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The Chemistry of Dialkoxy Disulfides and Related Compounds

by

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A Thesis Submitted to the Faculty of Graduate Studies And Research in
Partial Fulfillment of the Requirements for the Degree of
Doctor of Philosophy

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ABSTRACT

New acyclic dibenzyloxy disulfides substituted in the *para* position were prepared by a modified procedure in very high yield (*ca.* 85%). Each of them were found to display an AB quartet in the ^1H NMR spectrum, suggesting the possible existence of the isomeric thionosulfite structure $(RO)_2S{=}S$ in contrast to the more commonly proposed linear structure R-O-S-S-O-R. This structure question was addressed by preparing a series of closely related compounds including the analogous disulfide R_2S_2, tetrasulfide R_2S_4, "oxytrisulfide" R-O-S_3-R, sulfoxylate R-O-S-O-R, sulfite $(RO)_2S{=}O$, cyclic thionosulfite and corresponding cyclic sulfite, followed by comparative ^1H and ^{13}C NMR studies. The solid state structure was established to be linear according to X-ray analysis with somewhat short S-S bond length compared with conventional disulfide structures. The possible interconversion between the linear and the branched isomer was ruled out following an extensive spectroscopic study including ^{17}O NMR, IR, Raman and UV.

The solid/solution structure was established to be linear with a rigid *gauche* conformation dependent of a barrier to rotation of *ca.* 18 kcal mol^{-1} (T_c = 75°C). This barrier was responsible for the diastereotopicity of the adjacent benzylic protons, giving rise to asymmetric induction, and permitted the detection of the enantiomers with the chiral shift reagent $Eu(hfc)_3$ in chloroform at room temperature. The existence of rotational diastereomers was demonstrated by ^1H and ^{13}C NMR for chiral dialkoxy disulfides prepared from enantiomerically pure chiral and racemic alcohols.

A temperature dependent NMR study revealed that dibenzyloxy disulfides can deliver singlet diatomic sulfur S_2. The thermolysis was studied in different solvents in the presence of different dienes. The disulfide adduct and the diene were comparably competitive for the S_2 transfer. Tetrasulfide adducts were obtained in the presence of dimethyl and diphenyl butadiene, but converted to the disulfide adduct upon triphenylphosphine treatment. The related "oxytrisulfide" was demonstrated to also transfer the S_2 unit to dienes. A brief analysis of a known thionosulfite has shown its potential to transfer S_2 units to dienes. Mechanistic considerations were proposed to rationalized the olefinic compounds formed.

Triphenylphosphine desulfurization of dialkoxy disulfides yielded the corresponding sulfoxylates. The kinetics of the conversion of these to the corresponding sulfinates RO(S=O)R were examined and found to be first order; the Arrhenius parameters were determined.

RÉSUMÉ

Une procédure modifiée a été appliquée à la synthèse de nouveaux composés dérivés du dibenzyloxy de disulfure. Ces composés, incluant des modifications en position *para* du cycle benzénique, ont été isolés suivant des rendements moyens de 85%. La structure linéaire R-O-S-S-O-R de ces composés a été remise en question, suite à l'apparence des spectres RMN du proton, quadruplet associé à un système de protons couplés H_A et H_B, suggérant une structure isomérique branchée associée aux thionosulfites $(RO)_2S{=}S$. Une étude comparative des spectres RMN du proton et du carbone-13 suite à la préparation d'une série de composés analogues tels des disulfures R_2S_2, des tetrasulfures R_2S_4, des "oxytrisulfures" R-O-S_3-R, des sulfoxylates R-O-S-O-R, des sulfites $(RO)_2S{=}O$, des sulfites et thionosulfites cycliques a permis le morcellement structural de ces composés. Des structures cristallines par rayons X ont demontré un arrangement linéaire des liens O-S-S-O avec un lien S-S plus court comparativement aux disulfures ou tetrasulfures. La spectroscopie infra-rouge, ultra-violet et visible, Raman et la RMN de l'oxygène-17 ont permis d'abandonner la possibilité d'existence de la strucutre branchée pour ces composés.

Il a été clairement établit qu'en solution et à l'état solide, ces composés sont linéaires suivant une conformation *gauche* rigide des liens O-S-S-O avec une barrière de rotation évaluée à 18 kcal mole^{-1} (T_c = 75°C) qui est responsable de la diastéréotopicité des protons benzyliques adjacents. La mise en présence de ces composés avec un réactif chiral de complexation diastéréomérique tel Eu(hfc)$_3$ a démontré l'existence d'énantiomères de rotation. La RMN du proton et du carbone-13 ont confirmé l'existence des diastéréoisomères de rotation de différents dialkoxy de disulfure chiraux préparés à partir d'alcools chiraux et racémiques.

L'étude RMN de température a révélé que ces composés sont des précurseurs pour le transfert du soufre diatomique S_2. La réaction de thermolyse a été étudiée dans différents solvants avec des dienes. En présence des dienes telles la 2,3-diméthyle et la 2,3-diphényle butadiène, des disulfures et tétrasulfures cycliques ont été obtenus. Ces derniers tétrasulfures cycliques sont convertis en disulfures cycliques par l'action de la triphényle phosphine. Les "oxytrisulfures" sont aussi des précurseurs pour le transfert du soufre diatomique S_2. Le potentiel des thionosulfites cycliques comme précurseur au soufre diatomique a aussi été brièvement étudié, et différents mécanismes réactionnels sont proposés.

La désulfurisation de ces dialkoxy de disulfure a donné les composés sulfoxylates correspondants. La cinétique de l'isomérisation de ces sulfoxylates vers les sulfinates RO(S=O)R est d'ordre 1. Les paramètres d'activation d'Arrhénius pour cette réaction d'isomérisation ont été évalués.

ACKNOWLEDGEMENT

I would like to first thank Dr. I.S. Butler who was my first contact at McGill and who gave me the opportunity of pursuing my graduate studies in the Department of Chemistry. Thank you for your understanding and guidance; they really made a difference for me in those early days.

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[]	concentration
%	percent
Å	Ångstrom
b.p.	boiling point
°C	degrees Celsius
ca.	circa
calc'd	calculated
CCl_4	carbon tetrachloride
cm	centimeters
CNDO	complete neglect of differential overlap
Cp	cyclopentadienyl
d	deuterium
DMF	N,N-dimethylformamide
DMSO	methyl sulfoxide
DNMR	dynamic nuclear magnetic resonance
EI	electron impact
eq	equivalent
ESR	electron spin resonance
Et_2O	diethyl ether
EtOAc	ethyl acetate
EtOH	ethanol
eu	entropy units
FAB	Fast Atom Bombardment
g	gram
gc	gas chromatography
h	hour
Hg	mercury
i-Pr	isopropyl
IR	infrared
K	degrees Kelvin
kcal	kilocalories
kJ	kilojoules
L	liter

lit.	literature
M	molarity
m-CPBA	*meta*-chloroperbenzoic acid
m-CBA	*m*eta-chlorobenzoic acid
mg	milligram
$MgSO_4$	magnesium sulfate
MHz	megahertz
mL	milliliter
mm	millimeter
MM	molecular mechanics
mmHg	millimeter of mercury
mmol	millimole
µmol	micromole
MO	molecular orbital
mol	mole
m.p.	melting point
MS	mass spectrometry
N	normality
n	normal
NBA	4-nitrobenzyl alcohol
n-Bu	normal butyl
NCS	N-chlorosuccinimide
nm	nanometer
NMR	nuclear magnetic resonance
o-	ortho
p-	*para*
ppm	parts per million
Rf	relative mobility
s	second
s-	secondary
SOAO	singly occupied atomic orbital
SOMO	singly occupied molecular orbital
t-Bu	tertiary butyl
T_c	temperature of coalescence
TLC	thin layer chromatography
TMSCl	trimethylsilyl chloride
UV	ultraviolet

CHAPTER 1: GENERAL INTRODUCTION

1.1 Introduction

A substantial investigation on dialkoxy disulfides **1** was initiated in 1965 by Thompson and co-workers[1] in a series of papers entitled "Organic Esters of Bivalent Sulfur." Despite having been discovered 70 years earlier by Lengfeld[2] in 1895, only the di-*n*-propyl and di-*n*-butyl esters had been described[3] before Thompson's work. They can be defined as ester derivatives of the corresponding thiosulfurous acid[1a] $H_2S_2O_2$, or derivatives of the corresponding oxyacids (dihydroxides) of sulfur.[4] In 1970, Thompson[5] published a review including related bis(amino) sulfides **2** and disulfides **3**.

ROSSOR **1**

$R_2N(S)_nNR_2$ **2: n = 1** **3: n = 2**

In 1982, Kutney and Turnbull[6] reviewed the chemistry of dialkoxy disulfides as part of a variety of compounds containing the branch-bonded S=S moiety. This thiosulfoxide functionality is one of the interesting aspects of this "relatively" new class of compounds. The controversy relating to the assignment of their linear dialkoxy disulfide **4**, or branch-bonded thionosulfite **5**, structure about the disulfide bond has been raised before. In the past[7], various alternatives (**5,6,7**) to the linear structure **4** were considered; structure **6**,

---

1. a) Q.E. Thompson, M.M. Crutchfield, M.M. Dietrich and E. Pierron, *J. Org. Chem.*, **30**, 2692 (1965); b) Q.E. Thompson, M.M. Crutchfield and M.W. Dietrich, *ibid*, **30**, 2696 (1965); c) Q.E. Thompson, *ibid.*, **30**, 2703 (1965).

2. F. Lengfeld, *Ber.*, **28**, 449 (1895).

3. H. Stamm and H.Wintzer, *Ber.*, **70**, 2058 (1937).

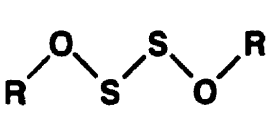
4. H. Schmidt and R. Steudel, Z. *Naturforsch.*, **45B**, 557 (1990).

5. Q.E. Thompson, *Quart. Rep. Sulfur Chem.*, **5**, 245 (1970).

6. G.W. Kutney and K. Turnbull, *Chem. Rev.*, **82**, 333 (1982).

7. a) A. Meuwsen, *Ber.*, **B68**, 121 (1935); b) H. Stamm, *ibid.*, **68**, 637 (1935); c) A. Meuwsen, *ibid.*, **B69**, 935 (1936); d) G. Sheibe and O. Stoll, *ibid.*, **71**, 1573 (1938); e) A. Clow, H.M. Kirton and J.M.C. Thompson, *Trans. Faraday Soc.*, **36**, 1029 (1940); f) M. Goehrig, *Ber.*, **80**, 219 (1947).

thiosulfonate, and **7**, thiosulfite, were eliminated based on spectroscopic evidence.[6] The difference between **4** and **5** was not clear and **5** could not be excluded.



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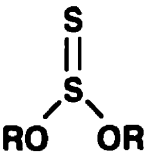

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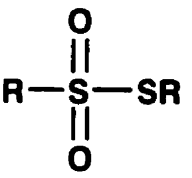

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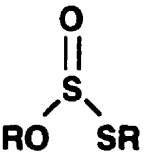

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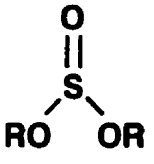
According to Thompson[1a], the linear isomer **4** is favored for acyclic esters $RCH_2OSSOCH_2R$ (R = alkyl, aryl) however, the observed diastereotopicity of the methylene protons in their ^1H NMR spectrum is known to be typical for these groups being adjacent to an asymmetric center. The temperature dependence of the ^1H NMR spectra of diethoxy disulfide (EtOSSOEt) has indicated that restricted rotation about the S-S bond and the dihedral angle of about 90° between the ethoxyl groups were at the origin of the asymmetry. The barrier of rotation was determined to be 8.6 ± 1.7 kcal mol^{-1}.[1a] Albeit this value is too low for a 90 °C barrier (*vide infra*). While the tetrahedral sulfur atom at the branched position provides asymmetry for adjacent CH_2s in the thionosulfoxide functionality **5**, this configuration is assumed to be stable at the coalescence temperature of 70 °C[8] estimated for the linear arrangement, by comparison to the stability of sulfite esters[9] **8** and cyclic thionosulfites[1b] **9a**. In fact, Thompson[1c] reported that the nonequivalence of the methylene protons was still maintained at 145 °C in diethyl sulfite **8** (R = CH_2CH_3).



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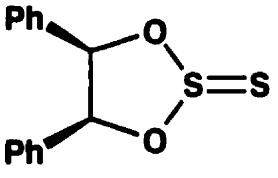
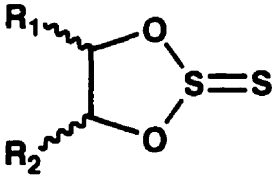


(α) **-9c**

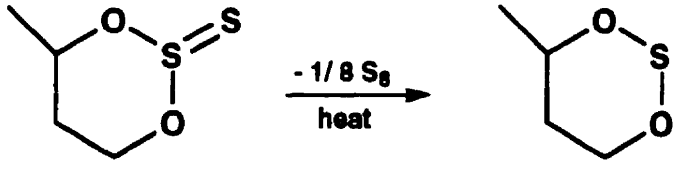


9a: $R_1 = R_2 = CH_3$
b: $R_1 = R_2 = C_6H_{10}$
c: $R_1 = R_2 = C_6H_5$
d: $R_1 = R_2 = H$

8. D.N. Harpp, *Perspectives in the Organic Chemistry of Sulfur;* B. Zwanenburg and A.J.H. Klunder, (Ed.), Elsevier, Amsterdam, 1987, pp. 1-22.

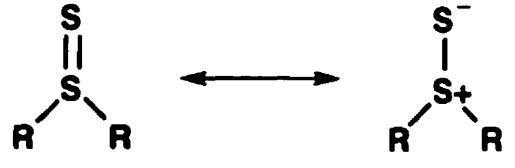
9. a) J.G. Pritchard and P.C. Lauterbur, *J. Am. Chem. Soc.*, **83**, 2105 (1961); b) P.C. Lauterbur, J.G. Pritchard and R.L. Vollmer, *J. Chem. Soc.*, 5307 (1963).

Up to now, only the 5-membered ring cyclic thionosulfites **9** ($R_1 = R_2 = CH_3$; C_6H_{10}; C_6H_5; H) have been claimed, being prepared from their corresponding 1,2-diols.[1b,10a] However, the thionosulfites (**9a, 9c, 9d**) obtained by Thompson[1b] (in less than 20% yield) were found to decompose at room temperature in the presence of light.[10b] The first fully characterized crystalline thionosulfite derivative was the O,O'-bicyclohexyl-1,1'-diyl thiosulfite **9b** described by Harpp, Steliou and Cheer.[10a] This compound was reported to be much more stable than any analogous derivatives reported by Thompson.[10b] Yet, no cyclic dialkoxy disulfides have been reported and defined.[10c] Apparently the unstable thionosulfite **10**, derived from 1,3-butanediol, easily loses sulfur in some fashion to give the sulfoxylate **11**.[1b]



10 **11**

The loss of sulfur from cyclic and acyclic polysulfides $R(S)_nR$ ($n \geq 2$) *via* the intermediacy of the thiosulfoxide **12** have been discussed in the context of sulfur extrusion processes.[8, 11] This rearrangement of the sulfide chain has been proposed to be induced thermally, photochemically and in the presence of solvent.[6, 11] The intermediacy of a thiosulfoxide was also proposed in their desulfurization reactions with trivalent phosphorous reagents.[12]



12

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10. a) D.N. Harpp, K. Steliou and C.J. Cheer, *J. Chem. Soc., Chem. Commun.*, 825 (1980); b) Their decomposition was observed when stored in the freezer at -5 °C in the dark: after a year for **9a**, few months for α-**9c**, 2 months for β-**9c** and few days for **9d**. However, no signs of decomposition were observed when a pure sample of **9b**, in the solid form, was exposed to light for over a period of 6 months; c) Very recently, a bis(dialkoxy disulfide) has been isolated. It is a 16-membered ring containing two alkoxy disulfide units; C. Abrams and D.N. Harpp, unpublished results.

11. D.N. Harpp and C.R. Williams, *Sulfur Reports*, **10**, 103 (1990); and references cited therein.

12. a) C.G. Moore and B.R. Trego, *Tetrahedron*, **18**, 205 (1962); **19**, 1251 (1963); b) D.N. Harpp, D.K. Ash and R.A. Smith, *J. Org. Chem.*, **45**, 5155 (1980).

The idea of a different arrangement for the S-S bond in polysulfides was raised by many groups.[13] According to Foss, the facile nucleophilic substitution (by alkali and alkoxides) at the divalent sulfur involving ionic scission of the S-S bond was due to the ability of sulfur to make use of its 3d-orbitals in the transition state.[14] Presumably, the branch-bonded structure **12** involving d-orbital expansion of the central sulfur atom, could only be stable when this atom was attached to electron-withdrawing groups thus causing a difference in electronegativity between the two sulfur atoms.[13] The branched sulfur atom would then act as a Lewis base to compensate the electron deficiency at the chain sulfur atom. However, R being electron-donating, the branch sulfur atom will be more electronegative than the chain sulfur atom and dative bonding ($3p_{\pi}$---3d) might be possible (**Figure 1**). This last type of bonding has been suggested for sulfoxides and phosphine oxides.

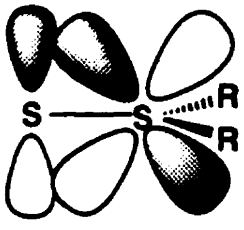
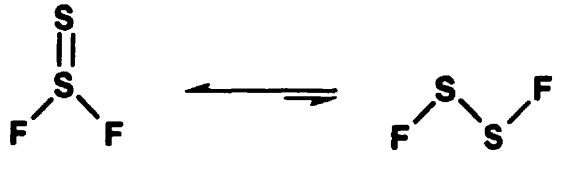


Figure 1: Overlap of a Sulfur 3p-orbital with a Sulfur 3d-orbital

The idea of a stable branch-bonded sulfur bonded to electron-withdrawing groups is supported by the existence of sulfur monofluoride (S_2F_2) in both forms **13** and **14**;[15] the thiosulfoxide arrangement **13** being the more stable isomer.



13 **14**

13. O. Foss in *Organic Sulfur Compounds*, Vol. 1, N. Kharasch, Ed., Pergamon Press Inc., New York, 1961, pp. 75-77; pp. 83-95.

14. O. Foss, *Acta Chem. Scand.*, 4, 404 (1950).

15. R.D. Brown, G.P. Pez and M.F. O'Dwyer, *Aust. J. Chem.*, 18, 627 (1965).

Early evidence for the possible equilibrium between linear and branch-bonded forms of disulfides has been reviewed.[6,16] In the next sections (1.2-1.8) the background material associated with this work on dialkoxy disulfides and related structures, branch-bonded sulfur species and diatomic sulfur chemistry will be outlined.

1.2 Acyclic Dialkoxy Disulfides

The first two dialkoxy disulfides, dimethoxy and diethoxy disulfides **1** (R = CH_3, CH_2CH_3), were prepared from the respective sodium alcoholates suspended in ligroin when treated with sulfur monochloride (S_2Cl_2) (**eq.1**).[2]

$$\mathbf{2\ RONa \xrightarrow[ligroin]{S_2Cl_2} ROSSOR} \qquad \textbf{(eq. 1)}$$

In 1937, using the Lengfeld procedure, the di-*n*-propyloxy and di-*n*-butyloxy disulfides **1** (R = *n*-Pr; *n*-Bu) were synthesized by Stamm.[3] In 1965, Thompson[1a] and his group reintroduced the class of compounds with a new methodology; the alcohol was treated with S_2Cl_2 in chloroform ($CHCl_3$) or methylene chloride (CH_2Cl_2) using tertiary amines (R' = Et) as acid acceptors (**eq.2**).

$$\mathbf{2\ ROH + 2\ R'_3N \xrightarrow{S_2Cl_2} \underset{\mathbf{1}}{ROSSOR} + 2\ R'_3N.HCl} \qquad \textbf{(eq. 2)}$$

The reaction addressed a wide variety of primary and secondary alcohols (**eq.2**; R = *i*-C_3H_7, *n*-$C_{18}H_{37}$, cyclohexyl, benzyl, allyl, cholesteryl).[1a] Due to a sluggish reaction, no pure esters of tertiary alcohols were obtained. In the case of diallyloxy disulfide **15**, internal disproportionation to acryloin **16**, allyl alcohol **17** and elemental sulfur was observed upon attempted distillations.[1a]

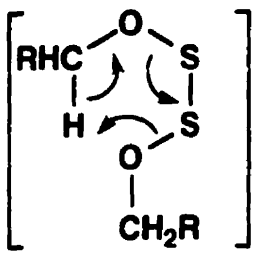
---

16. a) R. Rahman, S. Safe and A. Taylor, *Q. Rev., Chem. Soc.*, **24**, 208 (1970); b) S. Safe and A.Taylor, *J. Chem. Soc.*, 432 (1970).

$$(CH_2{=}CHCH_2OS)_2 \xrightarrow[\text{heat}]{} CH_2{=}CHC(=O)H + CH_2{=}CHCH_2OH + 1/4\ S_8$$

15 16 17

The observed order of thermal stabilities (secondary > primary > allyl) suggested that the 6-membered ring transition state **18** was involved in the elimination process (**Scheme 1**).



$$\longrightarrow RCH(=O) + RCH_2OH + 1/4\ S_8$$

18

Scheme 1

On acidic and basic alumina, the major decomposition products were those of disproportionation (**Scheme 1**). A more complex decomposition pattern was observed when chloroform solutions of dialkoxy disulfide **1** and pyridine hydrochloride ($C_5H_5N.HCl$) were allowed to stand for several days at room temperature. The major products were the sulfite **8** (~30%), the alcohol with elemental sulfur (~70%), as well as the sulfoxylate ester **19** (~2-5%). The following decomposition pattern was proposed[1a] (**Scheme 2**);

$$2\ ROSSOR \underset{}{\overset{2\ HCl}{\rightleftharpoons}} 2\ ROSCl + 2\ (ROSH) \longrightarrow 2\ ROH + 1/4\ S_8$$

1

$$2\ ROSCl + 2\ ROH \longrightarrow 2\ ROSOR + 2\ HCl$$

19

$$ROSOR + HCl \rightleftharpoons ROCl + (ROSH)$$

$$ROCl + ROSOR \longrightarrow RCl + ROS(=O)OR$$

8

Scheme 2

Dialkoxy disulfides were also prepared by reacting S_2Cl_2 with alkoxy (alkyloxy) silanes[17] and stannanes[18] of the type $ROMR'_3$ (R = *n*-Pr, *i*-Pr, CCl_3CH_2, Ph; M = Si, R' = Me and M = Sn, R' = n-Bu) **(eq.3 and eq.4)**.

$$S_2Cl_2 + 2\,Me_3SiOR \xrightarrow[-2\,Me_3SiCl]{} (RO)_2S_2 \qquad \textbf{(eq. 3)}$$

$$S_2Cl_2 + 2\,n\text{-}Bu_3SnOR \xrightarrow[-2\,n\text{-}Bu_3SnCl]{} (RO)_2S_2 \qquad \textbf{(eq. 4)}$$

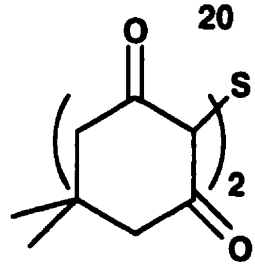
R = *n*-Pr (94%)
R = *i*-Pr (87%)

1.2.1 Chemistry and Reactions

Reactions of the S-S moiety of the ester involved treatment of dibenzyloxy disulfide with excess *n*-butyl lithium *via* the alcoholate **20** to give *n*-butyl sulfide **21** and benzyl alcohol ($C_6H_5CH_2OH$) as major products **(eq.5)**.[1a] Also, dimethoxy disulfide in the presence of 5,5-dimethyl-1,3-cyclohexanedione **22** and catalytic amounts of potassium *t*-butoxide gave the cyclohexyl sulfide **23** in 75% yield[1a] **(eq.6)**.

$$(PhCH_2OS)_2 + 4\,n\text{-}BuLi \longrightarrow \underset{\textbf{20}}{2\,PhCH_2OLi} + \underset{\textbf{21}}{2\,(n\text{-}Bu)_2S} \qquad \textbf{(eq. 5)}$$

$$(MeOS)_2 + 2\,(\textbf{22}) \xrightarrow{t\text{-}BuOK} \underset{\textbf{23}}{\text{cyclohexyl sulfide}} + MeOH + 1/8\,S_8 \qquad \textbf{(eq. 6)}$$



17. E. Wenschuk and R. Ritzel, *Sulfur Letters*, 4, 161 (1986).

18. D.A. Armitage and I.D.H. Towle, *Phosphorous and Sulfur*, 1, 37 (1976).

The alkoxide catalyzed decomposition of the corresponding dialkoxy disulfide for the preparation of the sulfoxylate ester **19** (R = Et) was described by Meuwsen and Gebhardt [19] **(eq.7)**.

$$\text{ROSSOR} \xrightarrow{\text{EtONa}} \underset{\textbf{19}}{\text{ROSOR}} + 1/8\ S_8 \qquad \textbf{(eq. 7)}$$

The heterolytic decomposition of **1** was studied by Kobayashi.[20,21] Alkylation of dimethoxy disulfide with triethyloxonium fluoroborate **24** gave dimethyl sulfite **25** (20-30%) with a trace of methyl methanesulfinate **26**, and precipitation of sulfur **(eq.8)**.

$$(MeOS)_2 \xrightarrow[CH_2Cl_2,\ rt]{24} \underset{\textbf{25}}{(MeO)_2S{=}O} + \underset{\textbf{26}}{MeS(=O)OMe} + 1/8\ S_8 \qquad \textbf{(eq. 8)}$$

No ethyl groups were incorporated in the sulfite product. Interestingly, when a catalytic amount of the Lewis acid **24** was used, higher yields of methyl methanesulfinate **26** were obtained. The reaction was reported to work in presence of other Lewis acids such as boron trifluoride etherate, $BF_3.OEt_2$, and antimony pentachloride, $SbCl_5$.

Unsymmetrical polysulfides could not be prepared directly from sulfur halides (SCl_2 or S_2Cl_2). However, Kagami and his group[21-23] had access to them by nucleophilic substitution on dialkoxy disulfide compounds.

1.2.2 Nucleophilic Substitution with S-O Bond Cleavage

Kagami and Motoki[21] demonstrated that nucleophilic substitutions on dialkoxy disulfide **1** (R = CH_3, C_2H_5) were feasible with cleavage at the sulfur-oxygen bond. In fact,

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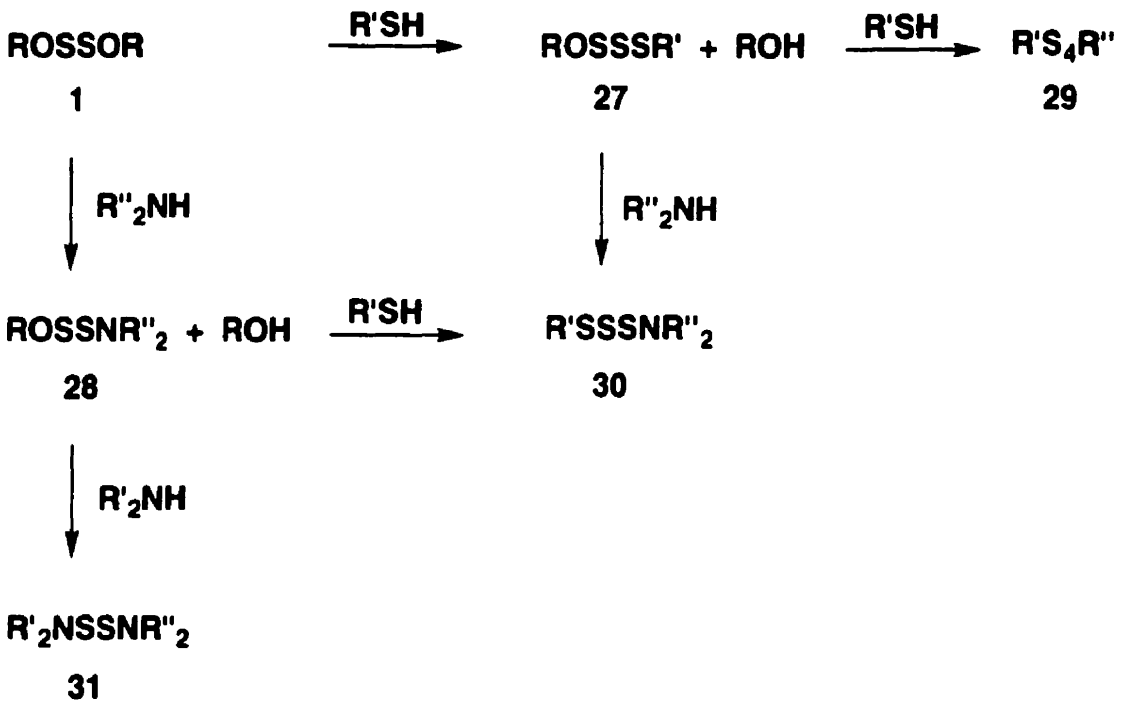
19. A. Meuwsen and H. Gebhardt, *Ber.*, **B68**, 1011 (1935); **B69**, 937 (1936).

20. M. Kobayashi, H. Minato and K. Shimada, *Int. J. Sulfur Chem.*, **1A**, 105 (1971).

21. H. Kagami and S. Motoki, *J. Org. Chem.*, **42**, 4139 (1977).

they readily react with mercaptans, R'SH (R' = C_2H_5, *n*-C_3H_7, *i*-C_3H_7, *t*-C_4H_9), or secondary amines, R"$_2$NH (R"$_2$ = $(C_2H_5)_2$, (*i*-C_3H_7), $(CH_2)_5$, $(CH_2)_4$), to give alkoxyalkyl trisulfides **27** (20-50%) or alkoxyamine disulfides **28** (19-74%) with elimination of alcohol. It is noteworthy that further reaction with R'SH or R"$_2$NH on **27** and **28** gave unsymmetrical dialkyl tetrasulfides **29** (60-63%), alkylamino trisulfides **30** (56-73%), and unsymmetrical diamine disulfides **31** (~37%) **(Scheme 3)**.



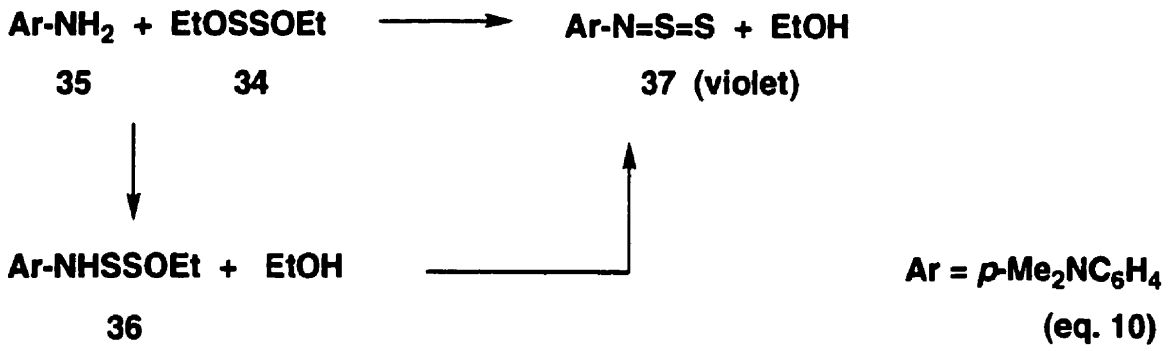
Scheme 3

The same group[22] have also found that thiocarboxylic acids **32** displace an alcohol moiety with S-O bond cleavage to afford acylalkoxy trisulfides **33** **(eq.9)**.

(eq. 9)

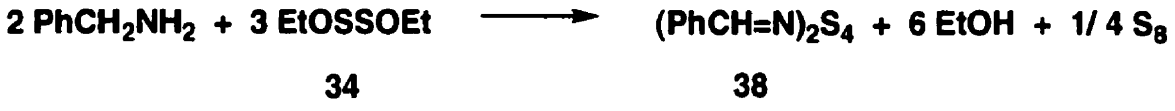
22. H. Kagami, H. Satsumabayashi and S. Motoki, *J. Org. Chem.*, **42**, 958 (1977).

The chemoselectivity depicted in **Scheme 3** was lowered when **1** was put in the presence of primary amines RNH_2; Kagami [22] reported that equimolar amounts of diethoxy disulfide **34** and N,N-dimethyl-*p*-phenylenediamine **35** were refluxed in benzene and afforded *p*-dimethylamino-N-thiosulfinylaniline **37** (a branch-bonded structure) after column chromatography of the reaction mixture **(eq.10)**. The formation of the product was rationalized by the elimination of ethanol from the intermediate ethoxyamino disulfide **36**.

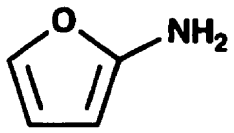


(eq. 10)

Interestingly, benzylamine, ($PhCH_2NH_2$), and **34** in benzene afforded dibenzylideneamino tetrasulfide **38** (~60%), sulfur and ethanol **(eq.11)**. When benzylamine was substituted by furfurylamine **42**, difurfurylideneamine tetrasulfide was obtained in 55% yield .



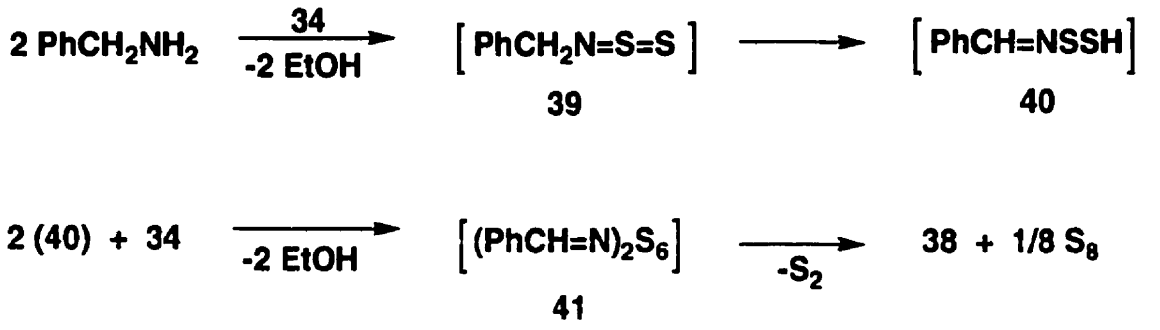
(eq. 11)



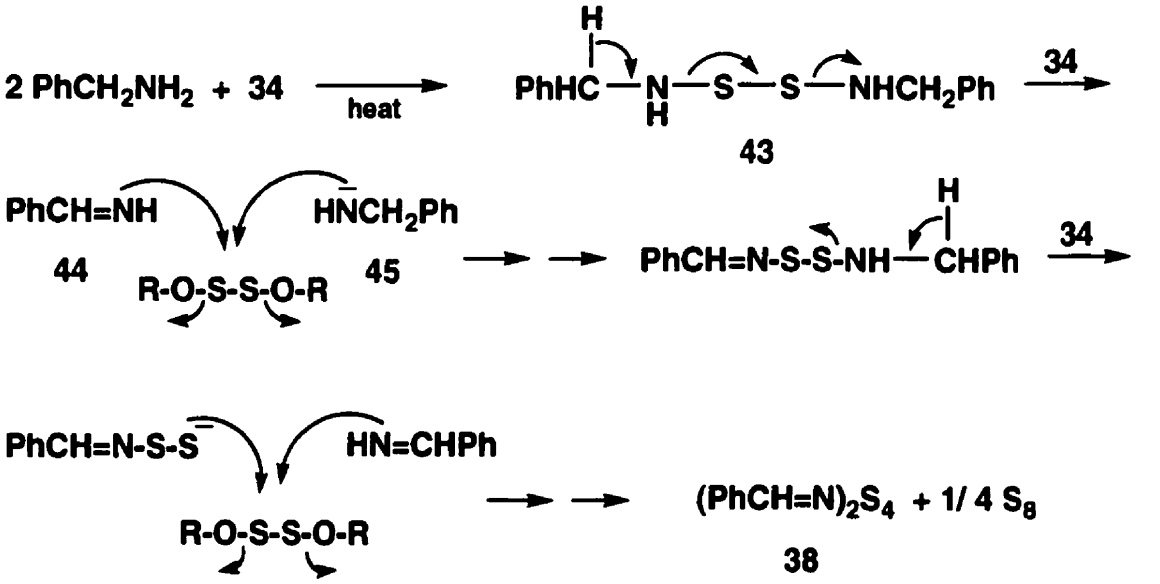
42

Since thiosulfinyl **37** was isolated, it was assumed that tetrasulfide **38** was formed *via* thiosulfinyl **39** which isomerizes to benzylideneamino hydrogen disulfide **40** with proton transfer. Two molecules of **40** react with **34** to form hexasulfide **41** which decomposes to give **38** with loss of sulfur **(Scheme 4)**. An alternative mechanism driven by the temperature involved might be the formation of dibenzylamine disulfide **43** that could lose S_2

to form the corresponding imine **44** and amide **45** that subsequently react with **34** to give **38** (**Scheme 5**).

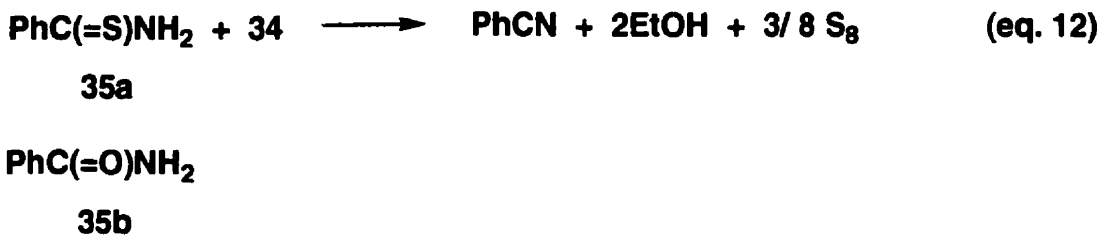


Scheme 4

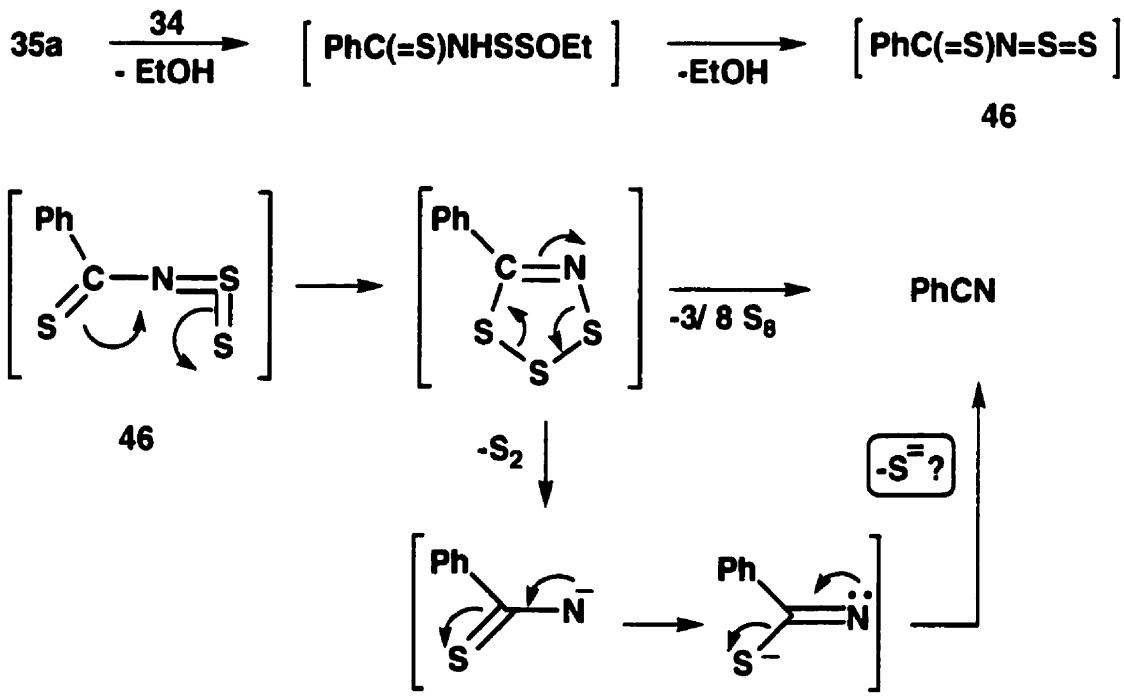


Scheme 5

Substitution of the aromatic amine **35**, in **eq.10**, by benzamide **35b**, gave no reaction at all, but substitution with thiobenzamide **35a**, using the same conditions, gave benzonitrile (75%), sulfur and ethanol **(eq.12)**.

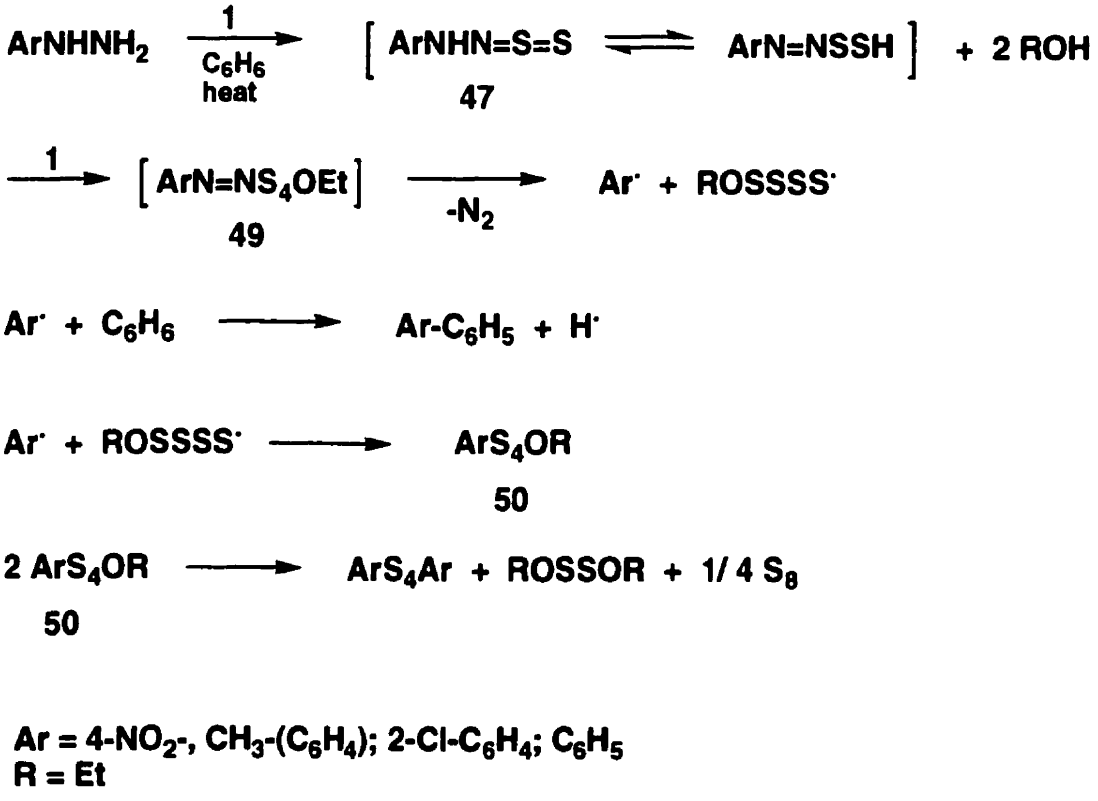


The rational was that the reaction proceeded again *via* this thiobenzoyl-N-thiosulfinylamine **46** followed by elimination of sulfur (S_3 or consecutively S_2 and S^{2-}) **(Scheme 6)**.



Scheme 6

Kagami and his group[23] have also studied the reaction of **1** with hydrazine derivatives, $RNHNH_2$, and found that not only the substitution of the alkoxyl group, but also the elimination of sulfur and nitrogen, takes place. They assumed that the reaction proceeded *via* a thiosulfinyl intermediate **47** followed by proton transfer to give an azo intermediate **48**. The latter, **48**, then replaces the alkoxyl group in **1** to give the intermediate arylazoalkoxy tetrasulfide **49** (**Scheme 7**). The intermediate is believed to decompose to the aryl radical with the evolution of nitrogen[24] and to react immediatly with the solvent used, benzene (C_6H_6), or the alkoxy tetrasulfanyl radical, ROSSSS·, to give biphenyl or arylalkoxy tetrasulfide **50** respectively. According to them, the symmetrical diaryl sulfide, ArSSAr, would always be formed by the thermal decomposition of arylalkoxy tetrasulfide **49**.

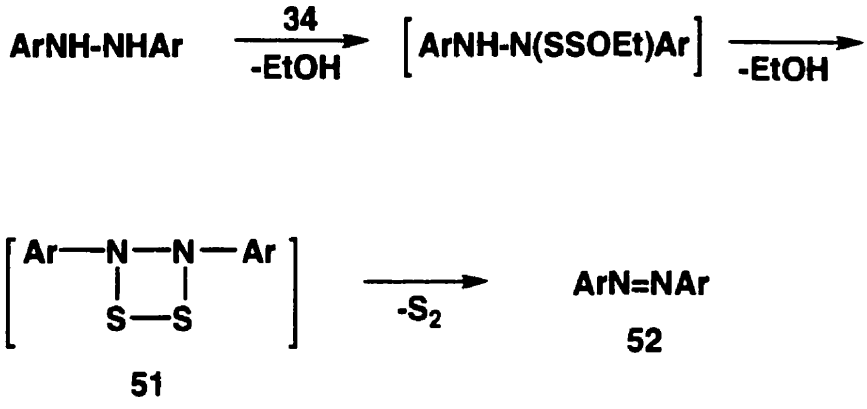


Scheme 7

23. H. Kagami and S. Motoki, *Bull. Chem. Soc. Jpn.*, **52**, 3463 (1979).

24. D.H. Hey and W.A. Waters, *J. Chem. Soc.*, 882 (1948).

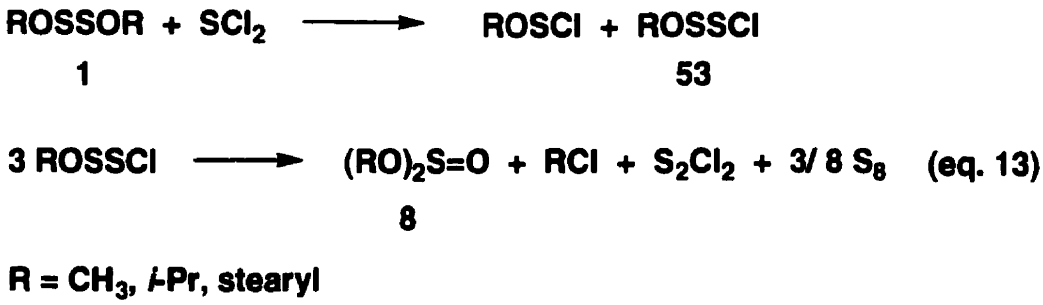
On the other hand, hydrazobenzene reacted with **34** to give azobenzene **52** in quantitative yield (99%) with the elimination of ethanol and sulfur **(Scheme 8)**. They assumed that hydrazobenzene reacts with **34** to give a cyclic disulfide **51** followed by the elimination of sulfur (initially as S_2) to form azobenzene **52**.



Ar = C_6H_4, 2-Br-C_6H_4, 2,2'-Br-C_6H_3

Scheme 8

Steudel and Schmidt[4] reported that the reaction of **1** with sulfur dichloride, SCl_2, produces alkoxychloro disulfide **53**. However, these species were reported to slowly decompose at 20°C, and very slowly even at -78°C according to **eq.13**.



R = CH_3, *i*-Pr, stearyl

However, **53** can rapidly be transformed by titanocenepentasulfide, $(C_5H_5)_2TiS_5$ to the corresponding nonasulfide **54 (eq.14)**.

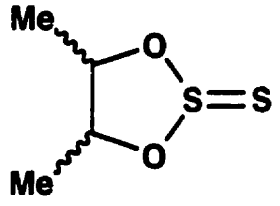
$$\underset{\textbf{53}}{2\,ROSSCl} + Cp_2TiS_5 \longrightarrow \underset{\textbf{54}}{ROS_9OR} + Cp_2TiCl_2 \qquad \textbf{(eq. 14)}$$

Neat **54** slowly decomposes with formation of **1** and other homologous dialkoxy sulfides $(RO)_2S_n$ with n up to at least 18. The formation of $(RO)_2S_{16}$ is the preferred route **(eq.15)**.

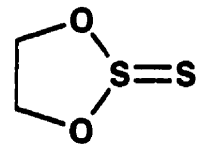
$$\underset{\textbf{54}}{2\,ROS_9OR} \longrightarrow ROS_{16}OR + \underset{\textbf{1}}{ROS_2OR} \qquad \textbf{(eq. 15)}$$

1.3 Cyclic Dialkoxy Disulfides

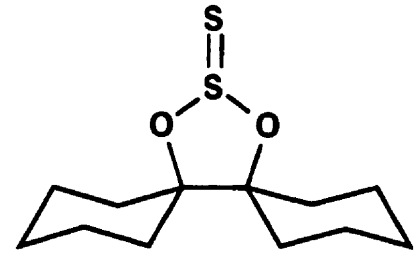
There appear to be no established cyclic dialkoxy disulfides.[10c] The **-OSSO-** unit appears only as the thionosulfite group. The list is short of cyclic thionosulfites prepared as pure materials. They are 1,2-dimethylethylene thionosulfite[16] **55**, ethylene thionosulfite[1b] **56**, and the fully characterized O,O- bicyclohexyl-1,1'-diylthiosulfite[10] **57**.



55

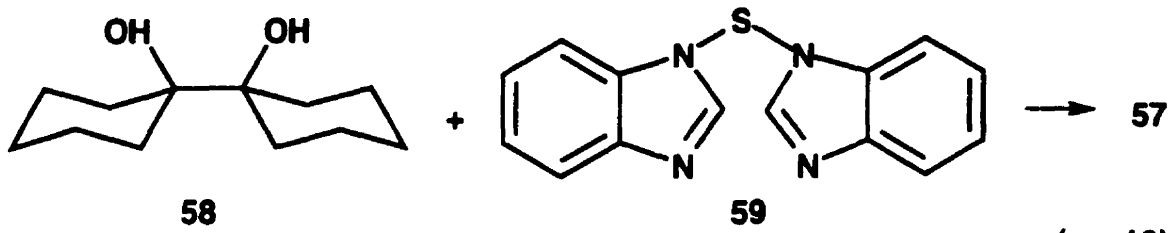


56



57

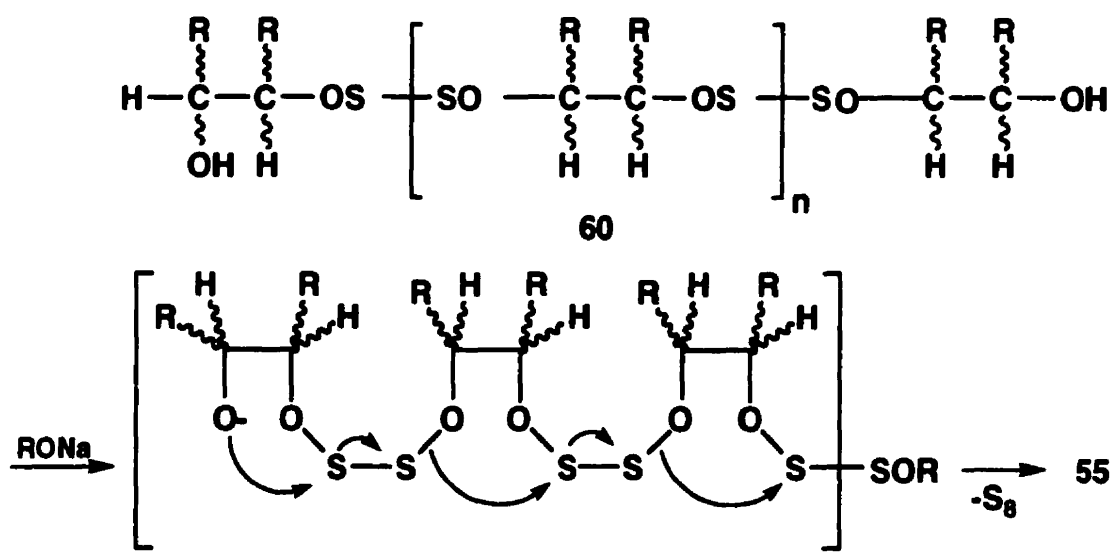
The two former compounds are reported to decompose at room temperature and in the light while the latter decomposes at 100 °C. The branch-bonded structure of thionosulfite **57** was confirmed by X-ray crystal analysis; the S-S bond length was reported to be 1.901Å. The cyclic thionosulfite ester **57** was prepared from (bicyclohexyl)-1,1'-diol **58** with the *mono*sulfur-transfer reagent bisbenzimidazol-1-yl sulfide **59** in refluxing CCl_4, **(eq.16)**.



58 59 57

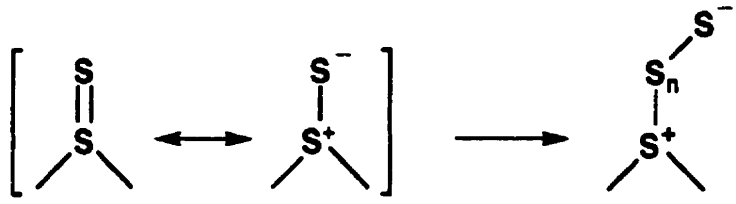
(eq. 16)

The thionosulfite ester **55** was obtained by Thompson's group.[1b] They reported that aliphatic 1,2-diols react with sulfur monochloride, S_2Cl_2, to give low molecular weight polymeric esters **60** (600 - 1100) that undergo, in the presence of alkoxide catalysts, a thermal decomposition described by Thompson[1b] as an "alkoxide-catalyzed intramolecular unzipping " of the polymer molecule to give **55** (20%) and elemental sulfur (**Scheme 9**). Interestingly, the only known stable cyclic dialkoxy disulfide **57** has been found to bear the branch-bonded arrangement of the disulfide bond. This arrangement of the disulfide bond has been proposed for intermediates to account for the products observed in the chemistry of linear disulfides and polysulfides; this type of intermediate apparently permits the concatenation of sulfur atoms that cyclize intramolecularly to eliminate elemental sulfur S_8.[8,13,14]



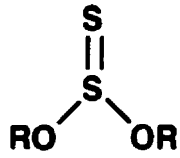
60

Scheme 9

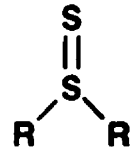


1.4 Intermediacy of Thiosulfoxides ($R_2S{=}S$)

One very important distinction to be made between thionosulfite arrangement **5** and thiosulfoxide arrangement **12** (R being different from alkoxide), is that they both contain the branch-bonded functionality but their adjacent groups are different.



5



12

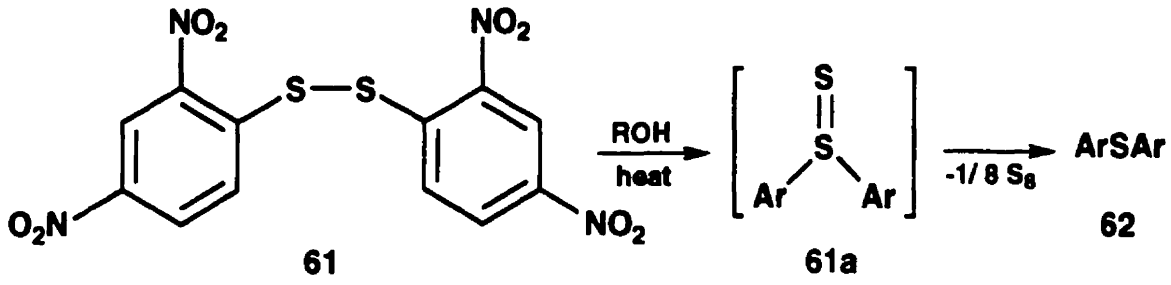
Spectrochemical evidence has been amassed for branch-bonded sulfur chains in polysulfides at low temperatures[25] (S-S(=S)-S). Bands in the region of 670 cm^{-1} have been observed in the infrared spectrum of the matrix-isolated (noble gases, nitrogen, carbon disulfide) condensate obtained by cooling sulfur vapor to and below -150 °C.[25]

The facile transformation of bis(2,4-dinitrophenyl) disulfide **61** to the sulfide **62** **(eq.17)** has been reported. Stepanov and co-workers[26] suggested that the withdrawing effect of the 2,4-dinitrophenyl group permits isomerization to the branched form; also, from product distribution, an equilibrium might have existed between the linear **61** and branched **61a** forms.

---

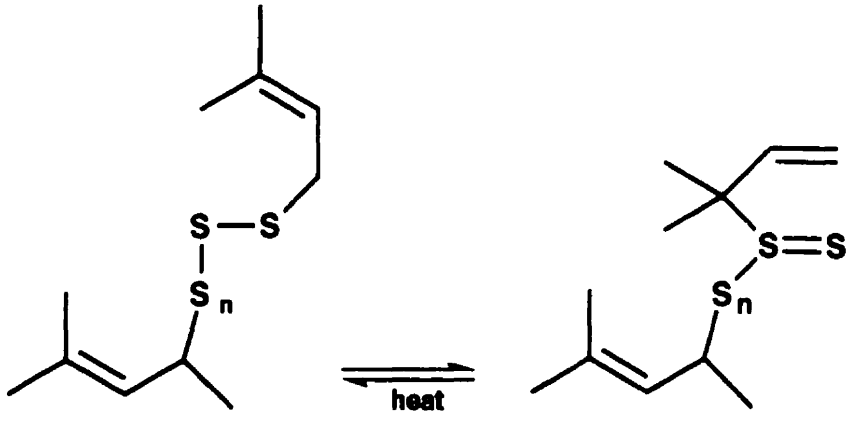
25. a) R Steudel, *Z. Anorg. Allg. Chem.*, **361**, 180 (1968); b) R. Steudel, *Z. Naturforsch.*, **27b**, 469 (1972).

26. a) B.I. Stepanov, V. Ya Rodionov and T.A. Chibisova, *J. Org. Chem. USSR (Engl. Transl.)*, **10**, 78 (1974); b) Ibid., *Chem. Abstr.*, **85**,495 (1976).



Ar = 2,4-NO_2-C_6H_3 (eq. 17)

The observed *cis-trans* double isomerization of allylic unsaturated di- and polysulfides **63** have been rationalized in terms of a thermal equilibrium between **63** and the thiosulfoxide **64**.[27]



Also, α-substituted allylic disulfides **65** rearrange at room temperature to the more stable isomer **67** with full double allylic inversion. An intramolecular double [2,3]-sigmatropic rearrangement of **65** *via* the thiosulfoxide **66** was proposed.[28]

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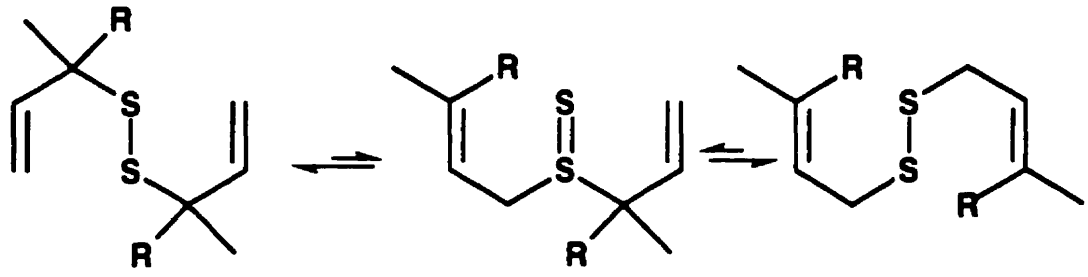
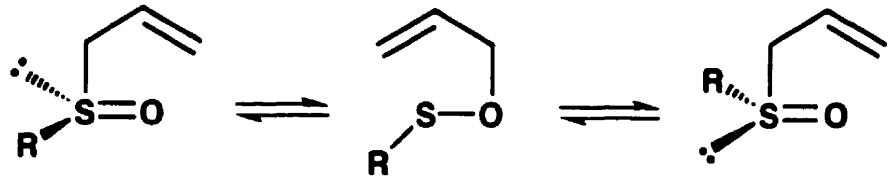
27. a) D. Barnard, T.H. Houseman, M. Porter and B.K. Tidd, *J. Chem. Soc. Chem. Commun.*, 371 (1965); b) B.K. Tidd, *Int. J. Sulfur Chem. C*, **6**, 101 (1971).

28. a) R. Tang and K. Mislow, *J. Am. Chem. Soc.*, **92**, 2100 (1970); b) G. Höfle and J.E. Baldwin, *J. Am. Chem. Soc.*, **93**, 6307 (1971); c) R.D. Baechler, J.P. Hummel and K. Mislow, *J. Am. Chem. Soc.*, **95**, 4442 (1973).



65 66 67

Evidence for **66** was obtained by means of interception experiments. Enhancement of the rate of desulfurization was observed for allylic disulfides. They react rapidly with triphenylphosphine, PPh_3, below 100 °C whereas alkyl and aryl disulfides are stable under these conditions;[29] the latter are known to be stable to PPh_3 up to 140 °C . This reaction is closely related to the allylic sulfoxide-sulfenate rearrangement; the activation parameters were measured by NMR spectroscopy for the conversion.[28c] The entropies of activation obtained were $\Delta S^{\ddagger} = -8.9 \pm 1$ eu for R = H and $\Delta S^{\ddagger} = -9.7 \pm 1$ eu for R = Me in **65**. These negative values were consistent with a cyclic transition state and in good agreement with the values reported for the rearrangement of allylic sulfenates to sulfoxides (-5 to -10 eu) which is proposed to take place by two consecutives [2,3]-sigmatropic processes.

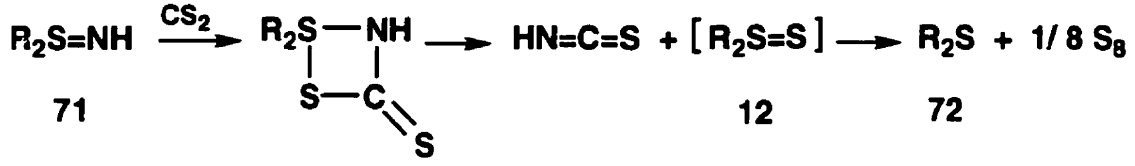


A thiosulfoxide intermediate has been proposed in some of the chemistry of sulfoxides **68**, sulfinimides **69** and sulfur ylides **70**. The subject was well reveiwed by Kutney and Turnbull.[6] A few illustrative examples are given.

68 **69** **70**

29. F. Challenger and D. Greenwood, *J. Chem. Soc.*, 26 (1950).

The reaction of alkyl sulfinimides **71** with carbon disulfide gives sulfides **72** and elemental sulfur **(eq. 18)**.[30]



71 12 72

(eq. 18)

Alkyl sulfinimides **73** gives sulfides[31] **(eq.19)** in the presence of the reductive reagent P_4S_{10}. These semipolar bonds and the one found in sulfur ylides **70** can also be reduced in the presence of thioacids like RC(=S)-SH and $R_2P(=S)$-SH to give the corresponding sulfide .[31]

(eq. 19)

73 12

X = $SO_2C_6H_4CH_3$-*p*

Thiosulfoxide intermediates have also been suggested to be formed prior to the formation of sulfide and elemental sulfur in the oxidative desulfurization reactions of S-trithianes **74** with iodine in DMSO **(Scheme 10)**.[31]

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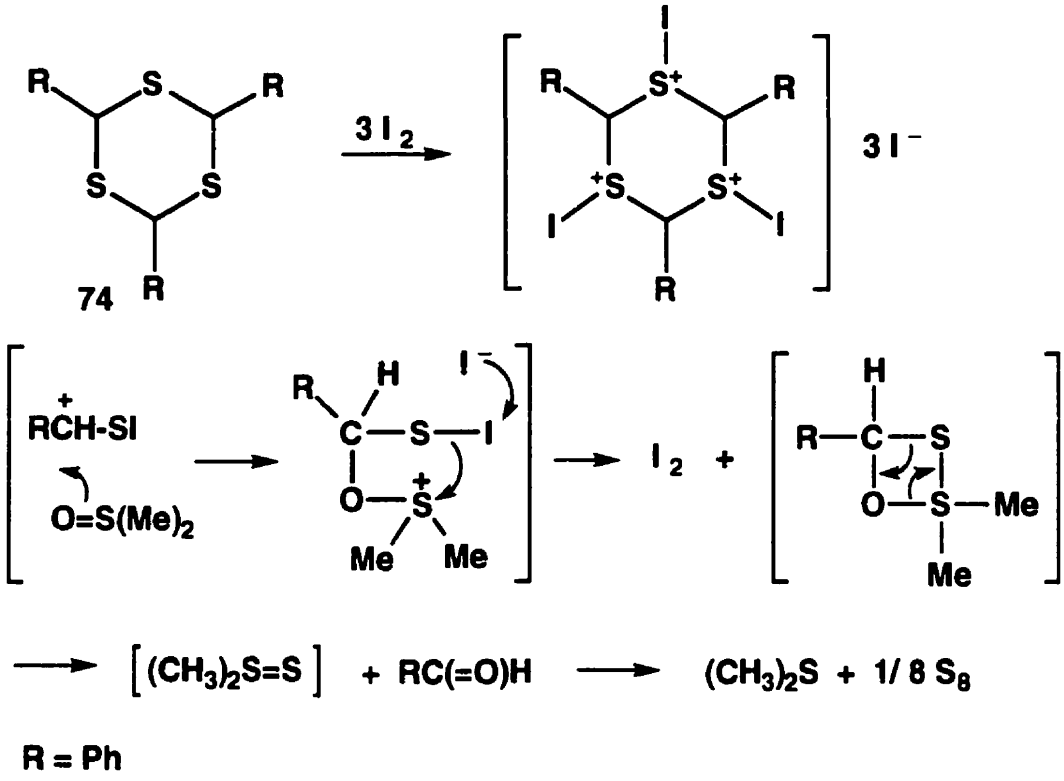
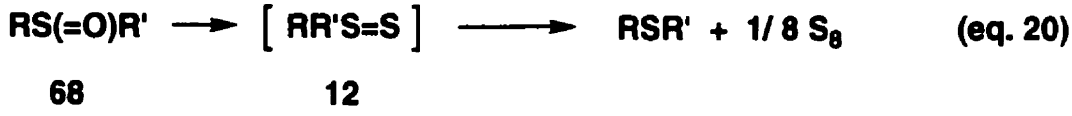
30. R. Appel and W. Buchner, *Chem. Ber.*, **95**, 855 (1962).

31. a) S. Oae, T. Yagihara and T. Okabe, *Tetrahedron*, **28**, 3203 (1972); b) A. Nakanishi and S. Oae, *Chem. Ind. (London)*, 960 (1971); c) S. Oae, A. Nakanishi and T. Sujimoto, *Tetrahedron*, **28**, 2981 (1972); d) I.W. Still and K. Turnbull, *Synthesis*, 540 (1978).



Scheme 10

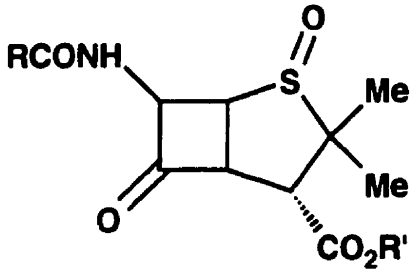
A thiosulfoxide was postulated as a potential intermediate in the reduction of sulfoxides **68** by the trifluoroacetic anhydride-hydrogen sulfide $(CF_3CO)_2O$-H_2S system;[32] or in the presence of hexamethyldisilathiane $[(CH_3)_3Si]_2S$;[33] the reduction gives the corresponding sulfides and sulfur likely *via* the thiosulfoxide **12** followed by extrusion of sulfur (**eq.20**).



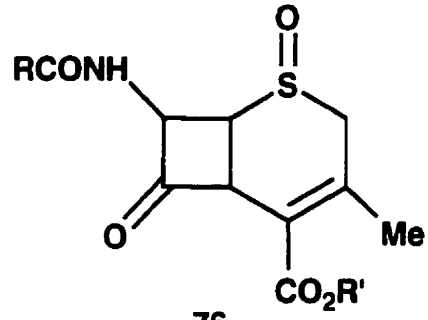
32. J. Drabowicz and S. Oae, *Chem. Lett.*, 767 (1977).

33. H.D. Soya and W.P. Weber, *Tetrahedron Lett.*, 235 (1978).

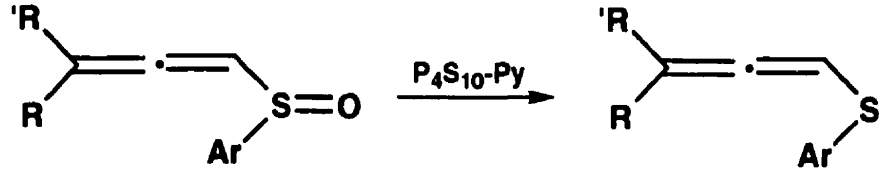
The same results were obtained with boron sulfide B_2S_3[34,35], silicon sulfide SiS_2[34a,b] and tetraphosphorus decasulfide P_4S_{10}[34,36,38a]. The latter reagent in the presence of pyridine was used for the conversion of penicillin and cephalosporin sulfoxides **75** and **76** to the corresponding sulfides.[37] In general, for sulfoxide deoxygenation, electron-donating substituents appears to accelerate the reaction.[38b] Allenic sulfoxides **77** were also reduced to their respective sulfides **78**.[39]



75



76



77 **78**

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34. a) R.D. Baechler, S.K. Daley, B. Daly and K. Mc Glynn, *Tetrahedron Lett.*, 105 (1978); b) R.D. Baechler, S.K. Daley, *Tetrahedron Lett.*, 101 (1978); c) J. Balint, M. Rakosi and R. Bognar, *Phosphorus Sulfur*, **6**, 23 (1979).

35. a) T. Li Lu, J.L. Kice and C.G. Venier, *J. Org. Chem.*, **44**, 610 (1979); b) R.D. Baechler, L.J. San Filippo and A. Schroll, *Tetrahedron Lett.*, **22**, 5247 (1981).

36. I.W. Still, J.N. Reed and K. Turnbull, *Tetrahedron Lett.*, 1481 (1979).

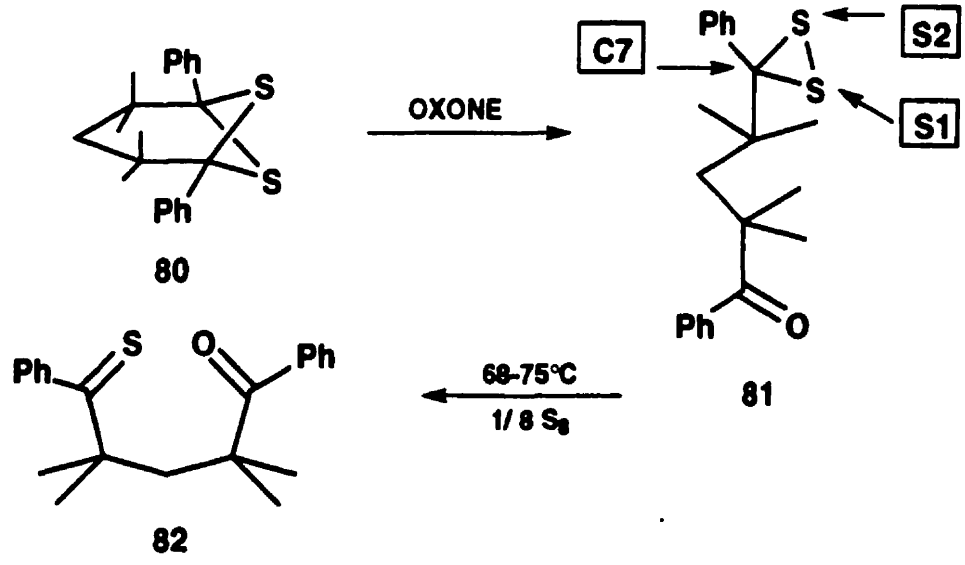
37. R.G. Micetich, *Tetrahedron Lett.*, 971 (1976).

38. a) I.W. Still, S.K. Hasan and K. Turnbull, *Synthesis*, 468 (1977); b) I.W.J. Still, S.K. Hasan and K. Turnbull, *Can. J. Chem.*, **56**, 1423 (1978).

39. R.C. Cookson and P.J. Parsons, *J. Chem. Soc., Chem. Commun.*, 822 (1978).

1.5 Intermediacy of Thiosulfine ($R_2C=S=S$), 79

To date, no stable thiosulfines has been isolated but several workers[40a,b] have proposed their transient existence. The chemistry of thiosulfines and dithiiranes have been reviewed by Senning and collaborators[40c] in 1986. Recently, another minireview was published by Senning.[40d] The first isolable dithiirane **81** was obtained by Nakayama[40e] in 1994 by oxidation of the bicyclic 1,3-dithietane **80** with potassium peroxomonosulfate (OXONE, $2KHSO_5.KHSO_4.K_2SO_4$) (**Scheme 11**). The crystalline compound was fully characterized by X-ray analysis. The bond length and angles found were S1-S2 2.073(2)Å, S2-S1-C7 55.07(8)°, S1-S2-C7 55.37(8)° and S1-C7-S2 69.55(9)°. It was stable at room temperature in air, but was found to decompose to give the thioketone **82** and elemental sulfur when heated at 68-75°C to determine the melting point. Still and co-workers[41] have proposed that the reductive deoxygenation of sulfine **83** to thione **84** may proceed through the intermediacy of **79** analogous to thiosulfoxide **12** proposed earlier as a short-lived intermediate in the sulfoxide deoxygenation.

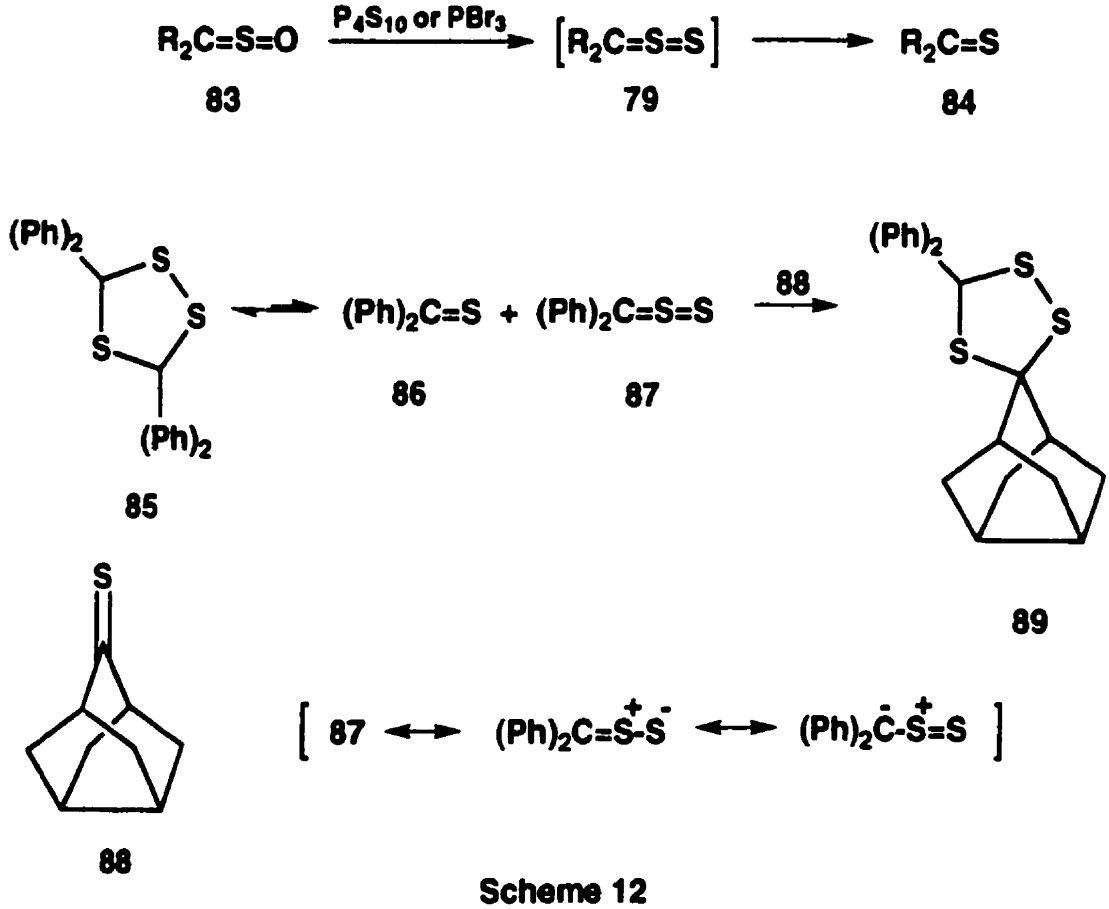


Scheme 11

40. a) A. Senning, *"IUPAC Organic Sulfur Chemistry"*, R. Kh. Freidlino and A.E. Skorova, Eds., Pergamon Press, Oxford, 1981, p.151; b) A. Senning and W. Mazurkiewicz, *Sulfur Lett.*, 1, 127 (1983); c) A. Senning, H.C. Hansen, M.F. Abdel-Megeed, W. Mazurkiewicz and B. Jensen, *Tetrahedron*, **42**, 739 (1986); d) A. Senning, *Sulfur Lett.*, 11, 83 (1990); e) J. Nakayama, A. Ishii, T. Akazawa, T. Maruta, M. Hoshino and M. Shiro, *Angew. Chem. Int. Ed. Engl.*, 33, 777 (1994).

41. I.J.W. Still, B. Zwanenburg, B.H.M. Lammerink and J.A.M. Kuipers, *Synthesis*, 295 (1981).

Huisgen and Rapp[42a] have offered the first unequivocal evidence for the existence of thiosulfine **79**; the thermal decomposition (1,3-dipolar cycloreversion) of 3,3,5,5-tetraphenyl-1,2,4-trithiolane **85** gave thiobenzophenone **86** and thiobenzophenone S-sulfide **87** in the presence of the dipolarophile adamantanethione **88**. This likely took place *via* 1,3-dipolar cycloaddition; the mixed 1,2,4-trithiolane **89** (81%) was obtained and fully characterized by ^{13}C,^{1}H NMR and MS (**Scheme 12**).



Scheme 12

Recently, less clear evidence was obtained by Harpp and Williams[42b] for the intermediacy of thiosulfine **79** or the isomeric dithiirane **90**. During their investigation of sulfur extrusion processes, they proposed that mono-4-fluorotriphenylmethanesulfenyl

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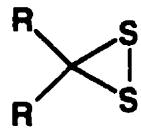
42. a) R. Huisgen and J. Rapp, *J. Am. Chem. Soc.*, **109**, 902 (1987); b) D.N. Harpp and C.R. Williams, *Tetrahedron Lett.*, **32**, 7633 (1991); c) Earlier work: J.P. Snyder, *J. Am. Chem. Soc.*, **96**, 5005 (1974); P. Metzner, M. Lemarié and T.-N. Pham, *Tetrahedron Lett.*, **32**, 7411 (1991); d) T. Machiguchi, M. Minoura, S. Yamabe and T. Minato, *Chem. Lett.*, 103 (1995).

chloride **91**, and 4,4'-dimethoxythiobenzophenone **92** formed an addition complex at low temperature which decomposed through the formation of **79** or **90** to regenerate the thioketone **92** and sulfur. Their proposal was supported by ^{19}F NMR spectral analysis. They observed that the addition complex was only stable below -40 °C but sulfur precipitation was not observed until about 0 °C.



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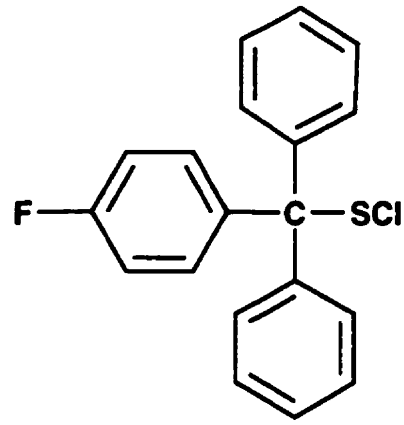
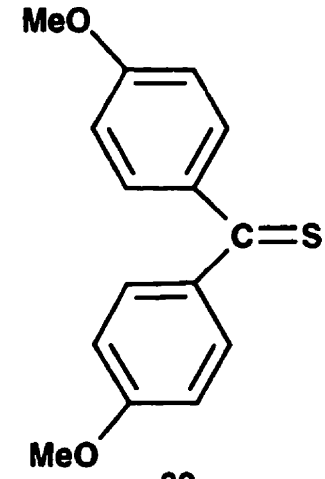
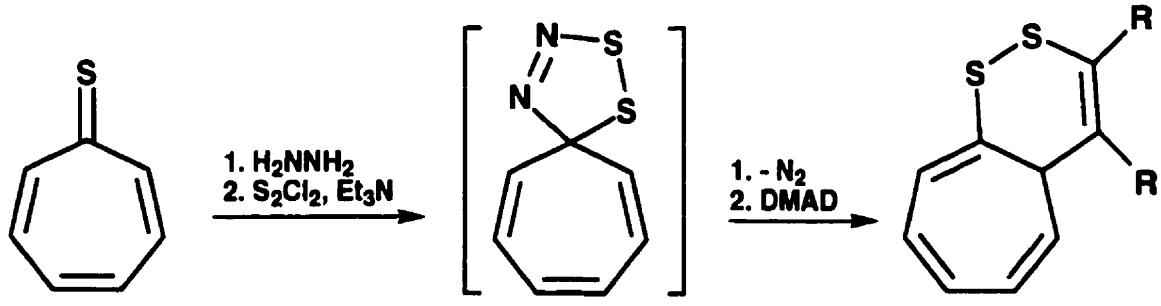


91



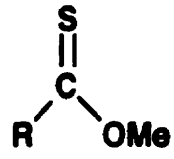
92

Cycloheptatrienethione S-sulfide (**79**; R_2C = tropone) was synthesized from tropone hydrazone with S_2Cl_2 in deuterated chloroform at -78 °C. The detection was an unprecedented [$10\pi + 2\pi$]-type cycloadduct formation with dimethyl acetylenedicarboxylate (DMAD).[42d]



R = CO_2Me

By analogy with dithiiranes **90**, oxathiiranes **95** were recently discussed by Metzner and co-workers[42c] during oxidative studies of thionoesters **93** to the corresponding sulfines **94**. The production of the corresponding ester RC(=O)OMe observed at room temperature was believed to result from a thermally allowed electrocyclization reaction of **94** to form **95** followed by loss of sulfur.



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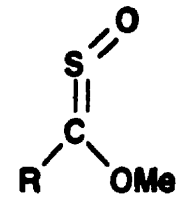
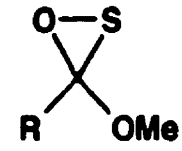


94



95

1.6 Intermediacy of N-(thiosulfinyl) Amine (RN=S=S)

The intermediacy of N-(thiosulfinyl)amines **97**, in the preparation of alkyl sulfur diimides **98** from N,N-bis(trimethysilyl) amines **96** and sulfur monochloride S_2Cl_2, has been postulated.[43]

96 **97** **98**

R = alkyl, aryl

p-Dimethylamino-N-thiosulfinylaniline **100** was the first of the class to be prepared by Barton and Robson[44] from the reaction of N,N-dimethyl-*p*-nitrosoaniline **99** and verified

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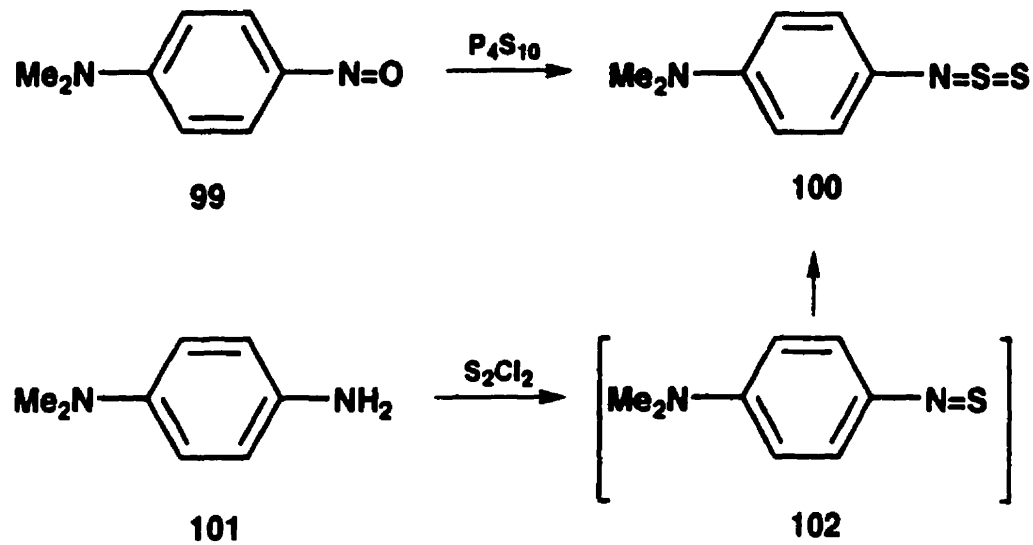
43. R. Mayer, E. Oestreich and S. Bleisch, *Z. Chem.*, **16**, 437 (1976).

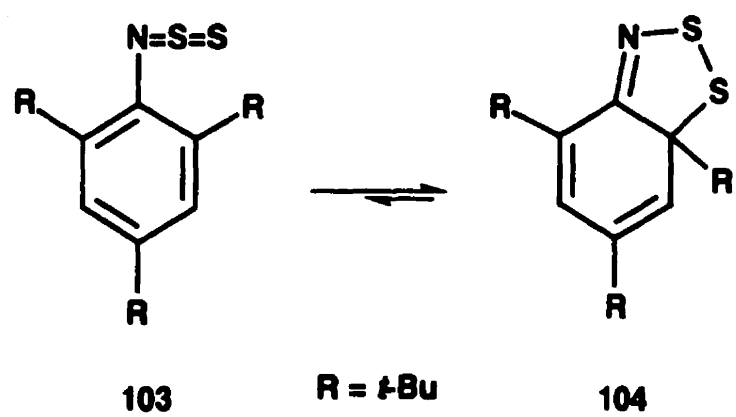
44. D.H.R. Barton and M.J. Robson, *J. Chem. Soc., Perkin Trans. 1*, 1245 (1974).

by the unambiguous synthesis from N,N-dimethyl-*p*-phenylene diamine **101**, probably *via* the "thionitroso" compound **102 (Scheme 13)**.



Scheme 13

Following that work, Okazaki and co-workers[45] demonstrated that the sterically hindered N-(thiosulfinyl)-2,4,6-tri-*t*-butylaniline **103** existed in equilibrium with the 5H-1,2,3-dithiazole **104**.



45. a) R Okazaki, N. Inamoto and Y. Inagaki, *Chem. Letters*, 1095 (1978); b) N. Inamoto, R. Okazaki and K. Inoue, *Tetrahedron Lett.*, **38**, 3673 (1979).

Interestingly, if a methyl group was substituted at the 6-position, the above equilibrium was not observed. Finally, N-thiosulfinylaniline was studied in the context of oxidation,[45,46] reduction,[44] cycloaddtion,[44] electrophilic[47] and nucleophilic[48] reactions.

1.7 NMR Considerations of Dialkoxy Disulfides

Acyclic dialkoxy disulfides were presented in **Section 1.1** and their structure was established to be linear by NMR considerations.[1a] However, cyclic derivatives (**Section 1.3**) are only known as the 5-membered ring cyclic thionosulfites (**9a-d**).[1b,10] The ABX_3 pattern observed by Thompson[1a] in the ^1H NMR spectrum of diethoxy disulfide **1** (R = CH_2CH_3) at 30°C closely resembles the one of ethylene sulfite[48a] **8** (R = CH_2CH_2) and diethyl sulfite[48b] **8** (R = CH_2CH_3). The two methylene protons of a given methylene group in diethyl sulfite are not stereochemically equivalent because of the lack of symmetry of the non-planar substituted sulfur atom with respect to internal rotation about the S-O-C bonds.

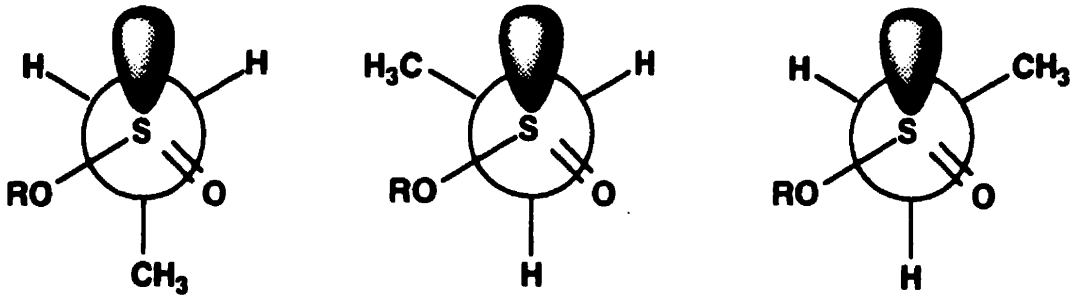


Figure 2: Three Possible Rotamers of $(CH_3CH_2O)_2S{=}O$; R = CH_2CH_3

46. Y. Inagaki, R. Okazaki and N. Inamoto, *Bull. Chem. Soc. Jpn.*, **52**, 2002 (1979).

47. Y. Inagaki, R. Okazaki and N Inamoto, *Bull. Chem. Soc. Jpn.*, **52**, 3615 (1979).

48. a) J.G. Pritchard and P.C. Lauterbur, *J. Am. Chem. Soc.*, **83**, 2105 (1961); b) F. Seel, W. Gombler and R. Budenz, *Justus Liebigs Ann. Chem.*, **735**, 1 (1970).

The diastereotopicity of the two methylene protons is depicted in **Figure 2**; the molecule is so oriented that we are looking along the sulfur-CH_2 axis. The two protons cannot be interchanged by symmetry operations in any of the rotamers. One could have imagined drawing the same type of rotamers for diethoxy disulfide in the thionosulfite arrangement **5**; the tetrahedral sulfur atom at the branched position conferring asymmetry on the adjacent CH_2 protons as in diethyl sulfite. However, the arrangement of diethoxy disulfide was suggested to be linear with a rigid *gauche* conformation (**Figure 3**). This conformation was determined to have a barrier of rotation of 8.6 ± 1.7 kcal mol^{-1}, and the ABX_3 pattern observed at 30 °C was simplified to an A_2X_3 pattern at 100 °C. There is no literature precedent for such behavior. Aliphatic disulfides normally have barriers in the range of *ca.* 9 kcal mol^{-1} and are considered to undergo "free" rotation at room temperature. By comparison, the nonequivalence of the methylene protons in diethyl sulfite was still observed at 145 °C.[1a] Apparently[1b], the ^1H NMR spectra of different cyclic thionosulfites remained unchanged at high temperatures. The spectra of the *cis*- and *trans*- isomers **9a** were constant from -40 to 158 °C, while **9d** exhibited an A_2B_2 pattern centered at 4.6 ppm up to 150 °C.

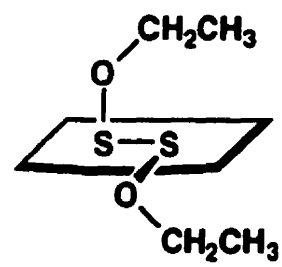


Figure 3: Gauche Conformation of the Two Ethoxy Groups Around the S-S Bond in $(CH_3CH_2O)_2S_2$

The rotational barrier of diethoxy disulfide was re-evaluated to be 17.75 ± 0.10 kcal mol^{-1} (T_c = 77.5 ± 2.5 °C) by Seel[48b], and at 18 kcal mol^{-1} (T_c = 75 °C) by Harpp and Ryan[8]. Harpp and Steliou[8] have carried out calculations using AMPAC with the MINDO/3 program on the linear *vs* the branch-bonded isomers and their results indicated the difference to be 9, 6, 6, and 5 kcal mol^{-1} for S_2Cl_2, $(CH_3O)_2S_2$, $(CH_3CH_2O)_2S_2$ and **57** respectively with the branch isomer being less stable in each instance. The conclusions drawn by Thompson about the linear arrangement with a rigid *gauche* conformation dependent of a

barrier to rotation are reasonable except for the value of the barrier.[49] Any rotational isomers with an internal barrier to rotation of that magnitude (8.6 ± 1.7 kcal mol^{-1}) are conformers and considered to undergo free rotation at room temperature. Apparently, Thompson made a miscalculation as well as a mis-reference that a barrier of 8.6 kcal mol^{-1} could be consistent with a coalesence temperature of *ca.* 75 °C

In spite of the very interesting structural aspects, this class of compounds may be considered as possible reagents for the release of diatomic sulfur (S_2). This is a reasonable consideration since diallyloxy disulfide **15** was found to disproportionate during the distillation to acryloin **16**, allyl alcohol **17** and elemental sulfur (**Scheme 1**).[1a] The proposed mechanism might be that the S_2 unit is thermally released, most likely in the singlet state ($^1S_2$) that subsequently converts to the triplet state ($^3S_2$), collecting other S_2 units to finally form S_8. In the presence of a diene, the S_2 moiety should act as a dienophile to form 1,2-dithiins (compounds **107**).

1.8 Precursors of Diatomic Sulfur S_2

This reactive dienophile has been regarded as part of methodologies related to hetero Diels-Alder reactions which are in turn important tools in the total synthesis of natural products.[50] Diatomic sulfur was first detected in the vapor phase of elemental sulfur S_8 heated at 1000 °C.[51a] The first report on diatomic sulfur generation that included trapping was credited to Jahn and Schmidt, in 1975,[51b] while studying the photolysis of thione ester **105**; S_2 was believed to be lost from **106** giving 2% of trapped disulfide **107** (**eq.21**).

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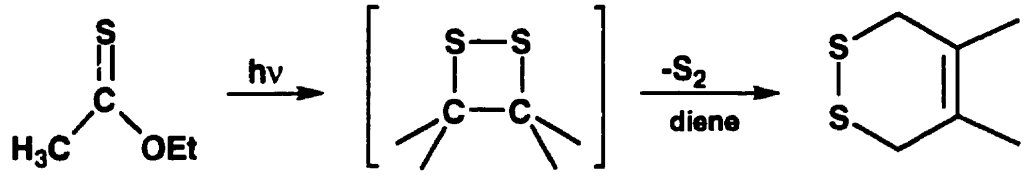
49. a) The same barrier was found to be about 18 kcal mol^{-1} after being re-evaluated, using Thompson's method, by Dr. D. Ryan in our laboratory in 1988 (ref. 8). The same magnitude was also found by another group (ref. 48a), and also calculations (ref. 8). *Ab initio* calculations seem to indicate that restricted rotation increases with shortening the S-S bond, and that a barrier to rotation of 18-20 kcal mol^{-1} was calculated for EtOSSOEt; unpublished work by D.N. Harpp and J.P. Snyder.

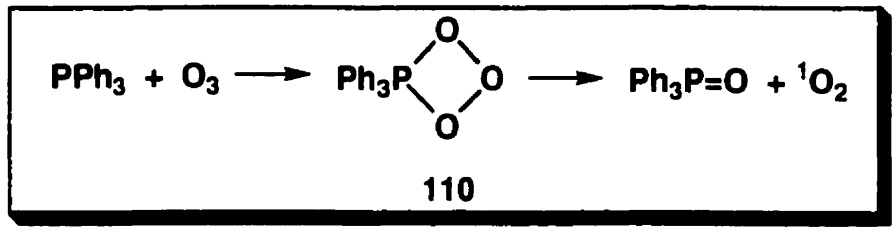
50. a) D.L. Boger and S.M. Weinreb, *Hetero Diels-Alder Methodology in Organic Synthesis*; H.H. Wasserman (Ed.), Academic Press, San Diego, CA, 1987; b) K. Steliou, Y. Gareau, G. Milot and P. Salama, *Phosphorus, Sulfur and Silicon*, **43**, 209 (1989); c) K. Steliou, *Acc. Chem. Res.*, **24**, 341 (1991).

51. a) B. Meyer, *Chem. Rev.*, **76**, 367 (1976); b) R. Jahn and U. Schmidt, *Chem. Ber.*, **108**, 630 (1975).

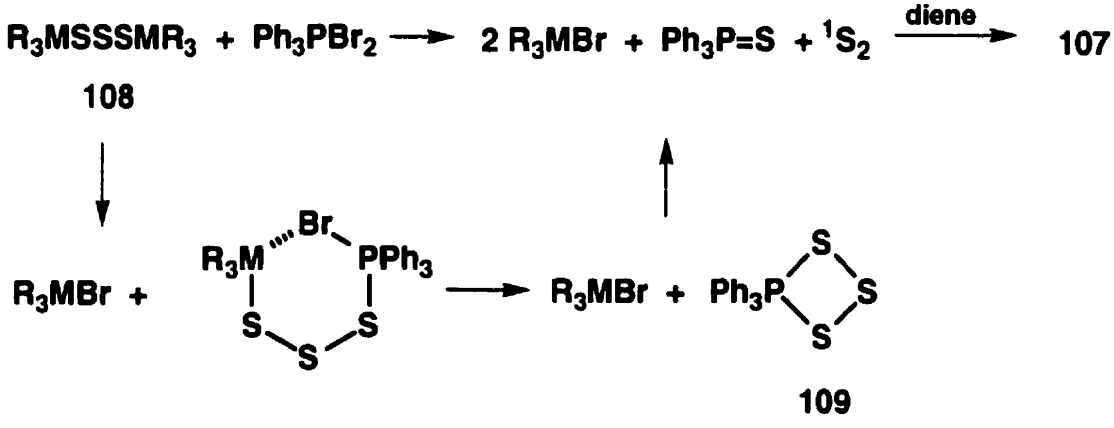


105 106 107

The first synthetically useful procedure to generate S_2 was elaborated in 1984 by Steliou using bis(triphenyl-germanium) trisulfide **108** to generate triphenylphosphine thioozonide **109** that can extrude $^1S_2$ spontaneously from -20 to 44 °C (**Scheme 14**).[52a] The clever method was elaborated to mimic the generation of singlet oxygen $^1O_2$ *via* phosphine ozonide **110**.[52b,c]



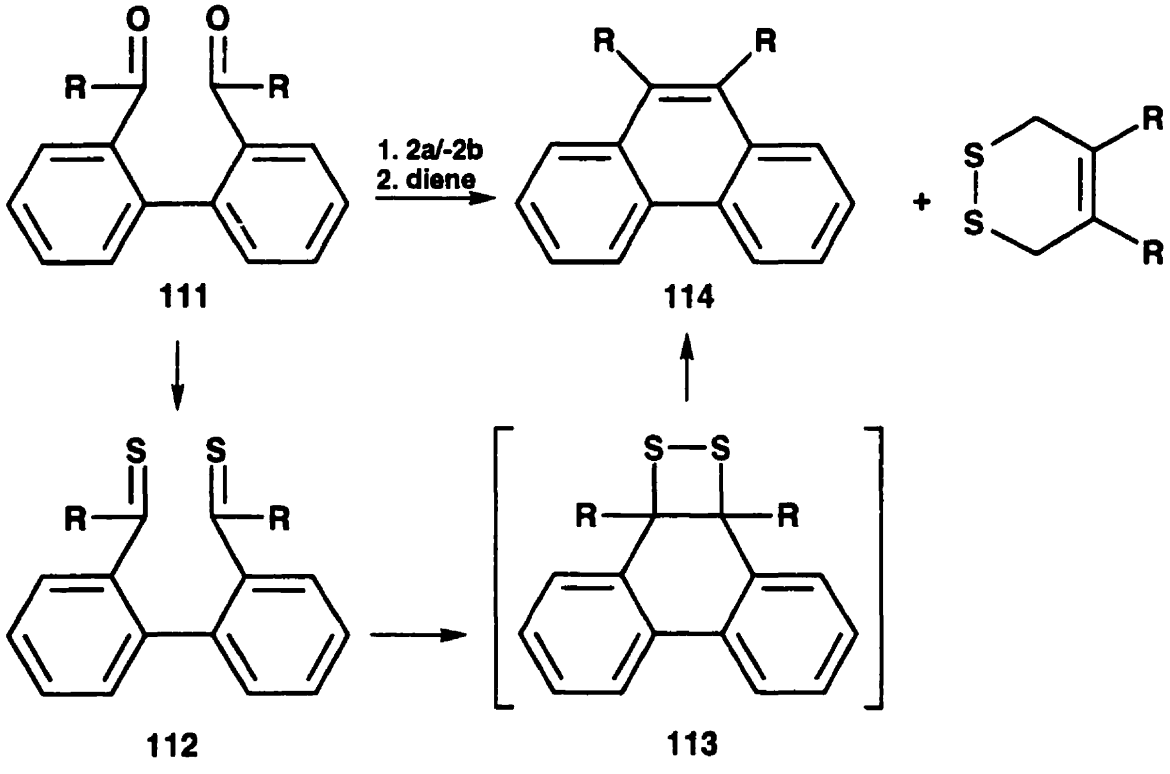
110



Scheme 14

52. a) K. Steliou, Y. Gareau and D.N. Harpp, *J. Am. Chem. Soc.*, **106**, 799 (1984); b) H.H. Wasserman and L.J. Ives, *Tetrahedron*, **37**, 1825 (1981); c) M. Balci, *Chem. Rev.*, **81**, 91 (1981).

Subsequently, an alternative method was developed by the same group to generate $^1S_2$ at higher temperature (80-131 °C); the 2,2'-dibenzoylbiphenyl **111** is converted to 2,2'-bis(thiobenzoyl)biphenyl **112** which spontaneously releases S_2 likely *via* a 1,2-dithietane intermediate **113**. The latter step driven by a favorable C-C bond formation to achieve the aromatic 9,10-diphenylphenanthrene **114** (ΔH = -37.08 kcal mol^{-1} for **112** → **114** to liberate S_2).[53a]

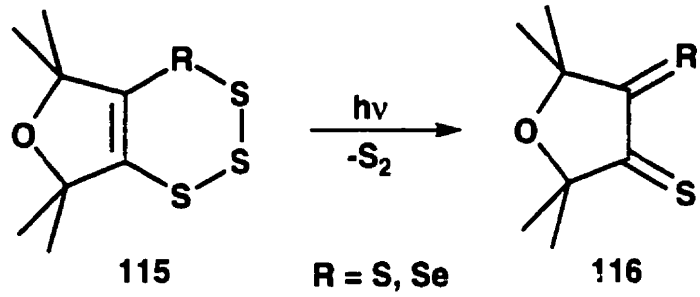


a: $(Me_3Si)_2S$ + 2/3 BCl_3; b: 2 Me_3SiCl + 1/3 B_2O_3

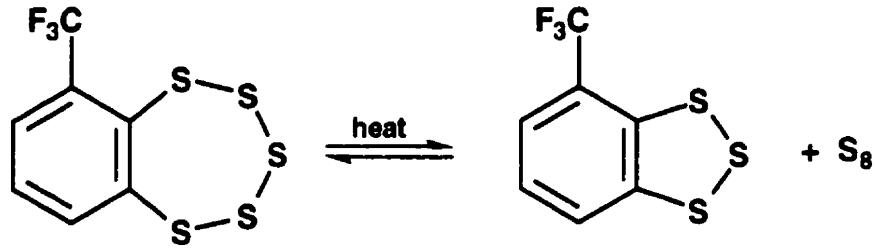
These efforts have led other groups considering the photochemical and thermal decomposition involving ring contractions of cyclic organosubstituted chalcogens.[53] Ando[53b] proposed the photochemical decomposition of **115** to **116** without providing evidence of trapping. Then, an S_2 intermediate was suggested to account for the formation of S_8 in the equilibrium benzopentathiepane-trithiolane (**117-118**).[53c] Although the sulfur

53. a) K. Steliou, P. Salama, D. Brodeur and Y. Gareau, *J. Am. Chem. Soc.*, **109**, 926 (1987); b) W. Ando, Y. Kumamoto and N. Tokitoh, *Tetrahedron Lett.*, **28**, 4833 (1987); c) B.L. Chenard, R.L. Harlow, A.L. Johnson and S.A. Vladerchick, *J. Am. Chem. Soc.*, **107**, 3871 (1985); d) P.D. Bartlett and T. Ghosh, *J. Org Chem.*, **52**, 4937 (1987); e) M. Schmidt and U. Görl, *Angew. Chem. Int. Ed. Engl.*, **26**, 887 (1987).

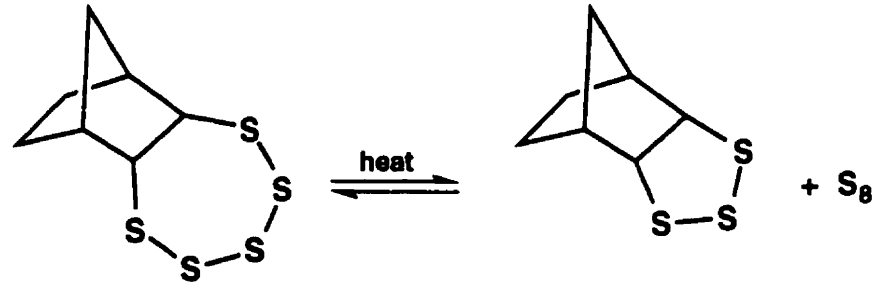
extruded in this equilibrium could sulfurate reactive olefins, a similar system studied by Bartlett and Ghosh on norbornene derivatives (**119-120**), in the presence of 2,3-dimethylbutadiene, was inconsistent with such an intermediate.[53d]



115 R = S, Se **116**

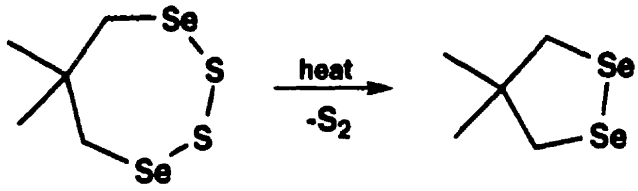


117 **118**



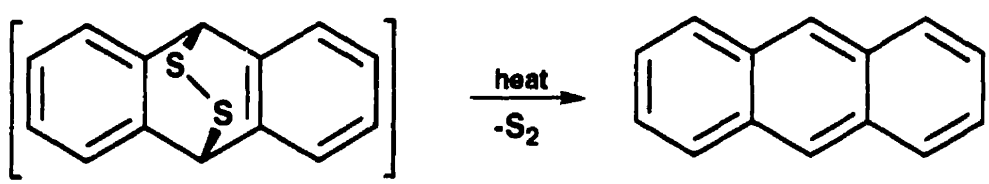
119 **120**

However, Schmidt and Görl[53e] have shown that 5,5-dimethyl-1,2-dithia-3,7-diselenacycloheptane **121** undergoes thermal decomposition with ring contraction to 4,4-dimethyl-1,2-diselenacyclopentane **122** and S_2 that was successfully trapped with a variety of dienes (2,3-dimethyl and 2,3-diphenyl butadiene, myrcene and 1,1'-bicyclohexenyl) in boiling chlorobenzene.

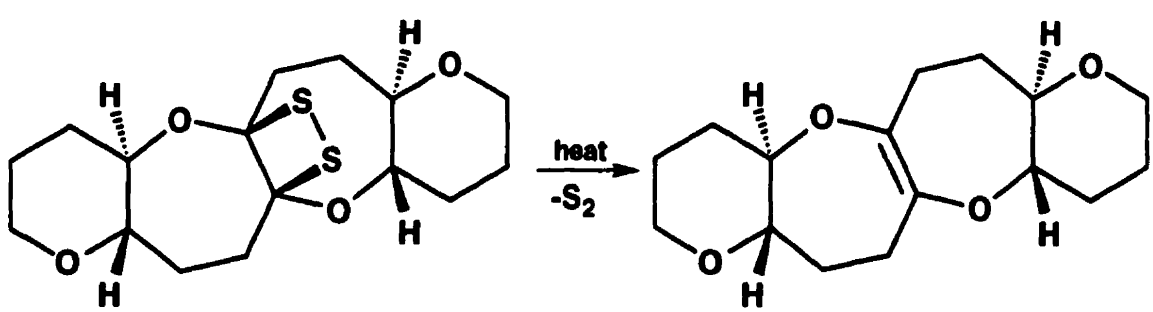


121 122

Ando devised an extrusion of S_2 *via* an intermediate anthracene endodisulfide **123** producing anthracene **124** at 55 °C.[54a] The process was regarded as a retro-Diels-Alder route and a mimic of the corresponding anthracene endoperoxide which reversibly generates molecular singlet oxygen $^1O_2$ and **124**;[54b,c] unfortunately no trapping was demonstrated. Another bridged disulfide system was described by Nicolaou and his team;[54d] dithiatopazine **125**, an intermediate in the total synthesis of brevotoxin B[54e], was isolated from the corresponding dithionolactone by photolysis. It was described and fully characterized as the first stable crystalline 1,2-dithietane system. When this stable system was photolyzed or heated to 100 °C, it extruded S_2, that was trapped with 2,3-diphenylbutadiene; the other product was the corresponding olefin **126**.



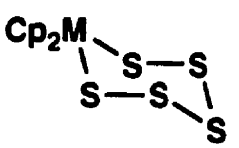
123 124



125 126

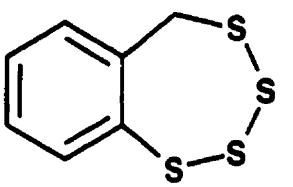
54. a) W. Ando, H. Sonobe and T. Akasaka, *Tetrahedron Lett.*, **28**, 6653 (1987); b) H.H. Wasserman, J.R. Sheffer and J.L. Cooper, *J. Am. Chem. Soc.*, **94**, 4991 (1972); c) E.J. Corey, M.M. Mehrotra and A.U. Khan, *ibid.*, **108**, 2472 (1986); d) K.C. Nicolaou, S.A. DeFrees, C.-K. Hwang, N. Stylianides, P.J. Carroll and J.P. Snyder, *J. Am. Chem. Soc.*, **112**, 3029 (1990); e) K.C. Nicolaou, C.-K. Hwang, M.E. Duggan and P.J. Carroll, *ibid.*, **102**, 3801 (1987).

Chronologically, the next precursors were described in our group in 1988[55a] as organometallic pentasulfide reagents **127**[55b]; the process was a parallel route to Steliou's germanium trisulfide approach, delivering S_2 at room temperature, in the presence of triphenylphosphine dibromide (**Scheme 14**). The next generation of processes, known to deliver S_2, involved organopolysulfide and disulfide molecules. They involve the thermolysis of cyclic 5H-benzo[f]-1,2,3,4-tetrathiepin (BTTP)[56a] **128** at 120 °C, of bicyclic 2,3-dithiabicyclo[2.2.1]hept-5-ene[56b] **129** at 130-160 °C and of the organometallic precursor **130** Cp_2MoS_4[56c] and the chlorination of tetramethylthiuram disulfide **131** with SO_2Cl_2 or Cl_2.[56d] Other molecules are known to react with dienes such as 2,3-dimethylbutadiene without necessarily delivering the S_2 unit. Triphenylmethanethiosulfenyl chloride (**132**) adds in 1,4-fashion to form adduct **133**.[56e] The same "precursor" was found to add in a 1,2-fashion to norbornene **134**, cyclopentene and cyclohexene and may deliver diatomic sulfur *via* a dithietane intermediate **135** (**Scheme 15**).[56f]



127

M = Ti, Zr, Hf



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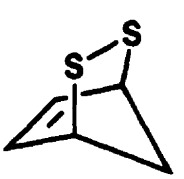
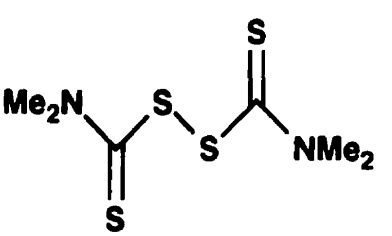


129



131

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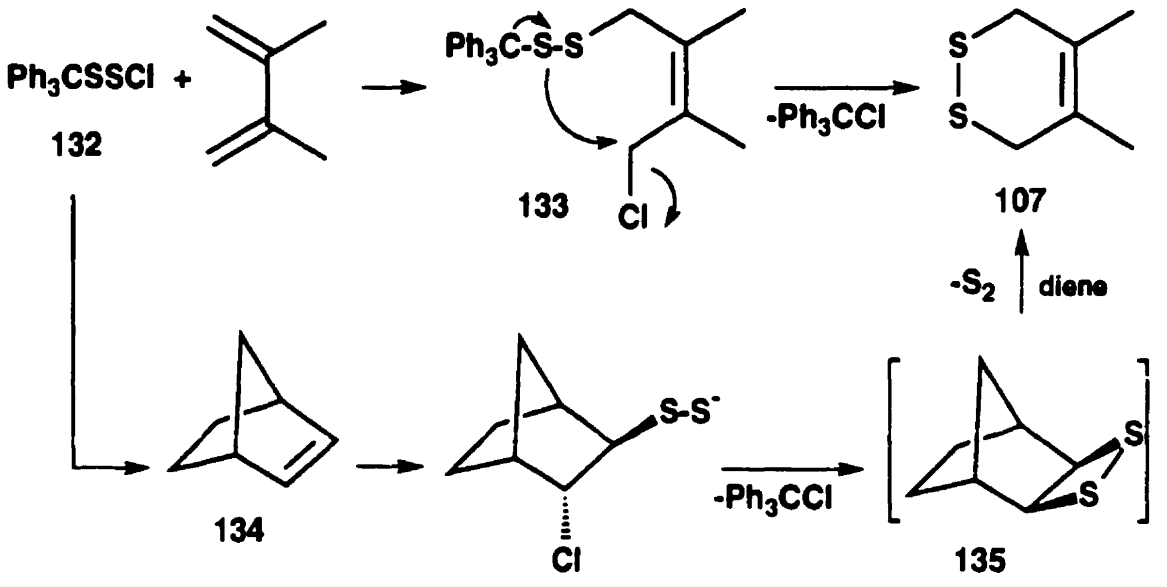
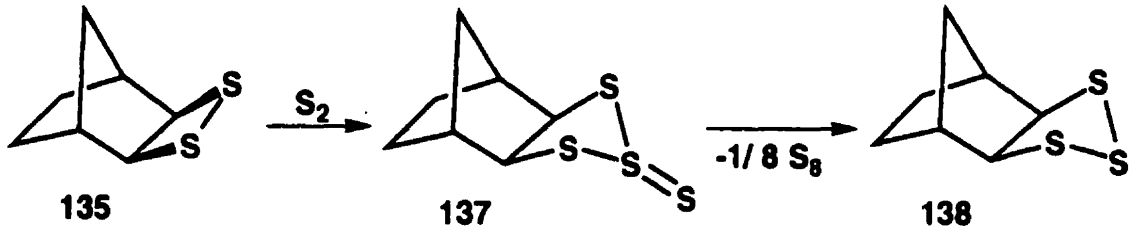
55. a) D.N. Harpp and J.G. MacDonald, *J. Org. Chem.*, **53**, 3812 (1988); b) J.M. McCall and A.G. Shaver, *J. Organomet. Chem*, **C37**, 193 (1980).

56. a) R. Sato, S. Satoh and M. Saito, *Chem. Lett.*, 139 (1990); b) T.L. Gilchrist and J.E. Wood, *J. Chem. Soc., Chem. Commun.*, 1460 (1992); *J. Chem. Soc., Perkin Trans. 1*, 9 (1992); c) D.N. Harpp and A. Rys, unpublished results; d) W. Chew and D.N. Harpp, *Sulfur Lett.*, **16**, 19 (1993); e) C.R. Williams, J.F. Britten and D.N. Harpp, *J. Org. Chem.*, **59**, 806 (1994); *Tetrahedron Lett.*, **32**, 7651 (1991); f) I.A. Abu-Yousef, R.C. Hynes and D.N. Harpp, *Tetrahedron Lett.*, **34**, 4289 (1993); *Tetrahedron Lett.*, **35**, 7167 (1994).



Scheme 15

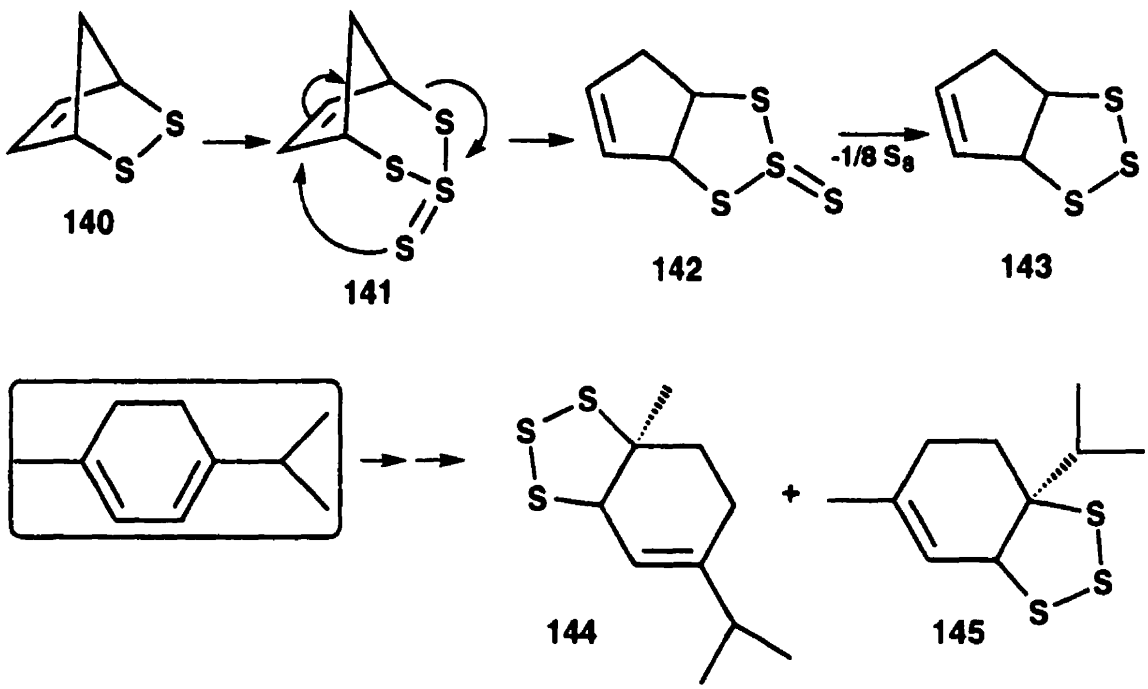
The last precursor **132** brings up the topic of S_2 addition to olefins. It seems that the S_2 addition to strained bicyclic olefins like norbornene **134** and norbornadiene **136** gives trithiolane (also called an epitrisulfide) product like **138**; the first S_2 addition possibly produces the dithietane intermediate **135** to which a second S_2 addition to the strained disulfide bond leads to thionotrisulfide **137** that deposits elemental sulfur to give **138**.[57]



The addition to the cyclic 1,3-diene, cyclopentadiene **(139)** gives bicyclic trisulfide **143**. The intermediate structure is the strained bicyclic adduct **140** to which a second addition occurs to give **141** which undergoes a 2,3-sigmatropic rearrangement to **142**

57. K. Steliou, Y. Gareau, G. Milot and P. Salama, *J. Am. Chem. Soc.*, **112**, 7819 (1990) and *Phosphorus, Sulfur Silicon Relat. Element.*, **43**, 209 (1989).

followed by elimination of elemental sulfur to form **143** (**Scheme 16**).[57] The same mechanism was suggested to account for the mixture of bicyclic trisulfide **144**:**145** (9:1) obtained in the case of α-terpinene.[57]



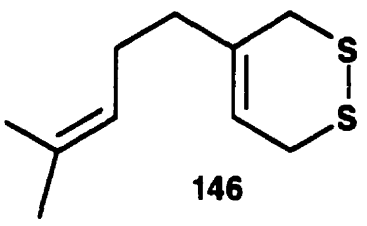
Scheme 16

1.9 The Chemistry of Activated Elemental Sulfur

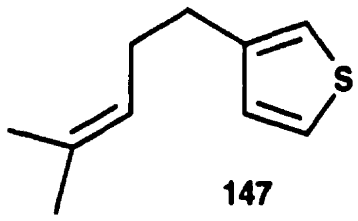
After considering the S_2 addition to acyclic 1,3-dienes, olefins and cyclic 1,3-dienes, it is important to mention that addition of "activated" elemental sulfur (S_n, n = 1-7) has also been observed on 1,3-dienes. The reactions are characterized by a variety of products ranging from the disulfide adduct to polysulfide compounds. In the presence of myrcene, the Diels-Alder adduct **146** was formed in low yield as well as thiophene **147** and polysulfide adducts **148**.[58a] In the presence of norbornadiene **136**, disulfides **149** and **150** were obtained.[53d] In the presence of 3H-benzo[d]-1,2-dithiole **151**, 5H-benzo[f]-1,2,3,4-

58. a) J.A. Elvidge, S.P. Jones and T.L. Peppard, *J. Chem. Soc., Perkin Trans 1*, 1089 (1982); b) T. Ghosh and P.D. Bartlett, *J. Am. Chem. Soc.*, **110**, 7499 (1988).

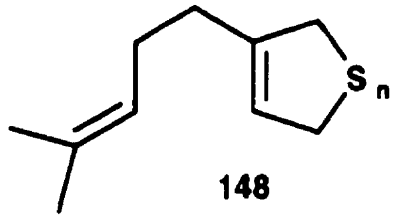
tetrathiepin (BTTP) **128** and 6-H-benzo[g]-1,2,3,4,5-pentathiocin (BPTC) **152** were produced.[56a]



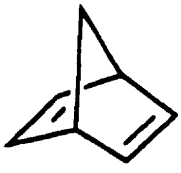
146



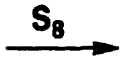
147

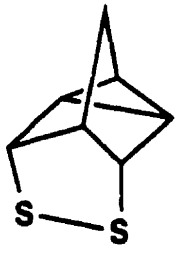


148



136





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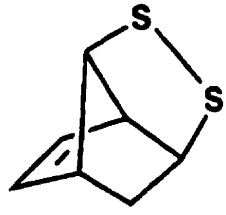

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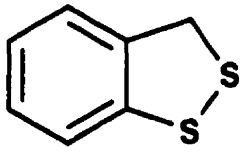

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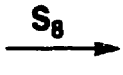

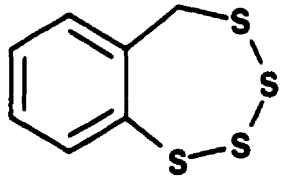

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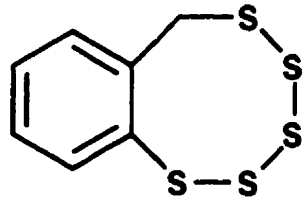
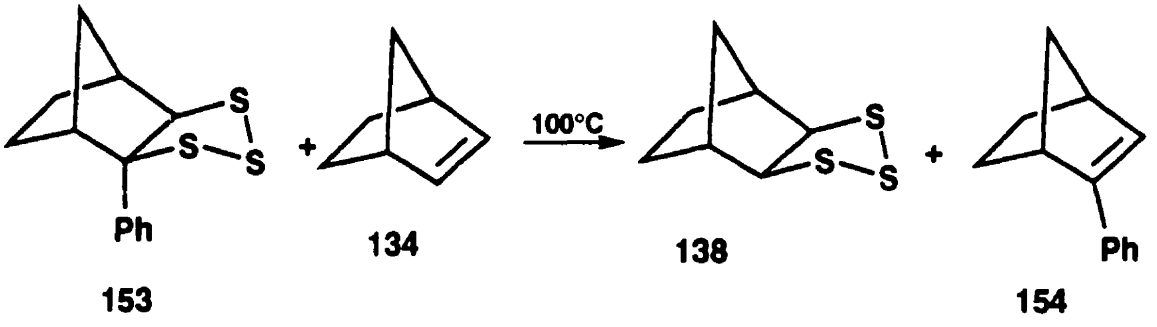


152

It seems that elemental sulfur is not the only source of activated sulfur, since norbornane trithiolane **153** can transfer a S_3 unit intermolecularly to norbornene **134** affording 2-phenyl-2-norbornene **154** and the trithiolane **138**.[58b] One may ask, what is activated elemental sulfur? Wasserman[59d] demonstrated that with time, S_8 is partially transformed to its allotropes S_6 and S_7 (to the extent of 1%), within minutes to hours, at room temperature when dissolved in polar solvents like methanol, acetonitrile and dimethyl sulfoxide. It seems that factors like irradiation[59c] and temperature, increase the allotropic

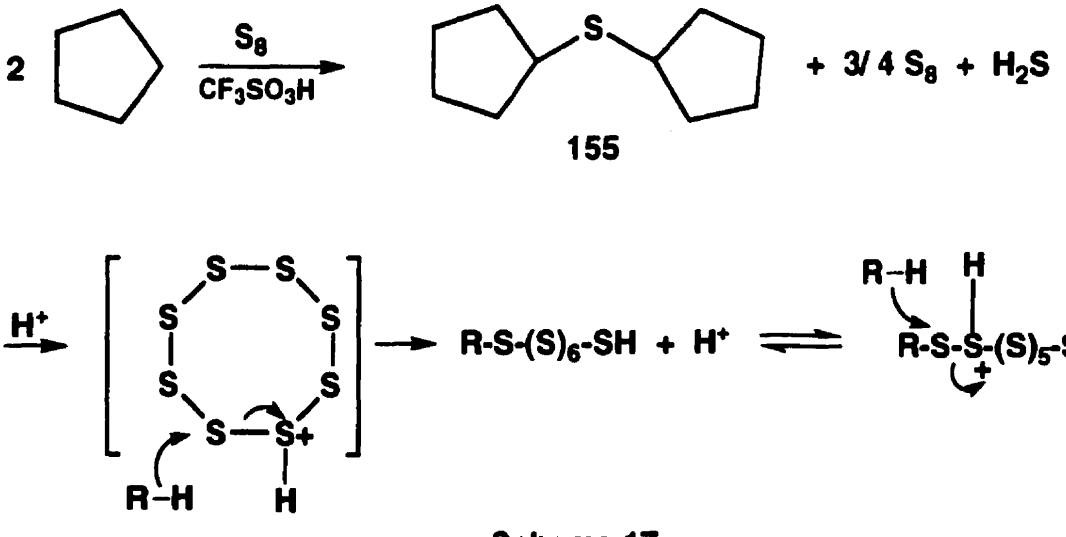
59. a) H. Jenne and M. Becke-Goehring, *Chem. Ber.*, **91**, 1950 (1958); b) H.G. Heal and J. Kane, *J. Inorg. Synth.*, **11**, 184 (1968); c) R. Steudel, J. Steidel, J. Pickardt and F. Schuster, *Naturforsch. B*, **35B**, 1378 (1980); d) F.N. Tebbe, E. Wasserman, W.G. Peet, A. Vatvars and A.C. Hayman, *J. Am.*

composition (S_6 and S_7) of cyclooctasulfur. These results are strongly indicative of polar intermediates in the interconversion processes; extended Hückel calculations indicate that a polar S_7=S is only 5-10 kcal mol^{-1} above S_8 in energy. In conclusion, they have proposed that the exo sulfur in S_7=S might be transferred to other sulfur rings.[59c]



153 134 138 154

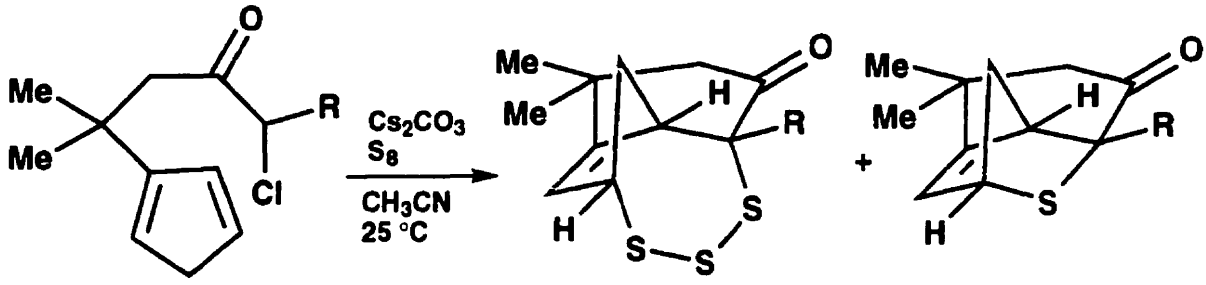
The interconversion to the different cyclic forms of elemental sulfur includes a related more soluble form, S_7=NH, which is prepared from S_8 in the presence of NH_3 in polar solvents.[56a,59a,b] The activation of S_8 in polar solvents corroborate one of our latest results where the disulfide adduct of 2,3-dimethyl butadiene was isolated from heating S_8 in DMSO in the presence of the diene.[59f] The protolytic activation of S_8 has also been considered to explain the acid catalyzed electrophilic sulfuration of cyclopentane with S_8 to dicyclopentyl sulfide **155 (Scheme 17)**.[59e]



Scheme 17

Chem. Soc., **104**, 4971 (1982); e) G.A. Olah, Q. Wang and G.K. Surya Prakash, *J. Am. Chem. Soc.*, **112**, 3697 (1990); f) D.N. Harpp and A. Rys, *Tetrahedron Lett.*, **38**, 4931 (1997).

The recent result reported on the subject led to the preparation of the novel tricyclictrithiapin **157** from ethyl 2-chloro-5-(1,4-cyclopentadienyl)-5-methyl-3-oxo-hexanoate **156**.[60] The idea was to generate the corresponding intermediate thiocarbonyl at the 2-position followed by intramolecular [4+2] cycloaddition to form **158**. Apparently, the inherent strain in this tricyclic sulfide renders the C-S bond susceptible to attack by the excess sulfur in the reaction to form **157**.



156 **157** **158**

R = CO_2Et

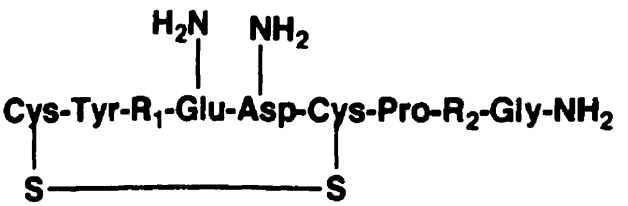
1.10 Naturally Occuring Cyclic Disulfides Including 1,2-Dithiins

Inasmuch as cyclic disulfides are the products of S_2 addition to dienes, it is appropriate to review some aspects of their occurence in nature. The disulfide (-S-S-) bridge is important as a chain-linking and ring-closing bridge in numerous bioproteins and polypeptides; it serve to preserve the essential stereochemical features to the biofunctions. Examples include immunoglobulins (antibodies), many enzymes like glutathione peroxidase, structural proteins like keratin and cyclic hormones like vasopressine **159**, oxytocin **160** and insulin (2 polypeptides of 21 and 30 residues). The disulfide bonds are formed between cysteine residues.[61a-f] Many studies and evaluations are carried out on potential mimic

60. D.A. Nugiel and M.M. Abelman, *J. Org. Chem.*, **60**, 3554 (1995).

61. a) C. Ressler, *Science*, **128**, 1281 (1958); b) A.V. Schally and R. Guillemin, *J. Biol. Chem.*, **239**, 1038 (1961); c) C. Walsh, *Enzymatic Reaction Mechanisms*, W.H. Freeman and Co., New York, 1979; d) G.L. Zubay, *Biochemistry*; 2nd Ed., Macmillan, New York, 1988; e) R.L. Baxter, S.S.B. Glover, E.M. Gorden, R.O. Gould, M.C. McKie, A.I. Scott and M.D. Walkinshaw, *J.*

catalysts of important enzymatic processes; the naturally occuring tripeptide glutathione (GSH; γ-glutamylcysteinylglycine) is oxidised to its corresponding disulfide (GSSG) by the enzyme glutathione peroxidase (GSH-Px) in the presence of reduced oxygen metabolites ($O_2^{\cdot-}$, H_2O_2, $OH^{\cdot}$). The catalytic activity of diaryl ditelluride was found to be higher than diaryl diselenide in thiol peroxidase activity.[62a,c] It was demonstrated that the oxidized form GSSG has antioxidant properties by protecting -SH groups in the enzyme carbonic anhydrase III againts oxidative damage by peroxide.[62e] Different molecular disulfides systems are developed, based on the thiol-disulfide interchange reaction to probe conformations in oligopeptides containing two cysteine residues.[62b,d]



159: R_1 = Phe; R_2 = Arg
160: R_1 = Ile; R_2 = Leu

The only reported saturated 4-membered ring 1,2-disulfide to be fully characterized is dithiatopazine **119**.[54d,e] Where the latter is called 1,2-dithietane, the corresponding unsaturated 4-membered ring 1,2-disulfides are referred as dithiete and only a few are known. Barton and his group reported the benzodithiete **161** as part of a steroid skeleton, and the structure was confirmed by X-ray analysis.[63] The 3,4-di-*t*-butyldithiete **163** was prepared in 45% yield from the thioxo-ketone **162** using the Lawesson's reagent **(eq.22)**.[64] The bicyclic dithietes **164** and **165** were synthesized from their corresponding 7-membered ring cycloalkyne and excess sulfur in refluxing DMF (77 and 51% yield).[65]

Chem. Soc. Perkin Trans. 1, 365 (1988); f) D.M. Rothwarf and H.A. Scheraga, *J. Am. Chem. Soc.*, **113**, 6293 (1991).

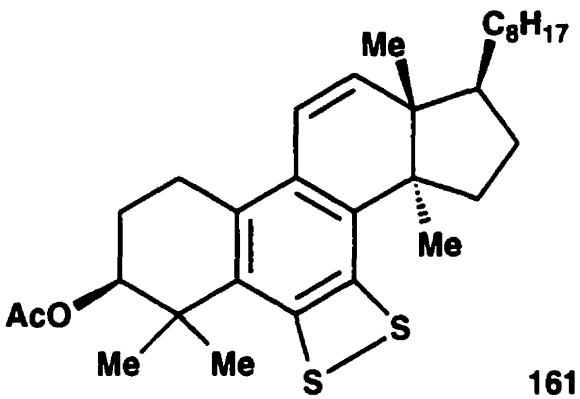
62. a) S.R. Wilson, P.A. Zucker, R.-R. Huang and A Spector, *J. Am. Chem. Soc.*, **111**, 5936 (1989); b) P.S. Kim and T.-Y. Lin, *Biochemistry*, **28**, 5282 (1989); c) L. Engman, D. Stern, I.A. Cotgreave and C.M. Anderson, *J. Am. Chem. Soc.*, **114**, 9737 (1992); d) W.J. Lees and G.M. Whitesides, *J. Am. Chem. Soc.*, **115**, 1860 (1993); e) M. Friedman, *Sulfur compounds in foods*; C.J. Mussinan, M.E. Keelan (Eds.), ACS Symposium Series 564, American Chemical Society, Washington, DC, 1994 pp-258-277.

63. a) R.B. Boar, D.W. Hawkins, J.F. Mc Ghie and D.H.R. Barton, *J. Chem. Soc., Perkin Trans I*, 515 (1977); b) R.B. Boar, D.W. Hawkins, J.F. Mc Ghie, S.C. Misra, D.H.R. Barton, M.F.C. Ladd and D.C. Povey, *J. Chem. Soc., Chem. Commun.*, 756 (1975).

64. B. Köpke and J. Voss, *J. Chem. Res. Synop.*, **11**, 314 (1982).

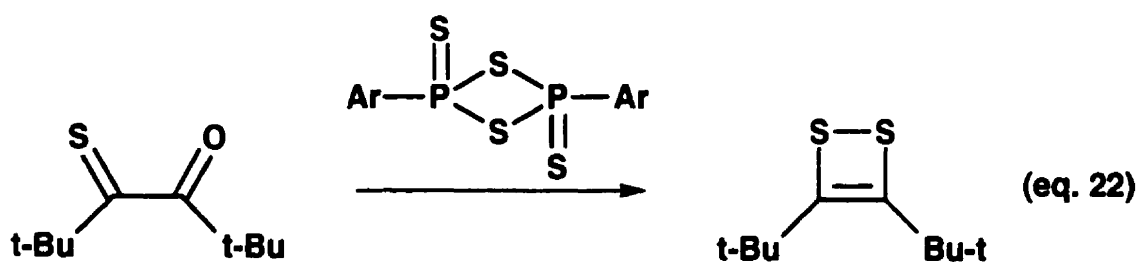
65. A. Krebs, H. Colberg, U. Höpfner, H. Kimling and J. Odenthal, *Heterocycles*, **22**, 1153 (1979).

Other dithietes **167** were shown to exist in a solvent dependent equilibrium with the tautomeric dithione **166** (R = 4-Me_2N-C_6H_4 and CN).[66a,b] For the 3,4-trifluoromethyl- (R = CF_3), the 1,2-dithiete was detected by IR and found to convert to the dimer **168**.[66c] Calculations have set the relative stabilizing effect of the substituents on the valence tautomeric forms in terms of their delocalization energies. Conjugative electron release by the substituent stabilizes the dithione structure **166** relative to the 1,2-dithiete **167**, while both conjugative and inductive electron withdrawing substituents stabilize **167** with respect to **166**.[66]



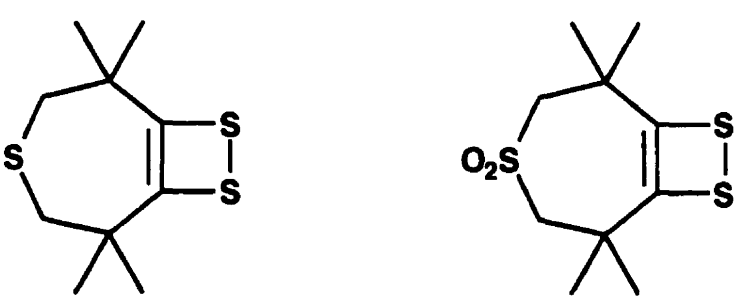
161

S-S: 2.12 Å



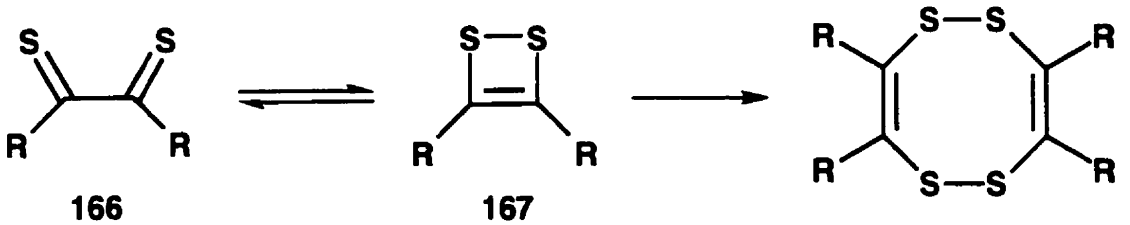
(eq. 22)

162 163



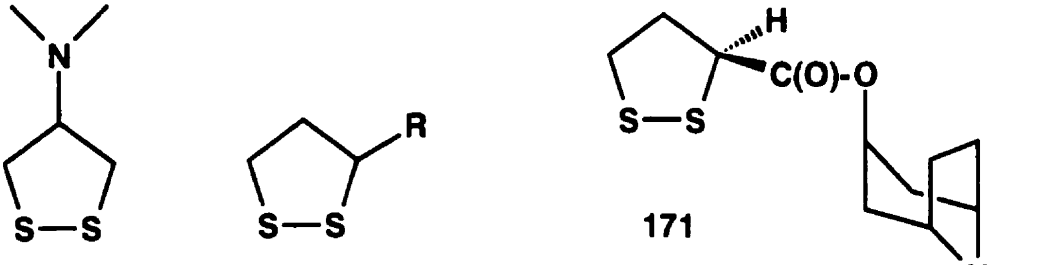
164 165

66. a) W.Küters and P. de Mayo, *J. Am. Chem. Soc.*, **96**, 3502 (1974); **95**, 2383 (1973); b) H.E. Simmons, D.C. Blomstrom and R.D. Vest, *J. Am. Chem. Soc.*, **84**, 4756, 4772, 4782 (1962); c) C.G. Krespan, *J. Am. Chem. Soc.*, **83**, 3434 (1961).



166 167 168

The 5-membered rings are named 1,2-dithiolanes and the first one reported was nereistoxin[67a] **169** found in marine annelids of the genera *Lumbriconereis* and *Lumbrenereis* in 1934 (later considered as an insecticide)[67k]. The next important one was α-lipoic acid **170a**, isolated from the liver, acting as co-factor in metabolism[67b,c] and being involved in oxidative decarboxylation[67h,i] and photosynthesis.[67d,e] Biological aspects of **170a** were reviewed[67l,m] including metabolite **170b** 1,2-dithiolane-3-carboxylic acid[67j] which upon esterification with tropine gave brugine **171** that was extracted from mangrove trees.[67f,g]



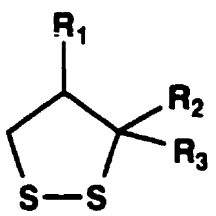
169

170a: R = $(CH_2)_4CO_2H$
170b: R = CO_2H

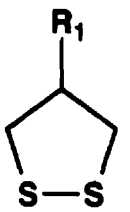
171

67. a) S. Nitta, *J. Pharm. Soc. Jpn.*, **54**, 648 (1934); T. Okaichi and Y. Hashimoto, *Agric. Biol. Chem.*, **26**, 224 (1962); b) L.J. Reed, B.G. Bebusk, I.C. Gunsalus and C.S. Hornberger, *Science*, **114**, 93 (1951); c) L.J. Reed, I.C. Gunsalus, G.H.F. Shakenberg, Q.F Soper H.E. Boaz S.F. Kern and T.V. Park, *J. Am. Chem. Soc.*,., **75**, 1267 (1953); d) M. Calvin and J.A. Barltrop, *J. Am. Chem. Soc.*, **74**, 6153, (1952); e) M. Calvin, *J. Chem. Soc.*, 1895 (1956); f) J.W. Loder and G.B. Russell, *Tetrahedron Lett.*, 6327 (1966); *Aust. J. Chem.*, **22**, 1271 (1969); g) A. Kato, *Phytochemistry*, **14**, 1458 (1975); h) D.E. Griffiths, *Genet. Biog. Chloroplasts Mitochondria, Interdiscip. Conf.*, Th. Buecher, W. Neupert and W. Sebald (Eds.), Amsterdam, North-Holland, 175 (1976); i) D.E. Griffiths, *Mol. Biol. Memb., (Proc. Symp.), 1977*, S. Fleisher, Y. Hatefi and D.H. Maclennan, (Eds), Plenum Presss, New York, 275 (1978); j) H.C. Furr, H.-H. Chang and D.B. McCormick, *Arch. Biochem. Biophys.*, **185**, 576 (1978); k) G.C. Scott, J.A. Pickett, M.C. Smith, C.M. Woodstock, P.G.W. Harris, R.P. Harman and H.D. Koetecha, *Proc. -Br.Crop Prot. Conf. - Pests Dis.*, **1**, 133 (1984); l) L. Teuder, *Sulfur Reports*, **9**, 257 (1990); m) L.I. Reed, I.C. Gunzalus, B.G. Debusk and C.S. Hornberger, *Science*, **114**, 93 (1993).

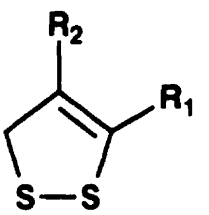
Altough very toxic, brugine has shown antitumor activity against Sarcoma 180 and Lewis Lung carcinoma. The alkyl substituted 1,2-dithiolanes **172-175** were isolated from the anal secretion of carnivores belonging to the genus *Mustela* (weasel, ferret, badger, otter).[68a-c] Besides their use in chemical communication[68d,f], they were also used as area repellents.[68e,g] Asparagusic acid **176** was isolated from etiolated and green asparagus shoots and has been investigated for use as a plant growth inhibitor.[69b,c] It has also been shown, *in vitro*, to have cytotoxic effect on Strain L mouse fibroblasts.[69a] Charactoxin **177** was isolated from *Chary* algae species;[70a,b] it was investigated for its intrinsic insecticidal properties because of its characteristic pungent smell.[70c,d] It has also been examined as a nerve poison.[70e] Interestingly, two naturally occuring, unsaturated 1,2-dithiolanes were isolated from garlic oil **178** and **179**.[71a]



172: R_1=H; R_2=CH_3; R_3=CH_3
173: R_1=H; R_2=H; R_3=CH_2CH_3
174: R_1=H; R_2=H; R_3=$(CH_2)_2CH_3$
175: R_1=CH_3; R_2=H; R_3=CH_3



176: R_1=CO_2H
177: R_1=SCH_3



178: R_1=CH_3; R_2=H
179: R_1=H; R_2=CH_3

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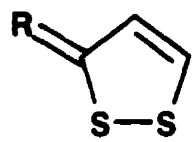
68. a) H. Schildknecht, I. Wilz, F. Enzmann, N. Grund and M. Ziegler, *Angew. Chem. Int. Ed. Engl.*, **15**, 242 (1976); b) E. Albone, *Chem. Brit.*, **13**, 92 (1977); c) D.R. Crump, *J. Chem. Ecol.*, **6**, 341, 837 (1980); d) V.E. Sokolov, E.S. Albone, P.F. Flood, P.F. Heap, M.Z. Kagan, V.S. Vasilieva, V.V. Roznov and E.P. Zinkevich, *J. Chem. Ecol.*, **6**, 805 (1980); e) E. Vernet-Maury, E.H. Polak and A. Damael, *J. Chem. Ecol.*, **10**, 1007 (1984); f) B.K. Clapperton, E.O. Minot and D.R. Crump, *Anim. Behav.*, **36**, 541 (1988); g) T.P. Sullivan, D.R. Crump and D.S. Sullivan, *J. Chem. Ecol.*, **14**, 363, 379 (1988).

69. a) J. Kieler, *Biochem. Pharm.*, **11**, 453 (1962); b) H. Yanagawa, *Plant and Cell Physiol.*, **17**, 931 (1976); c) R. Tressl, M. Holzer and M. Apetz, *J. Agric. Food Chem.*, **25**, 455 (1977).

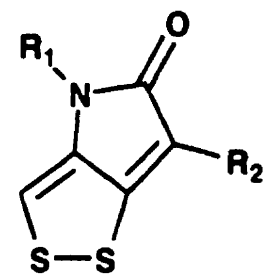
70. a) U. Anthony, C. Christophersen, J.O. Madsen, S. Wium-Anderson and N. Jacobson, *Phytochemistry*, **19**, 1228 (1980);b) S. Wium-Anderson, U. Anthony, C. Christophersen and G. Houen, *Oikos*, **39**, 187 (1982); c) N. Jacobsen and L.-E.K. Pederson, *Pestic. Sci.*, **14**, 90 (1983); d) L.-E. Nielsen and L.-E.K. Pederson, *Experimentia*, **40**, 186 (1984); e) S.M. Sherby, A.T. Eldefrawi, J.A. David, D.B. Satelle and M.E. Eldefrawi, *Arch. Insect Biochem.Physiol.*, **3**, 431 (1986).

71. a) Z. Ding, J. Ding, C. Yang and K. Amura, *Yunnan Zhiwu Yanjiu*, **10**, 223 (1988); *Chem. Abstr.*, **110**, 22443 (1989); b) Ref. 62e: M. Güntert, H.-J. Bertram, R. Emberger, R. Hopp, H. Sommer and P. Werkhoff, pp. 199-223.

Recently, 4,5-dehydro-1,2-dithiolan-3-one **180** was identified as a new thermal degradation compound of thiamin (vitamin B_1).[71b] Cruciferous vegetables like cabbage (*Brassica oleracea var capitata*) produce many volatile sulfur compounds such as 4,5-dehydro-1,2-dithiolan-3-thione **181** upon tissue disruption.[72] Cyclic disulfides such as homolycin **182**, thiolutin **183** and aureothricin **184** were identified from *Streptomyces* and found to have strong antibiotic activity parallel to high toxicity.[72]



180: R=O
181: R=S



182: R_1=H; R_2=CH_3
183: R_1=CH_3; R_2=CH_3
184: R_1=CH_3; R_2=C_2H_5

The only source of naturally occuring 1,2-dithiins are the compounds extracted from plants of the family *Compositae*.[73a] Example compounds are the dithiacyclohexadiene polyynes **185** and **186** known as thiarubrines A and B that are investigated for their antiviral and nematicidal activities.[73c,b] The known 3,6-dihydro-1,2-dithiins are **187** and the 3-vinyl derivative **188** both isolated from garlic and shown to be a component of the aroma of cooked asparagus.[74a,b] The 3-vinyl derivative has been shown to have antithrombotic activity.[74c] The well-known myrcene **189** isolated from steam-distilled hops[75a] and

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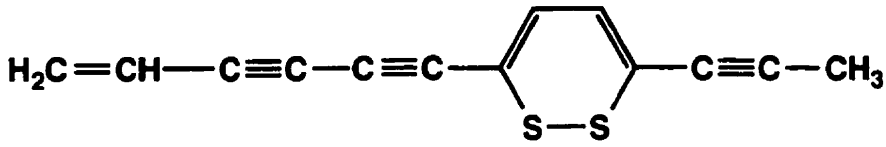
72. L. Field, *Organic Chemistry of Sulfur*, S. Oae, (Ed.), Plenum Press, New York, 1977, pp. 309-316.

73. a) F. Freeman, D.S.H.L. Kim and E. Rodriguez, *Sulfur Reports*, **9**, 207 (1989); b) J.B. Hudson, and G.H.N. Towers, *Bioact. Mol.*, **7**, 315 (1988); c) E. Rodriguez, *ACS Symp. Ser.*, **380**, 432 (1988).

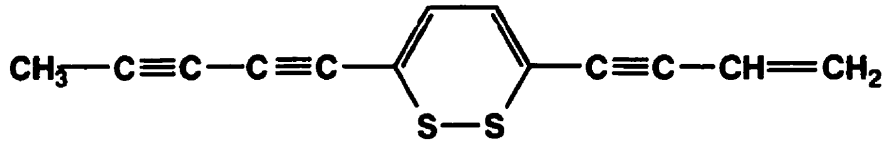
74. a) R. Tressl, M. Holzer and M. Apetz, *J. Agric. Food. Chem.*, **25**, 455 (1977); b) E. Block, S. Ahmad, J.L. Catalfamo, M.K. Jain and R. Apitz-Castro, *J. Am. Chem. Soc.*, **108**, 7045 (1986); c) H.H. Nishimura, C.H. Wijaya and J. Mizutani, *J. Agric. Food Chem.*, **36**, 563 (1988); *Chem. Abstr.*, **108**, 203507 (1988).

75. a) T. Uyehara, T. Ohnuma, T. Suzuki, T. Kato T. Yoshida and K. Takahashi, *Tennen Yuki Kagobutsu Tornkau Koen Yoshishu*, **22**, 235 (1979); *Chem. Abstr.*, **93**, 168433 (1980); b) A. Omata, K. Yomogida, Y. Ohta, S. Nakamura, T. Toyoda, A. Amado and S. Muraki, *Dev. Food Sci.*, **18**, 707 (1988); c) K. Steliou, Y. Gareau, G. Milot and P. Salama, *Developments in the Organic Chemistry of Sulfur, (Proc. XIII Int. Symp. Org. Chem. of Sulfur, 1988)*, C. Th. Pederson and J. Becher, (Eds.), Gordon and Breach Science Publishers, New York, 1989 pp. 209-241.

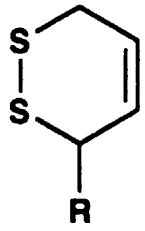
Bulgarian rose oil [75b] has demonstrated activity against Gram-positive bacteria and the HIV virus.[71c] Finally, 3-vinyl-3,4-dihydro-1,2-dithiin **190** was isolated from asparagus.[74a]



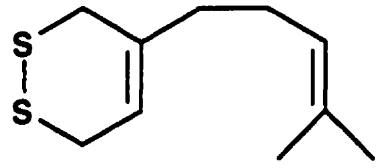
185



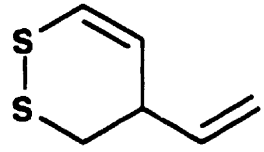
186



187: R=H
188: R=CH=CH$_2$



189



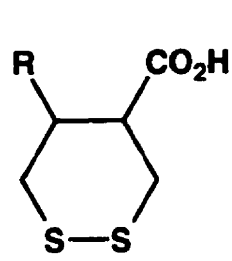
190

Saturated 6-membered ring disulfides are known as dithianes; 1,2-dithiane-4-carboxylic acid **191** and the 5-methyl derivative **192** have also been isolated from asparagus.[74a] Other peculiar cyclic disulfides include the seven membered ring **193** detected in the Hawaiian brown algae *Dictyopteris plagiogramma*;[76] the 1,2,4-trithiolane **194**, the sulfoxide derivative **195**, 1,2,4,5-terathiane **196**, lethionine **197**, tetrathiepane **198**, the sulfone derivative **199** and 1,2,4,5,7,8,10,11-octathiacyclododecane **200** from the red algae *Chondria californica* [77]; compounds **194**, **197**, **198** and the 1,2,3,4,5,6-hexathiepane **201**

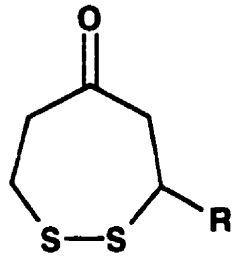
76. P. Roller, K. Au and R.E. Moore, *J. Chem. Soc., Chem. Commun.*, 503; 1168 (1971).

77. T.E. Kinlin, R. Muralidhara, A.O. Pittet, S. Sanderson and J.P. Walradt, *J. Agr. Food Chem.*, **20**, 1021 (1972).

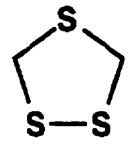
are reported to develop in drying the shiitake mushroom.[78a-e] 3,5-Dimethyl-1,2,4-trithiolane **202** and 3,6-dimethyl-1,2,4,5-tetrathiane **203** were detected by gas chromatographic analysis of milk[79a] and cooked meat;[79b,c] **202** has also been detected in other mushrooms (*Boletus edulis*).[80]



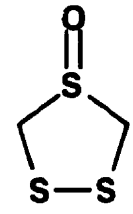
191: R=H
192: R=CH_3



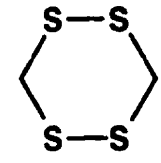
193: R=C_6H_{11}



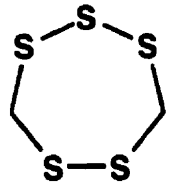
194



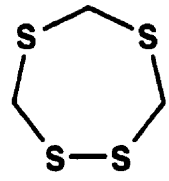
195



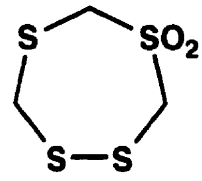
196



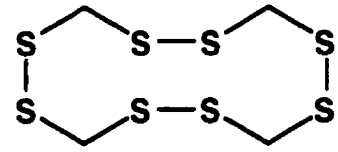
197



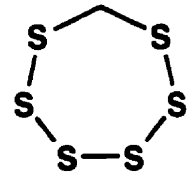
198



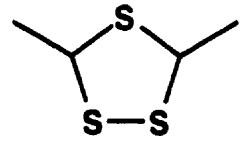
199



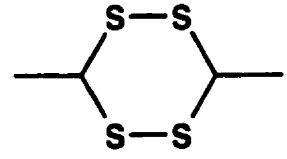
200



201



202



203

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78. a) K. Morita and S. Kobayashi, *Chem. Pharm. Bull.*, **15**, 988 (1967); b) S. Wada, H. Nakatani and K. Morita, *J. Food Sci.*, **32**, 559 (1967); c) K. Yasumoto, K. Iwami and H. Mitsuda, *Mushroom Sci.*, **9**, 371 (1976); d) C.C. Chen and C.T. Ho, *J. Agric. Food Chem.*, **34**, 830 (1986); e) E. Block, *J. Org. Chem.*, **59**, 2273 (1994).

79. a) P. Dubs and M. Johno, *Helv. Chim. Acta*, **61**, 1404 (1978); b) G. Ohloff and I. Flament, *Prog. Chem. Org. Nat. Prod.*, **36**, 231 (1979); c) G. Urback, *J. Chromatogr.*, **404**, 163 (1987).

80. a) A.F. Thomas, *J. Agric. Food Chem.*, **4**, 955 (1973); b) S.J. Wratten and D.J. Faulkner, *J. Org. Chem.*, **41**, 2465 (1976).

1.11 Naturally Occuring Bridged Bicyclic Disulfides

These compounds come from the family of fungal toxins characterized by the epidi- **204** and the epitrithiadioxopiperazine **205** systems. These systems have been extensively reviewed[81] and their array of biological properties[82e,g] range from antiviral/antifungal,[82a,b] immunosuppressive (inhibition of phagocytosis),[82c,h] oxidative DNA cleavage,[82f,i] and potential inhibitors of histamine release.[82j] Furthermore, the epipolythiapiperazine-2,5-dione moiety has been demonstrated to be responsible for the inhibitory effects on reverse transcriptase, one of the key enzymes in the life cycle of retro-viruses.[83] Despite this wide potential of bioactivity, no drug containing these systems (**204** and **205**) has been developed due to the high mammalian toxicity exhibited by most of these compounds.[84] A few specific examples include gliotoxin **206**, hialodendrin **207**, dithiosilvatin **208**, sirodesmin **209** and

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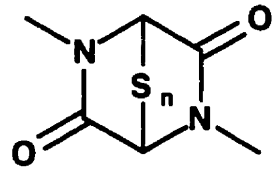
81. a) D.Brewer, D.E. Hannah and A. Taylor, *Can. J. Microbiol.*, **12**, 1187 (1966); b) R. Hodges and J.S. Shannon, *Aust. J. Chem.*, **19**, 1059 (1966); c) A. Taylor, *Biochemistry of some foodborne microbial toxins*, R.I. Mateles and G.N. Wogan (Eds.), M.I.T. Press, Cambridge, Mass, 1967, p.69; d) D. Brewer, R. Rahman, S. Safe and A. Taylor, *Chem. Commun.*, 1571 (1968); e) S. Safe and A. Taylor, *J. Chem. Soc. (c)*, 432 (1970); f) A. Taylor, *Microbial Toxins Vol. VII*, A. Ciegler ans S.J. Ajl (Eds.), Academic Press, New York, 337 (1971); g) T. Sato and T. Hino, *Tetrahedron*, **32**, 507 (1976); h) C. Leigh And A. Taylor, *Adv. Chem. Ser.*, **149**, 228 (1976); i) J.D.M. Herscheid, M.W. Tjhuis, J.H. Noordik and H.C.J. Ottenheijm, *J. Am. Chem. Soc.*, **101**, 1159 (1979); j) P.J. Curtis, D. Greatbanks, B. Hesp, A.F. Cameron and A.A. Freer, *J. Chem. Soc., Perkin I*, 180 (1979); k) G.W. Kirby and D.J. Robins, *The Biosynthesis of Mycotoxins*, P.S. Stein (Ed.), Academic Press 301 (1980); l) T. Fukayama, S. Nakatsuka and Y. Kishi, *Tetrahedron*, **37**, 2045 (1981); m) W.B. Turner and D.C. Aldridge, *Fungal Metabolites II*, Academic Press, New York, 417 (1983); n) G.W. Kirby, G.V. Rao, D.J. Robins and W.M. Stark, *Tetrahedron Lett.*, **27**, 5539 (1986); o) N. Kawahara, K. Nozawa, S. Nakajima, K. Kawai, *J. Chem. Soc., Perkin Trans. I*, 2099 (1987); p) M. Soledade, C. Padras, S.R. Abrams, G. Séguin-Swartz, J.W. Quail and Z. Jia, *J. Am. Chem. Soc.*, **111**, 1904 (1989).

82. a) W.A. Rightsel, H.G. Schneider, B.J. Sloan, P.R. Graf, F.A. Miller, Q.R. Bartz, J. Ehrlich and G.J. Dixon, *Nature*, **204**, 133 (1964); b) P.W. Trown, *Biochem. Biophys. Res. Commun.*, **33**, 402 (1968); c) A. Mullbacher and R.D. Eichner, *Proc. Natl. Acad. Sci. U.S.A.*, **81**, 3835 (1984); d) A. Mullbacher, P. Waring and R.D. Eichner, *Gen. Microbiol.*, **131**, 1251 (1985); e) T.W. Jordan ans S.J. Cordiner, *TIPS*, **8**, 144 (1987); f) A.W. Braithwaite, R.D. Eichner, P. Waring and A. Mullbacher, *Mol. Immun.*, **24**, 47 (1987); g) P. Waring, R.D. Eichner and A. Mullbacher, *Med. Res. Rev.*, **8**, 499 (1988); h) A. Mullbacher, A.F. Moreland, P. Waring, A. Sjaarda and R.D. Eichner, *Transplantation*, **46**, 120 (1988); i) P. Waring, *J. Biol. Chem.*, **265**, 14467 (1990); j) N. Kawahara, K. Nozawa, M. Yamazaki, S. Nakajima and K. Kawai, *Chem. Pharm. Bull.*, **38**, 73 (1990).

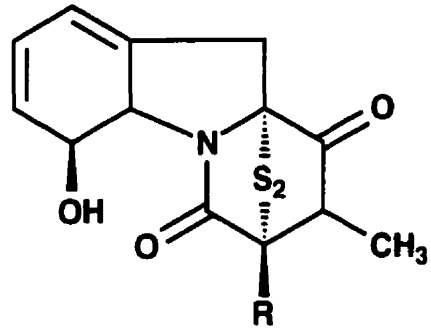
83. a) D. DeClercq, A. Billiau, H.C.J. Ottenheijm and J.D.M. Herscheid, *Biochem. Pharm.*, **27**, 635 (1978); b) P. Chandra, A. Vogel and T. Gerber, *Cancer Res.*, **45**, 46775 (1985); c) H. Mitsuya and S. Broder, *Nature*, **325**, 773 (1987); d) S.P.J. Goff, *AIDS*, **3**, 817 (1990); e) K.J. Connelly and S.M. Hammer, *Antimicrob. Ag. Chemother.*, **36**, 245 and 509 (1992).

84. a) A. Taylor, *Microbial Toxins*, S. Kadis, A. Ciegler and S.J. Ajl (Eds.), Academic Press, New York, Vol.7, Chap.10 (1971); b) R. Munday, *Chem. Biol. Interactions*, **41**, 361 (1982); c) R.D. Eichner and A. Mullbacher, *Aust. J. Exp. Biol. Med. Sci.*, **62**, 479 (1984); d) R.W. Jones and J.G. Hancock, *J. Gen. Microbiol.*, **134**, 2067 (1988).

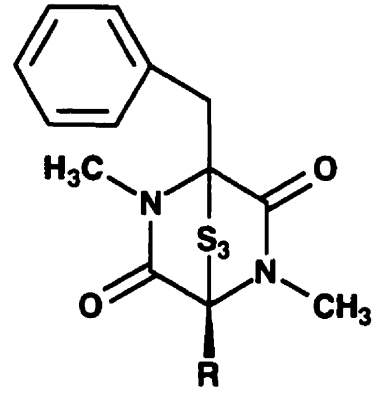
the 7-membered ring aspirochlorine **210** isolated from *Aspergillus tamari*,[85a] *A. flavus* [85b] and *A. oryzae*.[85c]



204: n=2
205: n=3



206: R=CH_2OH



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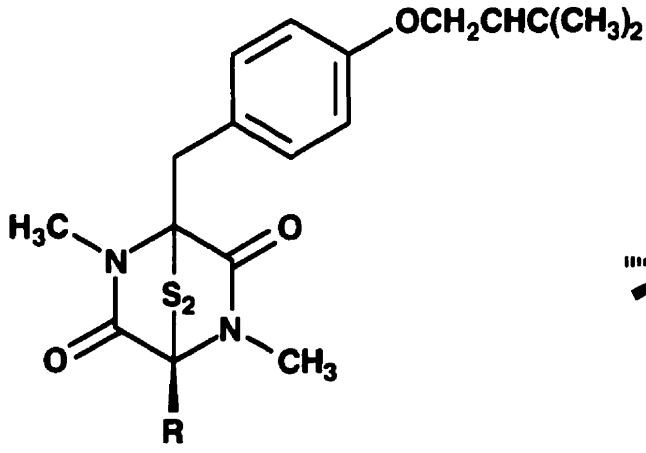
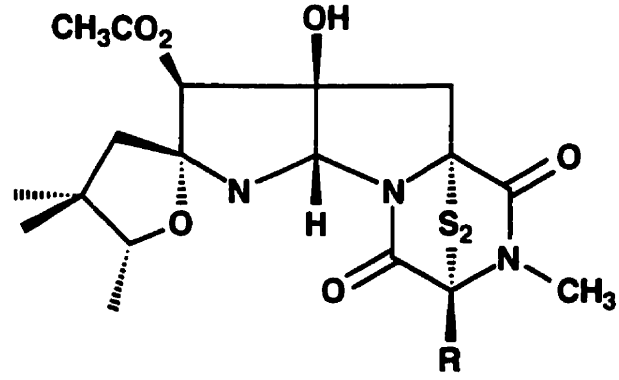
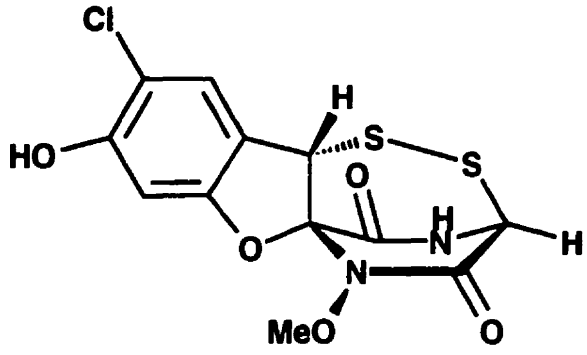


208: R=CH_2OH



209: R=CH_2OH

85. a) D.H. Berg, R.P. Massing, M.M. Hoehn, L.D. Boeck and R.L. Hamill, *J. Antibiot.*, **29**, 394 (1976); b) K. Sakata, H. Masago, A. Sakurai and N. Takahashi, *Tetrahedron Lett.*, **28**, 5607 (1982); c) K. Sakata, T. Kuwatsuka, A. Sakurai and N. Takahashi and G. Tamura, *Agric. Biol. Chem.*, **47**, 2673 (1983).



210

The potential bioactivity of all these different pools of naturally occuring cyclic, bridged bicyclic disulfide and related polysulfide compounds has been associated, in general, with the S-S bond which leads to activity which is lost upon reduction to the corresponding dithiol analogue. These cycles of bioreductive activation (originating from the cleavage of disulfide bond)/inhibition (resulting into the dithiol analogue) have generated many studies on the thiol-disulfide interchange reactions to clarify very important concepts like the structure-reactivity relations for the interchange,[86a] thermal stability of the S-S bond,[86b] the relationships between structure, effective concentration and equilibrium constants for the interchange,[86b,c] the thiolate-disulfide bond interchange,[86c,d] thiolate formation,[86e,h], hydrogen bonding between S-S bond and neighboring groups,[86g] and the structure of the S-S bond involved.[86f]

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86. a) G.M. Whitesides and J. Houk, *J. Am. Chem. Soc.*, **109**, 6825 (1987); and references cited therein; b) P. Magnus, R.T. Lewis and F. Bennett, *J. Chem.Soc., Chem. Commun.*, 916 (1989); c) G.M. Whitesides and J.A. Burns, *J. Am. Chem. Soc.*, **112**, 6296 (1990); G.M. Whitesides and R. Singh, *ibid*, **112**, 6304 (1990); d) P.M. Boorman, X. Gao and M. Parvez, *J. Chem. Soc., Chem. Commun.*, 1656 (1992); e) Ref. 62a; f) R.A. Volkman, J.G. Stroh, N.A. Saccomano, P.F. Thadeio, M.E. Kelly, P.R. Kelbaugh and N.D. Heck, *J. Am. Chem. Soc.*, **116**, 10426 (1994); g) T.-A. Okamura, N. Ueyama and Y. Yamada, *J. Org. Chem.*, **60**, 4893 (1995); h) S.J. Danishefsky and M.D. Shain, *J. Org. Chem.*, **61**, 16 (1996).

" Maybe the Absence of Evidence is not the Evidence of absence..."

CHAPTER 2: DIALKOXY DISULFIDES AND RELATED COMPOUNDS

2.1 Introduction

Despite having been discovered and known for almost 100 years, there are only a few synthetic methodologies available to prepare dialkoxy disulfides. To briefly review, the first one developed by Lengfeld[2] **(eq.1)** involves the treatment of sodium alkoxide, RONa, with sulfur monochloride, S_2Cl_2. The method elaborated by Thompson[1a] involves an alcohol treated with S_2Cl_2 in the presence of tertiary amines R'_3N **(eq.2)**; this last one is utilized most often. However, di-*n*-propyloxy and di-*iso*-propyloxy disulfide (**Table 1**, entries 5 and 10) were prepared in high yield by treating the respective alkoxy-tri-*n*-butylstannane derivative, *n*-Bu_3SnOR, with S_2Cl_2 at low temperature **(eq.4)**.[18] Interestingly, when phenyloxytrimethylsilane, $C_6H_5OSiMe_3$, was submitted to the same experimental conditions, bis(4-hydroxyphenyl) disulfide, $(4\text{-}HO\text{-}C_6H_4)_2S_2$, was obtained in 68% yield instead of the corresponding dialkoxy disulfide.[17] During our literature search on the title class of compounds, we realized that the lower members like diethoxy, dimethoxy and di-*iso*-propoxy disulfide were often used as the substrate of choice for nucleophilic substitution studies and other processes (Chapter 1, Section 1.2).

A number of groups reported using Thompson[1a] methodology to prepare their substrate without any notes on their experimental yields; the photolysis of dialkoxy disulfide **1** (R = Me, Et, *i*-Pr, *t*-Bu, *i*-Bu, neopentyl, benzyl) was studied as a convenient source of alkoxy radicals for addition to the sphere of fullerene C_{60} to yield the $RO\text{-}C_{60}$· adducts which are detected by ESR spectroscopy;[87] di-*iso*-propoxy disulfide and nonasulfide **54** (R = *i*-Pr) were used as sulfur transfer reagents, under mild conditions (40 °C, CH_2Cl_2), for the preparation of bis(2,3,4,6-tetra-*O*-acetyl-1-deoxy-β-D-glucopyranosyl) tetrasulfide **211** and undecasulfide **212 (eq.23)**.[88]

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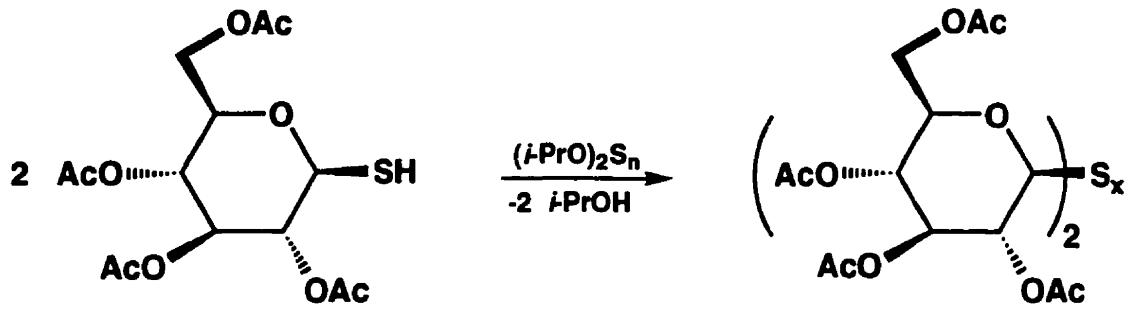
87. R. Borghi, L. Lunazzi and G. Placucci, *J. Org. Chem.*, **61**, 3327 (1996).

88. R. Steudel and H. Schmidt, *Chem. Ber.*, **127**, 1219 (1994).



(x = n+2)

211: x = 4
212: x = 11 (eq. 23)

Di-*n*-butyloxy disulfide **214** was prepared in 46% yield by Blaschette and collaborators[89] by reacting *n*-BuOH with the new sulfur transfer reagent bis(dimesylamino) disulfide **213** at ambient temperature (**eq.24**).

$$2\ n\text{-BuOH} + (CH_3SO_2)_2NSSN(SO_2CH_3)_2 \xrightarrow[CH_2Cl_2]{} (n\text{-BuO})_2S_2 \qquad \text{(eq. 24)}$$

213 **214**

The reaction of **214** with 1,1,1,3,3,3-hexamethyldisilazane (HMDS) gave silylated N,N,N',N'-tetrakis(trimethylsilyl) diamino disulfide, $([(CH_3)_3Si]_2N)_2S_2$, for which the crystal structure was determined at -95 °C. Further considerations regarding this compound will be included in later discussions related to the structure of dialkoxy disulfides **1**. We were interested in this last class of compounds from a synthetic and structural point of view. Thompson methodology was addressed with regard to alcohols.

89. A. Blaschette., M. Näveke and P.J. Jones, *Z. Naturforsch.*, **46b**, 5 (1991).

Table 1. Experimental Results for the Preparation of ROSSOR

Entry	Alcohol derivatives	R	Experimental conditions	Yields (%)	Ref.
1	RONa	CH_3	S_2Cl_2, ligroin	37	2
2		C_2H_5	S_2Cl_2, ligroin	41	2
3		*n*-C_3H_7	S_2Cl_2, ligroin	xx	3
4		*n*-C_3H_7	S_2Cl_2, Et_3N, CH_2Cl_2, 10°C	74[a]	1
5	ROSn(*n*-Bu)$_3$	*n*-C_3H_7	S_2Cl_2, CH_2Cl_2, -40°C	94	17,18
6	RONa	*n*-C_4H_9	S_2Cl_2, ligroin	xx	3
7	ROH	*n*-C_4H_9	S_2Cl_2, Et_3N, CH_2Cl_2, 10°C	70[a]	1
8		*n*-C_4H_9	$[(Ms)_2N]_2S_2$, CH_2Cl_2, rt	46	89
9		*i*-C_3H_7	S_2Cl_2, Et_3N, CH_2Cl_2, 10°C	71[a]	1
10	ROSn(*n*-Bu)$_3$	*i*-C_3H_7	S_2Cl_2, CH_2Cl_2, -40°C	87	17
11	ROH	benzyl	S_2Cl_2, Et_3N, CH_2Cl_2, 10°C	85[c]	1
12		allyl	S_2Cl_2, Et_3N, CH_2Cl_2, 10°C	85[b]	1
13		cholesteryl	S_2Cl_2, Et_3N, CH_2Cl_2, 10°C	48[c]	1

a) After distillation and correcting impurities by glc; b) Estimated content of ROSSOR by comparison of NMR of crude and pure materials; c) Recrystallized.

2.2 Results and Discussion

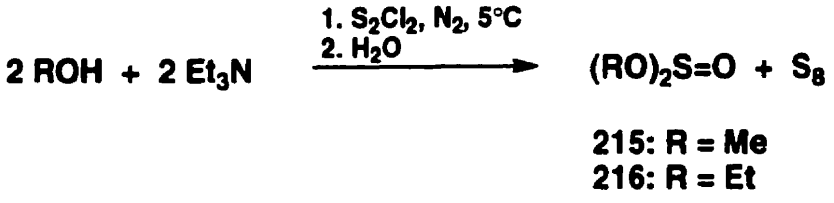
2.2.1 Preparation of Dialkyloxy Disulfides

Given the success obtained by Thompson in the preparation of a wide variety[90] of dialkoxy disulfides, this methodology was retained to prepare them. Before applying the above technique, every reagent was purified prior to use. The alcoholic substrates were distilled or recrystallized until they showed one spot on TLC. The other reagents were purified by distillation in the following way: methylene chloride (CH_2Cl_2) was distilled over P_2O_5; triethylamine (Et_3N) over KOH and S_2Cl_2[91] was flame distilled twice from sulfur flowers and charcoal; the red-yellowish fraction boiling at 135-137 °C was collected and stored in a dark bottle in the refrigerator under N_2. The preparation of dimethoxy **1** (R = CH_3) and diethoxy disulfide **34** following Thompson's procedure was fruitless. In the former case, after work-up and removal of CH_2Cl_2 under reduced pressure using the rotary

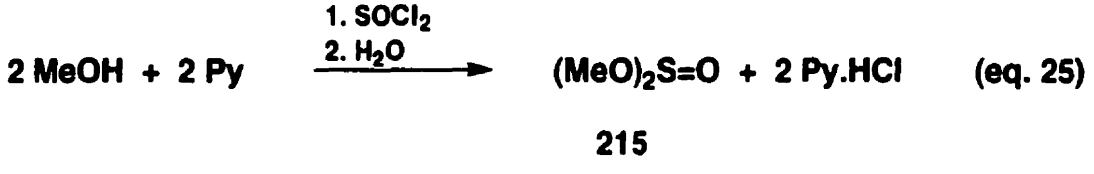
90. More details on Thompson's experimental results are summarized in Table 1 of ref.1a.

91. a) M. Fieser and L. Fieser, *Reagents for Organic Synthesis*; John Wiley & Sons, N.Y., Vol.1, 1967, p.1122.

evaporator, the residual ester was a yellowish oil containing dimethyl sulfite **215** with sulfur (S_8) as precipitate. The identity of **215** and elemental sulfur was confirmed by TLC with authentic samples.



Dimethyl sulfite **215** was independently prepared according to **eq.25** (65% yield). The product was characterized by ^1H NMR and IR; a sharp singlet was displayed at δ 3.50 ppm and a strong absorption at 1210 (S=O) cm^{-1}. Sulfites are known to absorb very strongly in the 1180-1240 cm^{-1} region[48a] while sulfoxides, $R_2S=O$, absorb in the 1010-1070 cm^{-1} region. The observed shift toward higher stretching frequency is explained by the electron-withdrawing effect of the alkoxy groups that renders the double bond stronger in the sulfonyl moiety (S=O) of sulfites.



The mechanism for the formation of elemental sulfur may be rationalized by the formation of diatomic sulfur, S_2, from the decomposition of dimethoxy disulfides *via* the six-membered transition state **18** proposed by Thompson for primary dialkoxy disulfides (**Scheme 1**). These diatomic sulfur species could concatenate[92] to form elemental sulfur. This concatenation of sulfur atoms to form stable sulfur species are likely initialized by the reaction of two sulfur species to form chain like intermediates **217** that cyclize to form S_8.

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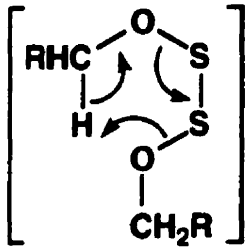
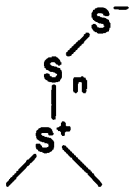
92. a) The idea of concatenation of sulfur atoms was first proposed by Foss in ref.13, 14; b) R.E. Davis, *J. Am. Chem. Soc.*, **80**, 3565 (1958).



18



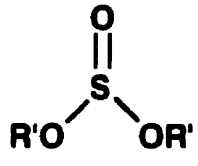
217

The formation of sulfite **215** in the reaction mixture may be related to the presence of triethylamine hydrochloride according to **Scheme 2** (Chapter 1, Section 1.2). Faced with the same "fate" for diethoxy disulfide (despite the use of dry EtOH)[93], we decided to look at the preparation of 4-substituted dibenzyloxy disulfides.

2.2.2 Preparation of 4-Substituted Dibenzyloxy Disulfides 218

Thompson and his group[1a] obtained very good results (**Table1**, entry 11) with the preparation of dibenzyloxy disulfide **218a**, 85% yield after recrystallization. We employed the same method to prepare a series of 4-substituted dibenzyloxy disulfides.[94] Our results are summarized in **Table 2**; the yields shown are the highest obtained for each disulfide derivative in a number of attempts. It is of note that the best yields were obtained with freshly distilled S_2Cl_2 in every case.

218 a: R = H
b: R = NO_2
c: R = Cl
d: R = OMe
e: R = Me



219: a-e

93. G. Hilgetag and A. Martini, *Preparative Organic Chemistry*, John Wiley and Sons, 1972, p.1096.

94. In general, this class of compound is stable for months at -15°C.

The following generalities for the reaction procedure were applied for each synthesis. The S_2Cl_2 solution was added at a rate to keep the reaction temperature at about 0-5 °C. One half of the S_2Cl_2 solution was added at -5 °C and the other half from -5 to +5° C in a dropwise fashion. The total addition time was never longer than 1-1.5 hour. The reaction mixture was never allowed to reach room temperature and vigorous stirring was applied; it was then quenched with cold water and thoroughly washed with cold water to eliminate any traces of HCl. This last step is very crucial for the successful isolation of each dialkoxy disulfide, preventing the formation of the corresponding sulfites **219**, once room temperature is reached and that the mixture is concentrated for the final purification steps. The organic layer was dried over anhydrous $MgSO_4$ and the solvents removed under reduced pressure. The crude solid residue (liquid residue for **218d** and **218e**), containing elemental sulfur S_8, the desired disulfide **218**, a very very small amount of sulfite **219** (except for **218d**) and the starting 4-substituted benzylic alcohol, was dissolved in 40% ethyl acetate in hexanes. The 4-substituted dibenzyloxy disulfide was found to crystallize in the solution upon standing in the fumehood or at -15°C. The filter was the pure desired disulfide **218**, while the residue from the mother liquor was chromatographed on silica gel using 30% ethyl acetate in hexanes. The order of elution on the column being first, the elemental sulfur, disulfide **218**, sulfite **219** and finally the alcohol. Isolation of each product gave the distribution reported in **Table 2**. The reaction residue for **218d** was found to be very unstable on silica gel, and almost no remaining bis(4-methoxybenzyloxy) disulfide **218d** was isolated by chromatography. The bis(4-nitrobenzyloxy) disulfide **218b** was found to decompose during purification by flash column chromatography on neutral alumina (80-200 mesh) to the corresponding alcohol, aldehyde, sulfite and elemental sulfur.

Table 2. Product Distribution in the Preparation of 218 (a-e)

ROSSOR 218	4-substituent	ROH (%)[a]	$(RO)_2S=O$ (%)[a]	218 (%)[b]	S_8 (%)[a]
a	H	4	3	88	1
b	NO_2	4	xx	90	1
c	Cl	3	4	86	1
d[c]	OMe	4	12	62[c]	8[c]
e	Me	6	3	82	1

a) Isolated yield from chromatography; b) Total isolated yield from crystallization and chromatography; c) 218d was very unstable on silica gel.

During the addition of S_2Cl_2, the reaction mixture changed from bright yellow to dark beige by the end of the reaction. An exception was observed when S_2Cl_2 was added to 4-chloro benzyl alcohol; the reaction color turned to mint green before evolving to beige. It is mandatory to mention that the isolation of the product must follow immediately after the work-up, otherwise the crude reaction mixture decomposed to the alcohol, the aldehyde and sulfur with an increase of the amount of sulfite. However, the reaction mixture can be kept in the refrigerator at -15 °C for few days (always after the work-up) without much decomposition (TLC). The disulfides **218c, d, e** did not crystallize upon standing at room temperature but did at -15 °C overnight in the refrigerator. The disulfide **218e** liquified upon filtration at ambient temperature.

The stability of the pure disulfide varies among the series. The more stable are **218b** and **218c**, they still remain stable at -15 °C after 8 months; they decompose after a few days at room temperature and in the light. The three others decompose after a day in the latter conditions but stay stable at -15 °C. The melting points for the disulfides and their corresponding sulfites are listed in **Table 3**. The sulfites **219** were prepared from the starting alcoholic substrate according to **eq.25**.

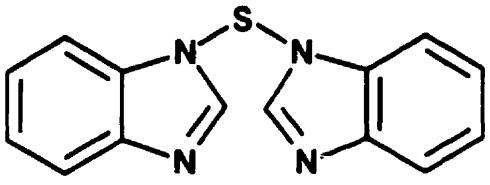
Table 3. Experimental Results for the Preparation of 219(a-e)

$(4\text{-X-}C_6H_4\text{-O})_2S{=}O$ **219**	**X**	**m.p. (°C)**	**Yield (%)[a]**	**m.p. (°C)**	$(4\text{-X-}C_6H_4OS)_2$ **218**
a	**H**	**liquid**	**61**	**50-51**	
b	**NO_2**	**81-82**	**66**	**92-93**	
c	**Cl**	**63-66**	**52**	**45-47**	
d	**MeO**	**liquid**	**73**	**34-36**	
e	**Me**	**40-42**	**65**	**liquid**	

a) Isolated yields after flash chromatography.

Many attempts towards the preparation of **218b** using the so called *mono*sulfur-transfer reagent bis(benzimidazol-1-yl) sulfide **59**, in refluxing CCl_4 (0.5, 1 and 2 equivalents) failed. The reaction was very slow, and the only products observed on TLC were elemental sulfur and 4-nitrobenzyl alcohol. Heat was required to initiate the reaction, but the presence of elemental sulfur during the process was indicative of the thermolability of

disulfide **218b**. Similar results were obtained with bis(benzimidazol-1-yl) disulfide (1 and 2 equivalents), the disulfide analogue of **59**, except that TLC monitoring showed the presence of some 4-nitrobenzaldehyde along with elemental sulfur and the alcohol. In each case benzimidazole precipitation was observed. The reaction mixture was allowed to reach room temperature and benzimidazole was collected, the mother liquor was evaporated under reduced pressure. The filtrate was taken up in methylene chloride; a meticulous search using TLC showed no signs of **218b**.



59

2.2.3 Preparation of Related Compounds

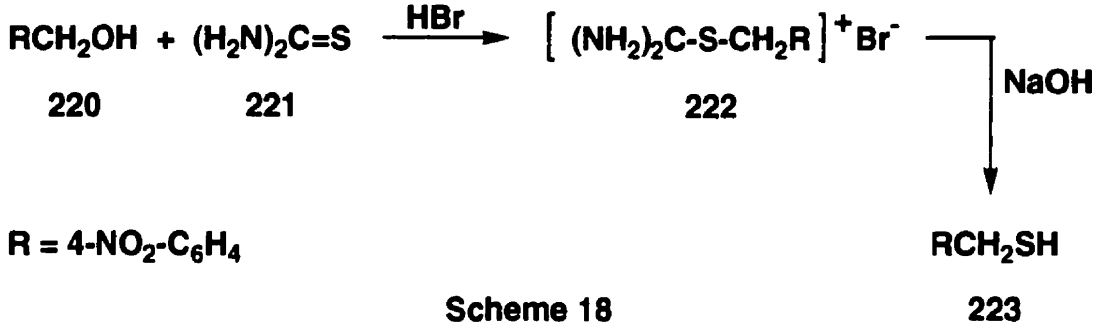
Since we were especially interested in the structural aspects of the molecular subunit **OSSO** of dialkoxy disulfides,[95] we required (*vide infra*) different compounds that were structurally related to the class of compounds. The approach taken for the selection of those compounds was the "**3D-Puzzle Approach**" where each atom, along the **OSSO** subunit, could be introduced/subtracted one by one to define overall related molecular structures. The logic of this approach gave a spectrum of molecules that helped clarify and characterize acyclic dialkoxy disulfides (Chapter 3).

2.2.3.1 Preparation of Bis(4-Nitrobenzyl) Tetrasulfide 226

We required a sample of bis(4-nitrobenzyl) tetrasulfide **226**, containing the **SSSS** subunit, as the starting point. This necessitated a sample of precursor 4-nitrobenzyl thiol **223** (R = 4-$NO_2C_6H_4$) to react with S_2Cl_2 to afford the tetrasulfide **226**. The condensation

95. a) The unusual aspects of the subunit **OSSO** were exposed clearly in Section 1.1 (pp. 1-5) and Section 1.7 (pp. 28-30); b) This new approach considers introducing the structure atom-by-atom and characterizing every resulting subunit along the process.

of thiourea **221** with active halides[96a] such as alkyl (*n*-, *sec*-, *t*-), allyl and benzyl halides to form S-thiouronium salts **222** followed by their hydrolysis with aqueous alkali or amines is a well-known method for the production of thiols. Frank and Smith[96c] have obtained yields of 73% with *n*-octanol, 77-90% with *n*-dodecanol, 91% with *n*-BuOH, 56% with *i*-BuOH and 72% with benzyl alcohol; they reported that the yields become poorer for tertiary alcohols due to their tendency to form olefins. The preparation of the thiol **223** by the isothiouronium salt[96a] methodology according to **Scheme 18** gave isolated yields in the range of 10%. The bis(4-nitrobenzyl) sulfide, m.p. 162-164 °C (lit.[97] m.p. 159 °C) along with the 4-nitrobenzyl alcohol **220** were the other reaction products obtained after column chromatography; the order of elution being the alcohol **220** (31%), the thiol **223** (56%) and the sulfide R_2S (12%) using 30% EtOAc-hexane.



Scheme 18

In our search to improve the yield of our desired thiol **223**; α-bromo-*p*-nitrotoluene **224** was treated with thiourea **221** in EtOH followed by the usual hydrolysis[98]. The only product identified was alcohol **220**. However, when **224** was treated with potassium thioacetate **225** in MeOH at room temperature followed by acid hydrolysis at 0 °C, 100% of 1-(methylthio)-4-nitrobenzene **223** m.p. 48-50 °C to m.p. 52-53 °C (once recrystallized from *i*-PrOH; lit.[95b,96] m.p. 52.5 °C) was obtained.

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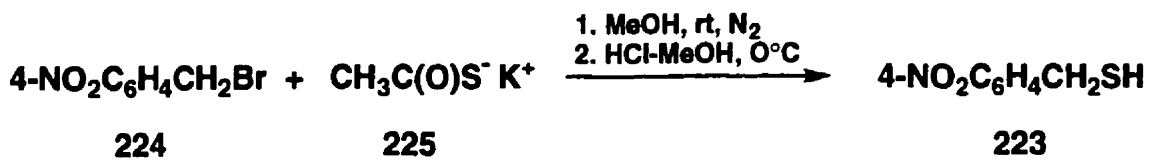
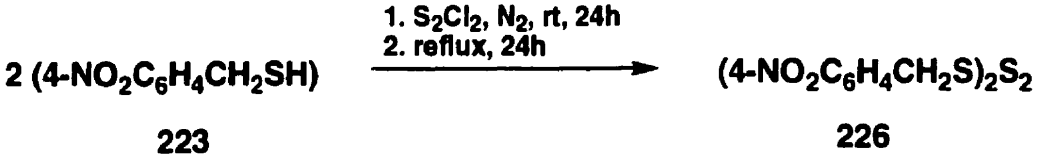
96. a) R.S. Sandler and W. Karo, *Organic Functional Group Preparations*, **Vol.3**, Academic Press, New York, N.Y., 1972, Chap.18; b) E.E. Reid, *Organic Chemistry of Bivalent Sulfur*, **Vol.1**, Academic Press, New York, N.Y., 1958; c) R. Frank and P.V. Smith, *J. Am. Chem. Soc.*, **68**, 2103 (1946).

97. T.S. Price and D.F. Twiss, *J. Chem. Soc.*, **95**, 1725 (1909); b) Tables in Ref. 95b.

98. Ref. 95a; Chap.12



Thiol **223** was reacted with S_2Cl_2 in dry ether, and the reaction mixture was gently refluxed overnight to afford, after column chromatography and recrystallization (toluene-petroleum ether) 45% yield of white fine needles m.p. 114-114.5 °C and identified as the bis(4-nitrobenzyl) tetrasulfide **226**. Interestingly, the product is only partially soluble in Et_2O and some of the tetrasulfide precipitated out of the reaction mixture at room temperature.



The successive loss of the four sulfur atoms was observed in the EI mass spectrum with the molecular ion m/z 400 (0.2%), m/z 368 (2.6%), m/z 336 (13.4%), m/z 304 (9.4%), m/z 272 (11.8%). The detailed spectroscopic results will be discussed in Chapter 3.

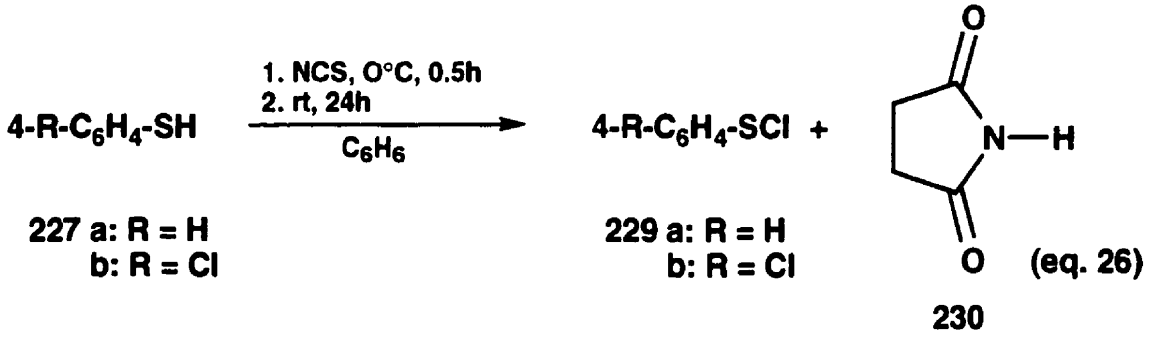
2.2.3.2 Preparation of *p*-Nitrobenzyl *p*-Chlorobenzenesulfenate

We were interested in looking at some features of the S-O bond of sulfenates R-S-O-R, since they are related to dialkoxy disulfides R-O-S-S-O-R. The above mentioned compound was prepared by condensing *p*-chlorophenylsulfenyl chloride **229b** with **220** in the presence of pyridine. Different methods[98] are available to prepare sulfenyl halides RSX (X = F, Cl, Br, I) which are known to undergo a wide variety of reactions: addition, displacement, oxidation, reduction, free-radical addition and Friedel-Crafts alkylation. The procedure used for the halogenation of benzenethiol **227a** and *p*-chlorobenzenethiol **227b** was a modification of the Emde's method further developed by Harpp and Mathiaparanam.[99]

---

99. a) E. Gebauer-Fulnegg, *J. Am. Chem. Soc.*, **49**, 2270 (1927); b) H. Emde, *Chem. Abstr.*, **46**, 529 (1952); c) D.N. Harpp and P. Mathiaparanam, *J. Org. Chem.*, **37**, 1367 (1972); d) Ref.97, p.159, Table IIA.

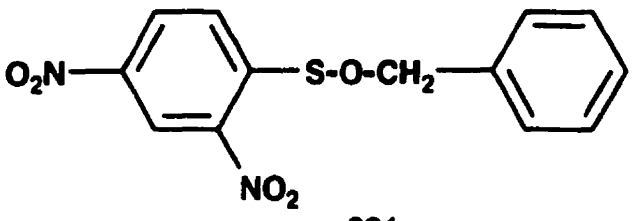
The thiol was chlorinated using N-chlorosuccinimide **228** at 0 °C followed by stirring at room temperature over a period of 24 hours according to **eq.26**. The color of the reaction mixture changed from yellow to orange at 0 °C and then to dark red at room temperature. The white precipitate of succinimide **230** was removed by filtration and the crude residual red oil was concentrated and distilled under reduced pressure. The fraction boiling at 57-58 °C under 1mm Hg (lit.[99d] b.p. 55 °C under 1mm Hg) was collected for **229a** in 96% yield, and the one boiling at 94-96 °C under 2 mm Hg (lit.[99d] b.p.68-69 °C under 0.5 mm Hg) was collected for **229b** in 97% yield. These arylsulfenyl chlorides were stored in dark brown bottles at -15 °C in the refrigerator.



Kharasch and his collaborators[100a,b] have prepared a wide variety of sulfenates (RSOR'; R = 2,4-dinitrobenzene, R' = *n*-, *i*-, *sec*-, *t*-alkyl, cyclohexyl, aryl, cholesteryl, benzyl, allyl, etc) with isolated yields over 80% except for the allyl analogue that was obtained in only 14% yield. They reported a yield of 95% for benzyl 2,4-dinitrobenzenesulfenate **231** and the bis(2,4-dinitrobenzene) disulfide **232** as the side product. *p*-Nitrobenzyl *p*-chlorobenzenesulfenate **233** was synthesized by reacting the sulfenyl chloride **229b** with the benzyl alcohol **220a** in the presence of pyridine according to **eq.27**.

---

100. a) N. Kharasch, D.P. Mc Quarrie, and M.C. Buess, *J. Am. Chem. Soc.*, **75**, 2568 (1953); b) L. Goodman and N. Kharasch, *J. Am. Chem. Soc.*, **77**, 6541 (1955); c) W.C., Hamilton and S.J. La Placa, *J. Am. Chem. Soc.*, **86**, 2289 (1964); d) Ref. 97, pp. 193-198; e) S. Braverman and B. Sredni, *Tetrahedron*, **30**, 2379 (1974).



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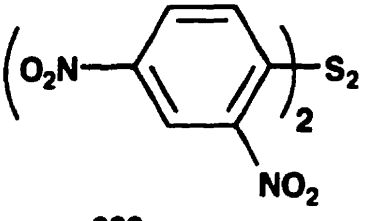

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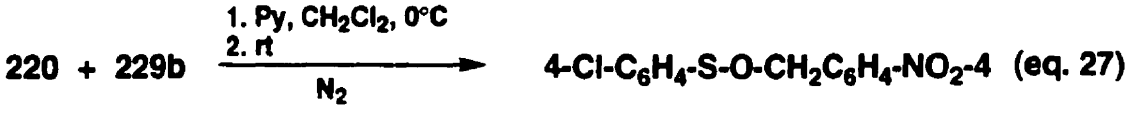
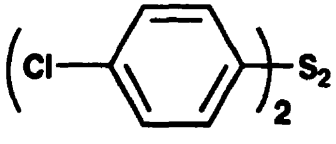


233

No signs of reactivity were observed at 0 °C (by TLC) after the addition of **229b**; the reaction temperature was increased to room temperature over a period of 2 hours; pyridine hydrochloride precipitate was collected and the residue concentrated under reduced pressure. Careful monitoring of the reaction by TLC showed the presence of four different products; about half of the residue was recrystallized at -15 °C in a solution of 10% ethyl acetate in hexanes while the other half was chromatographed on silica gel using 10% ethyl acetate in hexanes. What we thought to be the sulfenate **233** crystallized out overnight in the fridge and came out third from the chromatography column. The other products were identified as bis(4-chlorophenyl) disulfide, **234**, m.p.66-67 °C (lit.[101a-c] m.p. reported to be 73°, 71.5° and 71 °C); 4-nitrobenzyl chloride, **235** m.p. 72-73 °C (lit.[101d] m.p. 70-73 °C) and 4-nitrobenzyl alcohol **220** m.p. 92-93 °C (lit. 91-94 °C). The mass spectrum results reported in **Table 4** were obtained from electron-impact ionization.



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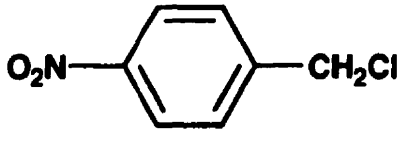


235

101. a) m.p. 71°C; F. Taboury, *Compt. Rend.*, **138**, 982 (1904); b) m.p. 71.5 °C; S.S. Bhatnagar and B. Singh, *J. Indian Chem. Soc.*, **7**, 663 (1930); c) m.p. 73 °C; M. B. Sparbe, J.L. Cameron and N. Kharasch, *J. Am. Chem. Soc.*, **75**, 4907 (1953); d) *Beil.* 5, 329.

Table 4. Product Identification by Mass Spectrometry

Compound	m/z, relative intensity (%), fragment
234	286/288/290, 48/35/8, $M^{+\cdot}$ Cl cluster
	222/224, 3/2, $M^{+\cdot}$- S_2
	143/145, 100/36, 4-Cl-$C_6H_4S^{+\cdot}$
	108, 52, $C_6H_4S^{+}$
235	171/173, 47/15, $M^{+\cdot}$ Cl cluster
	136, 100, 4-NO_2-$C_6H_4CH_2^{+}$
220	153, 53, $M^{+\cdot}$
	136, 24, 4-NO_2-$C_6H_4CH_2^{+\cdot}$
	107, 61, $M^{+\cdot}$- NO_2
	77, 100, Ph^{+}

What we thought to be the sulfenate **233** was in fact the *p*-nitrobenzyl *p*-clorobenzenesulfinate **236** (p.66). Recently, the chemistry related to the rearrangement of alkyl, aryl, and allyl sulfenates to their corresponding sulfoxides was reviewed by Braverman.[102d] The thermal sulfenate-sulfoxide interconversion for benzyl arylsulfenates, $ArCH_2$-O-S-Ar, to their sulfoxide,[102a-c] $ArCH_2$-S(=O)Ar, is believed to occur *via* a concerted intramolecular mechanism[102b, 103a] (**Scheme 19**).

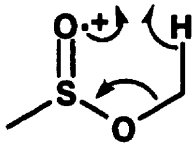
Scheme 19

102. a) D.R. Rayner, E.G. Miller, P. Bickart, A.J. Gordon and K. Mislow, *J. Am. Chem. Soc.*, **88**, 3138 (1966); b) D.R. Rayner, E.G. Miller, H.J. Thomas and K. Mislow, *J. Am. Chem. Soc.*, **90**, 4861 (1968); c) J.J. Jacobus, *J. Chem. Soc., Chem. Commun.*, 709 (1970); d) S. Braverman, *The Chemistry of Sulfones and Sulfoxides*, S. Patai, Z. Rappoport and C.J.M. Sterling (Ed.), Wiley, Chichester, 1988, Chap. 14.

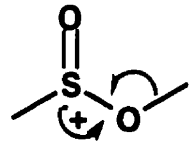
103. a) J.L. Kice, *Adv. Phys. Org. Chem.*, 100 (1980); b) E. Ciaffarin, S. Gambaretta, M. Isola and L. Senatore, *J. Chem. Soc., Perkin Trans 2*, 554 (1978).

This mechanism was preferred over a radical-pair[102c] path, according to the results obtained on the study of the rearrangement of (-)-(R)-benzyl-α-d *p*-toluenesulfenate to the (+)-benzyl-α-d-*p*-tolyl sulfoxide gave partial retention (35%) of configuration at the benzylic carbon and a negative entropy of activation ($\Delta S^{\ddagger}$ = -2 eu, $\Delta H^{\ddagger}$ = 29.7 kcal mol^{-1}, k = 8.7 x 10^{-5} s^{-1} at 120 °C).[98b] Analogously, Thompson[1c] noted that dibenzyl sulfoxylate, $(PhCH_2O)_2S$, rearranges to the benzyl α-toluenesulfinate, $PhCH_2S(=O)OCH_2Ph$ during the preparation. The expected sulfenate **233** was unambiguously identified as being the sulfinate **236**. The free energy difference is small between the sulfoxide ($R_2S=O$) and the sulfenate structure (R-S-O-R), with the sulfoxide being thermodynamically more stable.[103] At one point, we thought the sulfoxide **237** was the correct structure because of the presence of the characteristic S→O stretching frequency at 1110 cm^{-1} in the IR spectrum; however, an examination of the EI mass spectrum showed clearly the presence of the molecular ion at m/z 311/313, 4%/2%, $M^{+\cdot}$ Cl cluster, being the mass of the sulfenate **233** plus the mass 16 due to the addition of an oxygen atom **(Scheme 20)**.

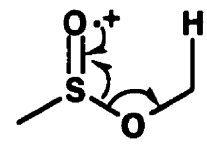
The structure of sulfinate **236** is analogous to benzyl benzoate, $Ph(C=O)OCH_2Ph$, in which C-S, C-O and S-O bond cleavage are possible fragmentation mechanisms. The fragmentation patterns of **Scheme 20** may involve abstraction of the α'-hydrogen followed as shown in Type I.



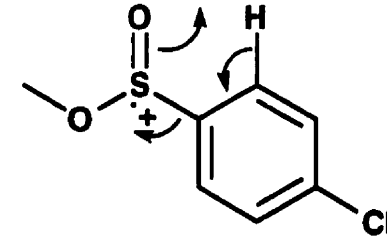
Type I-CO



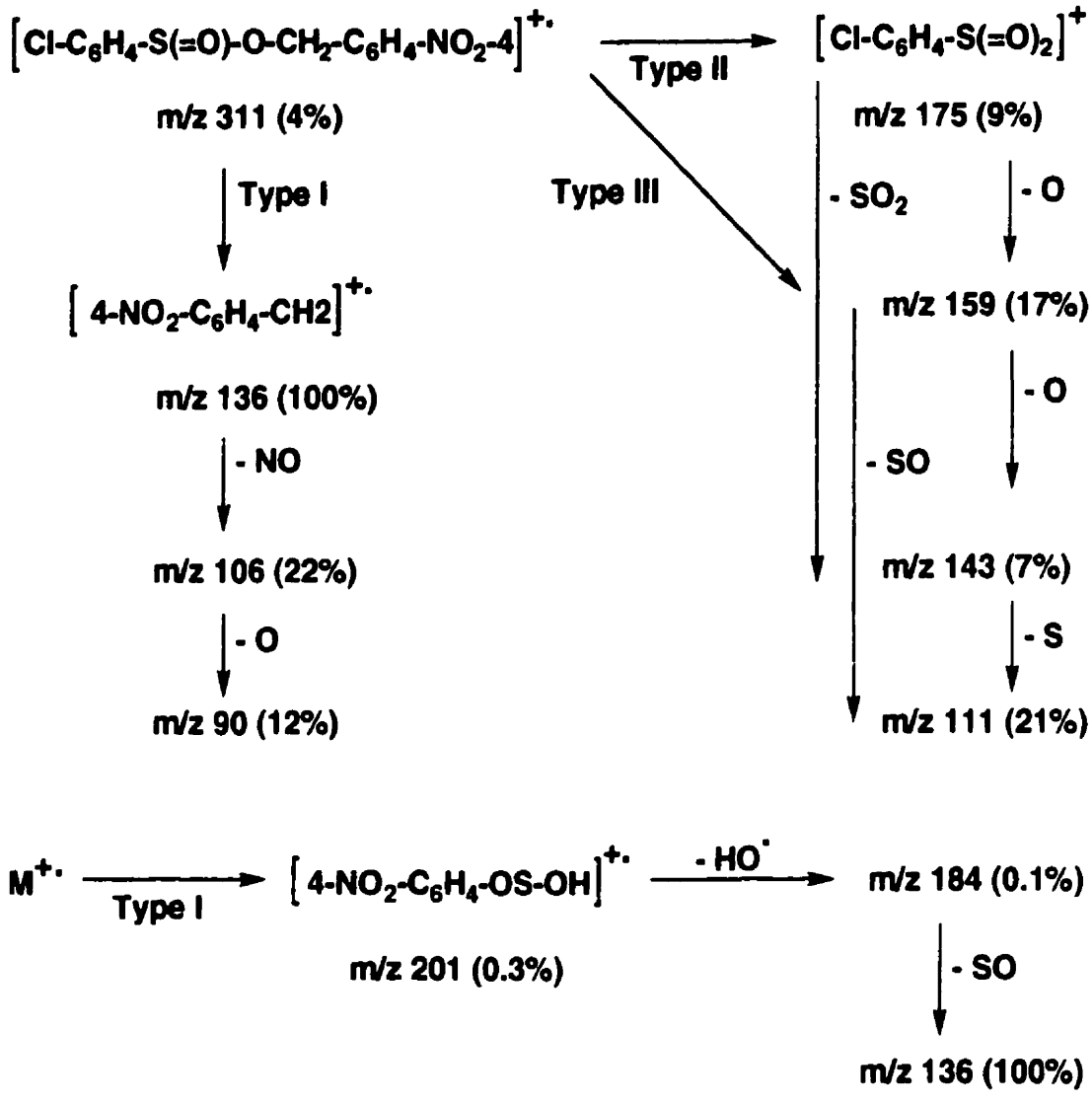
Type II-CO



Type III-SO



Type IV-CS



Scheme 20

Sulfenates are known to be easily oxidized by air and oxidizing agents to afford sulfinate esters in high yields. The ^1H NMR spectra of the samples being chromatographed and recrystallized showed that the products are identical and that oxidation probably occurred during the reaction process, even if the reaction was carried out under a nitrogen atmosphere. The acid catalyzed hydrolysis of alkyl arenesulfenates to sulfinate is known to proceed for concentrations of water that are smaller than 1%.[103b] The benzylic protons are diastereotopic (AB quartet) with a chemical shift difference $\Delta\nu = 91.8$ Hz, at the operating frequency of 200 MHz, and a geminal coupling constant $^2J_{HH} = 12.4$ Hz.

4-Cl-C_6H_4-S(=O)O-CH_2-C_6H_4-NO_2-4 **236**

4-Cl-C_6H_4-S(=O)CH_2-C_6H_4-NO_2-4 **237**

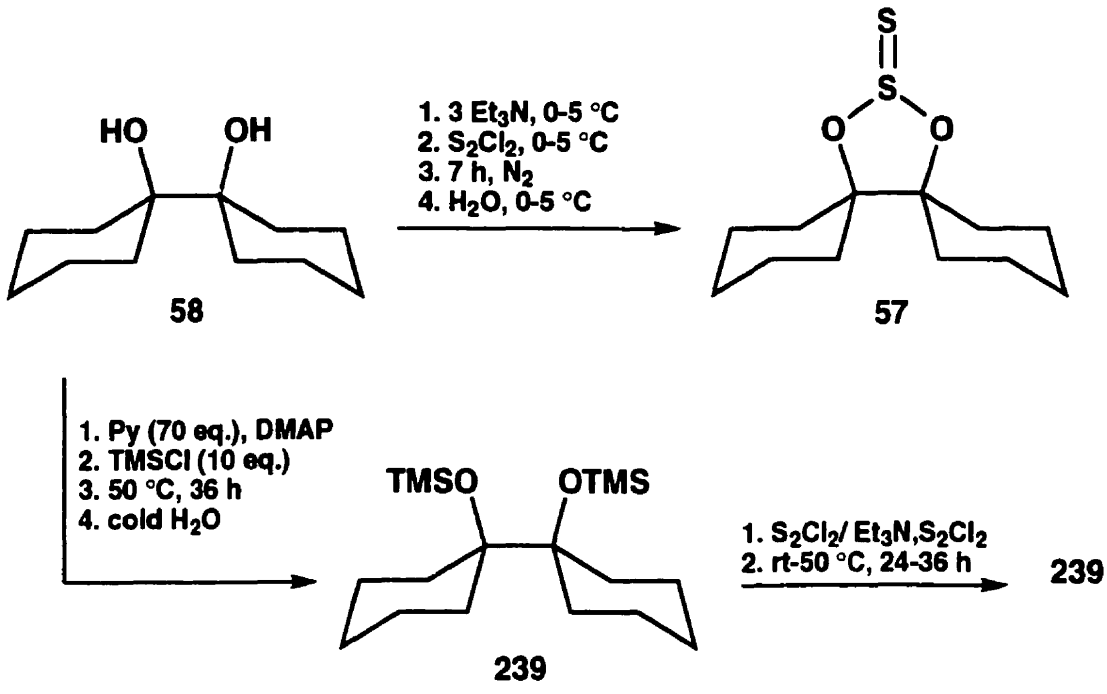
There is little doubt that the sulfenate **233** was formed but oxidized during the process. Alcohol **220** after purification by chromatography probably resulted from the hydrolysis of the sulfenate by water present in the silica gel. Discussion on the NMR spectroscopy of sulfinates will be included in Chapter 3 as part of the structure related to bis(4-substitutedbenzyloxy) disulfide **218**, as well as part to the structure related to the isomerization of sulfoxylates **246b-c** to their corresponding sulfinates (Chapter 4).

2.2.3.3 Preparation of O,O'-Bicyclohexyl-1,1'-diylthiosulfite 57 and Sulfite 240

The next task in the thorough evaluation of these closely related structures was to prepare pure samples of the only known stable thionosulfite[104a] O,O'-bicyclohexyl-1,1'-diylthiosulfite **57** and the corresponding sulfite. The thionosulfite **57** was prepared from the 1,2-diol (bicyclohexyl)-1,1'-diol **58** refluxing in a suspension of the *mono*sulfur-transfer reagent bis(benzimidazol-1-yl) sulfide **59** in CCl_4 for 72 hours according to **eq.16** (p.16).[104b] The mixture was cooled to room temperature and the benzimidazole collected. Some of the CCl_4 was evaporated under reduced pressure and the product was purified by flash chromatography on silica gel using CCl_4 to give **57** in 45% yield (based on **59**).[104c] An analytically pure sample was obtained from recrystallization in hexane, m.p. 100-101 °C (lit.[104a] 100-101 °C). Now, **57** can also be prepared by refluxing the 1,2-diol **58** in the presence of the disulfur-transfer reagent bis(benzimidazol-1-yl) disulfide **238** for 48 hours in CCl_4, or, by reacting the 1,2-diol **58** in the presence of Et_3N with S_2Cl_2 at 0-5 °C to yield respectively, after purification and recrystallization, 42% and 46% of **57 (Scheme 21)**.[104d] The preparation of **57** was also attempted by reacting the previously silylated 1,2-diol **239** with S_2Cl_2 or with SCl_2 in the presence of Et_3N (1-11 equivalents), both at room temperature and 50 °C but only **239** was recovered.

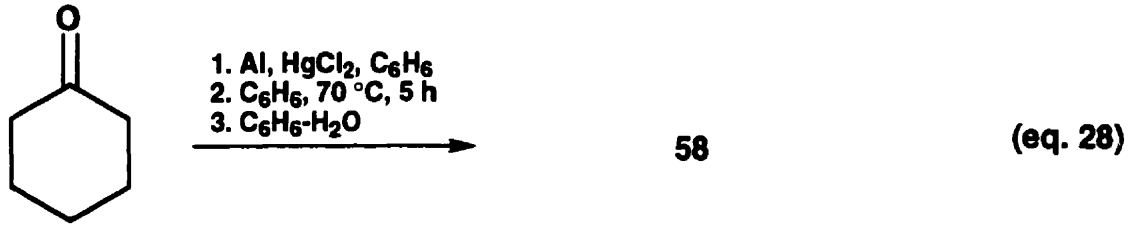
---

104. a) Ref. 10a; It was the only stable cyclic thionosulfite known at the time; b) A complex mechanism was proposed for this unusual transformation; see ref. 104e; c) Exposure for a long period of time on SiO_2 decomposes **57** to the corresponding sulfite **240**; d) D.N. Harpp, E. Martins and S.L. Tardif, unpublished results; e) K. Steliou, Ph. D. Thesis, McGill University, (1978).



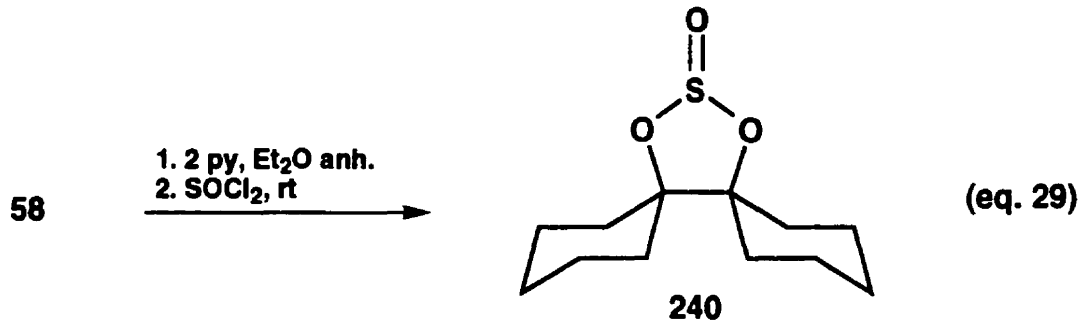
Scheme 21

The corresponding sulfite **240** was prepared according to **eq.29** in 87% m.p. 56-58 °C (lit.[104e] 58-59 °C). The starting 1,2-diol was obtained from intermolecular reductive coupling of cyclohexanone in the presence of aluminium and mercuric chloride according to **eq.28** (25%, m.p. 122-124 °C (hexanes; lit. 124.5-126.5 °C).[105]



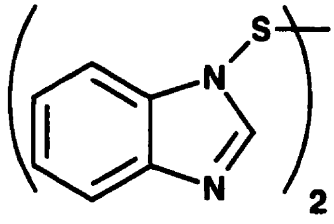
(eq. 28)

105. R.C. Walters, *J. Am. Chem. Soc.*, **74**, 5185 (1952); reported yield of 30%.



(eq. 29)

The results obtained for the synthesis of the thionosulfite **57** (**Scheme 21**) are very interesting and do raise the issue again of the molecular arrangement of the **OSSO** subunit. The branch-bonded arrangement, as a 5-membered ring system, for acyclic 1,2-diols was strongly suggested by Thompson[1b] based on ^1H NMR instead of the 6-membered 1,4,2,3-dioxadithiane **241**, but their structures were never confirmed by X-ray analysis. Recently, in our laboratory, a wide variety of symmetrical and unsymmetrical thionosulfites **242** have been prepared in order to study their thermal stability.[106a] At present, the only confirmed, shelf-stable compound bearing the branch-bonded structure remains to be **57**.



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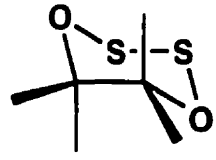
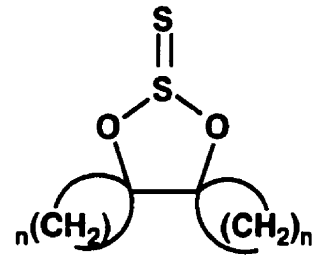


241

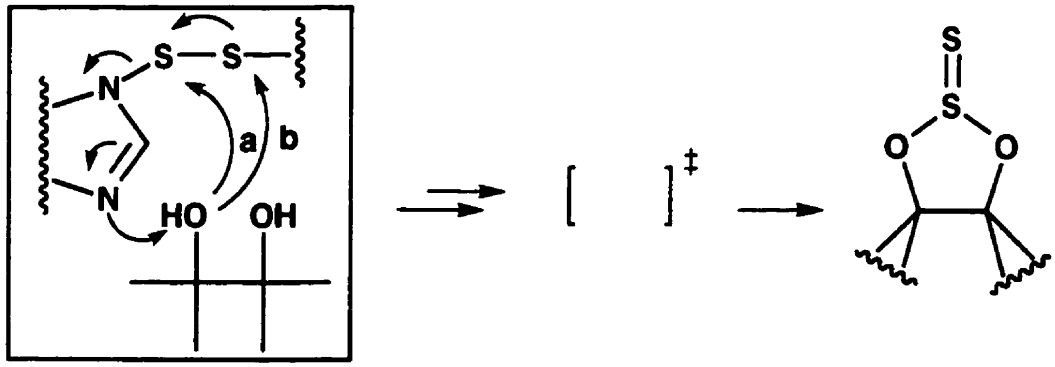
The facile formation of the 5-membered ring appears to be the driving force for the formation of **242** over the linear structure that seems to be favored for open-chain molecules (*vide infra*). From a mechanistic point of view and considering the linear nature of the disulfide bond in the reagents **238** and S_2Cl_2[106b], the 1,4,2,3-dioxadithiane **241** might be formed prior to the formation of the final structure **57** (**Scheme 22**). A consideration of a mechanistic rational for the product led us to consider path a over path b. The first two

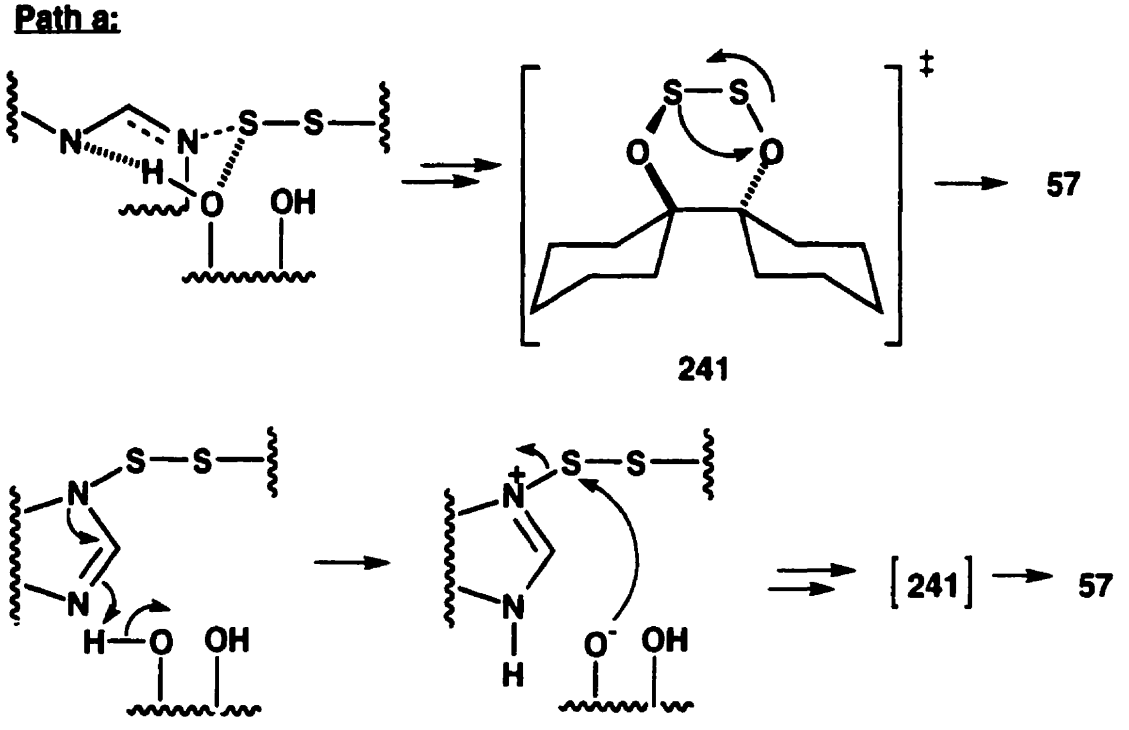
106. a) Private communication from C. Abrams: The shelf-stability of this class seems to vary considerably among the series for **242**; D.N. Harpp and C. Abrams, unpublished results; b) This material was freshly distilled prior to being use because unstable due to disproportionation; Ref. 91.

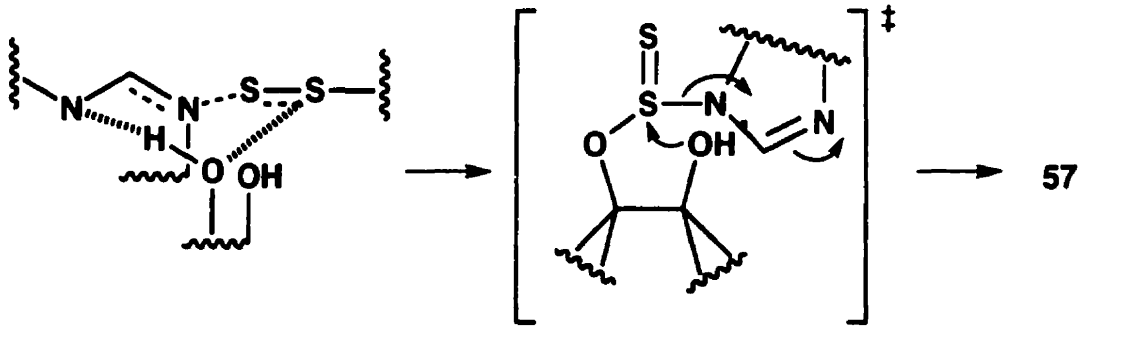
repetitive steps, before the formation of **241**, might proceed through a concerted 6-membered ring nucleophilic displacement process, or through two distinctive steps where the first one involves protonation of the imidazole ring followed by a nucleophilic attack and the displacement of benzimidazole (**Scheme 22**).



242: n = 0, 4-8







Scheme 22

2.2.3.4 Preparation of 4-Nitrobenzyloxy Benzyl Trisulfide 243

Nucleophilic substitution on diethoxy disulfide **34** by amines and thiols to give alkoxyalkyl trisulfides **27** and alkoxyamine disulfides **28** has been studied (Section 1.2.2.,

Scheme 3).[21] The yields reported by that group were 22-50% (**entries 1-5 in Table 5**). The title compound, containing the "oxytrisulfide" **OSSS** subunit, was prepared and reported, along with the experimental conditions, in **Table 5**. In our case, the best yield for $ArOSSSCH_2Ph$ **243** was obtained in a co-solvent system of acetonitrile-dichloromethane (50:50), a polar aprotic solvent (entry 10). The other products isolated were the corresponding 4-nitrobenzyl alcohol **220** and benzyl tetrasulfide **244** (m.p. 49-50 °C). The desired product was an oil that solidified upon standing m.p. 43-45 °C. The bis(4-nitrobenzyl) oxytrisulfide **245** could not be purified but was detected and the yield evaluated by NMR.

ROSSOR + R'SH ⟶ ROSSSR' + 2 ROH (eq. 30)

Table 5. Preparation of Oxytrisulfide Compounds (eq.30)

entry	ROSSOR R	R'SH R'	Yield (%)	Experimental Conditions[d]
1	Et	Et	45[a]	CCl_4, 50°C, 3h
2	Et	*n*-C_3H_7	43[a]	CCl_4, 50°C, 3h
3	Et	*i*-C_3H_7	50[a]	CCl_4, 50°C, 3h
4	Et	*t*-C_4H_9	40[a]	CCl_4, 50°C, 3h
5	Me	*t*-C_4H_9	22[a]	CCl_4, 50°C, 3h
6	218b	C_6H_5-CH_2	0[b]	CCl_4, rt, 12h
7	218b	C_6H_5-CH_2	10[b]	CCl_4-CH_2Cl_2, 50°C, 14h
8	218b	C_6H_5-CH_2	12[b]	CH_2Cl_2, 50°C, 3h
9	218b	C_6H_5-CH_2	39[b]	CH_3CN-CH_2Cl_2, rt, 2h
10	218b	C_6H_5-CH_2	62[b]	CH_3CN-CH_2Cl_2,50°C,2h
11	218b	4-NO_2-C_6H_4-CH_2	27[c]	CH_3CN, rt,1.5h

a) Ref.21; yields reported after distillation under reduced pressure; b) Isolated yield after column chromatography on silica gel; c) Could not be purified and NMR yield; d) Co-solvent sytems 50:50 ratio.

2.2.3.5 Preparation of 4-Substituted Benzyl Sulfoxylate 246

By analogy to the preparation of symmetrical 4-substituted dibenzyloxy disulfides **218a-e**, sulfur dichloride SCl_2[107a] was added to a cooled solution of the respective alcohol

107. a) SCl_2 a dark red colored pungent liquid (b.p. 60 °C) and S_2Cl_2, the most stable sulfur chloride, a dark yellow pungent liquid (b.p. 138 °C) hydrolyzes easily to HCl, H_2S, S_8 and SO_2.; b) This halide was freshly distilled over PCl_5 and cooled down to -40 °C (**eq.31**).

in the presence of triethylamine Et_3N. However, SCl_2 is prone to decomposition and easily gives S_2Cl_2 even at low temperature (**eq. 31**). The decomposition was minimized by adding SCl_2[107b] at -78 °C, followed by the work-up at 0 °C. The reaction products, besides the sulfoxylates **246**, were the corresponding dialkoxy disulfides **218**, sulfites **219**, sulfinates **249** and unreacted alcohols **220**. According to the product distribution reported in **Table 6**, the formation of **246b** was enhanced at the expense of the formation of dialkoxy disulfide **218b** as the reaction temperature was lowered. The rate of disproportionation of SCl_2 to S_2Cl_2 (**eq.31**) was slowed down at this very low temperature, thus accounting for the diminution in yield of **218b**. The formation of sulfite **219b** can be rationalized considering the "oxy-chloro-sulfide and disulfide" type of intermediate **247** and **248**; they are known to decompose to the sulfite at -78 °C (**eq.33-34**).[108] The intermediate **247** may also be generated at very low temperature (**eq.35**) and lead to the formation of **219** (**eq.36**) following **Scheme 23**. The acid (HCl) catalyzed decomposition of the sulfoxylate **246** and the dialkoxy disulfide **218** have to be considered as well for the sulfite formation (**Scheme 2**).

Table 6. Product Distribution[a] for the Preparation of 4-Substituted Benzyl Sulfoxylate 246

ROH[b] 220	RO(S=O)R 249	$(RO)_2S=O$ 219	ROSSOR 218	ROSOR 246	Experimental Conditions[d]
b[f]	xx	xx	xx	10	0-5°C, 2 h
b	09	15	26	27	-10°C, 2 h
b	xx	16	15	50	-40°C, 2 h
b	xx	11	10	58	-78°C, 2 h
e	07	23	18	21	-40°C, 2 h
d[c]	04	34	24	xx[e]	-40°C, 2 h
a	xx	16	22	27	-78°C, 2 h
a	xx	25	26	24	-40°C, 2 h
c	xx	17	17	46	-78°C, 2 h
c	03	24	19	38	-40°C, 2 h

a) % yield; b) R = 4-X-$C_6H_4CH_2$; 220a: X = H; b: X = NO_2; c: X = Cl; d: X = OMe; e: X = Me; c) NMR yields otherwise isolated yields using column chromatography; d) Solvent used was CH_2Cl_2; e) Compound was formed (NMR), but doesn't withstand column chromatography on silica gel; f) Product precipitated out of mixture in the fridge.

108. a) Ref.4; R= *i*-Pr; ROSSOR reacts with SCl_2 at -78 °C to give intermediates **247** and **248** that decompose to give the sulfite (**eq.32**). While the intermediate **247** decomposes rapidly at -78 °C, the intermediate **248** was detected and analysed at -20 °C.

$$\left[\ 2\,SCl_2 \rightleftharpoons S_2Cl_2 + Cl_2\ \right] \xrightarrow[\text{heat}]{PCl_5} 2\,SCl_2 + PCl_3 \qquad \text{(eq. 31)}$$

The formation of the dialkoxy disulfide **218b** seems to be unavoidable considering the multiple sources of S_2Cl_2 (**eq.33, 34** and **36**) even at low temperature. Interestingly, **218b** and sulfite **219b** were detected in a separate experiment where the sulfoxylate **246b** was treated with SCl_2, under the same experimental conditions (-78 °C followed by work-up at 0 °C). A potential rationale for their formation follows (**Scheme 24**). It is of interest that the formation of the sulfite in this reaction has, to our knowledge, not been previously explained.

$$ROSSOR + SCl_2 \longrightarrow \underset{\mathbf{247}}{[ROSCl]} + \underset{\mathbf{248}}{[ROSSCl]} \qquad \text{(eq. 32)}$$

$$3\,\underset{\mathbf{247}}{[ROSCl]} \xrightarrow[-78°C]{} (RO)_2S{=}O + RCl + S_2Cl_2 \qquad \text{(eq. 33)}$$

$$3\,\underset{\mathbf{248}}{[ROSSCl]} \xrightarrow[\text{slow}]{} (RO)_2S{=}O + RCl + S_2Cl_2 + 3/8\,S_8 \qquad \text{(eq. 34)}$$

$$ROH + SCl_2 \longrightarrow \underset{\mathbf{247}}{[ROSCl]} + HCl \qquad \text{(eq. 35)}$$

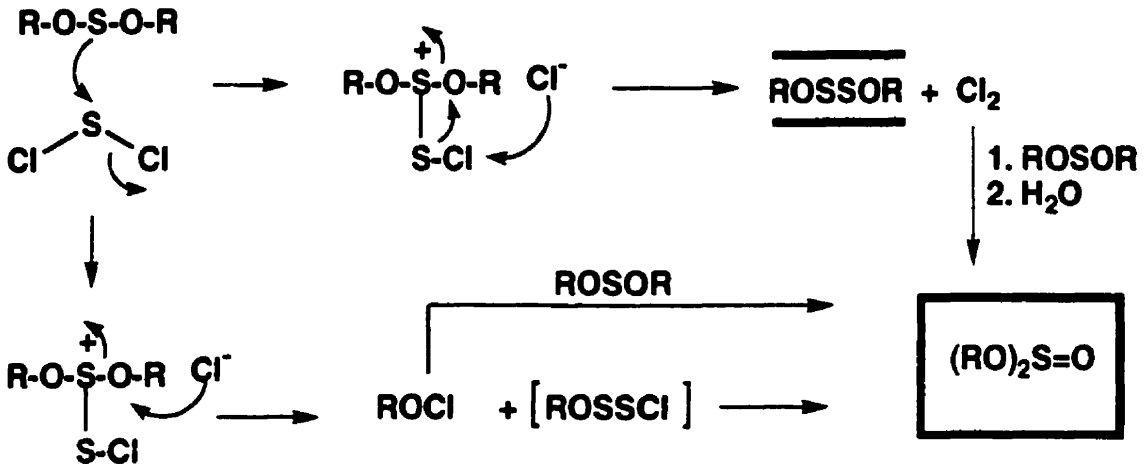
$$2\,\underset{\mathbf{247}}{[ROSCl]} \longrightarrow ROSOR + SCl_2$$

$$SCl_2 + \underset{\mathbf{247}}{[ROSCl]} \longrightarrow ROCl + S_2Cl_2$$

$$ROCl + ROSOR \longrightarrow RCl + (RO)_2S{=}O$$

$$ROH + SCl_2 + 2\,\underset{\mathbf{247}}{[ROSCl]} \longrightarrow (RO)_2S{=}O + S_2Cl_2 + RCl + HCl \qquad \text{(eq. 36)}$$

Scheme 23



Scheme 24

We also found, contrary to Thompson,[109] that sulfoxylates **246** could be isolated and were not that prone to readily rearrange to their corresponding sulfinates **249**. Precautions that were effective were not to let the reaction mixture temperature go above 0 °C, at which the work-up is performed, as well as to follow immediately with the isolation and purification using flash chromatography techniques on silica gel. To corroborate this we were able to obtain recrystallized analytical samples for **246b** and **c**. In the case of **246b** the crystals were suitable for X-ray analysis at room temperature and a full determination was obtained (discussed in Chapter 3). Sulfoxylate **246b** was found to rearrange slowly in chloroform-d over a period of time not exceeding 24 hours as shown in **Figure 4**. Unfortunately, the crystals for **246c** were not suitable for X-ray analysis (too fine) but a time-dependent NMR analysis has shown that about the same period of time was required for **246c** to rearrange to **249c** in $CDCl_3$ (**Appendix I**). Other linear sulfoxylates ROSOR were prepared by Thompson[1c] in good yield (R= *n*-Pr, 62%; R=*i*-Pr, 67%; R=*n*-Bu, 70%; R=*n*-C_5H_{11}, 56%; R=cholesteryl, 16%). In that same paper, some cyclic sulfoxylates were also reported with their yields (**250a**, 20%; **250b**, 8%; **251**, 58%). The sulfoxylates **252**[110a,b] and **253**[110c] were apparently prepared but no yields were reported.

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109. a) Ref.1c; reported that benzyl sulfoxylate **246a** readily rearranged to benzyl α-toluenesulfinate **249a** during preparation.

110. a) L. Birkofer and H. Niedrig, *Chem. Ber.*, **99**, 2070 (1966); b) J.S. Chapman, J.W. Cooper and B.P. Roberts, *J. Chem. Soc., Chem Commun.*, 835 (1976); c) H. Kogami and S. Motoki, *J. Org. Chem.*, **43**, 1262 (1978).

$(p\text{-}NO_2C_6H_4CH_2\text{-}O\text{-})_2S$

a: $-CH_2OSOCH_2-$
b: $-CH_2OSSOCH_2-$
c: $-O(S{=}O)CH_2-$
d: $-CH_2O(S{=}O)-$

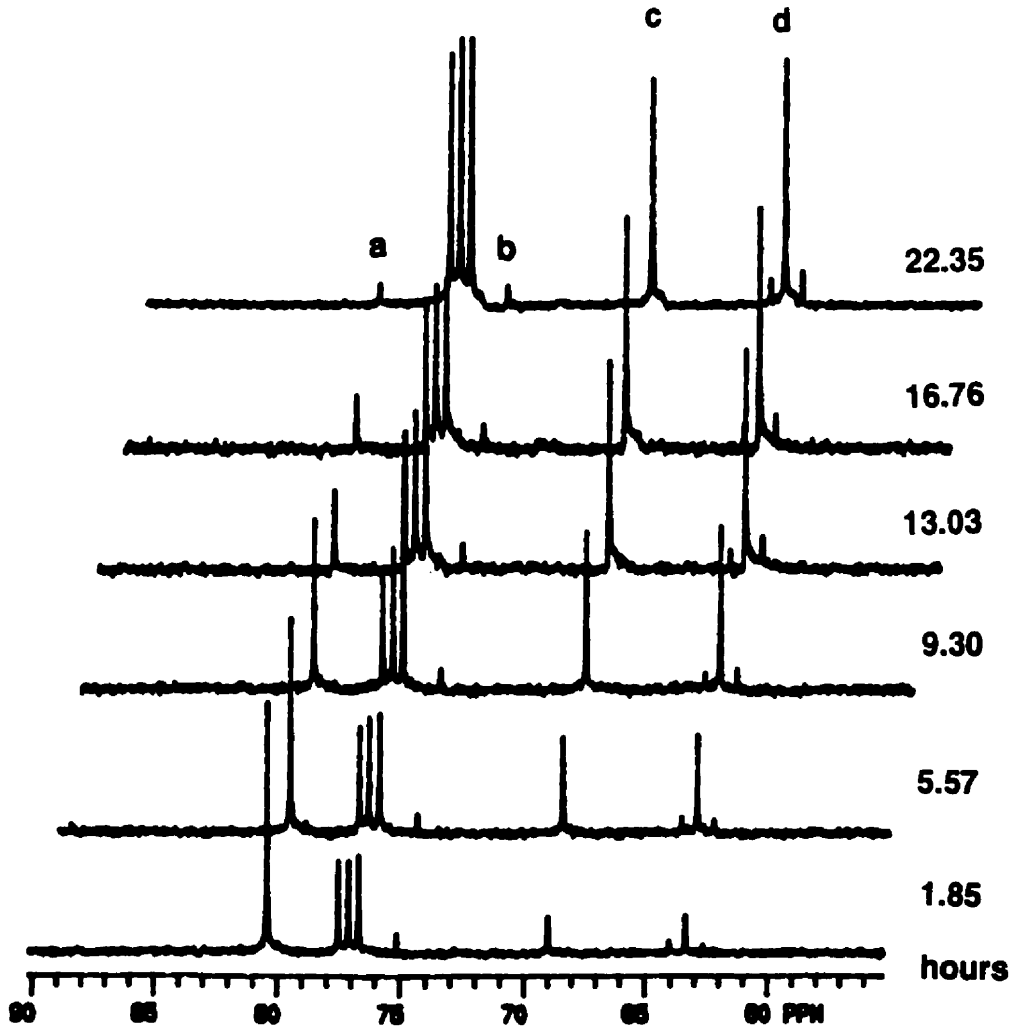
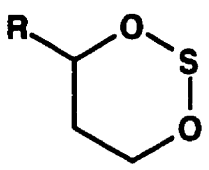
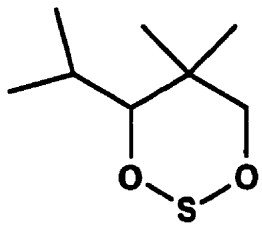


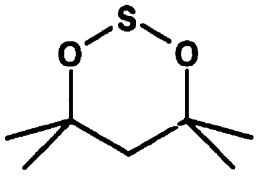
Figure 4: Isomerisation of 246b to 249b in $CDCl_3$ at 20.3 °C.



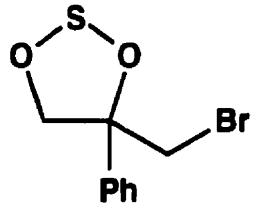
250a: R=CH_3
250b: R=H



251



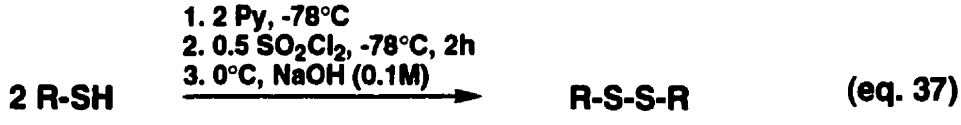
252



253

2.2.3.6 Preparation of 4-Nitrobenzyl disulfide 254

Disulfide **254** was synthesized by adding two equivalents of the thiol **223** and pyridine to a solution of one equivalent of sulfuryl chloride SO_2Cl_2 at -78 °C **(eq. 37)**. The yield was 93% after column chromatography. It was reported that SO_2Cl_2 was a good chlorinating agent[111a] and that pyridine enhances the nucleophilicity[111b] of the thiol thus trapping the HCl formed. Low temperatures prevented the decomposition of the sulfenyl chloride intermediate RSCl.[111c]



R = 4-O_2N-C_6H_4-CH_2

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111. a) W.A. Thaler, W.H. Mueller and P.E. Butler, *J. Am. Chem. Soc.*, **90**, 2069 (1961); b) W.H. Mueller and P.E. Butler, *J. Am. Chem. Soc.*, **97**, 2075 (1968); c) J.P. Danehy, B.T. Doherty and P. Hegan, *J. Org. Chem.*, **36**, 2525 (1971).

2.3 General Commentary

All the compounds prepared were identified using ^{1}H and ^{13}C NMR as well as mass spectrometry where required. The NMR values were not reported because they will be discussed extensively in the next chapter. Nevertheless, except for the *p*-nitrobenzyl *p*-chlorobenzenesulfenate **233** that we failed to obtain, four new, unreported symmetrical acyclic substituted dibenzyloxy disulfides (**218b-e:** 4-NO_2, 4-Cl, 4-MeO, 4-Me) and their corresponding sulfites (**219b-e:** 4-NO_2, 4-Cl, 4-MeO, 4-Me) were prepared. Other unreported compounds were also synthesized such as the 4-nitrobenzyloxy benzyl trisulfide **243** and the symmetrical acyclic substituted dibenzyl sulfoxylates (**246a-e:** 4-H, 4-NO_2, 4-Cl, 4-MeO, 4-Me). Recrystallized analytical samples for **218b-c**, bis(4-nitrobenzyloxy) tetrasulfide **226** and sulfoxylate **246b** were suitable for X-ray analysis at room temperature and full determinations were obtained. Interestingly, we have found that the thionosulfite **57** could also be prepared from the disulfur-transfer reagent bis(benzimidazol-1-yl) disulfide **238** and sulfur monochloride S_2Cl_2 from the corresponding 1,2-diol **58**.

CHAPTER 3: STRUCTURE OF DIALKOXY DISULFIDES AND RELATED COMPOUNDS

3.1 Introduction

Molecules containing disulfide and polysulfide moieties require further consideration, since the torsional potential about the S-S bond has a minimum near 90°, which minimizes electronic and steric repulsions. Even with force fields that include explicit lone pairs, additional two-fold torsional potentials are required to reproduce that behavior. The MM parametization[112] for disulfides works well for acyclic molecules as well as for di- and tetrathianes. In simple dialkyl sulfides, C-S bond lengths are around 1.82 Å[113a,b] and C-S-C bond angles are about 100-105°[113b,c]. Dimethylsulfide has a C-S bond length and C-S-C bond angle of 1.802 Å and 98.9° respectively.[114a] Sulfur-sulfur bond lengths of organic di- and trisulfides range about 2.03-2.08 Å and the range of C-S-S bond angles is 101-106°.[114b] X-ray crystal structures of a number of acyclic disulfides[115a-d] show the *gauche* conformation about the disulfide bond to be preferred, with an average C-S-S-C dihedral angle of about 85°. Such a conformational preference for disulfides is consistent with the gauche effect,[116] and has also been found using molecular orbital[117a-c] and force field[112,118] calculations. In addition , the barrier to rotation about an S-S bond is greater (*ca.* 2-5 kcal mol^{-1}) than that about a CH_2-CH_2 bond.[119] The Van der Waals radius for sulfur is 1.80-1.85 Å,[120] but this

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112. a) MM2: N.L. Allinger, M.J. Hickey and J. Kao, *J. Am. Chem. Soc.*, **98**, 2741 (1976); b) MM3-4: N.L. Allinger, J.-H. Lii and N. Nevins, *J. Comput. Chem.*, **17**, 695 (1996) and references cited.

113. a) S.C. Abrams, *J. Chem. Soc., Q. Rev.*, 407 (1956); b) W. Tagaki, *Organic Chemistry of Sulfur*, S. Oae (Ed.), Plenum Press, New York, 1977, Chap. 6; c) E. Block, *Reactions of Organosulfur Compounds*, Academic Press, New York, 1978.

114. a) L. Pierce, M. Hayaski, *J. Chem. Phys.*, **38**, 2753 (1963); b) L. Field, see Ref. 113b, Chap.7.

115. a) J.D. Lee and M.W.R. Bryant, *Acta Crystallogr., Sect. B*, **B 25**, 2094, 2497 (1969); **B 26**, 1729 (1970); **B 27**, 2325 (1971); b) J.S. Ricci and I. Bernol, *J. Am. Chem. Soc.*, **91**, 4078 (1969); *J. Chem. Soc., Sect. B.*, 806 (1970); c) T. Ottersen, L.G. Warner and K. Seff, *Acta Crystallogr., Sect. B.*, **B 29**, 2954 (1973); d) C.M. Woodard, D.S. Brown, J.D. Lee and A.G. Massey, *J. Organometal. Chem.*, **121**, 333 (1976).

116. S. Wolfe, *Acc. Chem. Res.*, **5**, 102 (1972).

117. a) D.B. Boyd, *J. Am. Chem. Soc.*, **94**, 8799 (1972); *J. Phys. Chem.*, **78**, 1554 (1975); b) H.E. Van Wart, L.L. Shipman and H.A. Sheraga, *J. Phys. Chem.*, **78**, 1848 (1974); c) J.P. Snyder, L. Carlsen, *J. Am. Chem. Soc.*, **99**, 2931 (1977).

118. F.S. Jorgensen and J.P. Snyder, *Tetrahedron*, **35**, 1399 (1979).

is probably not spherically uniform about the sulfur atom. Based on studies of close contacts to divalent sulfur found by X-ray determinations, there are directional preferences for non-bonded interactions.[121a-c] The orbital contributions in the S-S σ bond of acyclic disulfides are presumed to be practically pure p in character; one set of lone pairs on each sulfur occupies the 3s orbitals, while the remaining pairs of non-bonding electrons exist as 3p-π electrons.[13]

3.1.1 The Isomers of Disulfur Dihalides

Both isomeric forms of disulfur difluoride **13** and **14** ($S{=}SF_2$ and FSSF) were reported, and the linear isomer **14** is thermally less stable and rearranges slowly to the thiosulfoxide isomer **13**.[122a-d] The structural parameters were clearly determined by mass spectrometry,[122b] microwave,[122b] infrared and Raman,[122c] and photoelectron[122e] spectroscopy. For sulfur monochloride, S_2Cl_2, it has been claimed that UV irradiation of it in an argon matrix had produced the thiosulfoxide isomer **255** ($S{=}SCl_2$).[123c] However, from electron diffraction,[123a] and vibrational,[123b] photoelectron[122e] and microwave spectroscopy,[123d] no conclusive evidence was obtained to support the existence of the isomer **255**. It was established that the linear isomer **256** (ClSSCl) was the only dominant stable isomer present. The photoelectron spectrum of the bromo analog S_2Br_2 was compared to that of FSSF, and the linear isomer BrSSBr[124] was the only isomer detected.[122e] The

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119. a) R.R. Fraser, G. Broussard. J.K. Saunders, J.B. Lambert and C.E. Mixan, *J. Am. Chem. Soc.*, **93**, 3822, (1971); b) R. Steudel, *Angew. Chem. Int. Ed. Engl.*, **14**, 655 (1975).

120. L. Pauling, *The Nature of the Chemical Bond*, 3rd Ed., Cornell University Press, Ithaca, New York, 1960, p.260.

121. a) R.E. Rosenfield, R. Parthasarathy and J.D. Dunitz, *J. Am. Chem. Soc.*, **99**, 4860 (1977); b) D. B. Boyd, *J. Phys. Chem.*, **82**, 1407 (1978); c) T.N. Guru Row and R. Parthasarathy, *ibid.*, **103**, 477 (1981).

122. a) R.L. Kuczkowski, *J. Am. Chem. Soc.*, **85**, 3047 (1963); b) *Ibid.*, **86**, 3617 (1964); c) G.P.Pez and R.D. Brown, *Spectrochim. Acta*, **26A**, 1375, (1970); d) F. Seel, *Adv. Inorg. Chem. Radiochem.*, **16**, 297 (1974); e) H. Bock and B. Soulouki, *Inorg. Chem.*, **16**, 665 (1977).

123. a) E. Hirota, *Bull. Chem Soc. Japan*, **31**, 130 (1958); b) B. Beagley, G.H. Eckersley and D. Tomlinson, *Trans. Faraday Soc.*, **65**, 2300 (1969); c) B.M. Chadwick, J.M. Crzybowski and D.A. Long, *J. Mol. Spectroscopy*, **48**, 139 (1978); d) R.D.Brown, C.J. Marsden and P.D. Godfrey, *J. Chem. Soc., Chem. Comm.*, 399 (1979).

124. F. Feher and S. Ristic, *Z. Anorg. Allg. Chem.*, **293**, 311 (1958).

characterization of the unstable[125] diiodo disulfide S_2I_2 was attempted (**eq.38**), but no direct evidence for its generation could be obtained.[122e]

$$\text{Cl-S-S-Cl} + \text{KI} \longrightarrow [\text{I-S-S-I}] + 2\,\text{KCl}$$

$$\downarrow \qquad \text{(eq. 38)}$$

$$1/4\,S_8 + I_2$$

This compilation of qualitative results was confirmed by *ab initio* considerations[126a] and results.[126b] In the case of S_2F_2, the barrier of conversion ($S{=}SF_2$, **13**/FSSF, **14**) was evaluated to be 23-46 kcal mol^{-1},[122e,127] sufficient to permit the separate existence of both isomers, and for S_2Cl_2 (ClSSCl/$S{=}SCl_2$) to be 3.4 kcal mol^{-1}.[122e] Another interesting way to look at it, is to consider that the energy gap between the two linear isomers seems to increase as F gets replaced by Cl. New theoretical investigation indicated that the existence of any thiosulfoxide isomers is related to the electronegativity value of the attached substituents at the central sulfur atom.[128] In compound such as S_2X_2, a higher electronegativity value shortens the sulfur-sulfur bond, thus increasing its double bond character and the stability of any given thiosulfoxide isomer.[126]

3.2 Results and Discussion

3.2.1 Some Solution ^1H and ^{13}C NMR Considerations

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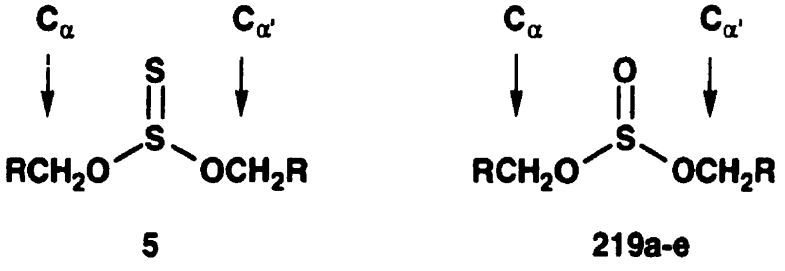
125. F. Feher and H. Muenzner, *Chem. Ber.*, **96**, 1150 (1963).

126. a) M. Solà, J. Mestres, R. Carbo and M. Duran, *J. Am. Chem. Soc.*, **116**, 5909 (1994); b) F. Matthias Bickelhaupt, M. Solà and P. von Ragué Schleyer, *J. Computational Chem.*, **16**, 465 (1995); and references cited therein.

127. J.P. Snyder and D.N. Harpp, unpublished results; a barrier of 36.7 kcal mol^{-1} at the MP2/6-31+G* level was found.

128. In ref. 126b; the relative stabilities (XSSX/$S{=}SX_2$ for X=F, Cl, CH_3 and H) is correlated to the electronegativity (EN) of X. EN are the Allred-Rochow electronegativity values (in the same order for X: 4.1, 2.8, 2.5 and 2.2).

An AB quartet pattern was observed in the ^1H NMR spectrum in each of the acyclic bis(4-substitutedbenzyloxy) disulfides **(218a-e)** studied. Their corresponding sulfites **219a-e**, were submitted to ^1H NMR analysis for comparison; the AB quartet observed for the benzylic protons attached to C_α and $C_{\alpha'}$ **(Scheme 25)** is rationalized in Section 1.7; the lack of symmetry of the non-planar substituted sulfur atom with respect to internal rotation about the S-O-C bonds was at the origin of the diastereotopicity observed **(Figure 2)**. The possibility of a thionosulfite arrangement **5** for compounds **218** would have depicted the same type of asymmetry with the tetrahedral sulfur atom at the branch position. The ^1H NMR spectra data are listed in **Table 7** for compounds **218** and **219**.



5 **219a-e**

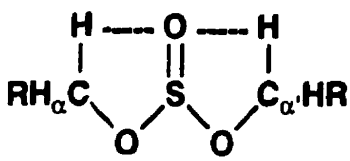
Scheme 25

Table 7. ^1H NMR Spectral Data[a] for "Dioxy Disulfides" 218a-e and Sulfites 219a-e

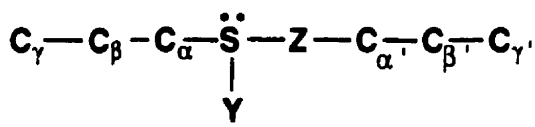
$(4\text{-R-}C_6H_4CH_2OS)_2$ $(4\text{-R-}C_6H_4CH_2O)_2S{=}O**	R	δ_H (ppm)[b]	$^2J_{HH}$ (Hz)[b]	$\Delta\nu$[a] (Hz)	$\Delta\nu / {}^2J_{HH}$
218a	**H**	**4.90, 4.79**	**11.67**	**20.87**	**1.79**
219a	**H**	**5.05, 4.93**	**9.75**	**22.01**	**2.25**
218b	**NO_2**	**4.99, 4.88**	**12.18**	**23.86**	**1.96**
219b	**NO_2**	**5.17, 5.03**	**12.40**	**29.22**	**2.36**
218c	**Cl**	**4.86, 4.76**	**10.41**	**20.78**	**2.00**
219c	**Cl**	**5.00, 4.90**	**11.05**	**19.79**	**1.79**
218d	**OMe**	**4.84, 4.72**	**9.85**	**20.46**	**2.08**
219d	**OMe**	**4.94, 4.83**	**9.15**	**18.65**	**2.04**
218e	**Me**	**4.92, 4.80**	**10.78**	**20.90**	**1.94**
219e	**Me**	**5.03, 4.91**	**10.90**	**22.97**	**2.11**

a) ^1H NMR (200 MHz, $CDCl_3$) at T = 18-20°C; b) Benzylic protons.

The diastereotopic α- or α'-benzylic protons of the sulfite derivatives **219** are more deshielded by comparison to the ones of the corresponding "dioxy disulfides" **218**, but not by very much! The interaction between the sulfinyl oxygen of the sulfite functionality and the α and α'- protons may account for the chemical shift difference (**Scheme 26**). This type of interaction is also encountered in sulfinate **257** and thiosulfinate **258** where a pseudo 5-membered ring renders possible the interaction with the protons attached to C_β and $C_{\beta'}$ or a pseudo 6-membered ring with the protons attached to $C_{\alpha'}$ and C_γ.[129]



Scheme 26



257: Y, Z = oxygen
258: Y = oxygen
Z = sulfur

The geminal coupling constants reported in **Table 7** are consistent with the ones found by Seel and collaborators[48b]; they reported for diethyl sulfite **8** and diethoxy disulfide **34**, 10.3 and 9.9 Hz respectively. The ^{13}C NMR spectra show the shielding effect at the benzylic carbon (C_α and $C_{\alpha'}$) on going from the "dioxy disulfide" **218b** to the sulfite **219b** and to the tetrasulfide **226** (**Table 8**). According to Freeman and others,[129a] the resulting deshielding effect observed by adding sulfur atoms is caused by strong lone pair interactions between them. The use of the 3d orbitals of sulfur atom give rise to pd-π bonds and to a partially positive sulfur atom adjacent to the Cα and Cα' (**Scheme 27**). These sulfur atoms exert a deshielding effect on the adjacent carbon atoms. Thus, the resonance between the sulfurs and the two additional sulfur atoms may be invoked to explain the greater deshielding of C_α and $C_{\alpha'}$ tetrasulfide **226** compared to the disulfide **254**. The deshielding effect of an additional sulfur atom was observed at the quaternary carbon in di-*t*-butyl disulfide (46.15 ppm) and in di-*t*-butyl trisulfide (48.91 ppm).[129a] The effect was also observed on comparing the ^1H NMR spectra of the methyl groups of di-*t*-butyl disulfide (δ_H = 1.31 ppm), trisulfide (δ_H = 1.37 ppm) and tetrasulfide (δ_H = 1.40 ppm).[129a]

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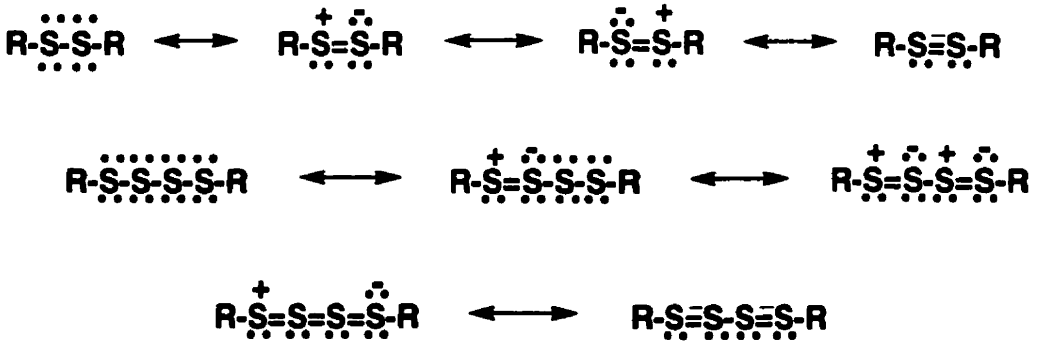
129. a) F. Freeman, *Mag. Res. Chem.*, **26**, 813 (1982); b) F. Freeman, C.N. Angeletakis and T.J. Maricich, *Org. Mag. Res.*, **17**, 53 (1981).

Table 8. ^{13}C NMR Chemical Shift for Benzylic Carbon in Some Related Compounds

Compound	Formula[b]	δ_C (-CH_2)[a]
218a	R = H	76.74
218b	R = NO_2	75.05
218c	R = Cl	75.76
218d	R = MeO	76.42
218e	R = Me	76.59
219b	(4-NO_2-$C_6H_4CH_2O)_2S$=O	62.93
246b	(4-NO_2-$C_6H_4CH_2O)_2S$	80.33
246c	(4-Cl-$C_6H_4CH_2O)_2S$	81.06
226	(4-NO_2-$C_6H_4CH_2S_2)_2$	45.10
220	4-NO_2-$C_6H_4CH_2OH$	64.37
254	(4-NO_2-$C_6H_4CH_2S)_2$	41.76
57	$(C_6H_{10}O)_2S$=S[c]	94.48[d]
240	$(C_6H_{10}O)_2S$=O	92.97[d]

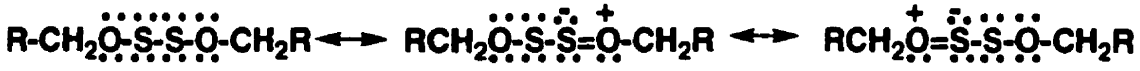
a) ^{13}C NMR (75 MHz, $CDCl_3$) at T = 17-20°C; b) Compound 218: (4-R-$C_6H_4CH_2OS)_2$; c) Stable thionosulfite; d) Quaternary carbon adjacent to the tetrachalcogenide moiety.



Scheme 27

The ^{13}C NMR substituent effects were defined and calculated for thiosulfinates **257** and thiosulfonates **259** (**Scheme 26**; lone pair, Y = O and Z = S);[129a] the α_{SO}, α'_{SO}, α_{SO2} and α'_{SO2} shifts are defined relative to their corresponding disulfide in the following way:

α_{SO} = δ C_α (thiosulfinate) – δ C_α (disulfide), α'_{SO} = δ $C_{\alpha'}$ (thiosulfinate) – δ $C_{\alpha'}$ (disulfide), etc. These values are positive or negative depending on whether the effect of substitution on sulfur atoms of the disulfide is deshielding or shielding. Using the same idea, we can define α_{SS} = δ C_α (**226**) – δ C_α (**254**), α_{OSSO} = δ C_α (**218b**) – δ C_α (**254**), $\alpha_{OS(=O)O}$ = δ C_α (**219b**) – δ C_α (**218b**). According to **Table 8**, the α_{SS} = 3.34 ppm, the α_{OSSO} = 33.29 ppm and the $\alpha_{OS(=O)O}$ = -12.12 ppm. The α_{OSSO} is very high in magnitude and much more deshielding than the α_{SS} value; this is probably associated with a double bond character between sulfur and oxygen in **218b**, arising from pd-π bonding in the valence bond resonance structure (**Scheme 28**). The $\alpha_{OS(=O)O}$ shielding value is governed by the electron-withdrawing effect of the adjacent benzyloxy groups to the sulfonyl moeity (S=O) in the sulfite **219b**. In the same order of idea, α_{OSO} = δ C_α (**246b**) – δ C_α (**218b**) = 5.28 ppm having a deshielding effect associated with the double bond character between sulfur and oxygen resulting at one point over time, to the isomerization to the corresponding sulfinate **249b** (**Figure 4**).



Scheme 28

At first, the similar ^{1}H NMR results obtained in **Table 7** for the "dioxy disulfides" **218a-e** and the sulfites **219a-e** seem to suggest the structure to be parallel (OS(=O)O and OS(=S)O for **219** and **218** instead of OSSO for **218**). However, some doubts were raised after looking at the ^{13}C NMR chemical shift differences, where $\Delta\delta CH_2$ (218b/219b) = δ(OSSO **218b** – OS(=O)O **219b**) = 12.12 > $\Delta\delta$C = δ(OS(=S)O **57** – OS(=O)O **240**) = 1.51 (**Table 8**), and where $\Delta\delta CH_2$ = δ(OSO **246b**– OSSO **218b**) = 5.28 was of the same order of magnitude; $\Delta\delta$C compares to $\Delta\delta CH_2$ (218b/219b), suggesting this time a linear arrangement for **218b** since the corresponding sulfoxylate **246b** was linear (δCH_2 = 5.17 (s,4H) ppm instead of two AB quartets for the sulfinate **246b**). These results were no more than qualitative comparisons; we were fortunate enough to obtain analytical recrystallized samples suitable for X-ray analysis for **218b-c**, **226** and **246b**.

3.2.2 X-Ray Results and Analysis

The structure of acyclic dialkoxy disulfides has been suggested to be linear by NMR considerations.[1a] In order to confirm the structure of **218** with some of their molecular parameters, X-ray crystallographic analysis of **218b** and **c** were undertaken Compound **218b** (4-NO_2) crystallizes (from 30% EtOAc in hexane) in the triclinic space group P1 (#2) **(Appendix II)**. **Figure 5** shows the ORTEP representation of the molecule **218b** and **Table 9** includes a number of characteristic bond lengths, bond angles and torsional angles. Of special interest is the rather short S1-S2 [1.968(2) Å] bond between the divalent sulfur atoms, the S1-O5 [1.648(3) Å] and S2-O6 [1.659(4) Å]; the bond angles S2-S1-O5 [107.3(2)°] and S1-S2-O6 [107.8(1)°]; the dihedral angle O5-S1-S2-O6 [-85.6(2)°][130]. Also interesting are the bond lengths including the hydrogen atoms attached to C13 (C13-H13a [0.955 Å] and C13-H13b [0.907 Å]) and C14 (C14-H14a [1.04(2) Å] and C14-H14b [1.081 Å]).

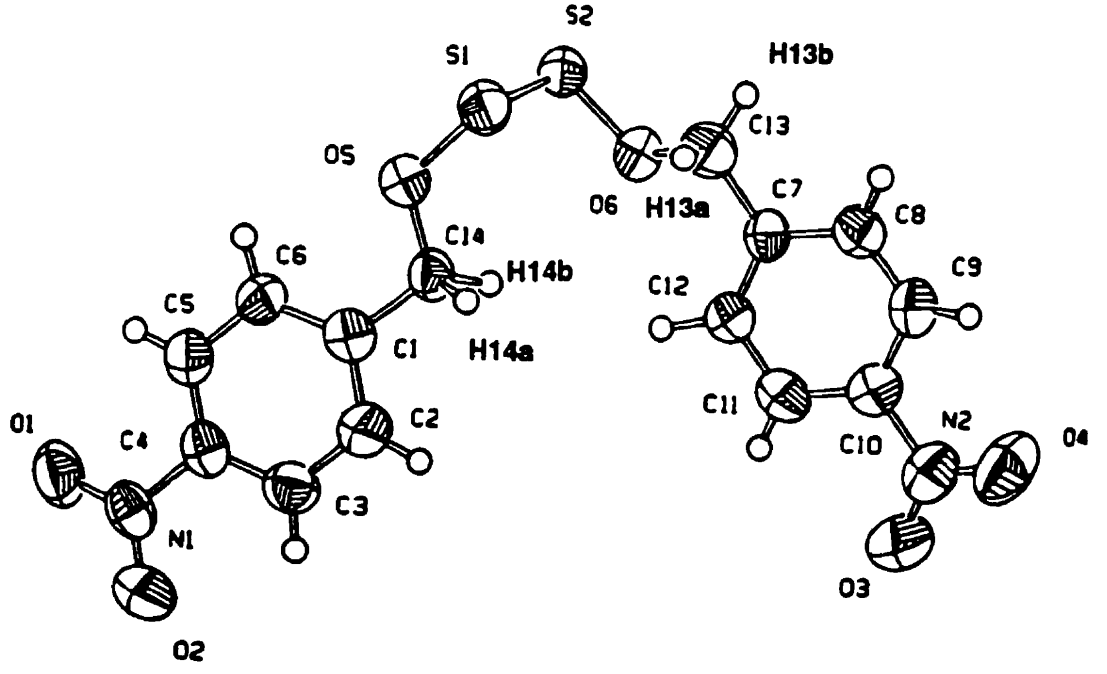


Figure 5: ORTEP Drawing of Bis(4-Nitrobenzyloxy) Disulfide 218b

130. The sign is positive if when looking from atom 2 to atom 3, a clockwise motion of atom 1 would superimpose it on atom 4. An article has just been published which apparently overlooked our announcement, S.L. Tardif, C.R. Williams and D.N. Harpp, *J. Am. Chem. Soc.*, **117**, 9067 (1995), on the X-ray structure of **218b**; R. Borghi, L. Lunazzi and G. Placucci, *J. Org. Chem.*, **62**, 4924 (1997).

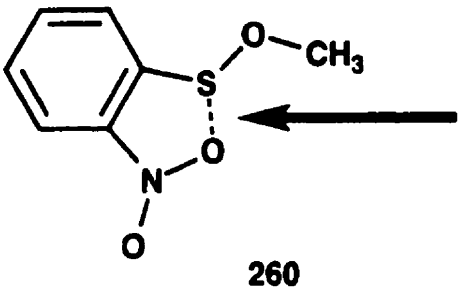
Table 9. Selected Bond Lengths, Valency Angles and Torsion Angles for 218b

(Å)		(°)		(°)	
S1-S2:	1.968(2)	S2-S1-O5:	107.3(2)	O5-S1-S2-O6:	-85.6(2)
S1-O5:	1.648(3)	S1-S2-O6:	107.8(1)	S1-S2-O6-C13:	-74.2(4)
S2-O6:	1.659(4)	S1-O5-C14:	114.6(3)	S1-O5-C14-C1:	175.1(3)
C1-C14:	1.503(6)	S2-O6-C13:	115.5(3)	S2-S1-O5-C14:	86.6(4)
C7-C13:	1.497(7)	O5-C14-C1:	110.1(4)	S2-O6-C13-C7:	170.5(3)
O6-C13:	1.432(6)	O6-C13-C7:	109.7(4)		
O5-C14:	1.427(6)	H14a-C14-H14b:	93.57		
C14-H14a:	1.042	H13a-C13-H13b:	113.52		
C14-H14b:	1.081	O5-C14-H14a:	118.59		
C13-H13a:	0.955	O5-C14-H14b:	109.69		
C13-H13b:	0.907	C1-C14-H14a:	113.10		
		C1-C14-H14b:	110.60		
		O6-C13-H13a:	109.96		
		O6-C13-H13b:	111.76		
		C7-C13-H13b:	111.11		
		C7-C13-H13b:	100.39		

The S1-S2 bond length is remarkably short in **218b** [1.968(2) Å] indicating some p-d conjugation along the disulfide (some π-bond character). The S-S bond lengths in polysulfides are known to range at about 2.03-2.08 Å[112] while the S-S bond length for the thionosulfoxide (R_2S=S) arrangement are closer to 1.90 Å (**Table 16**). As we have seen in Chapter 1, the necessary condition for branch-bonding is a difference in electronegativity between the two sulfur atoms. At this point, the X-ray results suggested that the 4-nitrobenzyloxy groups are not electron-withdrawing enough to permit such bonding. However, the S1-S2 bond length is approximately half-way between the S=S bond length found by Harpp, Steliou and Cheer[10a] in compound **57** (1.901 Å) and the "normal" disulfide bond length. The bond length difference between S1-O5 and S2-O6 bonds is 0.011 Å, but their range is comparable to the one found in methyl *o*-nitrobenzenesulfinate **260**, where the X-ray diffraction of the crystal structure gave an S-O bond length of 1.648 ± 0.012 Å, a ∠ S-O-CH_3 bond angle of 113° and an intermolecular short distance between S and one of the oxygen atoms on the *ortho*-nitro group [2.44 Å];[131] the sum of the van der Waals radii for S

131. W.C. Hamilton and S.J. La Placa, *J. Am. Chem. Soc.*, **86**, 2289 (1964).

and O being 3.25 Å,[120] the shortness of the found distance was indicative of a strong nonbonding attractive interaction between S and *o*-O. Their O-CH_3 bond length was 1.45 Å, while ours in **218b** are 1.427(6) and 1.432(6) Å for O5-C14 and O6-C13 respectively.



260

On average, the sulfur oxygen single bonds in sulfite S(IV)-O and in sulfenate S(II)-O were evaluated at 1.63 Å and 1.66 Å.[132] As expected, the molecule diplays a torsion angle φ (O5-S1-S2-O6) = -85.6(2)° about the S1-S2 bond, which is rather close to the ideal value of 90° associated with a minimum-energy conformation. Considering **Table 9** with **Figure 5**, the X-ray shows that the two geminal hydrogens attached to C13 (H13a and H13b) and C14 (H14a and H14b) are different among them and among each set; Δ **r (C14-H)** = r (C14-H14b) – r (C14-H14a) = 0.039 Å, Δ ∠ **(O5-C14-H)** = ∠ (O5-C14-H14a) – ∠ (O5-C14-H14b) = 8.9°. Application of the same simple mathematical treatment to H13a and H13b; Δ **r (C13-H)** = r (C13-H13a) – r(C13-H13b) = 0.048 Å, Δ ∠ **(O6-C13-H)** = (O6-C13-H13b) – (O6-C13-H13a) = 1.8°. No internal symmetry element was ascribed to the molecule itself, but the two crystals in the unit cell were P_1 related by inversion center (translational symmetry): one molecule sitting at x, y, z and the other one at -x, -y, -z. Intermolecular distance (out to 3.60 Å) are reported in **Table 10**. Contrary to the strong nonbonding attractive interaction between S and *o*-O observed in methyl *o*-nitrobenzenesulfinate **260**, any specific nonbonding interactions could be detected (van der Waals radii for H, O, S being 1.06, 1.42 and 1.80 Å).[133a] Another interesting aspect are the rather large valence angles S1-O5-C14 [114.6(3)°] and S2-O6-C13 [115.5(3)°] compared to H-O-H in water [104.5°],

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132. G.C. Barrett, *The Chemistry of Sulfenic Acids and their Derivatives*, Patai series Editors, John Wiley & Sons, Chichester, 1990, p.12.

133. a) A. Bondi, *J. Phys. Chem.*, **68**, 441 (1964); b) U. Blukis, P.H. Kasai and R. Myers, *J. Phys. Chem.*, **38**, 2753 (1963); c) Gas phase: B. Haas and H. Oberhammer, *J. Am. Chem. Soc.*, **106**, 6146 (1984); d) K.I. Gobbato, M.F. Klapdor, D. Mootz, W. Poll, S.E. Ulic, H. Willner and H. Oberhammer, *Angew. Chem. Int. Ed. Engl.*, **34**, 2244 (1995); e) Electron diffraction: J. Donohue and V. Shomaker, *J. Chem. Phys.*, **16**, 92 (1948).

C-O-C in dimethyl ether $(CH_3)_2O$ [111.7°],[133b] O-O-C in dimethyl peroxide $(CH_3O)_2$ [105.2(5)°][133c] or O-O-O and O-O-C in bis(trifluoromethyl)trioxyde $(F_3C\text{-}O)_2O$ [106.4(1)° and 106.5(1)°][133d] that could probably be ascribed to the size of the sulfur atom itself attached to the carbon.

Table 10. Some Intermolecular Distances for 218b

	(Å)
S1-H14b:	**3.222**
S2-H13a:	**3.282**
S2-H13b:	**3.289**
O6-H13a:	**3.210**
O6-H13b:	**2.999**
H14a-H14b:	**3.559**
H13a-H13b:	**3.357**
H14b-H13b:	**3.545**

The compound **218c** (4-Cl analogue) crystallized (out of pentane) in the monoclinic system with space group designation C_2 (**Appendix III**). **Figure 6** shows the ORTEP representation of the molecule **218c** and **Table 11** includes a number of characteristic bond lengths, bond angles and torsional angles. Of special interest is the even shorter S-Sa [1.932(3) Å] bond between the divalent sulfur atoms, and the S-O5 [1.644(9) Å]; the bond angle Sa-S-O5 [108.9(3)°]; the dihedral angle O5-S-Sa-O6 [76.815°][130]. Also interesting are the bond lengths including the hydrogen atoms attached to C14 (C14-H14a [1.04(5) Å] and C14-H14b[1.0(1) Å]). Contrary to **218b**, the molecule **218c** was found to occupy crystallographic sites of C_2 symmetry and containing an internal twofold symmetry axis. The other enantiomeric conformer (enantiomorph) was eliminated with a probability of being wrong of 0.7477×10^{-16}. The valence angle Sa-S-O5 [108.9(3)°] was in the same order as S2-S1-O5 [107.3(2)°] and S1-S2-O6 [107.8(1)°] in **218b**, and comparable to the one found in the the tetrasulfide analog of **218b** (**226**; *vide infra*), but these were somewhat larger than the S-S-S [104 °][133e] found in dimethyl trisulfide $(CH_3S)_2S$.

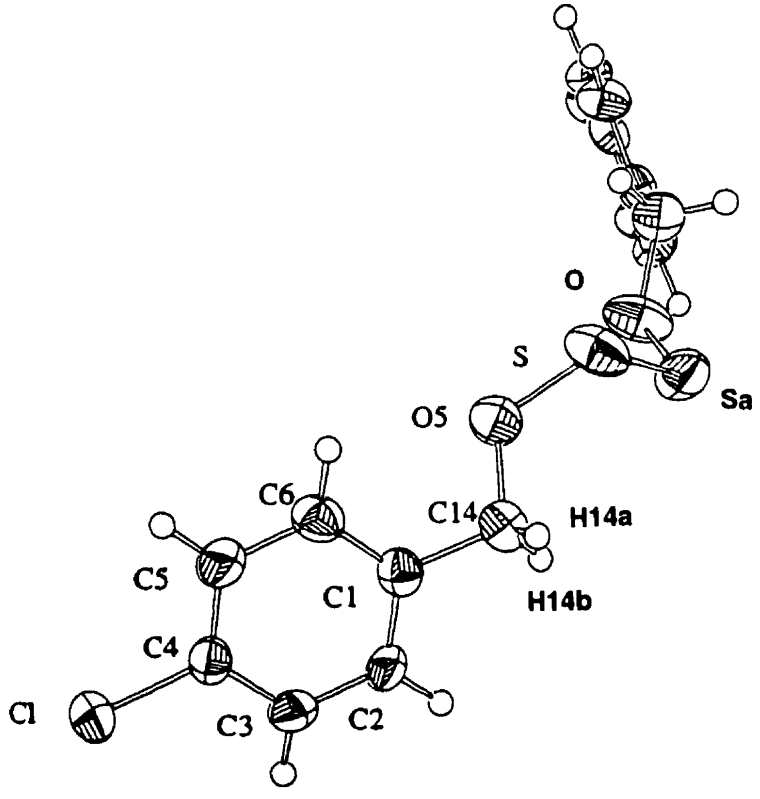

Figure 6: ORTEP Drawing of Bis(4-Chlorobenzyloxy) Disulfide 218c

Table 11. Selected Bond Lengths, Valency and Torsion Angles for 218c

(Å)		(°)		(°)	
S-Sa:	1.932(3)	Sa-S-O5:	108.9(3)	S-O5-C14-C1:	165.7(8)
S-O5:	1.644(9)	S-O5-C14:	116.1(7)	Sa-S-O5-C14:	78.2(5)
O5-C14:	1.428(8)	O5-C14-C1:	108.7(8)	O5-S-Sa-O:	76.8(5)
C1-C14:	1.504(1)	O5-C14-H14a:	112(3)		
C14-H14a:	1.04(5)	O5-C14-H14b:	105(4)		
C14-H14b:	1.0(1)	C1-C14-H14a:	111(4)		
		C1-C14-H14b:	117(4)		
		H14a-C14-H14b:	104.6		

Few years ago, Steudel and Miaskiewicz[134] published a theoritical paper on the structures and relative stabilities of seven isomeric forms of $H_2S_2O_2$ containing an S-S bond; they found that the most stable isomer was one of the two possible rotamers of the chain-like HOSSOH with C_1 symmetry **261**. The branch-bonded arrangement (C_s symmetry) **263** was in the third rank after the other rotamer with C_2 symmetry **262** and was found to be less stable by 12-20 kJ mol^{-1} (2.9-4.8 kcal mol^{-1}) relative to **261**; the energy difference between **261** and **262** being 1.01 kcal mol-1 at the MP2/6-311G**//HF/6-311G** + ZPE level of theory. In **Figure 5**, the structure of **218b** depicte a C_1 symmetry arrangement for the substructure unit C14-O5-S1-S2-O6-C13 while **218c** (**Figure 6**) depicte a C_2 symmetry element. Preliminary molecular modelling *via* MMX caculations using the PCMODEL[135] program (**Appendix VI**) was also performed on **218b**. The AB benzyl quartet observed in the ^1H NMR spectrum of the *anti*- **218b** seems justified due to restricted rotations around C14-O5, and S1-S2. The *syn* isomer seems to be more stable than the *trans* by 17.15 kJ mol^{-1} (4.1 kcal mol^{-1}), the *syn* arrangement being favored by π stacking (π–π interaction of the two facing aromatic rings) and by dipole charge reduction of 0.53 D over the *anti*. Calculations for the *syn* isomer by the rigid rotor approximation have also revealed that restricted rotations were encountered to a higher degree around S1-S2, S1-O5 and O5-C14 bonds. Missing parameters in the programs MACROMODEL and MODEL, for the molecular representation of **218b**, were believed to be at the origin of the discrepancy between the X-ray and the calculations (**Figure 8**). The final display mode using MODEL have calculated a few angles and distances for the *syn*-isomer of **218b** (**Table 12**). The calculated values for the valency angles and the bond lengths were related to the X-ray values by ± 1-10%, while both absolute values for the torsion angle O5-S1-S2-O6 (MODEL and X-ray) were close to the optimum 90° angle.

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134. R. Steudel, K. Miaskiewicz, *J. Chem. Soc. Dalton Trans.*, 2395 (1991): the calculations at the level of theory MP2/6-311G**//HF/6-311G** + ZPE means that the electron correlation in the form of the Moller-Plesset (MP) perturbation theory to the second order (MP2) using the triple zeta *ab initio* basis set (6-311G**) were used to calculate the energy of the optimized geometry (//). This energy was previously optimized using the *ab initio* basis set 6-311G** (including orbital function and atomic polarization) at the Hartree-Fock level (HF) including the zero point vibrational energies (ZPE) computed at the same level HF/6-311G**.

135. Calculations were done by Dr. K. Steliou then at the University of Montreal (presently at Boston University); the program is also available from Serena Software, P.O. Box 3076, Bloomington, Indiana, USA 47402-3076.

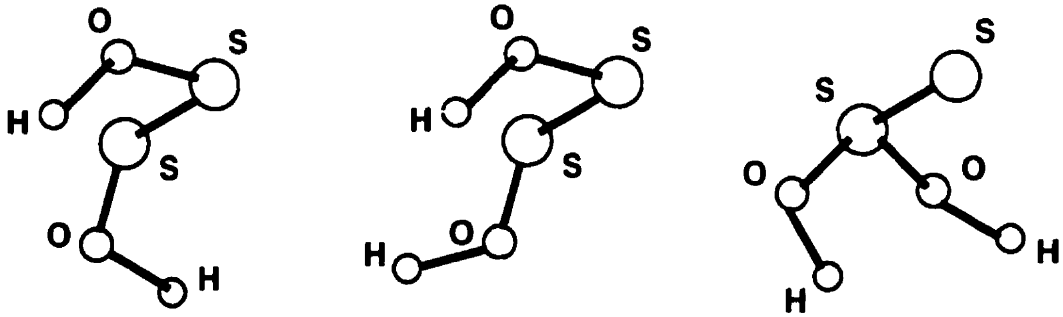

Figure 7: Representation of the Three More Stable Isomers of $H_2S_2O_2$

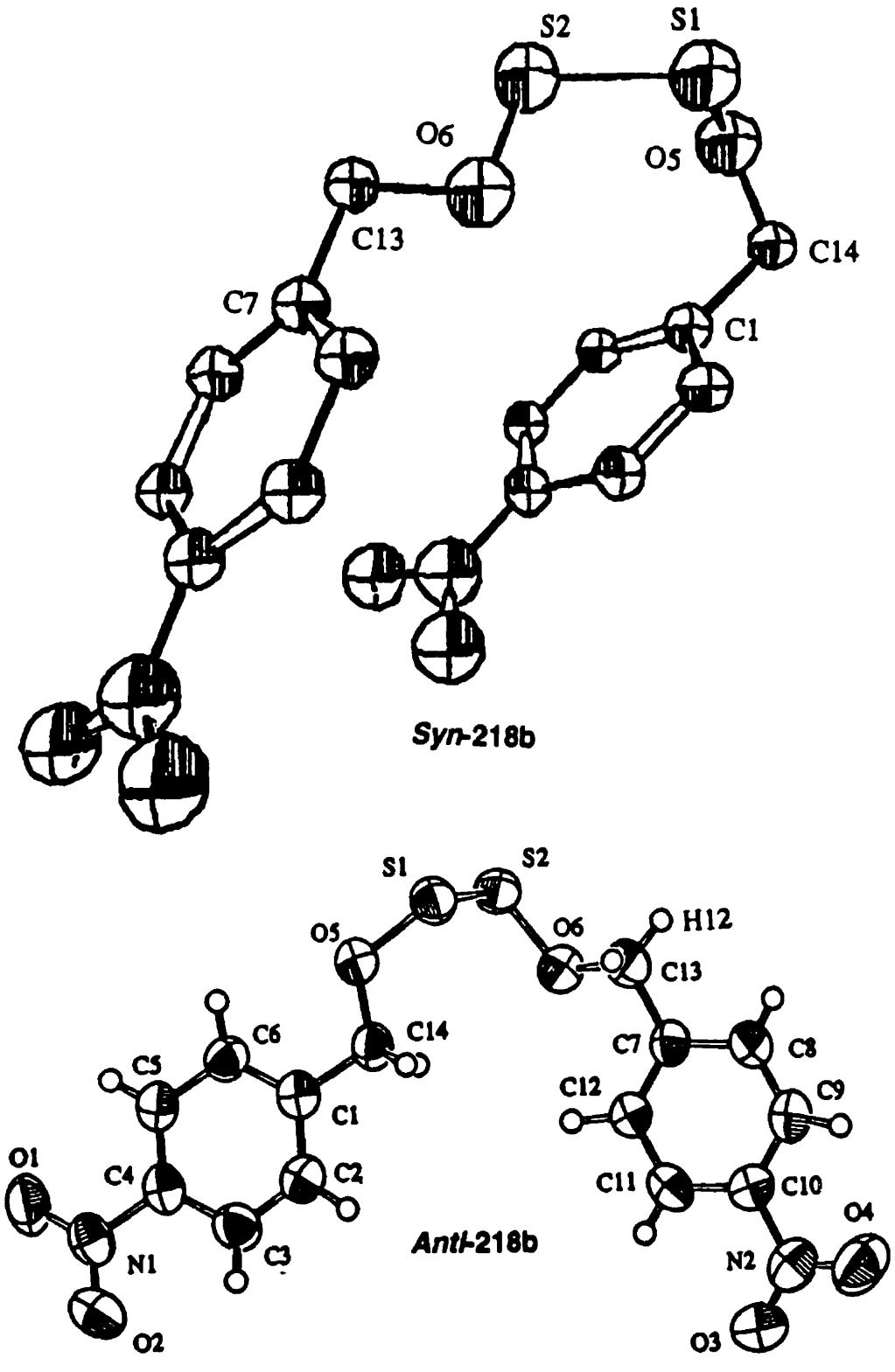

Figure 8: Representation of the *Syn*- and *Anti*-Isomers of 218b

Table 12. Calculated Parameters for *Syn*-218b

(Å)	MODEL	X-ray	(°)	MODEL	X-ray
S1-S2:	2.069	1.968(2)	S2-S1-O5:	111.27	107.3(2)
S2-O6:	1.533	1.659(4)	S1-S2-O6:	111.68	107.8(1)
			S2-O6-C13:	112.84	115.5(3)
			O6-C13-C7:	110.83	109.7(4)
			O5-S1-S2-O6:	87.81	-85.6(2)
			S1-O5-C14-C1:	67.03	175.1(3)
			S2-S1-O5-C14:	-104.68	86.6(4)
			C13-O6-S2-S1:	165.08	-74.2(4)
			C7-C13-O6-S2:	-177.64	170.5(3)

Recently, both the gas-phase structure and the solid-state molecular structure of dimethoxydisulfide CH_3-O-S-S-O-CH_3 were determined by electron diffraction[136] and X-ray diffraction[137] (at -158 °C) respectively. Both analyses revealed that the molecule adopts the chainlike arrangement along the **OSSO** subunit with C_1 symmetry **265** in the gas phase and an averaged C_2 symmetry **264** in the crystal since the molecular structure was found to deviate slightly from the absolute C_2 symmetry. *Ab initio* MO calculations at the HF/6-311G** level resulted in three enantiomeric pairs of conformational isomers [(+++), (++-), (-+-)] originating from rotation about the two S-O bond axis.[136] The rotamers of symmetry C_1 (++-) **264** were found to be more stable than the set of helical C_2 symmetry rotamers (+++) **265** by 4 kJ mol^{-1} (0.96 kcal mol^{-1}). The third set of conformers (-+-) **266** were found to be less favorable due to the steric interaction of the methyl groups **Figure 9**. The three different sets of rotamers were distinguished considering their intramolecular non-bonding interactions like C···C' and C'···O. The only set having the last non-bonding interactions in the 4.50-4.60 Å range displayed by the experimental radial distribution function was **265**. The C···C' interaction in **264** was expected to be 5.65 Å, while the C···C' and C'···O interactions in **266** were expected to be about 4.00 Å by calculations. Some geometrical parameters obtained by electron diffraction, X-ray diffraction and *ab initio* calculations are reproduced in **Table 13**.[136] Again, the calculated and X-ray values are related by ±1-10%.

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136. R. Steudel, H. Schmidt, E. Baumeister, H. Oberhammer and T. Koritsanszky, *J. Phys. Chem.*, **99**, 8987 (1995); **Figure 9:** the structures **264-266** were assigned considering the angles C'-O'-S'-S, O'-S'-S-O and S'-S-O-C; structure **265** was assigned (++-).

137. T. Koritsanszky, J. Buschmann, P. Luger, H. Schmidt and R. Steudel, *J. Phys. Chem.*, **98**, 5416 (1994).

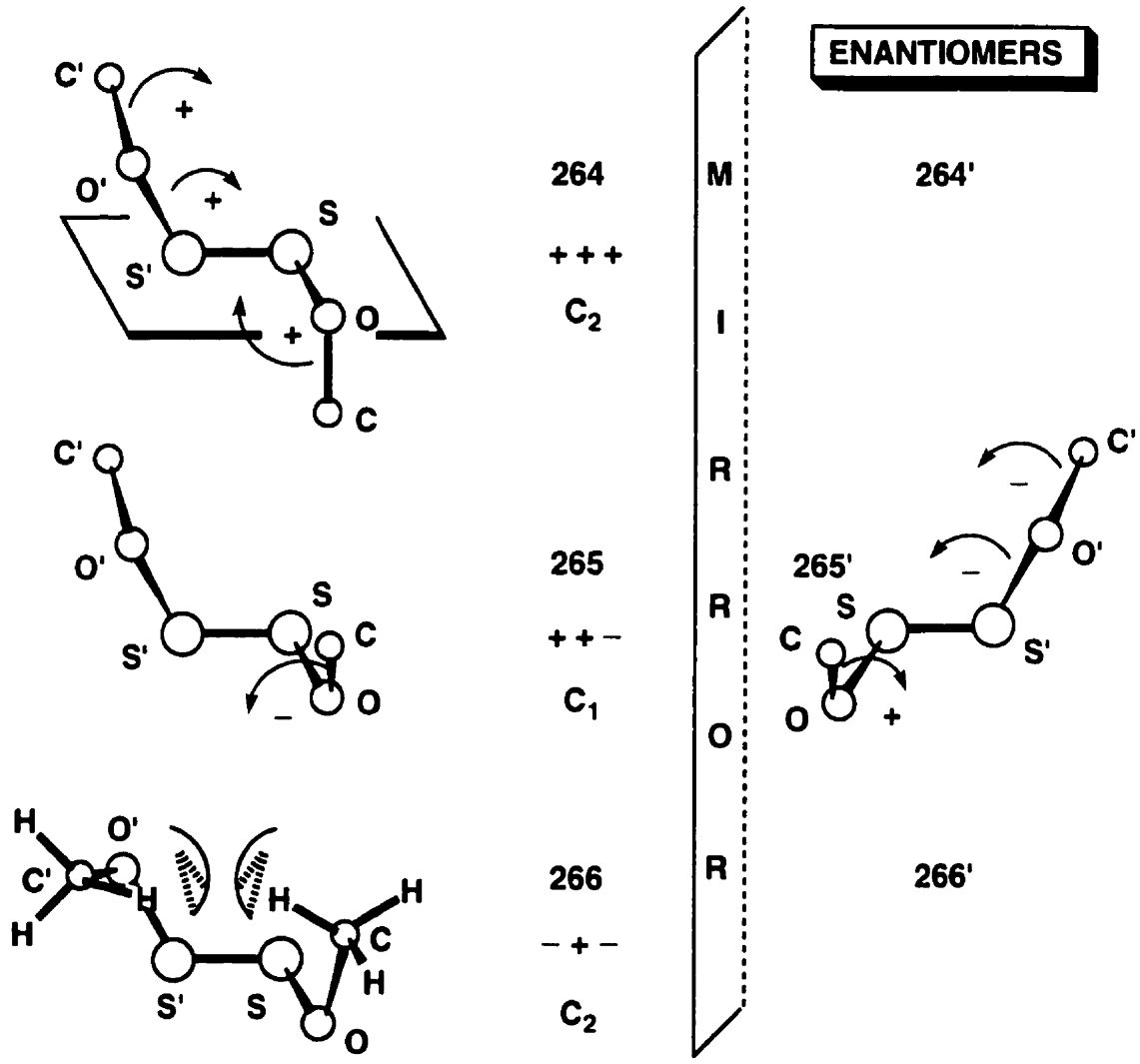

Figure 9: Calculated Enantiomeric Sets of Confomers for $(CH_3OS)_2$

The substructure unit C14-O5-S1-S2-O6-C13 in **218b** (4-NO_2) (**Figure 5**), can be correlated, once again, with a C_1 symmetry arrangement like **265'** where the sequence of atoms follows C-O-S-S'-O'-C' (**Figure 9**), while the same substructure unit in **218c** (4-Cl) (**Figure 6**) depicte a C_2 symmetry arrangement like **264** where the sequence of atoms follows C'-O'-S'-S-O-C (**Figure 9**).

Table 13. Geometrical Parameters[a] for $(CH_3OS)_2$

	gas phase	crystal	*ab-initio*[b]
S-S:	1.960(3)	1.972(1)	2.020
S-O:	1.653(3)	1.658(4)	1.635
O-C:	1.432(3)	1.435(1)	1.413
O-S-S:	108.2(3)	108.2(1)	105.3
C-O-S:	114.5(4)	114.5(1)	117.2
O-C-H:	110.6(10)	109.4(7)	109.3
O-S-S-O:	91(4)	81.5(1)	86.7
C-O-S-S:	±74(3)	75(3)	±82.8

a) Distances in Angstroms and angles in degrees; b) HF6-311G**; values for set of conformers 265.

By comparison, the X-ray structure of dimethoxysulfide (dimethylsulfoxylate, $(CH_3O)_2S$) was determined at -113 °C and reported. The molecule was found to adopt the C_2 structure in both the solid state[138a] and in the gas phase[138b]. Two helical rotamers of symmetry C_2 (++; --) **(267; 268)** and one of symmetry C_s (+-) **269** were considered **(Figure 10)**. Both enantiomers of C_2 symmetry were present in the unit cell and related by a center of inversion.[138a] Some important structural parameters were the bond lengths S-O [1.6212(7) Å], C-O [1.4444(6) Å] and C-H (averaged) [1.067(7) Å], the bond angles O-S-O [104.78(5)°], C-O-S [115.76(2)°], O-C-H (averaged) [108.3°] and the torsional angle C-O-S-O [81.75(2)°]. The S-O bond length was similar to the one found in methyl *o*-nitrobenzenesulfinate **260**.

138. a) J. Buschmann, P. Luger, T. Koritsanszky, H. Schmidt and R. Steudel, *J. Phys. Chem.*, **96**, 9243 (1992); b) E. Baumeister, H. Oberhammer, H. Schmidt and R. Steudel, *Heteroatom Chem.*, **2**, 633 (1991).

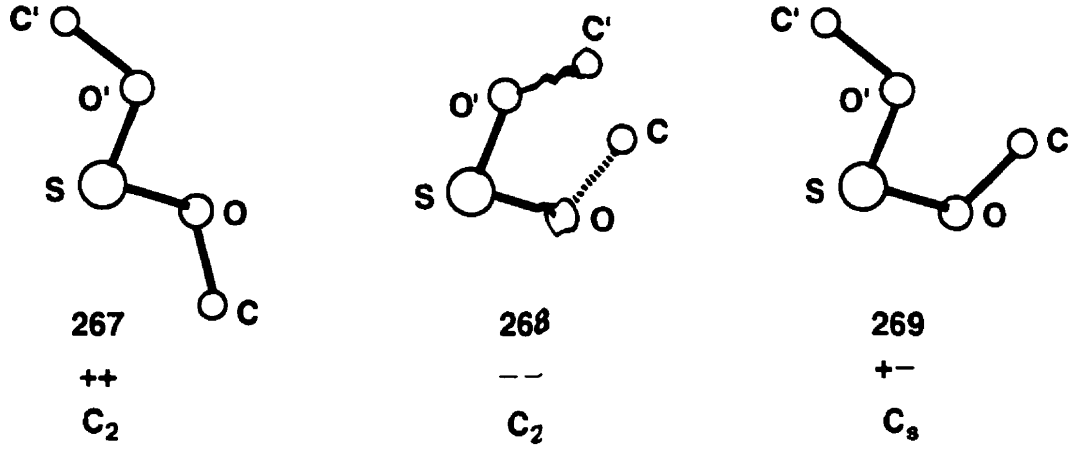

Figure 10: Theoretical Rotamers for $(CH_3O)_2S$

Interestingly, the prepared sulfoxylate bis(4-nitrobenzyl) sulfoxylate **246b** (4-NO_2) was found to crystallize (out of dichloromethane) in the triclinic system with space group designation p -1 (**Appendix IV**). **Figure 11** shows the ORTEP representation of the molecule **246b** and **Table 14** includes a number of characteristic bond lengths, bond angles and torsional angles. Of special interest are the bond lengths S1-O5 [1.648(3) Å] and the S1-O6 [1.622(3) Å]; the bond angle O6-S1-O5 [103.1(2)°]; the dihedral angles O6-S1-O5-C14 [75.1(3)°][130] and O5-S1-O6-C13 [88.9(3)°]. Also interesting are the bond lengths including the hydrogen atoms attached to C14 and C13 (C14-H14a/b and C13-H13a/b [0.97 Å]). By comparison to dimethylsulfoxylate (**Figure 10**, rotamer **267**), the sulfoxylate **246b** deviates from C_2 symmetry around the substructure unit C14-O5-S1-O6-C13 (**Table 12** and **Table 14**) following the sequence of atoms C-O-S-O'-C'.

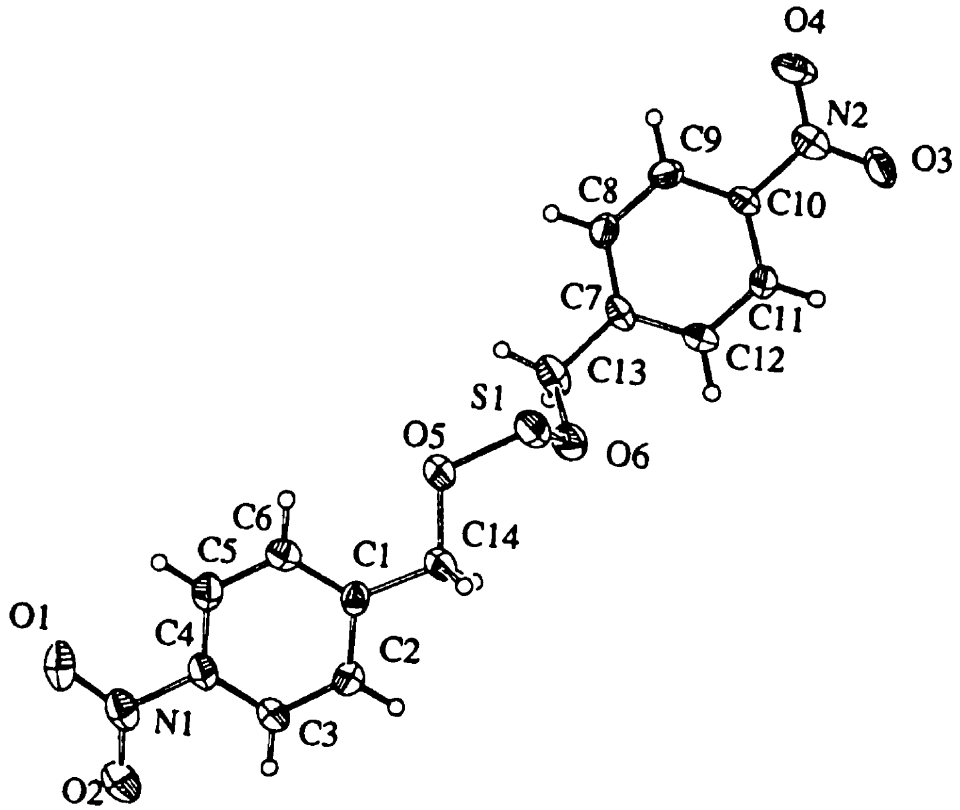

Figure 11: ORTEP Drawing of Bis(4-Nitrobenzyl) Sulfoxylate 246b

Table 14. Selected Bond Lengths, Valency and Torsion Angles for 246b

	(Å)		(°)		(°)
S1-O5:	1.648(3)	O6-S1-O5:	103.1(2)	O6-S1-O5-C14:	75.1(3)
S1-O6:	1.622(3)	C14-O5-S1:	113.3(3)	O5-S1-O6-C13:	88.9(3)
O5-C14:	1.434(5)	C13-O6-S1:	116.2(3)	S1-O6-C13-C7:	90.6(4)
O6-C13:	1.460(5)	O5-C14-C1:	111.3(4)	S1-O5-C14-C1:	-178.5(3)
C1-C14:	1.488(6)	O6-C13-C7:	110.2(4)		
C7-C13:	1.504(6)	O5-C14-H14a/b:	109.4(3)		
C14-H14a/b:	0.97	O6-C13-H13a/b:	109.6(2)		
C13-H13a/b:	0.97	C7-C13-H13a/b:	109.6(3)		
		C1-C14-H14a/b:	109.4(3)		

Since only a few sulfoxylates were prepared and characterized prior to **246b**, some parameters are worth diccussing and comparing with those compounds. The S1-O5 The S1-O5 [1.648(3) Å] and S1-O6 [1.622(3) Å] bond lengths are in the same range as the S-O bond in thiosulfonates **259** [1.65 Å],[131] in the sulfenic acid ArN=C(OAr)SOH **270** [1.624 Å],[139a] in methane sulfonic acid $CH_3S(=O)_2OH$ **271** [1.658Å],[139b] and in sulfoxylic acids $(HO)_2S$ **272** [1.632-1.666 Å].[139c] However, shorter S-O bonds were found in the bis(*i*-propyloxysulfide)-dichloropalladium (II) complex $[PdCl_2\{S(OPr^i)_2\}_2]$ **273** [1.586(6), 1.589(6), 1.592(6) and 1.611(6) Å].[140] The valence angle at the oxygen atoms C14-O5-S1 [113.3(3)°] and C13-O6-S1 [116.2(3)°] are somewhat larger than the one found in **270** [H-O-S: 105°], **271** [H-O-S: 107.7°] and **272** [107.4, 109.8°] but somewhat similar to the C-O-S angle found in **259** [113°]. As we have seen previously in the X-ray determination of **218b** (4-NO_2) [S1-O5-C14: 114.6(3)° and S2-O6-C13: 115.5(3)°], **218c** (4-Cl) [S-O5-C14: 116.1(7)°] and dimethoxydisulfide [C-O-S: 114.5(1)°], we can attribute the enlargement of the C-O-S angle to the size of the sulfur atom itself attached to oxygen.

The analogous tetrachalcogenide of **218b**, bis(4-nitrobenzyl) tetrasulfide **226** was prepared and recrystallized (from EtOH-$CHCl_3$) in the orthorhombic space group P cab. The molecule itself has no internal symmetry, but the 8 molecules in the unit cell are related by pairs, and these pairs are related among each others by mirror planes (**Appendix V**). **Figure 12** shows the ORTEP representation of the molecule **226** and **Table 15** includes a number of characteristic bond lengths, bond angles and torsional angles. Of special interest are the S1-S2 [2.0293(24) Å], S2-S3 [2.0574(22) Å] and S3-S4 [2.0274(23) Å] bond lengths between the divalent sulfur atoms; the bond angles S1-S2-S3 [108.02(10)°] and S2-S3-S4 [106.23(10)°]; the dihedral angle S1-S2-S3-S4 [-94.5(1)°][130].

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139. a) Solid state; K. Kato, *Acta Crystallogr.*, **B28**, 55 (1972); b) Vapor phase: R.E. Penn, E. Block and L.K. Revelle, *J. Am. Chem. Soc.*, **100**, 3622 (1978); c) *Ab-initio* MO calculations: T. Steiger and R. Steudel, *J. Mol. Struct. (Theochem)*, **257**, 313 (1992).

140. R. Steudel, M. Kustos, H. Schmidt, E. Wenschuh, M. Kersten and A. Wloszczynski, *J. Chem. Soc., Dalton Trans.*, 2509 (1994).

The middle S2-S3 bond length is longer than the adjacent terminal ones. This pattern of bond distances was also observed in bis(2-benzothiazolyl) tetrasulfide **274** and bis(4-chlorophenyl) tetrasulfide **275**.[141] The alternating pattern was also noted in sodium-crown hexasulfide $\{[Na(15\text{-crown-}5)]_2S_6$ **276** where the chain-like S_6^{2-} ion has transoid conformations.[142] This bond length pattern was suggested to be due to the repulsion of the $3p_\pi$ lone pairs of the two central sulfur atoms resulting in a tendency to delocalize electron density into σ^* molecular orbitals of neighboring bonds of suitable geometry for hyperconjugation (gauche effect).[143a,c] The shorter S1-S2 and S3-S4 bonds are likely the result of π-interaction between the lone pairs 3p atomic orbitals of S1 and S4 and the lowered σ^*-MO of S2-S3. The σ^*-MO of S2-S3 is lowered by the resulting weak σ-MO interaction along S2-S3 which is weakened by the repulsive lone pairs interactions. *Ab initio* MO caculations on the parent H_2S_4 have shown the existence of *all-trans* (+++; C_2 symmetry), *cis-trans* (++-; C_1 symmetry) and *all-cis* (+-+; C_2 symmetry) conformations and to be of almost identical energy, with the *cis-trans* rotamer being the more stable followed by the *all-cis* and the least stable, the *all-trans* by 0.66 kJ mol^{-1} (0.16 kcal mol^{-1}).[143b] The tetrasulfides **274-276** were of *all-trans* conformation, but **226** was of *trans-cis* (--+; C_1 symmetry)[144] conformation along the substructure unit C14-S1-S2-S3-S4-C13 since the atoms C14:S4 and S1:C13 were in a *trans* and *cis* relationship respectively. The calculated torsion angles around the S1-S2-S3-S4 unit for all the conformers of H_2S_4 were in the range of 79.9 to 80.5° and similar angles were observed for **274** [78.48(5)°], for **275** [75.5(3)°] and **276** [S2-S3-S4-S5: -79.4(4)°; S3-S4-S5-S6: -78.8(4)°]. It was proposed that cumulated sulfur-sulfur bonds prefer a somewhat smaller angle than isolated S-S bonds.[143b] In compound **226**, the angle was closer to the observed and calculated 90° angle for H_2S_2.[145] The enlargement of the dihedral angle in **226** resulted from partial repulsive interaction between the aromatic protons at C6 and C5 and the almost perpendicular aromatic ring to it (**Figure 12**).

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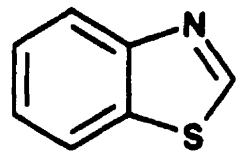
141. R. Steudel, P. Krüger, I. Florian and M. Kustos, *Z. anorg. allg. Chem.*, **621**, 1021 (1995).

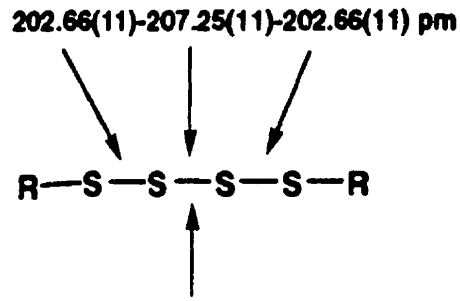
142. A.-D. Bacher and U. Müller, *Z. Naturforsch*, **47b**, 1063 (1992).

143. a) R. Steudel and F. Schuster, *J. Mol. Struct.* **44**, 143 (1978); b) Y. Drozdova, K. Miaskiewicz and R. Steudel, *Z. Naturforsch*, **50b**, 889 (1995); c) R. Steudel, Y. Drozdova, K. Miaskiewicz, R.H. Hertwig and W. Koch, *J. Am. Chem. Soc.*, **119**, 1990 (1997).

144. The assignment (- - +): C14-S1-S2-S3 (-92.7(3)°), S1-S2-S3-S4 (-94.5(1)°) and S2-S3-S4-C13 (86.4(2)°).

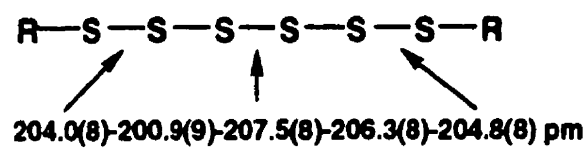
145. E. Herbst and G. Winnewisser, *Chem. Phys. Lett.*, **155**, 572 (1989).

274: R = 



275: R = 4-Cl-C_6H_4

276: R = Na(15-crown-5)



Recently, the X-ray crystallographic structure of bis(dimesylamino) disulfide[89] **213** was determined at -95 °C; the S-S bond length was 2.021 Å and the torsion angle (N-S-S-N) of -85 °. From the values of the S-S bond length and the torsion angle, compound **213** was characterized as a "normal" disulfide with a linear arrangement of the S-S bond. By comparison to **218b**, the presence of the electron-withdrawing dimesylamino groups ($N(SO_2CH_3)_2$) did not affect the S-S bond length extensively. It is clear that the S-S bond length in disulfides R-S-S-R depends of the electronegativity of the R groups attached (**Table 16**).[146] Recently, a comprehensive paper was published by Schleyer[126b] where a theoretical investigation of the relative stabilities of linear RSSR and branched isomers R_2SS was presented (R = F, Cl, H and CH_3). According to that paper, the short S-S bond lengths observed in **218b-c** may be rationalized by considering the MO interactions between the two equivalent antibonding singly occupied molecular orbitals (SOMOs) of the $S_2^{\cdot\cdot}$ biradical in its triplet ground state that are each available to form an electron pair bond with the singly occupied atomic orbital (SOAO) $2p_x$ or $2p_y$ of oxygen from the electronegative fragments $\cdot OCH_2Ar$ (**Figure 13**).[126b] It makes sense that the near 90° dihedral angle preference between the two SSO planes in **218b** and **c** is due to the perpendicular orientation of π_x^* and

146. a) B. Meyer, D. Jensen and T. Oommen, *Sulfur in Organic and Inorganic Chemistry*; Senning A., Ed.; M. Dekker: New York, **v.12**, 13 (1972); b) F.J. Loras, E. Tieman and D.R. Johnson, *J. Chem. Phys.*, **60**, 505 (1974); c) E. Tiemann, J. Hoeft, F.J. Loras and D.R. Johnson, *J. Chem. Phys.*, **60**, 5000 (1974); d) T. Chivers, R.T. Oakley, A.W. Cordes and P. Swepston, *J. Chem. Soc. Chem. Commun.*, 35 (1980).

π_y* SOMOs of $S_2^{\bullet\bullet}$. Based on their MO interaction diagram, the $2p_x$ or $2p_y$ SOAO of the oxygen from $\cdot OCH_2Ar$ also interacts with the two S-S bonding π_x and π_y MOs of $S_2^{\bullet\bullet}$ (3p sulfur lone pairs from each sulfur atom) leading to two equivalent 3-orbital-4-electron interactions, one in the xz plane and the other in the yz plane, leading to three degenerate pairs of S_2X_2 (X= OCH_2Ar) MOs: σ_{S-X} (bonding), n_{S-X} (nonbonding) and σ_{S-X}* (antibonding) **(Figure 13)**.[126b] They have clearly demonstrated that the S-S bond in S_2X_2 should contract as the electronegativity of $\cdot$X increases: decreasing the $\cdot$X SOMO and leaving the occupied n_{S-X} MOs with high $\cdot$X s-character and small π^* $S_2^{\bullet\bullet}$ amplitude. Therefore, we can advance that the partial electronic depopulation of the two equivalent $S_2^{\bullet\bullet}$ (SOMOs) π_x* and π_y* is responsible for the partial double bond character of the S-S bond in **218b-c**.

Table 16. A Variety of S-S Bond Lengths

Compound	r (S-S) (Å)
H_2S_2[143a]	2.065
$(CH_3)_2S_2$[143b]	2.029
S_2Cl_2[123b]	1.931
S_2Br_2[123a]	1.948
S_2F_2[122b]	1.888
S_2O_2[146b]	2.024
S=S[146a]	1.892
S=S=O[15, 146c]	1.882
$S=S(F)_2$[15, 122c]	1.860
9c $S=S(OR)_2$[10a]	1.901
Ph_3P=N-S-N=S=S[146d]	1.908

The "gauche-effect" was also suggested to be responsible for this S-S bond length reduction in S_2X_2 with the increasing electronegativity of X. The 3p lone pairs of the sulfur atoms were partly delocalized into σ_{S-X}* MOs in the same plane through hyperconjugation, creating two π bonds in planes almost perpendicular to each other. This configuration decreases the energy of σ_{S-X}* MOs as the strength of the perpendicular π bonds increases with the electronegativity of X **(Figure 14)**.[143a,c]

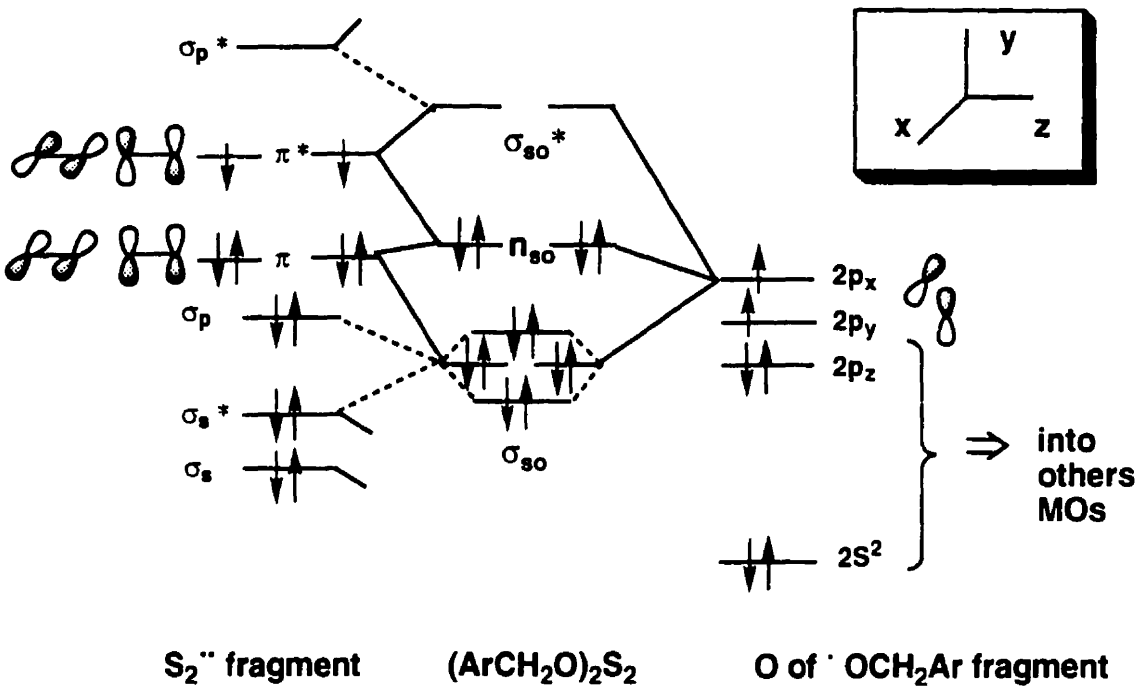


Figure 13: Qualitative MO Interaction Diagram for 218a-b

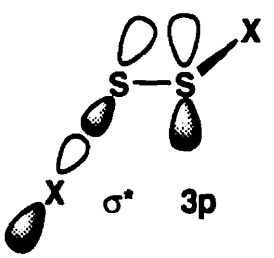


Figure 14: The Gauche Effect along X-S-S-X

The X-ray structure determination for acyclic dialkoxy disulfides have demonstrated that the arrangement of the **OSSO** subunit is linear in every instance with a significantly shorter S-S bond length than expected as compared with a "normal" disulfide. Interestingly,

the values are sitting half way on a scale where at one end there are compounds containing S=S bonds with the shortest S=S at *ca.* 1.86 Å, and at the other end, regular disulfides and polysulfides with the longest S-S at *ca.* 2.08 Å. In general, qualitative MO interaction diagrams, charge distribution considerations and *ab initio* MO calculations have shown that the disulfide (X-S-S-X) isomers are more stable than the thionosulfoxide (X_2S=S) isomers. The relative energies of X-S-S-X with respect to X_2S=S isomers were calculated at the MP4/6-31G**//6-31G** + ZPE level of theory for X=F, Cl, and CH_3 to give 0.2, -17.2 and -20.0 kcal mol^{-1}, at the MP2/6-311G**//HF/6-311G** + ZPE level for X=OH to give -3.3 kcal mol^{-1} and at the MP2/6-31G*//HF/4-31G* level for X=SH and H to give -31.5 and -33.7 kcal mol^{-1} respectively.[126b, 134, 143c]

According to *ab initio* calculations, the existence of linear conformers like **261** and **262** with the branched isomer **263** is highly possible under equilibrium conditions for HOSSOH.[134] The same sort of rationale can certainly be made for compounds like **218** since preliminary molecular modelling *via* MMX calculations using PCMODEL and MACROMODEL have shown the possible existence of distinct conformers for **218b** **(Figure 8)**.

3.2.3 Solid State NMR of 218a-b and 226

It seems that hindered rotation might be responsible for the diastereotopicity of the benzylic protons in **218b**. The ^{13}C shifts for the two benzylic carbon C13 and C14 in the solid state should be similar to the one observed in solution. A pure sample of **218b** was further characterized by solid state NMR techniques in order to examine the solid structure. For solid state NMR spectrocopy, the use of the techniques of cross polarization, CP,[147a] and magic-angle spinning, MAS,[147b,c] in many cases results in near solution-like spectra for solid compounds. Such methods yield the chemical shift and may also provide information regarding the overall crystallographic structure of the solid in question. For the two nuclei C13 and C14 of the solid **218b** to be equivalent in the NMR sense implies both symmetry of the local environment as well as equivalence with respect to the overall crystal geometry. The solid ^{13}C chemical shifts for compounds **218a**, **226** and **218b** are listed in **Table 17**, and the spectra are shown in **Figure 15** and **16**.

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147. a) A. Pines, M.G. Gibby and J.S. Waugh, *J. Chem. Phys.*, **59**, 569 (1973); b) E.R. Andrew, *Prog. Nucl. Magn. Reson. Spectrosc.*, **8**, 1 (1971); c) J. Schaefer and E.O. Stejskal, *J. Am. Chem. Soc.*, **98**, 1031 (1976).

Table 17. ^{13}C Solid[a] and Solution[b] Chemical Shifts for 218a-b and 226

	δ_c (CH_2) solid (ppm)	δ_c-aromatics	δ_c (CH_2) solution (ppm)	δ_c-aromatics
218a	79.50; 79.52	129.92; 137.73	75.05	128.48; 128.53 128.65; 136.54
218b	74.44; 78.73	125.22; 127.96 144.76; 147.49	76.74	123.70; 128.61 143.55; 147.77
226	38.15; 44.42	124.79; 131.05 134.19; 147.76	45.10	123.90; 130.30 143.72; 147.75

a) T=20.2°C, CP MAS NMR on Chemagnetics CMX-300 MHz (^{13}C NMR frequency 75 MHz) for 226 and on MX-100 MHz (^{13}C NMR frequency 25 MHz) for 218a-b; b) ^{13}C NMR (75 MHz, $CDCl_3$) at T=19.6°C using 300 MHz operating frequency.

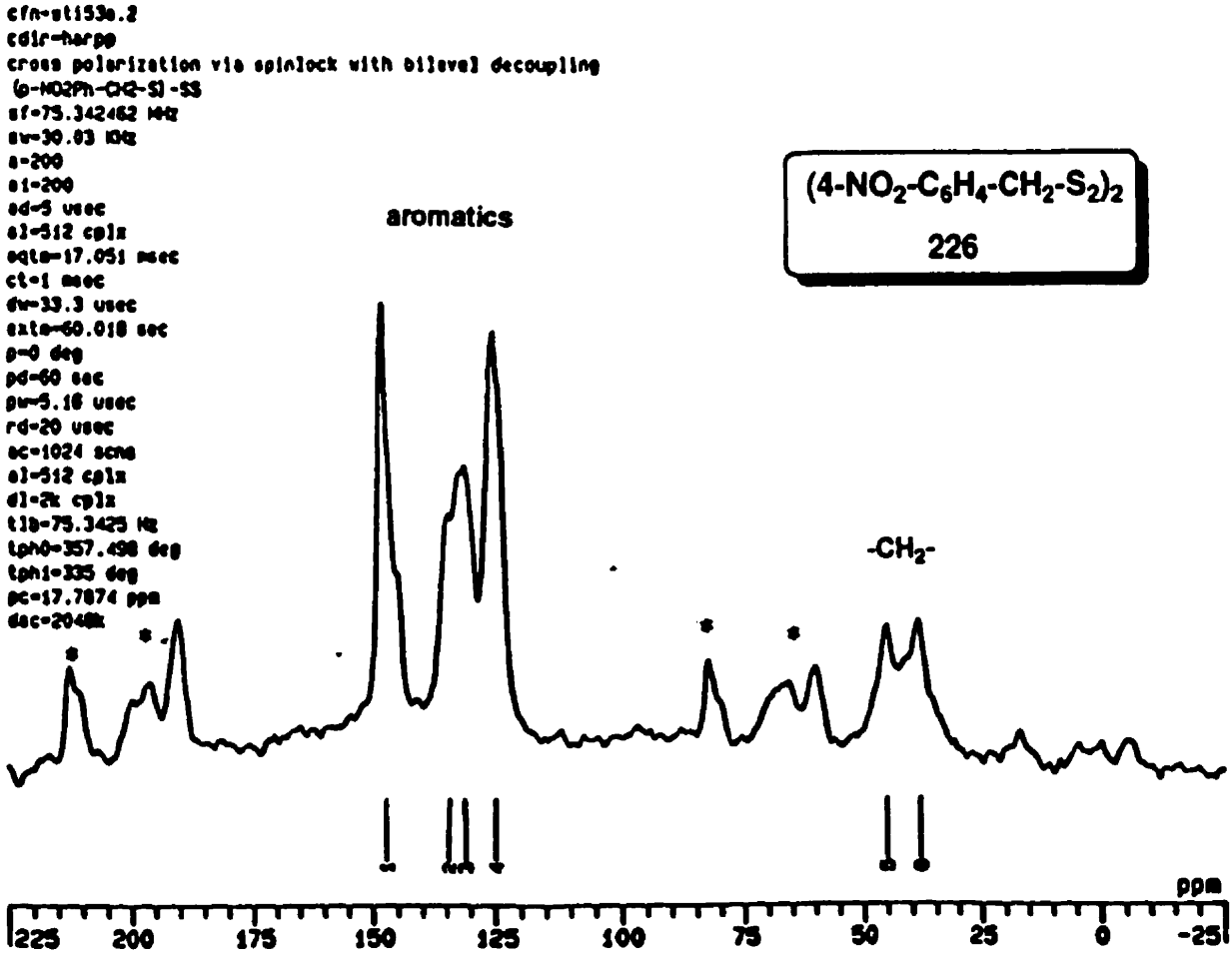


Figure 15: ^{13}C CP MAS NMR Spectrum of 226; (*) spinning sidebands.

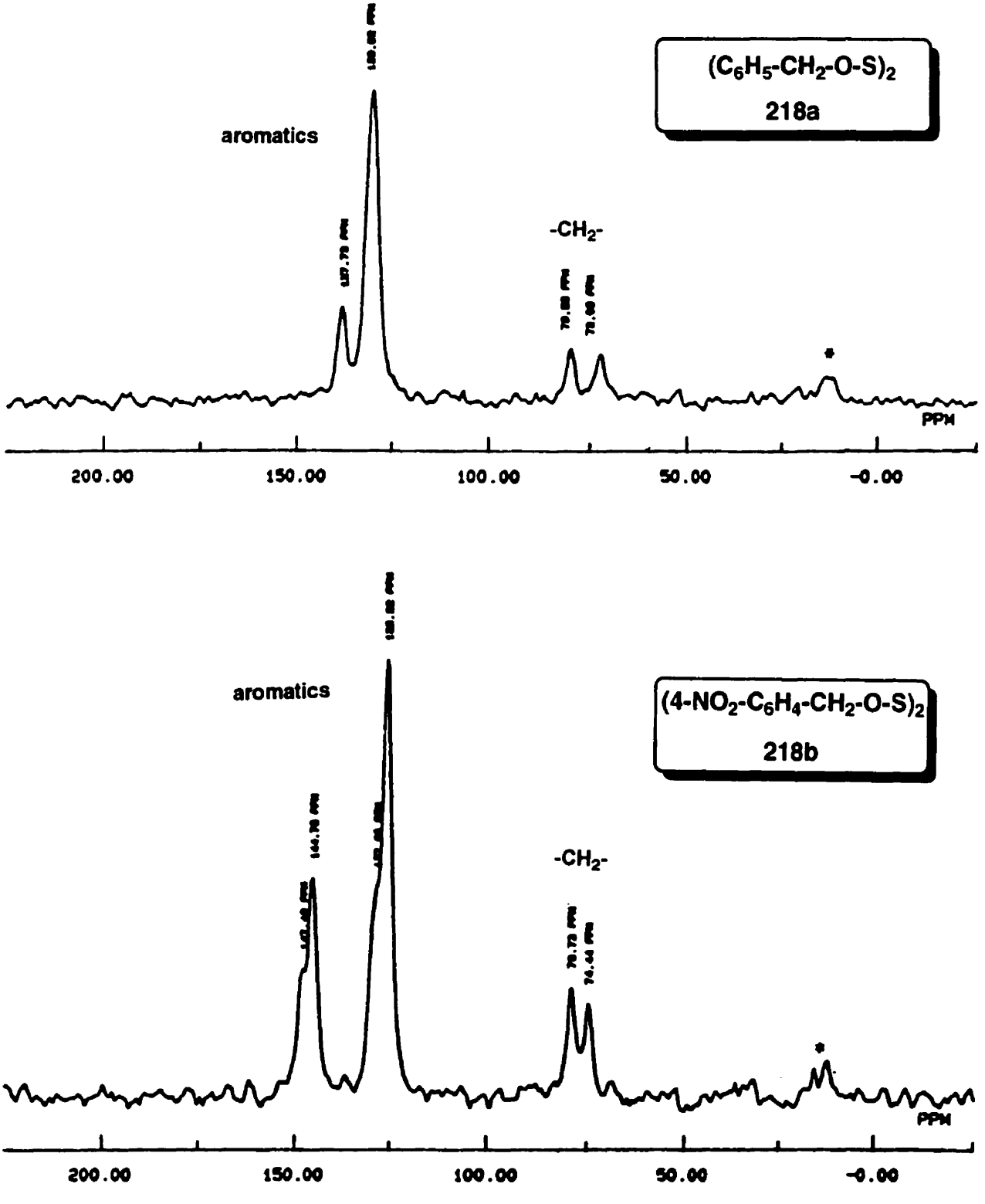


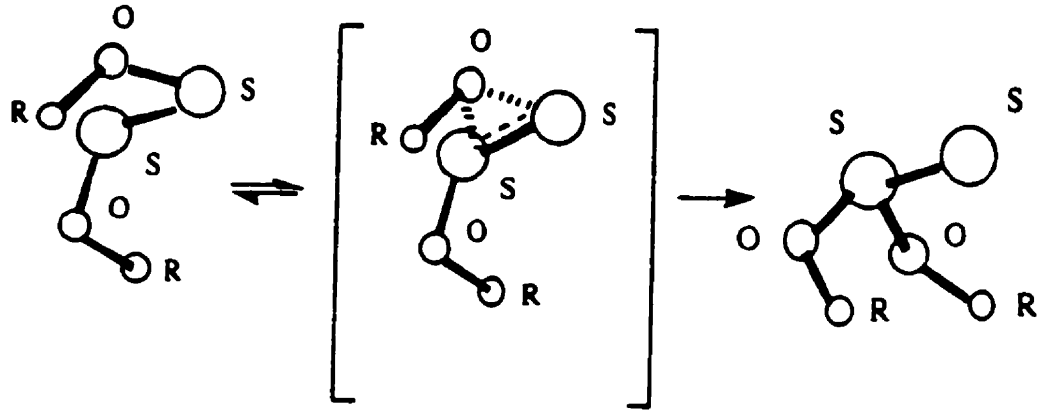
Figure 16: ^{13}C CP MAS NMR Spectra of 218a-b; (*) spinning sidebands

The results obtained indicate for **218b** that C13 and C14 are two distinctive crystallographic sites in the asymmetric unit, and the same conclusion can be drawn for the benzylic carbons in **218a** and the tetrasulfide **226**. The two distinctive lines observed in the ^{13}C solid spectra compared to the single signal in ^{13}C solution spectra may be attributed to the influence of surrounding molecules in the solid state and to changes in bond angles and distances between the solution and the solid state. Even if the two benzylic carbons, in each of the compounds studied, show two distinctive signals in their solid state spectra, their chemical shift values are very close to the ones observed in solution. This makes it a reasonable assumption that the solid state conformation must be very similar to the preferred conformation in solution. On this basis, it may be possible that **218b** crystallized in the *anti* isomer and rearranges preferentially to the *syn* isomer in solution as both isomers coexist. Since the somewhat energetically less favorable branch-bonded isomer is expected to have a dipole moment value higher than the linear isomer, therefore it is expected to be stabilized by polar environments.

3.2.4 Solvent Polarity and Temperature ^1H NMR Study for 218b

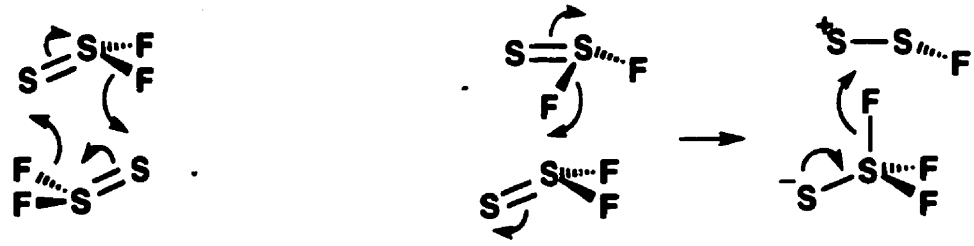
The generation of the branch-bonded isomer from **218b** would necessitate the migration of one OCH_2-C_6H_4-NO_2-*p* group from S1 to S2 probably *via* a three-membered ring transition state (**Scheme 29**). This unimolecular process is seen as a 2,3-sigmatropic rearrangement similar to the one postulated in the thermal racemization and isomerization of allylic disulfides.[28] The rearrangement through the proposed transition state **277** does not require a great deal of bond reorganization to form the thionosulfite isomer **278** from the linear disulfide isomer **218b**. However, this process was considered inconsistent for the observable isomerization of FSSF into F_2S=S and vice versa at temperatures of -100 °C and above in as much as the energy barrier calculated for the process was too high (40.7 kcal mol^{-1}).[126b] Less strained bimolecular processes were proposed (**Scheme 30**) like **279** with a 6-membered ring or like **280** where the negatively charged fluorine which undergoes a 1,2-shift is stabilized through the interaction with the positively charged central sulfur atom of the central sulfur atom of a second F_2S=S molecule. These processes would convert two F_2S=S molecules into F_2S=S + FSSF *via* a product complex [FSSF, F_2SS].[126b] Considering that the relative energy of FSSF to F2S=S (0.2 kcal mol^{-1}) and HOSSOH to $(HO)_2S$=S (-3.3 kcal mol^{-1}) are of the same order of magnitude and that thiosulfoxides should be stabilized by polar environments, compound **218b** was submitted to a solvent

study. Solvent polarity variation has also been studied in the context of sulfur extrusion[11] and desulfurization[148].



266' 277 278

Scheme 29



279 280

Scheme 30

148. a) D. Twiss, J. Am. Chem. Soc., 49, 491 (1927); b) L.D. Markley and J.E. Dunbar, *J. Org. Chem.*, 37, 2512 (1972); c) D.N. Harpp, D.K. Ash and R.A. Smith, *J. Org. Chem.*, 44, 4135 (1979); 45, 5155 (1980).

The results are reported in **Table 18** according to the increasing solvent polarity. Solvent shift effects were observed probably due to the formation of weak to strong interactions between solvent and solute molecules.[149] No special peak separation occurred during the course of the study. Comparison of the ^1H NMR chemical shifts for **218b** in aromatic solvents relative to $CDCl_3$, shows that the signals for the benzyl as well as for the aromatic protons are significantly shifted upfield in toluene-d_8 and benzene-d_6. The positive aromatic solvent induced shift ($\Delta ASIS = \delta CDCl_3 - \delta C_6D_6$ or C_7D_8) clearly indicate the formation of a collision complex between the aromatic solvents and **218b**.[150] The random distribution of the solvent molecules around the solute permits an overall orientation of the solute-solvent pair, which indicates that the solute molecules tend to spend more time facing onto the "pie" shaped aromatic molecules; this would result in shielding of the protons by the ring current anisotropy.

Table 18. Results of Solvent Polarity Study[a] for 218b

Solvent μ (D)	δ_H (CH_2) (ppm)	1/2 ($\delta_A + \delta_B$) (ppm)	$^2J_{HH}$ (Hz)	δ_H (Ar) (ppm)	$\Delta\nu/^2J_{HH}$
C_6D_6	4.23	4.30	12.19	6.68; 6.72	1.86
(0)	4.37			7.73; 7.77	
C_7D_8	4.33	4.40	12.21	6.78; 6.83	2.34
(0.36)	4.47			7.78; 7.83	
$CDCl_3$	4.87	4.94	12.40	7.40; 7.50	2.36
(1.01)	4.98			8.18; 8.22	
CD_2Cl_2	4.91	4.97	13.01	7.45; 7.50	1.72
(1.60)	5.03			8.19; 8.23	
DMSO	4.98	5.02	13.04	7.58; 7.63	1.25
(3.96)	5.06			8.18; 8.22	

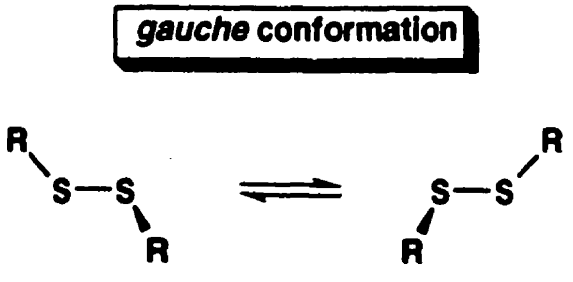
a) ^1H NMR frequency 200 MHz at T = 19.6-21.3°C.

149. a) D. Johnson and D. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958); b) E.D. Becker, *High Resolution Nuclear Magnetic resonance*, Academic Press, New York, 1969, Chap.11.

150. a) J. Ravayne and D.H. Williams, *J. Chem. Soc.*, **B**, 540 (1967); b) R.R. Fraser, T. Durst, R.R. McClory, R. Viau and Y.Y. Wigfield, *Int. J. Sulfur Chem.*, **A1**, 133 (1971).

The magnitude of this effect is known to depend upon the molecular arrangement, and was reported to increase with the tendency of polar groups within the molecule to interact with the aromatic π-electrons. Both sets of benzylic protons in **218b** seem to have experienced the same solvent shift effect; ΔASIS (C_6D_6) = 0.61 and 0.64 ppm while ΔASIS (C_7D_8) = 0.51 and 0.54 ppm. A small downfield shift was observed on going from $CDCl_3$ to DMSO, suggesting maybe some weak specific interactions between the O-S-S-O functionality of **218b** and the polar sulfoxide group of DMSO, since only one set of of the aromatics has been affected (the upfield doublet) as well as the benzylic protons. Also, interactions with the nitro groups cannot be ruled out. At any point in the experiment, a set of different peaks appeared or were overlapping with the AB quartet observed in each spectrum. Therefore, only one of the two possible isomers of **218b** was present in solution (linear or branch-bonded) to rationalize the AB quartet observed. The AB quartet is delivered in the linear arrangement if and only if hindered rotation is present with a preferred *gauche* conformation.

It is known and accepted that disulfides have a barrier to rotation about the S-S bond and that the low-energy conformations of disulfides are chiral by virtue of the chiral axis. The rotation barrier is generally so low that disulfides exist as a racemic mixture of rapidly equilibrating enantiomers at room temperatures.[132]



Measurements of the S-S bond rotation barrier were carried out by studying the temperature dependence of the NMR spectra (DNMR) of dibenzyl disulfides.[117c, 119a] The benzylic protons could only be diastereotopic under restricted rotation conditions like the ones shown with the *gauche* conformation about the S-S bond. The appearance of an AB quartet was observed when the rotation about the S-S bond was slowed down on the NMR time scale at

-128 °C.[119a] For dibenzyl disulfide $(PhCH_2S)_2$, the free energy of activation was found to be $\Delta G^{\ddagger} = 7.0$ kcal mol^{-1} for rotation about the S-S bond. In general, they conclude that the disulfide conformational isomerization occurs by way of the *trans* transition state.

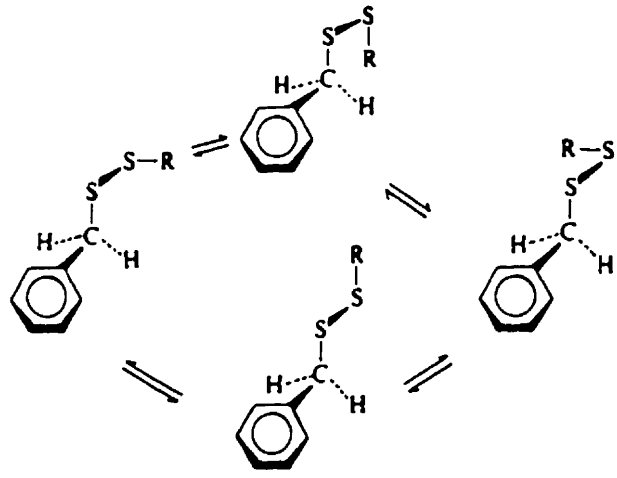


Figure 17: *Cis* and *Trans* Rotation about S-S in $(Ph\text{-}CH_2\text{-}S)_2$

CNDO/B optimization calculations have demonstrated that disulfides (R-S-S-R) and sulfenates (R-S-O-R) are both possessing adjacent divalent lone pair atoms and exhibit comparable molecular geometries and are predicted to undergo conformational transformation with qualitatively similar energy requirements.[117b]

DNMR studies on heteroatom-substituted disulfides are less abundant. For "dioxy disulfides", only diethoxy disulfide **30** $[(CH_3CH_2OS)_2]$ has been studied. Thompson[1a] found that the methylene protons were diastereotopic at 30 °C but collapsed to an A_2X_3 pattern at 100 °C with an activation energy of 36.1 ± 7.1 kJ mol^{-1} (8.6 ± 1.7 kcal mol^{-1}). Thompson suggested that the S-S bond was hindered, but made an error in assigning the barrier to be such a low value (8.6 kcal mol^{-1}) at room temperature. The re-evaluation of the rotational barrier by Seel[48] gave 17.75 ± 0.10 kcal mol^{-1} (T_c = 77.5 ± 2.5 °C), and by Harpp[8] 18 kcal mol^{-1} for T_c = 75 °C.[151a] For bis(amino) disulfides $[(R_2N)_2S_2]$ more elaborate studies were carried out where R = CH_3, CH_2CH_3, and $CH(CH_3)_2$.[151b-d] By

151. a) A very Recent paper (R. Borghi, L. Lunazzi and G. Placucci, *J. Org. Chem.*, **62**, 4924 (1997)) confirms the value of *ca.* 18 kcal mol^{-1}; b) V.W. Hu, J.W. Gilje and T.T. Bopp, *Inorg. Chem.*, **12**,

comparison, the temperature dependence of the proton NMR spectra of bis(amino) sulfides $[(Et_2N)_2S]$ **281** and $[(i\text{-}Pr_2N)_2S]$ **282** was interpreted in terms of restricted rotation about the S-N bond with rapid inversion at nitrogen.[151a] The $\Delta G^{\ddagger}$ values reported were 10.2 kcal mol^{-1} and 11.4 kcal mol^{-1} respectively ($T_c < -120$ °C). The same study was performed with the analogous disulfides and the barriers reported were 9.95 and 11.1 kcal mol^{-1} for **283** (at T = 30 °C the methylene protons were not all isochronous; at T = -120 °C, an overlapping ABX_3 and CDY_3 spectra were observed) and **284** respectively.[151a]

$[(CH_3CH_2)_2NS]_2$ $\{[(CH_3)_2CH]_2NS\}_2$

283 **284**

Since repulsive interactions between vicinal lone pairs of electrons have been generally cited as the origin of the barrier to rotation in disulfides (R-S-S-R) and sulfenates (R-S-O-R) where adjacent atoms are possessing non-bonding electrons; the existence of a more substantial barrier to rotation is expected for compounds like **218b**, in which the rotational barrier depends not only on rotation of the S-S bond, but also on rotation around the S-O bond, and to a lesser extent to the C-O bond. The barrier in **218b** would be expected to be higher than the one for dibenzyl disulfide reported by Fraser (7.0 kcal mol^{-1}).[119a, 118] **Figure 18** represents the high-temperature dependence of the ^1H NMR spectra of **218b** for the benzylic protons.

The identity of the AB quartet collapsed between 69.4 and 79.4 °C and was completely lost by 89.3 °C. The first sign of 4-nitrobenzyl alcohol **220** was detected at 59.5 °C (δ 4.27 ppm, $-CH_2-$), while the first sign for 4-nitrobenzaldehyde showed up at 69.4 °C (δ 9.58 ppm, -C(=O)H) in **Figure 19**. These results indicate that bis(4-nitrobenzyloxy) disulfide **218b** decomposes to the corresponding alcohol **220** and aldehyde. The shortness of the S-S bond found by X-ray crystallography may be an indication that the S-S bond rotation is already slow at room temperature and that the AB quartet is due mostly to restricted rotation around the S-S bond, or, that the branch-bonded arrangement of **218b** is the preferred structure in solution.

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955 (1973); c) L. Craine and M. Raban, *Chemical Reviews*, **89**, 689 (1989); d) D. Kost and H. Egozy, *J. Org. Chem.*, **54**, 4909 (1989).

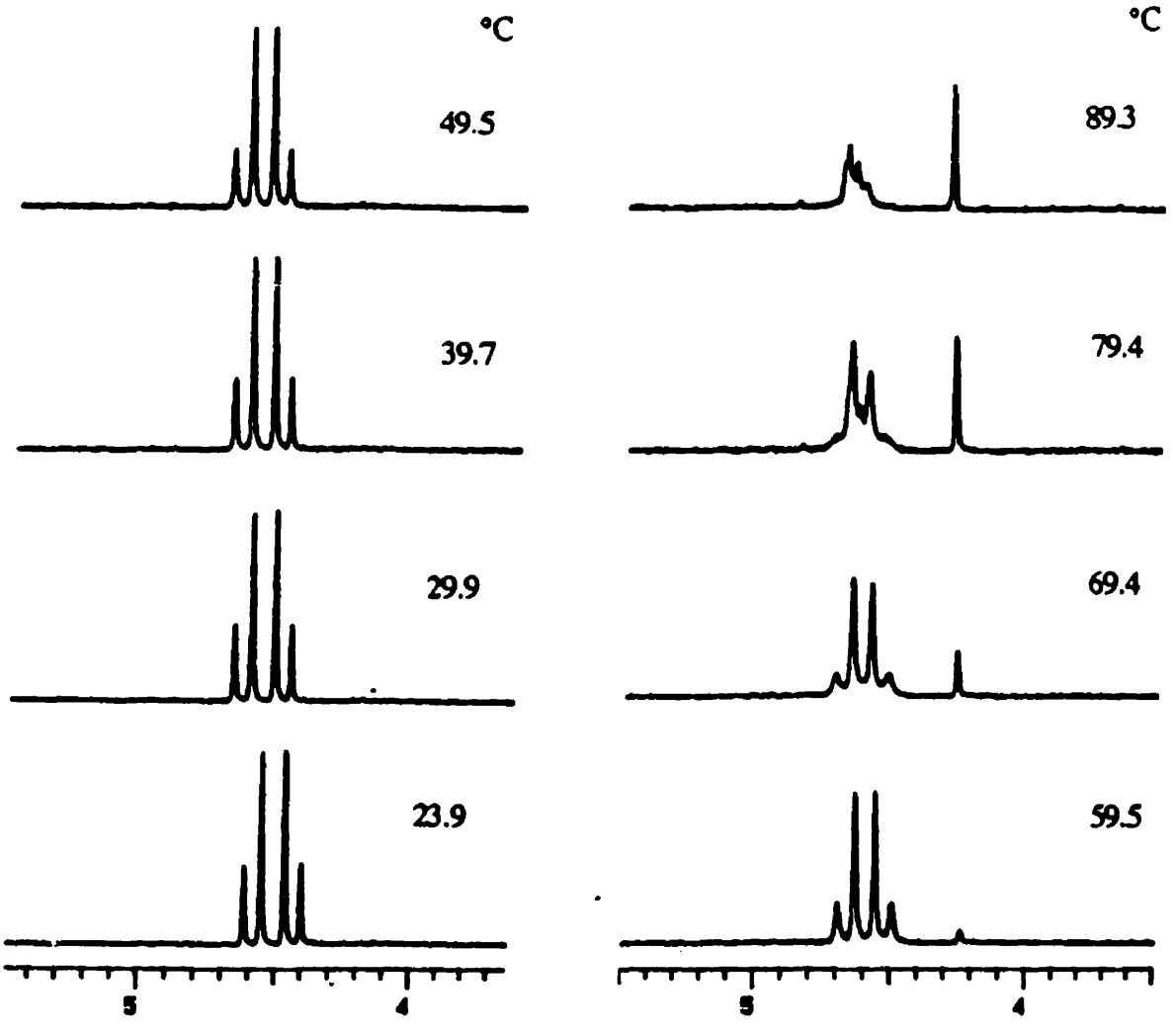


Figure 18: High-Temperature 200 MHz ^{1}H NMR spectra of 218b in Toluene-d_8 (benzylic protons from 23.9 to 89.3°C)

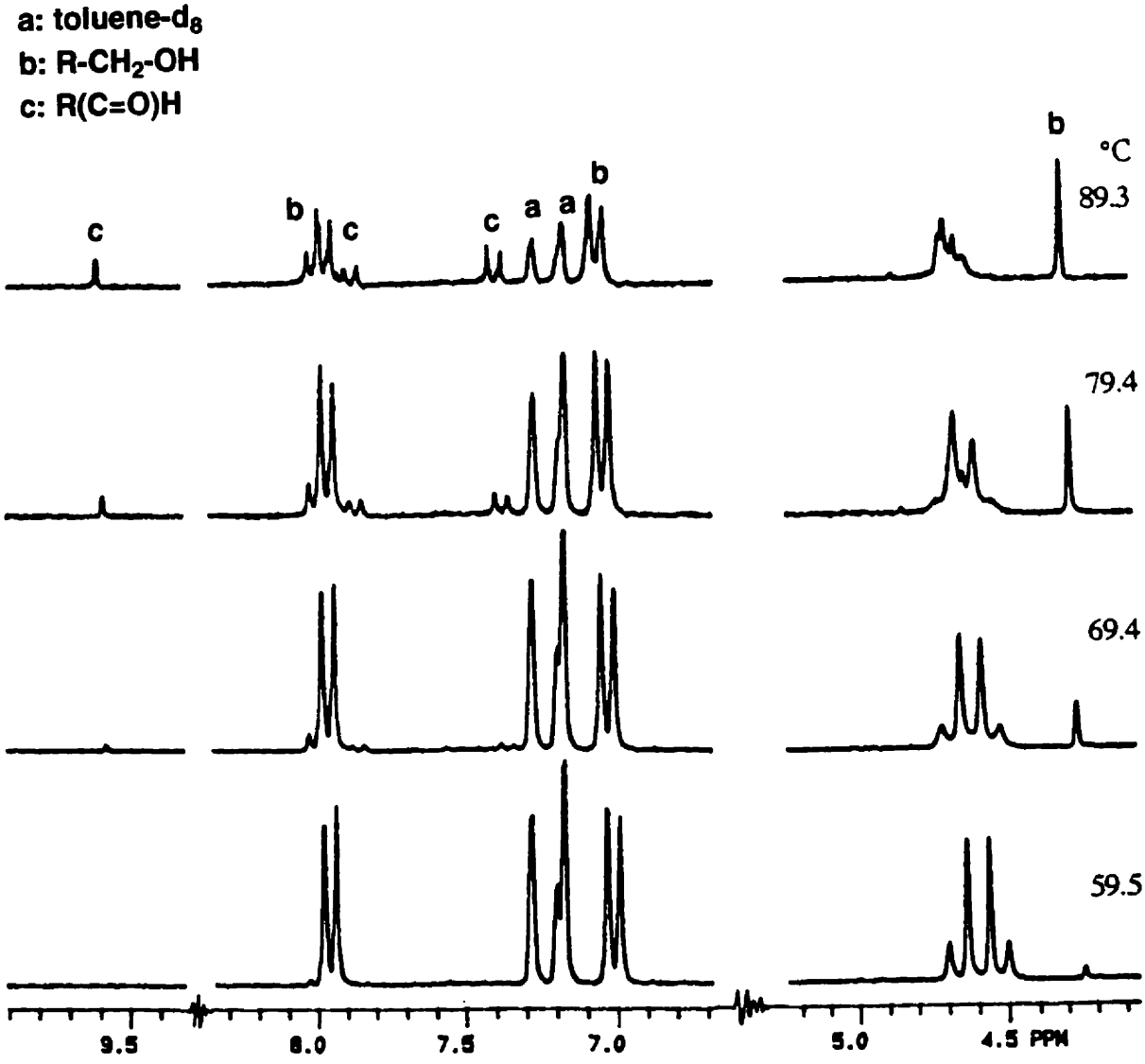
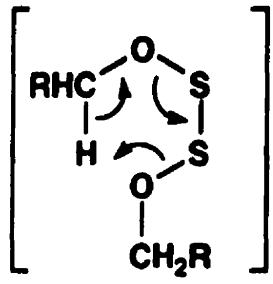
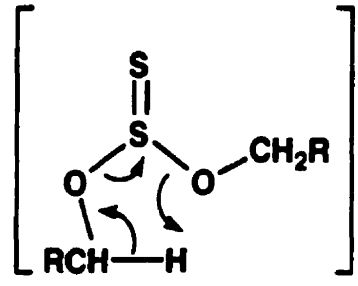


Figure 19: High-Temperature 200 MHz ^{1}H NMR spectra of 218b in Toluene-d_8 between 59.5 and 89.3°C (R = 4-NO_2-C_6H_4)

The decomposition of the linear arrangement of **218b** is possible *via* the 6-membered ring transition state leading to internal disproportionation to the alcohol **220** and the corresponding aldehyde . However, the decomposition of the branch-bonded arrangement of **218b** is certainly possible *via* a 5-membered ring transition state leading to the alcohol and aldehyde as well.



6-membered ring



5-membered ring

Whichever reaction process takes place in the high-temperature experiment, the rotational barrier was not reversible because of intramolecular decomposition. The low-temperature experiment is expected to hinder low barriers to rotation about S-S and S-O bonds (6.9-10.3[1] and 6-8[152, 118] kcal mol^{-1}), leaving the benzylic protons on each side of the -O-S-S-O- functionality as diastereotopic. The ^{1}H NMR low-temperature experiment was performed in CD_2Cl_2, and the lowest temperature that could be reached was -69.1°C (**Figure 20**). At that temperature it was possible to observe an early overlapping AB and CD pattern, showing that the two 4-nitrobenzyl groups were occupying two different environments resembling the ones experienced in solid state ^{13}C NMR, since the two benzylic carbons were found to be different in that case. The pattern of the aromatic protons was also affected. Only a clean AB quartet was detected on warming to ambient temperature, suggesting that some rotation was ceased around the bonds, and that maybe a new arrangement along -C14-O5-S1-S2-O6-C13- (**Figures 5** and **8**) was taking form at low temperatures. At this point, the possible branch-bonded isomer for **218b** could not be completely abandoned. In the above experiment, **218b** could be branched in solution and have two "frozen" aromatic rings that adopt a different orientation at low temperature.

The avenue of thermal isomerization using NMR techniques was unsuccesful at clearly distinguishing between the proposed linear arrangement in solid state (X-ray of **218b-c**) and the possible branch-bonded arrangement for compounds **218** in solution. The AB quartet for the benzylic protons of **218b** was present up to about -70°C and coalesced at about 75°C where decomposition was observed. Although this decomposition was very interesting from a synthetic point of view, (S_2 as dienophile, *vide infra*) the distinction between both isomers was far from crystal clear! Somewhat exotic ^{17}O NMR runs, using

natural abundance of ^{17}O, were performed on **218b**, **219b**, **57** (O,O'-bicyclohexyl-1,1'-diylthiosulfite) and **240** (corresponding sulfite of **57**).

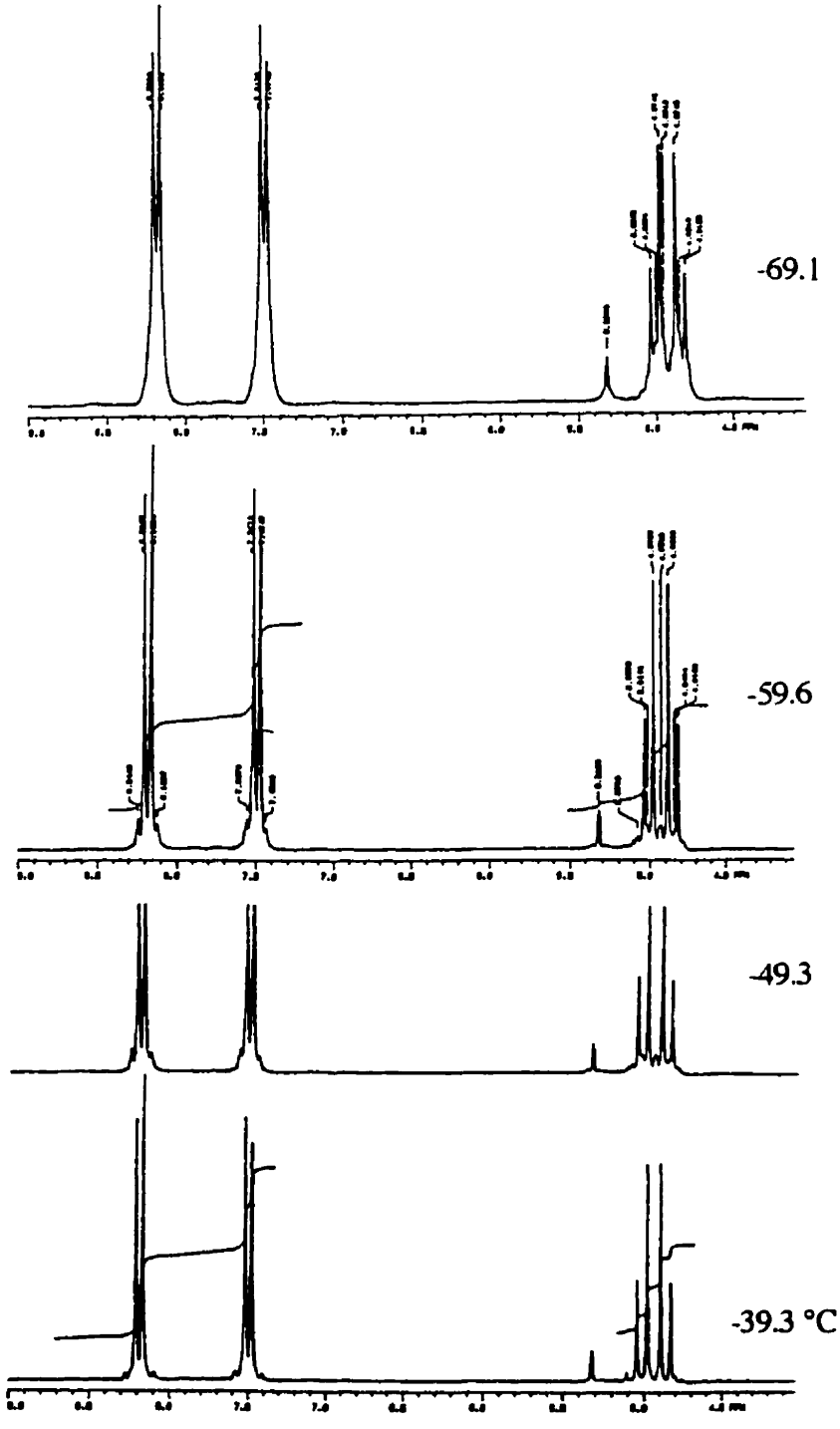


Figure 20: Low-Temperature 200 MHz ^1H NMR spectra of 218b in CD_2Cl_2

3.2.5 ^{17}O NMR of 218b, 219b, 57 and 240

Briefly, group VI of the Periodic Table includes tellurium-125 (^{125}Te) and selenium-77 (^{77}Se) that are useful NMR nuclei with spin 1/2 and adequate natural abundance (6.99% and 7.58% respectively)[152], while sulfur and oxygen do not have nuclear spin properties favoring NMR applications. For sulfur and oxygen, the dominant isotopes are ^{16}O and ^{32}S and both have zero for their spin value. However, they have available quadrupolar nuclei, ^{17}O (I = 5/2) and ^{33}S (I = 3/2) which are of low natural abundances and have large quadrupolar moments. The natural abundance for ^{17}O is 0.037% leading to weak signals and large linewidths because of its quadrupole moment that gives short relaxation times T_1 and T_2 due to the domination of the quadrupole relaxation mechanism.

The solutions were prepared in acetone-d_6 for **218b**, **219b** and **240** while **57** was dissolved in the minimal amount of $CDCl_3$ to which was added acetone-d_6 to ensure complete dissolution. The chemical shift values are reported in **Table 19** including values from the literature.[152] The nitro groups for compounds **218-219b** were not included in the spectral window analyzed (R-NO_2 $\delta > 600$ ppm). Ethers and alcohols were found to absorb close to water (having similar chemical shifts), thus indicating that the shielding of oxygen nuclei is very similar in molecules where the oxygen forms single bonds with either hydrogen and carbon (**Table 19**). However, branching of the hydrocarbon groups causes shifts to lower field. The upfield ^{17}O resonance found for **218b** compares to ether-like sites found in ether and alcohols, suggesting that the diamagnetic factors controlling the shielding of oxygen in -C-O-H and -C-O-C- bonds are very similar to the ones for oxygen in a -C-O-S- bond. The lower field ^{17}O resonance for oxygen attached to a quaternary carbon and a sulfur-sulfur double bond, in the thionosulfite **57**, compares to the effect observed for the singly-bonded oxygen attached to methyl-carbon and carbonyl in methyl acetate (Me-O-(C=O)-Me). The chemical shift difference of 27 ppm (δ ^{17}O (C-O-(S=S) **57** – δ ^{17}O (C-O-(C=O)) resulted probably from the nature of the carbon attachment (quaternary carbon *vs* primary carbon in methyl acetate) since the difference reported for *tert*-BuOH relative to MeOH was 29.2 ppm (**Table 19**). The chemical shift difference of 22.5 ppm for the singly-bonded oxygen in sulfites (**240** *vs* **219b**) was once again attributed to the carbon attachment. The ^{17}O resonances for the sulfonyl oxygen for **219b** and **240** were within reasonable range for comparison with the one found for dimethyl sulfite $(MeO)_2S=O$. While the resonance for the

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152. C. Rodger, N. Sheppard, H.C.E. McFarlane and W. McFarlane, *NMR and the Periodical Table*, Academic Press, London, 1978, p.396

singly bonded oxygen in **219b**, **240** and **57** compared to each other, being adjacent to a multiple bond (152.4, 151.8; 174.9, 174.3 and 165), the most striking difference was the one for **218b** compared to **57**; the absolute difference value was 131.2 ppm, suggesting the absence of structural equivalence in that particular case! This was strong additional evidence that compounds **218** might be linear in solution as well. This proposed situation was corroborated with theoretical ^{19}F and ^{17}O resonance calculations (F-S-S-F *vs* $F_2S{=}S$ and MeO-S-S-OMe *vs* $(MeO)_2S{=}S$) where the chemical shift differences were 196 and 87-111 respectively with the branch-bonded isomer sitting at lower field in both cases.[153a]

Table 19. ^{17}O Chemical Shifts

Compound[a]	δ (ppm)	Compound[b]	δ (ppm)
H_2O	0	218b	33.8 (CH_2-O-S)
Et-NO_2	600	219b	187.5 (S=O)
MeOH	37		152.4, 151.8 (CH_2-O-S)
i-PrOH	39	57	165.0 (C-O-(S=S))
tert-BuOH	66	240	221.6 (S=O)
Et_2O	12		174.9, 174.3 (C-O-S)
i-Pr_2O	61		
$Me_2C{=}O$	572		
$Me_2S{=}O$	17		
$(MeO)_2S{=}O$	113, 115 (Me-O-S)		
	174, 176 (S=O)		
$(MeO)_2SO_2$	101, 102 (Me-O-S)		
	145, 150 (SO_2)		

a) Ref. 152; b) ^{17}O NMR (40MHz, acetone-d_6) at T= 19.8°C using 300 MHz operating frequency.

Since both isomers were not clearly distinguished and different evidence pointed in two different directions, a comparative, exhaustive analysis including Raman, IR (solid and solution) and UV was carried out. The thionosulfite **57** and branch-bonded isomers for **218** were expected to deliver medium-intense signals in the IR, while linear isomers for **218** were expected to show strong bands in the Raman with both at somewhat different wavenumbers.

153. a) Private communication from Dr. J.P. Snyder presently at Emory University, Atlanta, Georgia; b) MM3 conformational analysis of **218a** followed by single point Becke3LYP/3-21G*/GIAO calculations of the proton chemical shifts of low energy conformations relatively to TMS; GAUSSIAN 94, M.J. Frisch et al., 1994; A.D.J. Becke, *J. Chem. Phys.*, **98**, 5648 (1993).

3.2.6 Infrared, Raman and UV Studies of 218a-b and Related Structure

In general, Raman excitation depends on bond polarizability changes during the vibration, while IR absorption depends on bond dipole moment changes. For example, weak IR absorption lines (e.g., S-H, C-S, $R_2C=CR_2$, -CN stretch) become strong Raman lines, and vice-versa. As a rule of thumb, symmetrical vibrations with a small oscillating dipole are strong in the Raman and weak in the IR; antisymmetrical vibrations are strong in the IR and weak in the Raman. The low-frequency modes are assigned to bonds with weak force constants and heavy atoms, to torsional modes and lattice vibrations of solids.[154]

The Raman spectrum of elemental sulfur S_8 was published in 1964[155a] and any signals below 250 cm^{-1} were attributed to ring deformation and torsion. The one for nitrobenzene was published in 1961[155b] and based on this assignment, we were able to apply an addition-iteration process from which the interesting group frequencies were assigned based on a qualitative analysis of related compounds. From the pool of compounds chosen was 4-nitrobenzene disulfide **285**, 4-nitrobenzyl thiol **223**, 4-nitrobenzyl disulfide **254** and tetrasulfide **226**, 4-nitrobenzyloxy benzyl trisulfide **243**, bis(4-nitrobenzyloxy) disulfide **218b**. Each individual powder Raman spectrum is reproduced in **Appendix VII**. For disulfide **285**, the stretching mode for S-S was found at 473.1 cm^{-1}. Generally, the literature indicates the stretching mode for a linear S-S bond at around 500 cm^{-1}. More specifically, Steudel reported that the radical anions $(S_2)^-$ and $(S_3)^-$ have been identified by Raman spectroscopy with values of 600 and 533, 580 cm-1 respectively.[119b] Lately, it was found that the vibrational wavenumbers were pratically identical for *all-cis*, *cis-trans* and *all-trans* rotamers of H_2S_4 in the IR and Raman spectra; ν(SS): 487, 484, 450; δ(SSS): 225, 184; τ(SSSS): 77 cm^{-1}.[143b] On this basis, the ν(SS) band at 527 cm^{-1} for the disulfide **254** and the ν(SS) bands at 442.5 and 488.3 cm^{-1} for the tetrasulfide **226** were identified. For the structure related to **218b** and **243** , the literature[4] has reported 526 and 717 cm^{-1} for ν(SS) and ν(SO) respectively in ROSSOR (R = *i*-Pr). In the same paper they reported ν(SS): 425, 442, 472, 492 and ν(SO): 724 cm^{-1} for RO-S_9-OR **(54)**. We are reporting for bis(4-nitrobenzyloxy) disulfide **218b** ν(SS): 525.3 and ν(SO): 682.1 and 645.7 cm^{-1}, and for 4-nitrobenzyloxy benzyl trisulfide **243** we report ν(SS): 461.3 and 484.5 cm-1 and ν(SO): 729.6 cm^{-1}.

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154. H.J. Sloane, *Appl. Spectrosc.*, **25**, 430 (1971).

155. a) D.W. Scott, J.P. Mc Cullough and F.H. Cruse, *J. Molec. Spectroscopy*, **13**, 313 (1964); b) J. H.J. Green, *Spectrochim. Acta*, **17**, 486 (1961); c) R. Steudel, *Z. Naturforsch.*, **27b**, 469 (1970).

The vibrational frequencies were calculated for the HO-S-S-OH conformers (ν(SS): 495-502 cm^{-1} and ν(SO): 737 and 758 cm^{-1}) and the isomer HO-(S=S)-OH (ν(SO): 793 and 811 cm^{-1}).[134] More recently, the gas-phase vibrational spectrum of $CH_3OSSOCH_3$ was published.[136] The IR and Raman wavenumbers for ν(SS) and ν(SO) are reported in **Table 20** along with the experimental values for **218a-b**, thionosulfite **57** and corresponding sulfite **240**. The closest related structure to the thionosulfite **240** reported was the claimed **225** $Cl_2S{=}S$ from N_2 matrix with ν(SS): 698.6 cm^{-1},[123c] and the ν(SS): 716 cm^{-1} for S_2[155c]. Density functional *ab initio* geometry optimizations (Becke3LYP/6-311G*) predicted ν(SS) at 639 and 643 cm^{-1} for $(MeO)_2S{=}S$ and **57**.[153]

Table 20. Observed Vibrational Data For MeO-S-S-OMe, 218a-b 54 and 240; wavenumbers in cm^{-1}

Compound	Infrared[c] solid	Infrared[c] solution	Raman powder	Raman solution	assignment[a]
$CH_3OSSOCH_3$[b]	688 m		684 vs	684 vs	ν(SO) i.p.
	662 s		667 vs	656 m	ν(SO) o.o.p.
	527 vw		525 s	530 vs	ν(SS)
218a[c]	669.4	[d]	695 w	too weak	ν(SO) i.p.
		[d]	660 m	too weak	ν(SO) o.o.p.
		526.2 w	527 ms	529 m	ν(SS)
218b[c]	678.8 w	[d]	682.1 vw	[d]	ν(SO) i.p.
	642.2 m	640.6 m	645.7 w	[d]	ν(SO) o.o.p.
	524.2 vw	527.7 vw	525.3 vw	530 vw	ν(SS)
57[c]	672.8 m	668.1 m	674.8 m		ν(SO)
	650.1 s	653.4 m	652 s		ν(SS)
	605.5 w	605.7 w	607.3 vw		ν(SO)
	561 vw		562.7 m		ν(SO)
240[c]	1217 vs		1202.2 s		ν(S=O)
			684.5 vs		ν(SO)

a) i.p. means in plane and o.o.p. means out of plane; b) Gas IR, Raman solid -120°C and neat liquid solution; c) Nujol-KBr and $CHCl_3$ solution for IR, Raman powder and $CHCl_3$ solution; d) Peaks are hidden under solvent peak.

The S-S stretching mode in thionosulfite **57** gave rise to a strong absorption both in the IR and Raman at *ca.* 650 cm^{-1} while the same mode was absent at that wavenumber for compounds **218a-b** (*ca.* 525 cm^{-1}) both for IR and Raman. However, the S-O stretching mode for **218a-b** also gave rise to weak absorption in the same region of ν(SS) for **57**. The wavenumbers for the S-O and S-S stretching modes in **218a-b** were not altered very much by going from powder to solution Raman. It seems that if compounds **218** were branch-bonded in solution, the intensity of the band at *ca.* 650 cm^{-1} would be very clear in both the IR and Raman. Therefore,we can confidently suggest that the structure for **218** is linear in the solid state and in solution.

The UV analysis of **218a-c** and **e** (4-H, NO_2, Cl and CH_3), **219b** (sulfite), **226** (tetrasulfide), **243** (oxy trisulfide), **57** and **240** (cyclic thionosulfite and sulfite) and benzyl disulfide **285** as chloroform solution were compared to pentane solutions of **218a**, **57** and **240 (Table 21)**. Solvent polarity affects the absorption characteristics, in particular, λ_{max}, since the polarity of a molecule changes when an electron is moved from one orbital to another. For example, the n -> π* absorption of acetone is shifted to shorter wavelength when the solvent is changed from hexane (279 nm) to ethanol (272 nm) to water (264.5 nm). This hypsochromic, or blue shift, is actually a measure of the strength of the hydrogen bond in polar solvents; the energy associated with the absorption in water is about 126 kcal mol^{-1}, and in hexane about 121 kcal mol^{-1}, this gives an energy change of about 5 kcal mol^{-1} which agrees well with the energy associated with a hydrogen bond.[156]

The nitro group absorbs at *ca.* 270 nm and is a very good absorbing chromophore (n -> π* transition with a high extinction coefficient value (ε), in compounds **218b**, **226** and **243**). We assume that compound **218b** was highly solvated in chloroform and that solvation and pressure broadening[156a] led to line broadening that prevented the identification of the S-S bond. This "blurring" was not observed in the other substituted benzyloxy disulfides **218a**, **c** and **e**. The spectral transition due to S-S n -> σ* was clearly identified (substitution by H, Cl, CH_3 instead of NO_2). For **218a**, the observed bathochromic shift (or red shift) on going from pentane to chloroform is best explained as a solvent effect where the solute-solvent interactions greatly diminishes on going from $CHCl_3$ to pentane, thus leaving the non-bonding electrons at lower energy level (ground-state) and giving rise to a

156. a) H.H. Jaffé and M. Orchin, *Theory and Applications of Ultraviolet Spectroscopy*, Wiley, New York, 1962; b) A.I. Scott, *Interpretation of the UV spectra of Natural Products*, Pergamon Press, New York, 1962; c) R.M. Silverstein and G.C. Bassler, *Spectrometric Identification of Organic Compounds*, Wiley, New York, 1967; d) D.J. Pasto and C. Johnson, *Organic Structures Determination*, Prentice Hall, New York, 1969.

maximum at a shorter wavelength. The experimental value of 196 nm was in full agreement with the calculated ones (194 nm (ε = 24000) and 198 nm (ε = 12000)).[157] The branch-bonded cyclic thionosulfite **57** was affected to a lesser extent in pentane; an additional band was found at 202 nm. Most likely, the bands observed in pentane are all associated with transitions (n –> π and n –> π^*) in the S=S functionality as it was calculated[157] (265nm (ε = 500), 241nm (ε = 2500) and 209 nm (ε = 6300)). The corresponding sulfite **240** showed that the sulfoxide (S=O) n –> π^* transition was shifted to a longer wavelength in pentane; this hypsochromic shift was a clear indication of strong solute-solvent interactions.

Considering the UV analysis of **218a**, **57** and **240** in pentane solution, the bands at 250 (ε = 2506) and 311 nm (ε = 195) for **57** are believed to be characteristic for the branch-bonded arrangement of the sulfur-sulfur bond along the **OSSO** subunit for "thiono" system, while the band at 196 nm (ε = 37300) for **218a** is characteristic of linear bonding (**figure 21**). It seems that hindered rotation is responsible for the diastereotopicity of the benzylic protons in compounds **218**. The proposed intramolecular process involving the migration of one OCH_2-C_6H_4-NO_2-*p* group from S1 to S2 probably *via* a three-membered ring transition state in **218b (Scheme 29)** is deemed a process to be to energetically demanding at room temperature (40.3 kcal mol^{-1} for MeOSSOMe)[157]. The possibility of demonstrating the existence of both torsional enantiomers for compounds **218** was further investigated.

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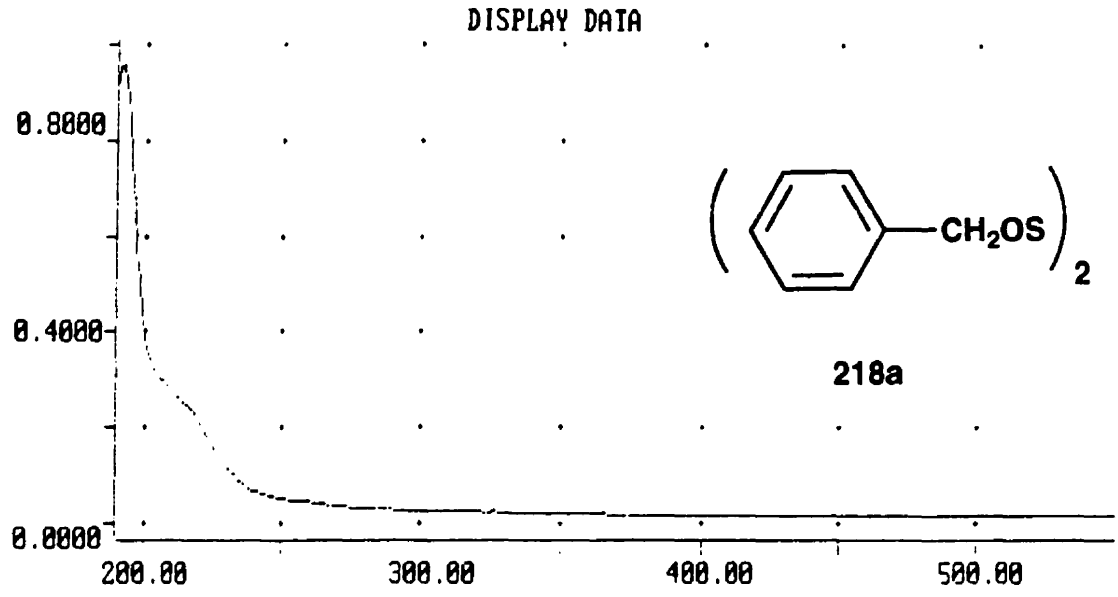
157. Private communications from Dr. J.P. Snyder (Emory University): values were calculated from the optimized isomers at the MP2/6-311G(3d) and Becke3LYP/6-311G* level of theory; GAUSSIAN 94, M.J. Frisch et al., 1994; A.D.J. Becke, *J. Chem. Phys.*, **98**, 5648 (1993); P.J. Stevens, F.F. Devlin, C.F. Chablowski and M.J. Frisch, *J. Phys. Chem.*, **98**, 11623 (1994); G. Rauhut and P. Pulay, *J. Phys. Chem.*, **99**, 3093 (1995); A.P. Scott and L. Radom, *J. Phys. Chem.*, **100**, 16502 (1996).

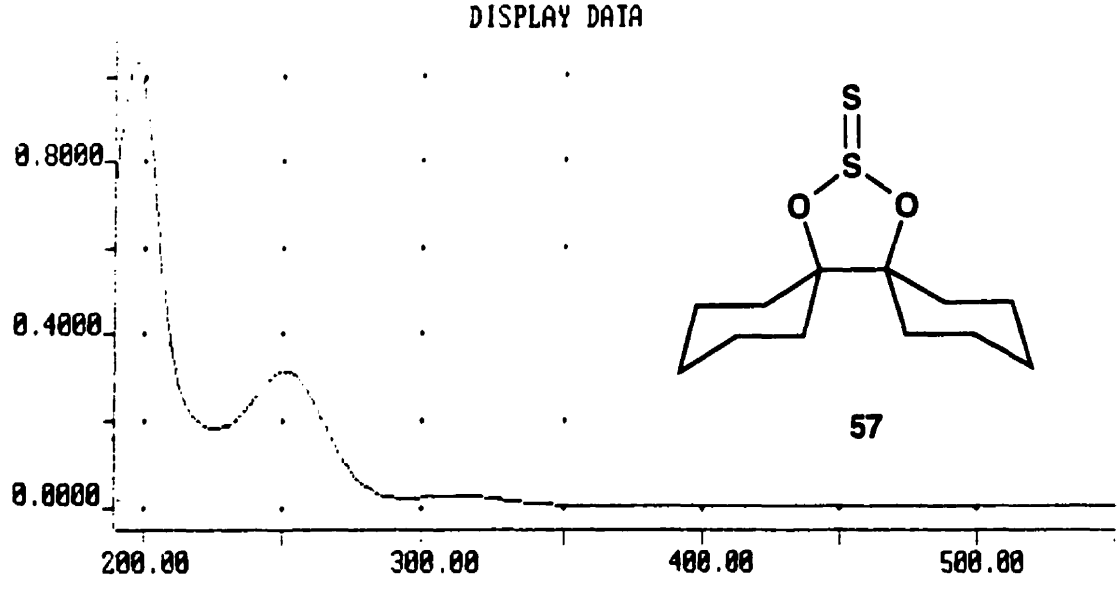
Table 21. Results of UV Analysis[a]

Compound	$^{\alpha}\lambda_{max}$ (nm)	ε L mol^{-1} cm^{-1}	assignment
285	241	15200	n –> σ* (S-S)
218b	269	47874	n –> π* (NO_2)
218c	241	13911	n –> σ* (S-S)
218e	241	13259	n –> σ* (S-S)
218a	240	8805	n –> σ* (S-S)
	196 (pentane)	37300	n –> σ* (S-S)
226	276	41589	n –> π* (NO_2)
	233	16152	n –> σ* (S-S)
	232	16826	n –> σ* (S-S)
243	267	27066	n –> π* (NO_2)
	246	22515	n –> σ* (S-S)
	242	23327	n –> σ* (S-S)
57	307	379	transitions originating from S=S bond
	311 (pentane)	195	
	255	3401	
	250 (pentane)	2506	
	202 (pentane)	4888	
240	240	16	n –> π* (S=O)
	276 (pentane)	518	n –> π* (S=O)
	204 (pentane)	1595	n –> π (S=O)[156a]
	191 (pentane)	2118	n –> π (S=O)[156a]
219b	265	38363	n –> π* (NO_2)
	235	14859	n –> π* (S=O)

a) Solution in $CHCl_3$ otherwise in pentane where indicated.



218a



57

Figure 21: UV Spectra of 218a and 57 in pentane

3.2.7 ^{1}H NMR Lanthanide-Induced-Shifts for 218a,b and 226

For disulfides R-S-S-R, the barrier to rotation about the S-S bond is generally so low there is a racemic mixture of rapidly equilibrating enantiomers at room temperatures. Like disulfides, compounds **218** have dihedral angle values in the 76-92° range (**218b**: -85.6°; **218c**: 76.85°) and can be defined as [+]- and [-]-torsional isomer ("torsional enantiomers") based on the right or left "handedness" turn with an axial transition away from the observer (**Figure 22**).

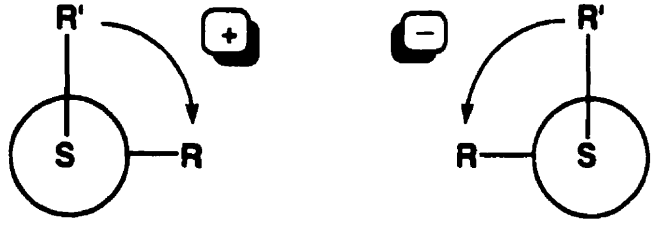


Figure 22: Enantiomers for a Rigid R-S-S-R Dihedral Angle

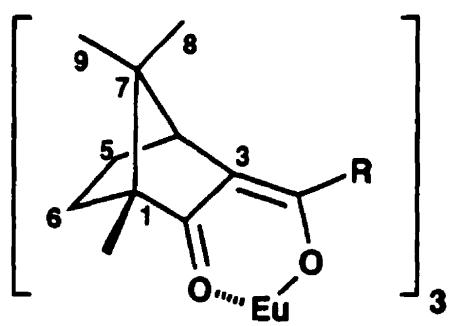
The related tetrasulfide **226**, benzyloxy trisulfide **243** and sulfoxylate **246b** were found to have a low barrier to rotation along the S-S and S-O bonds since the ^{1}H NMR pattern ($CDCl_3$) were perfect singlets for the adjacent benzylic protons (**226:** 4.13; **243:** 4.95, 4.17 and **246b:** 5.16 ppm). The barriers to rotation for the interconversion of torsional enantiomers in compounds **218a-b** were calculated to be at least 17.3-17.8 kcal mol^{-1} (T_c of *ca.* 75-80 °C) using the Eyring equation **(eq.39)** and assuming equal populations of the *syn*-and *anti*-conformers **(Figure 8)**; the rate constant (k_c) at the coalescence temperature (T_c) was calculated from **eq.40** where $\Delta\delta_{AB}$ is the measured shift difference (in Hertz) between the two exchanging nuclei at the slow exchange limit.[158] The ABq pattern for **218** suggested the possibility of the isolation of each separate torsional enantiomer (possibly at low temperature).

$$k_c = \frac{K_B T}{h} \exp(-\Delta G^{\ddagger}/RT) \qquad \textbf{(eq. 39)}$$

158. G. Binsch and H. Kessler, *Angew. Chem. Int. Ed. Engl.*, **19**, 411 (1980).

where $k_c = \pi \Delta\delta_{AB}/2^{1/2}$ (eq. 40)

The formation of labile diastereomeric complexes using chiral lanthanide shift reagents gave credence for such separation. Complexation changes the chemical shifts of the substrate according to the distance from the lanthanide ion (Eu, Yb and Pr) and the orientation relative to the axis of symmetry.[159] Compounds **218a,b** were treated with sequential additions of tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato] europium (III) **286** ($Eu(hfc)_3$), because the reagent is known to induce large paramagnetic shifts in the ^1H NMR spectrum of molecules bearing lone-pair functionalities. Lanthanide-induced shifts (LIS) were observed for the benzylic protons of **218a,b** but not in the case of tetrasulfide **226**.



286: R = C_3F_7
287: R = CF_3

The chemical shift difference between the ABq for the racemic mixture (both torsional enantiomers) and the prefered diastereomeric complex formed from one of the torsional enantiomers and the chiral reagent was not expected to be tremendously different. Modifications of the ABq of **218b** were observed only when 2.7 molar equivalents of reagent were added [^1H NMR (300 MHz, $CDCl_3$)]: 4.975, 4.938, 4.866, 4.827 evolved to 4.997, 4.992, 4.959, 4.953, 4.888, 4.827 ppm) with poor resolution. In **218b**, the nitro groups were believed to interact with the europium Lewis acid prior to interacting with the OSSO functionality. In the case of **218a**, 0.34 eq was needed to deliver a similar splitting pattern of the ABq [^1H NMR (500 MHz, $CDCl_3$)]: 4.93, 4.892, 4.819, 4.781 (ABq, 4H) which evolved to 5.011, 5.004, 4.988, 4.981 (2H); 4.904, 4.881 (2H) ppm) (**Figure 23**). Similar results were obtained at 300 MHz. Upon addition of more reagent (up to 1.1eq), no further splitting was recorded, and the resolution factor was fading due to the paramagnetic nature of the reagent. At high concentration, the loose electrons start to act as radicals. In the

159. D. Springer, *NMR Shift Reagents*, Sievers Ed., Academic Press, 1973.

presence of $Pr(hfc)_3$ and tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorato-]ytterbium (III) **287** ($Yb(tfc)_3$) , no splitting was detected, only a lowering of resolution of the ABq.

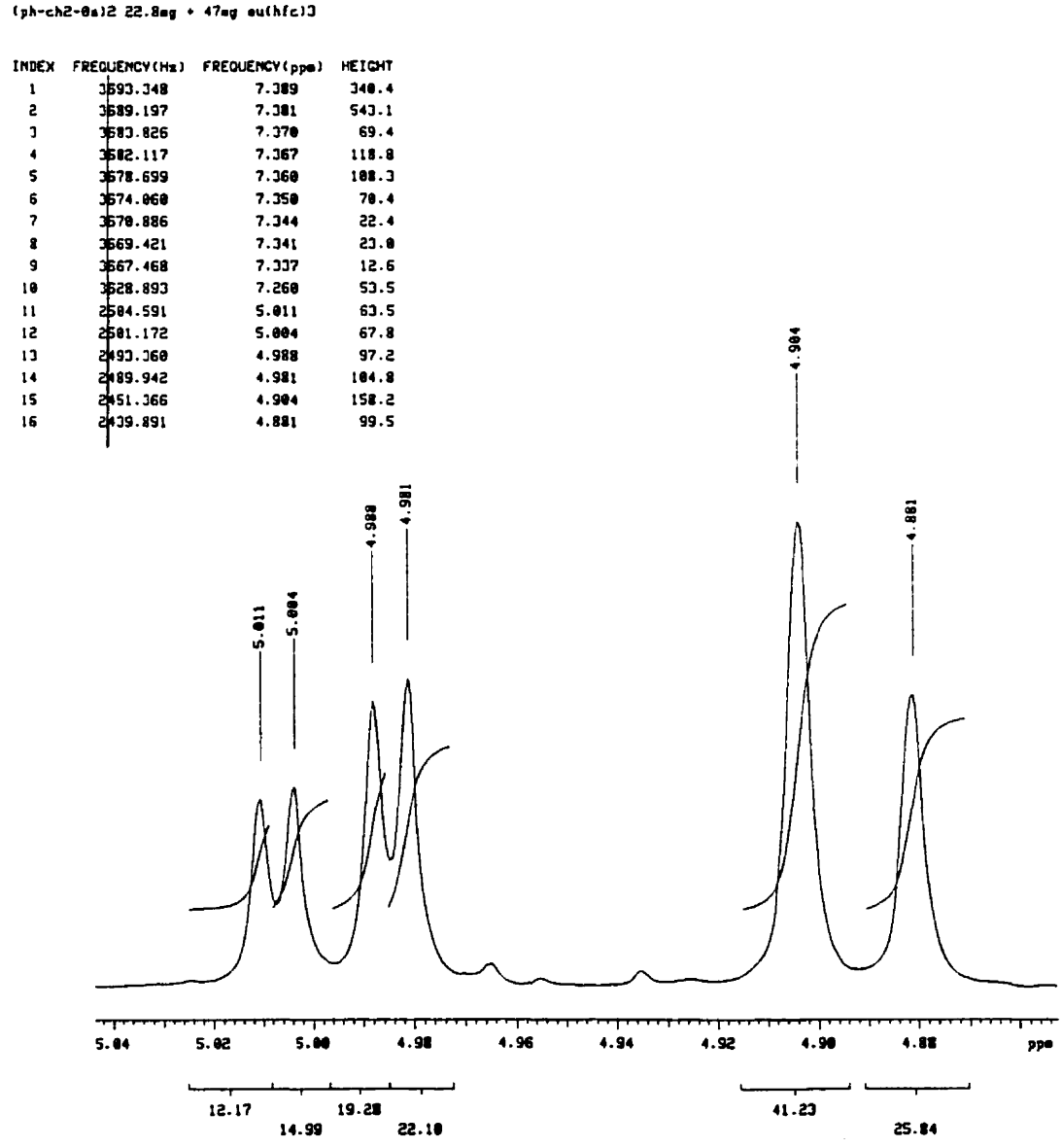


Figure 23: ^1H NMR ($CDCl_3$) 500 MHz of 218a + $Eu(hfc)_3$ (0.34 eq)

The solubility of the reagent **286** suggests that specific coordination of the metal complex to the solute molecules did occur. The questions are how, and why the doubling on only one of the two legs of the ABq? The reagent probably complexes to one of the oxygens and maybe to the sulfur to influence one CH_2, and is too far away to influence the second CH_2 group. Possibly the skewness of the **OSSO** subunit prevented the other CH_2 group to be influenced; interestingly, the peak doubling was reversed upon dilution with $CDCl_3$. Even if we were not able to accomplish the full resolution of the two ABq (AB and A'B'), the evidence obtained supports the presence of torsional isomers instead of a branch-bonded isomer.

Considering only the 4-nitrobenzyloxy group (p-NO_2-C_6H_4-CH_2-O-), the geminal benzylic protons are enantiotopic (proR-H and proS-H) because they are attached to a prochiral carbon and are in principle indistinguishable by ^1H NMR. However, they become diastereotopic H_A and H_B by virtue of the hindered rotation along the S-S bond of the **OSSO** subunit linear arrangement thus being left in an overall asymmetric conformational environment whether its the [+][160a] -torsional or [-]-torsional "enantiomer" of **218**. This effect of hindered rotation giving rise to [+]- and [-]-torsional isomers is described as "atropisomerism".[160b] These [+]- and [-]-torsional isomers, resulting from the phenomenon of atropisomerism, can be named "atropisomers" and are not distinguishable by NMR.[160c] However, compounds with adjacent benzylic chiral center to the **OSSO** subunit were believed to give rise to diastereomers.

3.3 More Acyclic Alkoxy Disulfides

Thompson reported that the observed order of stability of dialkoxy disulfides was secondary > primary > allyl.[1a] Esters of acyclic benzylic chiral secondary alcohols of known configuration were prepared and we found that, at room temperature under nitrogen, they were less stable than **218**. The esters of sec-phenethyl alcohol (racemic and (R)-) **288** and 1-naphthyl-ethanol (racemic and (S)-) **289** were prepared according to **eq.2**. We found that starting with the racemic alcohol and following with the enantiomerically pure (R)-**288**, that

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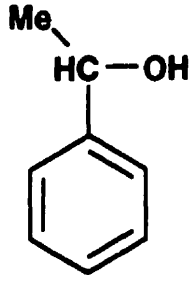
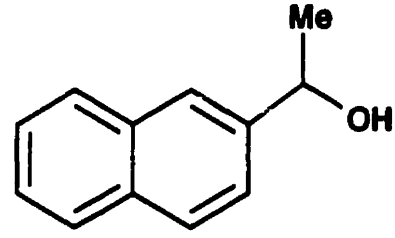
160. a) The squared brackets represent the chirality for the rigid O-S-S-O dihedral angle; in the case of chiral adjacent group attached to the O-S-S-O unit, the nomenclature (R)- and (S)- is employed; b) E.L. Eliel, *Stereochemistry of Organic Compounds*, S.H. Wilen Eds., John Wiley & Sons Inc., New York, pp. 1142-1163 (1994); c) Attempts to separate the enantiomers of **218b** on a chiral HPLC column at low temperature were unsuccessful; Dr. J.P. Snyder, Emory University, private communication.

the rotational or torsional [+]- and [-]- diastereomers were distinguishable using ^{1}H and ^{13}C NMR spectroscopy (**Table 22**). The hindered barrier to rotation along the S-S bond, previously evaluated at *ca.* 18 kcal mol^{-1}, permitted the observation of four diastereomeric conformers (**Figure 24**, two dl pairs (I and II; III and IV) and two other diastereomers (V and VII)).



288



289

Table 22. ^{13}C and ^{1}H NMR[a] **Results for the Identification of Esters of 288**

Compounds	δ (CH) (ppm)	δ (CH_3) (ppm)	δ (CH) (ppm)	δ (CH_3) (ppm)
(rac)-288	69.99	24.96	4.86, 4.84, 4.82, 4.80	1.49, 1.47
(rac)-OSSO-(rac)	83.50, 83.30 82.37, 82.27	23.61, 23.41 23.03, 22.65	see figure 25 for 4 quartets	1.66, 1.65 1.64, 1.63 1.61, 1.60 1.59, 1.58
(R)-OSSO-(R)	83.27, 82.24	23.41, 22.64	5.06, 5.04, 5.02, 5.00 4.94, 4.92, 4.90, 4.88	1.67, 1.65 1.62, 1.60

a) ^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$).

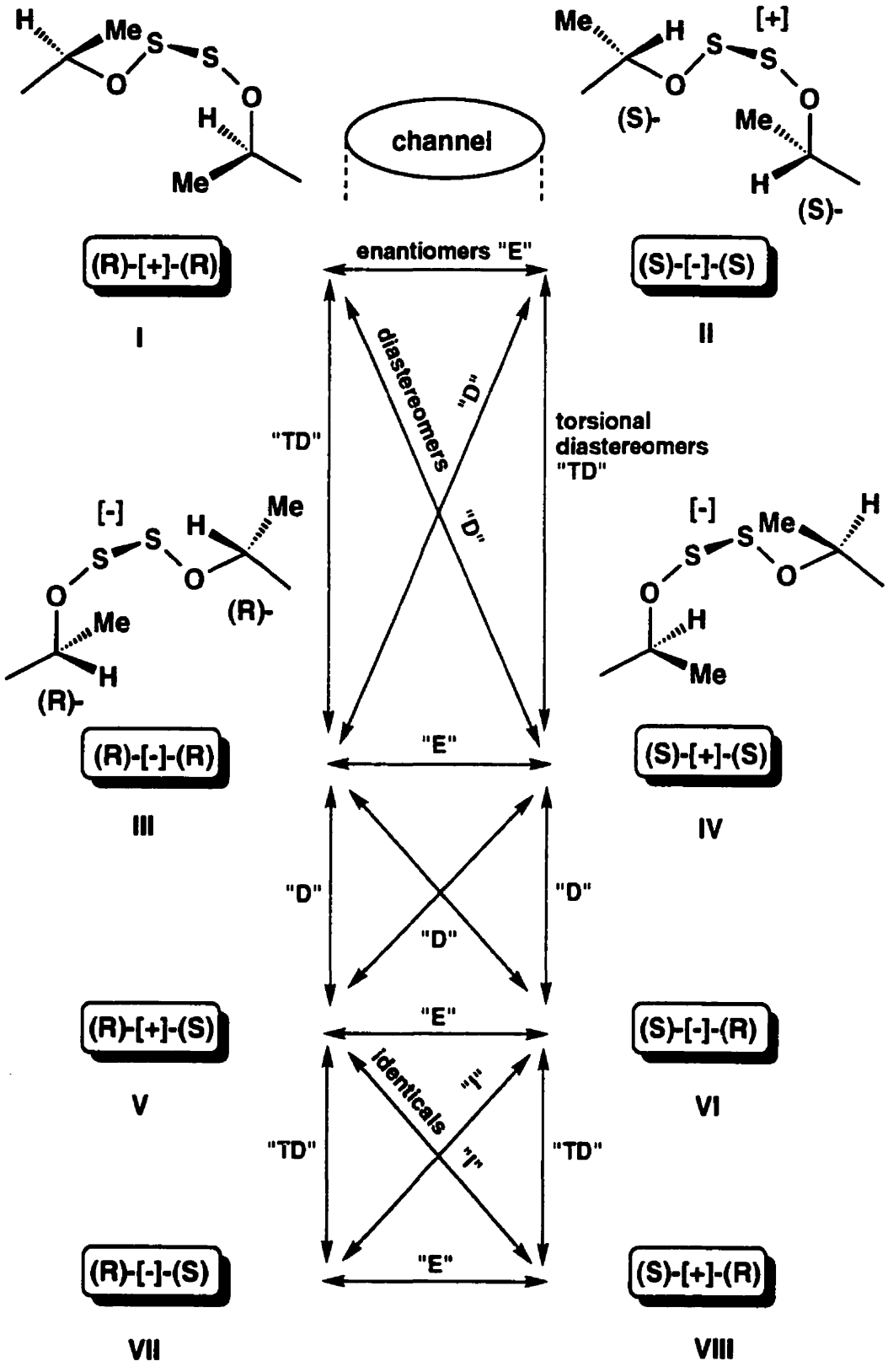


Figure 24: Stereoisomers of the OSSO Ester of (rac)-288

When chiral alcohol **288** was employed, ^{1}H and ^{13}C NMR spectra of (R)-OSSO-(R) showed two sets of signals for CH (two quartets) and CH_3 (two doublets) due to the presence of the two torsional diastereomers (R)-[+]-(R) and (R)-[-]-(R), which are not superimposable and seem to be present in equal amounts. The analytical considerations of the (rac)-OSSO-(rac) were simplified; the doubling of the two resolved quartets (for CH) and the appearance of two more doublets (for CH_3) were due to the presence of the other diastereomers (R)-[+]-(S) and (R)-[-]-(S) (**Figure 25**). The same rationale was applied to the alcohol **289** where this time the ester from the enantiomerically pure (S)-alcohol was prepared (**Table 23, Figure 26**). The esters prepared from the racemic and (R)-**288** were found to be more stable, at room temperature under N_2, than the esters from **289**. However, both types of ester could be kept at -30 °C, under N_2, for months in a dark bottle in the freezer.

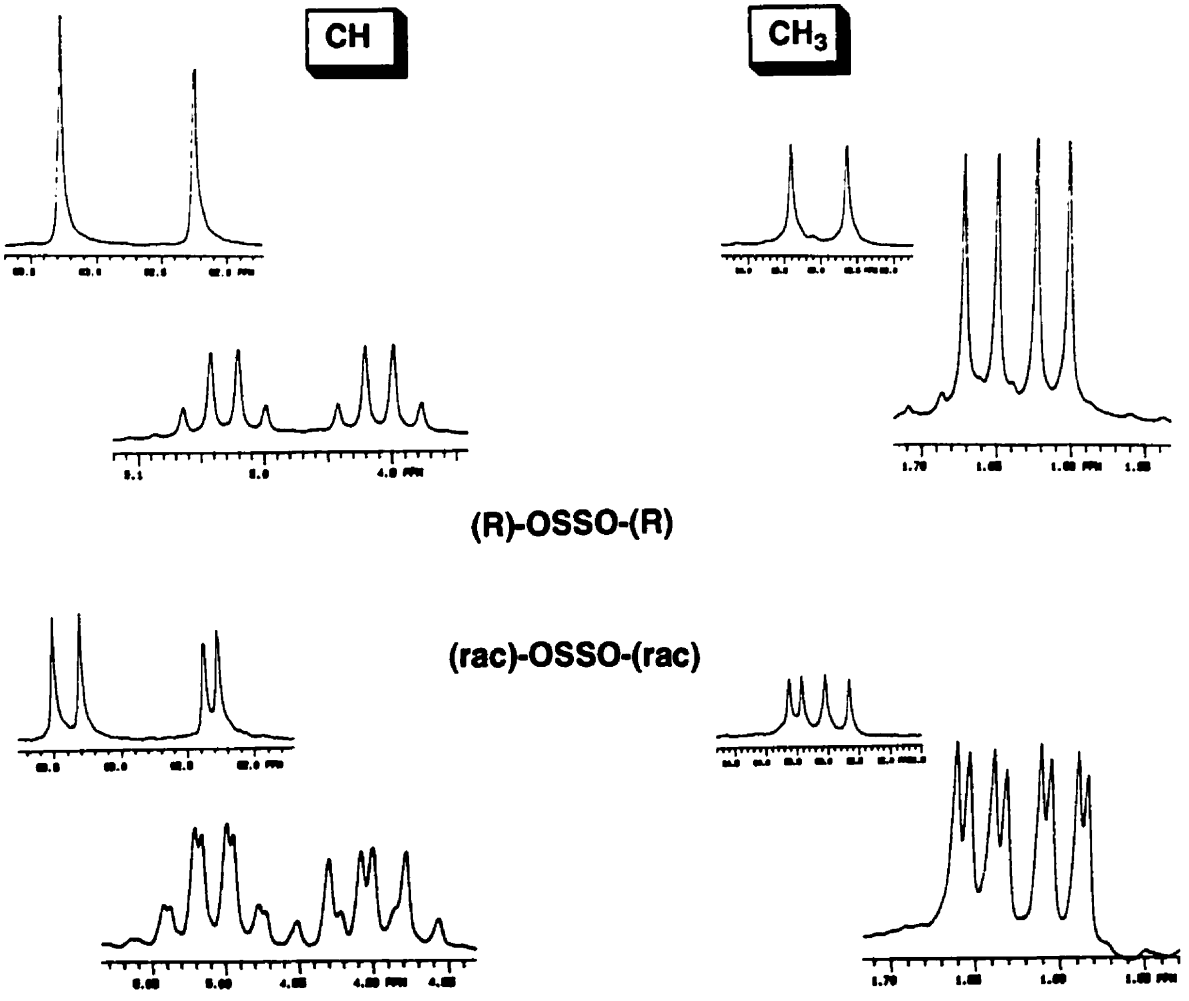


Figure 25: ^{1}H NMR Spectra for (R)- and (rac)-Ester of 288

Table 23. ^{13}C and ^{1}H NMR[a] Results for the Identification of Esters of 289

Compounds	δ (CH) (ppm)	δ (CH_3) (ppm)	δ (CH) (ppm)	δ (CH_3) (ppm)
(rac)-289	70.49	25.11	5.10-4.99 (two overlapping quartets)	1.59, 1.56
(rac)-OSSO-(rac)	83.56, 83.44 82.54, 82.45	23.68, 23.40 23.14, 22,93	see Figure 26	see Figure 26
(S)-OSSO-(S)	83.48, 82.48	23.43, 22.97	5.14, 5.12, 5.10, 5.08 5.03, 5.01, 4.99, 4.97	1.65, 1.63 1.62, 1.60

a) ^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (300 MHz, $CDCl_3$).

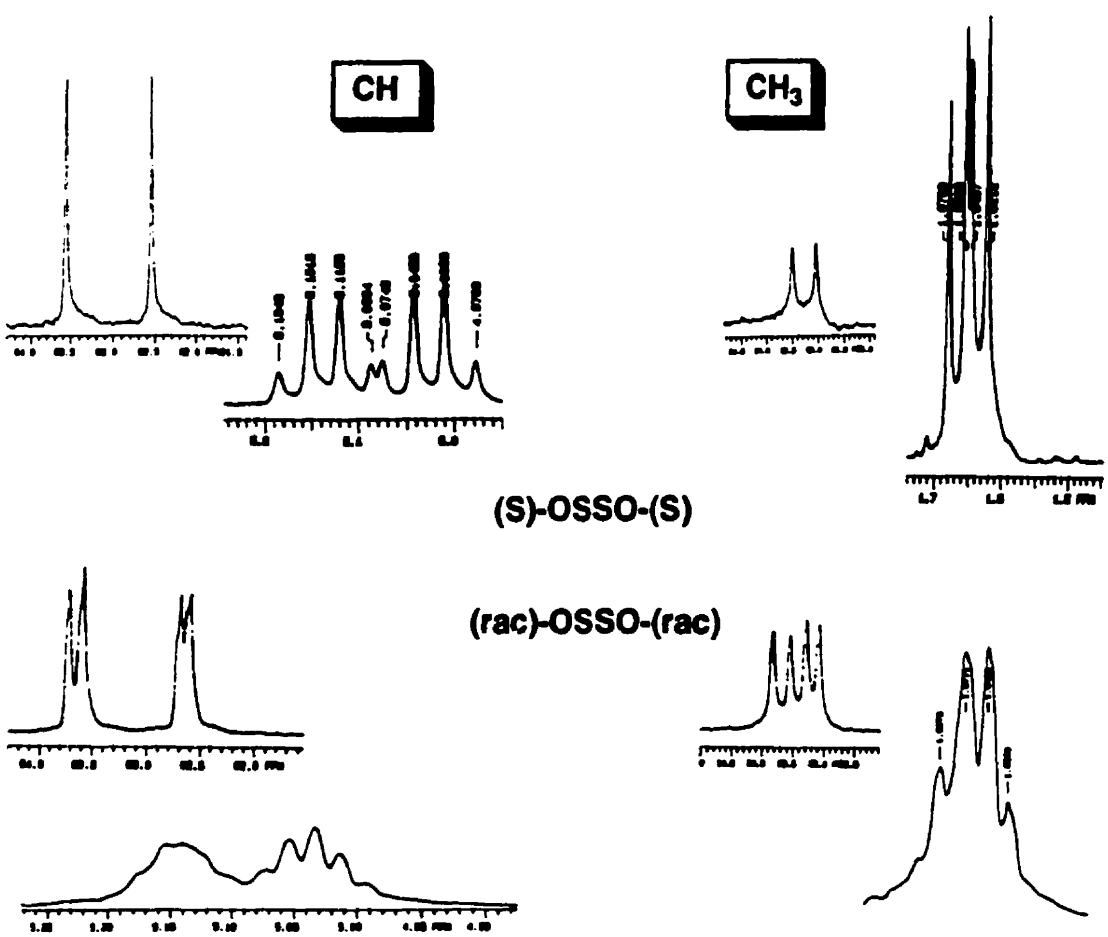
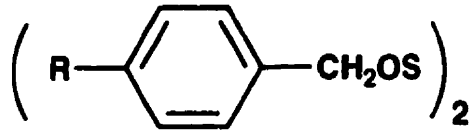
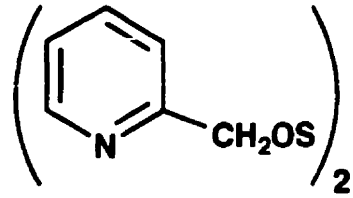


Figure 26: ^{1}H and ^{13}C NMR Spectra for (S)- and (rac)-Ester of 289

Other achiral 4-substituted benzylic esters were prepared and their stability was found to be related to the substitution pattern. For example, the dialkoxy disulfides **218f-g** and **290** were prepared and yields reported (**Table 24**). The crystalline stable ester **218f** was isolated, using flash column chromatography techniques, in 63% and judged as being moderately stable on silica gel. The other two esters were very unstable on silica gel: in the case of **218g**, we could only obtain from the column, 5% of the product and it decomposed to the corresponding alcohol, aldehyde and S_8 according to **Scheme 1**; the ester **290** was not very stable on SiO_2, and once isolated in pure form, it was more stable than **218g** but was found to decompose in a matter of hours at room temperature.



218f: R = CO_2Me
g: R = O(C=O)Me



290

Table 24. Results on the Preparation of 218f-g and 290

ROSSOR	Yield (%)	m.p. (°C)	δ (CH_2) (ppm)[b] ^1H; ^{13}C
218f	63	44.5-46	4.96, 4.90, 4.83, 4.77; 75.78
218g	25[a]	oil	4.90, 4.85, 4.79, 4.73; 75.80
290	78[a]	oil	4.99, 4.93, 4.87, 4.73; 77.00

a) NMR yield since very unstable on silica gel; b) ^1H NMR (300MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$).

Interestingly, using ^1H and ^{13}C NMR, the composition of the overall crude reaction mixture for **290** was found to remain constant when left for 14 hours at room temperature. Contrary to the other esters **218**, **290** seems to be stabilized in acidic media. We supposed that the nitrogen of the pyridinyl group was neutralizing the HCl present by forming the

pyridinium hydrochloride and therefore rendering the overall molecule less susceptible to decomposition and formation of sulfite **(Scheme 2)**. An extra proof of this was that the NMR of the crude showed only traces of sulfite (less than 3%).

3.4 General Commentary

Through the course of the discussion, a number of indicators pointed towards the existence of the isomeric thionosulfite of **218b** in solution. Although the X-ray structure of **218b-c** confirmed a linear arrangement of the S-S bond, the possibility of the branch-bonded one could never be completely erased. First, the similarity of the ^{1}H NMR spectral data between the series of dibenzyloxy disulfides **218** and the corresponding series of sulfites **219** suggests the structures to be parallel (O-S(=O)-O vs O-(S=S)-O). In the latter possibility, the chemical shifts for the benzylic protons would be expected to be upfield compared to their former as **Table 7** showed. However, the ^{13}C chemical shift difference would be expected to be smaller and in the same order of magnitude as the one found for **57** and **240** (12.12 **(218b – 219b)** >> 1.51 ppm **(57 – 240)**) even if one can argue about the intrinsic chemical nature of the carbon adjacent to the **OSSO** subunit (benzylic carbon *vs* quaternary carbon). Solid state ^{13}C CP MAS NMR of **218a-b** and **226** were recorded and compared with those carried out in solution. It is assumed to result from the same molecular arrangement both in the solid state and in solution for each case. The ^{1}H NMR thermal decomposition of **218b** was interesting from a synthetic point of view although no evidence could be extracted to distinguish one isomer over the other. The AB quartet was present from -70 °C to *ca.* 75 °C where coalescence was observed as well as decomposition to S_2 (source of S_2 as dienophile, *vide infra*), alcohol and corresponding aldehyde. Considering that the value of the relative energy of FSSF to $F_2S{=}S$ (0.2 kcal mol^{-1})[126b], HOSSOH to $(HO)_2S{=}S$ (-3.3 kcal mol^{-1})[143c] and $CH_3OSSOCH_3$ to $(CH_3O)_2S{=}S$ (2.3 kcal mol^{-1})[136a] are of the same order of magnitude and that thiosulfoxides should be stabilized by polar environments, compound **218b** was submitted to an ^{1}H NMR solvent study. However, the coexistence of both isomers was not detected in polar solvents. *Ab initio* calculations[153b] of the proton chemical shifts relative to TMS for **218a** have delivered values of 4.75, 4.59, 4.42 and 4.31 ppm for the AB quartet (experimental $CDCl_3$: 4.93, 4.87, 4.81 and 4.76 ppm), and by an MM3 calculation using the thionosulfite's conformations for **218a** have also provided an AB quartet in the same range (4.0-5.5 ppm). Strong evidence toward linear isomers for **218** was extracted from ^{17}O NMR spectroscopy using natural abundance of ^{17}O while comparing the

chemical shift differences among **218b**, **219b**, **57** and **240**. While the resonance for the singly-bonded oxygen in **219b**, **240** and **57** compared well to each other being adjacent to a multiple bond (152.4, 151.8; 174.9, 174.3 and 165), this same resonance was somewhat different on comparing **218b** to **57**; the absolute chemical shift difference value was 131.2 ppm, suggesting the absence of structural equivalence in that particular case. This was strong additional evidence that compounds **218** might be linear in solution as well.

Since both isomers were not clearly distinguished, a comparative analysis including Raman, IR (solid and solution) and UV was carried out. The S-S stretching mode in **47** gave rise to a strong absorption around 650 cm^{-1} in both the IR and Raman, while **218a-b** did not show absorption in that region, showing only medium to very weak absorption around 525 cm^{-1} in comparing from the Raman to the IR. Considering that the UV analysis of **218a**, **57** and **240** in pentane solution was meant to be used as an extra tool for comparison, we were able to establish that the bands at 250 (ε = 2506) and 311 nm (ε = 195) for **57** are believed to be characteristic for the branch-bonded arrangement of the sulfur-sulfur bond along the **OSSO** subunit for "thiono" system, while the band at 196 nm (ε = 37300) for **218a** was characteristic of linear bonding.

At this point, we felt that the distinction between branched and linear isomers was resolved and that new experimental spectroscopic values were defined. The S-S barrier to rotation along the **OSSO** subunit, evaluated at *ca.* 18 kcal mol^{-1}, was responsible for the diastereotopicity of the adjacent benzylic protons (atropisomerism). Contrary to disulfides, where the S-S barrier to rotation is too low, the rigidity of the S-S bond could be demonstrated; which produced, in effect an addition site of chirality in the molecule. Some evidence using the chiral lanthanide shift reagent $Eu(hfc)_3$ showed that a diastereomeric complex was formed, although the doubling of the ABq was not fully accomplished and resolved. However, the existence of the rotational diastereomers was demonstrated by ^{1}H and ^{13}C NMR for the chiral esters (R)-OSSO-(R) of **288** and (S)-OSSO-(S) of **289** by comparison to their corresponding racemic ester, since the S-S barrier to rotation gave rise to asymmetric induction **(Table 22 and 23)**. The torsional diastereomeric pairs (R)-[+]-(R)/(R)-[-]-(R) for **288** and (S)-[+]-(S)/(S)-[-]-(S) for **289** were not superimposable and showed two distinct signals in their ^{13}C NMR spectrum.

Two other 4-substituted dibenzyloxy disulfides were prepared **218f-g**. The behaviour and stability of **218f** (4-$MeCO_2$) was compared to **218b** (4-NO_2), while **218g** (4-Me(C=O)O) was compared to **218d** (4-MeO). It seems that substitution in the *para* position by an electron withdrawing group had an effect of stabilization for the overall molecule **218b** and **f**. The more peculiar ester **290**, made from the alcohol 2-pyridinyl carbinol, was stabilized in acidic media due to the formation of the HCl salt analogue of **290** bis(hydrochloride pyridinylium carbinoxy) disulfide; the salt free form was found to decompose, in the pure form at room temperature, to the corresponding alcohol, aldehyde and S_8.

CHAPTER 4: SOME CHEMISTRY ASSOCIATED WITH THE COMPOUNDS RELATED TO DIALKOXY DISULFIDES

4.1 Introduction

Significant comparisons were made with related compounds to establish, on firm grounds, the linearity of the **OSSO** subunit for 4-substituted benzyloxy disulfides both in solution and in the solid state. Some of these related compounds were never reported before. We have seen that the thermolysis of **218** gave the corresponding alcohol, aldehyde and S_2 that concatenates into S_8 in the absence of dienes (**Scheme1**), that sulfenate **233** was hydrolyzed to the sulfinate **236** (p.67) and that sulfoxylates **246b-c** isomerize to sulfinates **249b-c** at room temperature. The chemistry of compounds **218**, including S_2 and related trapping experiments, oxidation and desulfurization will be the topics of Chapter 5. The potential of the thionosulfite **57** and 4-nitro-benzyloxy benzyl trisulfide **243** as precursor for S_2 generation was never previously reported in the literature.

4.2 The Reaction of *p*-Nitrobenzyl *p*-Chlorobenzenesulfenate 233 to Sulfinate 236

The sulfenate **233** was never obtained; instead, the sulfinate **236** (81%) was isolated along with bis(4-chlorophenyl) disulfide **235** (92%), 4-nitrobenzyl chloride **235** (50%) and 4-nitrobenzyl alcohol **220** (26%) using column chromatography techniques. The acid catalyzed hydrolysis of alkyl arenesulfenates to sulfinates is known to proceed for concentrations of water that are smaller than 1%.[103b] A complex mechanism is proposed to rationalize the formation of sulfinate **236** along with the other compounds (**eq.41-46**). The yields were calculated based on **eq.45**, considering the formation of sulfenate **233** that follows the decomposition pattern to give **235**, **236** and **220**. The formation of thiosulfinate **292** followed **Scheme 31**, and the 4-nitrobenzyl chloride **235** was formed following **eq.46**. According to **eq.46**, the yield of alcohol **220** recovered should be *ca.* 76% (yield of **235** + yield of **220**). The yield of bis(4-chlorophenyl) disulfide **235** was somewhat higher than the other by about 10%, this being due to the excess 0.25 eq of 4-chlorobenzene sulfenyl chloride **229b** that was added. The oxidation of disulfides by halides to form sulfenyl halides is an equilibrium process that likely resulted in the formation of **235** (**eq. 47**).

$$\underset{233}{RSOR'} + H_2O \xrightarrow[\text{slow}]{HCl} \underset{291}{RSOH} + \underset{220}{R'OH} \qquad \text{(eq. 41)}$$

$$\underset{291}{2\,RSOH} \longrightarrow \underset{292}{RSS(=O)R} + H_2O \qquad \text{(eq. 42)}$$

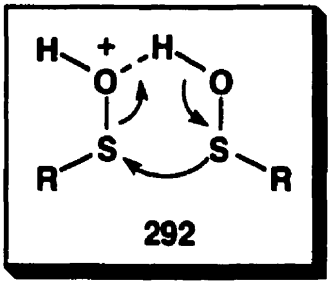
$$292 + \underset{233}{RSOR'} + HCl \longrightarrow \underset{293}{RSRS^{+}\,S(=O)R} + R'OH \qquad \text{(eq. 43)}$$

$$\underset{293}{293} + \underset{220}{R'OH} \longrightarrow \underset{234}{R_2S_2} + \underset{236}{RSO_2R'} + HCl \qquad \text{(eq. 44)}$$

$$\underset{233}{3\,RSOR'} + H_2O \xrightarrow{HCl} \underset{234}{R_2S_2} + \underset{236}{RSO_2R'} + \underset{220}{2\,R'OH} \qquad \text{(eq. 45)}$$

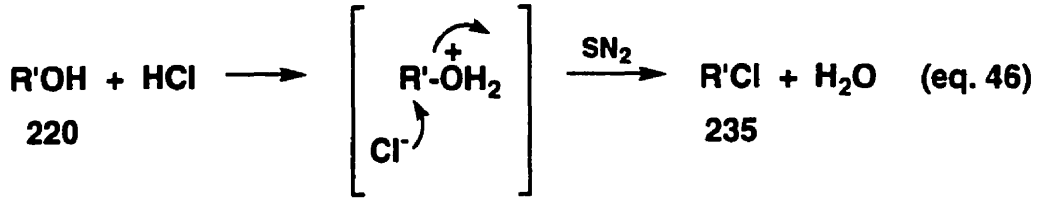
Where

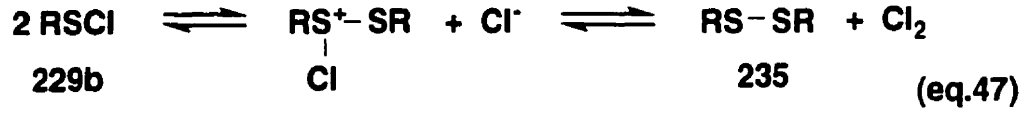
R = 4-Cl-C_6H_4
R' = 4-NO_2-C_6H_4-CH_2



292

Scheme 31



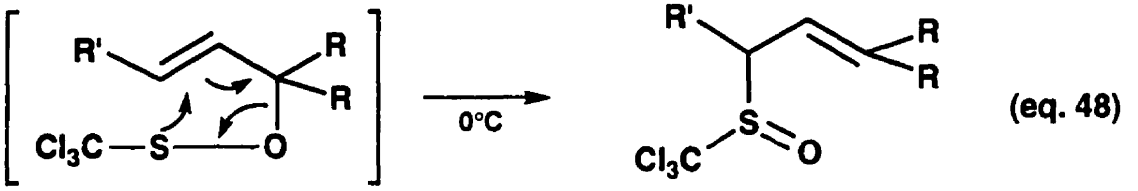


4.3 Some Chemistry of Sulfoxylates

4.3.1 Introduction

The chemistry of sulfoxylates RO-S-OR was briefly discussed in the context of the preparation for **246** (Section 2.2.3.5). In general, alkyl and aryl sulfenates RS-OR rearrange to the corresponding sulfoxides RS(=O)R at temperature above 70 °C, while sulfoxylates rearrange to their corresponding sulfinates RO-S(=O)R during their preparation at room temperature and below. The thermal sulfenate-sulfoxide interconversion for benzyl arylsulfenates, $ArCH_2$-O-S-Ar', to their sulfoxide, $ArCH_2$-S(=O)Ar', is believed to occur *via* a concerted intramolecular mechanism based on a thermal mechanistic study performed on chiral benzyl arylsulfenates (Ar = Ph and Ar' = *p*-Tol; k = 8.7 x 10-5 s^{-1} (120 °C), $\Delta H^{\ddagger}$ = 29.7 kcal mol^{-1}, $\Delta S^{\ddagger}$ = -2 eu)[102b] where partial retention of configuration and negative entropy of activation resulted at 120 °C (**Scheme 19**, p.65-66).[98b, 102a-c, 103a] The reversible [2,3]-sigmatropic rearrangement of allylic sulfenates to sulfoxides (p.19) is known to proceed at low and moderate temperature while the thermal isomerization (without allylic isomerization) of certain allylic sulfenates to sulfoxides proceeds at higher temperature **(eq.48-49)**.[132] The two processes were structurally related allylic sulfenates. The allyl trichloromethanesulfenates **294a-b** were readily transformed to the corresponding sulfoxide **295a-b** at 0 °C by allylic isomerization, while cinnamyl trichloromethanesulfenate **296a** and γ,γ-dimethylallyl trichloromethanesulfemate **296b** were relatively stable and could be heated at 80 °C to undergo thermal isomerization to sulfoxides **297a-b** without allylic shift.

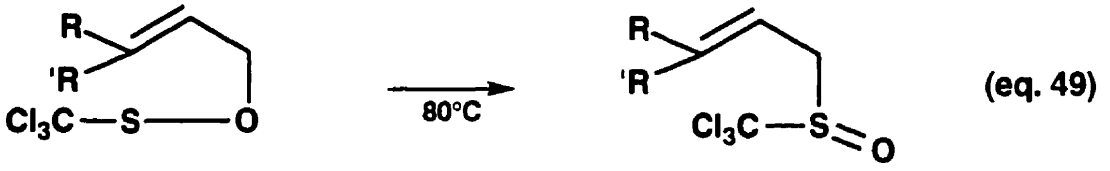
The thermal isomerization process was governed by thermodynamic factors (**eq.49**). For example, the expected α-phenylallyl sulfoxide **295c** resulting from allylic isomerization would have meant loss in conjugation energy and increase in steric interactions between the phenyl and trichloromethyl group.



(eq. 48)

294a: R =H; R'= H
294b: R = Me; R'= H

295a: R =H; R'= H
295b: R = Me; R'= H
295c: R = H; R'= Ph

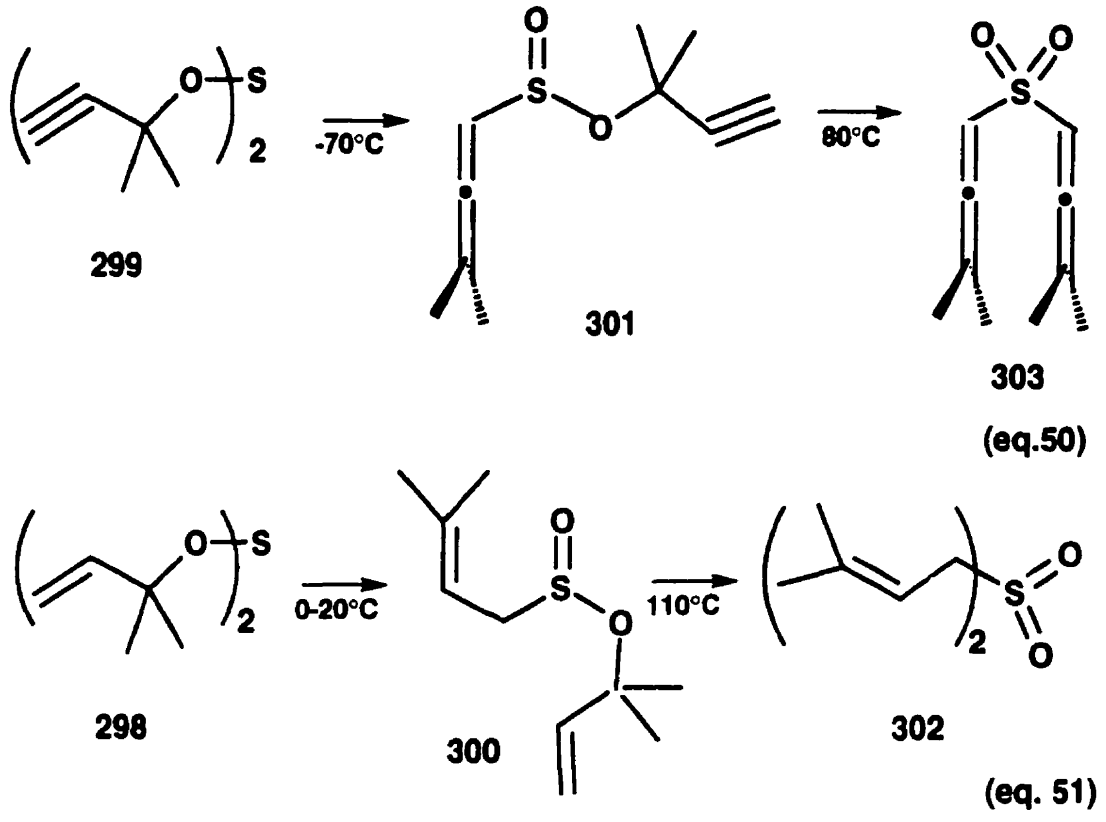


(eq. 49)

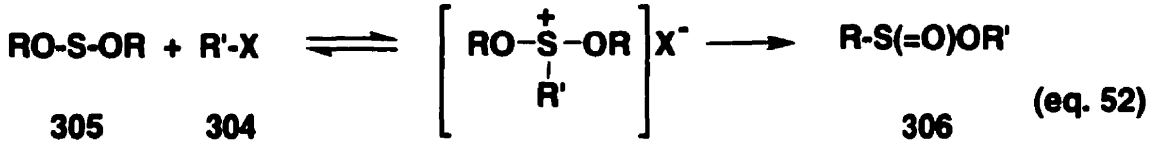
296a: R = Ph; R' = H
296b: R = R'= Me

297

Braverman[102d] reported that the rearrangement of allylic **298** and propargylic **299** sulfenates to the corresponding sulfones **302** and **303** involved a double [2,3]-sigmatropic shift. In both cases, the first rearrangement proceeded spontaneously even at low temperature to yield the sulfinates **300** and **301**, while somewhat higher temperature were required for the second rearrangement (**eq.50-51**). The enhanced rate for the first rearrangement was due to the greater nucleophilicity of the sulfur atom in the sulfenates **298-299** compared to sulfinates **300-301**. The only reported example related to dibenzyl sulfoxylate was dibenzyl sulfoxylate **246a** that was reported to rearrange, during preparation from -95-0 °C, to the sulfinate **249a**.[1c]



Sulfinates RS(=O)OR' **306** were prepared from dialkyl sulfoxylates ROSOR (R = Me, *n*-Pr, *i*-Pr, *n*-Bu, C_4H_8NO = morpholino, $C_5H_{10}N$ = piperidino) **305** and alkyl or benzyl halides **304** (R'= *n*-Pr, *i*-Pr, *n*-Bu; X = Br, I (44-79%) and R'= C_6H_5-CH_2, *p*-NO_2-C_6H_4-CH_2; X = Br (48-87%)) *via* the Thio-Arbuzov reaction **(eq.52)**.[161] The same sulfoxylates **305** (except for R = Me) in the presence $[PdCl_2(NCPh)_2]$ **307** gave the new compound **273**, $[PdCl_2\{S(OPr^i_2\}_2]$.[140] The postulated sulfonium-type intermediate in **eq.52** and the ligand function of sulfoxylates **305** in the transition-metal complex **273** indicates that the sulfur atom of **305** acted as a donor in both processes.



161. a) E. Wenschuh, R. Fahsl and R. Höhne, *Synthesis*, 829 (1976); b) E. Wenschuh and M. Kersten, *Sulfur Lett.*, **14**, 233 (1992).

4.3.2 Isomerization of Sulfoxylates 246b-c to Sulfinates 249b-c

Other previously encountered products were detected and/or isolated in the preparation of 4-substituted benzyl sulfoxylate **246**, like "oxy disulfides" **218**, sulfites **219** and sulfinates **249** (**Table 6**); their formation was rationalized (**eq.31-36, Scheme 23-24**). The sulfoxylates **246a** and **e** were able to withstand column chromatography conditions, at least to some extent and samples were isolated and found to isomerize in a matter of an hour once purified at ambient temperature. Where **246d** was only detected by NMR in the reaction mixture, **246b** (4-NO_2) and **c** (4-Cl) were stable enough, once purified, to be kept at -30°C under N_2 in the freezer over a period of a couple of months. Noteworthy was the exceptional stability in the solid state of **246b** at room temperature that permitted the X-ray determination (**Figure 11**)! The isomerization of sulfoxylates **246b,c** to the sulfinates **249b,c** was studied in solution at temperatures close to room temperature. In every kinetic run (in deuterated solvent using 300 MHz-^{13}C NMR), the process of isomerization was found to obey first order kinetics. The process was monitored in three different solvents at three different temperatures and each run was duplicated; in certain cases, 3-4 repetitions were carried out. The kinetics of the intensity change of the ^{13}C NMR signal of the benzylic methylene carbon was followed. ^{13}C chemical shifts for the sulfoxylates **246b-c** and sulfinates **249b-c** in different solvents are reported in **Table 25**.

Table 25. ^{13}C NMR Chemical Shifts[a] for 246b-c and 249b-c

Solvent[b,c] μ (D) ε	δ_c (CH_2) 246b	δ_c (CH_2) 246c	$\delta_{c\alpha}$ (CH_2)[d] $\delta_{c\alpha'}$ (CH_2)[d] 249b	$\delta_{c\alpha}$ (CH_2) $\delta_{c\alpha'}$ (CH_2) 249c
Toluene-d_8	80.37	81.07	67.81	68.47
0.36			63.31	63.58
2.38				
Chloroform-d	80.33	81.06	68.90	69.71
1.01			63.26	63.55
4.81				
Acetonitrile-d_3	81.61	81.88	69.62	69.93
3.92			63.49	63.40
35.94				

a) 13C NMR (75 MHz) in ppm at 19.6-20.3 °C; b) Dipole moment μ (Debye) and dielectric constant ε at 25°C; c) Ref. 163c; d) Cα and Cα' are on the left and right handside of (S=O)O functionality respectively.

The rate of the first-order reaction is proportional to the change in concentration of the sulfoxylate **246** (**b** or **c**) with time, and the rate law is described according to **eq.53**, where k is the rate constant for the isomerization process. Considering that the concentration of **246b,c** at t = 0 sec is the initial concentration $[246b\text{-}c]_0$, and at t = t , [246b-c], the first-order rate law can be written as **eq.54** and integrated between the limits t = 0 and t = t to give **eq.55**. The half-life $t_{1/2}$, being the time required for the concentration of **249b-c** to reach $[246b\text{-}c]_0/2$, is expressed by **eq.56**. The plots of ln[246b-c] against t were linear, for a first-order process, and k was obtained from the slope. The application of linear regression analysis to the experimental results to fit **eq.55**, shows that the correlation between the time and the natural logarithm of the concentration of sulfoxylate (ln [246b-c]) is reliable and that all the points are almost on line (correlation coefficient (r); **246b:** $0.9891 < r < 0.9990$ and **246c:** $0.9866 < r < 0.9984$).

$$\text{rate} = -\frac{d[246\ b\text{-}c]}{dt} = k\,[246b\text{-}c] \qquad \textbf{(eq. 53)}$$

$$-\frac{d[246\ b\text{-}c]}{[246b\text{-}c]} = k\,dt \qquad \textbf{(eq. 54)}$$

$$\boxed{\ln [246b\text{-}c] = -kt + \ln [246b\text{-}c]_0} \qquad \textbf{(eq. 55)}$$

and

$$\boxed{t_{1/2} = \frac{\ln 2}{k} = \frac{0.693}{k}} \qquad \textbf{(eq.56)}$$

The first-order rate constants k are interpreted in terms of energies. The temperature dependence of the experimental rate constant k usually follows the Arrhenius equation **(eq.57)**, where R is the gas constant (1.987 cal K^{-1} mol^{-1}) and T is the Kelvin temperature. The values of A, the preexponential factor related to the frequency of collisions with the correct geometry for the reactants, and E_a, the Arrhenius activation energy, are determined

experimentally by plotting the natural logarithm of k against 1/T according to **eq.58**.[162a] The isomerization process is considered to be a unimolecular process to which was applied the transition state theory[162b-d]. The bonds of sulfoxylates **246b-c** are believed to rearrange to form the activated complex depicted in **Scheme 32**. The central sulfur atom acts as an electron donor, interacting with the adjacent benzylic carbon as this atom is loosening its CH_2-O interaction to the profit of the forming sulfoxide group (S=O). This concerted three-membered ring transition state is in agreement with both the kinetic and thermodynamic parameters correlated in **Table 26**: the positive activation enthalpies and the low positive entropies (except for **246b** in CD_3CN, *vide infra*) are comparable to other pericyclic concerted processes[163c] like Diels-Alder reactions and the Cope rearrangement. The enthalpy factor is interpreted in terms of an increase in bond formation, and the entropy in terms of restricted internal rotation to achieve the activated complex in the transition state.

$$k = A \exp(-E_a/RT) \qquad \text{(eq. 57)}$$

$$\ln k = \ln A - \frac{E_a}{RT} \qquad \text{(eq. 58)}$$

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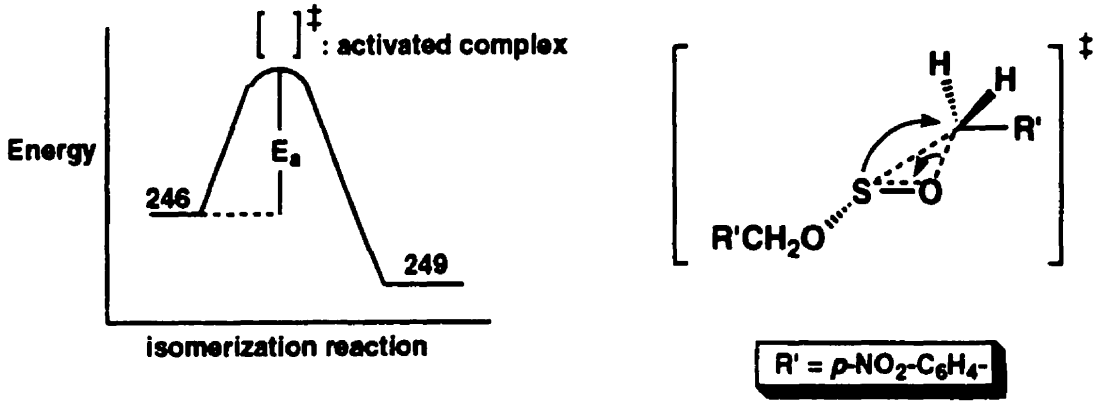
162. a) R. Breslow, *Organic Reaction Mechanism An Introduction*, W.A. Benjamin inc., New York (1965); b) In the transition state theory, the reactants and the activated complex are taken to be in equilibrium ($[A^{\ddagger}] = K_{\ddagger}[A]$), and that all activated complexes go on to the product at exactly the same rate ($k[A] = k^{\ddagger}[A^{\ddagger}]$) so that the rate constant k, of the reaction, depends only on the position of the equilibrium between the reactants and the activated complex ($k = k^{\ddagger}K_{\ddagger}$). The rate constant $k^{\ddagger}$is derived by a statistical mechanics method, and $k = (k_B T/h) K^{\ddagger}$ where k_B is the Boltzmann constant (3.2999×10^{-24} cal K^{-1}), h is the Planck's constant (1.5837×10^{-34} cal s^{-1}) and $K^{\ddagger}$ is a new equilibrium constant that excludes the contributions from the reaction coordinate. Then $K^{\ddagger}$ is written in terms of a free energy of activation $\Delta G^{\ddagger} = -RT \ln K^{\ddagger}$ that is divided in terms of enthalpy $\Delta H^{\ddagger}$ and entropy $\Delta S^{\ddagger}$ of activation, for $\Delta G^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$ that is in turn substituted in the Eyring equation **(eq.39)** for $k = (k_B T/h) \exp(-\Delta H^{\ddagger}/RT) \exp(\Delta S^{\ddagger}/R)$ and compared to the Arrhenius equation **(eq.57)** for $A = (ek_B T/h) \exp(\Delta S^{\ddagger}/R)$ **(eq.59)** and $E_a = \Delta H^{\ddagger} + RT$ **(eq.60)**: S.W Benson, *Thermochemical Kinetics*, Wiley, New York (1968); c) J.W. Moore and R.G. Pearson, *Kinetics and mechanisms*, 3rd Ed., Wiley, New York (1981); d) P.D. Pacey, *J. Chem. Educ.*, **58**,612 (1981).

163. a) J.H. Hildebrand and R.L. Scott, *The Solubility of Nonelectrolytes*, 3rd Ed., Dover, 1964; b) E.S. Amis and J.F. Hilton, *Solvent Effects on Chemical Phenomenon*, Academic Press, 1973; c) C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry*, 2nd revised Ed., VCH, Weinheim, 1990.



Scheme 32

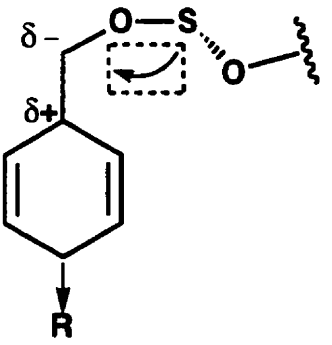
Table 26. Relative Rates and Activation Parameters[a] for Isomerization 246b-c to 249b-c

246	Solvent	k x 10^{-6} (s^{-1})	$(k_{rel})^c$	E_a	ln A	$\Delta G^{\ddagger}$	$\Delta S^{\ddagger}$ (eu)
b	Toluene-d_8	39.3	2.14	24.3 ± 0.3	31.6	23.1	2.3 ± 0.4
	$CDCl_3$	38.7	2.10	24.0 ± 0.2	31.2	23.0	1.6 ± 0.5
	CD_3CN	18.4	1.00	30.6 ± 0.1	41.9	23.4	22.7 ± 0.5
c	Toluene-d_8	14.5	0.76	27.2 ± 0.4	35.6	23.6	10.2 ± 0.4
	$CDCl_3$	37.9	1.98	b	b	b	b
	CD_3CN	19.1	1.00	b	b	b	b

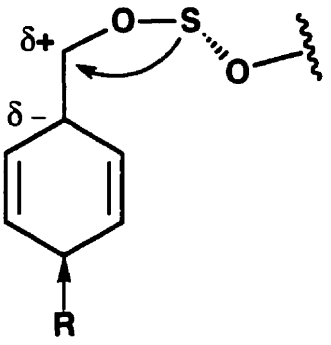
a) at 25°C; E_a and $\Delta G^{\ddagger}$ are expressed in kcal mol^{-1}, and error limits represent the standard deviation; b) Temperature dependence of k was not studied; c) Temperatures used for 246b: Toluene-d_8 (20.3, 27.3 and 35.3 °C); $CDCl_3$ (20.3, 27.2 and 35.3 °C); CD_3CN (19.9, 27.3 and 35.2 °C). For 246c: Toluene-d_8 (20.3, 27.3 and 35.2 °C); $CDCl_3$ (20.3 °C); CD_3CN (20.3 °C).

Considering that the process of isomerization was achieved *via* the same activated complex in the transition state, in the different solvents, the activation parameters were further interpreted. The energy of sulfoxylate **246b** was lowered in acetonitrile-d_3, due to an increase of solute-solvent interaction, dipole-dipole between the nitro group of **246b** and the cyano group of acetonitrile, thus increasing the activation energy and decreasing the rate. Therefore, the positive change in energy of activation on going from toluene-d_8 to acetonitrile-d_3 is expressed in terms of solvation (enthalpy; $\Delta H^{\ddagger}(CD_3CN) - \Delta H^{\ddagger}(C_7D_8) =$ 6.3 kcal mol^{-1}). The entropy was greatly reduced on passing from the reactant **246b** to the activated complex of the transition state ($\Delta S^{\ddagger}(CD_3CN) - \Delta S^{\ddagger}(C_7D_8) = 20.24$ eu); the highly ordered cohesive forces holding the solvent molecules together were scrambled upon dissolution and solvation of **246b** in acetonitrile-d_3. The values k_{rel} indicate that the change of solvent polarity had a very small effect on the rate of the reaction, and that the charge distribution in the activated complex of **246b** is very similar to the initial reactant **246b** itself (isopolar activated complex)[163]. Considering the rate diminution, the positive sign of the entropy of activation change and its greater value, in acetonitrile-d_3 for **246b**, it is reasonable to assume that the O-S-O functionality of **246b-c** is not highly solvated in the activated complex.

Both sulfoxylates **246b-c** were bearing an electronegative group in the *para* position causing the ring to be electron deficient; the chlorine atom is inductively electron withdrawing because of intrinsic electronegativity while the nitro group is electron withdrawing because of the functional group polarity. The inductive effects for **246b-c** as well as the resonance effect for **246b** transmitted through the aromatic ring, may be responsible for their stability compared to **246a, d** and **e**. The isomerization of **246** *via* the concerted process, where the sulfur from the O-S-O functionality acts as a donor, is predicted to be slowed down when the electron withdrawing groups are attached at the *para* position **(Scheme 33)**. The explanation depicted in **Scheme 33** is based on an inductive dipole; the development of positive charge at the *ipso* position of the benzene ring, due to the presence of the electron withdrawing group at the *para* position will leave negative charge on the benzylic carbon according to electrostatic theory. This negative charge reduces the attack of sulfur at that position. Now it is possible to appreciate why **246a, d** and **e** were found to isomerize at room temperature in a matter of an hour and less! In **246d** (*p*-OMe), the resonance electron-donating effect outweighed the possible inductive electron-withdrawal effect of the moderate electronegative oxygen atom of the methoxy group.



246b: R = NO_2
246c: R = Cl



246a: R = H
246d: R = OMe
246e: R = Me

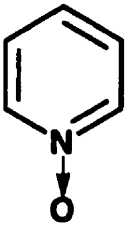
Scheme 33

4.3.3 The Oxidation of 246b-c

Sulfoxylates ROSOR are known to readily oxidize upon exposure to air, and were studied as possible deoxygenation agents (R=Et and *n*-Pr) in the presence of dibenzoyl peroxide **308**, pyridine N-oxide **309** and C-nitroso compounds **310** to give the corresponding sulfite in 77%, 85% and 60% respectively.[110c] Recently, 1,2-dioxetanes **311** (R= CH_3, CH_2Cl, CH_2Br, CH_2Ph and R'= Ph, CH_2Ph) were found to react with heteroatom nucleophiles and among them, the thiocyanate anion ^-SCN gave the corresponding sulfoxylates **312**, that readily oxidized to sulfites **313** **(eq.61)**.[164]

$(Ph(C=O)O)_2$

308

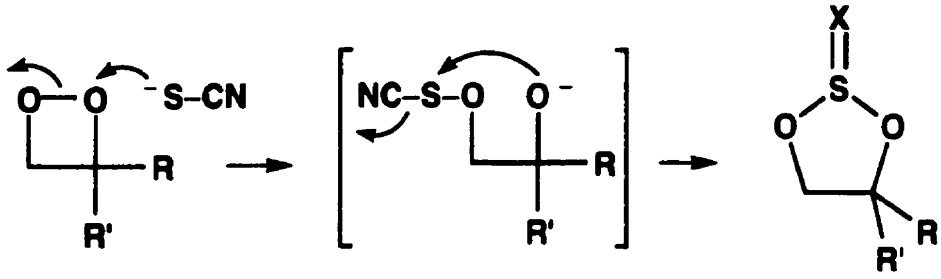


309

Ar-N=O

310

164. W. Adam and M Heil, *J. Am. Chem. Soc.*, **114**, 5591 (1992).

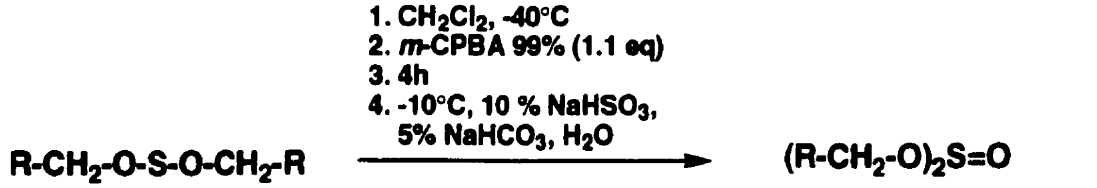


311

312: X = :
313: X = O

(eq. 61)

We were curious whether the *m*-CPBA oxidation of **246b-c** would give comparable results to the dibenzoyl peroxide oxidation mentioned previously. Both sulfoxylates **246b** and **c** gave the corresponding sulfites **219b** and **c** in 92% and 80% of isolated yields after column chromatography. The best isolated yields were obtained at *ca.* -40 °C using 1.1 equivalents of *m*-CPBA (99%)[165] in methylene chloride. Using thin layer chromatography techniques, the oxidation reaction at -78 °C was very slow (after *ca.* 14 hours, some sulfoxylate was detected), at 0 °C to -10 °C very "messy". However, at -40 °C, the reaction was monitored over a period of four hours and the oxidation was very clean and specific **(eq.62)**.



246b: R = *p*-NO_2-C_6H_4
246c: R = *p*-Cl-C_6H_4

219b: 92%
219c: 80%

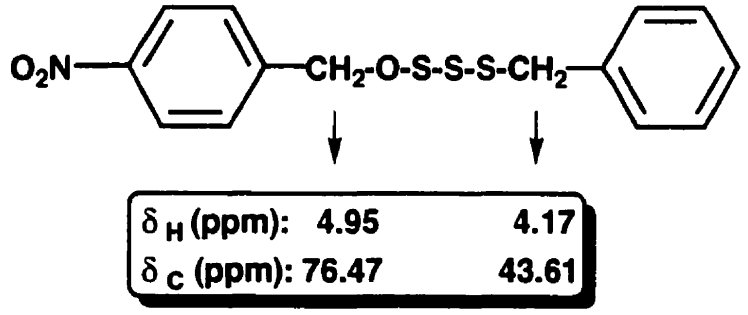
(eq. 62)

165. Prepared by washing the commercial 80-85% or 50-60% material with a phosphate buffer followed by recrystallization from methylene chloride (*vide infra*): N.N. Schwartz and J.H. Blumbergs, *J. Org. Chem.*, **29**, 1976 (1964).

4.4 Thermolysis of 4-Nitrobenzyloxy Benzyl Trisulfide 243

As discussed previously (Section 2.2.3.4) the only stable isolated compound of this class of "oxytrisulfide" was **243** (m.p. 43-45 °C). Other alkoxyalkyl trisulfides ROSSSR' **27** were prepared[21] and their yields reported (**Table 5**, entries 1-5). Their stability was not discussed but each compound was purified by distillation under reduced pressure (entries 1-5 b.p. (pressure in mmHg): 72.5°C (3.2), 66°C (0.9), 72°C (1.4), 53°C (0.6) and 51°C (1.0)) suggesting a certain degree of thermal stability. By analogy to bis(4-nitrobenzyloxy) disulfide **218b** which at high temperature delivers the corresponding alcohol, aldehyde and S_2, that concatenates in the absence of a diene to form S_8, the oxytrisulfide **243** could also decompose to give S_2 according to **Scheme 34**. Two different patterns of decomposition are theoretically possible (**I** and **II**), both entropically favored and each of them involving the cleavage of a C-H (100 kcal mol^{-1}), S-O (68 kcal mol^{-1}) and S-S (64 kcal mol^{-1})[166c] bond for a total of $\Delta H°_f$(**243**) of 232 kcal mol^{-1}.

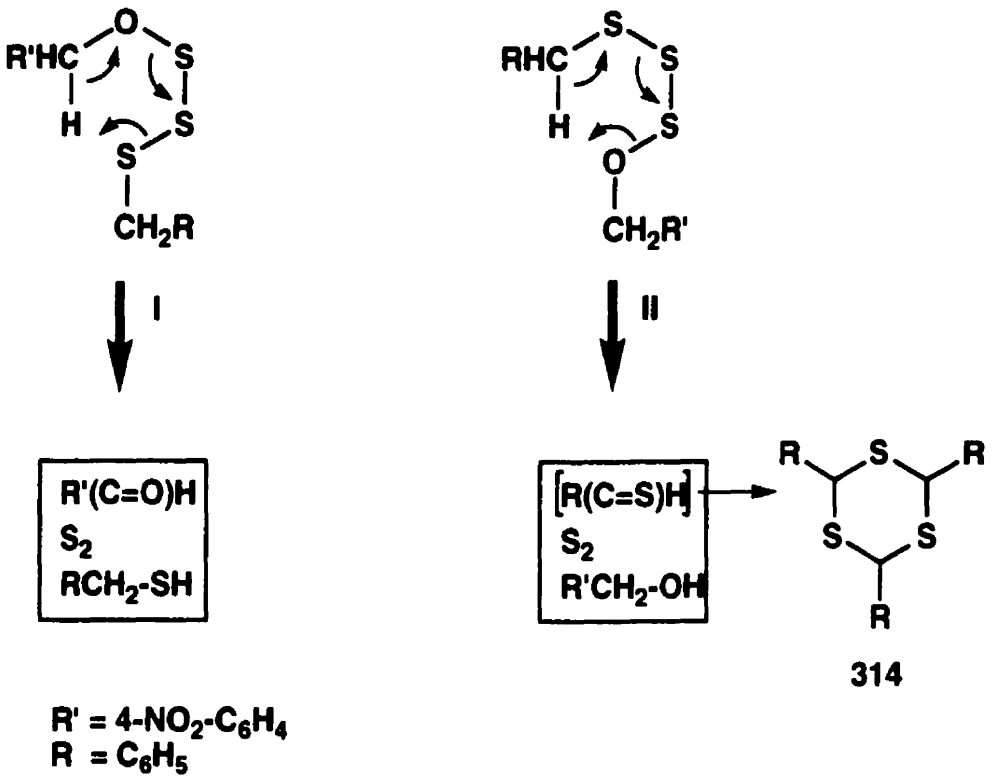
243



Consideration of the enthalpy of formation of the products for each process might favor one over the other; according to process **I**, the $\Delta°H_f$ (products) = 201 kcal mol^{-1}(S-H, C-O to C=O and S-S to S=S for 83, 87 and 31 kcal mol^{-1} respectively)[166] and process **II**, $\Delta°H_f$(products) = 206 kcal mol^{-1} (O-H, C-S to C=S and S-S to S=S for 110, 65 and 31 kcal mol^{-1})[166]. The enthalpy difference is somewhat small ($/\Delta\Delta H°_f$(products)/ = *ca.* 5 kcal mol^{-1}) and both processes are energetically favorable. In fact, the ^1H and ^{13}C NMR spectra of the thermolysis of **243**, in toluene-d_8 at 105-110 °C over a period of 8.5 hours, show the

166. a) A. Streitwieser and C.H. Heathcock, *Introduction to Organic Chemistry*, 3rd Ed., Macmillan, New, York, 1985; b) G.H. Whitam, *Organosulfur Chemistry*, Oxford, New York, 1995, p.26; c) The actual value might be smaller, but in this particular case it does not matter since the breaks are all equal and the issue is essentially the formation of C=O and S-H in **I** vs C=S and O-H in **II**.

formation of *p*-nitrobenzaldehyde, *p*-nitrobenzyl alcohol and the 1,3,5-trithiane **314** from thiobenzaldehyde Ph-(C=S)H. Chemical shifts in the range of 13 ppm, for the thial proton in ^{1}H NMR, and 250 ppm, for the thial carbon (C=S) in ^{13}C NMR, were not detected either at the early stage or at the end of the thermolysis experiment.[167]



Scheme 34

Thiobenzaldehydes are known to undergo self-condensation reaction to form the corresponding cyclic trimer **314** in the absence of dienes.[167] The alcohol and aldehyde were clearly identified in both toluene-d_8 and chloroform-d, using ^{1}H and ^{13}C NMR, upon addition of original material. Based on the results obtained after isolation of these two products we concluded that both processes were operating in a *ca.* 1:1 ratio (path **I** *vs* path **II**). Some elemental sulfur S_8 was also isolated. The other products were identified as dibenzyl tetrasulfide $(Ph\text{-}CH_2\text{-}S_2)_2$ and 1,3,5-trithia-2,4,6-triphenylcyclohexane **314** in both the *cis* (α-form) and *trans* (β-form) isomeric forms (^{1}H NMR). The tetrasulfide was formed

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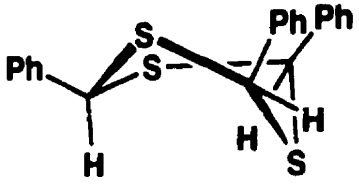
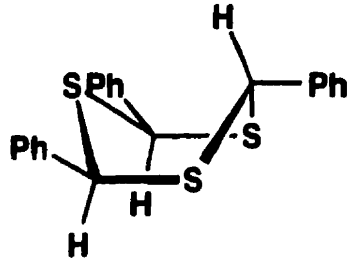
167. a) S. Jerumanis and J.M. Lalancette, *Can. J. Chem.*, **45**, 1928 (1964); J.E. Baldwin, R.C. Lopez, *J. Chem. Soc., Chem. Commun.*, 1029 (1982); R. Okazaki, A. Ishii, N. Fukuda, H. Oyama and N. Inamoto, *ibid.*, 1187; b) K. Steliou and M. Mrani, *J. Am. Chem. Soc.*, **104**, 3104 (1982).

according to **Scheme 3** (p.9) where the oxytrisulfide underwent nucleophilic substitution by benzyl mercaptan $PhCH_2$-SH.[22] *Cis*-**314** was reported to be less stable than *trans*-**314**, and both isomers were expected to be formed under thermolysis conditions.[167]

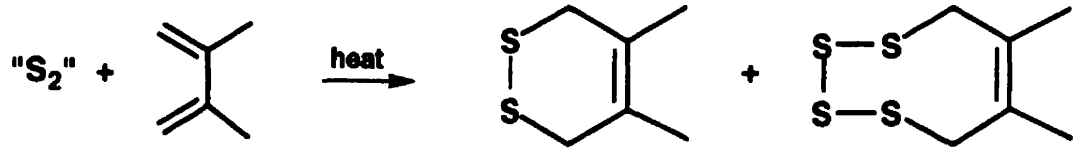


***Cis*-314**



***Trans*-314**

The same experiment was repeated in the presence of three equivalents of 2,3-dimethyl 1,4-butadiene **315** and monitored by ^{1}H NMR to explore the possibility of **243** as precursor for the S_2 dienophile (**eq.63**). The disulfide adduct **316** and tetrasulfide adduct **317** were detected (*vide infra*) and isolated in 8 and 22% yield respectively. The trapping of diatomic sulfur (S_2), generated from **243**, was not further investigated. However, a detailed investigation in terms of solvents, temperatures, dienes and ratio was addressed to dialkoxy disulfides **218 (Chapter 5)**. Nevertheless, the pseudo six-membered ring proposed for processes like **I** and **II** to give S_2, may actually be the preferred orientation in the transition state to liberate S_2 in any other related molecules with an S-S linear bond flanked between two electron withdrawing groups.



315 **316** **317** **(eq. 63)**

4.5 General Commentary

Related compounds to dialkoxy disulfides **218** included *p*-nitrobenzyl *p*-chlorobenzene sulfenate **233**. This sulfenate was never isolated and the formation of the corresponding sulfinate **236** resulted due to the acid-catalyzed hydrolysis of **233**. The sulfoxylates **246b-c** were found to isomerize following first order kinetics in toluene-d_8, chloroform-d_3 and acetonitrile-d_3. The experimental parameters of activation were interpreted according to transition state theory. The isomerization process was likely achieved *via* a three-membered ring activated complex, in the transition state, where the sulfur from the O-S-O functionality, acts as an electron donor on the adjacent benzylic carbon. The solvent polarity had little effect on the rate constant, and was interpreted in terms of solvation of the *para* substituent on the benzene ring of the sulfoxylate studied instead of solvation of the activated complex. The nature of the *para* substituent was probably very important in the overall stability of the sulfoxylate; electron withdrawing groups in the *para* position were believed to increase the stability of sulfoxylates **246**. The oxidation of these same sulfoxylates **246b-c** by *m*-CPBA gave the corresponding sulfites **219b-c** in very high yield.

The related "oxytrisulfide" **243** was found to have some potential as S_2 precusor. The elimination of S_2 took place by two different unimolecular processes, in a *ca.* 1:1 ratio, under thermolysis conditions, to give in the presence of diene **315**, the corresponding disulfide and tetrasulfide adduct **316** and **317** (*vide infra*). The suggested pseudo six-membered ring was probably the favored orientation in the transition state for the "oxytrisulfide" **243**, and as well for the dialkoxy disulfides **218 (Chapter 5)**.

CHAPTER 5: CHEMISTRY OF DIALKOXY DISULFIDES

5.1 Introduction

We have seen that the thermolysis of **218** provides the corresponding alcohol, aldehyde and S_2 which concatenates into S_8 in the absence of dienes (**Scheme 1**). It is of common belief that the S_2 unit is lost as singlet diatomic sulfur ($^1S_2$) by comparison to singlet diatomic oxygen ($^1O_2$) and adds as a dienophile to dienes in a Diels-Alder reaction. According to Hund's rule, the fundamental electronic configuration of both O_2 and S_2 molecules is a triplet (spin unpaired). Singlet diatomic sulfur is *ca.* 13 kcal mol^{-1} above the triplet state ($^3S_2$).[168] The lifetime of $^1S_2$ is expected to be less than that of $^1O_2$ which is about 130 ns in CCl_4.[169] As previously seen in Chapter 1 (Section 1.8), the S_2 reactive dienophile has been regarded as part of the methodologies related to hetero Diels-Alder reactions which are in turn very important tools in the total synthesis of natural products. Diverse precursors have been developed to generate and transfer the S_2 unit,[50-57] and the best isolated yields of the disulfide adduct like **316** (60-85%) resulted from Steliou's elegant biphenyl dithione approach reported on p.32 (**111** to **114**)[53a]. Dialkoxy disulfides **218** were investigated as a new class of precursor for the generation of S_2 unit.[170]

5.2 Generation of Diatomic Sulfur from 218

Preliminary results on the generation of S_2 from dialkoxy disulfides **218** were obtained in toluene and chlorobenzene in the presence of 2,3-dimethyl-1,4-butadiene **315** (**Table 27**). Each experiment gave only two purified trapped products; the disulfide adduct, 1,2-dithia-4,5-dimethyl-4-cyclohexene **316** and tetrasulfide adduct, 1,2,3,4-tetrathia-6,7-dimethyl-6-cyclooctene **317**. It appears that each of the alkoxy disulfides **218** is similarly efficient in transferring diatomic sulfur. Comparing the set of experiments in toluene and chlorobenzene indicates that the temperature of the trapping experiment seems to affect the yield of the disulfide adduct **316**; in chlorobenzene the yields were lowered. The reaction was addressed to precursor **218b** in terms of solvent and temperature (**Table 28**). It seems

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168. a) R.F. Barrow and R.D. duParcq, *Elemental Sulfur*, B. Meyer, Ed., Interscience, New York, 1965, p.251.

169. R. Schmidt and M. Bodesheim, *J. Phys. Chem.*, **98**, 2874 (1994).

170. S.L. Tardif, C.R. Williams and D.N. Harpp, *J. Am. Chem. Soc.*,**117**, 9067 (1995).

that toluene is a good solvent to investigate the reaction in terms of ratios of the disulfide and tetrasulfide adducts.

Table 27. Trapping Experiments[a] of 218 in the Presence of 2,3-dimethyl-1,4-butadiene 315

ROSSOR[b] 218	Solvent[c]	Time (h)	316 (%)[d]	317 (%)[d]
a	C_7H_8	5.0	23	49
c	C_7H_8	3.5	26	38
d	C_7H_8	2.5	36	41
e	C_7H_8	2.0	34	29
a	ClC_6H_5	1.0	20	45
b	ClC_6H_5	1.2	1[e]	25[f]
c	ClC_6H_5	1.0	18	38
d	ClC_6H_5	0.5	26	32
e	ClC_6H_5	1.0	<5	52

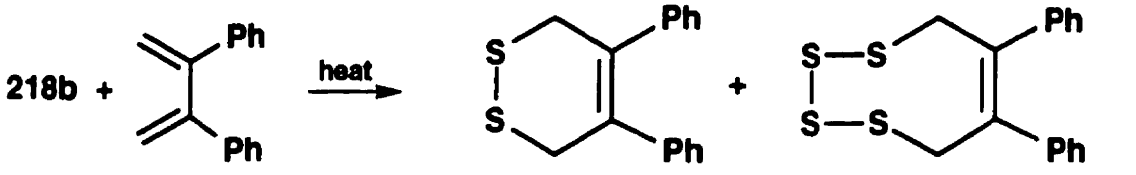
a) Ratio of 1:1.2 (218:315); b) R = 4-X-$C_6H_4CH_2$; 218a: X = H; b: X = NO_2; c: X = Cl; d: X = OMe; e: X = Me; c) For toluene, C_7H_8, (100-105°C) and for chlorobenzene, ClC_6H_5, (130-135°C); d) Isolated yield after flash chromatography (silica gel-CCl_4-hexanes 50:50); e) Evaluated by ^1H NMR (200 MHz) in $CDCl_3$; f) ^1H NMR yield using an internal standard ((4-NO_2-$C_6H_4CH_2$-S_2)$_2$, 226.

Table 28. Solvent Study of Trapping Experiments[a] for 218b

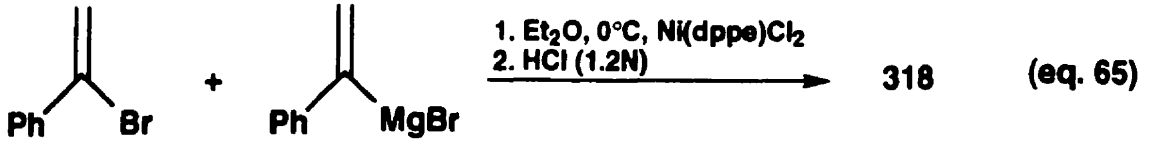
Solvent[b]	Time[c] (h)	316 (%)[d]	317 (%)[d]
EtOAc	14	4	10
DME	10	21	32
C_7H_8	36	19	69
ClC_6H_5	1.2	1[e]	25

a) Ratio of 1:1.2 (218b:315); b) For ethyl acetate, EtOAc, (70-75°C), dimethoxy ethane, DME, (80-85°C); C_7H_8 (100-105°C); ClC_6H_5 (130-135°C); c) Time afterwhich 218b was not detected by thin layer chromatography; d) Isolated yield after flash chromatography; e) Estimated using ^1H NMR.

Appropriate trapping experiments were developed using **218b**, in the presence of diene **315** and 2,3-diphenyl-1,3-butadiene **318** **(eq.64)**.[170] Diene **318** was prepared according to a Grignard reaction using α-bromo-styrene in the presence of the catalyst [1,2-bis(diphenylphosphino)ethane]dichloronickel(II) Ni(dppe)Cl_2 in 52% yield **(eq.65)**.[171] The yields reported in **Table 29** are the best experimental yields obtained after numerous trials. A previous paper dealing with diatomic sulfur transfer has reported yields of trapped disulfide adduct **316** ranging from unreported to low-medium (9-55%).[172a] By using an excess of **218b** to diene, we have obtained isolated yields of up to 79% of trapped disulfide adduct **316**. The previous highest yield (73%) ever reported was obtained according to the biphenyl dithione approach described by Steliou and his group.[53a] Interestingly, the corresponding tetrasulfide adduct **317** was never mentioned using the latter procedure.



318 **319** **320** **(eq. 64)**



318 **(eq. 65)**

However, most of the methodologies[50-57] provide the corresponding tetrasulfide adduct **317**; we also found that this tetrasulfide adduct is formed in our trapping experiments **(Tables 27-29)**. Concern has been expressed[50c] that diatomic sulfur transfer, as opposed to "activated" elemental sulfur, is actually not taking place when more than two sulfur atoms are transferred to the diene. As matter of fact, it was recently published from our group that when elemental sulfur S_8 is heated in excess with the diene **315** (4:1), in polar aprotic solvent (DMSO or pyridine), at *ca.* 120 °C, that disulfide adduct **316** was isolated in 65-

171. a) T. Nabeshima, A. Sakiyama, A. Yagyu and N. Furukawa, *Tetrahedron Lett.*, **30**, 5287 (1989); b) B.C. Fulcher, M.L. Hunter and M.L. Welker, *Synth. Comm.*, **23**, 217 (1993).

172. a) Ref.170; footnote (2); b) Ref.59f.

70%.[172b] However, treatment of elemental sulfur with diene **315** in the presence of the thermal decomposition products (alcohols and aldehydes of **218a-e**), never gave sulfurated adducts like **316** and **317**.

Table 29. Trapping Experiments with 218b in the Presence of Dienes

218b: diene[a]	Solvent	Time (h)	316 (%)[b]	317 (%)[b]
3:1.0	C_7H_8	24	(43) [75]	(36)
3:1.0	(100-102 °C)[c]	36	32 (31) [72]	47 (45)
5:1.0		24	(18) [75]	(63)
1:3.0		24	31 (28) [36]	19 (17)
1:3.0[d]		24	26 (24) [31]	18 (15)
3:1.0[d]		24	34 (35) [79]	48 (49)
1:1.2	ClC_6H_5	1.2	1[f]	25
1:2.0	(130-135°C)	1.2	1[f]	22
1:3.0		1.2	1[f]	51
			319 (%)[e]	**320 (%)[e]**
1:1.0	ClC_6H_5	2	26 (13) [39]	30 (28)
3:1.0		2	48 (26) [54]	34 (31)
5:1.0		2	50 (33) [61]	35 (31)

Typical amounts of 218b:diene in the case of the 3:1 ratio are 600 mg (1.63 mM):44.6 mg (0.54 mM) in 7 mL of solvent. In addition, for each mol of 218b used, 1 mol of MgO is added and the reactions are carried out until reagent 218b is depleted (tlc); b) ^{1}H NMR yield using an internal standard (tetrasulfide 226) are listed; brackets indicate isolated yield after flash chromatography (silica gel-CCl_4-hexanes 50:50); square brackets indicate isolated isolated yield after treatment of either 317 or 320 with triphenylphosphine to give respectively 316 and 319; c) The temperature of the oil immersion bath must not exceed 110 °C; d) 218c:diene; e) Flash chromatography for this system was 4% diethyl ether-petroleum ether on silica gel; f) Evaluated by ^{1}H NMR (200 MHz) in $CDCl_3$.

The total isolated yield of the disulfide adduct reported in square brackets in **Table 29**, came about after treating the reaction mixture with one equivalent of triphenylphosphine Ph_3P; for instance, the 6th entry, where the diene is the limiting reagent and **317** = 49% isolated yield, the conversion using Ph_3P gave 49% x 0.90 = 44% of disulfide adduct **316** isolated, for the combined yield of 79%. It is noteworthy that this combined 79% isolated yield required at least two separate chromatography columns! We have demonstrated by ^1H NMR, that upon treatment of a crude mixture with Ph_3P where adducts **316** and **317** are formed, that the tetrasulfide adduct is quantitatively converted to the disulfide adduct and isolated in 90% yield. The adducts **316**, **317**, **319** and **320** were identified using ^1H and ^{13}C NMR (**Table 30**).

Table 30. ^1H and ^{13}C NMR[a] Chemical Shifts of 316-317 and 319-320

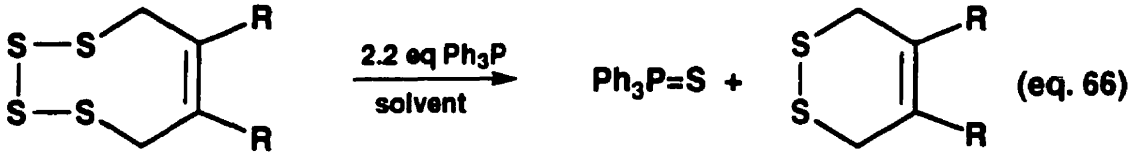
Compound (solvent)	δ (CH_2) ^1H	δ (CH_2) ^{13}C	δ (=C-CH_2-) ^{13}C	δ (CH_3) ^1H	δ (CH_3) ^{13}C
316 ($CDCl_3$)	3.18	34.15	125.16	1.75	20.80
316 (C_7D_8)	2.84	-	-	1.31	-
317 ($CDCl_3$)	3.64	42.78	130.30	1.79	18.14
317 (C_7D_8)	3.02	-	-	1.45	-
319 ($CDCl_3$)	3.67	-	-		
319 (C_7D_8)	3.42	-	-		
320 ($CDCl_3$)	4.07	-	-		
320 (C_7D_8)	3.52	-	-		

a) In ppm, using 200 and 300MHz operating frequencies at T = 19.2-20.3 °C.

5.3 Desulfurization and Stability of the Diels-Alder Adducts

A brief study of the desulfurization of **317**, using ^1H NMR, showed that the process is solvent dependent (**eq.66**). The desulfurization to the corresponding disulfide adduct was accomplished in 2 hours at room temperature in chloroform-d; 2 hours at 40 °C and 4-5 hours at room temperature in anhydrous diethyl ether (Et_2O) and 10 hours at 60 °C in benzene-d_6. Replacement of triphenylphosphine by the more reactive hexaethylphosphorustriamide,

$(Et_2N)_3P$ (HEPT), in **eq.66**, gave the disulfide adduct **316** in less than 2 hours at room temperature in benzene-d_6. By the time the addition of HEPT was terminated, half the tetrasulfide was converted to the disulfide adduct **316**. It is possible that the more reactive HEPT may convert the corresponding disulfide adduct **316** to the monosulfide adduct and then to the diene **315**. Neither the monosulfide adduct nor the diene **315** were detected during the experiment (^{1}H NMR). For the diphenyl analog **320**, in the presence of triphenylphosphine, 15 hours at 60 °C in benzene-d_6 were required for the conversion to **319**. Purification of the final disulfide adduct **316** from the reaction mixture gave an isolated yield for the conversion ≥ 90%.

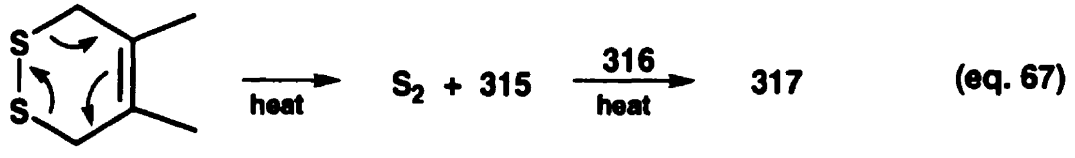


(eq. 66)

317: R = CH_3
320: R = Ph

316: R = CH_3
319: R = Ph

The thermal stability of the disulfide adduct **316** was monitored in toluene-d_8, at 98.1 °C over a period of 44 hours and only *ca.* 2% of tetrasulfide adduct was formed. Apparently, little reversion of **316** takes place **(eq.67)**.

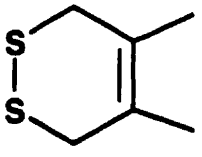


(eq. 67)

316

Different variations of **eq.67**, where the corresponding tetrasulfide **317** and a mixture of **316** and **317**, in a 1:1 ratio, were similarly heated, revealed that both adducts are stable at that temperature (*ca.* 100-105 °C) in toluene. A separate experiment showed that the trapped disulfide **316** and the diene **315**, in this case, are comparably competitive for the S_2 transfer reagent **218b (eq.68)**. Following these conditions, a 1:1 ratio (^{1}H NMR) of the trapped disulfide **316** and trapped tetrasulfide **317** along with elemental sulfur S_8 (TLC) resulted.

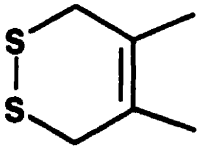
Another separate experiment where the disulfide adduct **316** was heated in the presence of one molar equivalent of the reagent **218b** resulted once again in a 1:1 ratio (^{1}H NMR) of adducts **316** and **317** **(eq. 69)**. In both cases, further heating over a period of 14 hours did not change the appearance of the spectrum. Therefore, the formation of tetrasulfide adducts **317** and **320** was rationalized by the rapid chelotropic insertion of a second equivalent of S_2 according to path **II**, path **I** being not allowed thermally[173] **(Scheme 35)**. It became clear why the best trapping experiments resulted from the presence of excess **218b** **(Table 29)**. Although the diatomic sulfur transfer process from dialkoxy disulfides **218** was not entirely chemoselective toward the formation of trapped disulfides, the corresponding tetrasulfides were easily converted back to the disulfides through desulfurization of the crude mixture.



316

1. 218b (1.0 eq)
2. 315
3. C_7D_8, 107.5°C, 2h

316 + 317 + S_8 **(eq. 68)**



316

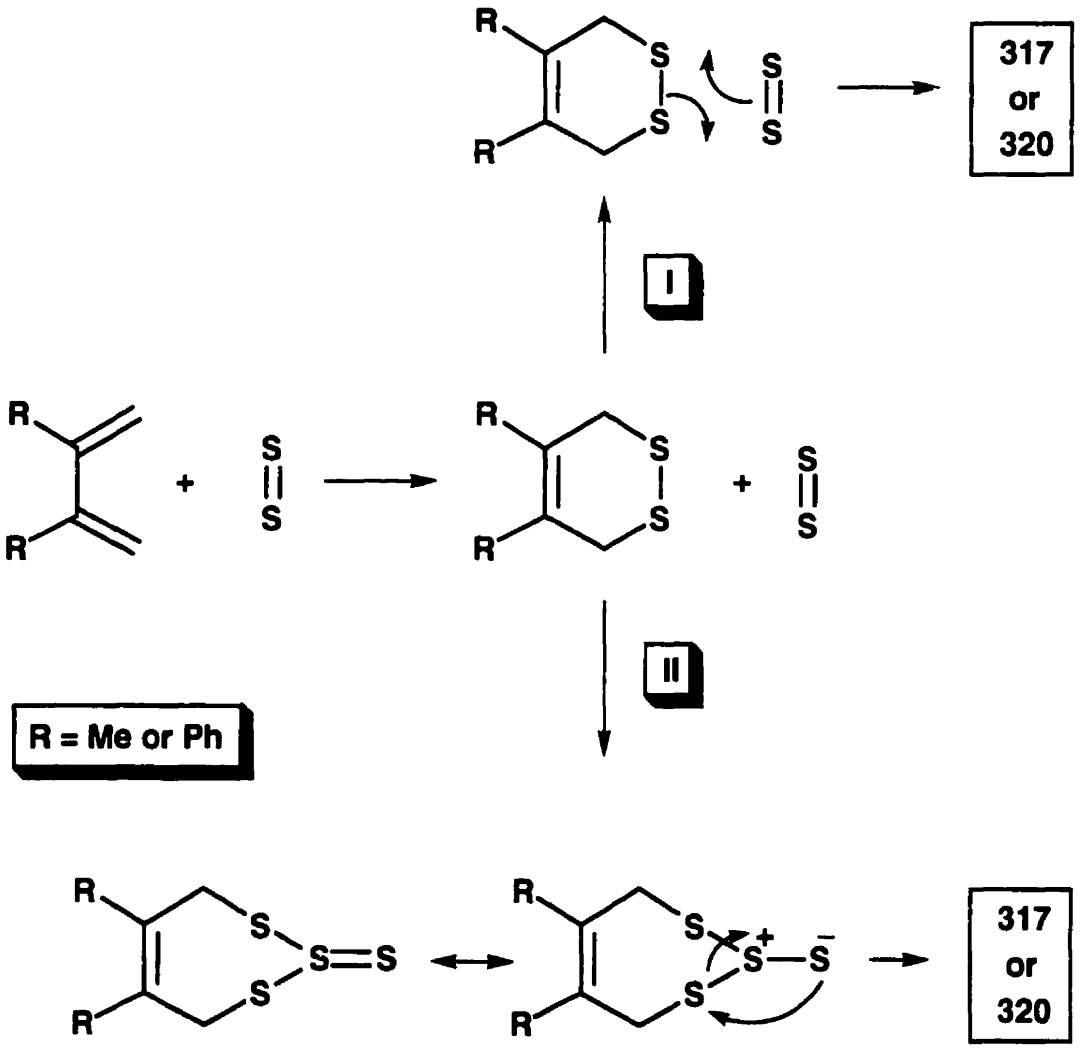
1. 218b (1.0 eq)
2. C_7D_8, 107.5°C, 2h

316 + 317 + S_8 **(eq. 69)**

Interestingly, when the disulfide adduct **316** was heated in chloroform-d (59.2 °C) over a period of 12 hours in the presence of the Lewis acid boron trifluoride diethyl etherate $BF_3.OEt_2$ (0.5 eq) the disulfide adduct was destroyed at the expense of the formation of the tetrasulfide adduct **317**. The formation of the tetrasulfide adduct may be rationalized **(Scheme 36)**. The precursor **218b** was also sensitive to the presence of Lewis acid, since it decomposed quickly in the presence of $BF_3.OEt_2$ (0.1 eq) at room temperature, to the corresponding sulfinate **249b**, sulfite **219b** and sulfur. The same decomposition was

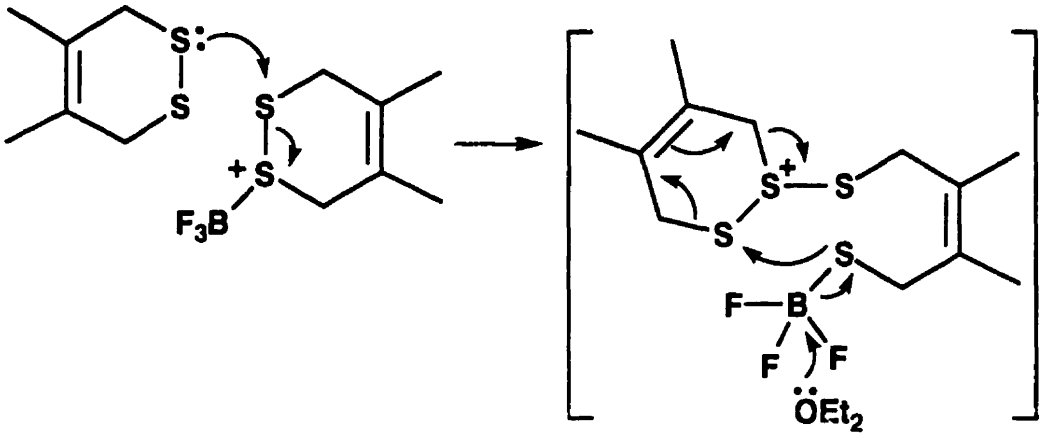
173. T.H. Lowry and K. Schueller Richardson, *Mechanism and Theory in Organic Chemistry*, 3rd Ed., Harper & Row, New York, Chap.10-11 (1987).

reported for diethoxy disulfide **34**.[174] For each sulfur transfer process reported in **Table 29**, we have found that with the addition of 1 molar equivalent of magnesium oxide MgO for each mole of **218b** or **c** used, consistent results were obtained.



Scheme 35

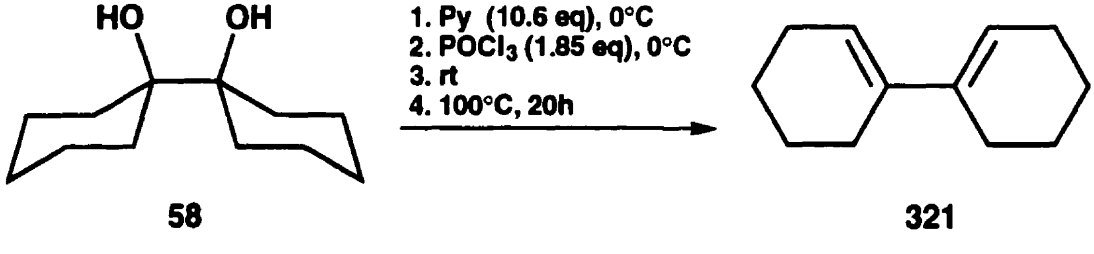
174. M. Kobayashi, H. Minato and K. Shimada, *Int. J. Sulfur Chem.*, 1, 105 (1971).



Scheme 36

5.4 Transfer of Diatomic Sulfur from 218b to Other Dienes

The diene 1,1'-bicyclohexenyl **321** was evaluated, believing that the chemoselectivity of the process toward the formation of disulfide adducts might be enhanced in the presence of a hindered diene. The diene **321** was prepared from the dehydration of bicyclohexenyl-1,1'-diol **58** according to **eq.70**.[175] Diene **321** was obtained as a clear, glassy oil in 56% yield after distillation (b.p. 79-80 °C under 1.5 mmHg; lit. b.p. 68 °C (0.4 mmHg)[175b] and b.p. 88 °C (2 mmHg)[175c]).

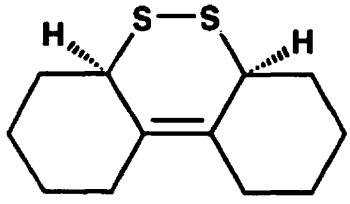


58 **321**

eq. 70

175. a) D.S. Greidinger and D. Ginsburg, *J. Org. Chem.*, **22**, 1406 (1957); b) M.E. Isabelle, D.H. Lake and R.H. Wightman, *Can. J. Chem.*, **55**, 3268 (1977); c) R.K. Haynes, *Aust. J. Chem.*, **31**, 131 (1978).

A set of trapping experiments performed in the presence of **321** using **218b** as precursor have shown no traces of the corresponding tetrasulfide adduct (**Table 31**). Unreacted diene, elemental sulfur S_8, *p*-nitrobenzyl alcohol **220** and corresponding *p*-nitrobenzaldehyde were the other products detected and isolated. Reasonable yields[176] of the disulfide adduct **322** were clearly obtained in the presence of excess reagent **218b**. Other methods involving the transfer of a discrete S_2 unit, including the precursors bis(triphenylgermanium) trisulfide **108**,[52a] bis(thiobenzoyl)biphenyl **112**[53a] and the 5,5-dimethyl-1,2-dithia-3,7-diselenacycloheptane **121**,[53e] reported the formation of **322** in 50%, 70% and 48% isolated yield respectively.



322

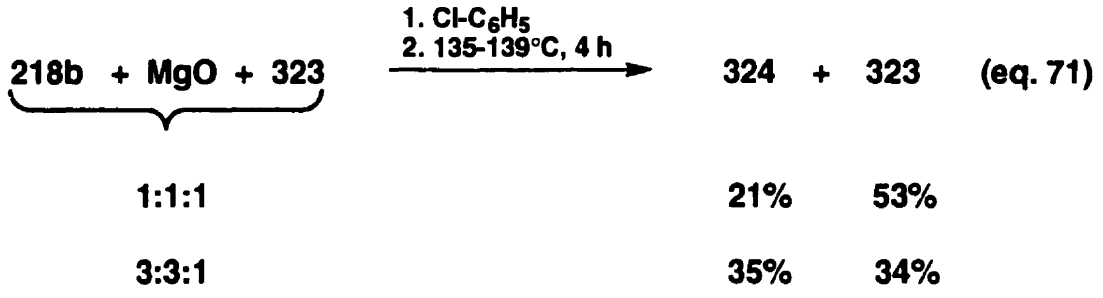
Table 31. Trapping Experiments in the Presence of 1,1'-Bicyclohexenyl

218b: 321[a]	Solvent	time (h)	322 (%)[b]
1.2: 1.0	ClC_6H_5	2	17
2.5: 1.0	(135-140°C)	2	41
3.5: 1.0		2	61

a) Molar equivalent of MgO compared to 218b were also added; b) Isolated yield using column chromatography.

176. This considers that **322** was reported to be sensitive toward light and acid as mentioned in ref. 52a.

The trapping reaction was not as successful in the presence of myrcene **323**. Myrcene **323** was found to contain a bit more than 25% of impurities[177] and was eluted on silica gel using 2% ether in petroleum ether prior to being use as a diene. The disulfide Diels-Alder adduct **324** was found to be very unstable once purified by chromatography. A combination of proton NMR using the internal standard tetrasulfide **226** and gas chromatography indicated yields of *ca.* 30% **(eq.71)**. Methodology using **108, 112** and **121** have reported 35%[52a], 75%[53a] and 40%[53e] isolated yield respectively.



The next interesting trapping experiment was performed in the presence of 1,2-divinylcyclohexane **329**. The unsaturation on the cyclohexane ring was introduced according to the vinylogous Ramberg-Bäcklund reaction where the base-induced conversion of 1-bromo-1-methyl-2-[(bromomethyl)sulfonyl]cyclohexane **328** gave **329 (eq.74)**.[178] Bromination of 1,3,5-trithiane **325** gave the corresponding α-bromomethanesulfonyl bromide **326** in 47% yield **(eq.72)**. The free radical addition of the sulfonyl bromide **326** to 1-methyl-1-cyclohexene **327** afforded the desired adduct for the vinylogous Ramberg-Bäcklund reaction **(eq.73)**. All the intermediates were analyzed by ^{1}H and ^{13}C NMR, and the final diene was used without any further purification. Thermolysis of **218b** in the presence of **329** (1:1 ratio), in toluene-d_8 at 105-110 °C for 14 hours, gave corresponding chemical shift for the formation a di- (3.42 ppm) **330** and a tetrasulfide adduct (3.61 ppm) **331** in a 43:57 ratio. Attempted separation and purification of the two different adducts resulted in decomposition and a complicated mixture.

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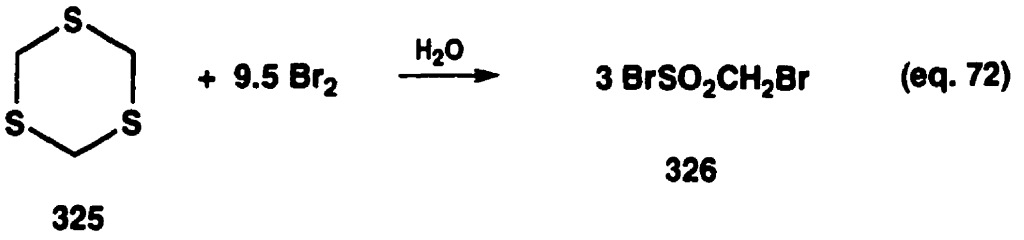
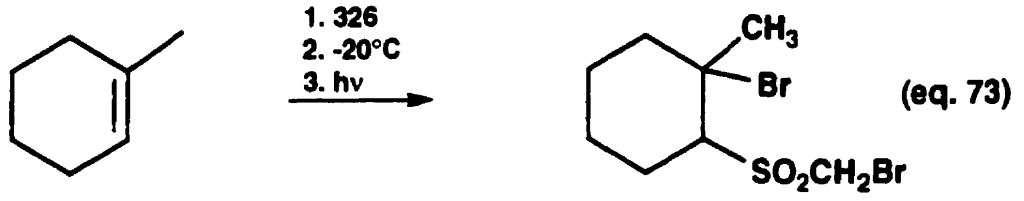
177. Gas chromatography of commercially available myrcene showed that an heptane solution contains more than 25% impurities. A pure sample left at room temperature for 5-6 hours regenerated the impurities. They were probably due to polymerization initiated by light and temperature.

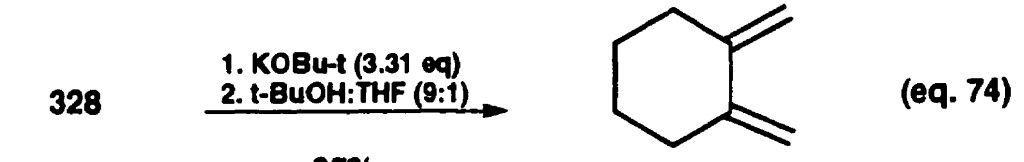
178. E. Block, M. Aslam, V. Eswarakrishan, K. Gebreyes, J. Hutchinson, R. Iyer, J.-A. Laffitte and A. Wall, *J. Am. Chem. Soc.*, **108**, 4568 (1986).



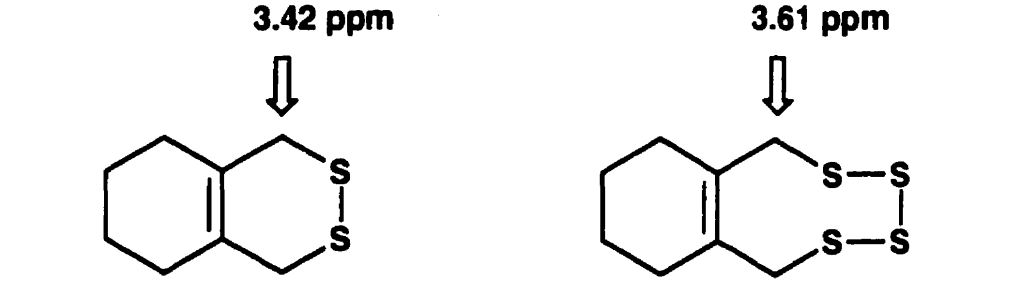
325 326



327 328



329

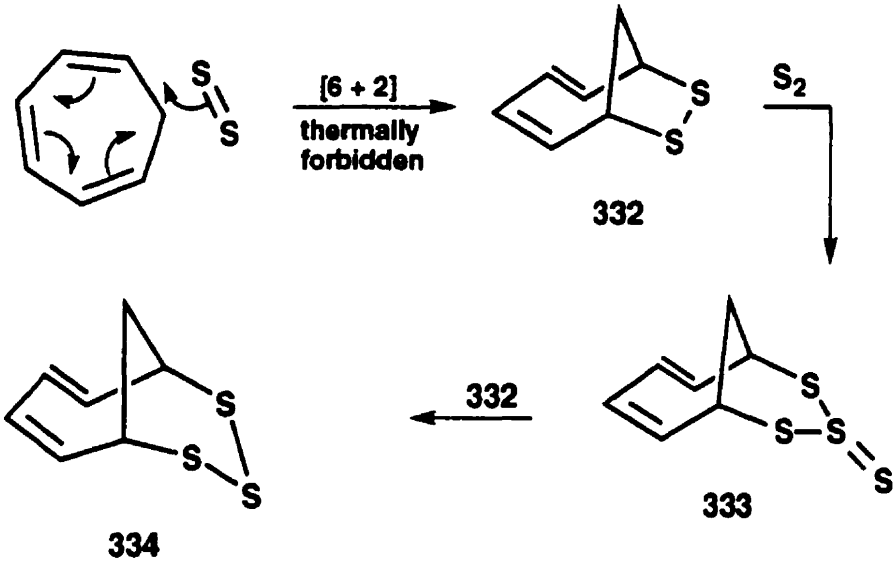


330 331

Interestingly, diatomic sulfur was also transferred from **218b** to cycloheptatriene (1:1.2 ratio), in refluxing chlorobenzene for 2 hours, to give 2,3,4-trithiabicyclo[4.3.1] deca-6,8-diene **334** in 48% isolated yield as a light yellow oil. The identity of this bridged bicyclic trisulfide was confirmed using ^{1}H, ^{13}C NMR and MS.[179] The net result was the

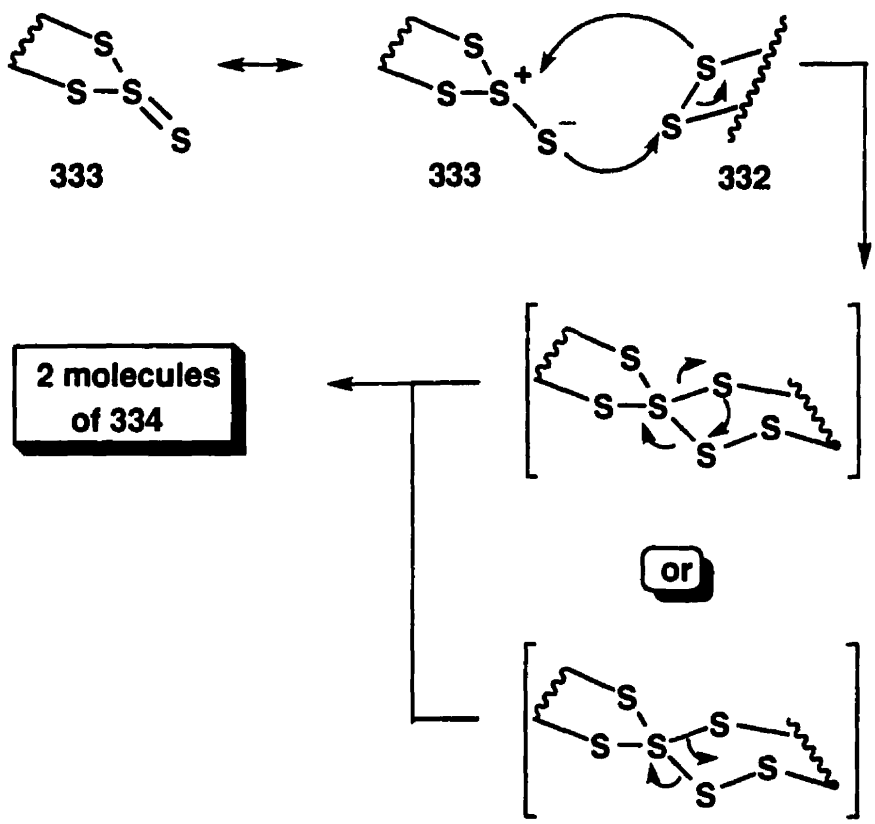
179. H. Fritz and C.D. Weis, *Tetrahedron Lett.*, **18**, 1659 (1974).

sulfuration of cycloheptatriene that resulted probably *via* a [6 + 2]-type addition in the first step, followed by the insertion of another S_2 unit in the strained bicyclic disulfide adduct **332** to give a thionotrisulfide intermediate **333**, that finally eliminates sulfur following a "ligand coupling process"[180] with another molecule of strained disulfide adduct (**Scheme 37**). Ligand coupling is a concerted reaction by orbital interaction between axial and equatorial ligands, where the ligands involved in the coupling retain their original configuration.[180] Previously seen processes like the sulfuration of norbornene derivatives (**119-120**), the S_2 addition to olefins (**135, 137, 138; Scheme 16**) and the chemistry related to activated elemental sulfur (**Chapter 1, Section 1.9**) could be rationalized using ligand coupling processes.



ligand coupling process between 332 and 333:

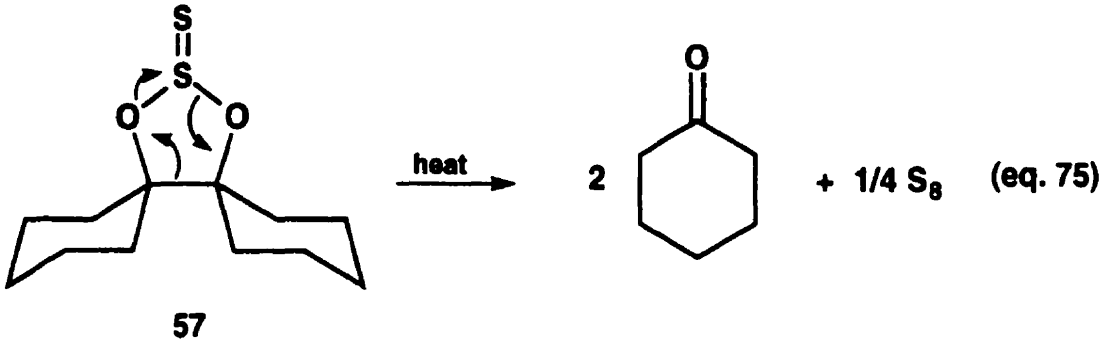
180. S. Oae, *Main Group Chemistry News*, **1**, 10 (1996).



Scheme 37

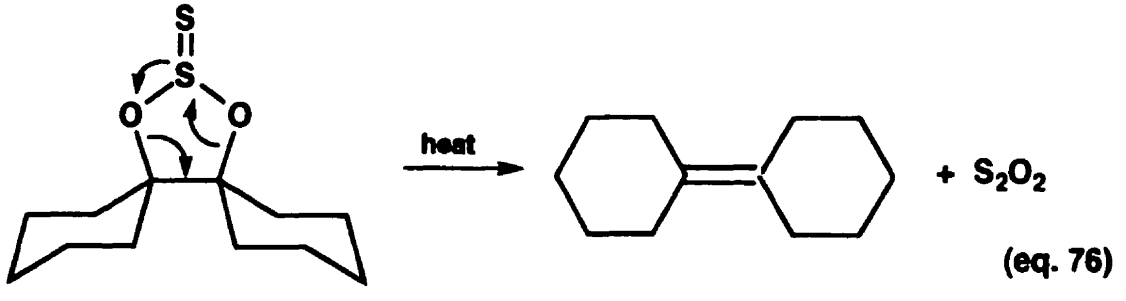
5.5 Transfer of Diatomic Sulfur from the Thionosulfite 57

It was reported that when the only fully characterized thionosulfite O,O-bicyclohexyl-1,1'-diylthiosulfite **57** was heated above its melting point (m.p. 100-101 °C) to *ca.* 150 °C, that an acidic gas evolved.[10] One possible mechanism for the transfer of S_2 may proceed according to **eq.75**, where most of the produced cyclohexanone could be removed during evaporation under reduced pressure leaving mainly the trapped disulfide or tetrasulfide adducts.



57

The thionosulfite **57** was heated in the presence 2,3-diphenyl butadiene **318** in polar solvents like DMSO and DMF (in a 1:1 ratio of diene to **57**) since in chlorobenzene, at 130-135 °C, no di- **(319)** nor tetrasulfide adduct **(320)** were detected after 24 hours. The same reaction in DMF, at 150-155 °C for 12 hours, has shown (^{1}H NMR) the formation of the disulfide adduct **319** exclusively . In DMSO at 155-160 °C, the formation of the disulfide adduct was detected but to a lesser extent. The above qualitative study shows that the S_2 unit was lost from the thionosulfite **57** under thermolysis condition in polar aprotic solvents. Recently, the dissociation of S_8 into S_2 molecules was studied in dimethylacetamide and it was concluded that the S_2 molecules were stabilized in a dipolar aprotic medium.[181] ^{13}C NMR analysis of the residual products of the thermolysis of **57** have indicated the presence of olefinic products, the sulfites **240**, a small amount of diol **58** and elemental sulfur S_8 (TLC). Considering that a gas was evolved under thermolysis condition and that sulfur oxide S_2O_2 was the major lost entity in the mass spectrum of **57**, another mechanism different from **eq.75** was considered where cyclohexylidenecyclohexane **335** was formed and detected by ^{13}C NMR **(eq.76** and **Table 32)**.



57 335

181. G. Bosser and J. Paris, *New J. Chem.*, **19**, 391 (1995).

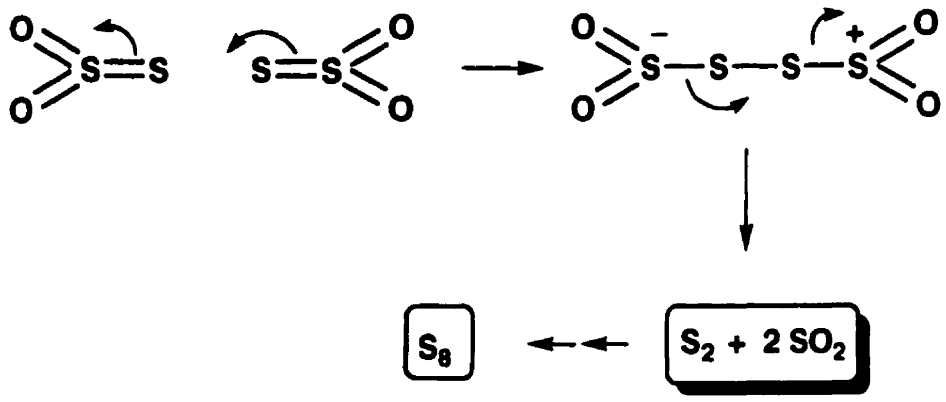
Table 32. ^{13}C NMR Chemical Shifts Related to the Thermolysis of 57

solvent[a]	compounds	δ (ppm)
$CDCl_3$	cyclohexanone	211.65, 41.65, 26.73, 24.67
DMSO-d_6		210.60, 41.28, 26.42, 24.29
$CDCl_3$	335	130.50, 30.75, 29.30, 27.65
DMSO-d_6		128.18[b]
$CDCl_3$	321	136.74, 121.25, 25.82, 25.47, 23.12, 22.49
DMSO-d_6		136.12, 120.78, 25.27, 24.94, 22.61, 22.02
$CDCl_3$	57	94.47, 31.78, 31.11, 25.21, 22.07, 21.92
DMSO-d_6		94.86, 30.91, 30.24, 24.51, 21.80
DMSO-d_6	240	92.96, 31.29, 30.75, 24.51, 21.46
$CDCl_3$	58	75.64, 30.68, 25.86, 21.76
DMSO-d_6		74.19, 29.89, 25.79, 21.50

a) ^{13}C NMR (75 MHz) using 300 MHZ operating frequency and referenced to 77.0 and 39.5 ppm in $CDCl_3$ and DMSO-d_6 respectively; b) Assigned based on ^{13}C NMR analysis of the residue.

The formation of the S_2 unit can certainly result from the previously seen "ligand coupling process"[180] between two S_2O_2 molecules (**Scheme 38**). The oxide S_2O_2 being known to disproportionate to S_8 and SO_2.[182]

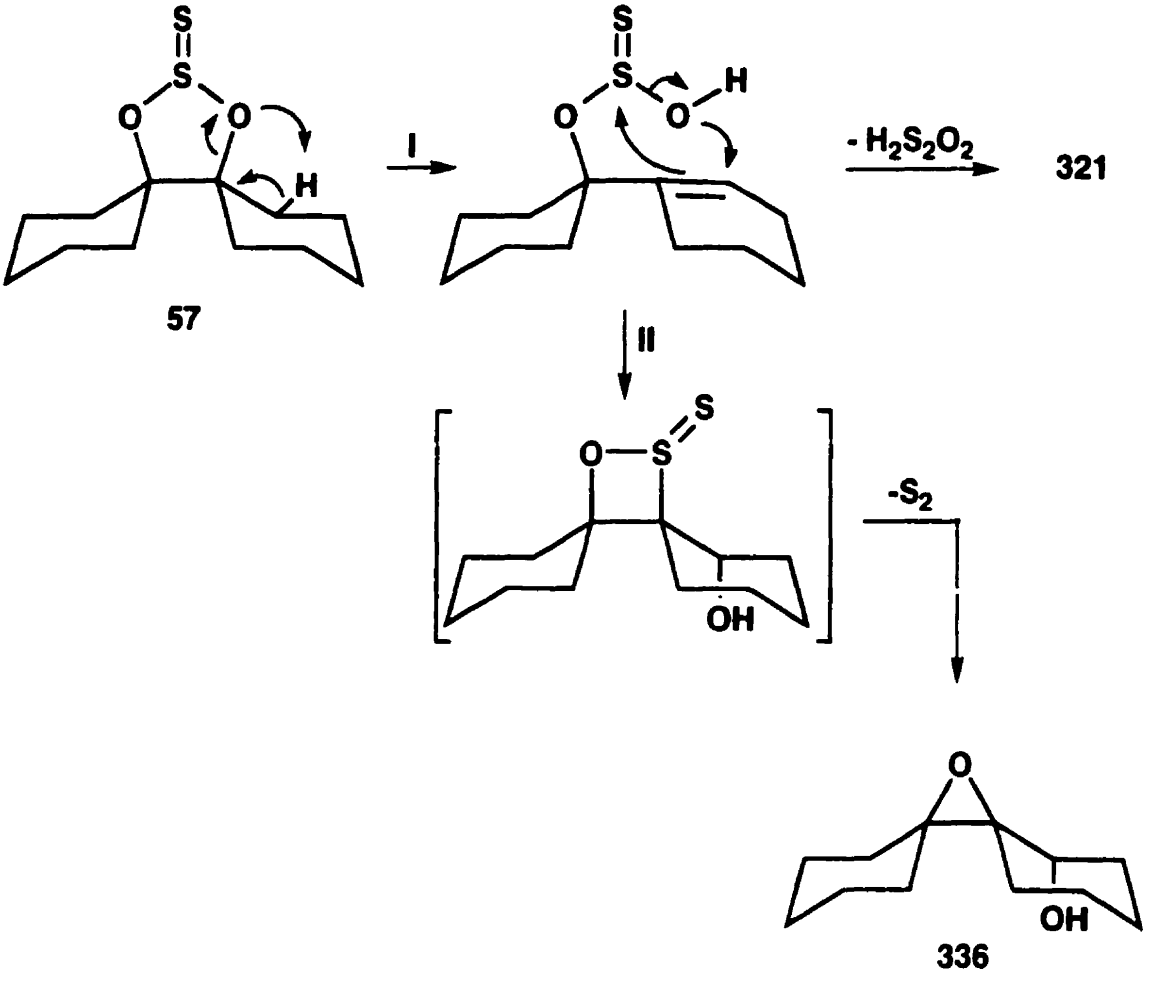
182. a) P.W. Schenk and R. Steudel, *Angew. Chem. Int. Ed.*, 4, 402 (1965); b) V. Haase,V. Heibel, G. Kirschstein, A. Kubny, H.-J. Richter-Ditten, H.-G. Horn and R. Steudel, *Gmelin Handbuch der Anorganischen Chemie*, H. Bitterer Ed., 8th Ed., vol.9, Spinger-Verlag, New York , pp. 1-69 (1980).



Scheme 38

Other mechanistic rationales are also possible since the ^{13}C chemical shift corresponds to 1,1'-bicyclohexenyl **321** (**Table 32**). The elimination of $H_2S_2O_2$ (path **I** in **Scheme 39**) followed by ligand coupling process can generate the S_2 unit (**Scheme 38**). However, there is no evidence (NMR) for the possible formation of the epoxide **336** (path **II** in **Scheme 39**). The ^{13}C NMR chemical shifts reported in **Table 32** do not shift by very much in changing solvents from chloroform-d to dimethylsulfoxide-d_6. While ^{1}H NMR was used to detect the disulfide trapped adduct **319**, ^{13}C NMR was employed as a tool to analyse the residual products, in hopes to propose a unique mechanism for the transfer of S_2. Careful analysis of the ^{13}C spectrum has shown that the cyclohexylidenecyclohexane **335**[183] and bicyclohexenyl **321** were formed in comparable amounts and that two different mechanisms were operating at the same time for the formation of S_2 *via* S_2O_2 (**eq.76** and path **I** of **Scheme 39**). Only traces of cyclohexanone were detected in the crude residue.

183. J.E. Murry, M.P. Fleming, K.L. Kees and L.R. Krepski, *J. Org. Chem.*, **43**, 3255 (1978).



Scheme 39

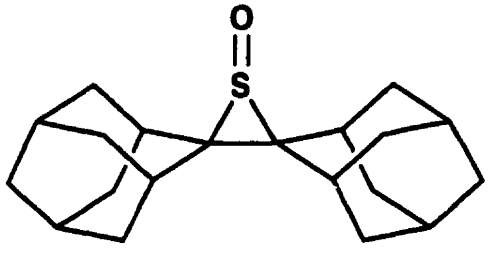
The detection of the trapped disulfide adduct **319** in the thermolysis of the thionosulfite **57**, in a polar aprotic solvent, raised the question whether the dialkoxy disulfide **218** may actually give the same adduct. At a somewhat lower temperature (90 °C) in DMSO-d_6, **218b** in the presence of 2,3-diphenylbutadiene **318** (1:0.75) was found to deliver the disulfide adduct **319** and unreacted diene after 2 hours (^{1}H NMR). Interestingly, only traces of the tetrasulfide adduct **320** were detected. A similar experiment in the presence of 3 equivalents of 2,3-dimethylbutadiene **315** at 113 °C for 1 hour gave a 1:1 ratio of the trapped di- and tetrasulfide **316** and **317** respectively.

5.6 Nucleophilic Substitution on 218b in the Presence of a Diene

The nucleophilic substitution of **218b** by benzylamine C_6H_5-CH_2-NH_2 in the presence of 2,3-dimethyl butadiene **315** was monitored using ^1H NMR in toluene-d_8 at 95 °C for 20 hours. The di- **(316)** and tetrasulfide adducts **(317)** were detected in a 30:70 ratio and isolated in 16% and 34% yield respectively. The adducts were supportive of the mechanism proposed in **Scheme 4** by Motoki[21] and the one suggested in **Scheme 5**, where both processes liberate a S_2 unit.

5.7 Thermolysis of the Sulfite 219

Recently, two different precursors for sulfur monoxide (S=O) transfer were prepared in our laboratory.[184] The hindered episulfoxides adamantylideneadamantane thiirane-1-oxide **337** and the analog **338** were found to deliver S=O to dienes **315** (dimethyl) and **318** (diphenyl) in optimized isolated yields of *ca.* 75% (in toluene at 110 °C from 14-24 hours).[184] Prior to these precursors, cyclic sulfites like **339** and **340** were found to decompose under thermolysis conditions to give benzil **341** and the diketone **342** along with S=O respectively.[185] Thompson reported that the nonequivalence of the methylene protons was still maintained at 145 °C for diethyl sulfite.[1c]



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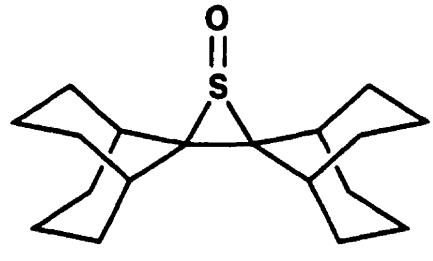
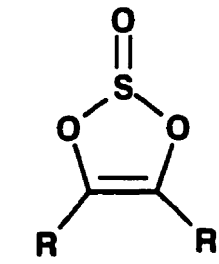


338

184. I.A. Abu-Yousef and D.N. Harpp, *Tetrahedron Lett.*, **36**, 201 (1995); I.A. Abu-Yousef and D.N. Harpp, *J. Org. Chem.*, **52**, 0000 (1997), in press.

185. a) Y. Okumura, *J. Org. Chem.*, **28**, 1075 (1963); b) A. DeGroot, J.A. Boerma and H. Wynberg, *J. Chem. Soc., Chem. Commun.*, 347 (1968).



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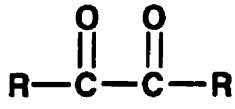
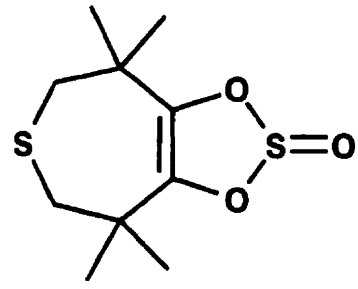


341

Heat - S=O



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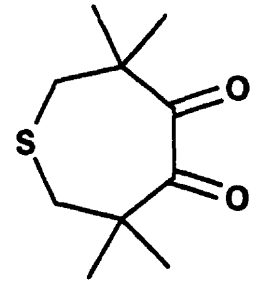
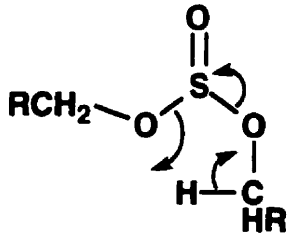
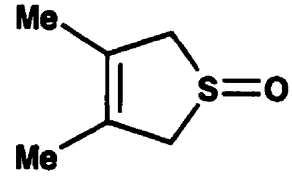


342

We investigated the decomposition of sulfite **219b** (4-NO_2) in the presence of 3 equivalents of diene **315** in DMSO-d_6 at 113 °C for 3 hours. Prior to the experiment, all the finger print ^{13}C NMR chemical shifts for all the possible related compounds were clearly determined in DMSO-d_6 (**Table 33**). We found that the sulfite **219b** was actually transferring S=O since the corresponding 2,5-dihydro-3,4-dimethyl-thiophene 1-oxide **343** was detected. The other major product in the mixture was the corresponding 4-nitrobenzyl alcohol along with the 4-nitrobenzaldehyde suggesting a pseudo 5-membered ring transition state (**Scheme 39**). The reaction was not further investigated, but the potential for S=O transfer is certainly present!



Scheme 39



343

Table 33. ^{13}C NMR Chemical Shifts Related to the Thermolysis of 219b

solvent[a]	compounds[b]	δ (ppm): assignment
DMSO-d_6	R-OH	61.98: CH_2
DMSO-d_6	$(ROS)_2$	74.91: CH_2
DMSO-d_6	$(RO)_2S{=}O$	62.51: CH_2
DMSO-d_6	RH(C=O)	192.19: C=O
DMSO-d_6	diene 315	20.23, 113.41, 142.70
DMSO-d_6 $CDCl_3$	343	60.05: CH_2, 14.08, 126.96 64.32: CH_2, 14.46, 126.07

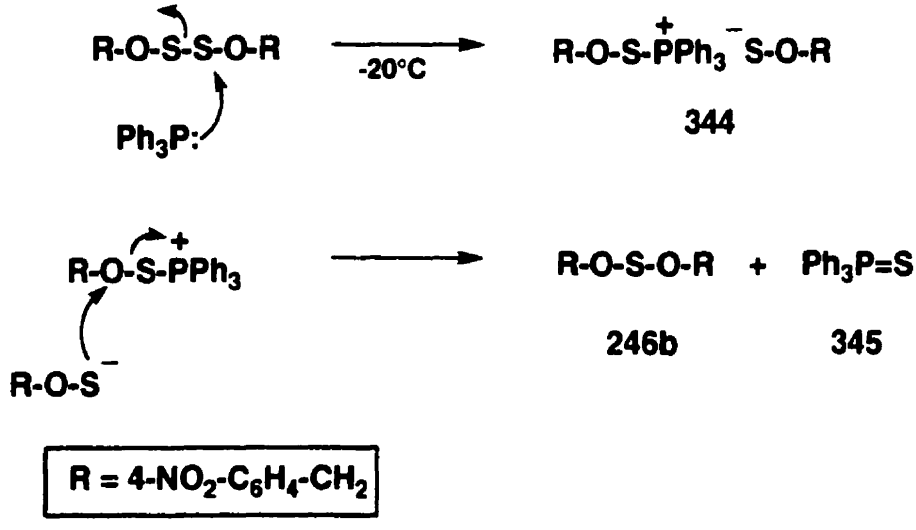
a) ^{13}C NMR (75 MHz) using 300 MHz operating frequency and referenced to 77.0 and 39.5 ppm in $CDCl_3$ and DMSO-d_6 respectively; b) R= 4-O_2N-C_6H_4-CH_2.

5.8 Desulfurization of 218b

The mechanism of desulfurization of trisulfide and polysulfides has been extensively studied.[186] The desulfurization of bis(4-nitrobenzyloxy) disulfide **218b** by an equimolar amount of triphenylphosphine Ph_3P was first examined at low temperature (^{13}C NMR-$CDCl_3$); the reaction was observed to proceed at -20 °C, below that temperature no signs of reactivity was detected. The reaction was followed up to room temperature, and the only compounds present in the reaction mixture were the sulfoxylate **246b**, the dialkoxy disulfide **218b** and 4-nitrobenzyl alcohol **220** (**Figure 27**). Leaving the mixture at room temperature for 20 hours resulted in a mixture of the corresponding sulfinate **249b** (isomerization of **246b** to **249b**) and alcohol **220**. Based on the low temperature results, the nucleophilic attack of triphenylphosphine on a sulfur atom of **218b** gives the ion pair **344**, followed by an attack of the thioalkoxide anion on the sulfur bonding oxygen atom of the phosphonium $SOCH_2C_6H_4$-NO_2-4 group to displace sulfoxylate **246b** and

186. a) D.N. Harpp, R.A. Smith and K. Steliou, *J. Org. Chem.*, **46**, 2072 (1981); D.N. Harpp and R.A. Smith, *J. Am. Chem. Soc.*, **104**, 6045 (1982).

triphenylphosphine sulfide **345** (**Scheme 40**). The reaction was repeated on a larger scale in Et_2O and the products isolated were the sulfinate **249b** and the alcohol **220** along with $Ph_3P{=}S$ (characterized by MS). The empty d-orbitals of the sulfur atoms in **218b** favor the attack of the phosphine on sulfur rather than on oxygen. This proposal is supported by the hard-soft acid-base (HSAB) principle developed by Pearson[187] where sulfur is a softer acceptor than oxygen and Ph_3P a soft base showing higher affinity for the sulfur atom than for the oxygen atom.



Scheme 40

When the same reaction was performed at room temperature, the corresponding sulfoxylate **246b**, dialkoxy disulfide **218b**, traces of sulfinate **249b**, alcohol **220** and the interesting sulfite **219b** were all detected after 1.5 hours (^{13}C NMR). After 20 hours, the sulfinate **249b**, the alcohol **220** and the sulfite **219b** were the only products in the reaction mixture along with elemental sulfur (TLC). We believe that a parallel mechanism for the formation of the sulfite **219b** was taking place.

187. R.G. Pearson, *Hard Soft Acids and Bases*, Dowden, Hutchinson and Ross, Pa, 1973; T.-L. Ho, *Hard and Soft Acids and Bases Principle in Organic Chemistry*, Academic Press, New York, 1977.

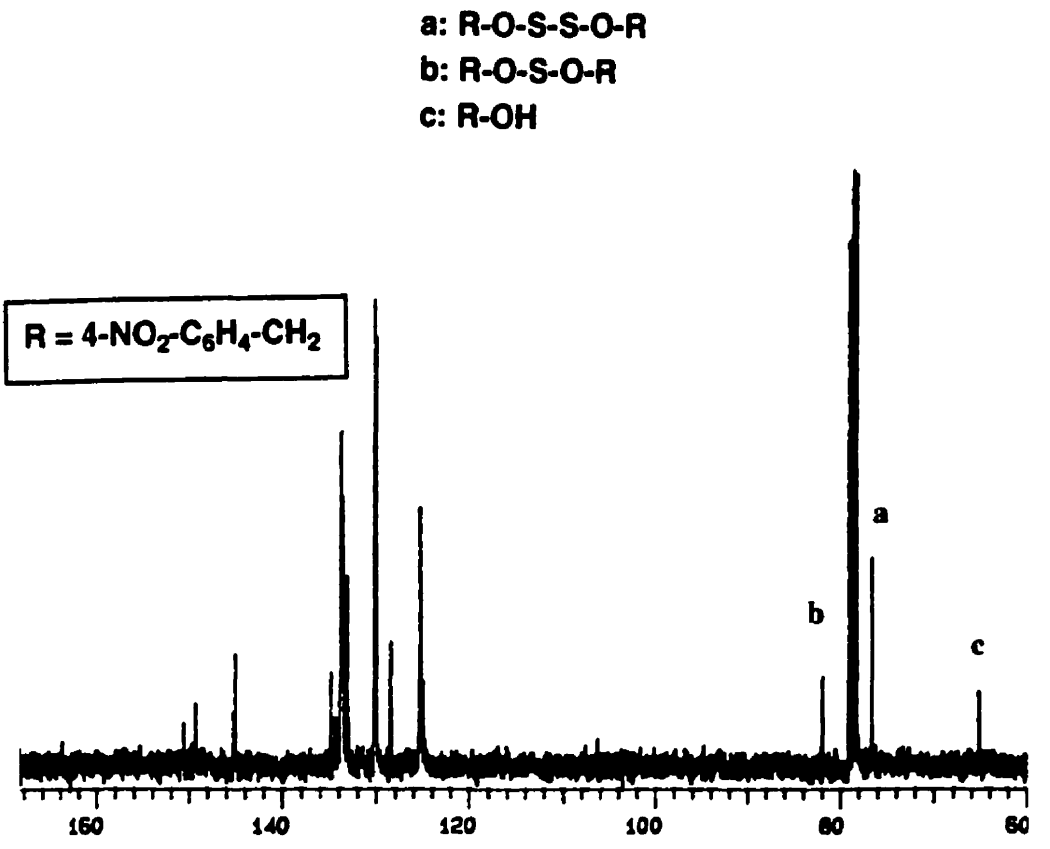


Figure 27: ^{13}C NMR of the Low-Temperature Desulfurization of 218b

5.9 Biological Testing

Dialkoxy disulfides 218a-c were tested for biocidal activity and found to be active. The tests were performed at Rohm & Haas Company in Pennsylvania United States under the supervision of Dr. T. Ghosh.

5.10 General Commentary

Bis(4-substituted benzyloxy) disulfides **218a-e** were found to be good precursors for the transfer of diatomic sulfur S_2. The disulfide adduct formation was related to the nature of the diene and comparably competitive toward the S_2 precursors **218**, hence leading to the formation of the corresponding tetrasulfide adducts **317** and **320** from 2,3-dimethyl and 2,3-diphenyl butadiene respectively. These tetrasulfide adducts were conveniently converted back to the disulfide adducts **316** and **319** upon triphenylphosphine treatment. In general, the beauty of compounds **218** is that the thermal decomposition gives, besides S_2, the corresponding alcohol and aldehyde that can be easily reduced back to the alcohol and reused for the preparation of precursors **218**. The S_2 unit was also transferred to other dienes such as 1,1'-bicyclohexenyl **321**, myrcene **323**, 1,2-divinylcyclohexane **329** and the triene cycloheptatriene where the formation of the bridged trisulfide adduct was rationalized by mechanistic considerations involving the "ligand coupling process".

Qualitative studies related to the thermolysis of the thionosulfite **57** in polar aprotic solvents have demonstrated the potential of those reagents as precursors for the transfer of S_2 unit.[188] Different mechanisms were proposed for the formation of the olefinic products detected. It was also demonstrated that the generation of S_2 unit as part of mechanistic considerations could be proven if the reactions are performed in the presence of dienes to generate di- and tetrasulfide adducts. The potential of bis(4-nitrobenzyl) sulfite **219b** as precursor for the generation of sulfur monoxide (S=O) was briefly investigated under thermolysis conditions and yielded positive results. Finally, the desulfurization of bis(4-nitrobenzyloxy) disulfide **218b** by triphenylphosphine Ph_3P, at low temperature in chloroform-d, was found to be very specific toward the formation of the corresponding sulfoxylate **246b** and 4-nitrobenzyl alcohol **220**. As anticipated, the sulfoxylate **246b** isomerized to the sulfinate **249b** when the reaction mixture was left at room temperature for 20 hours.

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188. I would like to express my thanks to Evelyn Martins, undergraduate student in the Honour's program who was involved with the experiments as part of her Honour's project (1995-1996), and Charles Abrams, fellow graduate student who is now looking into the potential of other cyclic thionosulfites as precursors for the transfer of the S_2 unit, and who shared the mass spectrometry results with us.

CONTRIBUTIONS TO ORIGINAL KNOWLEDGE

i) A series of unreported symmetrical acyclic dibenzyloxy disulfides substituted in the *para* position were prepared by a modified procedure in very high yield (*ca.* 85%: 4-NO_2, 4-Cl, 4-MeO, 4-Me, 4-CO_2-Me, 4-O(C=O)Me). The novel unreported bis(2-pyridinyl carbinoxy) disulfide was also prepared.

ii) The dichotomy related to the structure of of dialkoxy disulfides was resolved. The preparation of a series of closely related compounds including the unreported corresponding sulfoxylates (4-NO_2, 4-Cl, 4-MeO and 4-Me), sulfites (4-NO_2, 4-Cl, 4-MeO and 4-Me), the 4-nitrobenzyloxybenzyl trisulfide and bis(4-nitrobenzyl) tetrasulfide, along with the reported bis(4-nitrobenzyl) disulfide, O,O'-bicyclohexenyl-1,1'-diylthiosulfite and O,O'-bicyclohexenyl-1,1'-diylsulfite permitted a comparative spectroscopic study including ^{1}H, ^{13}C (solid and solution), ^{17}O NMR, IR and Raman (solid and solution) and UV analysis.

iii) X-ray analysis of bis(4-nitrobenzyloxy) disulfide, bis(4-chlorobenzyloxy) disulfide, bis(4-nitrobenzyl) tetrasulfide and bis(4-nitrobenzyl) sulfoxylate were obtained and compared. In the two former cases the S-S bond lengths were found to be linear and shorter than regular disulfides and polysulfides. Considering the data obtained in **ii)** and **iii)**, the structure of dialkoxy disulfides was established to be linear, and the diastereotopicity of the adjacent benzylic protons was due to a barrier to rotation along the **OSSO** subunit of *ca.* 18 kcal mol^{-1}.

iv) Dialkoxy disulfides represent another case of the more general phenomenon called **atropisomerism**. The resulting asymmetric induction gave rise to a diastereomeric complex in the presence of $Eu(hfc)_3$ and suggested the existence of the [+]- and [-]-torsional isomers. The existence of the rotational diastereomers was clearly demonstrated by ^{1}H and ^{13}C NMR for unreported chiral dialkoxy disulfides prepared from enantiomerically pure chiral and racemic alcohols sec-phenethyl alcohol and 1-naphthyl-ethanol.

v) The thermolysis study of dialkoxy disulfides in the presence of dienes 2,3-dimethyl and 2,3-diphenylbutadiene, 1,1'-bicyclohexenyl, myrcene, 1,2-divinylcyclohexane and the triene cycloheptatriene have established that these are good precursors for the transfer of S_2 unit.

vi) The tetrasulfide adduct sobtained in the presence of the dienes 2,3-dimethyl and 2,3-diphenylbutadiene were cleanly converted, under different conditions, to their corresponding disulfide adducts. In these cases, the disulfide adduct was competitive to the diene for the S_2 transfer.

vii) The cyclic thionosulfite O,O'-bicyclohexenyl-1,1'-diylthiosulfite was demonstrated to be a potential precursor for the transfer of S_2 unit under thermolysis conditions in DMSO. The mechanism is believed to proceed by the elimination of S_2O_2 molecules that undergo the ligand coupling process to liberate S_2 and two molecules of SO_2.

viii) Thermolysis of 4-nitrobenzyloxybenzyl trisulfide in the presence of 2,3-dimethyl butadiene gave the corresponding disulfide and tetrasulfide adduct. These were believed to come about *via* two different processes (1:1 ratio) that involved a pseudo 6-membered ring in the transition state, these two processes being energically different by *ca.* 5 kcal mol^{-1}.

ix) The thermolysis of bis(4-nitrobenzyl) sulfite in DMSO in the presence of 2,3-dimethyl butadiene gave the corresponding 2,5-dihydro-3,4-dimethyl-thiophene 1-oxide due to the transfer of sulfur monoxide.

x) The low temperature desulfurization of bis(4-nitrobenzyloxy) disulfide by triphenylphosphine was very specific toward the formation of the bis(4-nitrobenzyl) sulfoxylate and 4-nitrobenzyl alcohol. The sulfoxylate was found to isomerize to the corresponding sulfinate at room temperature.

xi) The kinetics of the isomerization of bis(4-nitrobenzyl) and bis(4-chlorobenzyl) sulfoxylates to their sulfinates was studied in different solvents and found to follow first order kinetics; the Arrhenius parameters were determined and interpreted following transition state theory. The isomerization is considered to be a unimolecular process where the central sulfur atom acts as an electron donor. Electron withdrawing substituents in the *para* position of the benzene ring are believed to increase the stability of the sulfoxylate.

xii) During the preparation of the sulfoxylates, the corresponding dialkoxy disulfides and sulfites were also formed and a novel mechanism for their formation was proposed. These sulfoxylates were found to give the corresponding sulfite in the presence of *m*-CPBA.

CHAPTER 6: EXPERIMENTAL

6.1 Generalities

The commercial reagents were obtained from Aldrich Chemical Company and tested by TLC, ^{1}H and ^{13}C NMR for purity. Solid reagents were recrystallized when needed and distillation was performed on liquid reagents when required. Sulfur monochloride, S_2Cl_2, was distilled twice from sulfur flowers and charcoal and the orange fraction boiling at 135-137 °C was collected and stored in a dark bottle under an atmosphere of N_2 in the freezer.[91] Sulfur dichloride, SCl_2, was distilled twice from 0.1% phosphorus pentachloride, PCl_5, and the red fraction boiling from 58-60 °C was collected and stored in the freezer under N_2.[91] Triethylamine, Et_3N (b.p. 89-90 °C), and pyridine, C_5H_5N, (b.p. 114-115 °C) were distilled over potassium hydroxide, KOH, and stored over 3Å molecular sieves that were activated at 400°C overnight and cooled in a dessicator. Thionyl chloride, $SOCl_2$, was distilled from triphenyl phosphite, $(C_6H_5O)_3P$, and the fraction boiling at 79 °C was collected and stored under nitrogen. Triphenylphosphine, Ph_3P, was recrystallized from absolute ethanol (m.p. 79-80 °C).

Different solvents were treated prior to use; methylene chloride, CH_2Cl_2, was distilled from anhydrous phosphorus pentoxide, P_2O_5, hexanes were distilled from concentrated sulfuric acid, H_2SO_4, and passed through an alumina column, tetrahydrofuran, THF, was distilled from the blue sodium-benzophenone ketal, and toluene and benzene were stored over metallic sodium. The dry ether used was diethyl ether, Et_2O, except when petroleum ether (low boiling 32-60 °C) is indicated.

Thin Layer Chromatography (TLC) was performed on 0.25mm Merck silica gel plates (60F-254) with polyester backing and visualized using UV light, a 10% aqueous sulfuric acid solution of ammonium molybdate-cerium sulfate developing dip followed by heating treatment and iodine adsorbed onto silica gel for the detection of sulfur containing compounds. Column chromatography was carried out on Merck Kieselgel 60 (230-400 mesh) using flash chromatography conditions.[189] Gas Chromatography was performed on a Varian Associates (VA) model 3700 gas chromatogram equipped with a model 4270 printing integrator and an FID detector. Separations were obtained using a 15m glass capillary column bonded with 3% silicone OV-101. Melting points (m.p.) were obtained using open

189. W.C. Still, M. Khan and A. Mitra, *J. Org. Chem.*, **43**, 2923 (1978).

end capillaries on a Gallenkamp melting point apparatus and uncorrected. Boiling points were measured directly and reported uncorrected.

The ^{1}H and ^{13}C NMR spectra were recorded on Varian XL-200 MHz, XL-300 MHz, Unity 500 MHz spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) relative to internal tetramethylsilane, TMS, or referenced to the solvent peak noted. Abbreviations for the multiplicity assignments follows: s for singlet, d for doublet, t for triplet, q for quartet and m for multiplet. ^{17}O NMR spectra were recorded on Varian XL-300 MHz and referenced using D_2O as an external reference and acetone-d_6 as an internal reference (**Appendix VIII**). The solid state ^{13}C NMR for **218a-b** were recorded on Chemagnetics CMX-300 MHz and **226** on Chemagnetics MX-100MHz by Dr. Fred Morin in the Department of Chemistry at McGill University.

Infrared spectra were recorded on an Analect ASQ-18 FTIR Spectrometer calibrated to the 1602 cm^{-1} line of polystyrene equipped with an Analect Instrument MAP-67 data System and an Analect Instrument RAM-56 Color Display or on a Nicolet Model 6000 FT-IR spectrometer. Ultra-Visible spectra were recorded on a Hewlett Packard 8452A Diode Array Spectrometer. The FT-Raman spectra were recorded on a Bruker Model IFS-88 spectrometer with the aid of a Bruker FRA-106 Raman module equipped with an air-cooled, 300-mW Nd:YAG laser operating in the near-IR region at 1064 nm. The data are reported in wavenumbers (cm^{-1}).

Low resolution electron impact (EI) and chemical ionization (CI) mass spectra were obtained using a DuPont Instrument model 21-492B equipped with a 70-eV ionizing energy source and used in direct-inlet mode and performed by Mr. Nadim Saade. The data are reported according to mass to charge ratio (m/z), assignment and relative intensity. Elemental analyses for **218a-b** and **219b** were obtained from the laboratory of Dr. Charles Larsen at Kemisk Laboratorium, University of Copenhagen in Denmark. The X-ray crystallography of compound **218b** was performed by Dr. James Britten, compound **226** was determined by Dr. Rosemary C. Hynes and compounds **218c** and **246b** by Dr. Anne-Marie Lebuis all at the Department of Chemistry, McGill University, Montreal, Quebec, Canada. Solutions and refinement were done using NRCVAX system program (see **Appendixes II-V**).

6.2 Methodology for the Preparation of Dialkoxy Disulfides and the Related Compounds Chapter 2

Preparation of Dimethyl Sulfite 215:

$(CH_3O)_2S=O$

Thionyl chloride (9.10 mL, 125 mmol) was added dropwise to a solution of dry methanol (10.2 mL, 250 mmol) mixed with pyridine (20.1 mL, 250 mmol) in anhydrous ether at -10 °C. Within a few minutes, pyridine hydrochloride, $C_5H_5N.HCl$, separated as a white precipitate. The mixture was stirred for 1h until room temperature was reached and quenched with 20 mL of water and transferred to a separatory funnel. A portion of 30 mL of dichloromethane was added and the aqueous layer was discarded. The remaining organic phase was washed with 5% HCl (2 x 20 mL) to remove the excess pyridine, then dried over anhydrous $MgSO_4$, filtered and evaporated to a colorless liquid (8.947g, 65%). Rf (EtOAc-hexanes, 1:4): 0.19; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.50 (s, 6H) ppm; IR (neat): 1210 (S=O) cm-1 that was found to be in the fingerprint region.[48a]

Attempt at the Preparation of Dimethoxy Disulfide:[1a-b]

$(CH_3OS)_2$

To a stirred solution of methanol (3.80 mL, 93.6 mmol) and triethylamine (13.1 mL, 93.6 mmol) in dichloromethane kept at 5-10 °C was added dropwise a solution of S_2Cl_2 (3.75 mL, 46.8 mmol) in 15 mL of dichloromethane. The addition rate was such that the mixture was kept at *ca.* 5 °C during the addition time of 0.5 h. The mixture was stirred for an extra 1 h without external cooling. Ice-water (30 mL) was then added, and the reaction was transferred to a separatory funnel where the aqueous phase was discarded. The organic phase was washed with cold water (3 x 25 mL) in order to remove triethylamine hydrochloride, $Et_3N.HCl$, dried over anhydrous $MgSO_4$, filtered and evaporated. The residual yellow oil containing sulfur precipitate was evaluated by TLC (hexanes): S_8 Rf: 0.61, $(CH_3O)_2S=O$ Rf: base line, $(CH_3O)_2S_2$ Rf: 0.11. A portion was kept in the freezer at -15 °C overnight and found to decompose to S_8 and dimethyl sulfite **215** (TLC). The other portion decomposed to S_8 and **215** during the process of distillation under reduced pressure.

Attempt at the Preparation of Diethoxy Disulfide 34:

The same procedure was used using dry ethanol instead of methanol. The results were as successful as for methanol!

$(CH_3CH_2OS)_2$

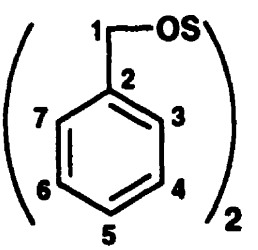
Preparation of Dry Ethanol:

EtOH (99%, 10 mL), magnesium turnings (1 g) and iodine (0.1 g) were boiled under reflux until the iodine color disappeared. The mixture was heated until all the magnesium was converted into ethoxide, then EtOH (180 mL) containing less than 1% of water was added and heated under reflux for an extra 5 hours, whereafter the EtOH was distilled.[93]

Preparation of 4-Substituted Dibenzyloxy Disulfides 218a-e:

The compounds were prepared based on Thompson's methodology.[1a] The reaction solvent was changed to a mixture of ether and dichloromethane 70:30. The S_2Cl_2 solution was added dropwise to keep the reaction temperature in the 0-5 °C range and when more than half the solution was added, the cooling bath was removed and the addition continued with vigorous stirring. Upon completion of the addition, the reaction was quenched with ice-water.

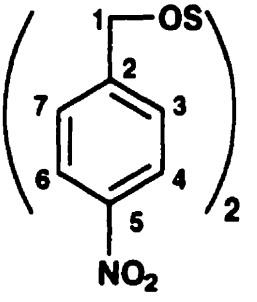
Preparation of Bis(Benzyloxy) Disulfide 218a:[1a]



To a solution of benzyl alcohol (4.44 mL, 42.9 mmol) and triethylamine (6.06 mL, 42.9 mmol) in ether (70 mL) and CH_2Cl_2 (30 mL) cooled to 0 °C was added a solution of S_2Cl_2 (1.72 mL, 22 mmol) in CH_2Cl_2 (8 mL) dropwise. Three quarters of the way through the addition, the ice bath was removed, the addition completed along with stirring for 1 hour then water (100 mL) was added. The organic phase was separated and further washed with water (3 x 80 mL) and a solution of NaCl sat'd (2 x 60 mL), dried over anhydrous $MgSO_4$, filtered and evaporated to give a crude off-white solid containing **218a** Rf(30% EtOAc in hexanes): 0.62 and traces of benzyl alcohol Rf: 0.27; ^1H NMR (200 MHz, $CDCl_3$) δ: 2.27

(s, 1H), 4.63 (s, 2H), 7.34 (s, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 65.13, 126.92, 127.52, 128.45, 140.79 ppm. Column chromatography using this solvent system gave an off-white solid (5.425 g) that was identified as **218a** compared to a recrystallized sample; m.p. (hexanes-*t*-BuOH) 50-51 °C (lit.[1a] 58-59 °C); ^1H NMR (200 MHz, $CDCl_3$) δ: 4.79, 4.90 (ABq J = 11.67 Hz, 2H), 7.34 (s, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 76.74 (C1), 128.48 (C3 and C7), 128.53 (C5), 128.65 (C4 and C6) and 136.54 (C2) ppm; MS (EI, direct inlet, 1.6 V) m/z: 278 ($M^{+\cdot}$, 38), 230 ($M^{+\cdot}$ -S=O, 100), 180 ($M^{+\cdot}$ - $H_2S_2O_2$, 33)[190], 105 (C_6H_5-$(CH_2)_2^+$, 30), 91 (C_6H_5-CH_2^+, 100), 77 (Ph^+, 14); Anal. ($C_{14}H_{14}O_2S_2$) C (calc. 60.41, found 40.7), H (calc. 5.07, found 3.61). Presumably, the product decomposed on transit to the analysis center. Spectroscopic data were never reported previously except for elemental analysis.[1a]

Preparation of Bis(4-Nitrobenzyloxy) Disulfide 218b:

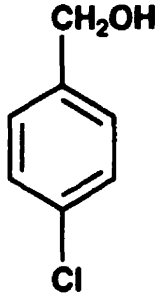


To a solution of 4-nitrobenzyl alcohol (6.6 g, 42.9 mmol) and triethylamine (6.06 mL, 42.9 mmol) in ether (70 mL) and CH_2Cl_2 (30 mL) cooled to 0 °C was added dropwise a solution of S_2Cl_2 (1.72 mL, 21.5 mmol) in CH_2Cl_2 (8 mL) .Three quarters of the way through the addition, the ice bath was removed, the addition completed along with stirring for 1 hour then water (100 mL) was added. The organic phase was separated and further washed with water (3 x 80 mL) and a solution of NaCl sat'd (2 x 60 mL), dried over anhydrous $MgSO_4$, filtered and evaporated to give a crude off-white solid containing **218b** Rf(30% EtOAc in hexanes): 0.45 and traces of 4-nitrobenzyl alcohol Rf: 0.13. Column chromatography using this solvent system along with recrystallization (70% of the total yield is obtained from the crude and the residue obtained from the mother liquor is chromatographed) gave a light yellow powder (7.043 g, 90%) identified as **218b**; m.p. (EtOAc-hexanes) 92-93 °C; ^1H NMR (200 MHz, $CDCl_3$) δ: 4.88, 4.99 (ABq, J = 12.18 Hz, 2H), 7.48 (d, J = 8.82 Hz, 2H), 8.20 (d, J = 8.71 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 75.05 (C1), 123.70 (C4 and C6), 128.61 (C3 and C7), 143.55 (C2) and 147.77 (C5) ppm; MS (EI, direct inlet, 423 mV) m/z: 320 ($M^{+\cdot}$ -S=O, 8), 272 ($M^{+\cdot}$ -SO_2, 15), 151 (HONO-C_6H_4-$C{=}O^+$, 47), 136 (O_2N-C_6H_4-CH_2^+, 100), 106 (136^+ -NO, 35), 89 (136^+

190. The mass spectrum of diisopropoxy disulfide $(C_3H_7O)_2S_2$ and $(C_3D_7O)_2S_2$ were also found to exhibit m/z peaks consistent with $H_2S_2O_2^{+\cdot}$ and $D_2S_2O_2^{+\cdot}$; H. Schmidt, R. Steudel, D. Sülzle and H. Schwarz, *Inorg. Chem.*, **31**, 941 (1992).

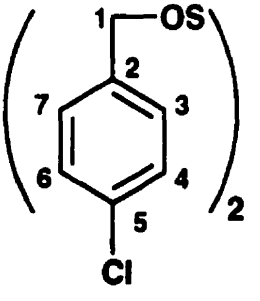
-HONO, 27), 77 (Ph^+, 63), 64 (S_2^+ or SO_2^+, 66); Anal. ($C_{14}H_{12}O_6N_2S_2$) C (calc. 45.62, found 45.53), H (calc. 3.28, found 3.07), N (calc. 7.61, found 7.23). This new coumpound was never reported in the literature.

Preparation of 4-Chlorobenzyl Alcohol:



To a solution of lithium aluminium hydride, $LiAlH_4$, (1.35 g, 35.6 mmol) in ether (40 mL) was added dropwise a solution of 4-chlorobenzaldehyde (10 g, 71 mmol) in ether (100 mL) over a period of 1.5 hours during which the exothermic addition was controlled using an ice bath. An extra portion of ether (75 mL) was syringed in the mixture that was stirred for 20 hours at room temperature. The reaction was quenched with the dropwise sequential addition of water (1.5 mL), NaOH 15% (1.5 mL), water (5 mL) followed by filtration and evaporation to give a white solid that was recrystallized from petroleum ether to afford 94% yield of the alcohol as white, shiny crystals; m.p. 71-73 °C (lit.[191a] 70-72 °C); Rf (EtOAc-hexanes, 40:60): 0.60; ^1H NMR (200MHz, $CDCl_3$) δ: 1.99 (s, 1H), 4.65 (s, 2H) and 7.29-7.30 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 64.51, 128.24, 128.64, 133.32, 139.19 ppm that were found to compare with reported values.[191b]

Preparation of Bis(4-Chlorobenzyloxy) Disulfide 218c:



To a solution of 4-chlorobenzyl alcohol (6.5 g, 46 mmol) and triethylamine (6.4 mL, 46 mmol) in ether (70 mL) and CH_2Cl_2 (30 mL) cooled to 0 °C was added dropwise a solution of S_2Cl_2 (1.8 mL, 23 mmol) in CH_2Cl_2 (8 mL). Half-way through the addition, the ice bath was removed, the addition completed along with stirring for 1 hour, then water (100 mL) was added. The organic phase was separated and further washed with water (3 x 80 mL) and a solution of NaCl sat'd (2 x 60 mL), dried over anhydrous $MgSO_4$, filtered and evaporated to give a crude light orange solid containing **218c** Rf(20% EtOAc in hexanes): 0.67 and traces of 4-chlorobenzyl alcohol Rf: 0.15. Column chromatography using this solvent system gave an off-white solid (6.781 g, 86%) that was identified as **218c** compared

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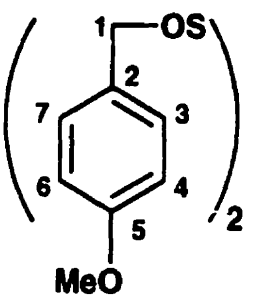
191. a) Catalog Handbook of Fine Chemicals, Aldrich, Milwaukee, USA, 324 (1996-1997); b) C.J. Pouchert and J. Behnke, The Aldrich Library of ^{13}C and ^1H FTNMR Spectra, Ed. 1, Aldrich Chemical Co., 1993.

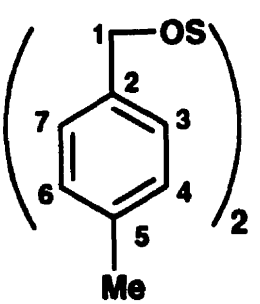
to a recrystallyzed sample (clear shiny pellets) that was prepared for X-ray determination; m.p. (pentane) 46-48 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 4.76, 4.86 (ABq J = 10.41 Hz, 2H), 7.24-7.36 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 75.76 (C1), 128.72 (C3 and C7), 129.91 (C4 and C6), 134.40 (C5) and 134.93 (C2) ppm. This new compound was never reported in the literature.

Preparation of Bis(4-Methoxybenzyloxy) Disulfide 218d:



To a solution of 4-methoxybenzyl alcohol (3.0 g, 22 mmol) and triethylamine (3.0 mL, 22 mmol) in ether (35 mL) and CH_2Cl_2 (20 mL) cooled to 0 °C was added a solution of S_2Cl_2 (868 μL, 11 mmol) in CH_2Cl_2 (4 mL) dropwise. Half way through the addition, the ice bath was removed, the addition completed along with stirring for 1 hour, then water (50 mL) was added. The organic phase was separated and further washed with water (3 x 30 mL) and a solution of NaCl sat'd (2 x 30 mL), dried over anhydrous $MgSO_4$, filtered and evaporated to give a light pinkish liquid containing **218d** Rf(20% EtOAc in hexanes): 0.66 and traces of 4-methoxybenzyl alcohol Rf: 0.10. Column chromatography using this solvent system gave a beige solid (2.278 g, 62%) that was identified as **218d** (recrystallized sample was obtained at -15 °C); m.p. (20% EtOAc in hexanes) 34-36 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.82 (s, 3H), 4.72, 4.84 (ABq J = 9.85 Hz, 2H), 6.88 (d, J = 6.63 Hz, 2H), 7.28 (d, J = 6.59 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 55.22 (CH_3O), 76.42 (C1), 113.85 (C4 and C6), 128.68 (C3 and C7), 130.43 (C2) and 159.78 (C5) ppm. The product is not very stable on silica gel and decomposed rapidly and liquefied at room temperature. This new compound was never reported in the literature.

Preparation of Bis(4-Methylbenzyloxy) Disulfide 218e:



To a solution of 4-methylbenzyl alcohol (2.7 g, 22 mmol) and triethylamine (3.0 mL, 22 mmol) in ether (35 mL) and CH_2Cl_2 (20 mL) cooled to 0 °C was added a solution of S_2Cl_2 (868 μL, 11 mmol) in CH_2Cl_2 (4 mL) dropwise. Half way through the addition, the ice bath was removed, the addition completed along with stirring for 1 hour, then water

(50 mL) was added. The organic phase was separated and further washed with water (3 x 30 mL) and a solution of NaCl sat'd (2 x 30 mL), dried over anhydrous $MgSO_4$, filtered and evaporated to give a crude off-white liquid residue containing **218e** Rf (20% EtOAc in hexanes): 0.67 and 4-methylbenzyl alcohol Rf: 0.13. Column chromatography using this solvent system gave an off-white clear liquid (2.763 g, 82%) that was identified as **218e**; ^1H NMR (200 MHz, $CDCl_3$) δ: 2.38 (s, 3H), 4.80, 4.90 (ABq J = 10.78 Hz, 2H), 7.20 (d, J = 7.86 Hz, 2H), 7.28 (d, J = 7.93 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.23 (CH_3), 76.59 (C1), 128.77 (C3 and C7), 129.18 (C4 and C6), 133.55 (C5) and 138.31 (C2) ppm; 4-methylbenzyl alcohol ^1H NMR (200 MHz, $CDCl_3$) δ: 1.89 (s, 1H), 2.35 (s, 3H), 4.62 (s, 2H), 7.17 (d, J = 8.06 Hz, 2H), 7.25 (d, J = 8.20 Hz, 2H) ppm; MS (EI, direct inlet, 150 °C) m/z: 258 ($M^{+\cdot}$ -S=O, 0.1), 242 ($M^{+\cdot}$ -SO_2, 0.2%), 210 (M+. -$H_2S_2O_2$, 0.5), 105 (CH_3-C_6H_4-CH_2^+, 100), 91 (C_6H_2-CH_2^+, 36), 77 (Ph^+, 16); MS (CI, direct inlet, 100 °C) m/z: 242 (M+. -SO_2, 21), 226 (M +$NH4^+$ -$H_2S_2O_2$, 11), 210 (226 -NH_3, 46) 209 (226 -$NH4^+$, 46), 105 (CH_3-C_6H_4-CH_2^+, 100). Compound **218e** was never reported in the literature.

Preparation of Dibenzyl Sulfite 219a:

To a solution of benzyl alcohol (960 µL, 9.28 mmol) and pyridine (740 µL, 9.28 mmol) in CH_2Cl_2 (15 mL) kept at -10 °C (ice-acetone bath) was syringed dropwise $SOCl_2$ (340 µL, 4.66 mmol). The reaction was stirred at -10 °C for 0.5 hour and then to room temperature for 1hour. The mixture was quenched following the procedure described for dimethyl sulfite **215**. Column chromatography using 40% EtOAc in hexanes gave the sulfite **219a** as a clear colorless oil (868 mg, 61%); Rf (20% ETOAc in hexanes): 0.50; benzyl alcohol Rf: 0.25; ^1H NMR (200 MHz, $CDCl_3$) δ: 4.93, 5.05 (ABq J = 11.75 Hz, 2H), 7.36 (s, 5H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 64.07 (CH_2), 128.49, 128.59, 128.64, 135.04 (aromatics) ppm; FTIR (neat): 1180s (S=O), 1080s (C-O) and 800-930 cm^{-1} several strong bands; MS (EI, direct inlet, 30 °C) m/z: 105 (C_6H_5-$CO^{+\cdot}$, 9), 91 (C_6H_5-$CH_2^{+\cdot}$, 100); MS (CI, direct inlet, 100 °C) m/z: 280 (M +NH_4^+, 100), 216 (M +$NH4^+$ -SO_2, 40). This compound was never reported in the literature.

Preparation of Bis(4-Nitrobenzyl) Sulfite 219b:

$(4\text{-}NO_2C_6H_4\text{-}CH_2O)_2S{=}O$

To a solution of 4-nitrobenzyl alcohol (3.55 g, 23.2 mmol) and pyridine (1.90 mL, 23.2 mmol) in ether (150 mL) kept at -10 °C (ice-acetone bath) was syringed dropwise $SOCl_2$ (850 µL, 11.6 mmol). The reaction was stirred at -10 °C for 0.5 hour and then to room temperature for 1hour. The mixture was quenched following the procedure described for dimethyl sulfite **215**. Column chromatography using 40% EtOAc in hexanes gave the sulfite **219b** as a yellow solid (2.7 g, 66%) m.p. 81-82 °C; Rf : 0.52; ^1H NMR (200 MHz, $CDCl_3$) δ: 5,03 5.17 (ABq J = 12.40 Hz, 2H), 7.50 (d, J = 8.50 Hz, 2H) 8.21 (d, J = 8.50 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 62.93 (C1), 124.27 (C4 and C6), 128.91 (C3 and C7), 142.34 (C2), 148.32 (C5) ppm; MS (EI, direct inlet, 3.9 V) m/z: 353 ($M\text{-}H^{+}\cdot$, 1), 336 ([$M\text{-}H^{+}\cdot$]-OH, 8), 288 ($M^{+}\cdot$ -SO_2, 65), 272 ($M^{+}\cdot$ -SO_3, 17), 242 ($O_2N\text{-}C_6H_4\text{-}CH_2O\text{-}CH_2\text{-}C_6H_4^{+}$, 78), 212 ($M^{+}\cdot$ -$O_2NC_6H_4\text{-}CH_2\text{-}C_6H_4^{+}$, 52), 165 (212-HONO, 82), 152 ($O_2N\text{-}C_6H_4\text{-}CH_2O^{+}\cdot$, 35), 136 ($O_2N\text{-}C_6H_4\text{-}CH_2^{+}$, 100), 120 ($O{=}N\text{-}C_6H_4\text{-}CH_2^{+}$, 44), 106 (136 -NO, 35), 77 (Ph^{+}, 20), 64 (SO_2^{+}, 10); Anal. ($C_{14}H_{12}O_7N_2S$) C (calc. 47.71, found 47.71), H (calc. 3.43, found 3.23), N (calc. 7.96, found 7.81); 4-nitrobenzyl alcohol Rf: 0.24. This compound was never reported in the literature.

Preparation of Bis(4-Chlorobenzyl) Sulfite 219c:

$(4\text{-}ClC_6H_4\text{-}CH_2O)_2S{=}O$

To a solution of 4-chlorobenzyl alcohol (1 g, 7 mmol) and pyridine (570 µL, 7 mmol) in CH_2Cl_2 (15 mL) kept at -10 °C (ice-acetone bath) was syringed dropwise $SOCl_2$ (260 µL, 3.50 mmol). The reaction was stirred at -10 °C for 0.5 hour and then to room temperature for 1hour. The mixture was quenched following the procedure described for dimethyl sulfite **215**. Column chromatography using 40% EtOAc in hexanes gave the sulfite **219c** as an off-white solid (606 mg, 52%) m.p. 63-66 °C; Rf (20% EtOAc in hexanes): 0.48; 4-chlorobenzyl alcohol Rf: 0.19; ^1H NMR (200 MHz, $CDCl_3$) δ: 4.90, 5.00 (ABq J = 11.05 Hz, 2H), 7.27 (d, J = 9.38 Hz, 2H), 7.34 (d, J = 6.42 Hz, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 63.30 (CH_2), 128.89, 129.81, 133.45, 134.64 (aromatics) ppm; FTIR (KBr): 1207vs (S=O), 1070s (C-O) and 780-880ms cm^{-1}; MS (EI, direct inlet, 30 °C) m/z: 330/332 ($M^{+}\cdot$, 0.5/0.4), 266 ($M^{+}\cdot$ -SO_2, 0.1), 125/127 ($Cl\text{-}C_6H_4\text{-}CH_2^{+}\cdot$, 100/33); MS (CI, direct

inlet, 130 °C) m/z: 348/350 (M +NH_4^+, 2/1.6), 142/144 (Cl-C_6H_4-$CH_2^{+\cdot}$ +NH_3, 26/8). This new compound was never reported in the literature.

Preparation of Bis(4-Methoxybenzyl) Sulfite 219d:

(4-$MeOC_6H_4$-$CH_2O)_2S$=O

To a solution of 4-methoxybenzyl alcohol (900 µL, 7.2 mmol) and pyridine (600 µL, 7.4 mmol) in CH_2Cl_2 (15 mL) kept at -10 °C (ice-acetone bath) was syringed dropwise $SOCl_2$ (300 µL, 4.1 mmol). The reaction was stirred at -10 °C for 0.5 hour and then to room temperature for 1hour. The mixture was quenched following the procedure described for dimethyl sulfite **215**. Column chromatography using 40% EtOAc in hexanes gave the sulfite **219d** as a clear yellowish oil (868 mg, 73%); Rf (20% EtOAc in hexanes): 0.57; 4-methoxybenzyl alcohol Rf: 0.16; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 4.83, 4.94 (ABq J = 9.15 Hz, 2H), 6.86, (d, J = 9.99 Hz, 2H) 7.30 (d, J = 8.78 Hz, 2H) ppm; FTIR (CCl_4): 1220vs (S=O), 1110s (C-O) cm^{-1}. This new compound was never reported in the literature.

Preparation of Bis(4-Methylbenzyl) Sulfite 219e:

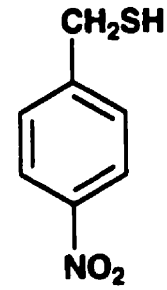
(4-MeC_6H_4-$CH_2O)_2S$=O

To a solution of 4-methylbenzyl alcohol (1.0 g, 8.2 mmol) and pyridine (660 µL, 8.2 mmol) in ether (15 mL) kept at -10 °C (ice-acetone bath) was syringed dropwise $SOCl_2$ (300 µL, 4.1 mmol). The reaction was stirred at -10 °C for 0.5 hour and then to room temperature for 1hour. The mixture was quenched following the procedure described for dimethyl sulfite **215**. Column chromatography using 40% EtOAc in hexanes gave the sulfite **219e** as a light yellow solid (868 mg, 65%) m.p. 40-42 °C (20% EtOAc in hexanes); Rf: 0.56; 4-methylbenzyl alcohol Rf: 0.26; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.32 (s, 3H), 4.83, 4.95, (ABq J = 11.53 Hz, 2H), 7.11-7.22 (m, 4H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 21.22 (CH_3), 64.06 (CH_2), 128.67, 129.32, 132.02, 138.53 (aromatics) ppm; FTIR (KBr): 1250s (S=O), 1080s (C-O) and 840-780 cm^{-1}; MS (EI, direct inlet, 30 °C) m/z: 290 ($M^{+\cdot}$, 1), 226 ($M^{+\cdot}$ -SO_2, 0.1), 105 (CH_3-C_6H_4-$CH_2^{+\cdot}$, 100); MS (CI, direct inlet, 70 °C) m/z: 308 (M +NH_4^+, 3), 244 (M +NH_4^+ -SO_2, 6), 226 ($M^{+\cdot}$ -SO_2, 2), 122 (CH_3-C_6H_4-$CH_2^{+\cdot}$ +NH_3, 100). This new compound was never reported in the literature.

Attempted Preparation of 218b using Bisbenzamidazol-1-yl sulfide 59 and Bisbenzamidazol-1-yl disulfide 238:

In the case of the *mono*sulfur-transfer reagent **59** (0.5, 1 and 2 equivalents) in the presence of 4-nitrobenzyl alcohol (1.0 g, 3.7 mmol) in refluxing CCl_4 gave only unreacted alcohol and S_8 (TLC). The progress of the reaction was monitored by TLC every 12 hours up to 72 hours to observe only the formation of elemental sulfur S_8. S_8 Rf (20% EtOAc in hexanes): 0.70; 4-nitrobenzyl alcohol Rf: 0.21. In the case of the disulfur-transfer reagent **238** (1 and 2 equivalents), also in refluxing CCl_4, some 4-nitrobenzaldehyde was detected along with the alcohol and S_8. S_8 Rf(30% EtOAc in hexanes): 0.83, 4-Nitrobenzaldehyde Rf: 0.42 and 4-nitrobenzyl alcohol **220** Rf: 0.31.

Preparation of 4-Nitrobenzyl thiol 223:

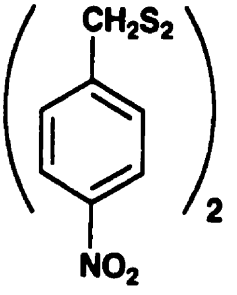


S-thiouronium salt:[96a] 4-Nitrobenzyl alcohol **220** (500 mg, 3.26 mmol), thiourea **221** (248.5 mg, 3.26 mmol) and HBr 48% solution (1.65g, 9.80 mmol) were refluxed together for 21 hours with stirring. NaOH 1.67M (6 mL) was syringed and the resulting mixture refluxed for an additional 3 hours. The organic phase was separated and the aqueous phase was acidified with HCl (1N) and extracted with ether (3 x 15 mL). Organic phases were combined, dried over anhydrous $MgSO_4$, filtered and evaporated under reduced pressure. Chromatography of the crude (162 mg) using 30% EtOAc in hexanes gave **220** (50 mg, 30%); m.p. 92-94 °C; Rf: 0.49; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.00 (s, OH), 4.83 (s, 2H), 7.52 (d, J = 8.28 Hz, 2H) 8.21 (d, J = 8.32 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 64.37 (C1) 124.11 (C4 and C6), 127.38 (C3 and C7), 147.63 (C2) and 148.57 (C5) ppm; MS (EI, direct inlet, 200 °C) m/z: 153 ($M^{+\cdot}$, 58), 136 ($M^{+\cdot}$ -OH, 36), 107 ($M^{+\cdot}$ -NO_2, 51), 105 ($136^{+\cdot}$ -HNO, 49), 89 ($136^{+\cdot}$ -HONO, 48), 77 (Ph^+, 100); the 4-nitrobenzyl thiol **223** (92mg, 56%); m.p. 48-50 °C (lit.[95b,96] 52.5 °C); Rf: 0.42; and the bis(4-nitrobenzyl) sulfide (20mg, 12%); m.p. 160-162 °C (lit.[97] m.p. 159 °C); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.65 (s, 2H), 7.42 (d, J = 8.57 Hz, 2H), 8.18 (d, J = 8.61 Hz, 2H) ppm.

Potassium Thioacetate: 4-Nitrobenzyl bromide **224** (1.0 g, 4.6 mmol), potassium thioacetate **225** (528.8 mg, 4.63 mmol) and MeOH (20 mL) were stirred together

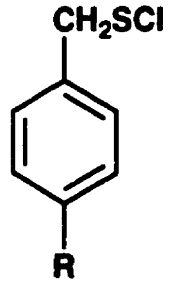
for 1 hour at room temperature. Concentrated HCl (2 mL) was added at 0 °C, and stirred to room temperature for 1 hour where potassium bromide precipitated. Extraction with chloroform (3 x 20 mL) gave a clear, yellowish organic phase that was dried over anhydrous $MgSO_4$, filtered and evaporated to a white solid residue (900 mg, 100%) identified as **223**; m.p. 52-53 °C (*i*-PrOH) (lit.[95b, 96] 52.5 °C); Rf (30% EtOAc in hexanes): 0.40 (0.48 for **224**); ^{1}H NMR (50 MHz, $CDCl_3$) δ: 1.83 (t, J = 7.87 Hz, 1H), 3.79 (d, J = 7.86 Hz, 2H) 7.47 (d, J = 8.55 Hz, 2H) 8.14 (d, J = 8.55 Hz, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 28.35 (CH_2), 123.90, 128.91, 146.71, 148.48 ppm; MS (EI, direct inlet, 60 °C) m/z: 169 ($M^{+\cdot}$, 20), 136 ($M^{+\cdot}$ -SH, 10), 106 (136$^{+\cdot}$ -NO, 5). The 4-nitro-benzylthioacetate (4-NO_2-C_6H_4-CH_2-S(C=O)CH_3) yellow solid; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.35 (s, 3H), 4.14 (s, 2H), 7.44 (d, J = 8.41 HZ, 2H), 8.13 (d, J = 8.54 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 30.25 (CH_3), 32.71 (CH_2), 123.82, 129.68, 145.51, 147.13, 194.22 ppm.

Preparation of Bis(4-Nitrobenzyloxy) Tetrasulfide 226:



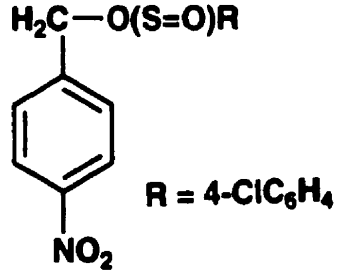
To a solution of **223** (1 g, 6 mmol) in ether (20 mL) was syringed S_2Cl_2 (400 mg, 3 mmol) in ether (2 mL) with stirring. The mixture was refluxed for 24 hours, after which time the product precipitated out as a white solid in a yellow solution. The precipitate was collected and the residue chromatographed (30% EtOAc in hexanes) and the combined product, after recrystallization, (toluene-petroleum ether) gave white, fine crystals (535 mg 45%) identified as **226**; m.p. 114-114.5 °C; Rf (30% EtOAc in hexanes): 0.33 ; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 4.28 (s, 2H), 7.44 (d, J = 8.57 Hz, 2H) 8.18 (d, J = 8.57 Hz, 2H) ppm; [^{13}C NMR (75 MHz, $CDCl_3$)] δ: 42.35 9 (CH_2), 123.90, 130.30, 143.72, 147.50 (aromtics) ppm; MS (EI, direct inlet, 200 °C) m/z: 368 ($M^{+\cdot}$ -S, 0.5), 336 (368$^{+\cdot}$ -S, 3), 304 (336$^{+\cdot}$ -S, 2), 272 (304$^{+\cdot}$ -S, 2), 167 (O_2N-$C_6H_4CH_2S^{+\cdot}$, 23), 151 (167-O, 10), 136 (O_2N-$C_6H_4CH_2^+$, 100), 121 (151 -NO, 33), 106 (136 -NO, 33). For comparison, dibenzyl disulfide ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.59 (s, 2H), 7.27 (s, 5H) ppm.[191b]

Preparation of Aromatic Sulfenyl Chlorides 229a-b:



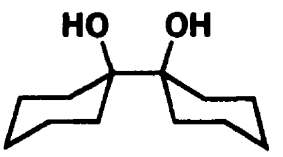
N-Chlorosuccinimide **228** (6.2 g, 45 mmol) was dissolved in benzene to form a slurry. 4-Chlorothiophenol **227b** (4.7 mL, 45 mmol) in benzene (15 mL) was added dropwise at 0°C over a period of 0.5 h. The resulting orange-red mixture was stirred for 24 hours at room temperature. Succinimide **230** was removed by filtration and the mother liquor concentrated under reduced pressure; CCl_4 was added to achieve precipitation of the remaining succinimide for a total of 4.23 g (94% recovery). The residual red oil was distilled under reduced pressure 94-95 °C (2 mmHg) (lit.[99d] b.p. 68-69 °C under 0.5 mmHg) for 97% of **229b** (R = Cl). For **229a** (R = H), 95% yield; b.p. 57-58 °C (1 mmHg) (lit.[99d] b.p. 55 °C under 1 mmHg) if **227b** is replaced by **227a**.

Preparation of *p*-Nitrobenzyl *p*-Chlorobenzenesulfinate 236:



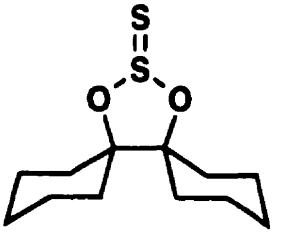
To a solution of 4-nitrobenzyl alcohol **220** (2 g, 13 mmol) and pyridine (1 g, 13 mmol) cooled at 0°C in CH_2Cl_2 (50 mL) was added dropwise *p*-chlorophenylsulfenyl chloride **229b** (3 g, 17 mmol). The mixture was stirred from 0 °C to room temperature over a period of 2 hours and concentrated under reduced pressure. The residue (2.318 g was taken up in EtOAc and chromatographed (25% EtOAc in hexanes) to give bis(4-chlorophenyl) disulfide **234** (709 mg, 18%); m.p. 66-67 °C; Rf: 0.72; MS [EI, direct inlet, 100 °C] m/z: 287 ($M^{+\cdot}$, 47.7), 222 ($M^{+\cdot}$ -S_2, 28), 143 (Cl-$C_6H_4S^{+\cdot}$, 100), 108 ($C_6H_4S^{+}$, 52.1); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.29 (d, J = 9.97 Hz, 2H), 7.44 (d, J = 10.03 Hz, 2H); 4-nitrobenzyl chloride **235** (363 mg, 9.4%); m.p. 72-73 °C; Rf: 0.39; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 4.68 (s, 2H), 7.59 (d, J = 8.63 Hz, 2H), 8.21 (d, J = 8.67 Hz, 2H); MS [EI, direct inlet, 30 °C] m/z: 173 ($[M+2]^{+\cdot}$, 15), 171 ($M^{+\cdot}$, 47), 136 (O_2N-$C_6H_4CH_2^{+}$, 100); *p*-nitrobenzyl *p*-chlorobenzenesulfinate **236** (1.815g, 47%); m.p. 63-64 °C; Rf: 0.27; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 4.64, 5.10 (ABq, J = 12.36 Hz, 2H), 7.54 (d, J = 8.79 Hz, 2H) 7.69 (d, J = 8.36 Hz, 2H) aromatics of 4-chlorobenzene substituent and 7.43 (d, J = 8.86 Hz, 2H), 8.17 (d, J = 8.82 Hz, 2H) ppm aromatics of 4-nitrobenzyl substituent; MS [EI, direct inlet, 120 °C] m/z: see **Scheme 20**; 4-nitrobenzyl alcohol **220** (171 mg, 0.04%); Rf: 0.1.

Preparation of (Bicyclohexyl)-1,1'-diol 58:[105]



A mixture of cyclohexanone (30g, 0.31 mol), aluminium powder (30g) and mercuric chloride (Hg_2Cl_2) (2.7 g, 9.9 mmol) in benzene (35 mL) was heated on a steam bath at 70 °C for 2 hours. Water (21 mL) and benzene (38 mL) were added and heating continued for 3 hours. The mixture was filtered and the residue extracted with a hot mixture of benzene (21 mL) and water (40 mL). Removal of the solvent under reduced pressure gave a white solid that crystallized on cooling. Petroleum ether (20 mL) was added and the white crystals were collected and recrystallized from petroleum ether (18.30g, 30%); m.p. 122-124 °C (lit.[105] m.p. 124.5-126.5 °C); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.07-1.81 ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.77, 25.87, 30.69, 75.66 ppm.

Preparation of O,O'-Bicyclohexyl-1,1'-diylthiosulfite 57 from 59 or 238:[192]



The preparation of bis-benzamidazol-1-yl sulfide **59** was previously described in detail.[104e] To a suspension of **59** (1.3 g, 5 mmol) in CCl_4 was added **58** (1 g, 5 mmol) and the mixture gently refluxed for 72 hours. It was cooled to room temperature; filtration collected benzimidazole (1.05 g). The filtrate was concentrated to a semi-solid residue that was chromatographed using CCl_4 to give **57** (585.9 mg, 45% yield); Rf: 0.65; m.p. 99-100 °C (hexanes) (lit.[10a] 100-101 °C); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.07-1.81 ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.92, 22.07, 25.21, 31.11, 31.78, 94.47 ppm. Thionosulfite **57** was also obtained in the presence of the disulfur-transfer reagent bisbenzamidazol-1-yl disulfide **238** (1.49 g, 5 mmol). The mixture was refluxed in CCl_4 for 48 hours and yielded **57** (547 mg, 42%); MS (FAB, NBA matrix) m/z: 261 ($M + H^+$, 12), 163 ($M + H^+ - H_2S_2O_2$, 66), 154 (NBA + H^+, 100).

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192. The preparation of **59** and **238** was previously reported in detail; D.N. Harpp, K. Steliou and T.H. Chan, *J. Am. Chem. Soc.*, 1222 (1978).

Preparation of O,O'-Bicyclohexyl-1,1'-diylthiosulfite 57 from S_2Cl_2:

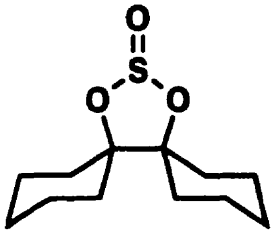
To a suspension of the diol **58** (1.5 g, 7.6 mmol) in CCl_4 (15 mL) was added triethylamine (2.13 mL, 15.3 mmol) and cooled to 0°C. A solution of S_2Cl_2 (0.7 mL, 7.5 mmol) in CCl_4 (3 mL) was added dropwise and stirred for 7 hours. The reaction was quenched with cold water (15 ml) and the organic phase separated and further washed with water (2 x 10 mL) and dried over anhydrous $MgSO_4$ to give a yellow solid residue that was chromatographed using the above conditions and yielded **57** (599 mg, 46%). This methodology toward the preparation of **57** was never reported previously.

Attempted Preparation of 57 using the Trimethylsilyl Chloride methodology:

Diol **58** (709 mg, 3.58 mmol) was dissolved in pyridine (20 mL) and dimethylaminopyridine (438 mg, 3.58 mmol) was added and the resulting mixture cooled to 0 °C with stirring. Trimethylsilyl chloride (10 eq, 4.5 mL, 35 mmol) was added dropwise for 2 hours. The mixture was stirred to room temperature and 50 °C for 36 hours and slowly added to cold water (200 mL) and a white precipitate was obtained. Filtration followed by extraction using EtOAc (4 x 30 mL) and treatment with anhydrous $MgSO_4$ gave the silylated diol **239** (95%); ^1H NMR (200 MHz, $CDCl_3$) δ: 0.19 (s, 9H), 1.38-1.72 (m, 6H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 4.51, 22.97, 26.52, 30.93 and 81.22 ppm. To compound **239** (119 mg, 0.346 mmol) and triethylamine (11 eq, 550 µL, 3.95 mmol) in CCl_4 (5 mL) cooled to 0 °C, was added a solution of S_2Cl_2 (2.6 eq, 72 µL, 0.90 mmol) in CCl_4 (2 mL) dropwise. The mixture was stirred for 2 hours and then to room temperature and finally to 50 °C for 36 hours to show only the presence of **239** (TLC).

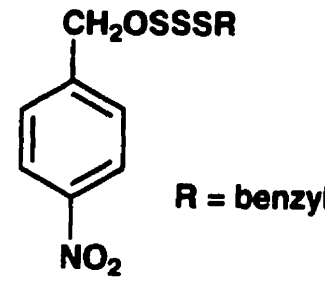
Preparation of the O,O'-Bicyclohexyl-1,1'-diylsulfite 240:[104e]

To a solution of diol **58** (2.0 g, 10 mmol) and pyridine (1.6 g, 20 mmol) in ether (100 mL) was added dropwise a solution of thionyl chloride (1.2 g, 10 mmol) in ether (25 mL) over a period of 0.5 hour. The white precipitate, pyridinium hydrochloride, formed during the addition of 2 hours was collected and the solvent evaporated under reduced pressure.



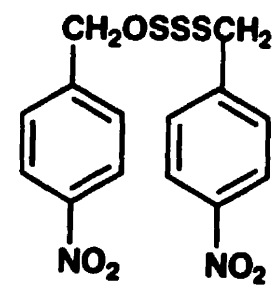
The residue was chromatographed using $CHCl_3$ to yield **240** (1.71 g, 70%); m.p. 58-59 °C; (lit.[104e] 58-59 °C); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 22.09, 22.14, 25.21, 31.69, 32.25, 92.97 ppm; MS (FAB, NBA matrix) m/z: 391 (M + NBA + 4 H+, 3), 245 (M + NBA -SO_2 -NO_2 -2 H_2O, 13).

Preparation of 4-Nitrobenzyloxy Benzyl Trisulfide 243:



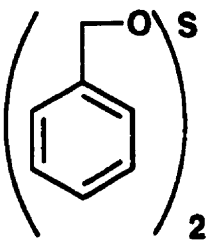
Benzyl thiol (182 mL, 1.55 mmol) was syringed dropwise to bis(4-nitrobenzyloxy) disulfide **218b** (572 mg, 1.55 mmol) dissolved in acetonitrile (6 mL) and dichloromethane (5 mL) at room temperature. Then the mixture was put into an oil bath at 50 °C for 2 hours, after which the solvents were evaporated and the residual semi-solid was chromatographed using (CH_2Cl_2 in hexanes 50:50) to yield a light yellow oil that solidified (62%) m.p. 43-45 °C; **243** Rf: 0.49; ^1H NMR (200 MHz, $CDCl_3$) δ: 4.16 (s, 2H), 4.94 (s, 2H), 7.30 (s, 5H), 7.47 (d, J = 8.49 Hz, 2H), 8.20 (d, J = 8.60 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 43.53, 76.40, 123.64, 127.77, 128.63, 129.33, 135.95, 143.72, 147.81, 149.91 ppm; MS (FAB, glycerol matrix) m/z: 401 (M +glycerol -NO^+, 0.1); MS (FAB, NBA) m/z: 460 (M +NBA -S, 1), 307 ($M^{+\cdot}$ -S, 3); MS (CI, direct inlet, 180°C) m/z: 357 (M +NH_4^+, 10). This compound was never reported in the literature.

Prepararion of Bis(4-nitrobenzyl)oxy Trisulfide 245:



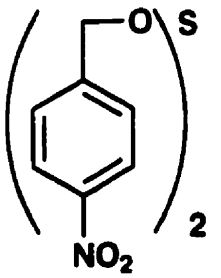
4-Nitrobenzyl thiol (1834 mg, 1.08 mmol) was added to bis(4-nitrobenzyloxy) disulfide **218b** (400 mg, 1.08 mmol) dissolved in acetonitrile (5 mL) at room temperature. Then the mixture was put into an oil bath at 50 °C for 1.5 hours, after which the solvent was evaporated and the residual semi-solid was chromatographed using (CH_2Cl_2 in hexanes 1:1) to yield a mixture of **245** and **218b** that was analyzed by NMR; ^1H NMR (200 MHz, $CDCl_3$) δ: 4.20 (s, 2H), 4.91 (s, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 43.53, 76.40, 123.64, 127.77, 128.63, 129.33, 135.95, 143.72, 148.03 ppm. This new compound was never reported in the literature.

Preparation of Dibenzyl Sulfoxylate 246a:



To a solution of benzyl alcohol (1.0 g, 9.3 mmol) and triethylamine (1.4 mL, 9.3 mmol) in dichloromethane (25 mL) cooled at -78 °C was added dropwise a solution of sulfur dichloride SCl_2 (314 µL, 4.65 mmol) in dichloromethane (4 mL) and the resulting mixture was stirred for 2 hours at -40 °C. The mixture was allowed to reach 0 °C, transferred to a separatory funnel and washed with water (3 x 10 mL) dried over anhydrous $MgSO_4$ and the solvent evaporated under reduced pressure. Column chromatography of the crude mixture (hexanes-CH_2Cl_2-toluene in 2:1:1) gave **218a** (276 mg, 22%); Rf: 0.49; **246a** (305 mg, 27%); Rf: 0.44; ^1H NMR (200 MHz, $CDCl_3$) δ: 5.11 (s, 2H), 7.39 (s, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 81.86, 128.44, 128.48, 128.61, 136.92 ppm; **219a** (195 mg, 16%); Rf: 0.15.

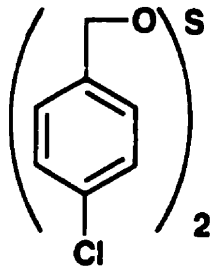
Preparation of Bis(4-Nitrobenzyl) Sulfoxylate 246b:



To a solution of 4-nitrobenzyl alcohol (1.0 g, 6.5 mmol) and triethylamine (910 µL, 6.53 mmol) in dichloromethane (25 mL) cooled at -78 °C was added dropwise a solution of sulfur dichloride SCl_2 (207 µL, 3.27 mmol) in dichloromethane (3 mL) and the resulting mixture was stirred for 2 hours at -40 °C. The mixture was allowed to reach 0 °C, transferred to a separatory funnel and washed with water (3 x 10 mL) dried over anhydrous $MgSO_4$ and the solvent evaporated under reduced pressure. The crude was taken up in CH_2Cl_2 until almost completed dissolution and filtered once more. The filtered solution was left overnight at -30 °C under N_2. Light orange crystals were collected to give **246b** (530 mg, 50%); ^1H NMR (200 MHz, $CDCl_3$) δ: 5.17 (s, 2H), 7.46 (d, J = 8.79 Hz, 2H), 8.18 (d, J = 8.54 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 80.33, 123.71, 128.50, 143.73, 147.91 ppm; the corresponding sulfinate **249b** ^1H NMR (200 MHz, $CDCl_3$) δ: 4.18 (d, J = 1.46 Hz, 2H), 5.08, 5.13 (ABq, J = 13.13 Hz, 2H), 7.38-7.53 (m, 4H aromatics), 8.16-8.31 (m, 4H aromatics) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 63.25, 68.89, 123.72, 123.82, 128.51, 131.59, 135.34, 143.73, 147.76, 147.91 ppm; the remaining solution was chromatographed (20% CH_2Cl_2 in hexanes) to give **218b** (179 mg, 15%); Rf: 0.67; **219b** (180 mg, 16%); Rf: 0.27; MS (CI, direct inlet, 300 °C) m/z:

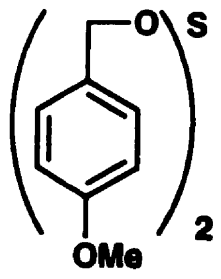
354 (M +NH_4^+, 4%), 272 ($M^{+\cdot}$ -SO_2, 6), 226 (272 -NO, 2), 166 (HONO-$C_6H_4C{=}O^+$ +NH_3 -H_2, 100), 151 (HONO-$C_6H_4C{=}O^+$, 56), 136 (O_2N-$C_6H_4CH_2^+$, 60), 107 (136^+ -NO +H, 56), 89 (136^+ -HONO, 17), 77 (Ph^+, 27). This compound was never reported in the literature.

Preparation of Bis(4-Chlorobenzyl) Sulfoxylate 246c:



To a solution of 4-chlorobenzyl alcohol (1 g, 7 mmol) and triethylamine (978 µL, 7 mmol) in dichloromethane (25 mL) cooled at -78 °C was added dropwise a solution of sulfur dichloride SCl_2 (238 µL, 3.5 mmol) in dichloromethane (3 mL) and the resulting mixture was stirred for 2 hours at -40 °C. The mixture was allowed to reach 0 °C, transferred to a separatory funnel and washed with water (3 x 10 mL) dried over anhydrous $MgSO_4$ and the solvent evaporated under reduced pressure. The crude was chromatographed (60% CH_2Cl_2 in hexanes) very quickly to give fractions as mixture of **218c** and **246c**; Rf: 0.68; the sulfite **219b** (195 mg, 17%). The mixted fractions were chromatographed (hexanes-CH_2Cl_2-toluene 2:1:1) very quickly to give **218c** (204 mg, 17%); Rf: 0.60; the sulfoxylate **246c** (500mg, 46%); Rf: 0.56; ^1H NMR (200MHz, $CDCl_3$) δ: 5.0 (s, 2H) 7.28 (d, J = 10.28 Hz, 2H), 7.32 (d, J = 7.21 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 81.05, 128.71, 129.81, 129.91, 135.34. Isomerization to the sulfinate **249c** was observed; ^1H NMR (200MHz, $CDCl_3$) δ: 3.98, 4.02 (ABq, J = 12.94 Hz, 2H), 4.90, 5.01 (ABq, J = 11.96 Hz, 2H), 7.11-7.38 (m, 8H aromatics) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 63.54, 69.71, 128.70, 128.82, 128.96, 129.62, 129.80, 131.79, 133.95, 134.54; MS (EI, direct inlet, 30° C) m/z: 266/268 ($M^{+\cdot}$ Cl cluster -HONO, 0.15/0.15), 142/144 (4-Cl-C_6H_4-$CH_2OH^{+\cdot}$ Cl cluster, 83/27), 107 ($142^{+\cdot}$ -Cl, 100), 77 (Ph^+, 96). This new compound was never reported in the literature.

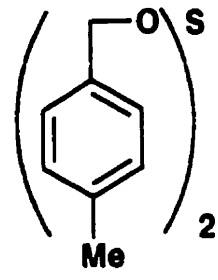
Preparation of Bis(4-Methoxybenzyl) Sulfoxylate 246d:



To a solution of 4-methoxybenzyl alcohol (1.0 g, 7.2 mmol) and triethylamine (1.0 mL, 7.2 mmol) in dichloromethane (25 mL) cooled at -40 °C was added dropwise a solution of sulfur dichloride SCl_2 (246 µL, 3.60 mmol) in dichloromethane (3 mL) and the resulting mixture

was stirred for 2 hours at -40 °C. The mixture was allowed to reach 0 °C, filtered, transferred to a separatory funnel andwashed with water (3 x 10 mL) dried over anhydrous $MgSO_4$ and the solvent evaporated under reduced pressure. See **Table 6** on p.72. This compound was never reported in the literature.

Preparation of Bis(4-Methylbenzyl) Sulfoxylate 246e:



To a solution of 4-methylbenzyl alcohol (1.0 g, 8.2 mmol) and triethylamine (1.14 mL, 8.2 mmol) in dichloromethane (25 mL) cooled to -40 °C was added dropwise a solution of sulfur dichloride SCl_2 (278 µL, 4.1 mmol) in dichloromethane (3 mL) and the resulting mixture was stirred for 2 hours at -40 °C. The mixture was allowed to reach 0 °C, transferred to a separatory funnel and washed with water (3 x 10 mL) dried over anhydrous $MgSO_4$ and the solvent evaporated under reduced pressure. The semi-solid residue was chromatographed (50% dichloromethane in hexanes) to give the dialkoxy disulfide **218e** (225mg, 18%); Rf: 0.55; the sulfoxylate **246e** (236 mg, 21%); Rf: 0.47; ^1H NMR (200 MHz, $CDCl_3$) δ: 5.12 (s, 2H), 7.25-7.32 (broad signal, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.58, 77.30, 129.34, 129.70, 134.28, 139.04 ppm; the sulfite **219e** (273 mg, 23%); Rf: 0.20; the sulfinate **249e** (oil, 79 mg, 7%); Rf: 0.04; ^1H NMR (200 MHz, $CDCl_3$) δ: 2.33 (s, 3H), 3.93, 4.02 (ABq, J = 13.18 Hz, 2H), 4.89, 4.99 (ABq, J = 11.48 Hz, 2H) 7.12, 7.13 (two singlets, 8H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.18, 21.23, 64.10, 70.31, 125.64, 128.43, 129.25, 129.46, 130.36, 132.64, 138.08, 138.46 ppm. Compounds **246e** and **249e** were never reported in the literature.

Preparation of 4-Nitrobenzyl Disulfide 254:

$(4\text{-}NO_2\text{-}C_6H_4\text{-}CH_2S)_2$

To a solution of sulfuryl chloride SO_2Cl_2 (73 µL, 0.91 mmol) in ether (10 mL) at -78 °C was added dropwise very slowly a solution of 4-nitrobenzyl mercaptan **223** (306 mg, 1.8 mmol) and pyridine (147 mL, 1.8 mmol) in ether (25 mL) over a period of 0.75 hour. The mixture was further stirred at -78 °C for 0.75 hour and then transferred to a separatory funnel and washed with NaOH (0.1M) (2 x 25 mL) and water (2 x 25 mL), dried over anhydrous $MgSO_4$, filtered and evaporated under reduced

pressure to give a light solid residue that was chromatographed using 70% dichloromethane in hexanes to give 284.4 mg (93% yield) of **254**; Rf: 0.28; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.68 (s, 2H), 7.37 (d, J = 8.79 Hz, 2H), 8.18 (d, J = 8.84 Hz, 2H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 42.34, 123.82, 130.06, 144.66, 147.84 ppm.

6.3 Methodology Related to Chapter 3:

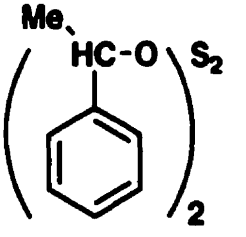
i) Bis(4-nitrobenzyloxy) disulfide **218b**, bis(4-chlorobenzyloxy) disulfide **218c**, bis(4-nitrobenzyl) tetrasulfide **226** and bis(4-nitrobenzyl) sulfoxylate **246b** were recrystallized and X-ray determinations were obtained **(Appendixes II-V)**.

ii) The room temperature solid state ^{13}C NMR study of dibenzyloxy disulfide **218a**, bis(4-nitrobenzyloxy) disulfide **218b** and bis(4-nitrobenzyl) tetrasulfide **226** was performed on recrystallized samples.

iii) The ^{1}H NMR solvent polarity and temperature studies, the ^{17}O NMR **(Appendix VIII)** and UV analysis were performed on freshly prepared material. The IR and Raman used recrystallized material.

iv) For the ^{1}H NMR Lanthanide-Induced-Shifts experiments, the shift reagent was added in 0.10 molar equivalent portion directly to the NMR tube, and the resulting solution was analyzed

Preparation of the Dialkoxy Disulfide from the Racemic sec-Phenethyl 288:



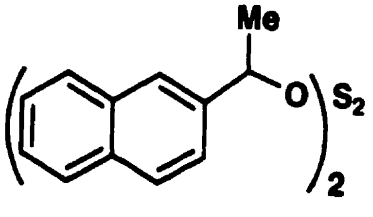
To the racemic alcohol **288** (987 μL, 8.2 mmol) and triethylamine (1.14 mL, 8.2 mmol) cooled to 0 °C in dichloromethane (12 mL CH_2Cl_2 and 6 mL Et_2O) was added dropwise a solution of S_2Cl_2 (327 μL, 4.1 mmol) in dichloromethane (3 mL). The reaction was further stirred for an extra 1 hour at 0 °C and worked up with water. The organic layer was dried over anhydrous $MgSO_4$, filtered and evaporated under reduced pressure to give a clear yellow oil that was chromatographed (50% EtOAc in hexanes) to give the **dialkoxy disulfide** of **288** (1 g, 80% yield); Rf: 0.81; ^{1}H NMR (300 MHz, $CDCl_3$) δ: see **Table 22** and **Figure 25**: 1.58 (d, J = 1.74 Hz),

1.61 (d, J = 1.79 Hz), 1.63 (d, J = 2.25 Hz), 1.65 (d, J = 2.25 Hz), 4.88-5.03 (two dq, 2H), 7.28-7.45 (broad, aromatics 10H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 22.65, 23.03, 23.41, 23.61, 82.27, 82.37, 83.30, 83.50, 126.57, 126.63, 126.70, 126.73, 127.98, 128.04, 128.32, 128.42, 141.84, 141.88, 141.91, 141.99 ppm; the **sulfite** ^1H NMR (300 MHz, $CDCl_3$) δ: 1.35 (d, J =6.59 Hz, 3H), 1.53 (d, J = 6.59 Hz), 1.58 (d, J = 6.59 Hz, 3H), 1.63 (d, J = 6.56 Hz, 3H), 5.38-5.47 (two overlapping quartets for 1H each), 5.57-5.67 (two overlapping quartets for 1H each), 7.30-7.40 (broad aromatics) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 23.02, 23.78 (double intensity), 24.17, 72.20, 72.52, 72.68, 72,78, 126.05, 126.12, 126.20, 128.02, 128.09, 128.15, 128.20, 128.40, 128.51, 128.59, 141.00, 141.27, 141.33, 141.67 ppm; the **alcohol 288** (139 mg, 145) Rf: 0.42; ^1H NMR (300 MHz, $CDCl_3$) δ: 1.48 (d, J = 6.35 Hz, 3H), 3.69 (d, J = 3.56, OH), 4.83 (q, J = 3.56 Hz, 1H), 7.31-7.40 (broad, aromatics, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 25.26, 70.12, 125.59, 127.34, 128.47, 146.08 ppm. The corresponding sulfite and dialkoxy disulfide of racemic *sec*-phenethyl alcohol were never reported in the literature.

Preparation of Dialkoxy Disulfide from the (R)-sec-Phenethyl Alcohol 288:

^1H NMR (300 MHz, $CDCl_3$) δ: see **Table 22** and **Figure 25**; 1.61 (d, J = 6.49 Hz, 3H), 1.66 (d, J = 6.54 Hz, 3H), 4.91 (q, J = 6.54 Hz, 1H), 5.03 (q, J = 6.46 Hz, 1H) ppm; [^{13}C NMR (75 MHz, $CDCl_3$)] δ: 22.64, 23.41, 82.24, 83.27, 126.60, 126.65, 127.95, 128.01, 128.30, 128.45, 141.85 ppm. This dialkoxy disulfide was never reported in the literature.

Preparation of Dialkoxy Disulfide from Racemic 1-(2-Naphthyl) Ethanol 289:



To the racemic alcohol **289** (1.0 g, 5.8 mmol) and triethylamine (809 μL, 5.8 mmol) cooled to 0 °C in dichloromethane (25 mL) was added dropwise a solution of S_2Cl_2 (232 mL, 2.9 mmol) in dichloromethane (3 mL). The reaction was further stirred for an extra 1 hour at 0 °C and worked up with water. The organic layer was dried over anhydrous $MgSO_4$, filtered and evaporated under reduced pressure to give a beige residue that was chromatographed (20% EtOAc in hexanes) to give the **dialkoxy disulfide** of **289** (208 mg, 12% yield); Rf: 0.58; ^1H NMR (300 MHz, $CDCl_3$) δ: see **Table 23** and **Figure 26**; ^{13}C NMR (75 MHz,

$CDCl_3$) δ: 22.93, 23.14, 23.40, 23.68, 82.45, 82.54, 83.44, 83.56, 124.13, 124.21, 124.31, 126.64, 125.89, 125.93, 126.07, 126.18, 127.63, 127.95, 128.22, 128.40, 133.05, 133.13, 139.14, 139.20, 139.35, 139.37; the corresponding **sulfite** (10 mg, 1% yield); Rf: 0.41; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 23.81, 23.88, 23.92, 24.02, 72.29, 72.46, 73.11, 73.55, 123.65, 123.80, 125.21, 126.11, 126.20, 126.29, 126.39, 127.59, 127.71, 127.98, 128.04, 128.26, 128.41, 128.61, 132.97, 133.02, 133.10, 133.15, 138.12, 138.62 ppm; the corresponding **alcohol 289** (548 mg, 55%); Rf: 0.13; ^1H NMR (300 MHz, $CDCl_3$) δ: 1.58 (d, J = 6.46 Hz, 3H), 5.06 (q, J = 6.54 Hz, 1H), 7.45-7.53 (broad, aromatics, 3H), 7.81-7.87 (broad, aromatics, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 25.05, 70.39, 123.77, 125.72, 126.07, 127.61, 127.87, 128.22, 132.83, 133.23, 143.12 ppm. The corresponding sulfite and dialkoxy disulfide of **289** were never reported in the literature.

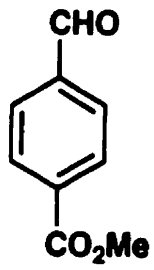
Preparation of Dialkoxy Disulfide from (S)-1-Naphthyl-Ethanol 289:

(S)-OSSO-(S)

To the enantiomeric (S)-alcohol **289** (0.50 g, 2.9 mmol) and triethylamine (405 μL, 2.9 mmol) cooled to 0 °C in dichloromethane (25 mL) was added dropwise a solution of S_2Cl_2 (116 μL, 1.45 mmol) in dichloromethane (2 mL). The reaction was further stirred for an extra 1 hour at 0 °C and worked up with water. The organic layer was dried over anhydrous $MgSO_4$, filtered and evaporated under reduced pressure to give a beige residue that was chromatographed (20% EtOAc in hexanes) to give the **dialkoxy disulfide** of **289** (407 mg, 69% yield); Rf: 0.58; ^1H NMR (300 MHz, $CDCl_3$) δ: 1.64 (d, J = 6.52 Hz, 3H), 1.66 (d, J = 6.53 Hz, 3H), 5.00 (q, J = 6.60 Hz, 1H), 5.11 (q, J = 6.59 Hz, 1H), 7.35-8.54 (broad multiplet,aromatics 14H);^{13}C NMR ($CDCl_3$, 75 MHz) δ: 22.97, 23.43, 82.48, 83.49, 124.22, 124.32, 125.66, 125.92, 126.04, 126.16, 127.64, 127.97, 128.01, 128.24, 128.40, 133.01, 133.09, 133.14, 139.19, 139.36 ppm; the alcohol **289** (84 mg, 17%). This dialkoxy disulfide was never reported in the literature.

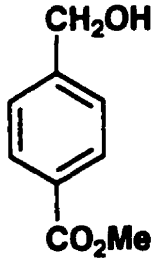
Preparation of Methyl 1-Hydroxymethylbenzoate

i) Esterification of 4-Carboxybenzoic Acid:



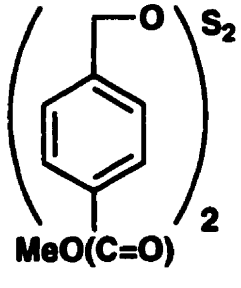
4-Carboxybenzoic acid (4 g, 27 mmol), DBU (4 mL, 27 mmol) and methyl iodide (1.7 mL, 27 mmol) were mixed together in benzene (50 mL) at room temperature. The mixture was immersed in an oil bath at 90 °C, and refluxed for 20 hours. Cooled to room temperature, the mixture was evaporated and the residue taken up in dichloromethane and washed with water (3 x 30 mL), the organic phase was dried over anhydrous $MgSO_4$ and filtered to give the desired product methyl 4-formylbenzoate (3.7 g, 85%) m.p. 59.5-61 °C; ^1H NMR (300 MHz, $CDCl_3$) δ: 3.94 (s, 3H), 7.93 (d, J = 8.55 Hz, 2H), 8.17 (d, J = 8.60 Hz, 2H), 10.08 (s, 1H) ppm; ^{13}C NMR (75 MHZ, $CDCl_3$) δ: 52.53, 129.46, 130.12, 135.01, 139.07, 165.99, 191.59 ppm. The analytical data were found to compare with previously reported ones.[191b]

ii) Reduction of Methyl 4-Formylbenzoate:



Methyl 4-formylbenzoate (2.6 g, 16 mmol) was dissolved in ethanol and cooled to 0 °C, then $NaBH_4$ was added potionwise and the mixture was stirred to room temperature and at room temperature for 1 hour. Then water and HCl (1.2 N) were added to pH~8 and the ethanol was evaporated. The pH was lowered to ~6 using HCl (1.2N) and at then extracted with dichloromethane. The organic phase was washed with water and dried over anhydrous $MgSO_4$ to give methyl 1-hydroxymethylbenzoate (2.15 g, 80%) m.p. 41.5-43 °C.

Preparation of Dialkoxy Disulfide 218f from Methyl 1-Hydroxymethylbenzoate:

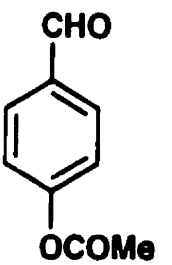


To methyl 1-hydroxymethylbenzoate (1.5 g, 9.1 mmol) and triethylamine (1.27 mL, 9.1 mmol) cooled to 0 °C in dichloromethane (12 mL) and Et_2O (6 mL) was added dropwise a solution of S_2Cl_2 (366 μL, 4.6 mmol) in dichloromethane (2 mL) for 0.5 hour. Extra stirring for 0.5 hour at 5-10 °C followed by the addition of water (2 x 10 mL)

and separation of the organic phase treated with anhydrous $MgSO_4$, gave a crude beige solid that was chromatographed (50% EtOAc in hexanes) to give the dialkoxy disulfide **218f** (1.1 g, 63%) m.p. 44-46 °C; Rf: 0.60; ^1H NMR (300MHz, $CDCl_3$) δ: 3.91 (s, 3H), 4.83, 4.94 (ABq, J = 12.15 Hz, 2H), 7.38 (d, J = 8.52 Hz, 2H), 8.01 (d, J = 8.49 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 52.14, 75.85, 128.12, 129.81, 130.13, 141.45, 166.68 ppm. This new compound was never reported in the literature.

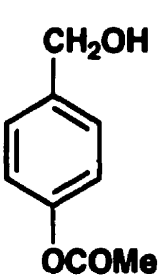
Preparation of 4-Acetoxybenzyl Alcohol:

i) Acetylation of 4-Hydroxybenzaldehyde:



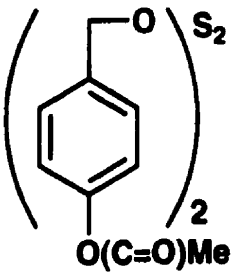
To 4-hydroxybenzaldehyde (5. g, 41 mmol) dissolved in dichloromethane and chloroform (50 ml + 50mL) was added dropwise pyridine (3.3 mL, 41 mmol) and the resulting burgundy solution was cooled to 0 °C. A solution of acetyl chloride in dichloromethane (20 mL) was added dropwise over an hour to turn the solution to orange. Stirring at room temperature for 11 hours followed by washing with water (5 x 100 mL) gave a clear solution that was evaporated. Dichloromethane (50 mL) was added to the residue and the solution was further washed with HCl (1.2N) (2 x 40 mL) and water (3 x 30 mL) to pH~6. The organic phase was dried over anhydrous $MgSO_4$, filtered and evaporated to give the desired 4-acetoxybenzaldehyde (5.5 g, 97%) of an orange oil that was distilled under reduced pressure b.p. 135-138°C °C (10 mmHg) (lit. 153 °C under 17 mmHg)[191]; ^1H NMR (300MHz, $CDCl_3$) δ: 2.29 (s, 3H), 7.23 (d, J = 8.55 Hz, 2H), 7.88 (d, J = 8.30 Hz, 2H), 9.94 (s, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 21.04, 122.28, 131.10, 155.23, 168.61, 190.93 ppm.

ii) Reduction of 4-Acetoxybenzaldehyde:



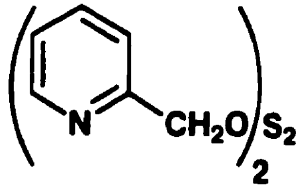
4-Acetoxybenzaldehyde (3.6 g, 22 mmol) was reduced using sodium borohydride $NaBH_4$ (300 mg, 7.9 mmol) as described for methyl 4-formylbenzoate to give a clear yellow oil for 4-acetoxybenzyl alcohol (3.2 g, 90%); ^1H NMR (300MHz, $CDCl_3$) δ: 2.27 (s, 3H), 2.71 (s, 1H), 4.57 (s, 2H), 7.02 (d, J = 8.60 Hz, 2H), 7.30 (d, J = 8.74 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.99, 64.31, 121.46, 127.91, 138.50, 149.79, 169.67 ppm.

Preparation of Dialkoxy Disulfide 218g from 4-Acetoxybenzyl Alcohol:



To 4-acetoxybenzyl alcohol (680 mg, 4.1 mmol) and triethylamine (578 μL, 4.1 mmol) cooled to 0 °C in dichloromethane (12 mL) and Et_2O (6 mL) was added dropwise a solution of S_2Cl_2 (166 μL, 2.1 mmol) in dichloromethane (2 mL) for 0.5 hour. Extra stirring for 0.5 hour at 5-10 °C followed by the addition of water (2 x 10 mL) and separation of the organic phase treated with anhydrous $MgSO_4$, gave a crude burgundy oil that was chromatographed (50% EtOAc in hexanes) to give the dialkoxy disulfide **218g** (260 mg, 25%); Rf: 0.68; ^1H NMR (300MHz, $CDCl_3$) δ: 2.26 (s, 3H), 4.76, 4.87 (ABq, J = 11.47 Hz, 2H), 7.03 (d, J = 8.25 Hz, 2H), 7.32 (d, J = 9.03 Hz, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.90, 75.80, 121.51, 129.60, 134.00, 150.58, 169.14 ppm. This new compund was never reported in the literature.

Preparation of Dialkoxy Disulfide 290 from 2-Pyridinyl Carbinol:



To 2-pyridinyl carbinol (2.0 g, 18 mmol) and triethylamine (2.55 mL, 18.3 mmol) cooled to 0 °C in dichloromethane (30 mL) was added dropwise a solution of S_2Cl_2 (733 μL, 9.2 mmol) in dichloromethane (2 mL) for 0.5 hour. Extra stirring for 1 hour at 5-10 °C followed by the addition of water (2 x 10 mL) and separation of the organic phase treated with anhydrous $MgSO_4$, gave a crude burgundy oil that showed over 75% yield by NMR. However, when chromatographed (EtOAc), it gave the dialkoxy disulfide **290** that decomposed right away once purified; Rf: 0.25; ^1H NMR (300 MHz, $CDCl_3$) δ: 4.91, 5.01 (ABq, J = 12.69 Hz, 2H), 7.13-7.38 (broad, aromatics, 2H), 7.59-7.69 (broad, aromatics, 1H), 8.50-8.53 (broad, aromatics, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 77.00, 122.05, 122.81, 136.55, 149.14, 156.31 ppm. This new compound was never reported in the literature.

6.4 Methodology Related to Chapter 4 and Chapter 5

Purification of *m*-CPBA:[165]

m-CPBA (commercial 50-85%) (10 g) was dissolved in Et_2O (250 mL). This ether solution was washed with a phosphate buffer (5 x 100 mL) which was made from KH_2PO_4 (5.92 g) and K_2HPO_4 (26.5 g) dissolved in water (1 L) for a pH of *ca.* 7.5. The ether phase was also washed with water (2 x 50 mL) and with a saturated NaCl solution (2 x 50 mL) followed by treatment with anhydrous $MgSO_4$, filtration and evaporation of the ether to give a white solid residue. The residue was recrystallized in dichloromethane to give pure *m*-CPBA of 99% purity.

m-CPBA Oxidation of 246b-c:

The sulfoxylates **246b-c** were oxidized by *m*-CPBA according to **eq.62**. The corresponding pure sulfites **219b-c** were obtained by chromatography using 40% EtOAc in hexanes; **219b** Rf: 0.52 and **219c** Rf: 0.67. For example, bis(4-nitrobenzyl) sulfoxylate **246b** (150 mg, 0.45 mmol) was dissolved in ether (7 mL) and the solution cooled to -40 °C. To this well stirred solution, was added dropwise a solution of *m*-CPBA (85 mg, 0.50 mmol) in 5 mL of Et_2O. After stirring for 4 hours, the solution was warmed up to about 0 °C, transferred to a separatory funnel and washed with a solution of $NaHSO_3$ 10% (2 x 5 mL) followed by a solution of 5% $NaHCO_3$ (2 x 5mL) and water (2 x 5 mL). Treatment with anhydrous $MgSO_4$, filtration and evaporation of the solvents under reduced pressure gave a light yellow residue that was chromatographed using 40% EtOAc in hexanes to give the sulfite **219b** (145 mg, 92% yield) m.p. 81-83 °C; Rf: 0.52; the ^1H and ^{13}C NMR spectra were compared with a previously prepared sample of **219b** and found to be identical. For bis(4-chlorobenzyl) sulfoxylate **246c**, the reaction was conducted in dichloromethane with the addition of a solution of *m*-CPBA in Et_2O.

Thermolysis of Oxytrisulfide 246: Formation of 1,3,5-Trithiane 314:

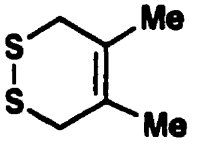
Compound **243** (30 mg, 89 µmol) and MgO (4 mg, 89 µmol) were heated in toluene-d_8 for 16 hours at 105-110 °C in the probe 300 MHz spectrometer and followed according to ^1H NMR signals. The 1,3,5-trithia-2,4,6-triphenylcyclohexane **314** is believed to be

identified in the ^1H NMR spectra in both the *cis* and *trans* form; ^1H NMR (300MHz, toluene-d_8) δ: 3.77 (s, 1H) and 3.82 (s, 2H) ppm for the *cis*-form; 3.78 (s, 3H) ppm for the *trans*-form.[193] The aromatics for the phenyl groups are at 7.04 ppm. The 4-nitrobenzyl alcohol gives a signal at 4.05 (s, 2H) ppm for the benzylic protons and the 4-nitrobenzaldehyde gives a signal at 9.31 (s, 1H) ppm for the (C=O)H group.

Trapping Experiments in the presence of 2,3-Dimethyl and 2,3-Diphenyl Butadiene:

Typical amounts of reagents are reported in **Table 29**. The reagents were mixed together and immersed in an oil bath at the desired temperature for the indicated time period. At the end of that period the solvent was evaporated under reduced pressure and the residue was triturated in carbon tetrachloride (5 x 10 mL) followed by hexanes (3 x 10 ml). These extracts were combined and evaporated prior to chromatography.

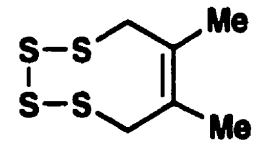
The 1,2-Dithia-4,5-dimethyl-4-cyclohexene 316:



The resulting light yellow clear oil has an unpleasant smell that can cling for long periods of time; Rf (5% $CHCl_3$ in hexanes): 0.30; Rf (25% CS_2 in cyclohexane): 0.33; Rf (50% CCl_4 in hexanes): 0.33; Rf (CCl_4): 0.43; ^1H NMR (300MHz, $CDCl_3$) δ: 1.74 (3H), 3.19 (s, 2H) ppm; ^1H NMR (300MHz, toluene-d_8) δ: 1.33 (s, 3H), 2.80 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.81, 34.19, 125.16 ppm; MS (EI, direct inlet, 30 °C) m/z: 146 ($M^{+\cdot}$, 100), 114 ($M^{+\cdot}$ -S, 3), 113 ($M^{+\cdot}$ -SH, 18), 82 ($M^{+\cdot}$ -S_2, 71), ($M^{+\cdot}$ -SH -S, 15), 67 ($M^{+\cdot}$ -CH_3, 80).

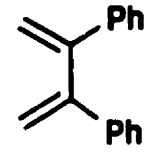
193. The corresponding *cis*-form was assigned δ ($CDCl_3$): 5.5 (s, 2H) and 5.8 (s, 1H) ppm while the *trans*-form was assigned 5.43 (s, 3H) ppm; B.F. Bonini, G. Mazzanti, P. Zani and G. Maccagnani, *J. Chem. Soc. Perkin Trans. I*, 1499 (1988).

1,2,3,4-Tetrathia-6,7-dimethyl-6-cyclooctene 317:



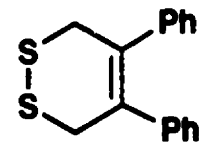
This is a yellow oil; Rf (5% $CHCl_3$ in hexanes): 0.38; Rf (25% CS_2 in cyclohexane): 0.35; Rf (50% CCl_4 in hexanes): 0.43; Rf (CCl_4): 0.50; ^1H NMR (300MHz, $CDCl_3$) δ: 1.78 (s, 3H), 3.62 (s, 2H) ppm; ^1H NMR (300MHz, toluene-d_8) δ: 1.44 (s, 3H), 3.01 (s, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 20.81, 34.19, 125.16 ppm; MS (EI, direct inlet, 30 °C) m/z: 210 ($M^{+\cdot}$, 5), 146 ($M^{+\cdot}$ -S_2, 44), 113 ($M^{+\cdot}$ -S_2 -H, 13), 82 (146 -S_2, 98), 81 (113 -S_2, 17), 67 (82 -CH_3, 100).

Preparation of 2,3-Diphenylbutadiene 318:[171b]



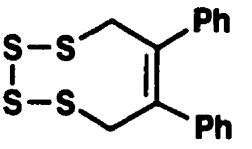
The compound was prepared exactly as referenced; Rf (hexanes): 0.26; ^1H NMR (300 MHz, $CDCl_3$) δ: 5.34 (d, J = 1.66 Hz, 2H), 5.57 (d, J = 1.71 Hz, 2H), 7.26-7.35 (m, 4H), 7.41-7.46 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 116.33, 127.49, 127.90, 127.93, 128.17, 140.19, 149.85 ppm.

1,2-Dithia-4,5-diphenyl-4-cyclohexene 319:



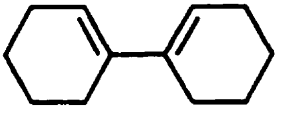
This is a beige solid m.p. 100-102 °C (lit.[54d] m.p. 101-102 °C); Rf (2% Et_2O in petroleum ether): 0.21; ^1H NMR (300 MHz, $CDCl_3$) δ: 3.67 (s, 2H), 6.95-7.10 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 34.67, 126.58, 127.90, 129.19, 134.76, 142.58 ppm.

1,2,3,4-Tetrathia-6,7-diphenyl-6-cyclooctene 320:



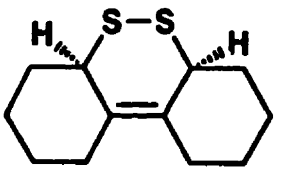
This is a beige solid m.p. 136-139 °C (lit.[54d] m.p. 137-139 °C) ; Rf (2% Et_2O in petroleum ether): 0.35; ^1H NMR (300 MHz, $CDCl_3$) δ: 4.07 (s, 2H), 7.06-7.14 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 42.91, 126.85, 126.95, 127.75, 127.96, 129.53, 138.03, 140.85 ppm; MS (EI, direct inlet, 100 °C) m/z: 334 ($M^{+\cdot}$, 3), 270 ($M^{+\cdot}$ -S_2, 7), 206 (270 -S_2, 100), 205 (270 -SH -S, 83).

Preparation of 1,1'-Bicyclohexenyl 321:



Previously distilled pyridine (86.7 mL, 1.07 mol) and phosphorus oxychloride, $POCl_3$, (17.4 mL, 187 mmol) were syringed slowly into a cooled 500 mL flask (0 °C) containing (bicyclohexyl)-1,1'-diol **58** (20 g, 101 mmol). The exothermic reaction was stirred cautiously to room temperature. The resulting pink creamy solution was heated at 100 °C for 20 hours using an oil bath. Once cooled to room temperature, water (250 mL) was added and stirring continued for 1 h. The mixture was extracted with pentane (3 x 100 mL). The combined extracts were sequentially washed with HCl 10% (4 x 75 mL), $NaHCO_3$ 5% (4 x 85 mL) and water (4 x 100 mL), dried over anhydrous $MgSO_4$ and evaporated to give a crude clear yellow oil (12.387 g). The crude oil was distilled under reduced pressure to give a clear oil in 56% yield (9.169 g); b.p. 79-80 °C (1.5 mmHg); ^1H NMR (300 MHz, $CDCl_3$) δ: 1.52-1.81 (m, 4H), 2.04-2.21 (m, 4H), 5.78 (bs, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 22.07, 23.12, 25.48, 25.82, 121.25, 136.70 ppm.

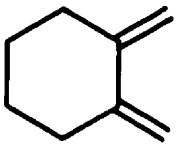
Trapping Experiment of 218b in the presence of 1,1'-bicyclohexenyl 321:



Typical amounts of **218b** (900 mg, 2.5 mmol) to **321** (114 mg, 0.7 mmol) in the case of the 3.5:1.0 ratio **(Table 31)** in 7 mL of chlorobenzene. In addition, for each mol of **218b** used, 1 mol of MgO was also added to the mixture. The reaction was immersed in an oil bath at 135-140 °C and

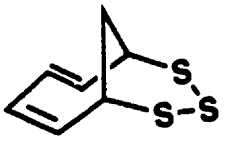
stirred for 2 hours. Most of the solvent was evaporated under reduced pressure and the residue was taken up in carbontetrachloride, CCl_4, and chromatographed on silica gel using 10% carbon disulfide, CS_2, in CCl_4; **321** Rf: 0.58, **322** (disulfide adduct, a clear yellow oil) Rf: 0.31; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 26.62, 27.96, 31.95, 34.52, 44.55, 132.44 ppm; MS (EI, 70 eV, 100 °C) m/z: 226 ($M^{+\cdot}$, 10); 162 ($M^{+\cdot}$ -S_2, 100).

Preparation of 1,2-Divinylcyclohexane 329:[178]



The compound was prepared exactly as referenced. α-Bromomethanesulfonyl bromide **326**; ^1H NMR (300 MHz, $CDCl_3$) δ: 5.00 (s, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 54.41 ppm; the adduct 1-bromo-1-methyl-2-[(bromomethyl)sulfonyl]cyclohexane **328**; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 22.58, 23.15, 24.15, 29.55, 43.63, 44.29, 65.65, 67.05 ppm; 1,2-Divinylcyclohexane **329**; ^1H NMR (300 MHz, $CDCl_3$) δ: 1.58-1.62 (m, 2H), 2.16 (broad, 2H), 4.60 (d, J = 1.46 Hz, 1H), 4.89 (d, J = 1.81 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 26.74, 35.25, 107.76, 149.64 ppm.

2,3,4-Trithiabicyclo[4.3.1] deca-6,8-diene 334:



This compound was isolated by chromatography using 20% chloroform in hexanes Rf: 0.27; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 29.23, 40.65, 127.05, 134.29 ppm; MS (EI, direct inlet, 30°C) m/z: 188 ($M^{+\cdot}$, 100), 155 ($M^{+\cdot}$ -SH, 3), 124 ($M^{+\cdot}$ -S_2, 0.7), 123 ($M^{+\cdot}$ -SH -S, 0.7), 92 ($M^{+\cdot}$ -S_3, 55), 91 ($M^{+\cdot}$ -SH -S_2,100); MS (CI, direct inlet, 70 °C) m/z: 206 (M +$NH4^+$, 2), 188 ($M^{+\cdot}$, 100), 155 ($M^{+\cdot}$-SH, 13), 124 ($M^{+\cdot}$ -S_2, 53), 123 ($M^{+\cdot}$-SH -S, 55).

Thermolysis of O,O'-Bicyclohexyl-1,1'-diylthiosulfite 57:

The thionosulfite **57** was heated in DMSO-d_6 at the desired temperature and the resulting products were analyzed by ^{13}C NMR spectroscopy. In the presence of 2,3-diphenyl butadiene **318**, trapped disulfide adduct **319** was obtained. The residual products of the thermolysis were analyzed by ^{13}C NMR in DMSO-d_6 and compared with the spectrum of authentic samples in the same deuterated solvent (**Table 32**).

Thermolysis of 218b in the Presence of the diene 315 and Benzylamine:

The reaction was monitored by ^1H NMR for 20 hours in toluene-d_8 at 95 °C. Bis(4-nitrobenzyloxy) disulfide **218b** (300 mg, 0.82 mmol), benzylamine (59 µL, 0.54 mmol) and 2,3-dimethylbutadiene **315** (93 µL, 0.82 mmol) were dissolved in toluene-d_8 and immersed in an oil bath at 95 °C. The reaction was monitored every 2 hours at first, and after 10 hours every 5 hours. The corresponding di- **316** and tetrasulfide adduct **317** were detected. The reaction solvent was evaporated under reduced pressure, and the residue triturated in CCl_4 (4 x 7 mL), the extracts were combined and evaporated. The desired adducts were isolated using chromatography (50% CCl_4 in hexanes) to give **316** (20 mg, 16% yield) and **317** (22 mg, 34% yield).

Thermolysis of the sulfite 219b in the Presence of Diene 317:

Bis(4-nitrobenzyl) sulfite **219b** (50 mg, 0.14 mmol) and 2,3-dimethylbutadiene **315** (48 µL, 0.43 mmol) were dissolved in DMSO-d_6 and immersed in an oil bath at 113 °C. The reaction was followed every hour for 8 hours and then every 5 hours up to 18 hours using ^{13}C NMR (**Table 33**).

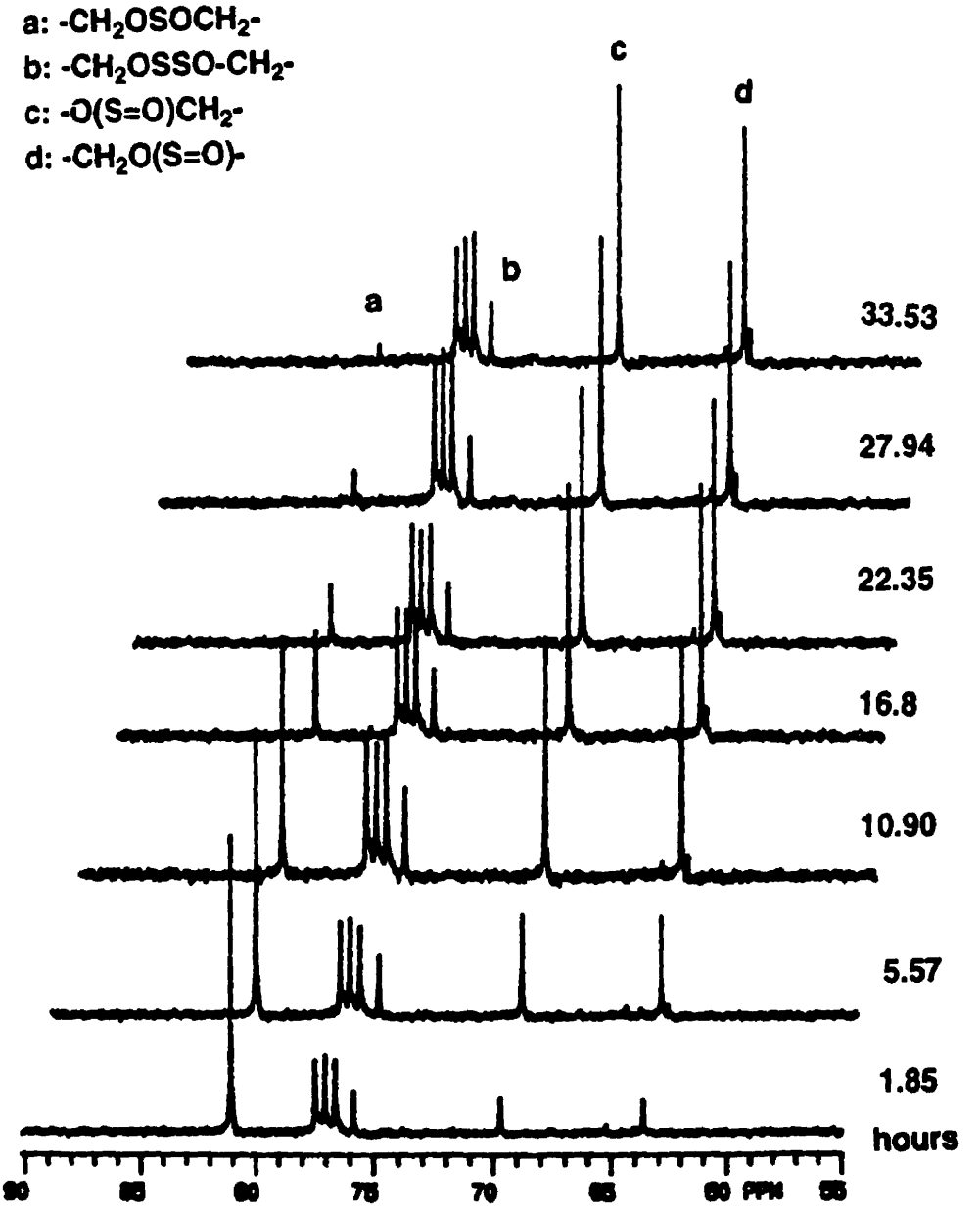
Desulfurization of Bis(4-Nitrobenzyloxy) Disulfide 218b:

The desulfurization was followed from -40 to 20 °C in chloroform-d and the products identified by comparing the spectrum of authentic samples and by adding authentic samples to the final reaction mixture.

APPENDIX I

Time Dependence Isomerisatiom of 4-Chloro-Benzyl Sulfoxylate 246c to the Sulfinate 249c in CDCl3 at 20.3 °C.

$(p\text{-Cl-C}_6\text{H}_4\text{CH}_2\text{-O-})_2\text{S}$



APPENDIX II

X-Ray Structure Determination of Bis(4-Nitro-Benzyloxy) Disulfide 218b

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The data were collected at T = 21°C on a Rigaku AFC6S diffractometer using the ω -2θ scan technique. The calculations were performed using TEXRAY program of the TEXSAN crystallographic software package from Molecular Structure Corporation (1985).

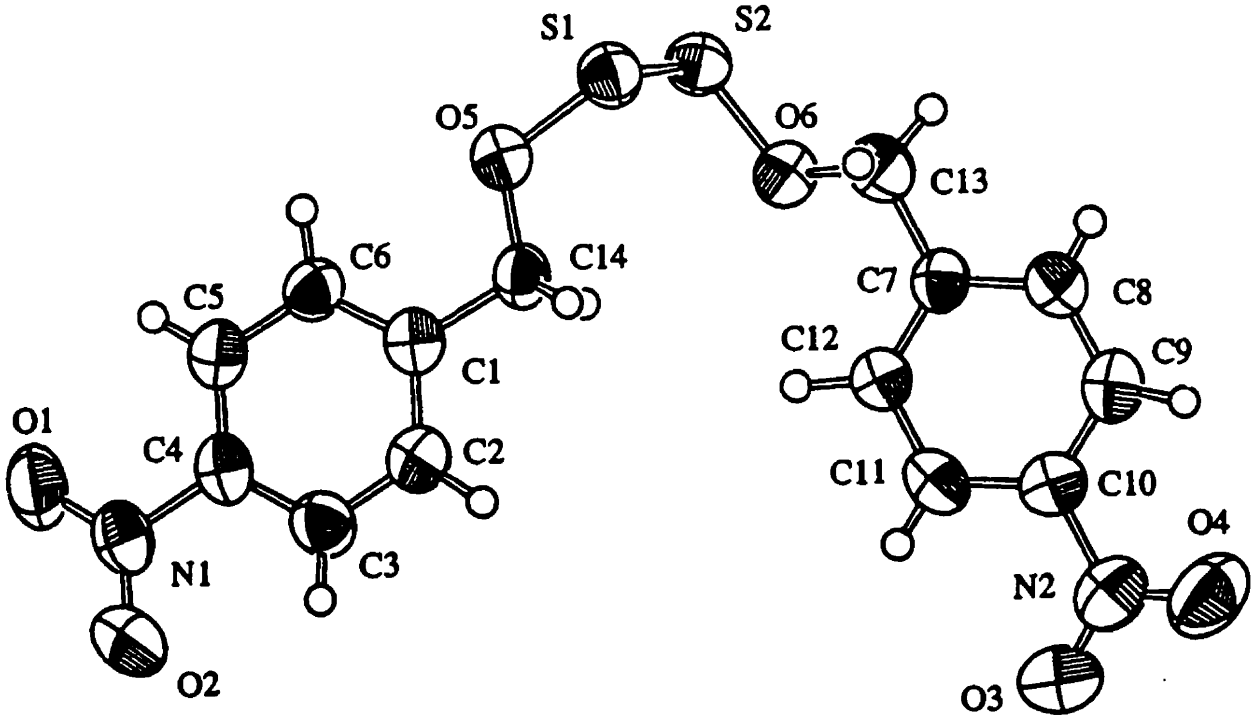

Figure II: ORTEP[194] Diagram Showing Complete Atomic Number Scheme for 218b (4-NO_2-C_6H_4-CH_2-O-S)$_2$ (50% Probability Ellipsoids).

194. C.K. Johnson, ORTEP II, Report ORNL-5138, Oak Ridge, National Laboratory, Tennessee (1976).

Table-II-1: Crystal Data for the Structure Determination of 218b

Data:	
Chemical Formula	$C_{14}H_{12}N_2O_6S_2$
Formula weight	368.38
Crystal Color, Habit	colorless, plate
Crystal Dimensions (mm)[a]	0.250 x 0.120 x 0.480
Crystal System	triclinic
Space Group	p1 (#2)
Lattice Parameters:	
a (Å)	12.810(2)
b (Å)	13.730(1)
c (Å)	4.6436(4)
α (°)	97.483(7)
β (°)	96.29(1)
γ (°)	83.96(1)
V $(Å)^3$	801.4(2)
Z	2
D_{cal} (g cm^{-3})	1.526
F(000)	380
μ (cm^{-1})	32.76
Collection and Refinement Parameters:	
Radiation	Graphite-monochromated CuKα
λ (Å)	1.54178
2θ max (°)	119.9
Scan Width (°)	(1.57 + 0.30 tanθ)
No. of reflections Measured	2507
No. of Unique reflections	2381 (R_{int} = 0.131)
No. of Reflections with $I_{net} > 3.00\ \sigma\ (I_{net})$	1612
Significant Reflections: RF[b], R_w[c], G_oF[d]	0.053, 0.058, 2.25
Maximum Shift/σ ratio	0.01
Maximum Peak in Final D-Map ($e/Å^3$)	0.28
Minimum Peak in Final d-Map ($e/Å^3$)	-0.30
p-factor	0.01
Structure Determination	by direct methods[195]
Structure Refinement	full-matrix least-squares

a) Obtained from 25 reflections with $74.82 < 2\theta < 78.46$ °; b) $RF = \Sigma (F_o - F_c) / \Sigma (F_o)$;
c) $R_w = (\Sigma[w(F_o - F_c)^2 / \Sigma(wF_o^2)])^{1/2}$; d) $G_oF = (\Sigma[w(F_o - F_c)^2 / (\#\text{ reflections} - \#\text{ parameters})])^{1/2}$

195. a) C.J. Gilmore, an integrated direct methods computer program, *J. Appl. Cryst.*, **17**, 42 (1984); b) P.T. Beurskens, *DIRDIF: Direct Methods for Difference Structures -an automatic procedure for phase extension and refinement of differences structure factors*, Technical Report 1984/1, Crystallography Laboratory, Toernooiveld, 6525 Ed. Nijmegen, Netherlands

Table II-2: Atomic Parameters (x, y, z) and B(eq)[a] for 218b[b]

atom	x	y	z	B(eq)
S(1)	0.5426(1)	0.2754(1)	0.2629(3)	4.82(7)
S(2)	0.4905(1)	0.1655(1)	0.4213(3)	4.71(7)
O(1)	0.7371(4)	0.7011(3)	1.651(1)	6.7(2)
O(2)	0.8913(4)	0.6241(3)	1.714(1)	7.5(3)
O(3)	1.0774(4)	-0.1535(4)	0.820(1)	8.5(3)
O(4)	1.0561(4)	-0.2572(4)	0.443(1)	8.3(3)
O(5)	0.5807(3)	0.3548(2)	0.5423(8)	5.0(2)
O(6)	0.5933(3)	0.0860(2)	0.4992(7)	4.5(2)
N(1)	0.8033(4)	0.6335(3)	1.586(1)	4.8(2)
N(2)	1.0267(4)	-0.1833(4)	0.596(1)	5.6(3)
C(1)	0.7160(4)	0.4161(4)	0.899(1)	3.8(2)
C(2)	0.8144(5)	0.4071(4)	1.053(1)	5.0(3)
C(3)	0.8446(4)	0.4785(4)	1.274(1)	5.1(3)
C(4)	0.7730(4)	0.5586(4)	1.342(1)	4.0(2)
C(5)	0.6768(4)	0.5696(4)	1.192(1)	4.6(3)
C(6)	0.6472(4)	0.4976(4)	0.969(1)	4.5(2)
C(7)	0.7375(4)	-0.0281(3)	0.350(1)	3.8(2)
C(8)	0.7681(5)	-0.1190(4)	0.200(1)	5.0(3)
C(9)	0.8619(5)	-0.1701(4)	0.279(1)	4.9(3)
C(10)	0.9253(4)	-0.1306(4)	0.510(1)	4.3(3)
C(11)	0.8962(5)	-0.0397(4)	0.662(1)	5.8(3)
C(12)	0.8024(4)	0.0105(4)	0.580(1)	4.9(3)
C(13)	0.6354(5)	0.0273(4)	0.253(1)	5.3(3)
C(14)	0.6869(4)	0.3347(4)	0.664(1)	4.3(2)
H(1)	0.8698	0.3581	1.0042	5.6
H(2)	0.9104	0.4800	1.3644	6.1
H(3)	0.6260	0.6197	1.2475	5.0
H(4)	0.5806	0.5122	0.8651	4.9
H(5)	0.7451	0.3133	0.5226	4.8
H(6)	0.6954	0.2646	0.7506	4.8
H(7)	0.7223	-0.1426	0.0717	5.4
H(8)	0.8980	-0.2222	0.1702	5.7
H(9)	0.9368	-0.0145	0.8113	6.5
H(10)	0.7876	0.0770	0.7036	5.5
H(11)	0.5856	-0.0167	0.1601	5.7
H(12)	0.6579	0.0651	0.1303	5.7

a) B(eq) is the mean of the principal axes of the thermal ellipsoid for atoms refined anisotropically. For hydrogens, B(eq) = B(iso); b) Estimated standard deviations refers to the last digit printed in ().

Table II-3: Bond Distances for 218b (in angstroms (Å))[a]

S1-S2	1.968(2)	C1-C14	1.503(6)
S1-O5	1.648(3)	C2-C3	1.377(7)
S2-O6	1.659(4)	C3-C4	1.382(7)
O1-N1	1.220(6)	C4-C5	1.352(7)
O2-N1	1.218(6)	C5-C6	1.385(7)
O3-N2	1.210(6)	C7-C8	1.386(7)
O4-N2	1.212(6)	C7-C12	1.366(7)
O5-C14	1.427(6)	C7-C13	1.497(7)
O6-C13	1.432(6)	C8-C9	1.365(7)
N1-C4	1.475(6)	C9-C10	1.361(7)
N2-C10	1.461(7)	C10-C11	1.387(7)
C1-C2	1.382(7)	C11-C12	1.363(8)
C1-C6	1.378(7)		
C2-H1	0.951	C11-H9	0.877
C3-H2	0.900	C12-H10	1.024
C5-H3	0.928	C13-H11	0.955
C6-H4	0.948	C13-H12	0.907
C8-H7	0.848	C14-H5	1.042
C9-H8	0.932	C14-H6	1.081

a) Estimated standard deviation in the least significant figure are given in ().

Table II-4: Bond Angles (in degrees (°))[a]

S2-S1-O5	107.3(2)	N1-C4-C5	119.6(5)
S1-S2-O6	107.8(1)	C3-C4-C5	121.8(5)
S1-O5-C14	114.6(3)	C4-C5-C6	119.6(5)
S2-O6-C13	115.5(3)	C1-C6-C5	120.0(5)
O1-N1-O2	123.7(5)	C8-C7-C12	119.3(5)
O1-N1-C4	117.4(5)	C8-C7-C13	119.8(5)
O2-N1-C4	118.8(5)	C12-C7-C13	120.9(5)
O3-N2-O4	122.1(6)	C7-C8-C9	121.1(5)
O3-N2-C10	119.5(5)	C8-C9-C10	118.8(5)
O4-N2-C10	118.4(6)	N2-C10-C9	119.8(5)
C2-C1-C6	119.3(5)	N2-C10-C11	119.2(5)
C2-C1-C4	118.5(5)	C9-C10-C11	121.0(5)
C6-C1-C14	122.2(5)	C10-C11-C12	119.5(5)
C1-C2-C3	121.0(5)	C7-C12-C11	120.3(5)
C2-C3-C4	118.3(5)	O6-C13-C7	109.7(4)
N1-C4-C3	118.695)	O5-C14-C1	110.1(4)
C1-C2-H1	124.88	C12-C11-H9	119.43
C3-C2-H1	113.63	C7-C12-H10	125.50
C2-C3-H2	124.04	C11-C12-H10	114.17
C4-C3-H2	117.31	O6-C13-H11	109.96
C4-C5-H3	122.25	O6-C13-H12	111.76
C6-C5-H3	177.66	C7-C13-H11	111.11
C1-C6-H4	124.78	C7-C13-H12	100.39
C5-C6-H4	115.00	H11-C13-H12	113.52
C7-C8-H7	115.55	O5-C14-H5	118.59
C9-C8-H7	123.00	O5-C14-H6	109.69
C8-C9-H8	128.13	C1-C14-H5	113.10
C10-C9-H8	111.34	C1-C14-H6	110.60
C10-C11-H9	121.04	H5-C14-H6	93.57

a) Estimated standard deviation in the least significant figure are given in 0.

Table II-5: Torsion Angles (in degrees (°))[a]

S1-S2-O6-C13	-74.2(4)	N2-C10-C9-C8	-179.3(5)
S1-O5-C14-C1	175.1(3)	N2-C10-C11-C12	179.1(5)
S2-S1-O5-C14	86.6(4)	C1-C2-C3-C4	1.4(9)
S2-O6-C13-C7	170.5(3)	C1-C6-C5-C4	-0.9(8)
O1-N1-C4-C3	-176.7(5)	C2-C1-C6-C5	0.1(8)
O1-N1-C4-C5	3.2(8)	C2-C3-C4-C5	-2.2(9)
O2-N1-C4-C3	2.3(8)	C3-C2-C1-C6	-0.4(6)
O2-N1-C4-C5	-177.8(5)	C3-C2-C1-C14	-178.8(5)
O3-N2-C10-C9	-171.8(6)	C3-C4-C5-C6	1.9(9)
O3-N2-C10-C11	9.4(9)	C5-C6-C1-C14	178.4(5)
O4-N2-C9-C10	6.5(8)	C7-C8-C9-C10	0.5(9)
O4-N2-C10-C11	-172.3(6)	C7-C12-C11-C10	0(1)
O5-S1-S2-O6	-85.6(2)	C8-C7-C12-C11	0.0(9)
O5-C14-C1-C2	176.6(5)	C8-C9-C10-C11	-0.5(9)
O5-C14-C1-C6	-1.7(7)	C9-C8-C7-C12	-0.2(9)
O6-C13-C7-C8	150.0(5)	C9-C8-C7-C13	178.4(5)
O6-C13-C7-C12	-31.4(7)	C9-C10-C11-C12	0(1)
N1-C4-C3-C2	177.7(5)	C11-C12-C7-C13	-178.6(6)
N1-C4-C5-C6	-178.0(5)		

a) The sign is positive if when looking from atom to atom, a clockwise motion of atom 1 would superimpose it on atom 4.

APPENDIX III

X-Ray Structure Determination of Bis(4-Chloro-Benzyloxy) Disulfide 218c

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The data were collected at T = 20°C on a Rigaku AFC6S diffractometer using the $\omega/2\theta$ scan technique. The calculations were performed using TEXRAY program of the TEXSAN crystallographic software package from Molecular Structure Corporation (1985).

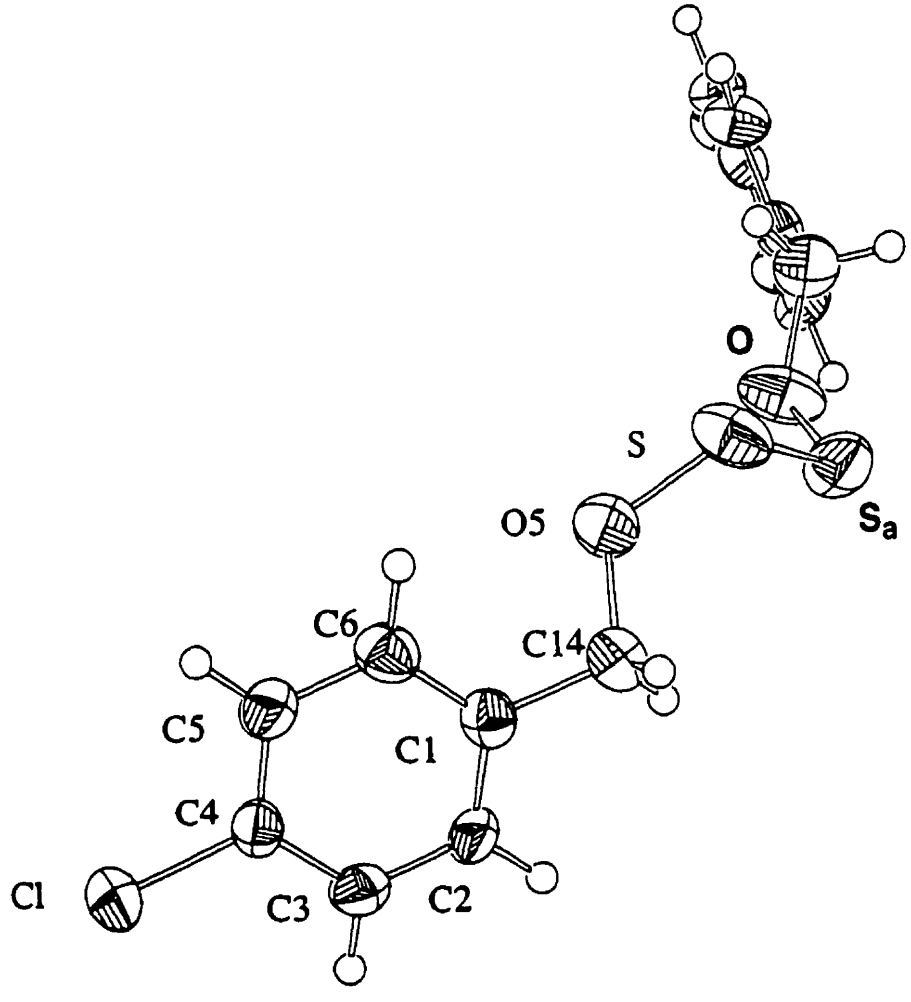

Figure III: ORTEP[194] Diagram Showing Complete Atomic Number Scheme for 218c (4-Cl-C_6H_4-CH_2-O-S)$_2$ (40% Probability Ellipsoids).

Table-III-1: Crystal Data for the Structure Determination of 218c

Data:	
Chemical Formula	$C_{14}H_{12}Cl_2O_2S_2$
Formula weight	347.27
Crystal Color, Habit	colorless, plate
Crystal Dimensions (mm)[a]	0.48 x 0.30 x 0.08
Crystal System	monoclinic
Space Group	C2
Lattice Parameters:	
a (Å)	26.606(4)
b (Å)	4.9201(5)
c (Å)	5.8484(1)
β (°)	95.282(13)
V (Å)^3	762.34(19)
Z	2
D_{cal} (Mg m^{-3})	1.513
F(000)	359.43
μ (mm^{-1})	6.42
Collection and Refinement Parameters:	
Radiation	Graphite-monochromated CuKα
λ (Å)	1.54056
2θ max (°)	140.0
h, k, l ranges	-32, 32; 0, 5; 0, 7
No. of reflections Measured	1585
No. of Unique reflections (+ Friedel mates)	1346
No. of Reflections with $I_{net} > 2.50\ \sigma(I_{net})$	1192
Significant Reflections: RF[b], R_w[c], G_oF[d]	0.050, 0.065, 3.10
Maximum Shift/σ ratio	0.013
Maximum Peak in Final D-Map (e/Å^3)	0.320
Minimum Peak in Final d-Map (e/Å^3)	-0.350
p-factor	0.02
Structure Determination	by direct methods[195]
Structure Refinement	NRCVAX system programs[196]

a) Obtained from 24 reflections with $55.00 < 2\theta < 60.00$ °; b) $RF = \Sigma (F_o - F_c) / \Sigma (F_o)$;
c) $R_w = (\Sigma[w(F_o - F_c)^2 / \Sigma(wF_o^2)])^{1/2}$; d) $G_oF = (\Sigma[w(F_o - F_c)^2 / (\#\text{ reflections} - \#\text{ parameters})])^{1/2}$

196. E.J. Gabe, Y. Le Page, J.-P. Charland, F.L. Lee and P.S. White, *J. Appl. Cryst.*, **22**, 384(1989).

Table III-2: Atomic Parameters (x, y, z) and B(eq)[a] for 218c[b]

	x	y	z	Beq
C1	0.79432(6)	0.01190	0.6134(3)	5.14(10)
S	0.99894(6)	1.0210 (10)	1.3344(3)	5.77(12)
O5	0.96191(17)	0.7734 (21)	1.2326(8)	6.5 (3)
C1	0.88174(24)	0.6121 (18)	1.0740(10)	3.7 (3)
C2	0.83522(22)	0.524 (3)	1.1263(10)	4.4 (3)
C3	0.80876(21)	0.3373 (21)	0.9873(11)	4.2 (3)
C4	0.82846(23)	0.2470 (20)	0.7899(9)	3.8 (3)
C5	0.87527(25)	0.3305 (24)	0.7381(10)	4.5 (4)
C6	0.90145(23)	0.518 (3)	0.8785(11)	4.4 (4)
C14	0.9089 (3)	0.8240 (24)	1.2238(11)	4.8 (4)
H2	0.821	0.591	1.259	5.2
H3	0.777	0.271	1.026	5.0
H5	0.889	0.259	0.608	5.3
H6	0.933	0.583	0.842	5.2
H14A	0.898	0.815	1.374	5.6
H14B	0.901	0.999	1.161	5.6

a) B(eq) is the mean of the principal axes of the thermal ellipsoid for atoms refined anisotropically. For hydrogens, B(eq) = B(iso); b) Estimated standard deviations refers to the last digit printed in ().

Table III-3: Bond Distances for 218c (in angstroms (Å))[a]

C1-C4	1.748(8)	C1-C14	1.504(12)
S1-Sa	1.932(3)	C2-C3	1.376(13)
S1-O5	1.644(9)	C3-C4	1.384(9)
O5-C14	1.428(8)	C4-C5	1.372(10)
C1-C2	1.373(10)	C5-C6	1.381(14)
C1-C6	1.381(10)		

a) Estimated standard deviation in the least significant figure are given in ().

Table III-4: Bond Angles (in degrees (°))[a]

Sa-S-O5	108.9(3)	(Cl)-C4-C3	119.3(6)
S-O5-C14	116.1(7)	(C1)-C4-C5	120.1(5)
C2-C1-C6	119.8(8)	C3-C4-C5	120.6(7)
C2-C1-C14	119.0(7)	C4-C5-C6	119.2(6)
C6-C1-C14	121.0(7)	C1-C6-C5	120.4(7)
C1-C2-C3	120.2(6)	O5-C14-C1	108.7(8)
C2-C3-C4	119.6(6)		

a) Estimated standard deviation in the least significant figure are given in ().

Table III-5: Torsion Angles (in degrees (°))[a]

S1-O5-C14-C1	165.7(8)	C6-C1-C2-C3	1.5(5)
C14-C1-C2-C3	177.6(1)	C2-C1-C6-C5	-1.7(5)
C14-C1-C6-C5	-177.7(1)	C2-C1-C14-O5	146.3(9)
C6-C1-C14-O5	-37.7(5)	C1-C2-C3-C4	-2.4(4)
C2-C3-C4-(Cl)	-179.6(8)	C2-C3-C4-C5	3.5(5)
(Cl)-C4-C5-C6	179.4(9)	C3-C4-C5-C6	-3.6(5)
C4-C5-C6-C1	2.8(4)		

a) The sign is positive if when looking from atom to atom, a clockwise motion of atom 1 would superimpose it on atom 4.

APPENDIX IV

X-Ray Structure Determination of Bis(4-Nitro-Benzyl) Tetrasulfide 226

The data were collected at T = 21°C on a Rigaku AFC6S diffractometer using the $\theta/2\theta$ scan technique. The calculations were performed using TEXRAY program of the TEXSAN crystallographic software package from Molecular Structure Corporation (1985).

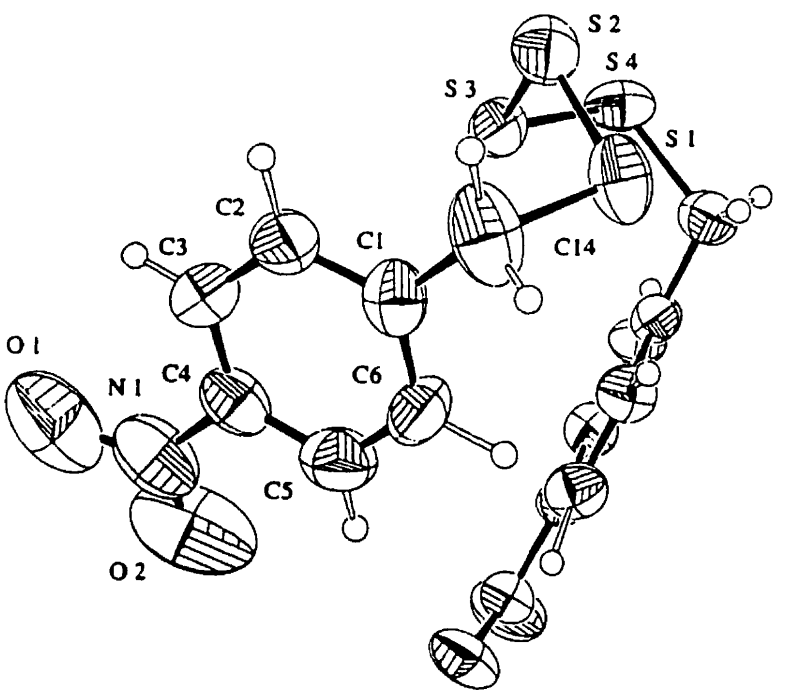

Figure IV: ORTEP[194] Diagram Showing Complete Atomic Number Scheme for 226 (4-NO_2-C_6H_4-CH_2-S-S)$_2$ (40% Probability Ellipsoids).

Table-IV-1: Crystal Data for the Structure Determination of 226

Data:	
Chemical Formula	$C_{14}H_{12}N_2O_4S_4$
Formula weight	400.50
Crystal Dimensions (mm)[a]	0.50 x 0.20 x 0.07
Crystal System	orthorhombic
Space Group	P cab
Lattice Parameters:	
a (Å)	9.3573(9)
b (Å)	12.5743(13)
c (Å)	29.134(4)
γ(°)	83.96(1)
V (Å)^3	3427.9(7)
Z	8
D_{cal} (Mg m^{-3})	1.552
F(000)	1662.39
μ (mm^{-1})	5.23
Collection and Refinement Parameters:	
Radiation	Graphite-monochromated CuKα
λ (Å)	1.54056
2θ max (°)	100.0
h, k, l ranges	0, 9; 0, 12; 0, 28
No. of reflections Measured	2045
No. of Unique reflections	1777
No. of Reflections with $I_{net} > 2.5\ \sigma\ (I_{net})$	1249
Significant Reflections: RF[b], R_w[c], G_oF[d]	0.038, 0.037, 1.51
Maximum Shift/σ ratio	0.144
Maximum Peak in Final D-Map (e/Å^3)	0.230
Minimum Peak in Final d-Map (e/Å^3)	-0.210
Structure Determination	by direct methods[195]
Structure Refinement	NRCVAX system programs[196]

a) Obtained from 24 reflections with $60.00 < 2\theta < 80.00$ °; b) $RF = \Sigma (F_o - F_c) / \Sigma (F_o)$;
c) $R_w = (\Sigma[w(F_o - F_c)^2 / \Sigma(wF_o^2)])^{1/2}$; d) $G_oF = (\Sigma[w(F_o - F_c)^2 / (\#\text{ reflections} - \#\text{ parameters})])^{1/2}$

Table IV-2: Atomic Parameters (x, y, z) and B(eq)[a] for 226[b]

Atom	x	y	z	Beq
S 1	0.04569(18)	0.51796(12)	0.06537(6)	6.08(10)
S 2	0.15511(18)	0.61906(13)	0.02399(5)	5.68(8)
S 3	0.31045(16)	0.69202(13)	0.06280(5)	5.16(8)
S 4	0.22536(19)	0.83153(12)	0.08448(5)	5.29(8)
O 1	0.8034(7)	0.3667(5)	0.1028(3)	11.2(5)
O 2	0.7263(8)	0.4177(5)	0.1687(2)	12.6(5)
O 3	0.5264(5)	0.5425(3)	0.2772(1)	7.0(3)
O 4	0.5738(5)	0.7018(4)	0.2983(2)	7.6(3)
N 1	0.7088(8)	0.3945(5)	0.1295(3)	8.0(5)
N 2	0.5104(6)	0.6382(4)	0.2744(2)	5.1(3)
C1	0.2902(7)	0.3944(4)	0.0764(2)	5.1(3)
C2	0.4052(9)	0.3951(5)	0.0473(2)	5.6(4)
C3	0.5416(9)	0.3950(5)	0.0639(3)	5.8(4)
C4	0.5624(7)	0.3959(4)	0.1101(3)	5.1(4)
C5	0.4523(10)	0.3965(6)	0.1400(3)	6.2(4)
C6	0.3156(9)	0.3956(5)	0.1236(2)	5.8(4)
C7	0.2283(6)	0.7556(4)	0.1737(2)	4.1(3)
C8	0.2303(7)	0.6479(4)	0.1840(2)	4.6(3)
C9	0.3211(7)	0.6086(5)	0.2171(2)	4.7(3)
C10	0.4084(6)	0.6790(4)	0.2398(2)	3.9(3)
C11	0.4074(7)	0.7866(5)	0.2310(2)	4.3(3)
C12	0.3160(7)	0.8244(5)	0.1978(2)	4.4(3)
C13	0.1309(8)	0.7956(6)	0.1370(2)	5.1(3)
C14	0.1433(9)	0.3933(6)	0.0566(4)	7.5(5)
H2	0.389(6)	0.394(4)	0.012(2)	7.0(16)
H3	0.614(7)	0.394(5)	0.043(2)	8.6(23)
H5	0.471(7)	0.401(5)	0.172(2)	8.5(21)
H6	0.225(6)	0.395(4)	0.146(2)	6.6(15)
H8	0.157(6)	0.601(4)	0.166(2)	7.4(17)
H9	0.322(5)	0.522(4)	0.228(2)	5.7(13)
H11	0.467(4)	0.830(3)	0.248(1)	2.5(11)
H12	0.325(5)	0.904(3)	0.189(1)	4.6(12)
H13A	0.050(6)	0.739(4)	0.126(2)	6.8(16)
H13B	0.084(6)	0.858(4)	0.142(2)	6.3(18)
H14A	0.091(6)	0.356(4)	0.077(2)	5.4(18)
H14B	0.112(11)	0.376(7)	0.021(3)	20.0(44)

a) B(eq) is the mean of the principal axes of the thermal ellipsoid for atoms refined anisotropically. For hydrogens, B(eq) = B(iso); b) Estimated standard deviations refers to the last digit printed in ().

Table IV-3: Bond Distances for 226 (in angstroms (Å))[a]

S1-S2	2.0293(24)	C5-C6	1.366(13)
S1-C14	1.832(8)	C5-H5	0.94(6)
S2-S3	2.0574(22)	C6-H6	1.07(5)
S3-S4	2.0274(23)	C7-C8	1.387(8)
S4-C13	1.824(7)	C7-C12	1.385(8)
O1-N1	1.229(11)	C7-C13	1.492(9)
O2-N1	1.191(10)	C8-C9	1.378(9)
O3-N2	1.216(7)	C8-H8	1.05(5)
O4-N2	1.215(7)	C9-C10	1.374(9)
N1-C4	1.481(10)	C9-H9	1.13(5)
N2-C10	1.478(7)	C10-C11	1.378(8)
C1-C2	1.370(10)	C11-C12	1.376(9)
C1-C6	1.395(10)		
C11-H11	0.93(4)	C1-C14	1.492(11)
C12-H12	1.04(4)	C2-C3	1.365(11)
C13-H13a	1.08(5)	C2-H2	1.03(5)
C13-H13b	0.91(5)	C3-C4	1.360(11)
C14-H14a	0.90(5)	C3-H3	0.91(6)
C14-H14b	1.09(9)	C4-C5	1.349(12)

a) Estimated standard deviation in the least significant figure are given in ().

Table IV-4: Bond Angles (in degrees (°))[a]

S2-S1-C14	101.6(3)	C8-C7-C13	119.6(6)
S1-S2-S3	108.02(10)	C12-C7-C13	121.0(5)
S2-S3-S4	106.23(10)	C7-C8-C9	120.7(6)
S3-S4-C13	103.74(24)	C7-C8-H8	115(3)
O1-N1-O2	125.3(8)	C9-C8-H8	123(3)
O1-N1-C4	115.4(7)	C8-C9-C10	118.2(5)
O2-N1-C4	119.3(8)	C8-C9-H9	122.7(24)
O3-N2-O4	123.5(5)	C10-C9-H9	119.0(24)
O3-N2-C10	118.0(5)	N2-C10-C9	119.2(5)
O4-N2-C10	118.5(5)	N2-C10-C11	118.2(5)
C2-C1-C6	118.4(7)	C9C10-C11	122.6(5)
C2-C1-C14	119.0(7)	C10-C11-C12	118.3(6)
C6-C1-C14	122.6(7)	C10-C11-H11	118(3)
C1-C2-C3	121.0(7)	C12-C11-H11	122(3)
C1-C2-H2	119(3)	C7-C12-C11	120.6(5)
C3-C2-H2	119(3)	C7-C12-H12	121.3(25)
C2-C3-C4	119.0(7)	C11-C12-H12	117.62(5)
C3-C3-H3	116(4)	S4-C13-C7	112.8(5)
C4-C3-H3	124(4)	S4-C13-H13a	104(3)
N1-C4-C3	120.6(7)	S4-C13-H13b	99(3)
N1-C4-C5	117.5(7)	C7-C13-H13a	114(3)
C3-C4-C5	122.0(7)	C7-C13-H13b	117(3)
C4-C5-C6	119.3(7)	H13a-C13-H13b	106(4)
C4-C5-H5	119(4)	S1-C14-C1	113.4(5)
C6-C5-H5	121(4)	S1-C14-H14a	94(4)
C1-C6-C5	120.3(7)	S1-C14-H14b	99(5)
C1-C6-H6	117(3)	C1-C14-H14a	104(4)
C5-C6-H6	122(3)	C1-C14-H14b	128(5)
C8-C7-C12	119.5(5)	H14a-C14-H14b	112(6)

a) Estimated standard deviation in the least significant figure are given in ().

Table IV-5: Torsion Angles (in degrees (°))[a]

C14-S1-S2-S3	-92.7(3)	S2-S1-C14-C1	69.3(4)
S1-S2-S3-S4	-94.5(1)	S2-S3-S4-C13	86.4(2)
S3-S4-C13-C7	63.4(3)	O1-N1-C4-C3	-17.1(5)
O1-N1-C4-C5	162.0(10)	O2-N1-C4-C3	164.2(10)
O2-N1-C4-C5	-16.6(5)	O3-N2-C10-C9	9.3(3)
O3-N2-C10-C11	-169.1(7)	O4-N2-C10-C9	-170.8(7)
O4-N2-C10-C11	10.7(3)	C6-C1-C2-C3	1.2(4)
C14-C1-C2-C3	-179.3(9)	C2-C1-C6-C5	-0.6(5)
C14-C1-C6-C5	179.9(9)	C2-C1-C14-S1	-110.4(7)
C6-C1-C14-S1	69.1(6)	C1-C2-C3-C4	-1.0(4)
C2-C3-C4-N1	179.3(9)	C7-C8-C9-C10	0.5(9)
N1-C4-C5-C6	-178.7(9)	C3-C4-C5-C6	0.4(4)
C4-C5-C6-C1	-0.2(4)	C12-C7-C8-C9	-1.7(3)
C13-C7-C8-C9	178.9(7)	C8-C7-C12-C11	1.7(3)
C13-C7-C12-C11	-178.9(7)	C8-C7-C13-S4	-106.4(6)
C12-C7-C13-S4	74.2(5)	C7-C8-C9-C10	0.6(3)
C8-C9-C10-N2	-177.8(7)	C8-C9-C10-C11	0.6(4)
N2-C10-C11-C12	177.9(7)	C9-C10-C11-C12	-0.6(4)
C10-C11-C12-C7	-0.6(3)		

a) The sign is positive if when looking from atom to atom, a clockwise motion of atom 1 would superimpose it on atom 4.

APPENDIX V

X-Ray Structure Determination of Bis(4-Nitro-Benzyl) Sulfoxylate 246b

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The data were collected at T = 20°C on a Rigaku AFC6S diffractometer using the $\omega/2\theta$ scan technique. The calculations were performed using TEXRAY program of the TEXSAN crystallographic software package from Molecular Structure Corporation (1985).

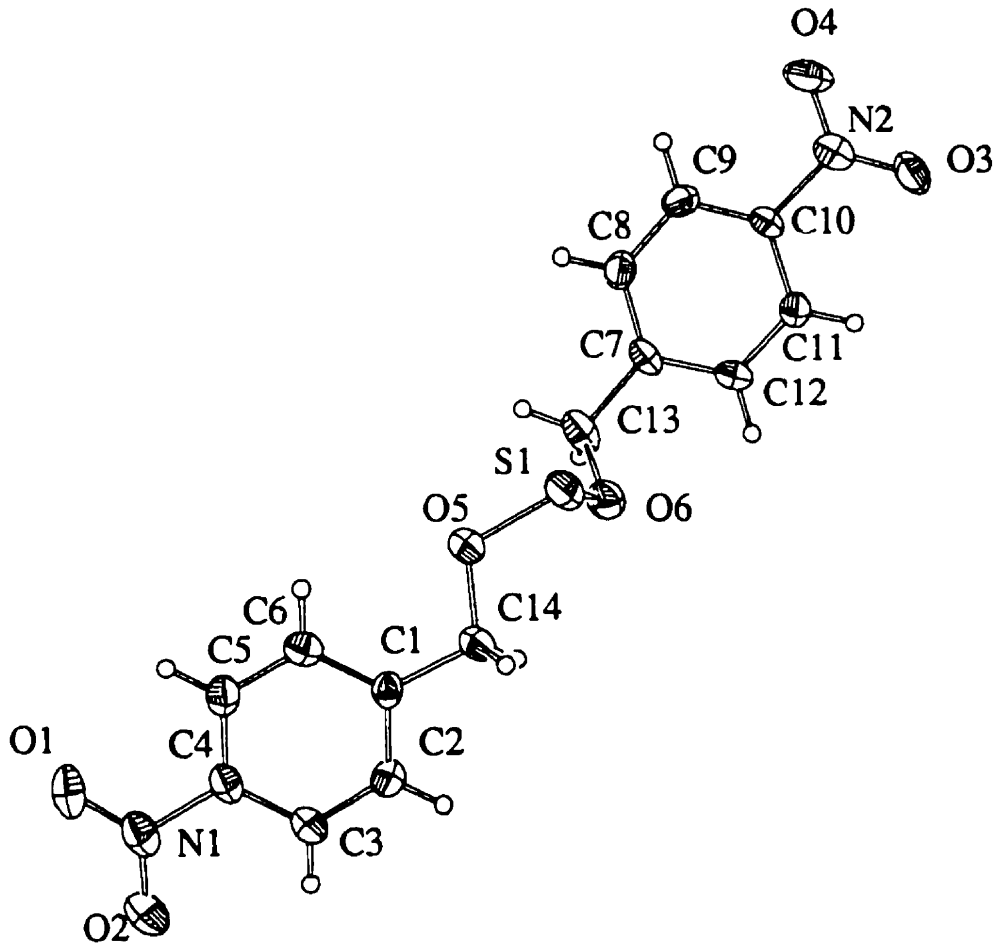

Figure V: ORTEP[194] Diagram Showing Complete Atomic Number Scheme for 246b $(4\text{-}NO_2\text{-}C_6H_4\text{-}CH_2\text{-}O)_2S$ (40% Probability Ellipsoids).

Table-V-1: Crystal Data for the Structure Determination of 246b

Data:	
Chemical Formula	$C_{14}H_{12}N_2O_6S$
Formula weight	336.32
Crystal Color, Habit	colorless, block
Crystal Dimensions (mm)[a]	0.28 x 0.16 x 0.08
Crystal System	triclinic
Space Group	p -1
Lattice Parameters:	
a (Å)	7.728(2)
b (Å)	8.011(2)
c (Å)	12.553(3)
α (°)	89.13(2)
β (°)	79.74(2)
γ (°)	73.73(2)
V (Å)^3	733.6(3)
Z	2
D_{cal} (Mg m^{-3})	1.523
F(000)	348
μ (mm^{-1})	0.255
Collection and Refinement Parameters:	
Radiation	Mo K\a
λ (Å)	0.70930
h, k, l ranges	-8, 9; 0, 9; -14, 14
No. of reflections Measured	5176
No. of Unique reflections	2588 (R_{int} = 0.061)
No. of Reflections with $I_{net} > 2.00\ \sigma\ (I_{net})$	1244
Significant Reflections: RF[b], R_w[c], G_oF[d]	0.074, 0.1132, 0.962
Maximum Shift/σ ratio	0.01
Maximum Peak in Final D-Map (e/Å^3)	0.229
Minimum Peak in Final d-Map (e/Å^3)	-0.262
Structure Determination	by direct methods[195]
Structure Refinement	NRCVAX[196] and system SHELXL-93[197] programs

a) Obtained from 22reflections with $20.00 < 2\theta < 25.00$ °; b) $RF = \Sigma (F_o - F_c) / \Sigma (F_o)$;
c) $R_w = (\Sigma[w(F_o - F_c)^2 / \Sigma(wF_o^2)])^{1/2}$; d) $G_oF = (\Sigma[w(F_o - F_c)^2 / (\#\text{ reflections} - \#\text{ parameters})])^{1/2}$

197. G.M. Sheldrick, SHELXL-93 (1995), Program for Structure Analysis, *J. Appl. Cryst.*, manuscript in preparation.

Table V-2: Atomic Parameters (x, y, z) and B(eq)[a] for 246b[b]

	x	y	z	U~eq~
S(1)	0.4531(2)	0.9369(2)	0.27374(11)	5.30(4)
O(1)	1.1343(5)	0.5182(5)	0.7346(3)	6.54(11)
O(2)	1.3550(6)	0.6063(5)	0.6425(3)	8.35(14)
O(3)	-0.0414(5)	0.9103(5)	-0.1870(3)	6.08(11)
O(4)	-0.1843(5)	0.7560(5)	-0.0841(3)	7.01(12)
O(5)	0.5808(4)	0.8507(4)	0.3636(2)	5.01(9)
O(6)	0.5615(4)	0.8254(4)	0.1632(2)	5.26(9)
N(1)	1.1997(7)	0.5917(5)	0.6580(4)	5.27(12)
N(2)	-0.0563(6)	0.8180(5)	-0.1094(3)	4.86(11)
C(1)	0.8592(6)	0.8173(5)	0.4339(3)	3.73(12)
C(2)	1.0446(7)	0.8070(6)	0.4133(4)	4.73(13)
C(3)	1.1565(7)	0.7355(6)	0.4860(4)	4.76(13)
C(4)	1.0809(7)	0.6705(6)	0.5802(4)	4.09(12)
C(5)	0.8981(7)	0.6775(6)	0.6018(4)	4.62(13)
C(6)	0.7871(6)	0.7507(6)	0.5291(4)	4.36(13)
C(7)	0.3598(6)	0.7066(6)	0.0788(4)	3.94(12)
C(8)	0.2041(7)	0.6549(6)	0.1103(4)	4.64(13)
C(9)	0.0665(6)	0.6894(6)	0.0503(4)	4.51(13)
C(10)	0.0873(6)	0.7779(6)	-0.0427(4)	3.56(11)
C(11)	0.2413(6)	0.8320(6)	-0.0777(4)	4.61(13)
C(12)	0.3772(6)	0.7946(6)	-0.0166(4)	4.86(13)
C(13)	0.5122(7)	0.6671(7)	0.1431(4)	5.6(2)
C(14)	0.7465(6)	0.9020(6)	0.3529(4)	4.92(13)

a) B(eq) is the mean of the principal axes of the thermal ellipsoid for atoms refined anisotropically. For hydrogens, B(eq) = B(iso); b) Estimated standard deviations refers to the last digit printed in ().

Table V-3: Bond Distances for 246b (in angstroms (Å))[a]

S1-O6	1.622(3)	C1-C14	1.488(6)
S1-O5	1.648(3)	C2-C3	1.377(6)
		C3-C4	1.384(6)
O1-N1	1.226(5)	C4-C5	1.376(6)
O2-N1	1.219(5)	C5-C6	1.376(6)
O3-N2	1.222(5)	C7-C8	1.371(6)
O4-N2	1.219(5)	C7-C12	1.386(6)
O5-C14	1.434(5)	C7-C13	1.504(6)
O6-C13	1.460(5)	C8-C9	1.375(6)
N1-C4	1.473(6)	C9-C10	1.365(6)
N2-C10	1.469(5)	C10-C11	1.376(6)
C1-C2	1.390(6)	C11-C12	1.372(6)
C1-C6	1.390(5)		
C2-H2	0.93	C11-H11	0.93
C3-H3	0.93	C12-H12	0.93
C5-H5	0.93	C13-H13a	0.97
C6-H6	0.93	C13-H13b	0.97
C8-H8	0.93	C14-H14a	0.97
C9-H9	0.93	C14-H14b	0.97

a) Estimated standard deviation in the least significant figure are given in ().

Table V-4: Bond Angles (in degrees (°))[a]

O6-S1-O5	103.1(2)	C14-O5-S1	113.3(3)
C13-O6-S1	116.2(3)	O2-N1-O1	124.7(4)
O2-N1-C4	117.7(5)	O1-N1-C4	117.6(5)
O4-N2-O3	123.5(4)	O4-N2-C10	117.6(4)
O3-N2-C10	118.8(4)	C2-C1-C6	118.9(4)
C2-C1-C14	118.0(4)	C6-C1-C14	123.2(4)
C3-C2-C1	121.3(4)	C3-C2-H2	119.3(3)
C1-C2-H2	119.3(3)	C2-C3-C4	118.5(4)
C2-C3-H3	120.7(3)	C4-C3-H3	120.7(3)
C5-C4-C3	121.2(4)	C5-C4-N1	119.8(5)
C3-C4-N1	119.0(5)	C4-C5-C6	119.8(5)
C4-C5-H5	120.1(3)	C6-C5-H5	120.1(3)
C5-C6-C1	120.3(5)	C5-C6-H6	119.9(3)
C1-C6-H6	119.9(3)	C8-C7-C12	118.4(4)
C8-C7-C13	122.0(4)	C12-C7-C13	119.5(4)
C7-C8-C9	121.7(4)	C7-C8-H8	119.2(3)
C9-C8-H8	119.2(3)	C10-C9-C8	118.4(4)
C10-C9-H9	120.8(3)	C8-C9-H9	120.8(3)
C9-C10-C11	122.0(4)	C9-C10-N2	120.3(4)
C11-C10-N2	117.7(4)	C12-C11-C10	118.4(4)
C12-C11-H11	120.8(3)	C10-C11-H11	120.8(3)
C11-C12-C7	121.2(4)	C11-C12-H12	119.4(3)
C7-C12-H12	119.4(3)	O6-C13-C7	110.2(4)
O6-C13-H13a	109.6(2)	C7-C13-H13a	109.6(3)
O6-C13-H13b	109.6(2)	C7-C13-H13b	109.6(3)
O5-C14-C1	111.3(4)	O5-C14-H14a	109.4(2)
C1-C14-H14a	109.4(3)	O5-C14-H14b	109.4(2)
C1-C14-H14b	109.4(3)	H14a-C14-H14b	108.0

a) Estimated standard deviation in the least significant figure are given in ().

Table V-5: Torsion Angles (in degrees (°))[a]

O6-S1-O5-C14	75.1(3)	O5-S1-O6-C13	88.9(3)
S1-O5-C14-C1	175.1(3)	N2-C10-C11-C12	179.1(5)
C6-C1-C2-C3	-1.1(7)	C14-C1-C2-C3	177.9(4)
C1-C2-C3-C4	1.1(7)	C2-C3-C4-C5	-0.4(7)
C2-C3-C4-N1	179.3(4)	C3-C4-C5-C6	-0.2(7)
O1-N1-C4-C5	7.5(7)	N1-C4-C5-C6	-179.9(4)
O2-N1-C4-C3	8.8(7)	C4-C5-C6-C1	0.1(7)
C2-C1-C6-C5	0.5(7)	C14-C1-C6-C5	-178.5(4)
C12-C7-C8-C9	-0.5(7)	C13-C7-C8-C9	-179.1(4)
C7-C8-C9-C10	-0.1(7)	C8-C9-C10-C11	0.3(7)
C8-C9-C10-N2	-179.9(4)	O4-N2-C10-C9	-6.6(6)
O3-N2-C10-C9	173.7(4)	O4-N2-C10-C11	173.2(4)
O3-N2-C10-C11	-6.5(6)	C9-C10-C11-C12	0.2(7)
N2-C10-C11-C12	179.6(4)	C10-C11-C12-C7	-0.9(7)
C8-C7-C12-C11	1.0(7)	C13-C7-C12-C11	179.7(4)
S1-O6-C13-C7	90.6(4)	C8-C7-C13-O6	-129.4(5)
C12-c7-C13-O6	52.0(6)	S1-O5-C14-C1	-178.5(3)
C2-C1-C14-O5	159.7(4)	C6-C1-C14-O5	-21.3(6)

a) The sign is positive if when looking from atom to atom, a clockwise motion of atom 1 would superimpose it on atom 4.

APPENDIX VI

Summary of the Calculations using MODEL and MACROMODEL on Bis(4-Nitro-Benzyloxy) Disulfide 218b

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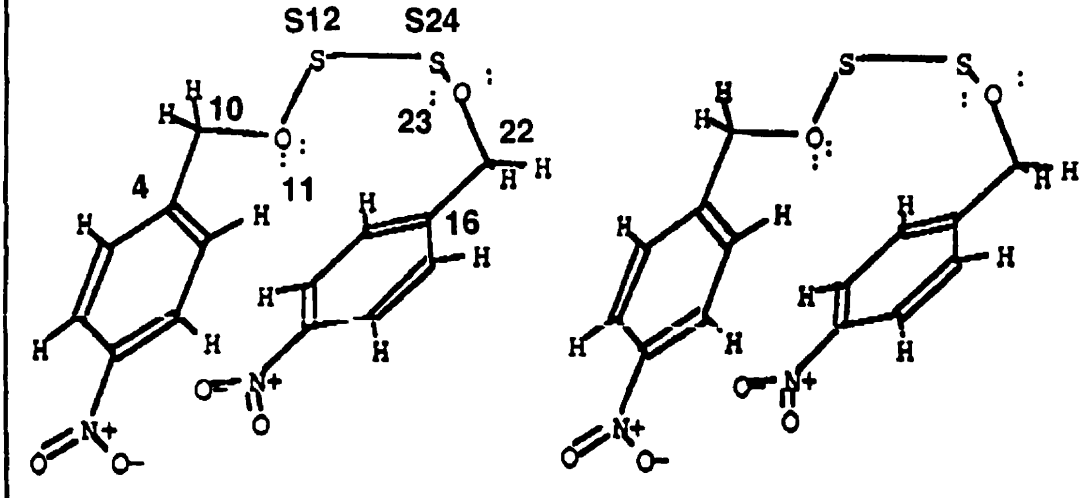
MODEL

Syn-

MODEL Version KS 2.96 MINIMIZATION MODE

CPU TIME = 9 SEC

MM ENERGY	20.50 (		20.50)
STR	0.79	BND	3.71
S-B	0.28	TOR	3.74
VDW	14.98	DIP	-3.00
Dipole moment		7.95 D	



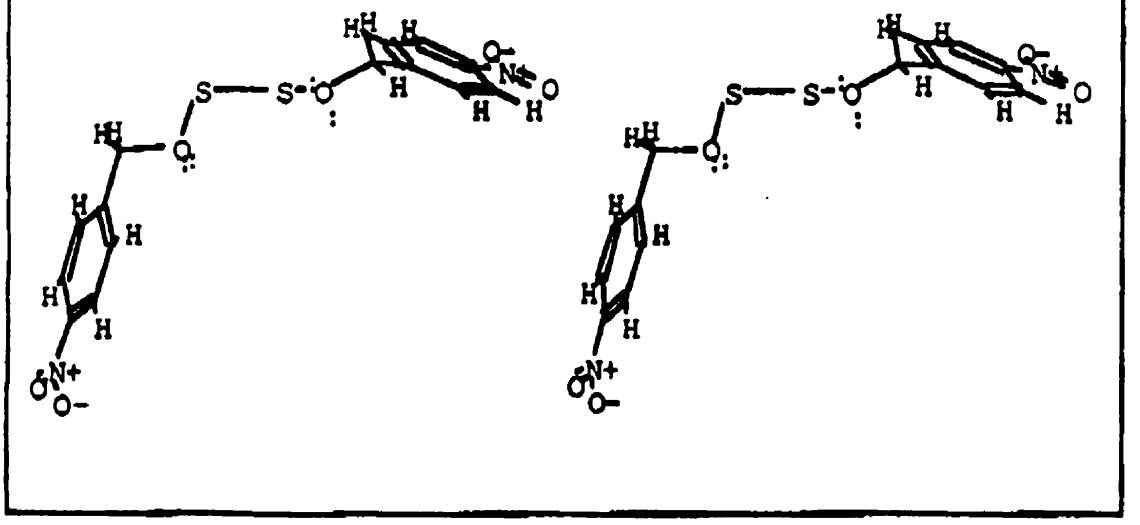
MODEL

Anti-

MODEL Version KS 2.96 MINIMIZATION MODE

CPU TIME = 92 SEC

MM ENERGY	25.71	(	25.71)
STR	0.86	BND	3.50
S-B	0.26	TOR	3.60
VDW	19.20	DIP	-1.70
Dipole moment	8.48 D		

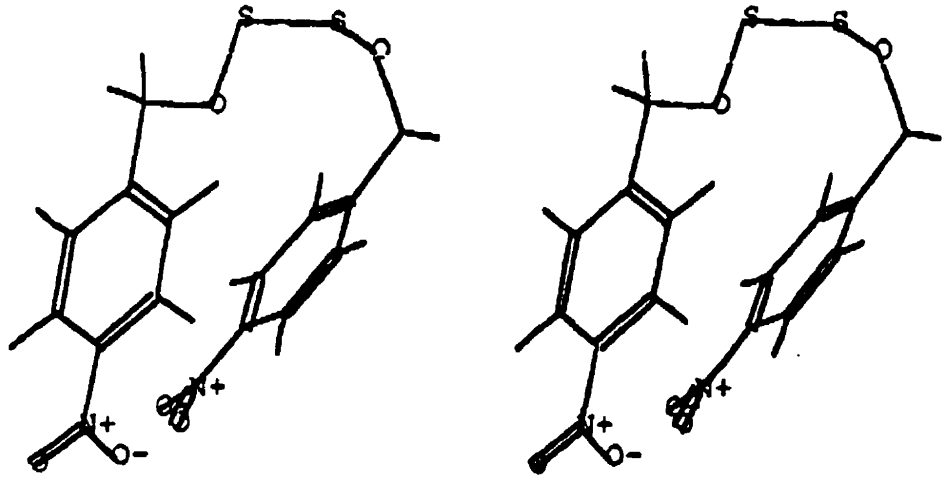


MACROMODEL

Syn-

MacroModel Gradient RMS = 0.0172 kJ/A-mol
Version 3.0 Minimization Time = 232.3 CPU Sec

	Energy =	74.48	kJ/mol (	17.8	kcal/mol)		
Str=	3.6	Bnd=	16.7	S-B=	0.9	HBd=	0.0
VDW=	62.2	Tor=	-12.9	Imp=	0.1	Ele=	3.9

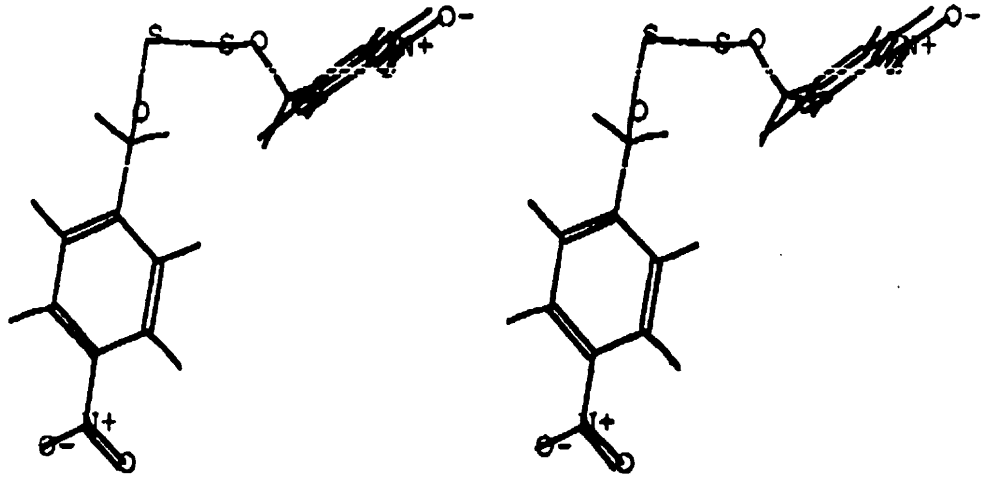


MACROMODEL

Anti-

MacroModel Gradient RMS = 0.6865 kJ/A-mol
Version 3.0 Minimization Time = 3.7 CPU Sec

	Energy =	91.63	kJ/mol	(	21.9	kcal/mol)	
Str=	3.7	Bnd=	15.9	S-B=	0.8	HBd=	0.0
VDW=	75.0	Tor=	-14.3	Imp=	0.0	Ele=	10.4



APPPENDIX VII

Powder Raman Spectroscopy of Related Compounds to 218b

Bis(4-Nitrobenzene) Disulfide 285

4-Nitrobenzene Mercaptan 223

Bis(4-Nitrobenzyl) Disulfide 254

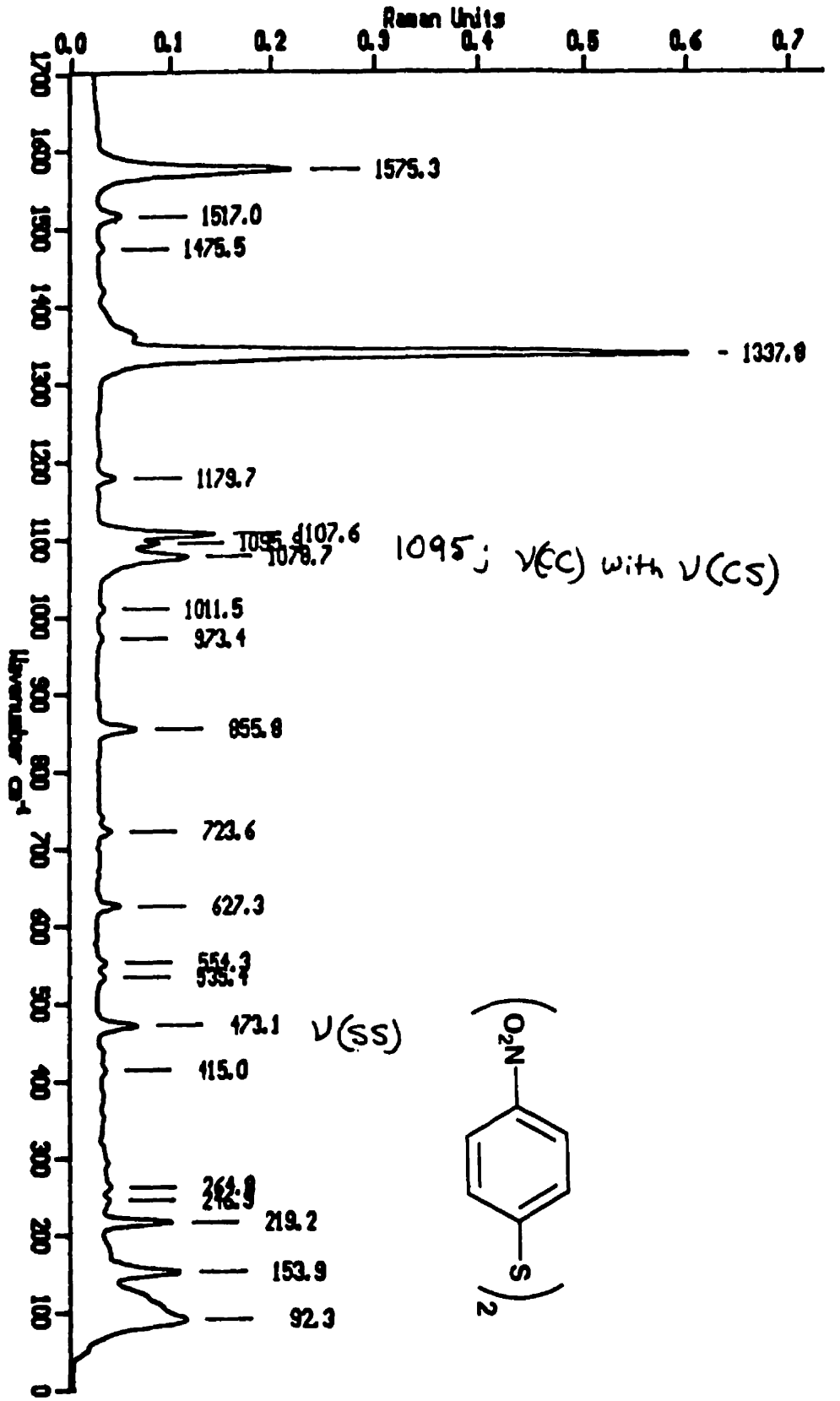
Bis(4-Nitrobenzyl) Tetrasulfide 226

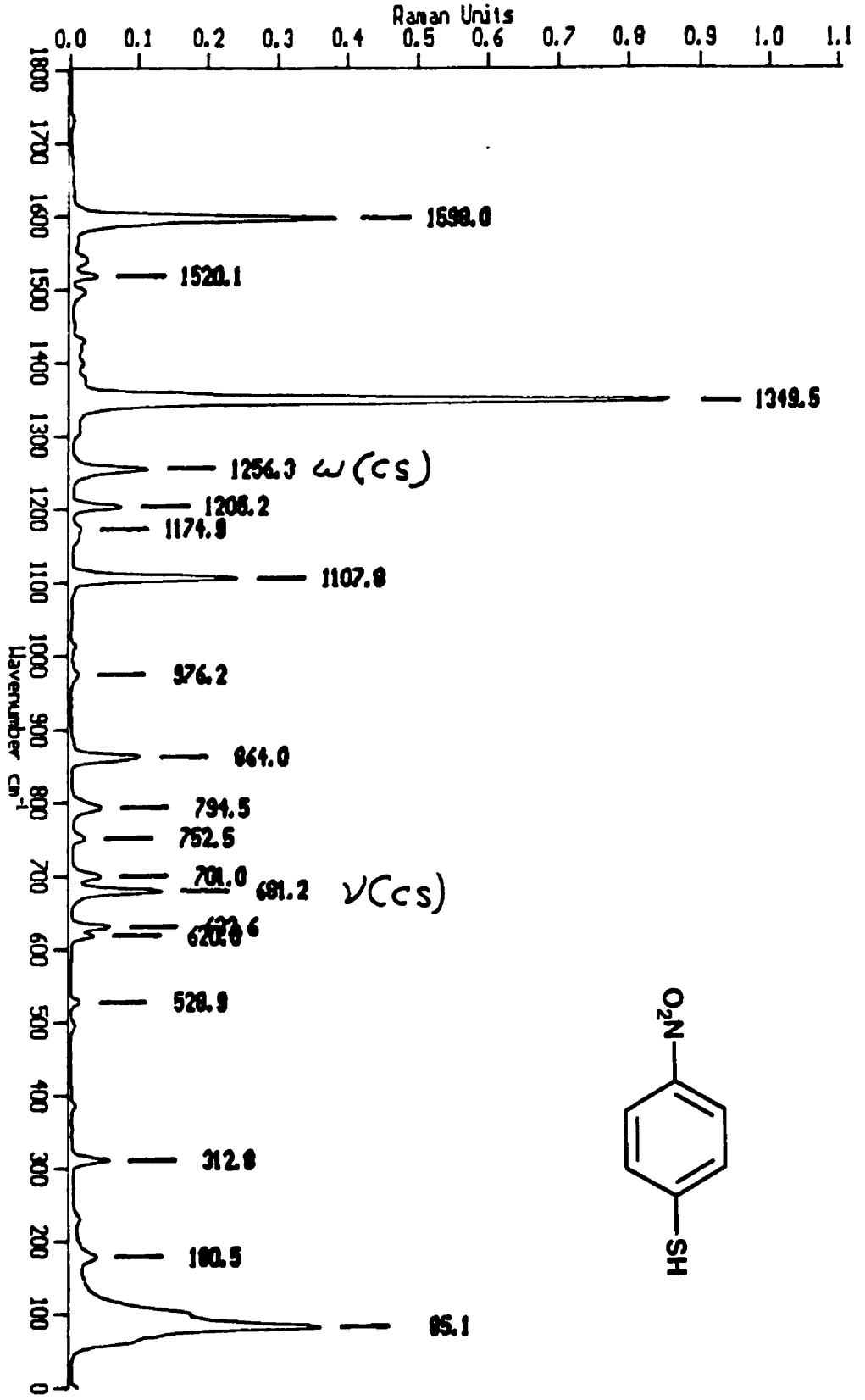
4-Nitrobenzyloxy Benzyl Trisulfide 243

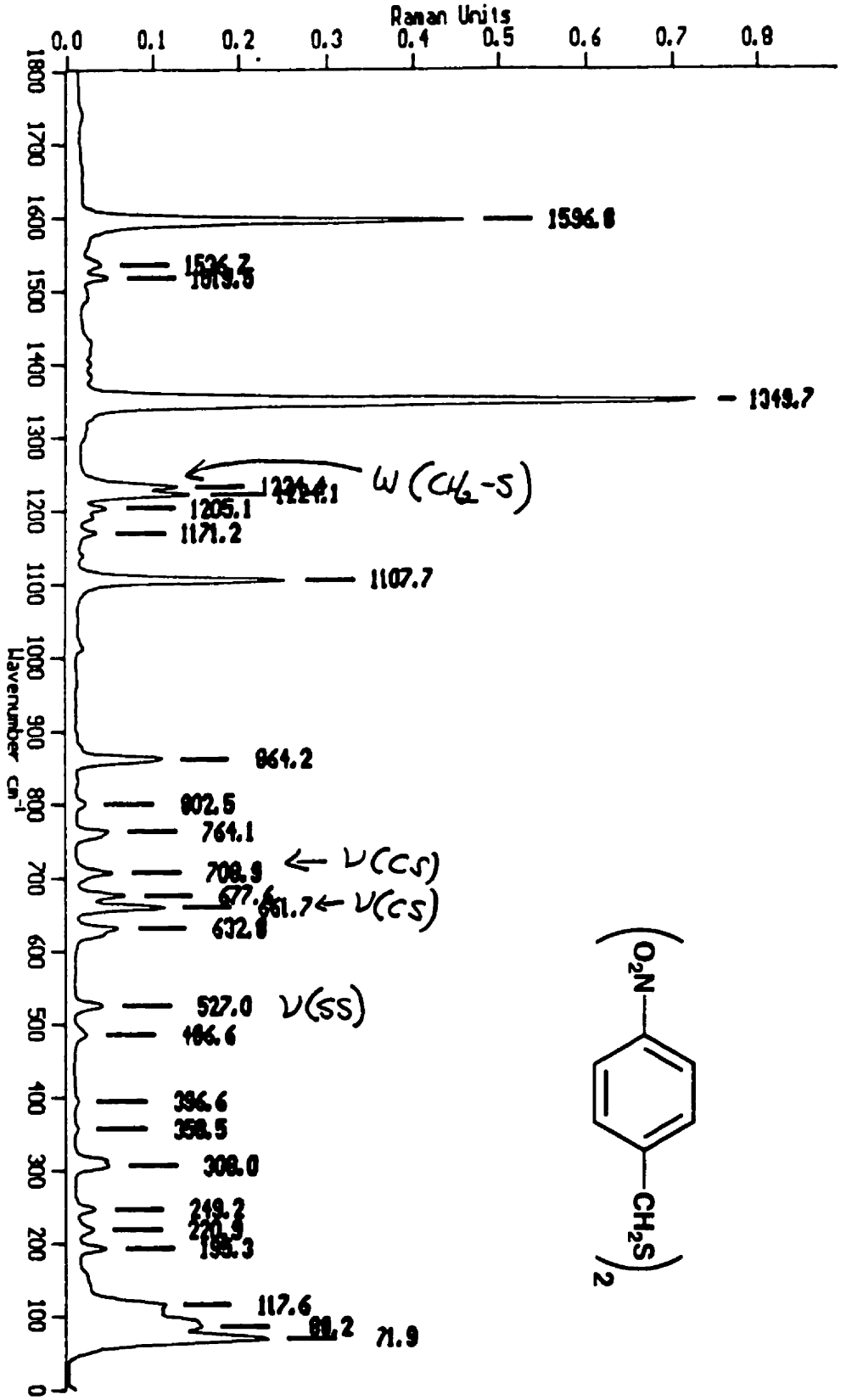
Bis(4-Nitrobenzyloxy) Disulfide 218b

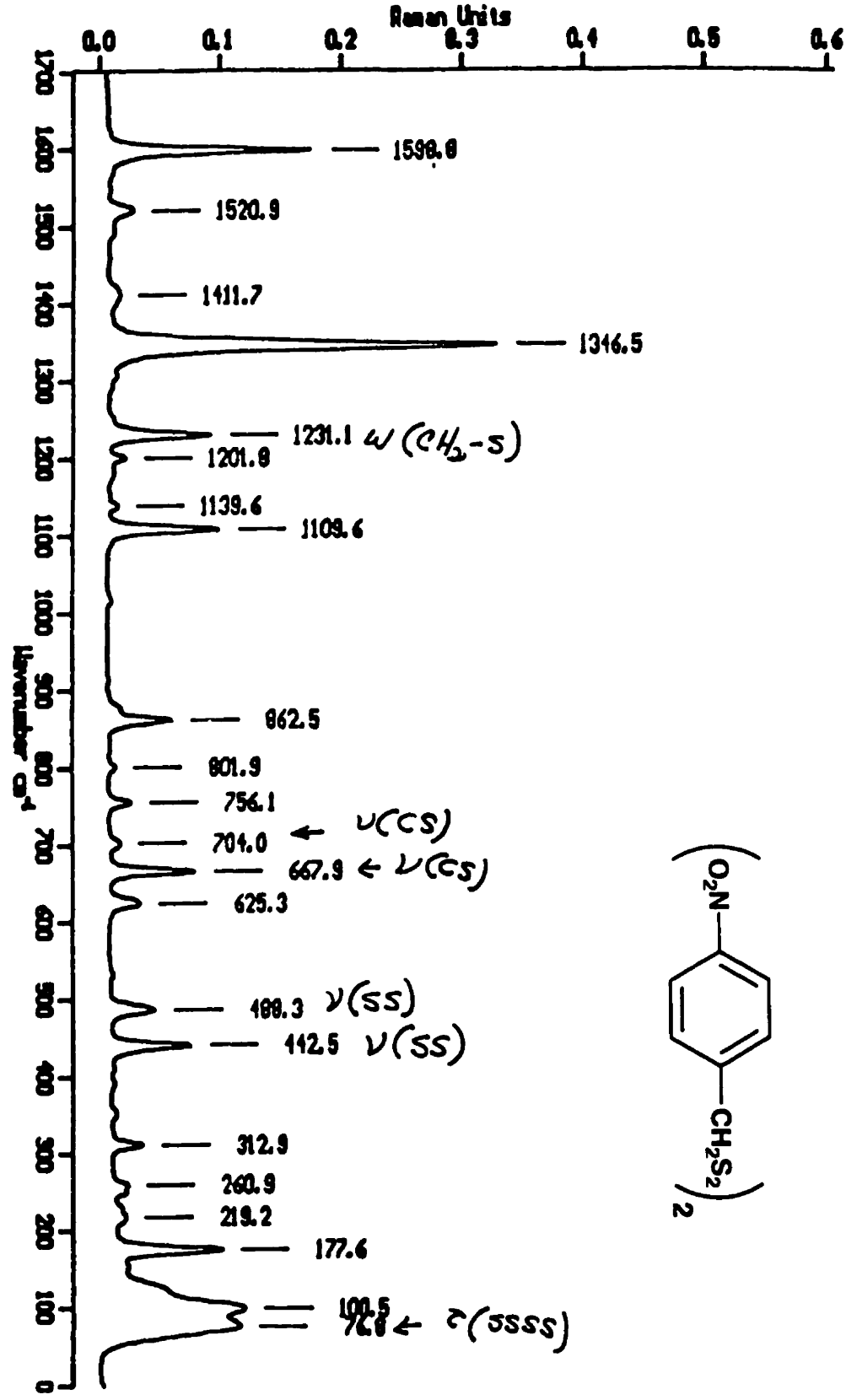
Dibenzyloxy Disulfide 218a

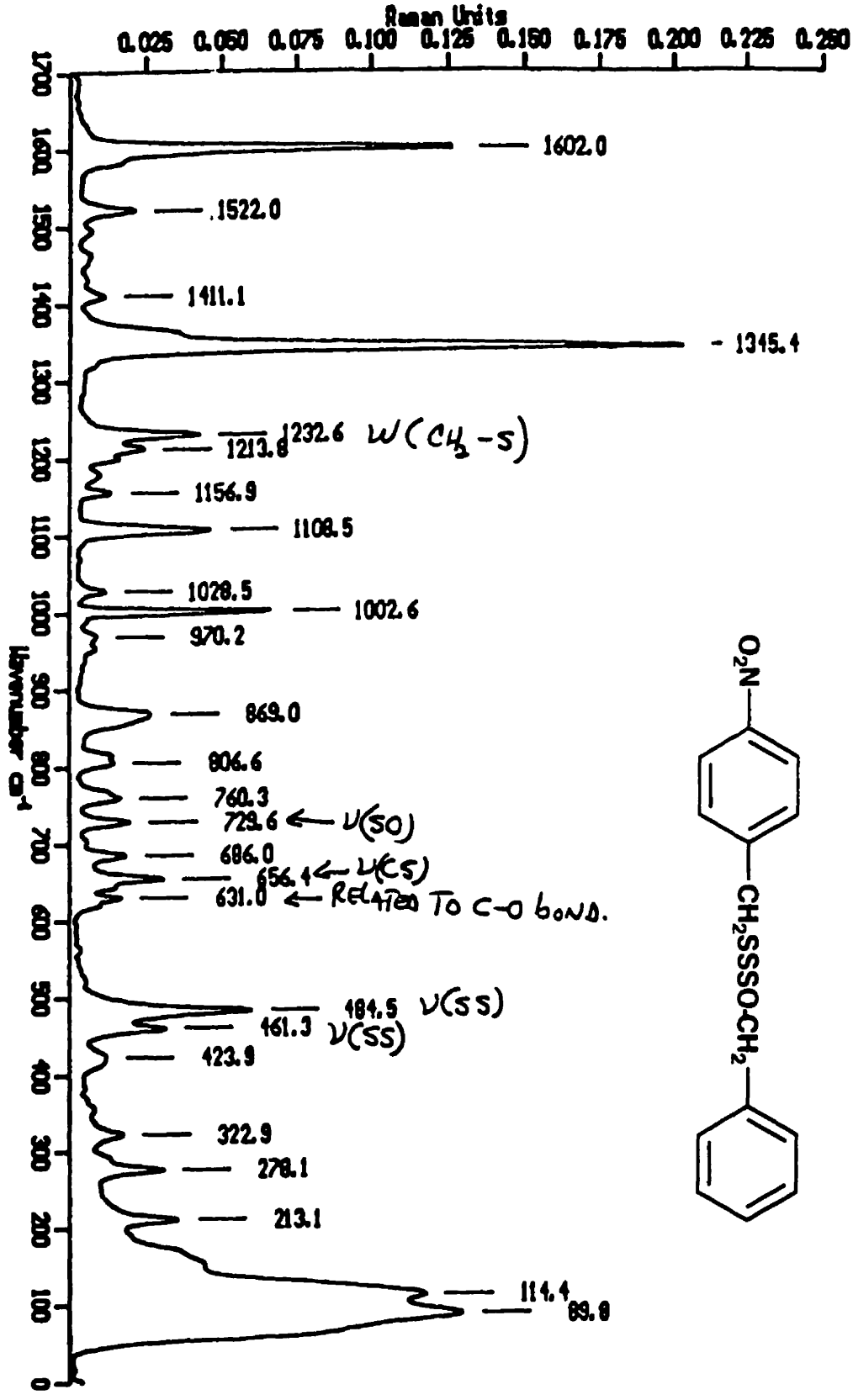
O,O'-Bicyclohexyl-1,1'-diylthiosulfite 57

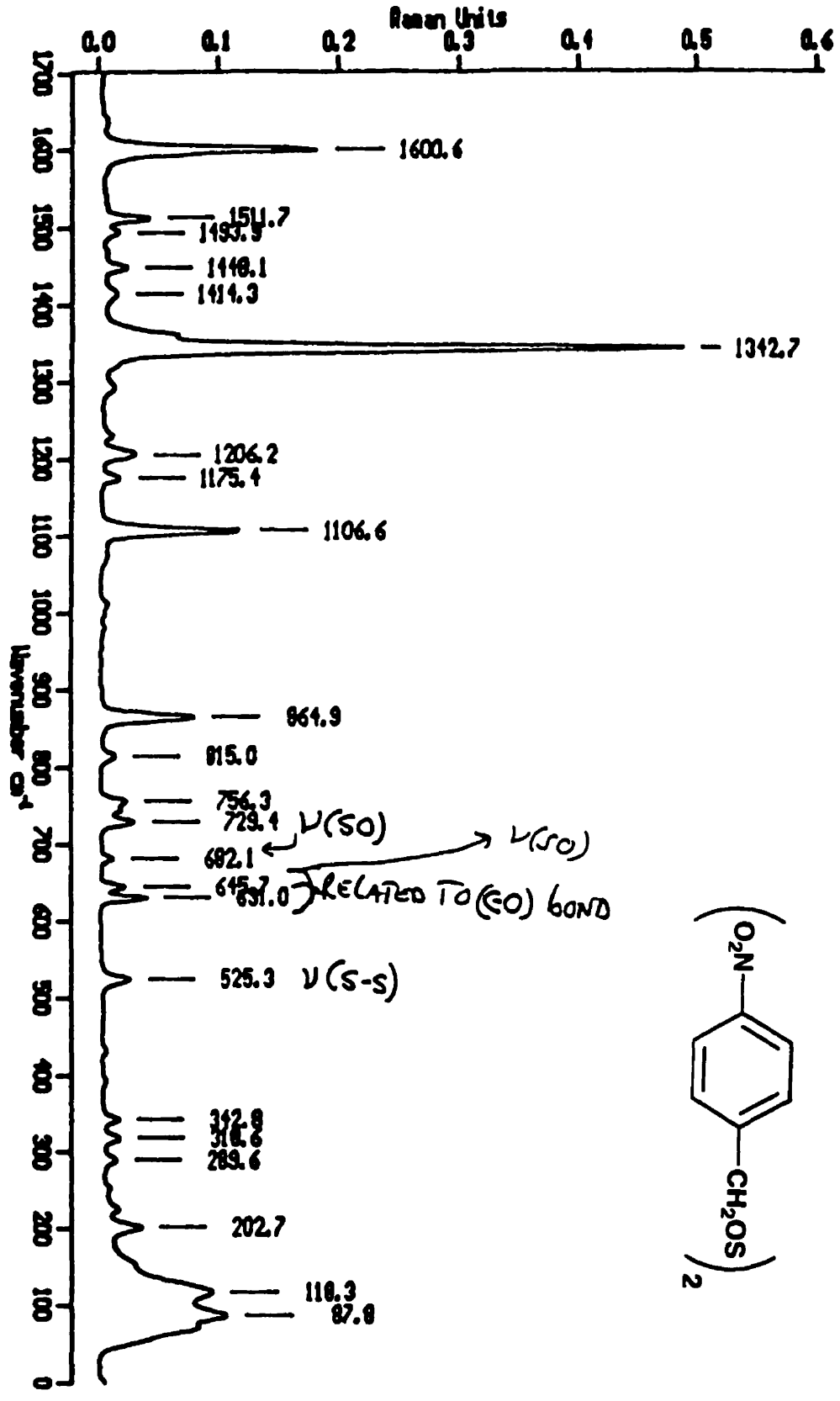

Raman Units
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
Wavenumber cm⁻¹
1575.3
1517.0
1475.5
1337.8
1179.7
1107.6
1095
1078.7
1095; ν(CC) with ν(CS)
1011.5
973.4
855.8
723.6
627.3
554.3
535.4
473.1
ν(SS)
415.0
264.8
242.5
219.2
153.9
92.3
O2N
S
2

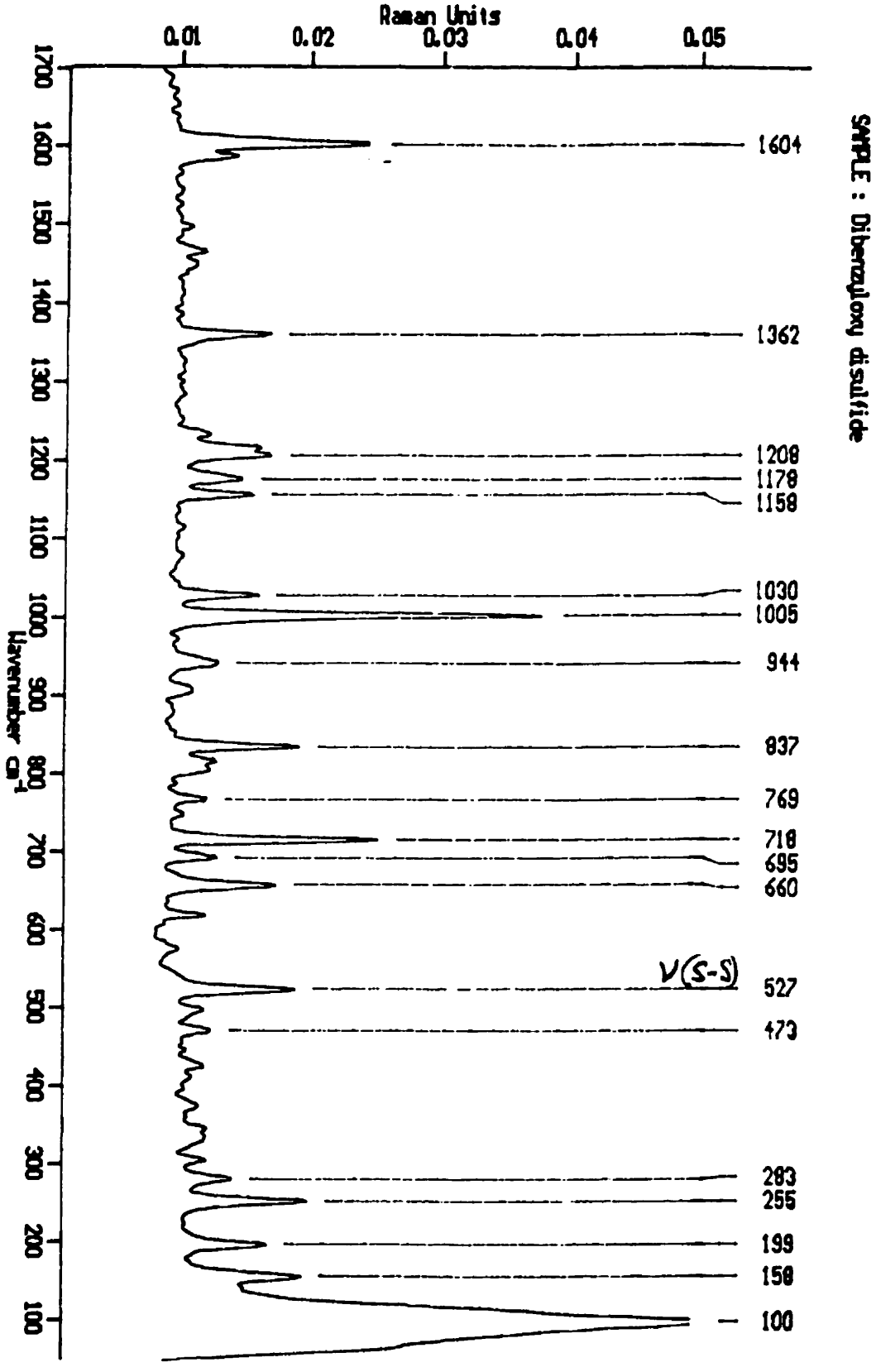

Raman Units
0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0 1.1
1800 1700 1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0
Wavenumber cm-1
1598.0
1520.1
1349.5
1256.3 ω(CS)
1206.2
1174.9
1107.0
976.2
864.0
794.5
752.5
701.0
691.2 ν(CS)
620.6
528.9
312.9
180.5
85.1
O2N
SH

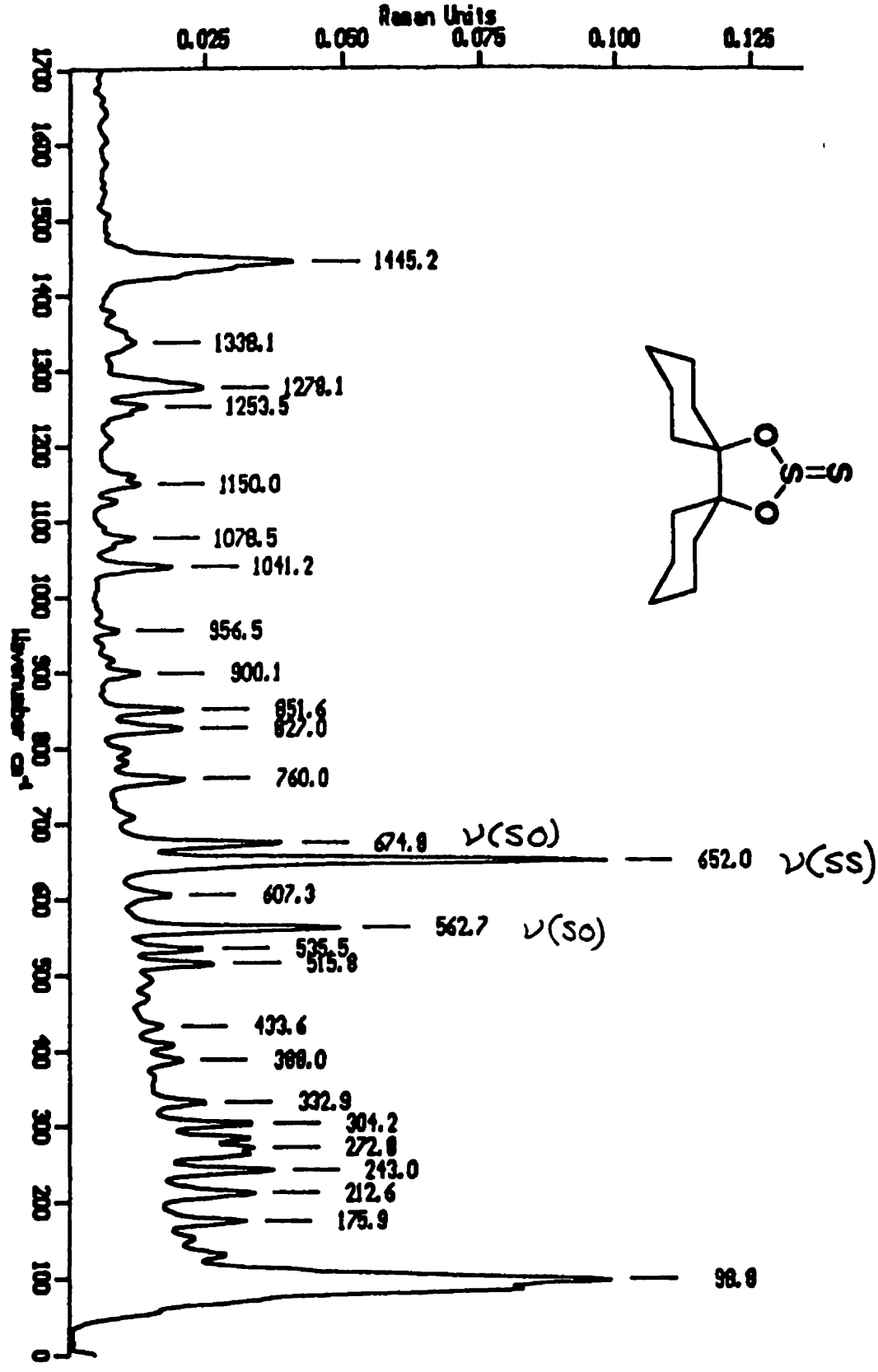

Raman Units
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
Wavenumber cm⁻¹
1800
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
1596.8
1536.2
1349.7
1224.1
1205.1
1171.2
1107.7
864.2
802.5
764.1
708.9
677.6
661.7
632.8
527.0
486.6
396.6
358.5
308.0
249.2
198.3
117.6
88.2
71.9
ν(CH2-S)
ν(CS)
ν(CS)
ν(SS)
O2N
CH2S
2


Raman Units
0.0
0.1
0.2
0.3
0.4
0.5
0.6
Wavenumber cm⁻¹
1598.8
1520.9
1411.7
1346.5
1231.1 ω(CH₂-S)
1201.8
1139.6
1109.6
862.5
801.9
756.1
704.0 ← ν(CS)
667.9 ← ν(CS)
625.3
488.3 ν(SS)
442.5 ν(SS)
312.9
260.9
219.2
177.6
100.5
τ(SSSS)
O₂N
CH₂S₂
2


Raman Units
0.025 0.050 0.075 0.100 0.125 0.150 0.175 0.200 0.225 0.250
1700 1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0
Wavenumber cm⁻¹
1602.0
1522.0
1411.1
1345.4
1232.6 W(CH2-S)
1213.8
1156.9
1108.5
1028.5
1002.6
970.2
869.0
806.6
760.3
729.6 ← ν(SO)
686.0
656.4 ← ν(CS)
631.0 ← RELATED TO C-O bond.
484.5 ν(SS)
461.3 ν(SS)
423.9
322.9
278.1
213.1
114.4
89.8
O2N
CH2SSSO-CH2


Raman Units
0.0
0.1
0.2
0.3
0.4
0.5
0.6
Wavenumber cm⁻¹
1600.6
1511.7
1493.9
1448.1
1414.3
1342.7
1206.2
1175.4
1106.6
864.9
815.0
756.3
729.4
692.1
645.7
631.0
525.3
342.8
316.6
289.6
202.7
118.3
87.8
ν(SO)
ν(SO)
RELATED TO (SO) BOND
ν(S-S)
O2N
CH2OS
2


Raman Units
0.01
0.02
0.03
0.04
0.05
Wavenumber cm⁻¹
1700
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
1604
1362
1208
1178
1158
1030
1005
944
837
769
718
695
660
ν(S-S)
527
473
283
255
199
158
100
SAMPLE : Dibenzoyloxy disulfide

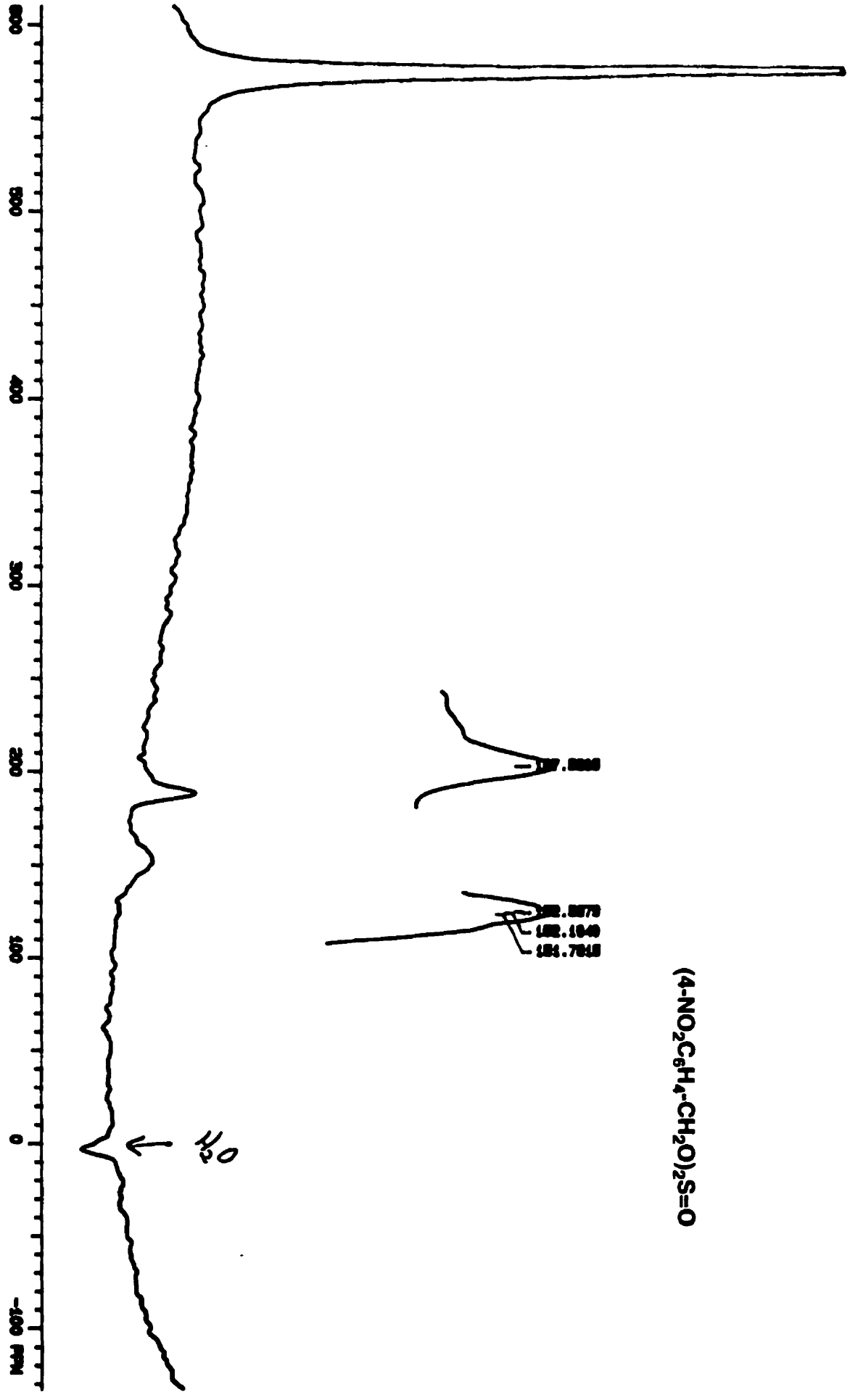

Raman Units
0.025
0.050
0.075
0.100
0.125
Wavenumber cm⁻¹
1445.2
1338.1
1278.1
1253.5
1150.0
1078.5
1041.2
956.5
900.1
851.6
827.0
760.0
674.8 ν(SO)
652.0 ν(SS)
607.3
562.7 ν(SO)
535.5
515.8
433.6
388.0
332.9
304.2
272.8
243.0
212.6
175.9
98.8
S=S
O
O

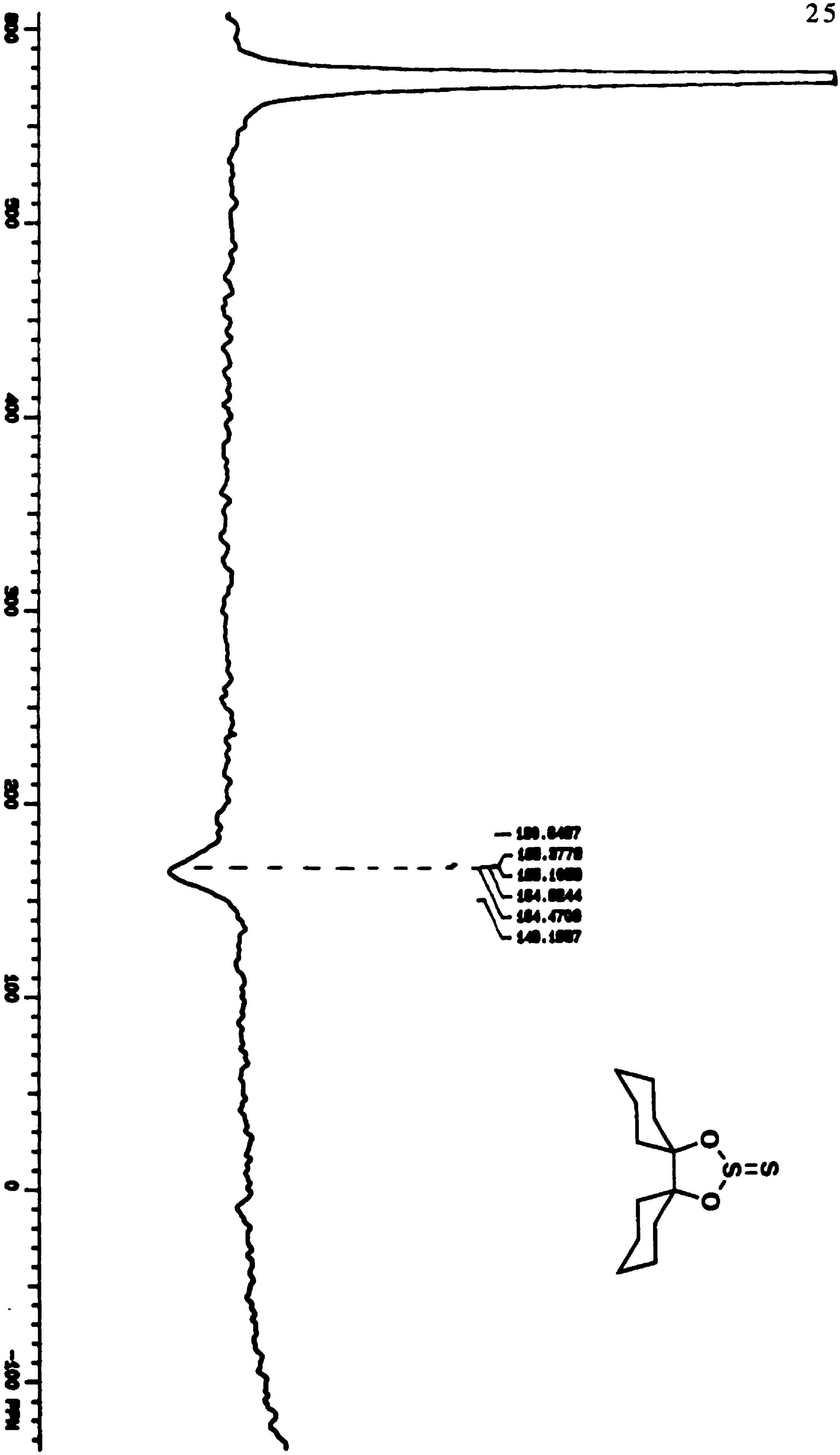
APPENDIX VIII

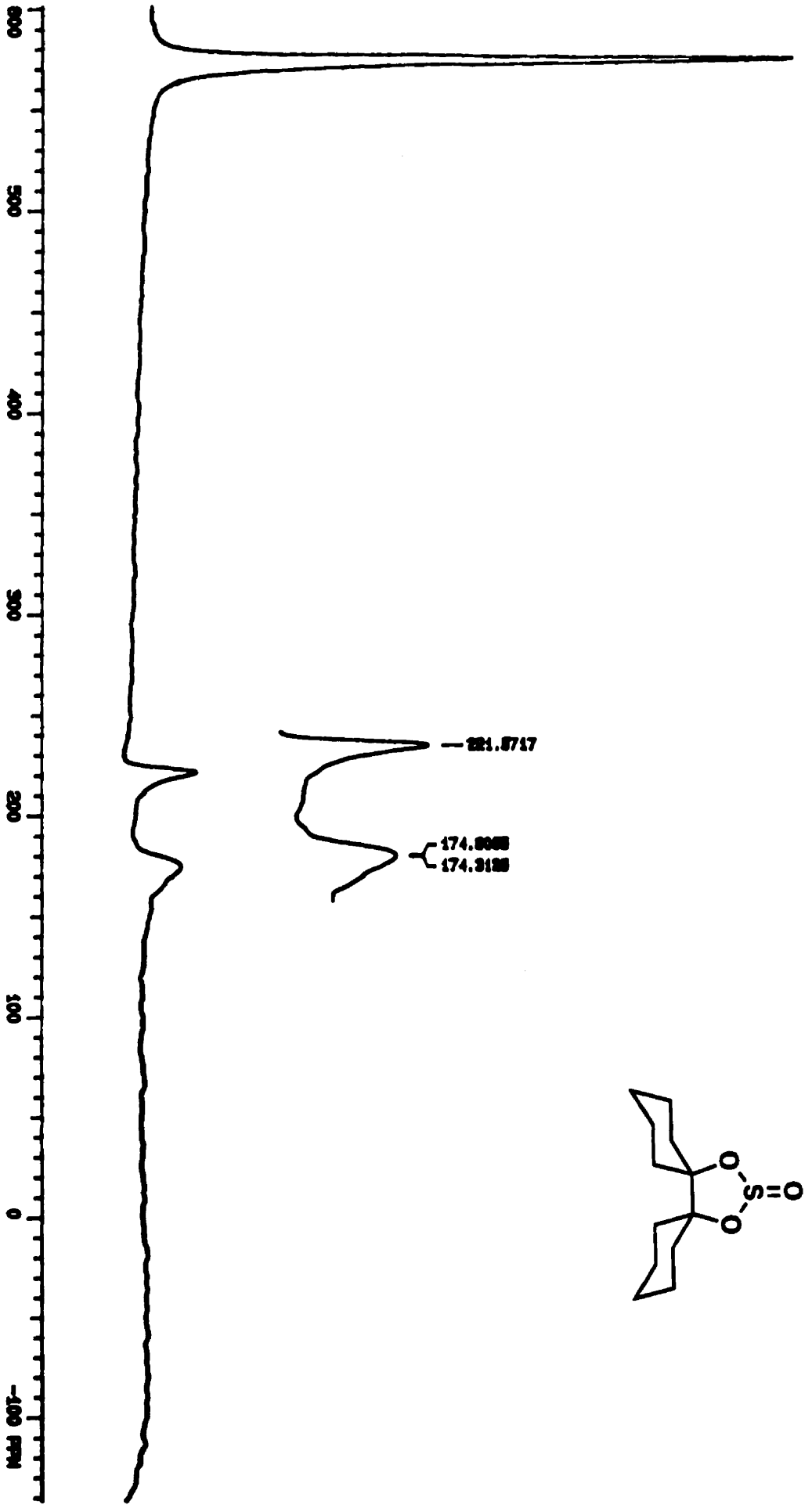
^{17}O NMR Spectroscopy of Related Compounds to 218b

Bis(4-Nitrobenzyloxy) Disulfide 218b
Bis(4-Nitrobenzyl) Sulfite 219b
O,O'-Bicyclohexyl-1,1'-diylthiosulfite 57
O,O'-Bicyclohexyl-1,1'-diylsulfite 240

-100 PPM
0
100
200
300
400
500
3375.9
NO2
OS
2


H2O
(4-NO2C6H4-CH2O)2S=O


600
500
400
300
200
100
0
-100 PPM
O
S=S
O


600
500
400
300
200
100
0
-100 PPM
221.8717
174.8088
174.8128
O
Sn=O
O