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OXIDATIONS OF AROMATIC KETOXIMES

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by

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ABSTRACT

The bis-aryl ketoximes; fluorenone and benzophenone oximes, are oxidized in glacial acetic acid with lead tetraacetate to parent ketones, geminal dinitromethanes, iminyl ketal derivatives (9,9-difluorenylideneiminoxylfluorene and 1,1-bis(diphenylmethylen-iminoxyl)-diphenylmethane) and minor amounts of oxime O-acetate. Benzophenone nitrimine is also formed, but only in the absence of oxygen. Side reactions due to nitric oxide, oxygen, and nitrogen dioxide are taking place in these oxidations. Separate studies with these oxidizing agents have therefore been conducted. The lead tetraacetate oxidation of these oximes in methylene chloride (or any other solvent) is complete with a half-mole equivalent of lead tetraacetate, is insensitive to molecular oxygen, and affords mainly parent ketones and ketazinemonoxides. No ketazine-N-bis-oxides, obtained from the ferricyanide oxidation of these oximes, are ever formed. The model oximes; benzil anti-monoxime, xanthone oxime, and indanone oxime, have been studied in the light of these observations. Mechanisms involving iminoxyl radicals have been postulated for all the reactions studied and a qualitative correlation of variations in products with stabilities of the iminoxyl radicals of the oximes studied has been made. No intramolecular reactions involving iminoxyl cations or radicals, leading to benzisoxazoles, have been detected.

To
Mother
and
Vivian

ACKNOWLEDGEMENTS

I sincerely thank Dr. G. Just for his patience, understanding and constructive criticism which have guided this work to its completion.

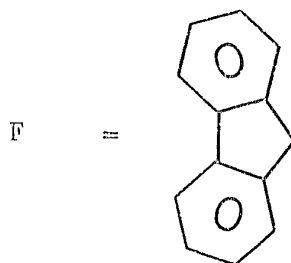
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Thanks are also extended to Miss A. Mylchreest who is responsible for the typing of this manuscript and who was always available when needed. The same thanks are extended to A. Brucher for having drawn most of the diagrams.

(ii)

Frequent Terms



me = mole equivalent with respect to oxime.

TABLE OF CONTENTS

	<u>page</u>
ABSTRACT	(i)
FREQUENT TERMS	(ii)
TABLE OF CONTENTS	(iii)
LIST OF TABLES	(vii)
LIST OF FIGURES	(viii)
MECHANISTIC SCHEMES	(ix)
INTRODUCTION	1
RESULTS	
Chapter 1 - Structural Elucidation of the Oxidation Products from Bis-Aryl Ketoximes	
1-1 Oxidation Products from Fluorenone Oxime	15
1-2 Oxidation Products from Benzophenone Oxime	41
Chapter 2 - Oxidation of Fluorenone Oxime	
2-1 Oxidation in Glacial Acetic Acid	
2-1.1 Lead tetraacetate	51
1.2 Molecular oxygen	56
1.3 Nitrogen oxides	61
1.4 Ionic-type oxidizing agents	62
2-2 Oxidation in Methylene Chloride	
2-2.1 General solvent effect in lead tetraacetate oxidations	64
2.2 Lead tetraacetate oxidations in methylene chloride	65
2-3 Oxidation of Fluorenone Oxime with Potassium Ferricyanide	
2-3.1 Formation of fluorenonazinemonoxide and bis-oxide	67
3.2 Comparative study of the lead tetraacetate oxidations of fluorenone oxime	71
Chapter 3 - Oxidations of Other Aromatic Ketoximes	
3-1 Oxidation of Benzophenone Oxime	
3-1.1 Lead tetraacetate oxidations in glacial acetic acid	73

TABLE OF CONTENTS (cont'd.)

	<u>page</u>
3-1.2 Lead tetraacetate oxidations in methylene chloride	75
1.3 Molecular oxygen	77
1.4 Nitrogen dioxide	77
3-2 Oxidation of Xanthone Oxime	80
3-3 Oxidation of Indanone Oxime	82
3-4 Oxidation of Benzil Anti-Monoxime	84
Chapter 4 - Geminal Dinitromethanes	
4-1 Introduction	86
4-2 Geminal Dinitromethanes from Aromatic Ketoximes ..	89
4-3 Structural Elucidation	91
DISCUSSION	
Chapter 5 - Mechanistic Aspects of the Oxidations of Aromatic Ketoximes	
5-1 Brief Summary of Results	99
5-2 Oxidations with Nitrogen Dioxide: Gem-Dinitro Derivatives	102
5-3 Autoxidations of Aromatic Ketoximes	111
5-4 Nitrogen Dioxide as a One-Electron Oxidizing Agent	117
5-5 Oxidations with Nitric Oxide	119
5-6 Lead Tetraacetate Oxidations of Aromatic Ketoximes	
5-6.1 Initiation steps and parent ketone formation ..	120
6.2 Ketal formation	129
6.3 Formation of nitro products	131
6.4 Azine-N-bis-oxide formation	134
6.5 Azinemonoxide formation	137
5-7 General Mechanistic Scheme for the Oxidation of Aromatic Ketoximes	138

<u>TABLE OF CONTENTS (cont'd.)</u>	<u>page</u>
EXPERIMENTAL	140
Chapter 1	
1-1	143
1-2	156
Chapter 2	
2-1.1	160
1.2	164
1.3	166
1.4	168
2-2.1	169
2.2	169
2-3.1	173
3.2	175
Chapter 3	
3-1.1 and 1.2	177
1.3	177
1.4	178
3-2	178
3-3	180
3-4	181
Chapter 4	
4-2 and 4-3	184
Chapter 5	
5-3	188
5-5	188

<u>TABLE OF CONTENTS (cont'd.)</u>	<u>page</u>
CONCLUSIONS AND CONTRIBUTIONS TO KNOWLEDGE	189
BIBLIOGRAPHY	194
APPENDIX A	199
APPENDIX B	202

LIST OF TABLES

<u>TABLE</u>		<u>page</u>
I	Half-Lives of Iminoxyl Nitroxides	8
II	UV Data of Fluorene and Fluorenone Derivatives	17
III	UV Spectral Study of 9,9-Difluorenylideneiminoxyl-fluorene	18
IV	R_F Values of Fluorenonazine and Its N-Oxides (T.L.C.)..	33
V	IR Data of Fluorenone Derivatives and Anhydride-N-oxides	38
VI	UV Data of Fluorenonazine and N-oxides	39
VII	UV Data of Benzophenone Oxime and Its Oxidation Products	42
VIII	Lead Tetraacetate Oxidation of Fluorenone Oxime in A. Oxygen-containing Glacial Acetic Acid	57
	B. Oxygen-free Glacial Acetic Acid	58
IX	Autoxidation of Fluorenone Oxime	59
X	Lead Tetraacetate Oxidation of Fluorenone Oxime in Methylene Chloride	68
XI	Ferricyanide Oxidation of Fluorenone Oxime	70
XII	Lead Tetraacetate Oxidation of Benzophenone Oxime ...	78-79
XIII	Nitrogen Dioxide Oxidation of Aromatic Ketoximes	92
XIV	IR and Melting Point Data of Dinitromethanes	93
XV	UV Data of Xanthene and Xanthone Compounds	96
XVI	Lead Tetraacetate Oxidations of Aromatic Ketoximes	101

LIST OF FIGURES

<u>FIGURE</u>		<u>page</u>
1	Probable Fragmentation Pattern of 9,9-Difluorenylideneiminoxylfluorene	20
2	Hydrolysis of Azinemonoxides	25-26
3	Probable Fragmentation Pattern of Fluorenonazine-monoxide	28
4	The IR Spectrum of Fluorenonazinemonoxide	29
5	Probable Fragmentation Pattern for Fluorenonazine-N-bis-oxide	35
6	The IR Spectrum of Fluorenonazine-bis-N-oxide	40
7	Probable Fragmentation Pattern of 1,1-Bis(diphenylmethylideniminoxyl)-diphenylmethane	44
8	The IR Spectrum of 1,1-Bis(diphenylmethylideniminoxyl)-diphenylmethane	45
9	Probable Fragmentation Pattern for Benzophenone Nitrimine	48
10	The IR Spectrum of Benzophenone Nitrimine	49
11	The IR Spectrum of Dinitrodiphenylmethane	97
12	The IR Spectrum of 9,9-Dinitroxanthene	98
13	General Mechanistic Scheme for the Oxidations of Aromatic Ketoximes	139

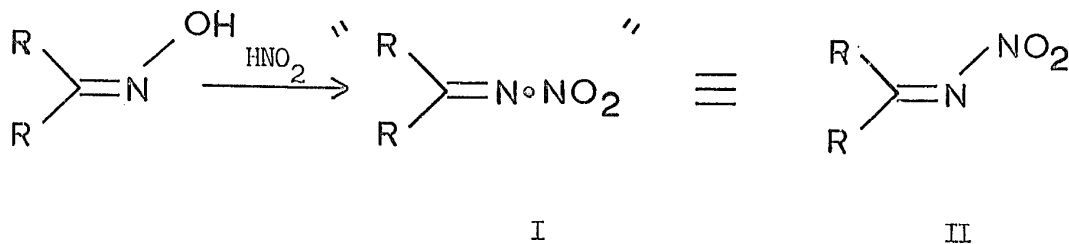
MECHANISTIC SCHEMES

<u>SCHEME</u>		<u>page</u>
I	Gem-Dinitromethane Formation	109
II	Autoxidation of Fluorenone Oxime	114
III	Iminyl Ketal Formation	118
IV	Lead Tetraacetate Oxidations of Aromatic Ketoximes	126
V	Nitration Products from Lead Tetraacetate Oxidations	131

INTRODUCTION

Many reviews have been devoted to the Beckman rearrangement of oximes, but relatively little is known of the mechanism of oxidation of these compounds. This has been mainly due to the very limited scope of the oxidation reactions investigated, which often afforded the parent ketone as sole isolable product.

The oxidation of aliphatic oximes with hydrogen peroxide, potassium permanganate, and chromic acid led to the isolation of parent ketone only (1). The use of nitrous acid usually led to ketone formation but in a few cases (2) labile "pernitroso" compounds (I) were isolated; later (3) shown to be the nitrimine derivatives (II).



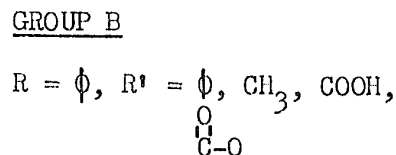
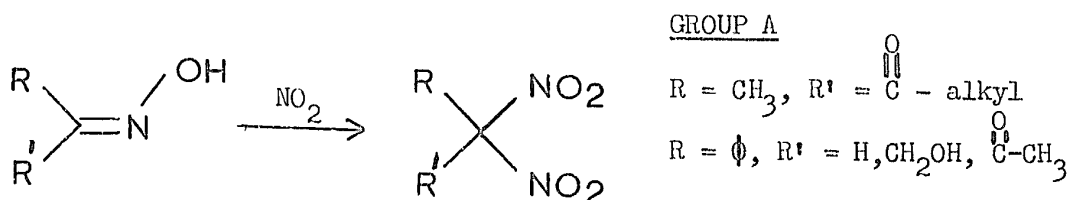
R = alkyl

Oxidations of aliphatic and alicyclic oximes with nitrosyl halides led to geminal nitrosohalide derivatives (4,5) which were readily further oxidized to the nitrohalide derivative. No such reactions were observed in the corresponding oxidations of aromatic oximes (4).

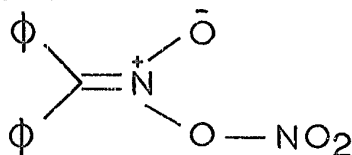
The oxidations of aromatic aldoximes and ketoximes with nitrous gases (N_2O_3 - N_2O_4), $\text{Na}_2\text{CO}_3/\text{I}_2$, $\text{K}_3\text{Fe}(\text{CN})_6$, and other standard oxidizing agents led to complex reaction mixtures containing furoxans and so-called

"oxime peroxides" (6,7).

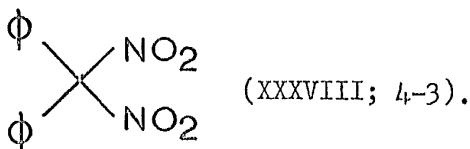
Very few generally useful methods of oxidation were discovered. Peroxytrifluoroacetic acid oxidized a variety of oximes to the nitro derivatives in good yields (8), while a similar reaction using hypobromite was limited to aliphatic oximes (9). Geminal dinitromethanes (III) were isolated in good yields from the oxidations of aliphatic α-diketomoximes and certain aromatic oximes (Group A) with nitrogen dioxide (10), but were reportedly not formed from benzophenone oxime* and other oximes shown in Group B.



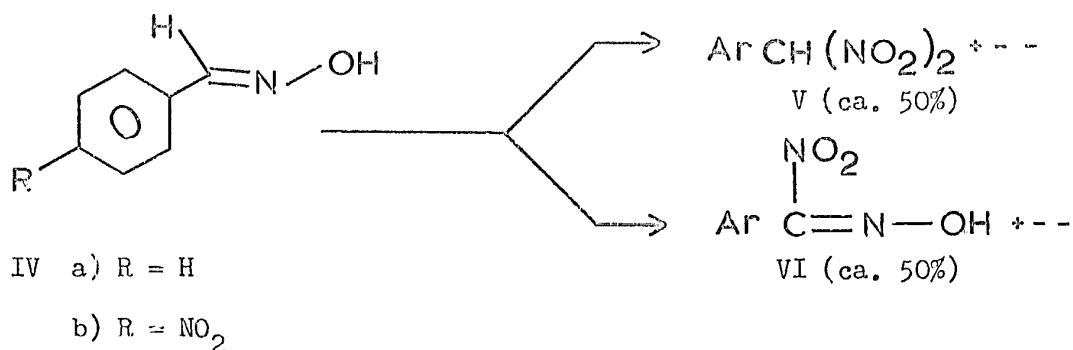
* A conflicting report (11) published at about the same time, indicated that benzophenone oxime reacted with NO_2 to give high yields of a product believed to be



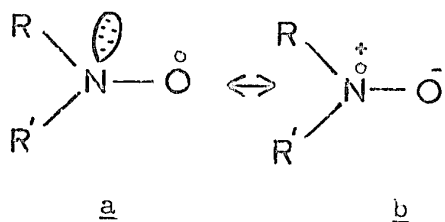
but shown in our work to be



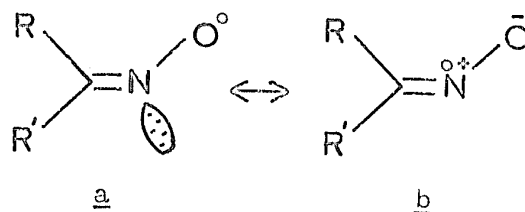
These results, reported at the turn of the century, were not further investigated. The nitrogen dioxide oxidation of aldoximes was comprehensively studied (12,13) only for benzaldoxime (IVa) and p-nitrobenzaldoxime (IVb). These afforded geminal dinitromethanes (V) or nitrolic acids (VI), depending on the reaction conditions.



It is only in the last few years that studies of the mechanism of oxime oxidations have been undertaken. In 1964, reports were published concerning the electron spin resonance spectra (ESR) of radicals obtained by the action of lead tetraacetate (14,15), ceric ammonium nitrate (16) and potassium ferricyanide (17) on aliphatic and aromatic oximes. The authors reported the formation of iminoxyl nitroxide radicals (VIII) which all had large nitrogen coupling constants ranging from 28-33 gauss. Aminoxyl nitroxides (VII), already well characterized (18), have smaller coupling constants in the range of 10-16 gauss. Theoretical calculations for the charge distribution of the unpaired electron on nitroxides (19) have shown that both the aminoxyl (VII) and iminoxyl (VIII) radicals exist as the following hybrids a and b:



VII

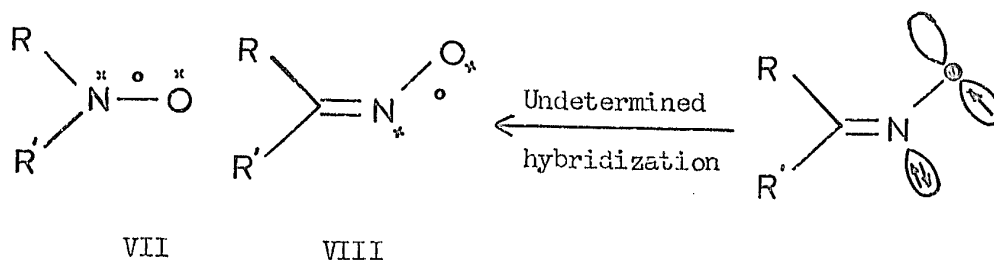


VIII

R, R' = alkyl or aryl.

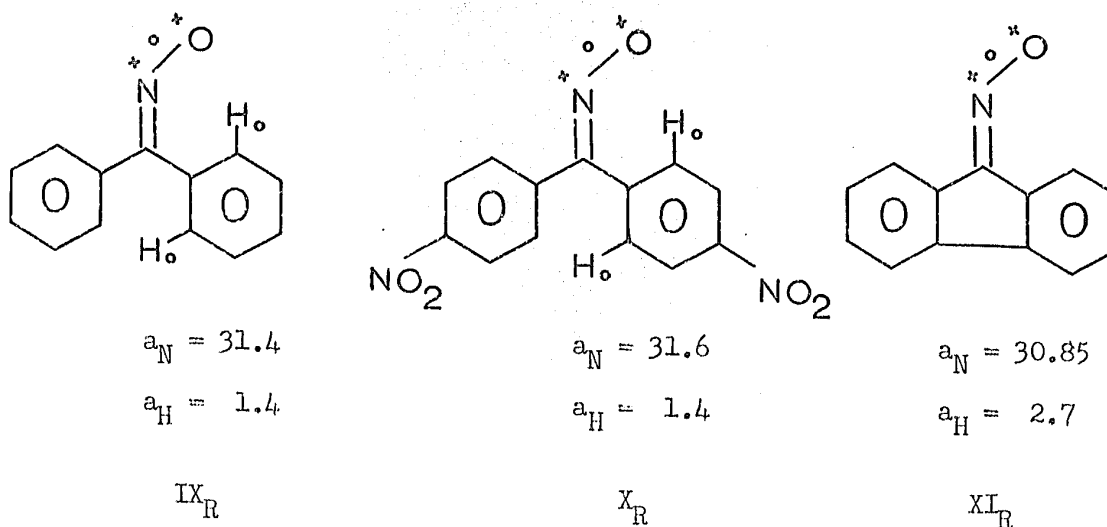
The importance of resonance form b for iminoxyl nitroxides (VIII) was also derived from calculations based on experimental ESR measurements which indicated that about 45 percent of the lone electron is actually on the nitrogen (20).

The hybrid structure of nitroxides may best be represented by using the Linnett three-electron bond model (21).



The aminoxyl nitroxides (VII) are π -type radicals (18). The iminoxyl nitroxides (VIII) are σ -type radicals because the unpaired electron is in a π -type orbital derived from nitrogen $s-p^2$ orbitals and an oxygen p -orbital which lies in the nodal plane of the C-N π -bond (14,22).

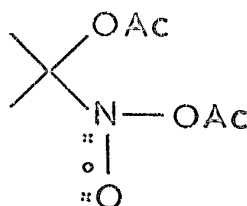
Experimental evidence for the assignment of the iminoxyl radicals as σ -radicals comes from a measurement of nitrogen and hydrogen coupling constants for a wide variety of these intermediates (15). In particular, the interaction of the unpaired electron with both β - (i.e. O-N=C-C-H) and γ -protons (i.e. O-N=C-C-C-H) was angular-dependent and was strongest when the interconnecting σ -bond system was coplanar*. Also, interaction in aromatic-substituted radicals was observed only with ortho-protons, in contrast to π -type radicals (18,23), and was unaffected by substituents such as p-nitro which interact with the π -system. Particular examples demonstrating these ideas are the benzophenone iminoxyl (IX_R), 4,4'-dinitrobenzophenone iminoxyl (X_R) and fluorenone iminoxyl (XI_R) nitroxides.



Further ESR studies in this area have shown that iminoxyl radicals were the major primary products in the oxidations of oximes, and that secondary nitroxides were also formed (14,24). Specifically, oxidations

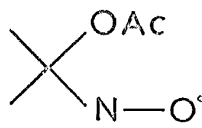
* The authors suggest 1,6-interaction through space as a possible mechanism for coupling with γ -protons (15).

of aliphatic oximes under varied conditions led to the primary iminoxyl radical which rapidly decayed to secondary nitroxide radicals (24a) of the following type:*



$$a_N = \text{ca. } 15.5 \text{ Oe.}$$

XI



$$** a_N = \text{ca. } 13.2 \text{ Oe.}$$

XII

Substituted acetophenone oximes showed a similar behaviour (24b). Acetophenone oxime and its p-methoxy and p-methyl analogues afforded unstable iminoxyl radicals which rapidly decayed to two secondary nitroxides* (XII and another as yet unidentified radical). The order of effectiveness of ring substituents to promote conversion of the iminoxyl radical into secondary radicals was qualitatively in the order $p\text{-MeO} > p\text{-Me} > \text{H} > \text{F, Cl, Br} > p\text{-NO}_2$. Aromatic aldoximes, in general, † gave unidentified secondary radicals (14). Bis-aryl ketoximes, not yet studied in great

* Lead tetraacetate oxidations in benzene (14) also led to secondary nitroxyl radicals but the actual identification of the latter was done for lead tetraacetate oxidations in methylene chloride (24).

** Obtained only from alicyclic oximes.

† Benzaldoxime, oxidized with lead tetraacetate, did afford the primary iminoxyl radical.

detail, led to primary iminoxyl radicals (14,24b).^{*} The measured half-lives of the iminoxyl nitroxides obtained from biacetyl monoxime (XIII), fluorenone oxime (XI), 4,4'-dinitrobenzophenone oxime (X), benzo-phenone oxime (IX), and cyclohexanone oxime (XIV) (see Table I) showed the surprising stability of the aromatic radicals with respect to their aliphatic analogues. A stabilization by ring substituents, such as p-NO₂, was also observed (24b).

Although the ESR spectra of the radicals from a variety of oximes have been studied in detail, the chemistry of these radicals has received only cursory attention.

Iffland (24) and Kropf (27) reported that the lead tetra-acetate oxidation of unsubstituted alicyclic and straight-chain aliphatic ketoximes gave unstable nitrosoacetates (XV). A more general study, conducted in this laboratory by Dahl and Just (26), showed that the oxidation of a) sterically hindered ring ketoximes (e.g. 2,2,6,6-tetramethylcyclohexanone oxime) led to N-acetoxhydroxamic acids (XVI) formed from corresponding intermediary nitrile oxides (path A in reaction scheme below); b) strained ketoximes (e.g. camphor oxime) also afforded the hydroxamic acids (XVI) which probably formed through rearrangement of an intermediate geminal nitrosoacetate (XV, paths B and C); c) simple aliphatic ketoximes (e.g. cyclohexanone oxime) led to gem-nitrosoacetates (XV, path B).

* Minor secondary radicals, appearing in the ESR spectra, have not been discussed.

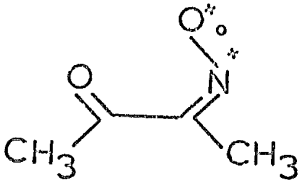
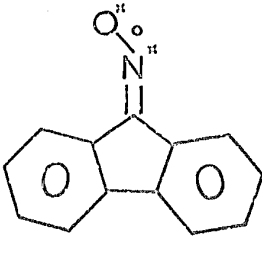
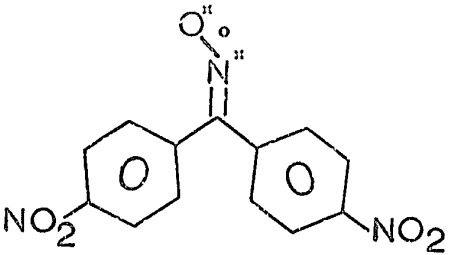
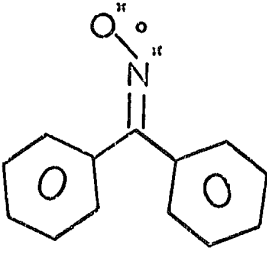
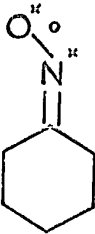
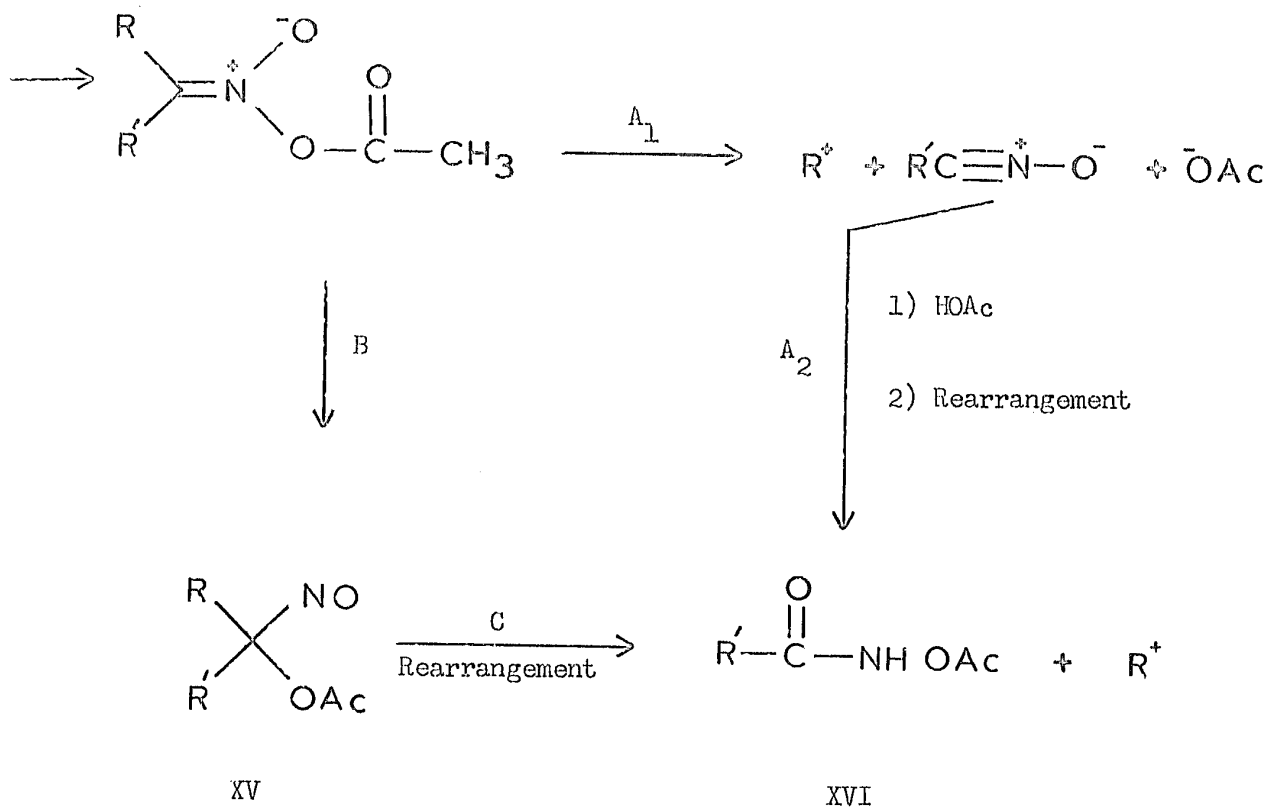
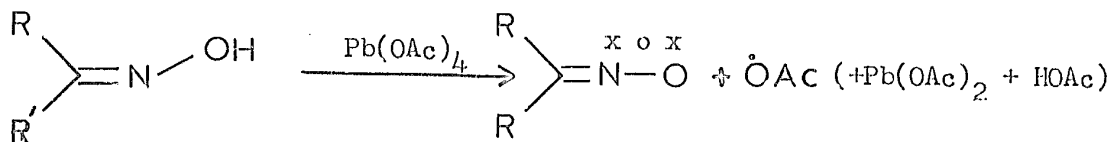
<u>Iminoxyl Nitroxide</u>	<u>Half-Life (minutes)</u>
	10.5
	5.5
	3.0
	0.5
	<<1.0

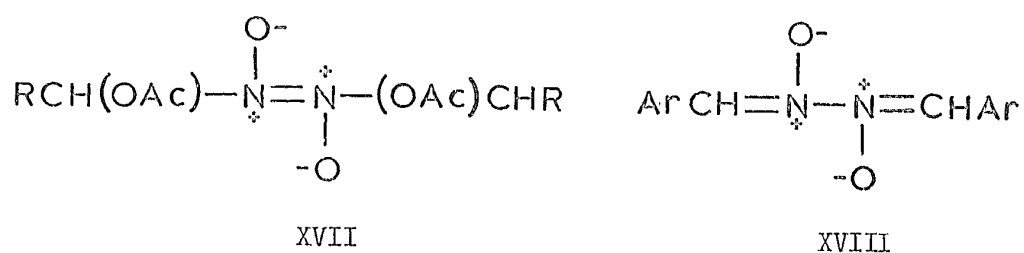
TABLE I - Stabilities of Iminoxyl Nitroxides



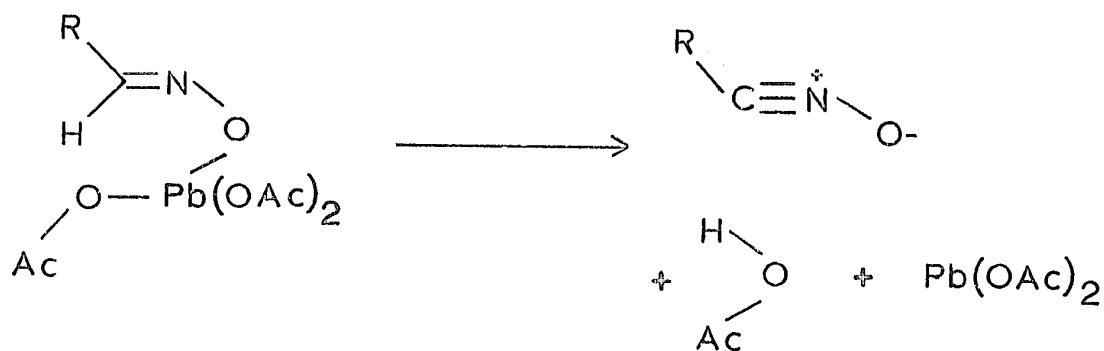
R = alkyl; more substituted than R'.

Kropf (27) reported that the lead tetraacetate oxidation of straight chain aliphatic aldoximes (e.g. butyraldoxime) led to stable, isolable dimeric gem-nitrosoacetates (XVII). Dahl and Just (26) have found that low temperature oxidations of all syn-aldoximes afforded nitrile oxides which could further react to the N-acetoxyhydroxamic

acids* (XVI, path A in above scheme); the oxidation of aliphatic anti-aldoximes or aliphatic syn-aldoximes (at room temperature) gave gem-nitrosoacetates (XV, path B) and secondary products, notably N-acetoxyhydroxamic acids (XVI, path C); and aromatic anti-aldoximes (e.g. benzaldoxime) led to arylaldazine-N-bis-oxides (XVIII)**.

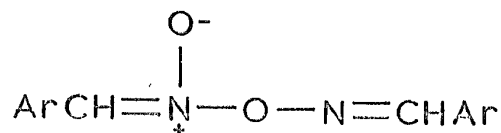


* Nitrile oxide formation was postulated via a concerted mechanism.

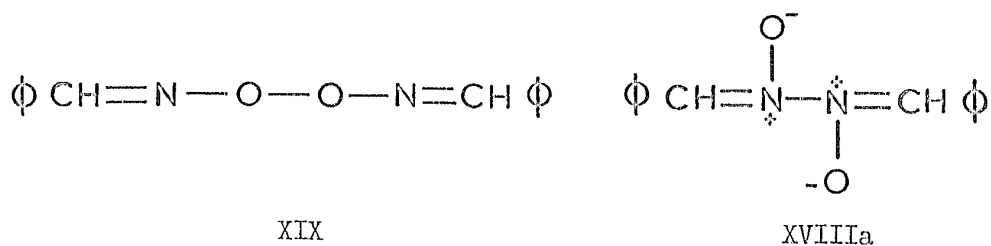


R = alkyl or aryl.

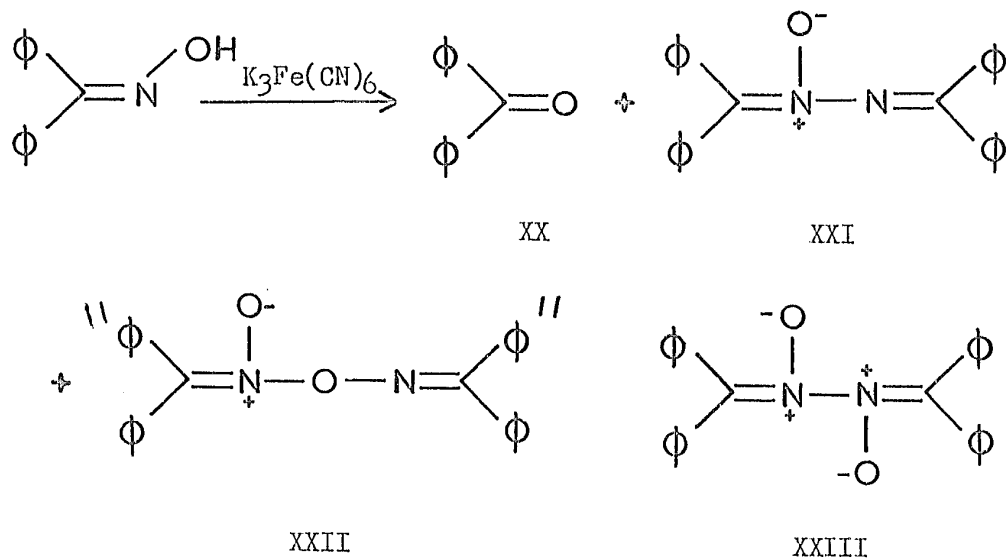
** Kropf (28) has reported that the oxidation of aromatic and α,β -unsaturated aldoximes in aprotic solvents at 0-5° with a half-mole equivalent of Pb(OAc)_4 (Dahl used 1 mole Pb(OAc)_4 at -20°) led to aldoxime anhydride N-oxides.



The potassium ferricyanide oxidation of aldoximes was studied as early as 1885 by Beckman (29) who reported the formation of an "oxime peroxide" (XIX) from benzaldoxime, which was conclusively shown, by Horner et al. (30), to be actually benzaldazine-bis-N-oxide (XVIIIa).



The corresponding oxidation of ketoximes was reported only for benzophenone oxime (31). It led to parent ketone (XX), benzophenone azine-monoxide (XXI) and "anhydride N-oxide" (XXII), which we believe was probably the azine-bis-oxide (XXIII).*



* The similar oxidation of fluorenone oxime led to the azine-bis-oxide (Chapter I, p.

No publications on the chemistry of the ceric ammonium nitrate oxidations of oximes have appeared to date.*

In summary, it has been shown that some chemistry of the oxidation of aliphatic oximes and aromatic aldoximes has been reported. The one-electron oxidation of aromatic ketoximes, while affording the most stable, well characterized iminoxyl radicals, has received some attention only in the case of benzophenone oxime (31).**

Lead tetraacetate was chosen as the oxidizing agent to be used in a study of the chemistry of iminoxyl radicals from aromatic ketoximes because of its well documented reactivity in a large number of solvents (covering the spectrum of dielectric constants) and over a very wide range of temperatures (-70° to $> 100^{\circ}\text{C.}$) (33). Other oxidizing agents, such as molecular oxygen and nitrogen dioxide, were also used in order to probe deeper into the mechanisms operating in the lead tetraacetate oxidations.

Bis-aryl ketoximes: fluorenone oxime (XI) and benzophenone oxime (IX), were chosen as the models to be initially investigated because of their symmetry and extended delocalization of the π -electrons. They were also chosen in the hope of obtaining 1,2-benzisoxazoles (XXIV) which are neutral compounds very stable to acids and bases (34):

* A private communication was received just prior to thesis writing (32).

** This work was reported in 1942.



This class of compounds would be most expected if an iminoxyl cation (XXV) were formed as an intermediate in the lead tetraacetate oxidation of aromatic ketoximes.

The possible formation of an intermediate iminoxyl cation from the lead tetraacetate oxidation of oximes has not been ruled out from the results of the ESR experiments since the actual concentrations of observed radicals were not reported. Anhydride N-oxide (XXIIa) formation from aromatic aldoximes (28) was, for instance, explained by assuming the intermediacy of iminoxyl cations (XXVa).



Work conducted in our laboratory on aliphatic oximes (26) also led us to suspect the possibility of an ionic mechanism.

The choice of model compounds was therefore dictated by a consideration of both free radical and ionic pathways presented in the foregoing introduction.

RESULTS

Chapter 1

Structural Elucidation of the Oxidation Products from Bis-Aryl Ketoximes

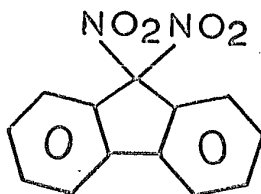
The lead tetraacetate oxidation of bis-arylketoximes such as fluorenone oxime (XI), and benzophenone oxime (IX) led to products whose types had not been observed in the similar oxidations of other oximes. The formation of some of these products was markedly affected by the solvent used, the presence of atmospheric oxygen, and the amount and mode of addition of oxidizing agent. The use of oxidizing agents other than lead tetraacetate led to changes in product distribution, with another new product appearing in the particular case of the potassium ferricyanide oxidation.

In order to simplify the presentation of results, the structure proofs for the new products will be discussed first.

1-1. Oxidation Products from Fluorenone Oxime

9,9-Dinitrofluorene (XXVI)

The structure proof is provided in Chapter IV.

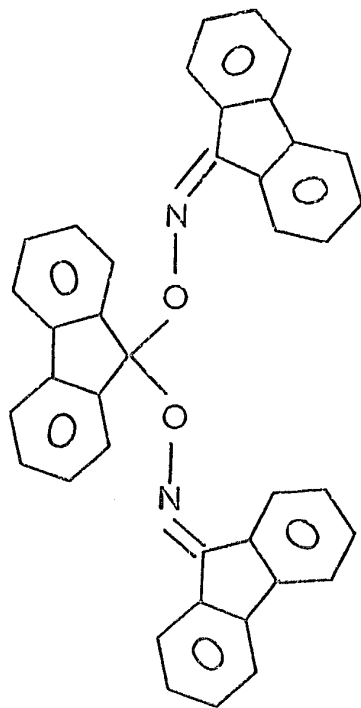


XXVI

9,9-Difluorenylideneiminoxylfluorene (XXVII)

The lead tetraacetate oxidation of fluorenone oxime (XI) in oxygen-free glacial acetic acid afforded a compound XXVII, $C_{39}H_{24}N_2O_2$, m.p. 267° (dec.), which had an osmometric molecular weight of 597.

The ultraviolet spectrum of compound XXVII was similar to that of fluorenone oxime. The absorption band at $256\text{ m}\mu$ was probably due to a conjugated $C=N$ electron transfer excitation (compare the spectral values in Table II). If the trimeric structure XXVII had two iminoxyl groups per molecule, the extinction coefficient at $256\text{ m}\mu$ for fluorenone oxime would be 0.529 for trimer XXVII. Excellent agreement was obtained for calculations made at $256\text{ m}\mu$, as well as at $247\text{ m}\mu$ (Table III). Furthermore, a model solution prepared from fluorenone oxime and 9,9-dinitrofluorene (XXVI) to simulate the following ketal structure gave



XXVII

TABLE II

UV DATA OF FLUORENE AND FLUORENONE DERIVATIVES

<u>Solvent</u>	<u>Fluorene</u>		<u>Fluorenone oxime</u>		<u>Fluorenone</u>		<u>9,9-Dinitro- Fluorene (XXVI)</u>	
	<u>λ max.</u>	<u>ϵ</u>	<u>λ max.</u>	<u>ϵ</u>	<u>λ max.</u>	<u>ϵ</u>	<u>λ max.</u>	<u>ϵ</u>
MetOH	248	18,800	247	15,800	247	63,000	246*	26,000
	255	24,400	256	20,500	256	102,000		
	260	23,700						
	271**	15,600					276**	6,800
	288	7,400						
	300	10,200	310*	3,500				
			350**	1,900	378	244	325	930

* broad

** shoulder

TABLE III

UV SPECTRAL STUDY OF 9,9-DIFLUORENYLIDENIMINOXYLFLUORENE

COMPOUND	ϵ^*		$\frac{\epsilon}{\epsilon_{XXVII}}$
	a) $\lambda = 256 \text{ m}\mu$	b) $\lambda = 247 \text{ m}\mu$	
$\begin{array}{c} \text{O}-\text{N}=\text{F} \\ \diagup \\ \text{F} \\ \diagdown \\ \text{O}-\text{N}=\text{F} \end{array}$ XXVII	1.23×10^5	9.78×10^4	a) 0.55 b) 0.54 Av. 0.545
			Calculated = 0.529
$\begin{array}{c} \text{OH} \\ \diagup \\ \text{F}=\text{N} \end{array}$ XI	0.68×10^5	5.28×10^4	% Difference = 3%

COMPOUND	% Absorption					
	226 m μ	247 m μ	256 m μ	278 m μ	305 m μ	315 m μ
$\begin{array}{c} \text{O}-\text{N}=\text{F} \\ \diagup \\ \text{F} \\ \diagdown \\ \text{O}-\text{N}=\text{F} \end{array}$ XXVII (3.7 x 10 ⁻³ mg/ml)	63	66	83	24	17	11
$\begin{array}{c} \text{OH} \\ \diagup \\ \text{F}=\text{N} \end{array} + \begin{array}{c} \text{NO}_2 \\ \diagup \\ \text{F} \\ \diagdown \\ \text{NO}_2 \end{array}$ XI (2 : 1) XXVI	58	82	97	22	14	9

* Ethanol-methylene chloride (2 : 3) was used as solvent.

** Concentrations equivalent to that shown for ketal XXVII were used.

absorptions which differed only by 10-20% from absorptions obtained for an equivalent solution of compound XXVII (Table III).

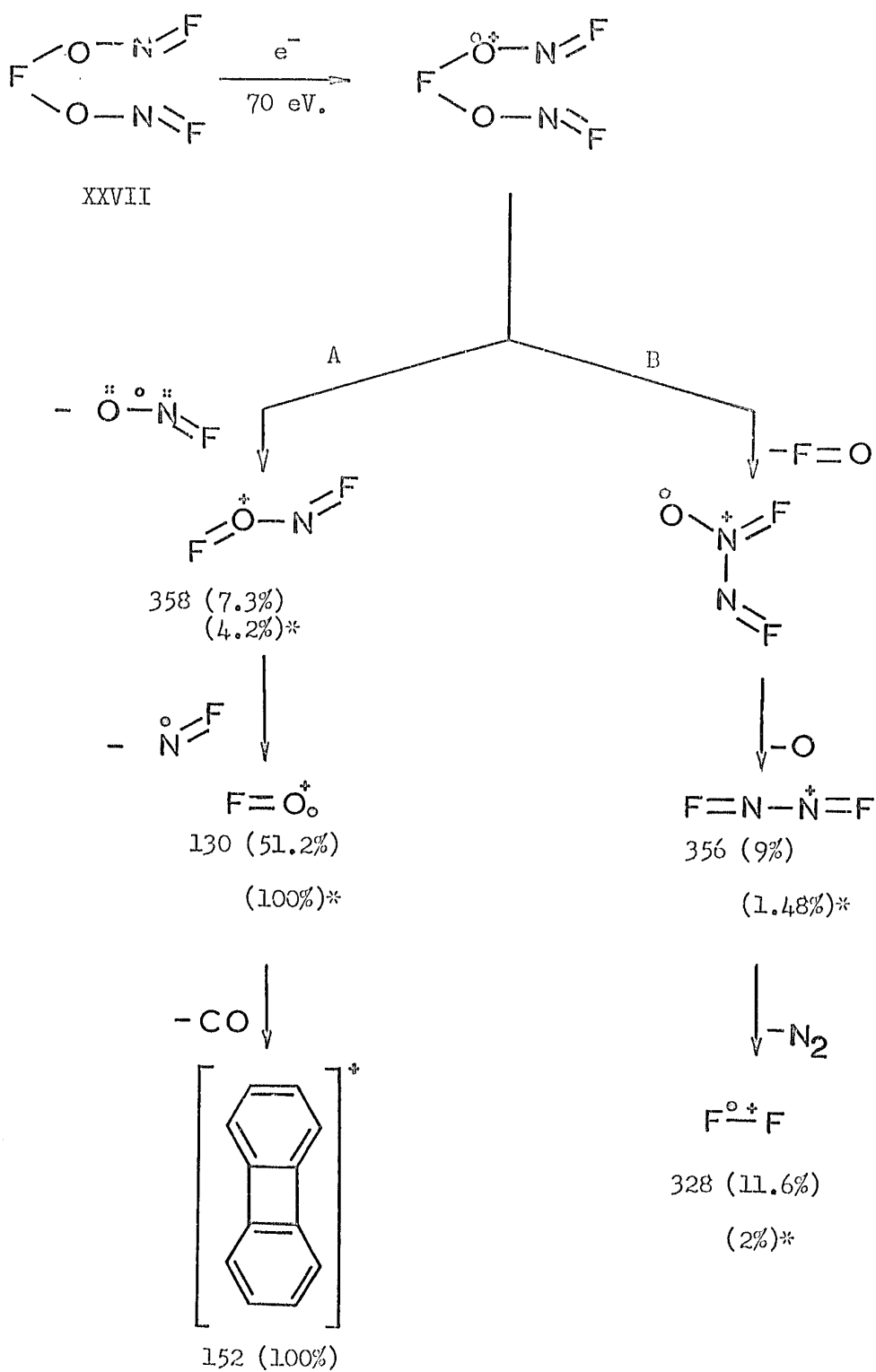
The infrared spectrum of compound XXVII in potassium bromide gave absorption bands between 4000 and 1100 cm^{-1} which were all approximately correlated with bands due to the fluorenylidene skeleton of fluorenone oxime (see Table V, p. 38) except for the band at 1625 cm^{-1} which was assigned to C=N stretching frequency. The set of peaks between 1090 and 1030 cm^{-1} could not be definitely assigned although their unique appearance in the spectrum of compound XXVII (compare other fluorene derivatives in Table V) suggested that they were due to absorptions of the ketal* function.

Although sublimation of compound XXVII between 150 and 240° resulted in partial decomposition, a meaningful mass spectrum was obtained. The fragmentation pattern observed (Fig. 1) is fully consistent with a structure corresponding to 9,9-difluorenylideneiminoxylfluorene (XXVII)**. Scheme A shows the fragmentation pattern which involves loss of an iminoxyl radical (known to be long-lived in the ground state (Table I)) to form the resulting ion at $m/e = 358$. This was obtained in significant yield even at 10 e.V. Scheme B indicates a mechanism for formation of the ketazine cation ($m/e = 356$).

Compound XXVII was found to be inert to oxidizing agents such as bromine and hydrogen peroxide. It underwent facile acid hydrolysis. Two mole equivalents of fluorenone oxime (XI) and one mole equivalent of

* Bergman et al. (35) found three to four bands for ketal absorptions in the 1200-1000 cm^{-1} region with extinction coefficients less than five.

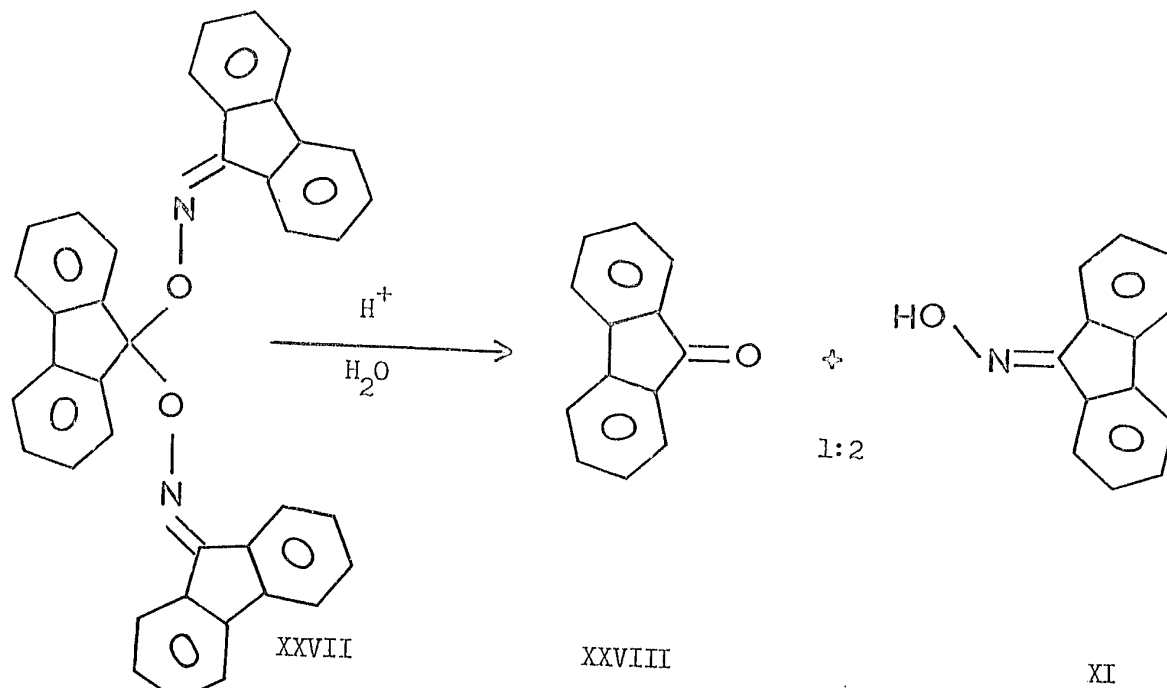
** For a further study of this spectrum, see Appendix A.



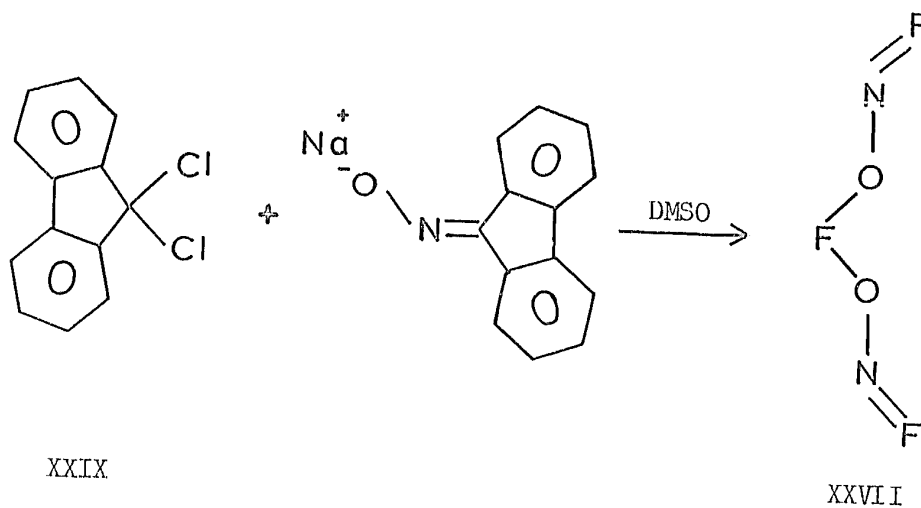
* Intensities at 10 eV.

FIG. 1. Probable Fragmentation Pattern of 9,9-Difluorenylideneiminoxyfluorene (XXVII).

fluorenone (XXVII), expected from the assigned ketal structure of XXVII, obtained.



As a final confirmation of the above structure, an independent synthesis from 9,9-dichlorofluorene (XXIX) and the sodium salt of fluorenone oxime was carried out.



Fluorenonazinemonoxide (XXX) - Structure and Chemistry

The lead tetraacetate and potassium ferricyanide oxidations of fluorenone oxime led to the formation of a compound XXX, $C_{26}H_{16}N_2O$, which was obtained as red crystals, m.p. 178° .

The infrared spectrum of compound XXX (KBr) contained strong absorption peaks at 1540 cm^{-1} and 1268 cm^{-1} , which may be related to the $N \rightleftharpoons O$ asymmetric and symmetric stretching frequencies respectively (36). The absorption band at 1630 cm^{-1} indicated the presence of a C=N (Fig. 4, p. 29) functionality. The ultraviolet spectrum of XXX contained absorptions at 255 and 261 m μ (ϵ 53000 and 65000 respectively), characteristic of the electron transfer band found in the spectrum of fluorenone oxime (255 m μ , ϵ 20800).

The chemical test for an N-oxide structure was made by reduction of XXX with triphenylphosphine. The red crystals isolated were identical with fluorenonazine (XXXI), prepared by the method of Curtius (37)*. Reduction of XXX was much more facile with lithium aluminum hydride ($LiAlH_4$) but it led to fluorenonazine (XXXI) and products of further reduction**. Comparison of the infrared spectra (CCl_4) of the azinemonoxide (XXX) and the azine XXXI showed the $N \rightleftharpoons O$ stretch at 1260 cm^{-1} as the only absorption not appearing for both compounds.

Hydrolysis of the azinemonoxide XXX in glacial acetic acid containing concentrated hydrochloric acid gave mainly fluorenone (XXVIII, 63%) and, unexpectedly, 9-chlorofluorene (XXXII, 33%), identified by comparison

* A much milder method using fluorenone hydrazone (XLIV) and oxygen was later discovered.

** Comparison by t.l.c. of these products with those obtained by $LiAlH_4$ reduction of azine XXXI indicated that they were reduction products.

with an authentic sample.

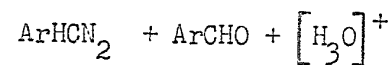
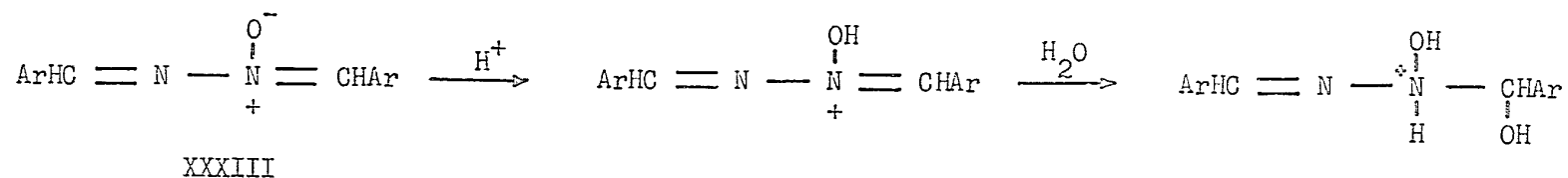
It has been shown (36) that the hydrolysis of aldazinemonoxides (XXXIII) in alcohols, phenols, or acetic acid containing catalytic amounts of mineral acids leads to the corresponding aldehyde and ether (or ester for acetic acid), the latter arising from solvolysis of the intermediate arylldiazomethane (XXXIV) (see Fig. 2). The 9-chlorofluorene (XXXII) which we obtained was most likely formed from the solvolysis of the expected intermediate 9-diazofluorene (XXXIVa) (path a in Fig. 2). The latter was prepared and subjected to treatment with glacial acetic acid containing conc. hydrochloric acid*. 9-Chlorofluorene (XXXII) was formed quantitatively. Formation of this product from the acid hydrolysis of fluorenonazinemonoxide (XXX) is therefore consistent with the structure assigned.

The hydrolysis of fluorenonazinemonoxide (XXX) led to 33% of chlorofluorene (XXXII), 33% of fluorenone (XXVIII), probably** formed along with the latter (path a of Fig. 2), as well as an additional 30% of fluorenone which must have formed by another mechanistic pathway. Path b shown in Fig. 2-B can be ruled out as leading to fluorenone since fluorenone oxime was found to be stable under the conditions used. Path c represents a possible mechanism which would explain the formation of fluorenone from intermediates similar to those observed from the aldazinemonoxide (XXXIII)

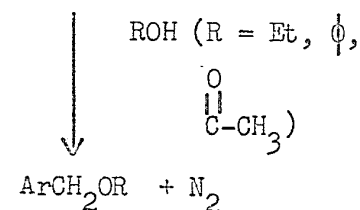
* Solvolysis of 9-diazofluorene (XXXIVa) in glacial acetic acid led to instantaneous and quantitative formation of 9-fluorenyl acetate. Glacial acetic acid containing conc. hydrochloric acid therefore has the chloride ion as the exclusively active nucleophile in the above solvolysis.

** The hydrolysis of benzaldazinemonoxide in conc. hydrochloric acid was reported (36) to lead to equimolar amounts of benzaldehyde and benzylchloride (35% each).

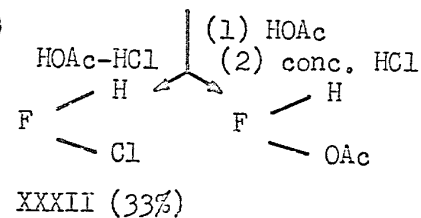
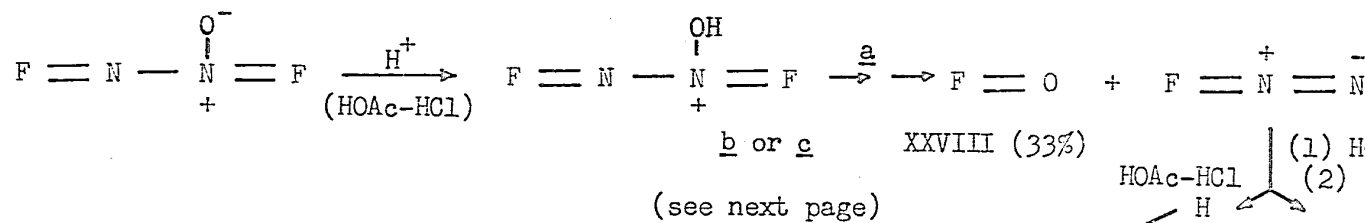
A. ALDAZINEMONOXIDES (36)



XXXIV



B. FLUORENONAZINEMONOXIDE



(continued)

FIG. 2. HYDROLYSIS OF AZINEMONOXIDES

B. FLUORENONAZINEMONOXIDE (cont'd.)

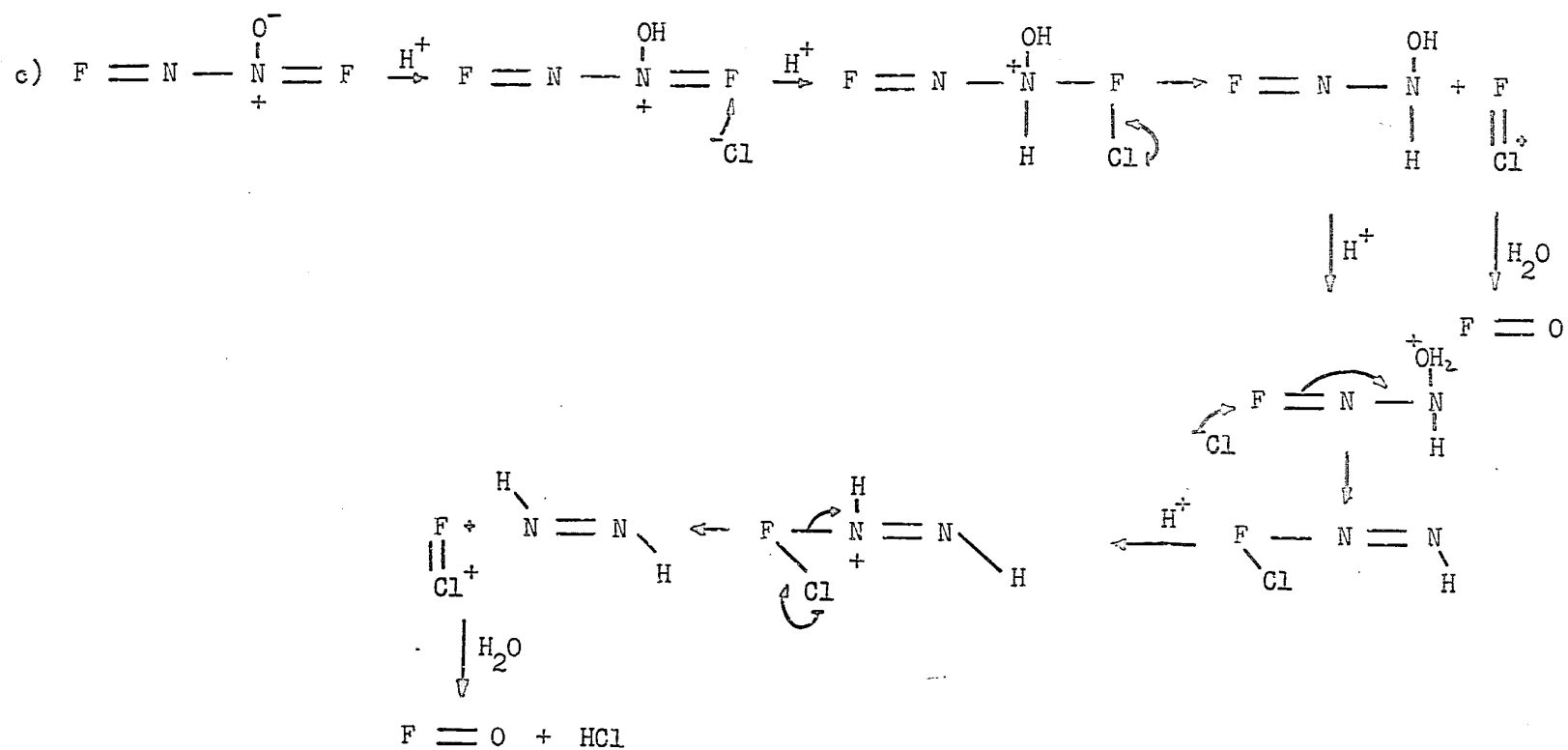
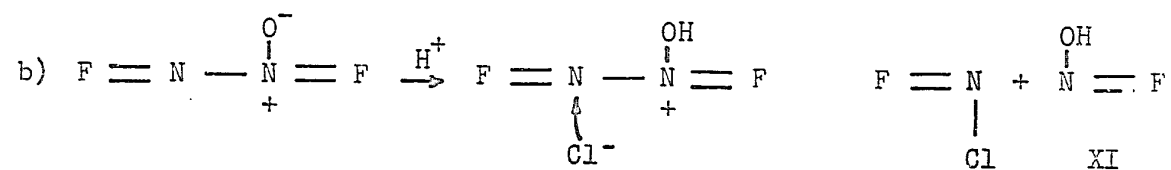


FIG. 2 (continued)

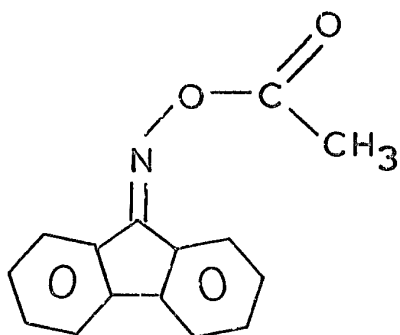
hydrolyses.

Finally, the mass spectrum of 9-fluorennonazinemonoxide (XXX) was readily explained (Fig. 3). The heaviest ion appearing in it corresponded to M-16 (M = molecular ion peak at 372 mass units). This facile loss of oxygen is a well recorded process for compounds containing an N-oxide functionality (38).

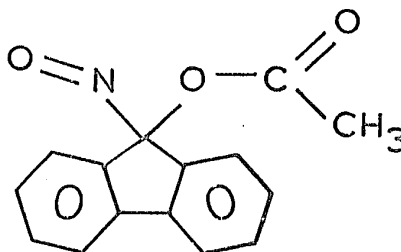
Fluorenone Oxime O-acetate (XXXV)

The NMR spectrum of a crude reaction mixture from the lead tetraacetate oxidation of fluorenone oxime contained an absorption band at 2.35 p.p.m. The infrared spectrum of this mixture had a weak absorption band at 1765 cm^{-1} .

Fluorenone oxime O-acetate (XXXV) and 9-nitroso-9-acetoxyfluorene (XXXVI) were considered as possible structures.



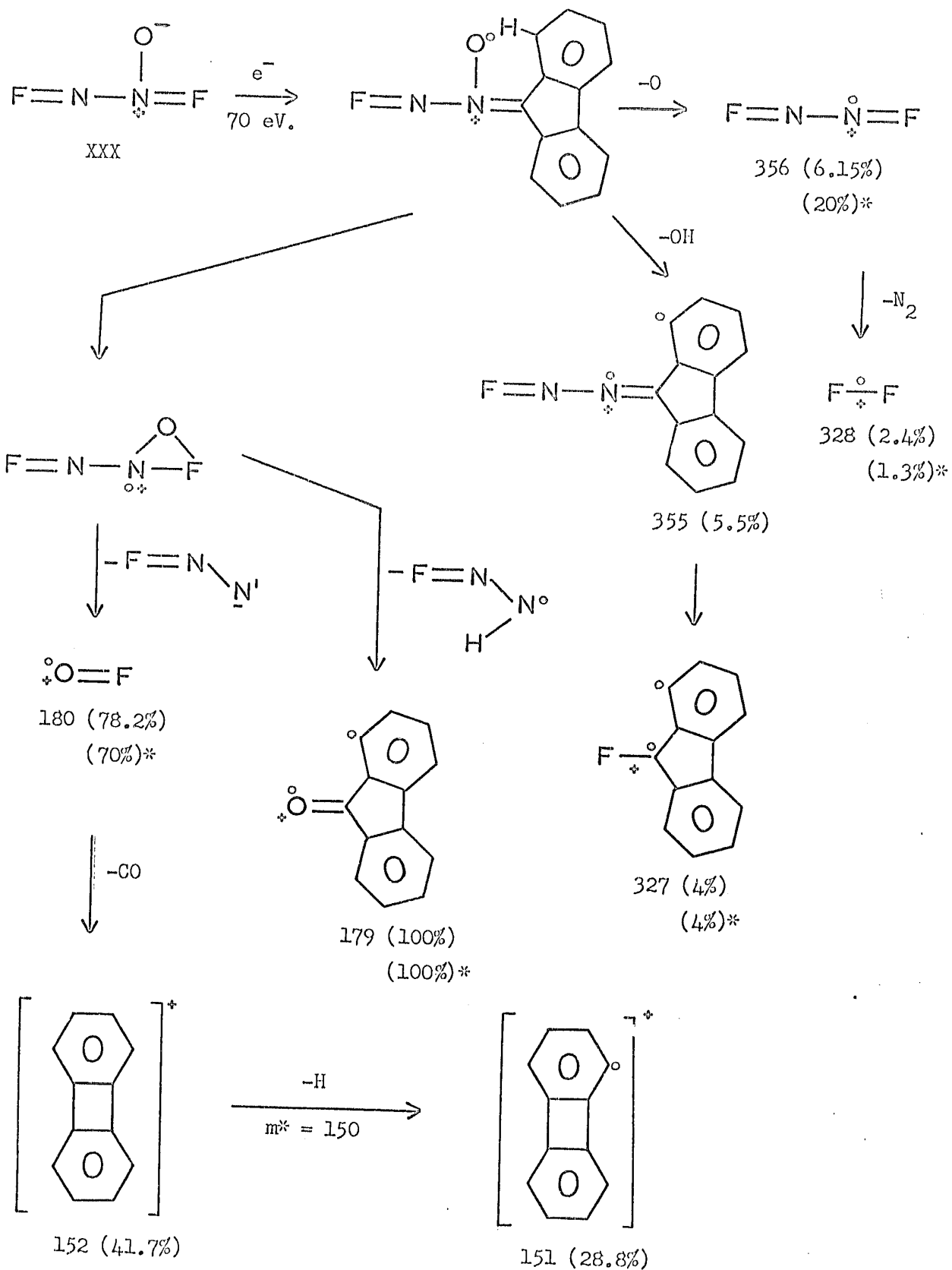
XXXV



XXXVI

However, the absence of a strong absorption band at about $1560\text{-}1555\text{ cm}^{-1}$ for the N=O stretching frequency and the stability of the reaction mixture to concentrated hydrochloric acid made the gem-nitrosoacetate (XXXVI) assignment improbable (27).

A synthetic sample of fluorenone oxime O-acetate had identical spectral properties to those described above.



* Intensity at 12 eV. m^* = metastable peak (see Appendix A for further data).

FIG. 3. Probable Fragmentation Pattern of Fluoren-9-yl azide (XXX).

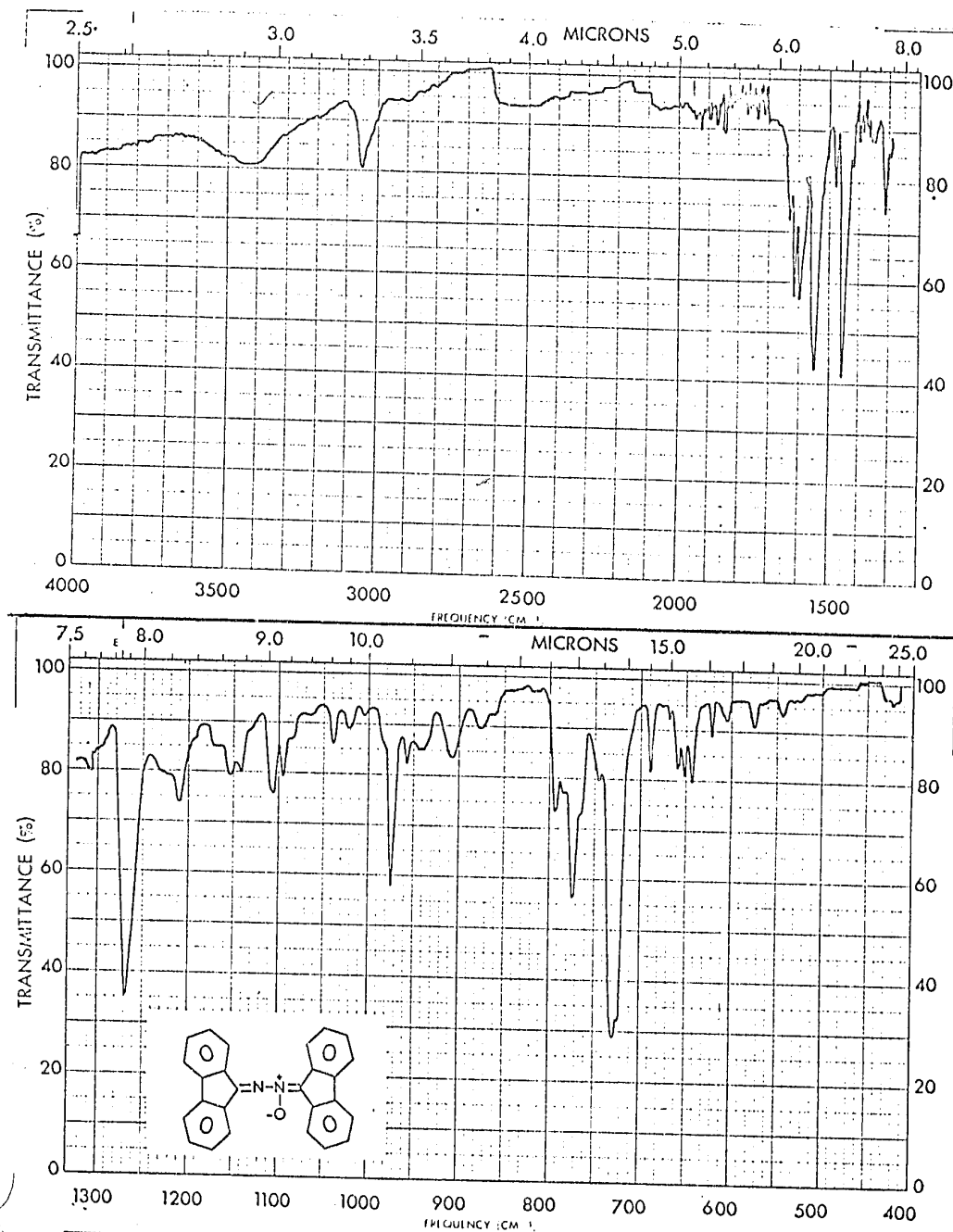
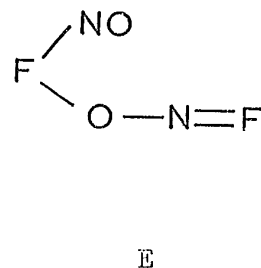
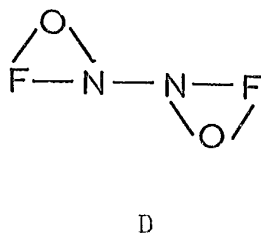
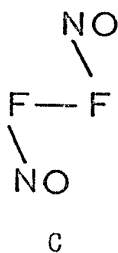
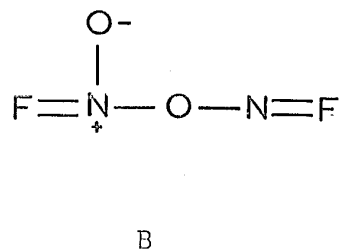
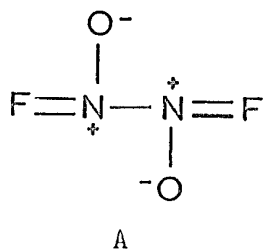


FIG. 4. The IR Spectrum of Fluorenemonoxide.

Chromatography of the crude products from the lead tetraacetate oxidation of fluorenone oxime led to mixtures of the oxime and oxime O-acetate (XXXV)*. The amount of compound XXXV present in the various reaction mixtures was estimated from standard absorption peaks obtained in the IR and NMR spectra of authentic fluorenone oxime O-acetate.

Fluorenonazine-bis-N-oxide (XXXVII)

The potassium ferricyanide oxidation of fluorenone oxime in an alkaline aqueous medium afforded yellow microcrystals, m.p. 212.5° (dec.) having the composition $C_{26}H_{16}N_2O_2$. Five structures with this empirical formula will be considered, two of which (A and B) are most probable.



* Fluorenone oxime and synthetically prepared oxime O-acetate (XXXV) were found to have identical R_f values on t.l.c. silica gel plates. Activation of the plates and variations in eluting solvents did not aid in effecting a separation.

The ultraviolet spectrum of compound XXXVII (Table VI, p. 39) had a strong absorption band at $256 \text{ m}\mu$ (ϵ 7,275) which most likely corresponded to the electron transfer excitation of $\text{C}=\text{X}$ conjugated with the fluorenylidene skeleton. The UV spectra of fluorenone (XXVIII), its oxime (XI), fluorenonazine (XXXI) and the N-monoxide (XXX) contained this band, which was not observed for 9,9-dinitrofluorene (XXVI) (see Tables II and VI).

The infrared spectrum (Fig. 6, p. 40) of compound XXXVII in potassium bromide showed a band at 1620 cm^{-1} (medium intensity) which was assigned to the $\text{C}=\text{N}$ stretching vibration (see spectral data in Table V, p. 38). A very strong absorption found at 1520 cm^{-1} was assigned to the $\text{N} \longrightarrow \text{O}$ stretching frequency.

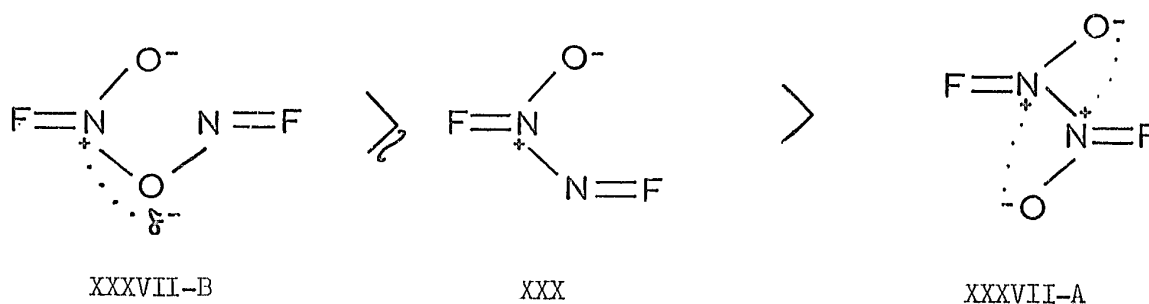
From these considerations, we can eliminate C and related structures, as well as D. Structure D was also ruled out since no positive starch-iodide test expected for an isonitrone group (39,40) was obtained. Structure E would be expected to have an $\text{N}=\text{O}$ stretching frequency between 1550 and 1560 cm^{-1} , since this was the range found for aliphatic and alicyclic geminal nitrosobenzoates (27). Moreover, both E and C can be ruled out from the observed mass spectrum (Appendix A) of compound XXXVII which did not contain a strong peak due to the loss of nitric oxide (M-30).

Therefore, only fluorenone oxime anhydride N-oxide (B) and fluorenonazine-bis-N-oxide (A) remain as probable structures for compound XXXVII.

A comparison of the infrared spectrum of fluorenonazinemonoxide (XXX) with that of compound XXXVII showed a striking similarity in the

overall absorption pattern (Table V)*. This pattern did not correspond to that reported by Kropf (28b) for a large number of oxime anhydride N-oxides and furoxans (see Table V).

The R_f value of compound XXXVII on t.l.c. was larger than that of fluorenazonemonoxide (XXX), indicating that XXXVII is less polar than the azinemonoxide XXX. A comparison of the R_f values of fluorenazonine (XXXI) and its azinemonoxide (XXX) indicated (Table IV) that the latter was more polar due to the N-oxide group. A comparison of the $N \longrightarrow O$ polarities of structures A and B with that of the azinemonoxide XXX indicated the following order of polarities.



Structure A would be expected to be the least polar of the above compounds due to the partial electrostatic neutralization provided by neighbouring positive and negative centres and therefore best corresponds to the observed R_f value of compound XXXVII (Table IV).

The mass spectrum of compound XXXVII, obtained below its melting point to avoid decomposition, contained a weak mass peak at M-16

* The strong absorption peak at 1268 cm^{-1} assigned to the $N \longrightarrow O$ symmetric stretching vibration in the azinemonoxide XXX was not found for XXXVII. However, an absorption peak at 1235 cm^{-1} (m) may be due to the $N \longrightarrow O$ symmetric stretch.

TABLE IV

R_f VALUES OF FLUORENONAZINE AND ITS N-OXIDES (t.l.c.)

Compound	R _f Value
----------	----------------------

$\text{F}=\text{N}-\text{N}=\text{F}$ XXXI	0.69
---	------

XXXVII	0.45
--------	------

$\begin{array}{c} \text{O}^- \\ \\ \text{F}=\text{N}-\text{N}=\text{F} \\ \vdots \end{array}$ XXX	0.26
--	------

$\begin{array}{c} \text{O}^- \\ \\ \text{F}=\text{N}-\text{N}=\text{F} \\ \\ \text{O} \end{array}$ XXXVII-A	> 0.26*
--	---------

$\begin{array}{c} \text{O}^- \\ \\ \text{F}=\text{N}-\text{O}-\text{N}=\text{F} \\ \vdots \end{array}$ XXXVII-B	< 0.26*
--	---------

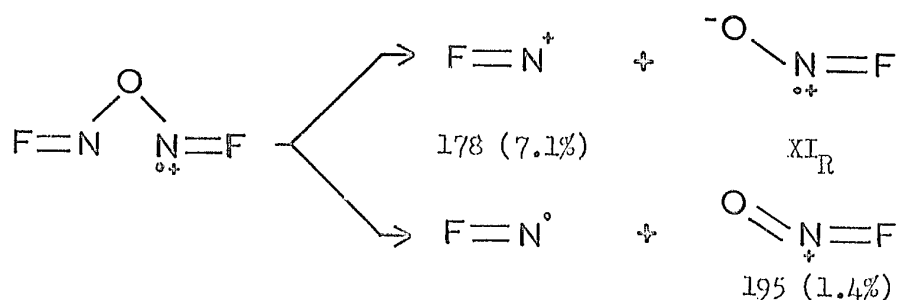
* Predicted Values

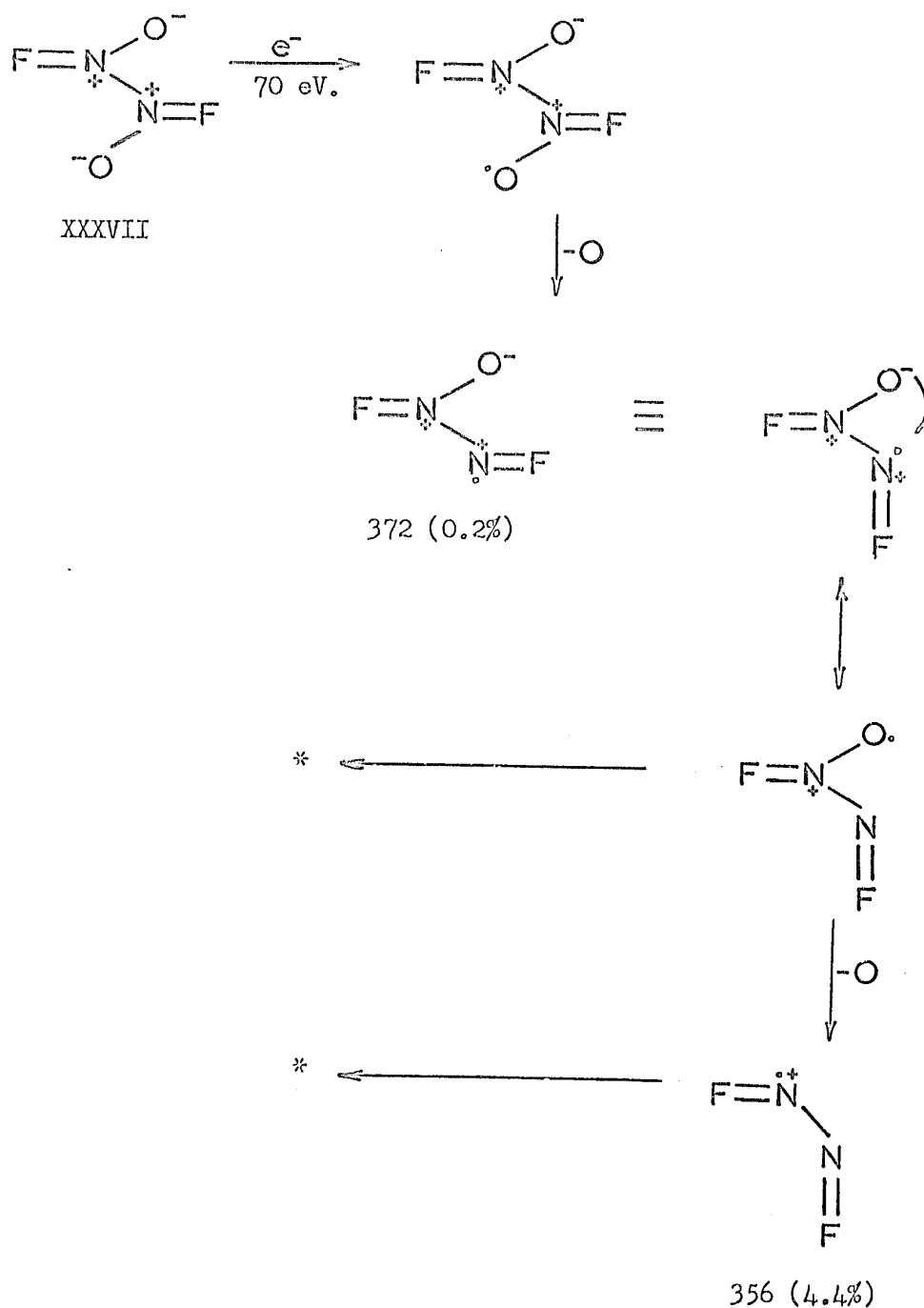
corresponding to a loss of oxygen from the molecular ion peak. This would be expected for both A and B, due to the presence of an N-oxide functionality ((38); also see Fig. 3). Further fragmentation of this resulting ion (mass 372, Fig. 5) proceeded in a manner which was strikingly similar to the fragmentation pattern observed for fluorenon-azinemonoxide (XXX; see Appendix A). The fragmentation pattern for structure D* would be expected to be very different from that actually observed for compound XXXVII.

In the light of the forementioned results, it seems that compound XXXVII may best be represented by structure A, fluorenonazine-bis-N-oxide.

The acid hydrolysis of compound XXXVII occurred very rapidly to give a one-to-one mixture of fluorenone and its oxime XI. A possible mechanistic scheme for this process was derived in analogy with the mechanism which had been proposed by Horner et al. for the hydrolysis of aldazinemonoxides (XXXIII; Fig. 2-A).

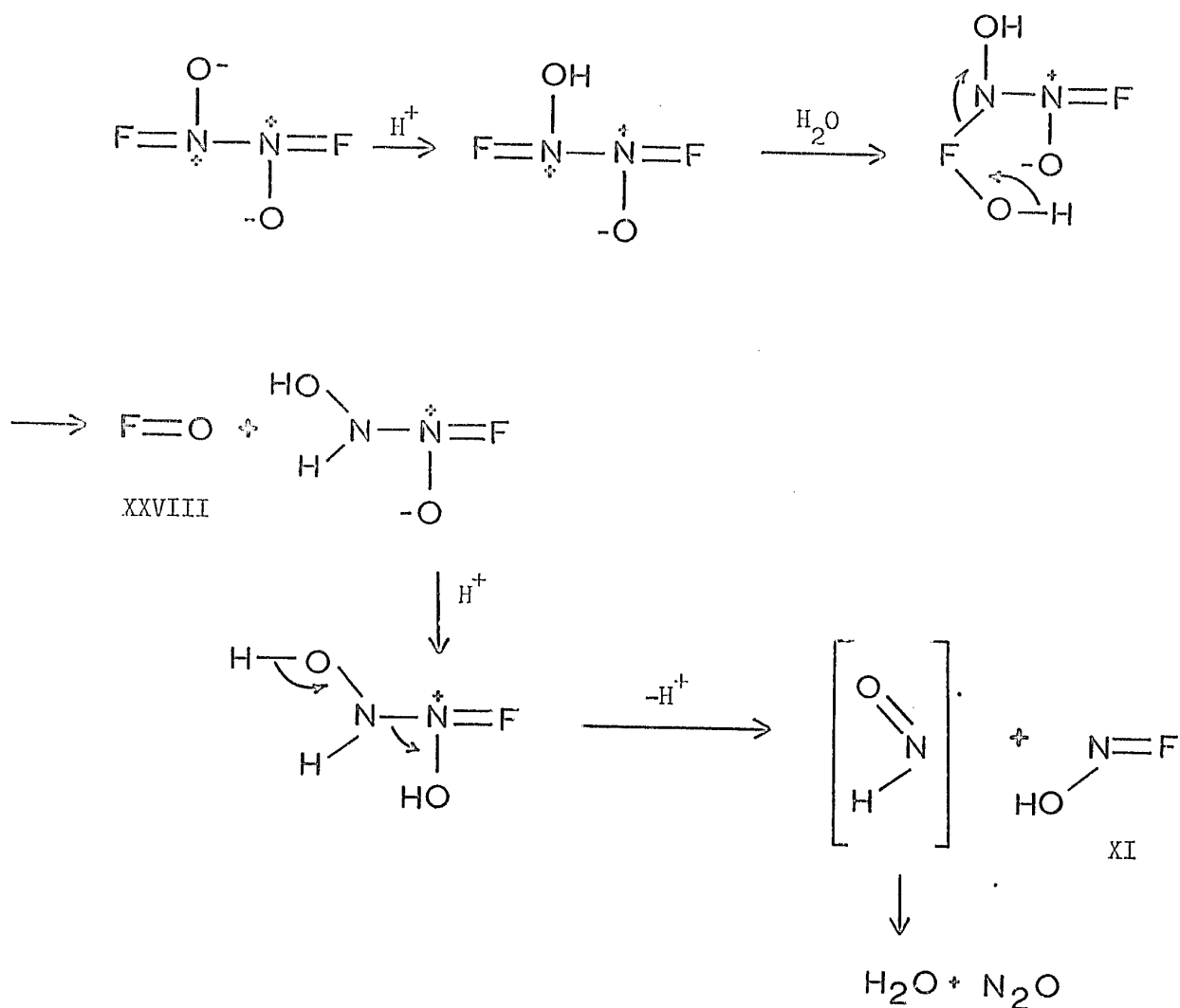
* A large abundance of iminyl cations ($m/e = 178$) might be expected due to the known stability of the fluorenone iminoxyl radical (XI_R). The base peak, however, corresponded to the fluorenone cation ($m/e = 180$), while the 178 peak was only 7.1% of the base peak.



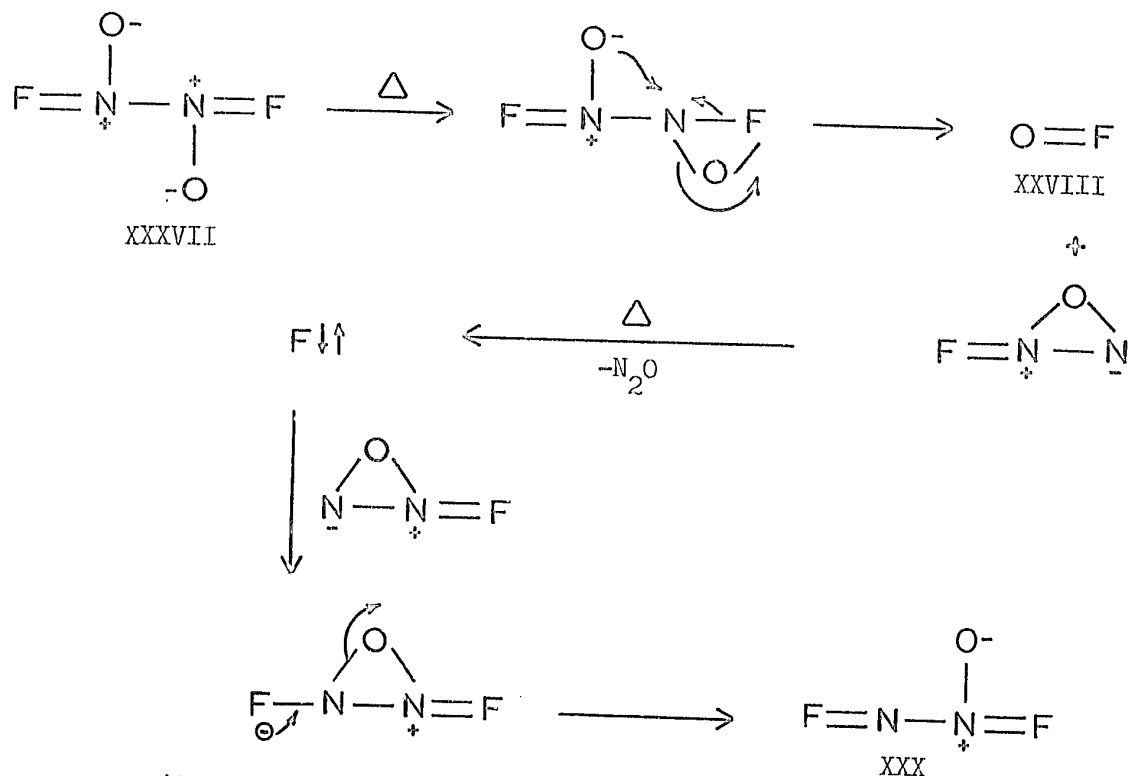


* Similar to fluorenonazinemonoxide (p. 28) fragmentation pattern (see Fig. 3 and Appendix A).

FIG. 5. Probable Fragmentation Pattern for Fluorenonazine-N-bis-oxide (XXXVII).



The pyrolysis of fluorenazine-bis-N-oxide (XXXVII) resulted in the formation of fluorenone (XXVIII) and fluorenazinemonoxide (XXX) in major and minor yield respectively. The reaction scheme below was formulated in analogy with the mechanism proposed for formation of parent ketone and azine from the photolysis of azinemonoxides (36); the azine formation arising from the reactions of intermediary diazomethanes (41).



Attempts to reduce fluorenonazine-bis-N-oxide (XXXVII) with triphenylphosphine under a variety of conditions were unsuccessful. This was surprising in the light of the facile reduction of aldazine-bis-N-oxides (XVIII) at room temperature (30)*, leading to the corresponding aldazines.

* Differences in reactivity between ketazinemonoxides and aldazinemonoxides have been previously described (Fig. 2) for acid hydrolyses.

TABLE V

IR DATA OF FLUORENONE DERIVATIVES AND ANHYDRIDE-N-OXIDES

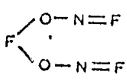
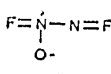
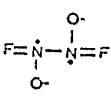
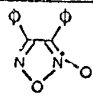
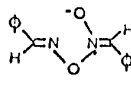
 XXVII	 XXVI	 XI	 XXX	 XXXVII	 (1650-650 cm ⁻¹)	 (1650-650 cm ⁻¹)
3050 (w-n)		3050	3040 (w)			
1940, 1910 (w)	1940, 1910 (w)	2710 (w-n)		1750 (w-n)		
1740 (w)				1710 (w-n)		
1720 (n)	1700 (w)			1640 (w)		
1625 (n)		1600 (w-n)		1620 (w)		
1605 (s)	1605 (sh, w-n)	1630 (n)	1620 (w-n)	1620 (n)		
1590 (sh, w-n)	1590 (s)	1605 (s)	1610 (n)	1610 (sh, n)		
		1590 (sh, w)	1580 (n)	1590 (sh, w)		
	1560 (s)		1570 (sh, n)		1582 (s)	1575 (s)
			1540 (s)	1520 (s)	1567 (s)	
1440 (s)	1450 (s)	1440 (s)	1470 (w-n)	1500, 1470 (sh, w-n)	1495 (n)	1479 (n)
	1375 (n)	1410 (n)	1450 (s)	1450 (n)	1448 (n)	
	1360 (n)			1410 (w)		1444 (s)
	1350 (s)			1380, 1370 (w)		1419 (s)
1320 (n)	1320 (s)	1320 (n)	1350 (w)	1350 (w)		
1300 (n)	1300 (s)		1340 (w)	1330 (w-n)	1320 (n)	
1230, 1210 (n)	1290 (sh, n)		1310 (w-n)	1310 (n)		1313 (n)
	1200 (n) 1134 (n-s)		1268 (s)	1235, 1212 (n)		
1158 (w-n)	1158, 1112 (w-n)	1158 (w-n)	1210 (w)	1208 (n)		
1109 (w-n)	1110 (n)	1110 (w-n)	1170 (w)	1170 (w-n)	1160 (n)	1142 (n)
1090, 1065 (w)		1110 (w-n)	1040 (w)	1070 (n-s)		
1042 (w)	1032 (w)			1038 (n-s)		
1038, 1030					990 (n)	991 (n)
978 (n-s)	972 (w)	988 (n)	975 (n)	975 (s)		
965 (n-s)	968 (w)					
942 (sh, s) 931, 904 (s)	932 (w)	935, 918 (w-n)	910 (w)	915 (s)		
			878, 860 (w)	878, 860 (n)		
					825 (s)	835 (s)
780 (n-s)			785 (w-n)	782 (n)		858, 848 (n)
768 (n-s)	752 (n)		770, 765 (n)	765, 749 (n-s)		
736, 728 (n, s)	735 (s)	749, 720 (w, s)		730 (s)		
675, 666 (w)	655 (n)					
639 (n)			640 (w-n)	642 (n)		
620 (w)	618 (w-n)	620 (w-n)				
575 (w)	575 (n)		572, 540 (w)	590, 580 (w)		

TABLE VI

UV DATA OF FLUORENONAZINE AND N-OXIDES

$\lambda_{\text{max.}}$ (m μ)	$\lambda_{\text{max.}}$			
	$\text{F}=\text{N}-\text{OH}$	$\text{F}=\text{N}^+-\text{N}=\text{F}^-$	$\text{F}=\text{N}-\text{N}=\text{F}$	$\text{F}=\text{N}^+-\text{N}^+=\text{F}^-$ -O
226	3,555		6,580	
230				10,710
232	3,148			9,902
240		5,723		
247	5,281			7,275
250				7,275
255		5,342		
256	6,805			
257				8,487
261		6,486	7,227	
276	1,523*			
278				3,840
280			2,157*	
305	1,117			1,819
310		763		
315	609			
320			1,942	1,010
337		2,098		
350		2,480		
360			1,726	
Solvent	CH_2Cl_2 -Ethanol (2:3)			
* shoulder				

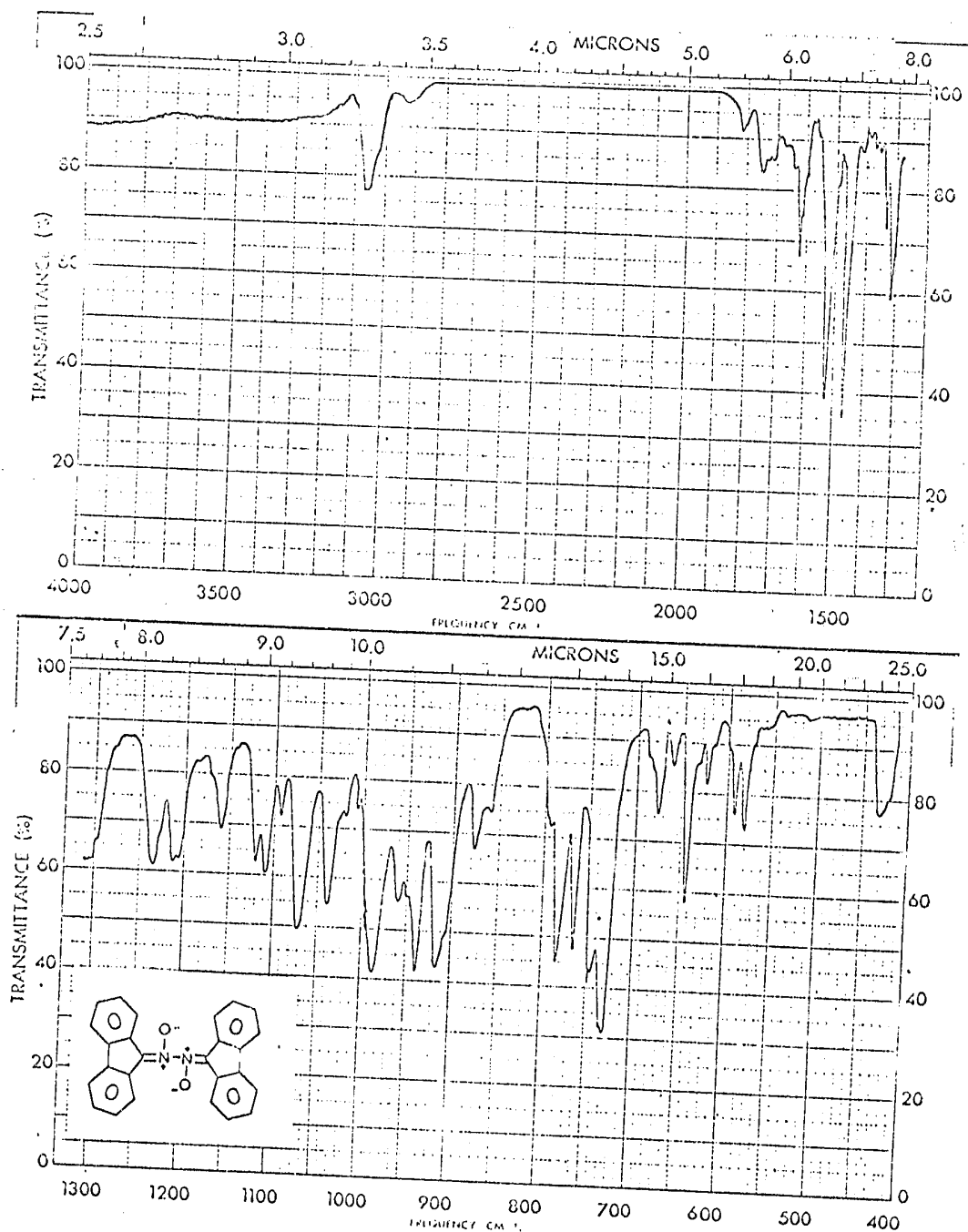
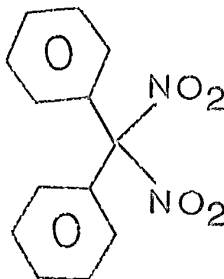


Fig. 6 - The IR Spectrum of Fluorennonazine-bis-N-oxide

1-2. Oxidation Products from Benzophenone Oxime

Dinitrodiphenylmethane (XXXVIII)

See Chapter IV for structure proof.



XXXVIII

1,1-Bis(diphenylmethyleniminooxyl)-diphenylmethane (XXXIX)

This compound, $C_{39}H_{30}N_2O_2$, was obtained from the lead tetraacetate oxidation of benzophenone oxime (IX) in glacial acetic acid. It was readily hydrolysed by acid to one part of benzophenone (XL) and two parts of benzophenone oxime (IX).

The ultraviolet spectrum of compound XXXIX (Table VII) contained absorptions at 233 and 264 $m\mu$ which were probably due to the presence of the C=N group (compare the different compounds entered in Table VII). This assignment was supported by the 1630 cm^{-1} absorption band found in the infrared* spectrum of XXXIX (Fig. 8, p. 45).

The above properties suggested a ketal structure analogous to the one established for 9,9-difluorenylideneiminooxylfluorene (XXVII). A calculation of extinction coefficient ratios for benzophenone oxime and compound XXXIX at each of the two wavelengths shown in Table VII

* A number of absorption peaks between 970 and 760 cm^{-1} were unique to this compound compared to other benzophenone derivatives, but no assignments could be made.

TABLE VII

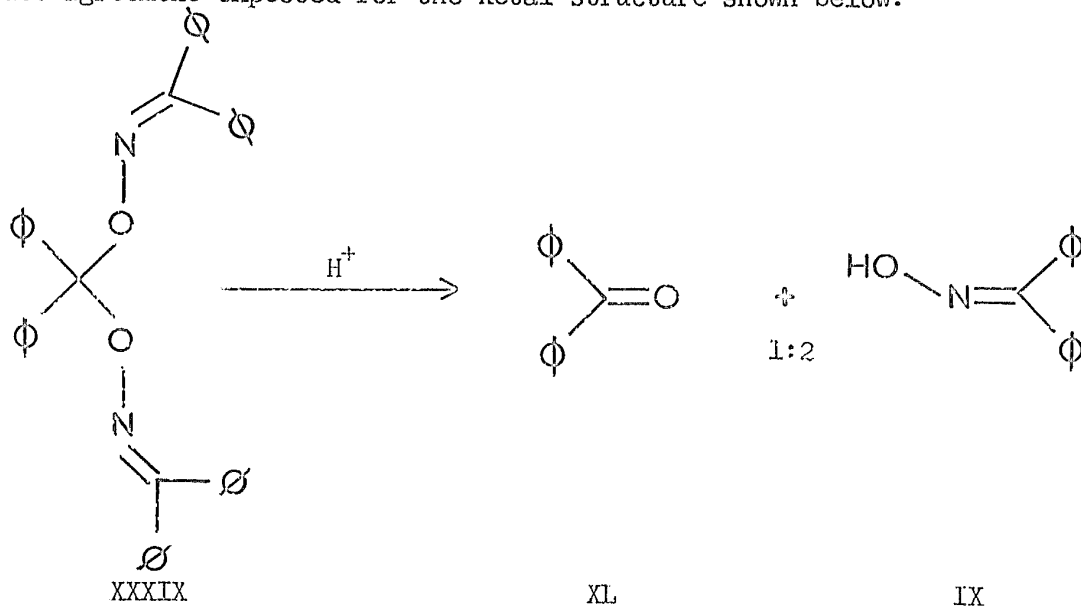
UV DATA OF BENZOPHENONE OXIME AND ITS OXIDATION PRODUCTS

$\text{Ph}_2\text{C}=\text{N}-\text{OH}$ IX		$\text{Ph}_2\text{C}=\text{N}-\text{O}-\text{N}(\text{Ph})_2$ XXXIX		$\text{Ph}_2\text{C}=\text{N}-\text{NO}_2$ XXXVIII		$\text{Ph}_2\text{C}=\text{N}-\text{NO}_2$ XLI	
λ_{max} (m μ)	ϵ_{max}	λ_{max} (m μ)	ϵ_{max}	λ_{max} (m μ)	ϵ_{max}	λ_{max} (m μ)	ϵ_{max}
						207	23,000
214	16,420	208	68,900	214	18,280		
230	14,140						
		233**	29,800				
250	10,360					258*	13,220
		264*	24,200	265*	1,985		
λ_{max} (m μ)	$\epsilon_{\text{IX}}/\epsilon_{\text{XXXIX}}$						
	Obs.	Calc.					
233	0.475	0.53					
264	0.428						
	% Deviation	15%					

* broad

** shoulder

(as had been done for the ketal of fluorenone, Table III) gave approximate agreement expected for the ketal structure shown below:



The mass spectrum of XXXIX contained a fragmentation pattern consistent with the assigned ketal structure (Fig. 7). A heavy fragment corresponding to the loss of an iminoxyl radical from the parent ion was observed as in the case for the ketal of fluorenone (Fig. 1-A).

Benzophenone nitrimine (XLI)

The lead tetraacetate oxidation of benzophenone oxime (IX) in oxygen-free glacial acetic acid afforded, in 11% yield, a compound XLI with elemental analysis C₁₃H₁₀N₂O₂. It was readily hydrolysed and pyrolysed to benzophenone, with evolution of brown nitrous fumes in the latter case.

The following structures A-D are consistent with this behaviour.

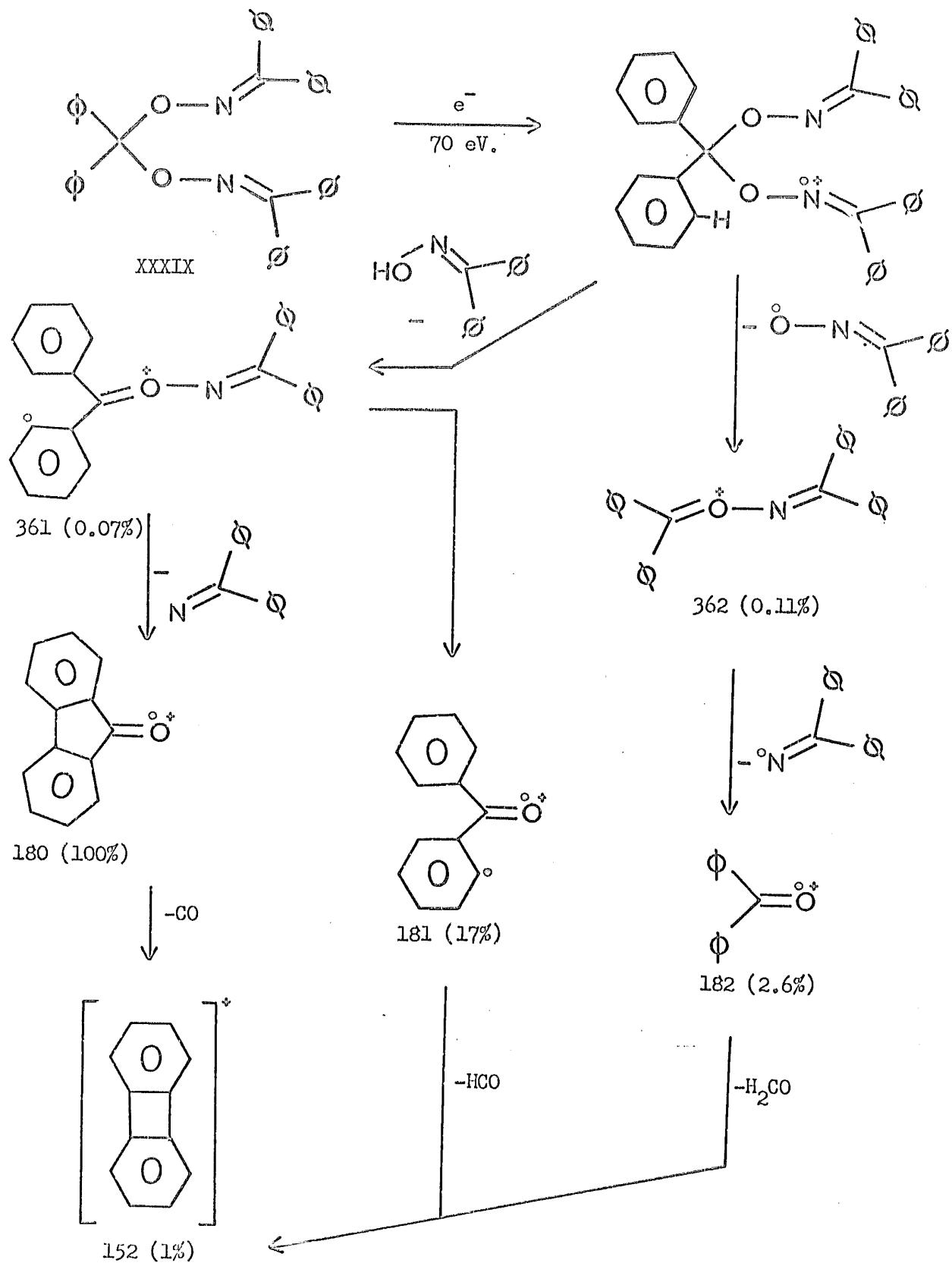
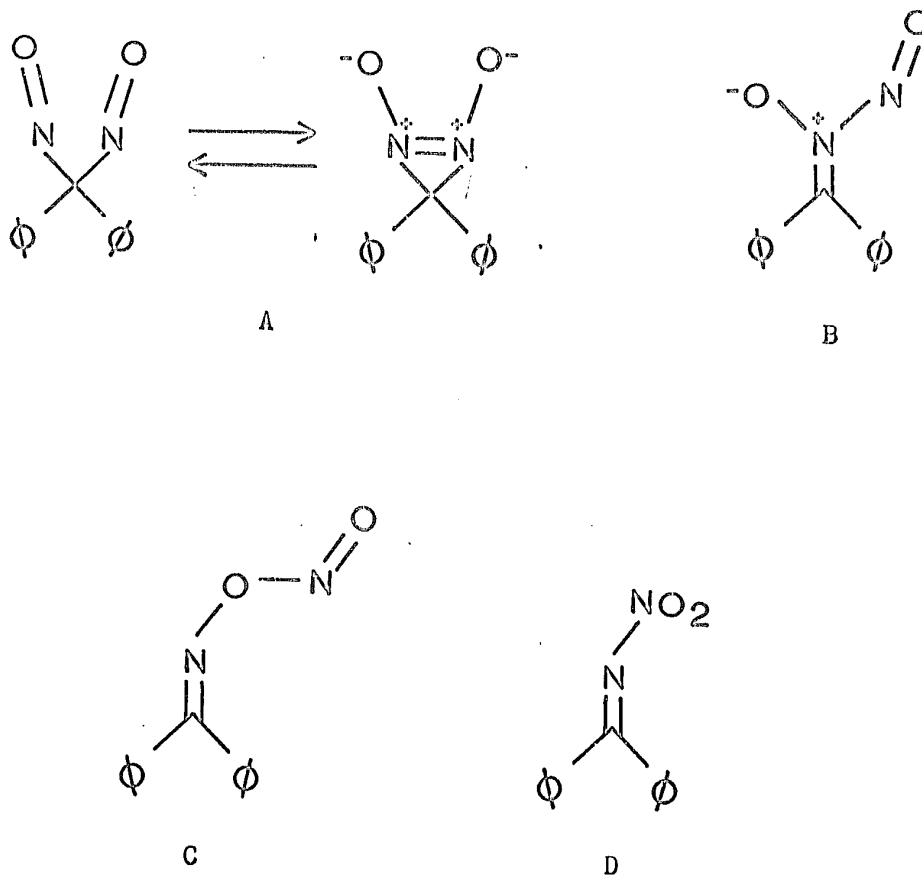


FIG. 7. Probable Fragmentation Pattern of 1,1-Bis(diphenylmethylenediminoxy)-diphenylmethane (XXXIX).



The infrared spectrum of compound XLI in KBr (Fig. 10, p. 49) had strong absorption bands at 1540 cm^{-1} and 1270 cm^{-1} , characteristic of the $\text{N} \rightarrow \text{O}$ stretching vibrations found in azine N-oxides and nitrimines (36). The spectrum of XLI in chloroform had two strong bands at 1575 and 1300 cm^{-1} , assigned as above, as well as a weak absorption at 1630 cm^{-1} corresponding most probably to the $\text{C}=\text{N}$ stretch.

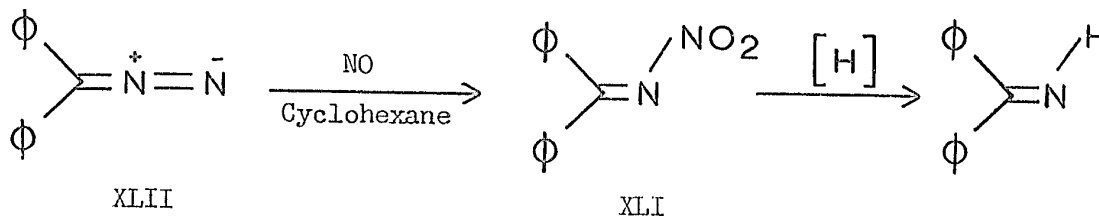
The ultraviolet spectrum of XLI (Table VII) contained a strong absorption band at $258\text{ m}\mu$ (ϵ 13,220) which was probably due to the electron transfer excitation of the diphenylmethylenimine skeleton. This supported the above (IR) $\text{C}=\text{N}$ functional assignment.

Structure A can be ruled out since it is lacking the $\text{C}=\text{N}$

functionality and would not have the above two intense bands in its infrared spectrum. Structure C does not have any N $\longrightarrow$ O functionalities.

The mass spectrum of compound XLI contained a fragmentation pattern fully consistent with the nitrimine structure D (Fig. 9) but inconsistent with structure B. A weak parent peak at mass 226, with no heavy ions corresponding to the loss of atomic oxygen or nitric oxide (expected for structure B), was observed. The formation of a base peak at mass 30, corresponding to NO^+ , has been reported for other nitro compounds (42).

An independent synthesis of the nitrimine of benzophenone from diazodiphenylmethane (XLII) was carried out according to the method of Horner et al. (30). This synthetic sample was found to be identical* with compound XLI (IR, t.l.c., mixed melting points). Horner and Kirmse et al. (30) assigned the nitrimine structure to their compound from the observation that catalytic hydrogenation led to the corresponding imine derivative.



* Spectral evidence for the structure proof of the nitrimine XLI was provided, in addition to the independent synthesis, because of the controversy which existed in the literature concerning the true structure of these compounds.

*** 165 (4.2%) and 164 (0.9%) due to loss of H radicals were also observed.

FIG. 2. Probable Fragmentation Pattern for Benzophenone Nitrimine (XLI).

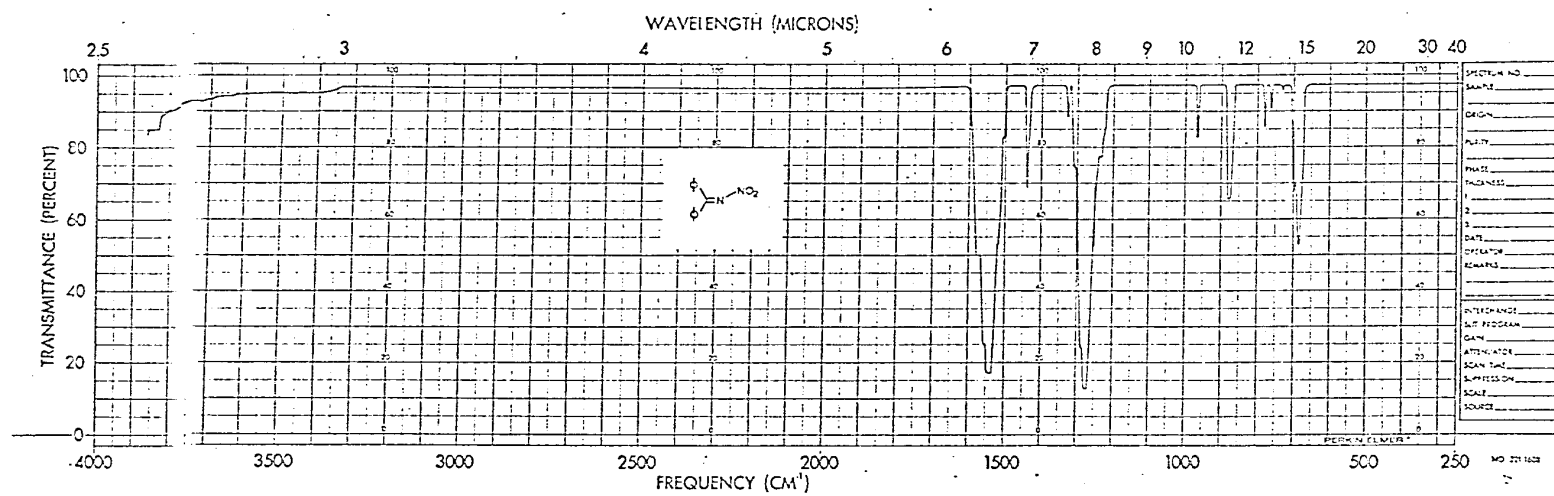


FIG. 10. The IR Spectrum of Benzophenone Nitrimine.

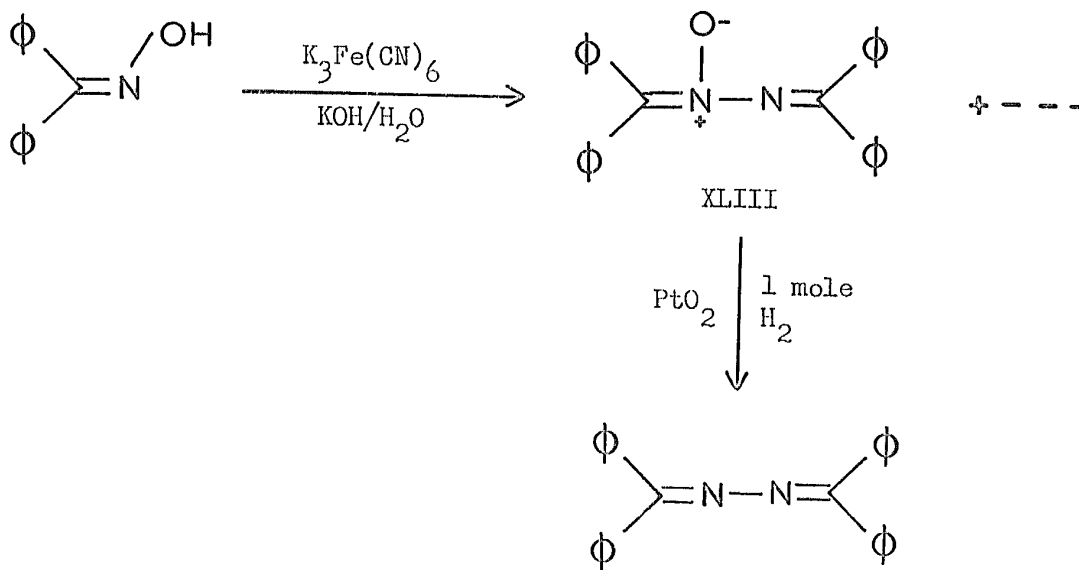
Benzophenonazinemonoxide (XLIII)

The lead tetraacetate oxidation of benzophenone oxime (IX) in methylene chloride led to the formation of a compound XLIII in 35% yield, m.p. 153-4.5° (dec.), having an R_f value (t.l.c.) smaller than that of oxime IX. The infrared spectrum of compound XLIII contained strong absorption peaks at 1552, 1512 and 1238 cm^{-1} . Similar absorption peaks, observed at 1570 (m), 1540 (s), and 1268 (v.s.) cm^{-1} for fluorenonazine-monoxide (XXX), had been assigned to the $\text{N} \longrightarrow \text{O}$ group in the azine-monoxide structure.

The foregoing observations lent strong support to the assignment of an azinemonoxide structure for compound XLIII.

An authentic sample of benzophenonazinemonoxide was prepared by the ferricyanide oxidation of benzophenone oxime described by Lauer and Dyer (31,43) and shown to be identical with compound XLIII (t.l.c., IR, mixed melting point).

The authentic sample had been characterized by its quantitative reduction to diphenylketazine.



Chapter 2

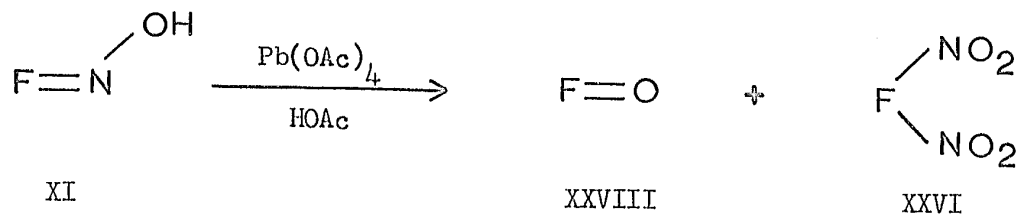
Oxidation of Fluorenone Oxime

2-1. Oxidation in Glacial Acetic Acid

2-1.1. Lead tetraacetate

As shown in the introduction, iminoxyl nitroxides were readily formed when oximes were oxidized with lead tetraacetate. Fluorenone oxime (XI) was chosen as the model compound for thorough investigation because of its symmetry and fixed geometry. Fortuitously, when the investigation was already in progress it was reported that the iminoxyl radical of fluorenone oxime (XI_R) was one of the most stable of all known iminoxyl nitroxides (Table I).

Upon addition of lead tetraacetate to fluorenone oxime (XI) in glacial acetic acid, the yellow solution turned dark amber. After two minutes, nearly all of the oxime was consumed (t.l.c.). Fluorenone (XXVIII) was the major product formed (50%, chromatography). Chromatography or direct crystallization of the crude product obtained upon work-up afforded colourless crystals of 9,9-dinitrofluorene (XXVI) in 20% yield:



Variations in the amount of lead tetraacetate added, from a half-mole to two mole equivalents, and in the mode of addition did not give any significant change in the yield of dinitrofluorene (XXVI) (Table VIII-A). It was however very significant that a half-mole equivalent of lead tetraacetate led to complete consumption of the fluorenone oxime and that another product, ketal XXVII, was formed in 3-4% yield.

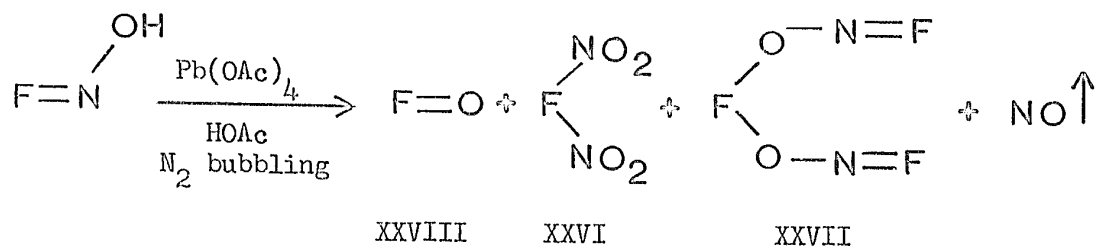
The stoichiometry of this reaction strongly suggested that the same oxygen atoms in the nitro groups of 9,9-dinitrofluorene were being provided by molecular oxygen which had not been excluded from the acetic acid reaction solutions.

Reaction of a one mole equivalent of lead tetraacetate with fluorenone oxime in glacial acetic acid saturated with oxygen indeed led to a small* increase in the yield of 9,9-dinitrofluorene.

The above experiment was repeated with bone-dry nitrogen passing through the glacial acetic acid just prior to and during the reaction, in order to remove most of the dissolved oxygen. A decrease in the yield of 9,9-dinitrofluorene (XXVI) was observed. The nitrogen exhaust was led through liquid air traps. After completion of the reaction, these traps contained a blue solid which when warmed up and exposed to air gave a dark brown gas. This indicated that nitric oxide** had been formed (confirmed by IR).

* The commercial acetic acid used already contained dissolved oxygen (see section 1.2).

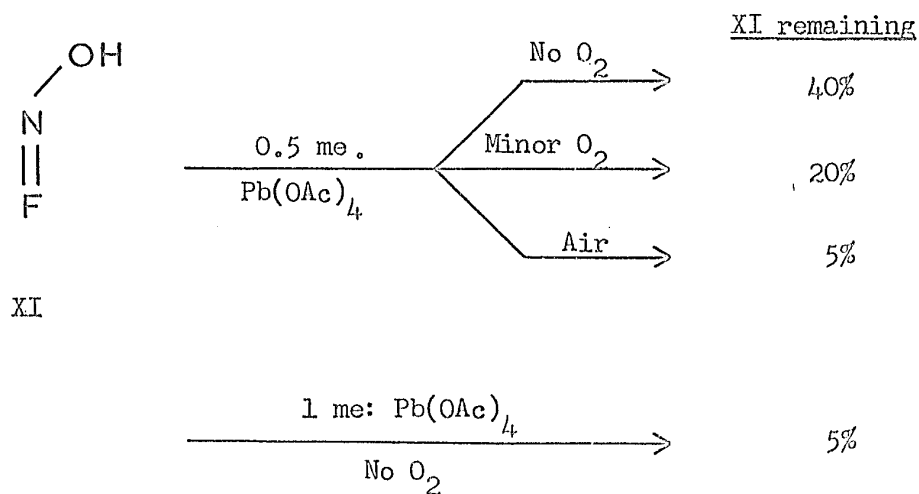
** In the presence of oxygen, it seemed likely that nitrogen dioxide would be involved in the reaction. This study will be taken up in Section 1.3).



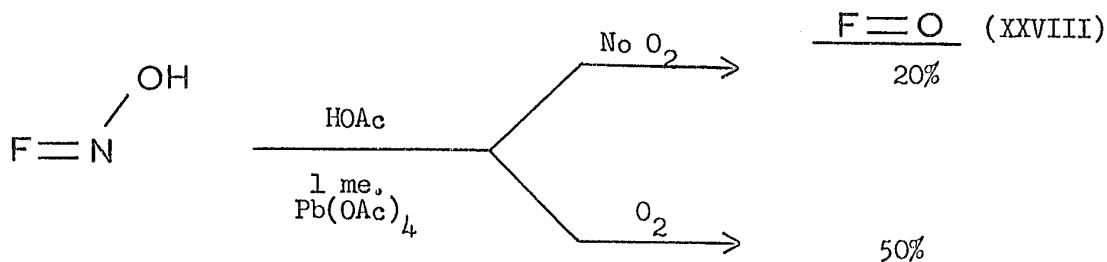
Under these conditions, 9,9-difluorenylideneiminoxyfluorene (XXVII) was also formed, in ca. 4% yield (Table VIII-A).

Having found that oxygen influences the product distribution in these oxidations, experiments were conducted in oxygen-free acetic acid.

With a half-mole equivalent of lead tetraacetate (entry 1, Table VIII-B), only 0.6 mole equivalents of fluorenone oxime were consumed, in sharp contrast to the oxidation in the presence of oxygen. Under the same reaction conditions, a one mole equivalent of lead tetraacetate (entry 5, Table VIII-B) led to complete reaction of the oxime. Removal of nitric oxide from these reaction media by purging with inert gas did not affect the yield of oxime consumed. When glacial acetic acid, freed of most of its dissolved oxygen by brief purging with inert gas prior to addition of reagents (entries 3 and 4), was used in the reaction of a half-mole equivalent of lead tetraacetate with fluorenone oxime, up to 80% of the oxime was consumed.



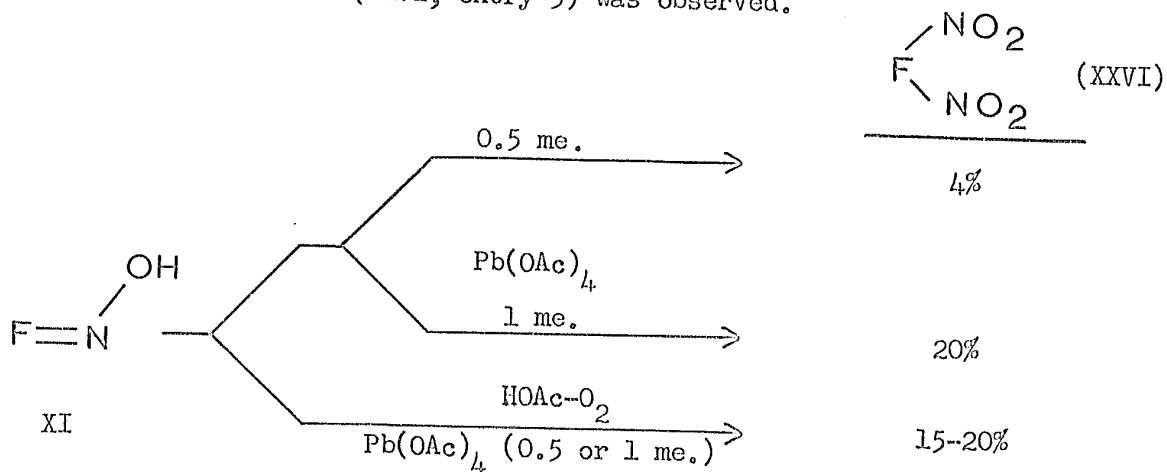
The yield of fluorenone (XXVIII) decreased by about 30% when the oxidation of fluorenone oxime was conducted in oxygen-free glacial acetic acid (Table VIII-B) rather than in commercial acetic acid in the presence of air (Table VIII-A).



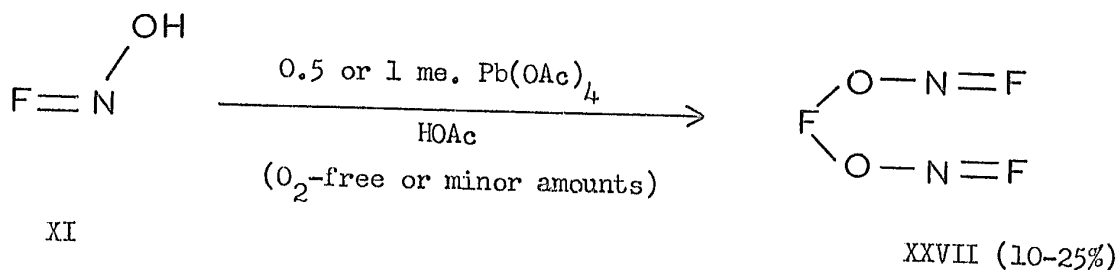
me = mole equivalent

A very minor amount of dinitrofluorene (XXVI) was formed when a half-mole equivalent of lead tetraacetate was reacted with fluorenone oxime in oxygen-free acetic acid (Table VIII-B). This low yield of 4% was maintained when helium was bubbled through the reaction solution and was also unchanged when acetic acid containing minor amounts of oxygen (entries 3 and 4, Table VIII-B) was used as solvent. However, when oxidation of oxime XI was effected with one mole equivalent of lead tetraacetate in oxygen-free acetic acid, a large increase in the production of

9,9-dinitrofluorene (XXVI, entry 5) was observed.



Finally, it was found that the yield of ketal XXVII in the absence of oxygen remained nearly* constant for 0.5-1 mole equivalent of lead tetraacetate used (entries 1 and 5, Table VIII-B) and was unaffected by the mode of addition of the lead tetraacetate (entry 6) or removal of nitric oxide from the reaction solution (entry 2). The yield of XXVII produced was still about 25% when acetic acid containing very minor amounts of dissolved oxygen was used (entries 3 and 4).

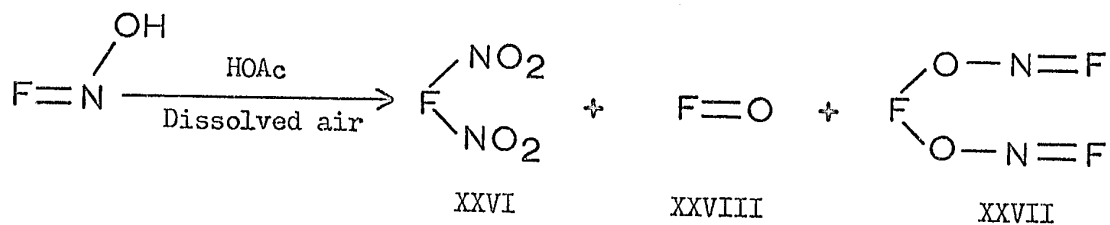


* A more careful report for variations in yields of XXVII is not given since some experiments were not more reproducible than the range indicated.

In all the reactions described above (Table VIII) there was also formed, in minor amounts, a compound identified as fluorenone oxime O-acetate (XXXV). Its mode of formation will be taken up in the discussion.

2-1.2. Molecular oxygen

The stability of fluorenone oxime in glacial acetic acid containing dissolved air* was tested by leaving it in solution, at room temperature, for twenty-four hours**. A precipitate was obtained in 13% yield consisting of the fluorenylideneiminyll ketal of fluorenone (XXVII). The mother liquor consisted of 60% fluorenone (XXVIII) and 25% 9,9-dinitrofluorene (XXVI) (t.l.c. and IR).



A reaction conducted as above in the absence of light led to the same product distribution.

In a blank run, bone-dry nitrogen was passed through a solution of the oxime in glacial acetic acid. Fluorenone oxime was recovered quantitatively. On the other hand, when oxygen was blown through the solution, the formation of ketal XXVII was suppressed, while fluorenone

* A freshly opened commercial bottle (Anachemia) was used. Saturation with oxygen did not alter the results.

** The disappearance of oxime was monitored by t.l.c. Only a minor amount of products had formed after 12 hours.

TABLE VIII-A
LEAD TETRAACETATE OXIDATION OF FLUORENONE OXIME IN
OXYGEN-CONTAINING GLACIAL ACETIC ACID

PRODUCT	PRODUCT YIELD (MOLE %)					
	ATMOSPHERIC				OXYGEN BUBBLING	NITROGEN BUBBLING
	1:1 ¹	1:2 ²	1:2	1: $\frac{1}{2}$	1:1	1:1
$\begin{array}{c} \text{O}-\text{N}=\text{F} \\ \diagup \\ \text{F} \\ \diagdown \\ \text{O}-\text{N}=\text{F} \end{array}$ XXVII	0	0	0	3	0	⁴ (10) ³
$\begin{array}{c} \text{NO}_2 \\ \diagup \\ \text{F} \\ \diagdown \\ \text{NO}_2 \end{array}$ XXVI	20	22	20	15	25	12
$\begin{array}{c} \text{F}=\text{O} \\ \text{XXVIII} \end{array}$	50	-	-	-	-	-
$\begin{array}{c} \text{OAc} \\ \diagup \\ \text{F}=\text{N} \\ \text{XXXV} \end{array}$	≤ 10	≤ 10	≤ 10	≤ 5	≤ 10	≤ 9
$\begin{array}{c} \text{OH} \\ \diagup \\ \text{F}=\text{N} \end{array}$	≤ 5	≤ 5	≤ 5	≤ 5	≤ 5	≤ 5

¹ Molar ratio of oxime XI to lead tetraacetate.

² Dropwise addition of lead tetraacetate. In all other cases the latter was added in one scoop.

³ Yield obtained when 1 g oxime XI was used in place of usual 585 mg.

TABLE VIII-B

LEAD TETRAACETATE OXIDATION OF FLUORENONE OXIME IN OXYGEN-FREE GLACIAL ACETIC ACID

ENTRY	Reactant Ratio ¹	Time in hours	Reaction Conditions	PRODUCT YIELD (%)				
				$\text{F} \begin{cases} \text{O}-\text{N}=\text{F} \\ \text{O}-\text{N}=\text{F} \end{cases}$ XXVII	$\text{F} \begin{cases} \text{NO}_2 \\ \text{NO}_2 \end{cases}$ XXVI	$\text{F}=\text{O}$ XXVIII	$\text{F}=\text{N} \begin{cases} \text{OH} \end{cases}$ XI	$\text{F}=\text{N} \begin{cases} \text{OAc} \end{cases}$ XXXV
1	1: $\frac{1}{2}$	2	Helium atmosphere	11-25% ⁴	4%	22%	40%	≤5%
2		2	Helium bubbling	15%	3%	20%	40%	≤5%
3		1	Helium atmosphere ²	26%	4%	21%	20%	≤7%
4		2	Nitrogen ² bubbling	16% (32%) ³	4%	17%	25%	≤7%
5	1:1	$\frac{1}{2}$	Nitrogen atmosphere	25%	20%	24%	≤5%	≤6%
6		$\frac{1}{2}$	Nitrogen atmosphere ⁵	20%	-	-	-	-

¹ Molar ratio of oxime to lead tetraacetate.² Glacial acetic acid was purged with dry gas just prior to use. In all the other experiments, oxygen-free acetic acid was used.³ Double the reagents were used.⁴ Variations under similar experimental conditions were obtained.⁵ Dropwise addition of lead tetraacetate solution.

and 9,9-dinitrofluorene were obtained in 65% and 30% yield respectively.

The oxidation of fluorenone oxime by molecular oxygen dissolved in glacial acetic acid was suppressed by the addition of water (~10%), concentrated hydrochloric acid or trifluoroacetic acid (50%). No reaction occurred in pure trifluoroacetic acid either. The use of other solvents (see Table IX) also led to no reaction.

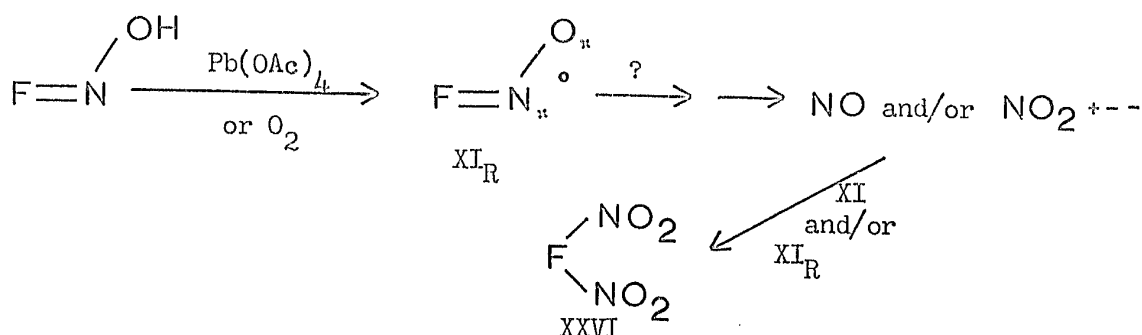
The oxidation did not proceed in absolute ethanol containing potassium hydroxide nor in glacial acetic acid saturated with anhydrous sodium acetate*.

TABLE IX
AUTOXIDATION OF FLUORENONE OXIME

Reaction conditions	Yield of Products (mole %)		
	$\text{F}=\text{O}$ XXVIII	$\text{F} \begin{array}{l} \nearrow \text{NO}_2 \\ \searrow \text{NO}_2 \end{array}$ XXVI	$\text{F} \begin{array}{l} \nearrow \text{O}-\text{N}=\text{F} \\ \searrow \text{O}-\text{N}=\text{F} \end{array}$ XXVII
HOAc-saturated with oxygen	60%	25%	13%
HOAc-blowing oxygen	65%	30%	0%
HOAc-blowing nitrogen	-	-	-
HOAc-O ₂ /H ⁺ (H ₂ O, HCl or CF ₃ COOH)	-	-	-
HOAc-O ₂ -NaOAc	-	-	-
Benzene-O ₂	-	-	-
EtOH/Ether (9:1)-O ₂	-	-	-
EtOH/KOH-O ₂	-	-	-

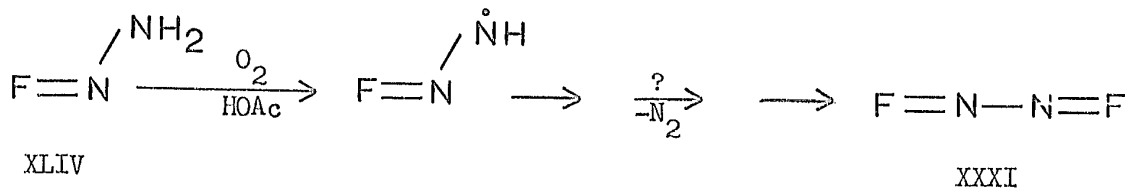
* Sodium acetate is a weaker base than the sodium salt of fluorenone oxime (see experimental).

Since the autoxidation reaction described above (summarized in Table IX) led to the same products as those obtained in the lead tetraacetate oxidation of fluorenone oxime in glacial acetic acid, it seemed likely that the formation of the iminoxyl radical XI_R was probably the same primary process in both cases, leading to the formation of nitric oxide and/or nitrogen dioxide in secondary steps. The formation of



9,9-dinitrofluorene (XXVI), in particular, may have been due to secondary reactions with nitrogen dioxide.

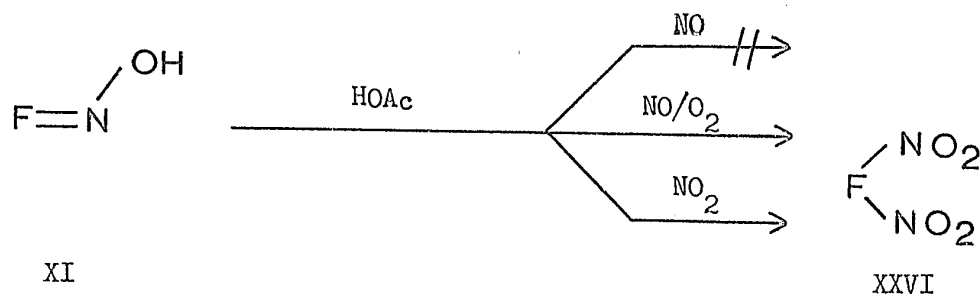
It is interesting to note that the autoxidation of fluorenone hydrazone (XLIV), conducted as for fluorenone oxime, led to quantitative formation of fluorenonazine (XXXI)*. If the autoxidation followed a reaction path similar to that shown for fluorenone oxime (XI), secondary products would be minimized since inert nitrogen, rather than nitrogen oxides, might be expected as a side product.



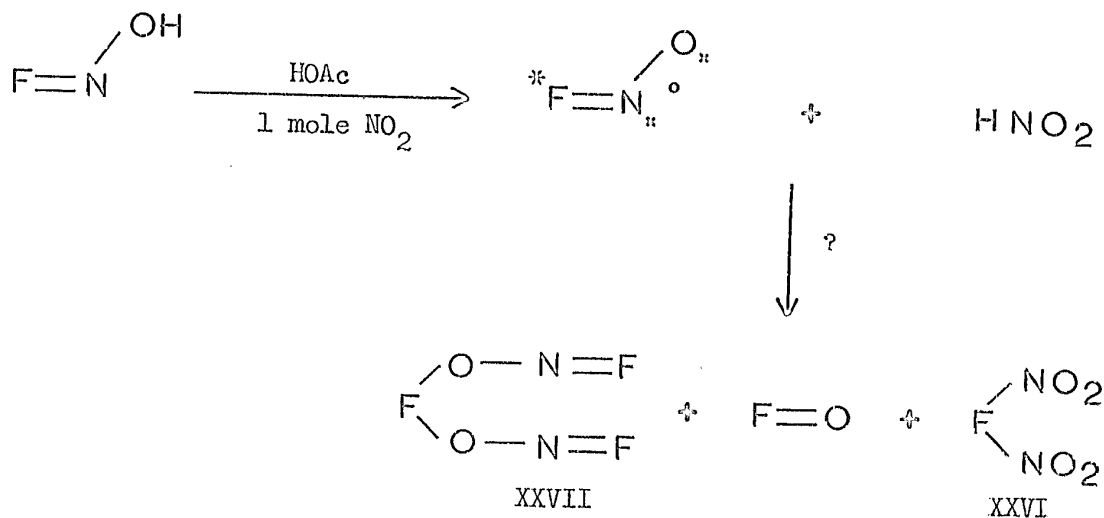
* This represents a new, facile method for formation of XXXI.

2-1.3. Nitrogen oxides

It was shown in section 1.1 that nitric oxide was generated in situ in the lead tetraacetate oxidation of fluorenone oxime (XI) in glacial acetic acid. When nitric oxide was passed through an oxygen-free acetic acid solution of oxime XI, no reaction occurred. However, addition of the oxime to an acetic acid solution saturated with nitric oxide exposed to air led to quantitative formation of 9,9-dinitrofluorene (XXVI). When the reaction was repeated with an acetic acid solution saturated with nitrogen dioxide, the same results were obtained.



Since nitrogen dioxide is a potential one-electron oxidizing agent, it was decided to use it to simulate the lead tetraacetate oxidation of fluorenone oxime. The dropwise addition of a dilute solution of a one mole equivalent of nitrogen dioxide in glacial acetic acid to the oxime in oxygen-free acetic acid led to the formation of 9,9-difluorenylidene-iminoxyfluorene (XXVII) in four percent yield. Unreacted oxime still remained (40%), while fluorenone and 9,9-dinitrofluorene (XXVI) were formed as the major products in about 15 and 30% yields respectively.



2-1.4. Ionic-type oxidizing agents

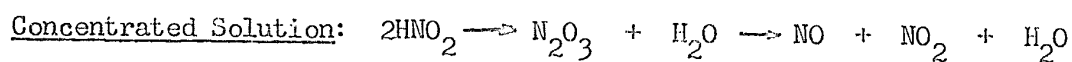
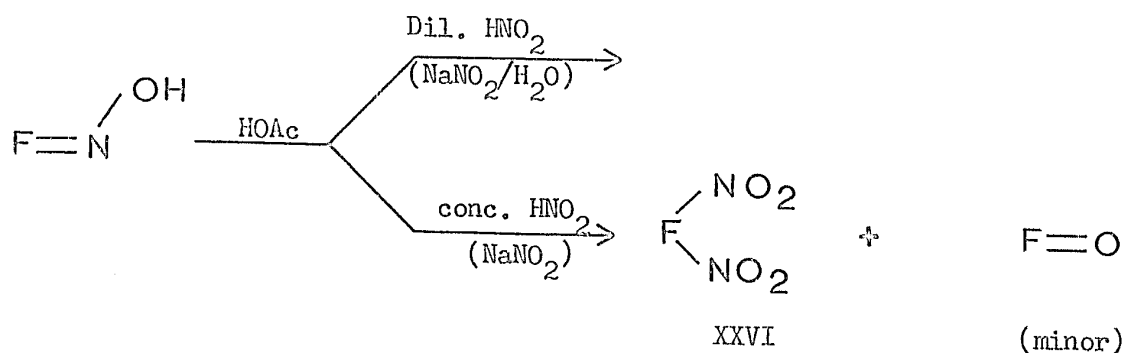
In the oxidation of fluorenone oxime with nitrogen dioxide, the primary step probably led to formation of nitrous acid. Its effect as a nitrosating agent was therefore investigated.

A dilute solution of aqueous sodium nitrite was slowly added to fluorenone oxime in acetic acid. No reaction occurred. Since these were typical nitrosating conditions (44), it was clear that fluorenone oxime did not react in an ionic fashion with the nitrous acid generated in situ.

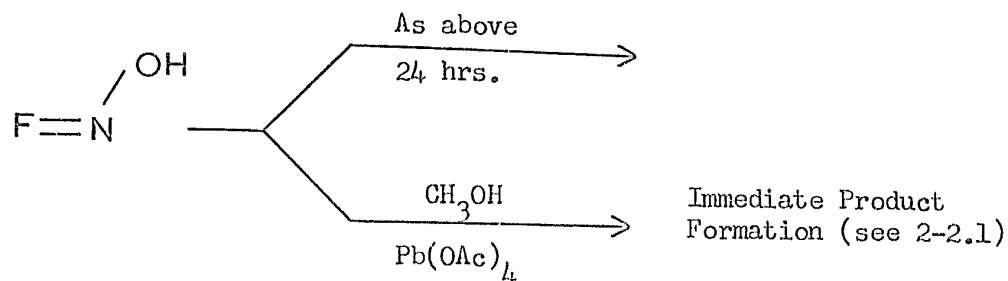
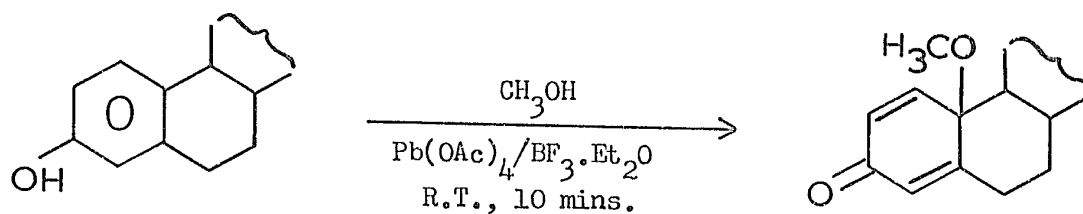
When the reaction was repeated by adding solid sodium nitrite all at once, mainly 9,9-dinitrofluorene (XXVI) was formed due to the expected generation of nitrogen dioxide in situ** (44,45).

* The mechanism is dealt with in the discussion (5-4).

** Reported for aqueous solutions but a qualitative study for the above systems indicated analogous results (see experimental).



The selective oxidation of fluorenone oxime via a free radical process was further demonstrated by its resistance to oxidation by 50% hydrogen peroxide, 40% peracetic acid, and by the lead tetraacetate-boron trifluoride etherate oxidizing mixture. The last-mentioned procedure has been used to convert a phenol to a dienone (46), as shown below.

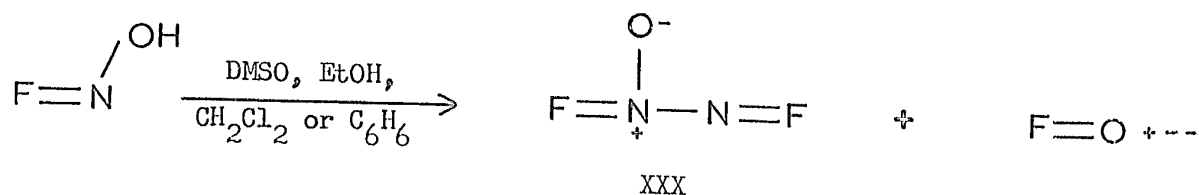


2-2. Oxidation in Methylene Chloride

2-2.1. General solvent effect in lead tetraacetate oxidations

Glacial acetic acid has been reported as favouring ionic or free radical reactions in lead tetraacetate oxidations (47), according to the substrate being oxidized. In the oxidation of fluorenone oxime, the nitroxyl radical (XI_R) is produced in glacial acetic acid as well as in methylene chloride (48). However, when solvents other than glacial acetic acid were used in the lead tetraacetate oxidation of fluorenone oxime, a radical change in product formation occurred.

Reaction of a one mole equivalent of lead tetraacetate with fluorenone oxime in methanol was immediate. A yellow solution was obtained from which about 30% of starting oxime was recovered. Aside from four minor unidentified products and fluorenone (XXVIII), a new major compound XXX, fluorenonazinemonoxide, was formed. The use of highly polar dimethyl sulfoxide, wet ether, benzene or methylene chloride as solvents in the above reaction led in all cases to formation of fluorenone (XXVIII) and XXX as major and minor products respectively. Other minor impurities were formed depending on the solvent used.



The lead tetraacetate oxidation of fluorenone oxime was investigated in detail in methylene chloride because (i) the simplest product distribution was obtained (t.l.c.), (ii) the existence of the

nitroxyl radical of fluorenone oxime has been shown in this particular solvent, (iii) the solvent can readily be evaporated at room temperature, (iv) lead acetate produced in the reduction of lead tetraacetate is very insoluble in this solvent.

2-2.2. Lead tetraacetate oxidation of fluorenone oxime in methylene chloride

Addition of a half-mole equivalent of lead tetraacetate to fluorenone oxime in methylene chloride, flushed with nitrogen, immediately led to a light orange solution. The solution turned brown and after five minutes, lead acetate precipitated out. A negative starch-iodide test, indicating absence of lead tetraacetate and/or any other reducible compounds, was only obtained after 1.5 hours (entry 2, Table X). A careful chromatography of the red oil obtained after work-up gave about 15% of fluorenonazinemonoxide (XXX), 50% of fluorenone (XXVIII) and minor amounts of dinitrofluorene (XXVI, < 1%) and ketal XXVII (1-3%).

When one mole equivalent of lead tetraacetate was used in the above experiment repeated in the presence of oxygen, the same product distribution was obtained (entry 1, Table X) except that much unreacted lead tetraacetate remained even after twenty-four hours.

The effect of the mode of addition of the lead tetraacetate on the product distribution was next tested.

The addition (over a period of 0.5 hour) of a dilute methylene chloride solution (O_2 present) of fluorenone oxime to a half-mole equivalent of lead tetraacetate in methylene chloride led to the same product distribution obtained from the addition (all at once) of lead

tetraacetate to the oxime (compare entries 6 and 2, Table X).

When the above experiment was repeated with the dropwise addition of a half-mole equivalent of lead tetraacetate to fluorenone oxime in oxygen-free methylene chloride, the yields of fluorenonazine-monoxide (XXX) and fluorenone (XXVIII) remained essentially unaffected, even though the reaction proceeded faster than in the case of addition of the oxidizing agent all at once (compare entries 3 and 2, Table X). However, the yield of 9,9-difluorenylideneiminoxylfluorene (XXVII) increased from 2% to about 10% (entry 3, Table X) under these reaction conditions.

In order to test the temperature dependence of fluorenonazine-monoxide (XXX) formation, the reaction was repeated at -15° . The reaction was slowed down considerably, but product distribution remained unaffected (entry 4, Table X).

An experiment was conducted to test the role of acetic acid in quenching the formation of fluorenonazinemonoxide (XXX) since it had not been formed in the lead tetraacetate oxidation of fluorenone oxime in glacial acetic acid.

A half-mole equivalent of lead tetraacetate was added to fluorenone oxime in methylene chloride containing six mole equivalents of glacial acetic acid. The reaction proceeded as for the case where no acetic acid had been added (compare entries 5 and 2, Table X) but was complete in less time. When the reaction was similarly carried out in ether containing dry hydrogen chloride gas or concentrated hydrochloric acid, the formation of fluorenonazinemonoxide (XXX) was not quenched.

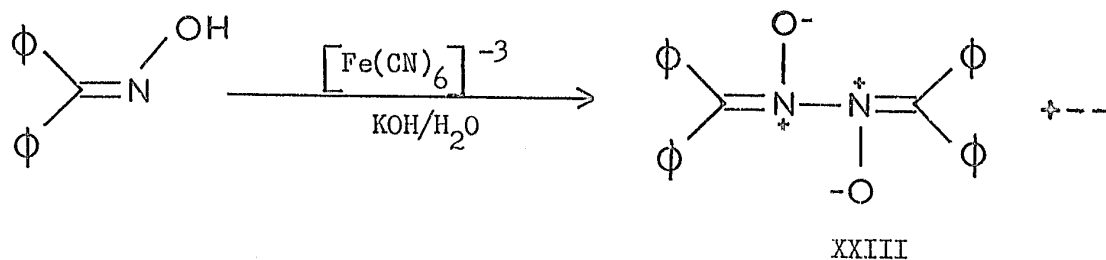
It is important to note that only trace amounts of 9,9-dinitro-

fluorene (XXVI) were formed in the above reactions, even in the presence of air (entries 1 and 6). This was in sharp contrast to the results obtained for the oxidations carried out in glacial acetic acid*. Moreover, a major amount of fluorenone (XXVIII) was isolated in the foregoing reactions whose formation cannot be attributed to participation by molecular oxygen, as its yield was constant in the presence and absence of oxygen.

2-3. Oxidation of Fluorenone Oxime with Potassium Ferricyanide

2-3.1. Formation of fluorenonazinemonoxide (XXX) and the bis-oxide (XXXVII)

The potassium ferricyanide oxidation of ketoximes has been reported only for benzophenone oxime (31) (see Introduction). The "anhydride N-oxide" of benzophenone oxime (XXII) was reported as one of the products, but no rigorous structure proof was provided. It had already been indicated (Introduction) that the more correct assignment might be the azine-bis-oxide structure (XXIII).



* The solubility of oxygen in methylene chloride is comparable to that in glacial acetic acid (43).

TABLE X
LEAD TETRAACETATE OXIDATION OF FLUORENONE OXIME IN METHYLENE CHLORIDE

ENTRY	Reactant Ratio ²	Mode ¹ of Addition	Reaction		PRODUCT YIELD (mole %)				
					$\begin{array}{c} \text{F}=\text{N}-\overset{*}{\text{N}}=\text{F} \\ \\ \text{O}- \end{array}$	F=O	$\begin{array}{c} \text{O}-\text{N}=\text{F} \\ \text{F} \diagup \quad \diagdown \\ \text{O}-\text{N}=\text{F} \end{array}$	$\begin{array}{c} \text{NO}_2 \\ \text{F} \diagup \quad \diagdown \\ \text{NO}_2 \end{array}$	$\text{F}=\text{N}-\text{OAc}$
			Time (min.)	Conditions					
					XXX	XXVIII	XXVII	XXVI	XXXV
1 ³	1:1	a	5	Air	11	43	1	2	-
2		a	90 ⁴	Nitrogen	15	50	1-3	0-1	-
3		b	20	Nitrogen	14	50-60	8-10	0	-
4	1: $\frac{1}{2}$	b	120	Nitrogen -15 ⁰⁴	15	60	7	0	-
5		a	25	Nitrogen ⁵	10-15	50	2	2	≤ 1%
6		c	50	Air	10-15	50	3	2	-

- ¹ a. Addition of lead tetraacetate to oxime solution all at once.
b. Above addition made dropwise.
c. Dropwise addition of oxime solution to lead tetraacetate solution.
- ² Molar ratio of oxime to lead tetraacetate.
- ³ 100 mg. oxime was used, compared to 585 mg. of oxime used in the other experimental runs.
- ⁴ All other reactions conducted at room temperature.
- ⁵ 1% acetic acid was added to the methylene chloride.
IR and t.l.c. analysis only.

It was hoped that the corresponding oxidation of fluorenone oxime might lead to the analogous azine-bis-oxide product. The intermediacy of this product in the lead tetraacetate oxidation of fluorenone oxime could then be tested.

Fluorenone oxime was slowly added (25 minutes) to potassium ferricyanide (1.7 mole equivalents) in aqueous potassium hydroxide solution. A deep orange solution was formed similar to that obtained in the lead tetraacetate oxidation of fluorenone oxime in methylene chloride (Part II). Work-up gave a red oil from which was readily obtained microcrystals of fluorenonazine-N-bis-oxide (XXXVII) in 3% yield. The remaining products consisted of fluorenone (XXVIII) and fluorenonazinemonoxide (XXX) in major and minor yields respectively (entry 1, Table XI).

When the above reaction was repeated at -5° , a light yellow suspension was formed. Upon warming up to room temperature a red oil was formed. Although the yields of fluorenone (XXVIII) and azinemonoxide XXX remained approximately constant, a five to six-fold increase in the yield of the azine-N-bis-oxide XXXVII was obtained (entry 3, Table XI).

The light yellow suspension formed in the above reaction conducted at -5° could be filtered to give a pale yellow** solid which spontaneously decomposed to a red oil upon warming up above 0° , with evolution of nitrous fumes. Attempts to characterize this solid were

* The oxidation of benzophenone oxime at this temperature was reported to give a higher yield of the "anhydride-N-oxide" (XXIII), with azine-monoxide (XXI) formation being quenched (31).

** Lauer and Dyer (31) had observed a blue oil as an unstable intermediate in the ferricyanide oxidation of benzophenone oxime at -5° .

unsuccessful*. Since the red oil derives its colour from the red azine-monoxide (XXX), the latter compound XXX was apparently formed from the unstable solid XLV**. The variations in yield of the azine-N-bis-oxide (XXXVII) with the reaction conditions (Table XI) also suggested that

TABLE XI
FERRICYANIDE OXIDATION OF FLUORENONE OXIME

<u>Reaction Conditions</u>				
<u>Temperature</u>	<u>Mode of Decomposition</u>	<u>XXXVII</u>	<u>XXVIII</u>	<u>XXX</u>
22°	I* decomposed in situ as it formed	3%	Major product	Minor product (ca. 10-20%)
-5°	I* was filtered after completion of addition. Spontaneous decomposition on warming (NO ₂)	7%	(ca. constant yield (t.l.c. and IR))	(ca. constant yield (t.l.c. and IR))
-5°	I* decomposed on warming to room temperature in suspension after completion of addition	15-18%		

* An infrared analysis of the chloroform solution of this solid at -10° warmed up to R.T. showed the bands for fluorenone and its azinemonoxide XXX, but showed no absorption peaks in the 2300-2000 cm⁻¹ region. This ruled out the possibility of any cyanide-containing intermediate (50).

** The solid XLV, which may be a homogeneous compound, is labelled for future reference.

this compound was formed, at least in the greater part, from the unstable solid XLV.

A comparison between the potassium ferricyanide and the lead tetraacetate oxidations of fluorenone oxime could now be made in the hope of shedding some light on the mechanisms responsible for the formation of observed products.

2-3.2. Comparative study of the lead tetraacetate oxidations of fluorenone oxime

Glacial acetic acid

In the lead tetraacetate oxidation of fluorenone oxime in glacial acetic acid, not a trace of fluorenonazine-bis-oxide (XXXVII) was obtained. The intermediate formation of this compound XXXVII can rigorously be ruled out because

(i) it was found to be inert to lead tetraacetate in methylene chloride and in acetic acid-methylene chloride (1:1);

(ii) it was insoluble in glacial acetic acid but was readily precipitated, unchanged, from methylene chloride with the addition of glacial acetic acid.

Other solvents

Although oxidation of fluorenone oxime with lead tetraacetate in solvents other than glacial acetic acid led to the formation of the azinemonoxide XXX, no azine-bis-oxide XXXVII was ever detected (see 2-2).

When the lead tetraacetate oxidation of fluorenone oxime was carried out in ether-methylene chloride (92:8) at -80° , a pale yellow

suspension formed which turned light brown at -30° and orange at -10° . After 12 hours of stirring, the suspension at -10° was filtered to give a solid consisting only of unreacted lead tetraacetate (30% of total). No unstable intermediate such as XLV nor any azine-bis-oxide XXXVII was detected nor isolated. The mother liquor contained fluorenone, fluorenon-azinemonoxide (XXX), and unreacted fluorenone oxime.

The above reaction was repeated at -70° in methylene chloride-ether (3:2). Addition of lead tetraacetate immediately afforded a suspension which was filtered after 17 hours at -70° to give about 50% of fluorenone oxime. However, addition of formic acid to the filtered solution at -70° precipitated out lead acetate corresponding to about 35% of unreacted lead tetraacetate. The yellow solution at low temperature contained fluorenone (IR analysis) but no azinemonoxide (XXX) which readily formed, however, when the solution was warmed up to room temperature. Again, no azine-bis-oxide (XXVII) product had at all been formed.

The possibility remained that any azine-bis-oxide XXXVII formed in the lead tetraacetate oxidations of fluorenone oxime in methylene chloride may have rapidly reacted with iminoxyl radicals (XI_R) or other intermediates to form fluorenonazinemonoxide (XXX). The oxidation of fluorenone oxime in methylene chloride with a half-mole equivalent of lead tetraacetate was therefore conducted in the presence of some added fluorenonazine-bis-oxide (XXXVII). The product distribution was unaffected and the azine-bis-oxide was quantitatively recovered.

Chapter 3

Oxidation of Other Aromatic Ketoximes

3-1. Oxidation of Benzophenone Oxime

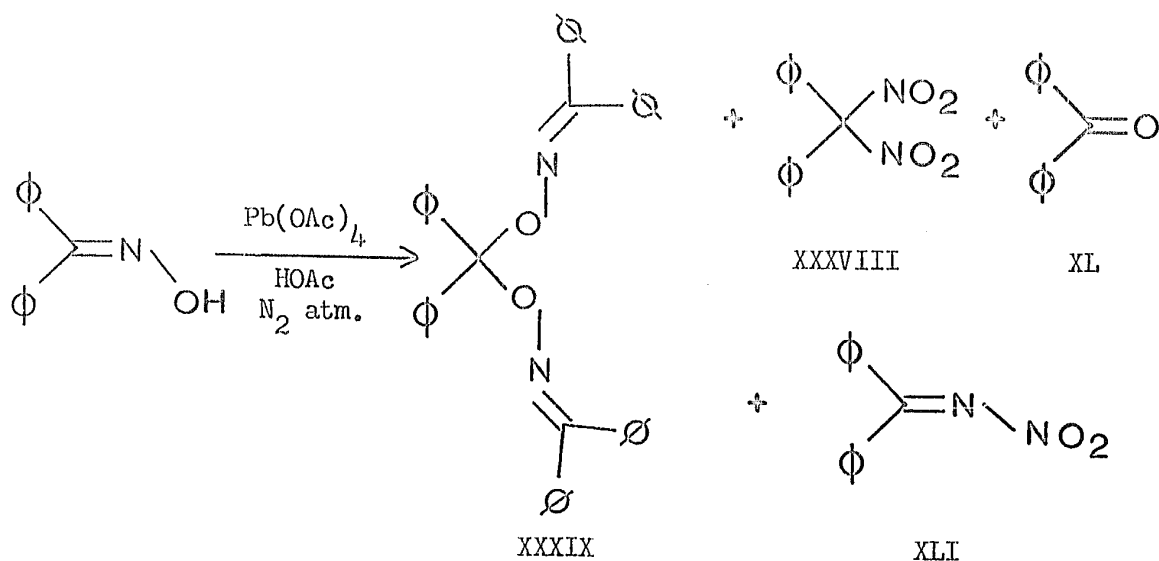
3-1.1. Lead tetraacetate oxidation in glacial acetic acid

Addition of a one mole equivalent of lead tetraacetate to benzophenone oxime in glacial acetic acid in the presence of air led to rapid consumption of the lead tetraacetate (2 min.), accompanied by the appearance of a light yellow-brown colour. After six minutes, the pale yellow solution was worked up. The resulting oil crystallized from methanol to give colourless crystals of 1,1-bis-(diphenylmethylideniminoxyl)-diphenylmethane (XXXIX) in 3% yield (entry 1, Table XII, p. 78). Chromatography of the mother liquor on silica gel with hexane afforded colourless plates of dinitrodiphenylmethane (XXXVIII) in 30% yield. Further elution with benzene gave 50% of benzophenone (XL) (identified by t.l.c. and IR analysis). Elution with ether gave 12% of an oil containing a 1:1 mixture of benzophenone oxime and a compound tentatively assigned (t.l.c. and IR) as benzophenone oxime O-acetate (XLVI, analogous to XXXV).

When lead tetraacetate was added to benzophenone oxime in oxygen-free glacial acetic acid in an inert atmosphere, immediate reaction occurred to give a brown solution which turned green after a few seconds and green-brown after one minute. The lead tetraacetate was consumed during this time.

Extraction and crystallization from methanol again gave compound XXXIX in 2.6% yield (entry 2, Table XII). Chromatography of the

mother liquor gave dinitrodiphenylmethane (9%) and, in 11% yield, nitrimine XLI. Further elution on silica gel afforded, in 64% yield, crystals of benzophenone (XL). Finally, about 5% of an oil was obtained which consisted mainly of benzophenone oxime and a minor amount of benzophenone oxime O-acetate (t.l.c. and IR).



The results obtained so far for the reaction of lead tetraacetate with benzophenone oxime in glacial acetic acid are shown in Table XII (entries 1 and 2). The presence of oxygen in the above oxidation caused an increase in the yield of dinitrodiphenylmethane (XXXVIII), as was found in the analogous oxidation of fluorenone oxime. The formation of the nitrimine of benzophenone (XLI) in the absence of oxygen, the formation of ketal XXXIV in a low yield (3-4%) which was unaffected by oxygen, and the short reaction time, represent the major differences from the results obtained for fluorenone oxime.

Dropwise addition (15 minutes) of lead tetraacetate to benzophenone oxime in glacial acetic acid in the presence of air led to rapid

and quantitative reaction of the oxime. If formation of ketal XXXIV were dependent on free oxime concentration, an increase in its yield might be expected under these conditions. In fact, no change in the yield of ketal XXXIV was obtained (compare entry 3, Table XII). Benzophenone was still formed in about 50% yield, while there was little change in the yield of dinitrodiphenylmethane (XXXVIII) (compare entries 3 and 1, Table XII).

3-1.2. Lead tetraacetate oxidation in methylene chloride

Addition of a half-mole equivalent of lead tetraacetate to a rapidly stirred solution of benzophenone oxime in methylene chloride (O_2 present) gave instantaneously a yellow suspension which turned to a brown-green and then to a yellow-green. These colour changes all took place within one minute, at which time the lead tetraacetate was completely consumed. Filtration gave 85% of the expected lead acetate. Chromatography (t.l.c.) of the mother liquor gave benzophenone (60%), an oil (5%) containing mainly benzophenone oxime O-acetate (XLVI) (see experimental), and a new crystalline compound XLIII (35%), having an R_f value smaller than that of the oxime. One crystallization from ethanol afforded yellow microcrystals of benzophenon-azinemonoxide (XLIII). The infrared spectrum of the crude mixture was compatible with the presence of these compounds and showed strong peaks at 1765 and 1710 cm^{-1} due to acetic acid formed in the course of the reaction.

A half-mole equivalent of lead tetraacetate added to benzophenone oxime in methylene chloride in 15 minutes was completely consumed

by the end of the addition. Infrared and t.l.c. analysis indicated essentially the same product distribution as for rapid addition (compare entries 5 and 4, Table XII).

Addition of a one mole equivalent of lead tetraacetate to benzophenone oxime in methylene chloride led to immediate precipitation of lead acetate and formation of a green suspension. After two minutes, t.l.c. analysis indicated the presence of minor amounts of a compound having the same R_f value as starting oxime (oxime or oxime acetate) and major amounts of benzophenone (XL) and dinitrodiphenylmethane (XXXVIII). Infrared analysis confirmed the presence of ketone XL and gem-dinitro compound XXXVIII and showed bands characteristic of acetic acid. No benzophenonazinemonoxide (XLIII) could be detected. Unreacted lead tetraacetate remained even after 48 hours. Work-up afforded lead acetate (50% of theoretical) and lead oxide corresponding to ca. 20% of unreacted lead tetraacetate. An infrared analysis of the crude oil obtained after work-up showed approximately the same product distribution as had been obtained in the oxidation conducted in glacial acetic acid (compare entries 6 and 1, Table XII).

Benzophenonazinemonoxide (XLIII) had not been formed in the above oxidation nor been further oxidized by unreacted lead tetraacetate, since it was found to be unreactive towards this oxidizing agent.

3-1.3. Molecular oxygen

It has been shown that fluorenone oxime reacted with oxygen in dry glacial acetic acid as solvent (2-1.2). Although oxygen did not participate in the formation of benzophenone from the lead tetraacetate oxidation of benzophenone oxime (see Table XII), it was of mechanistic interest to know what products would form in the autoxidation reaction of the latter.

When benzophenone oxime was left in 10% aqueous acetic acid saturated with oxygen, no reaction occurred. However the oxime was completely converted to benzophenone (major) and dinitrodiphenylmethane (XXXVIII, minor) when allowed to stand for 24 hours in dry glacial acetic acid saturated with oxygen.

3-1.4. Nitrogen dioxide

The addition of benzophenone oxime to a solution of nitrogen dioxide in methylene chloride or acetic acid led to formation of dinitrodiphenylmethane (XXXVIII) as major product. A more detailed study is presented in Chapter 4.

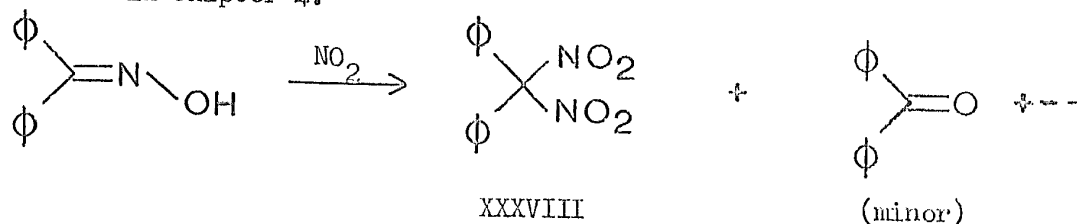
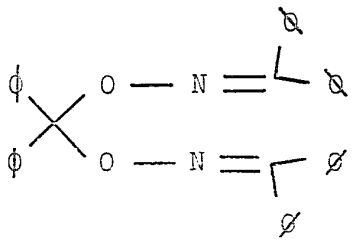
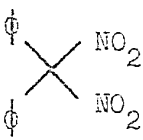
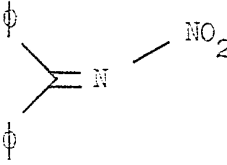


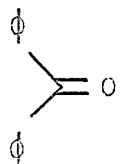
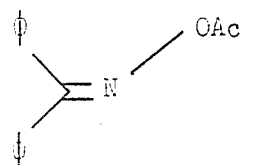
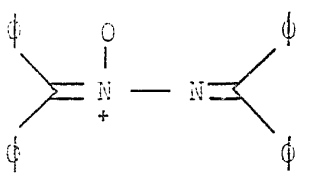
TABLE XII

LEAD TETRAACETATE OXIDATION OF BENZOPHENONE OXIME

PRODUCT	*1/1 HOAc/air 1	1/1 HOAc/N ₂ **2	1/1 HOAc/air **3 [†]	1/ ¹ / ₂ 4	1/ ¹ / ₂ CH ₂ Cl ₂ /air [†] 5	1/1 6
 XXXIX	3%	3% *(4%)	3%	0%	0%	0%
 XXXVIII	30%	9%	25%	0%	0%	[†] ca. 30%
 XLI	0%	11%	1%	0%	0%	0%

(continued)

TABLE XII (continued)

PRODUCT	*1/1 HOAc/air 1	1/1 HOAc/air **2	1/1 HOAc/air **3†	1/1/2 4	1/1/2 CH ₂ Cl ₂ /air ‡5	1/1 6
 XL	50%	60%	50%	60%	ca. 60% ‡	ca. 50% ‡
 XLVI	5%	5%	10%	5%	5%	5-10%
 XLVIII	0%	0%	0%	35%	ca. 35% ‡	0%

* Ratio of oxime to lead tetraacetate. Unless otherwise stated, 500 mg. of oxime was oxidized.

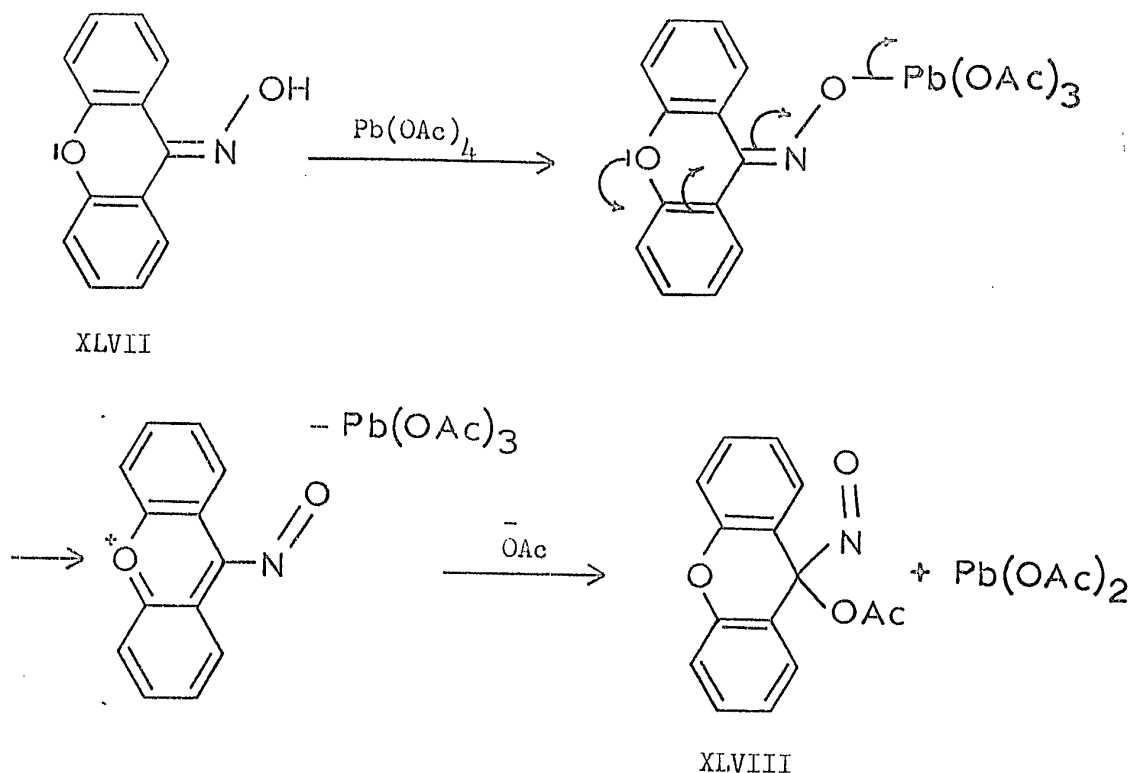
** 2 g. of oxime were oxidized.

† Dropwise addition of lead tetraacetate. Unless otherwise stated, the latter was added all at once.

‡ Infrared and t.l.c. analysis.

3-2. Oxidation of Xanthone Oxime

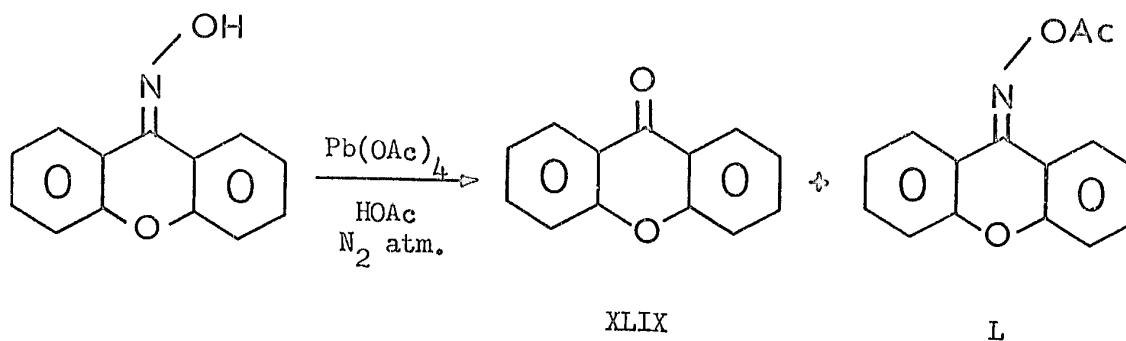
The lead tetraacetate oxidation of xanthone oxime (XLVII) might be expected to proceed differently from that of fluorenone oxime because of the electromeric effect of the bridged oxygen. An ionic reaction proceeding through heterolytic* cleavage of the organolead intermediate shown below might be expected to lead to the gem-nitrosoacetate XLVIII. This type of product was obtained by Iffland (25) from unhindered aliphatic ketoximes.



In order to investigate this effect, a study of the lead tetraacetate oxidation of xanthone oxime was undertaken.

* The electron-feeding effect of the bridged oxygen was clearly demonstrated by the inability of xanthone to react with hydroxylamine hydrochloride to form xanthone oxime. In contrast, fluorenone oxime was readily formed under these conditions.

Lead tetraacetate reacted rapidly and quantitatively (3 minutes) with a one mole equivalent of xanthone oxime in glacial acetic acid in an inert atmosphere. The initial dark brown solution faded to a pale yellow solution after 10 minutes. Addition of water gave a colourless solid which consisted mainly of xanthone ($\sim 90\%$, XLIX). Only one other product, tentatively identified (t.l.c. and IR) as the oxime O-acetate ($\sim 10\%$, L) was detected.



When the reaction was repeated in the presence of air, a yellow solution immediately formed. The product consisted of three major and six minor components. No xanthone (XLIX) or 9,9-dinitro-xanthone (LI; 4-2) could be detected (t.l.c.).

Xanthone oxime reacted quantitatively with a one mole equivalent of lead tetraacetate (5 minutes) in oxygen-free methylene chloride. Lead acetate (92% Th.) and xanthone (100% yield; t.l.c., IR and mixed m.p.) were obtained. When the reaction was repeated in the presence of air, xanthone ($\approx 75\%$) and a minor unidentified product (t.l.c.) were formed immediately.

It was apparent from the above observations that 1) a free radical process must be important in the lead tetraacetate oxidation of

xanthone oxime carried out in glacial acetic acid since the product distribution was markedly affected by molecular oxygen.

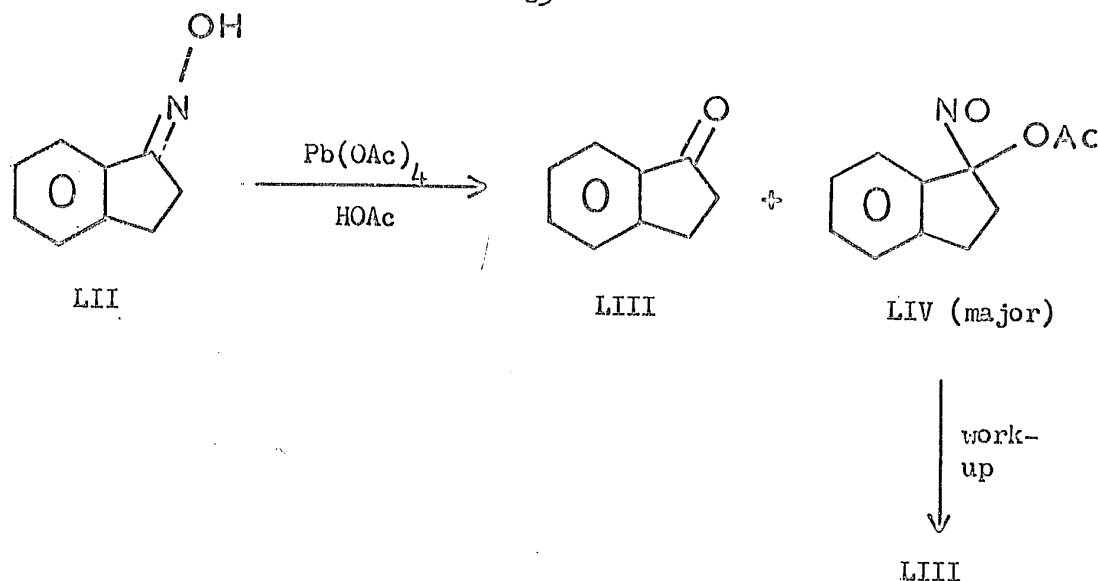
2) The expected ionic reaction of xanthone oxime with lead tetraacetate might be operative in the oxidation carried out in methylene chloride since oxygen had a minor effect on the yield of xanthone.

3-3. Oxidation of Indanone Oxime

While the lead tetraacetate oxidation of unhindered aliphatic ketoximes (25) led to gem-nitrosoacetate (XV), the oxidation of bis-aryl-ketoximes led to a number of rather different products (Chapters 2 and 3). It was therefore of interest to study the lead tetraacetate oxidation of indanone oxime (LII), which had a structure intermediate between the above oximes.

The addition of a one mole equivalent of lead tetraacetate to indanone oxime (LII) in oxygen-free glacial acetic acid afforded a fluorescent green solution (1 min.). When the lead tetraacetate was completely consumed (16 min.), a dark turquoise solution remained containing indanone (LIII) and a new product LIV, which decomposed mainly to indanone upon work-up (t.l.c.). The colour of this new product (turquoise spot when eluted on t.l.c.) and its facile decomposition to indanone made the gem-nitrosoacetate structure LIV likely*.

* Analogous results were reported for the lead tetraacetate oxidation of acetophenone oxime while our work was in progress (24b).



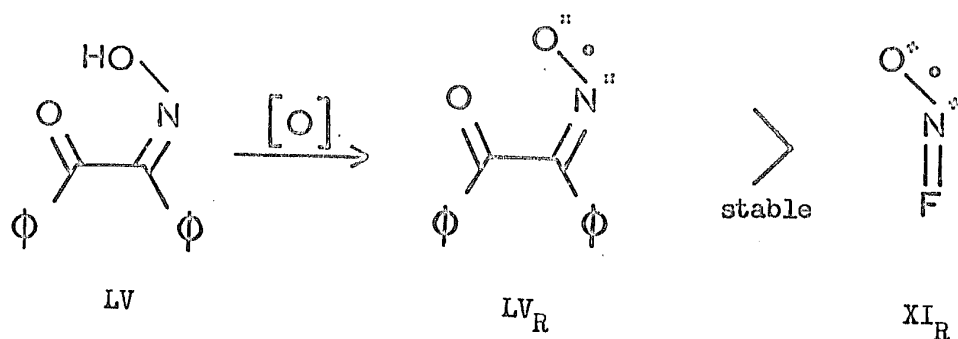
When the reaction was repeated in the presence of oxygen, the same reaction time and colour changes were obtained. Work-up gave indanone as the major product (ca. 75% yield). The absence of any nitration products, obtained in the analogous oxidation of fluorenone oxime, was confirmed by comparison (t.l.c.) of the reaction mixture with nitration products independently obtained from indanone oxime (4-2).

This distinct difference in behaviour between indanone oxime and fluorenone oxime was also found when the lead tetraacetate oxidation was carried out in methylene chloride.

A one mole equivalent of lead tetraacetate was completely and rapidly (2 min.) consumed by indanone oxime in methylene chloride to afford a green suspension. Lead acetate was isolated in 90% yield. Analysis of the mother liquor (IR and t.l.c.) indicated the presence of acetic acid and indanone (> 50%). No product with an R_f value corresponding to that of an azinemonoxide (see Table IV and 3-1.2) could be detected.

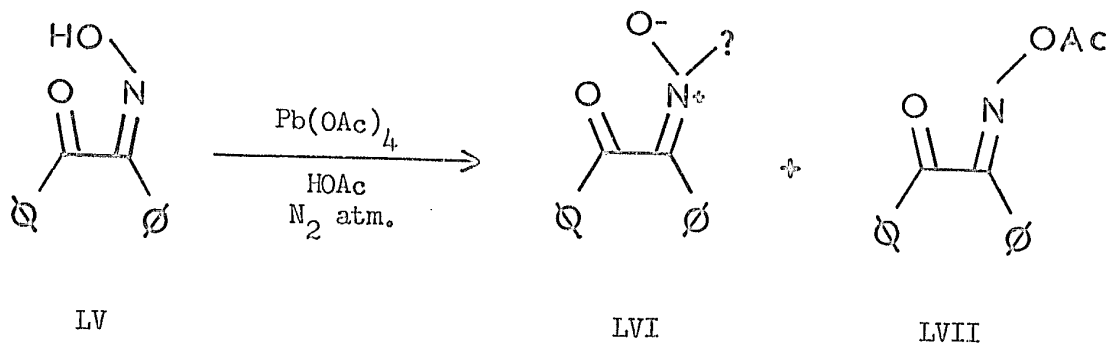
3-4. Oxidation of Benzil Anti-monoxime

The iminoxyl radical of biacetyl monoxime (XIII_R) was reported to be more stable than that of fluorenone oxime (XI_R) (see Table I). If this stabilization were due to the α -keto group, then the iminoxyl radical of benzil anti-monoxime (LV_R) would be stabilized in an analogous fashion.



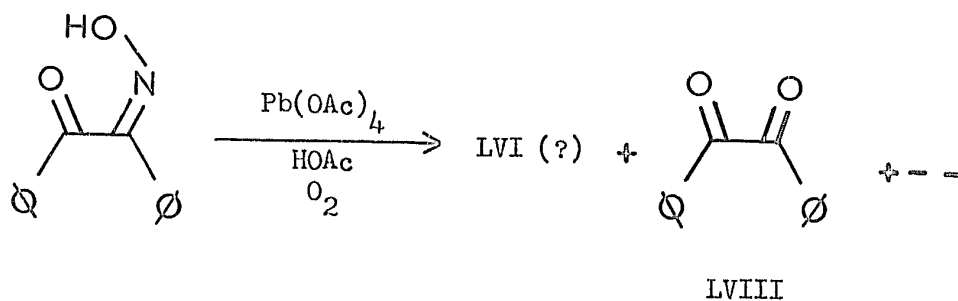
The lead tetraacetate oxidation of benzil anti-monoxime was therefore studied.

The oxidation of benzil anti-monoxime (LV) with one mole equivalent of lead tetraacetate in oxygen-free glacial acetic acid proceeded instantaneously and quantitatively. Pale yellow crystals consisting mainly of a new compound LVI and a minor amount of a product tentatively identified as benzil anti-monoxime O-acetate (VLII, see experimental) were obtained. Attempts to purify the new compound LVI were unsuccessful. Chromatography of the crystals on silica gel gave mainly benzil (LVIII). The following partial structure for LVI was tentatively assigned from the strong absorption bands at 1580 cm^{-1} and 1360 cm^{-1} (IR, CHCl_3), characteristic of the $\text{N} \rightarrow \text{O}$ functional group (36).



An azine-bis-N-oxide structure (cf. XXIII) seemed unlikely in the light of the observed stability of compound LVI to concentrated hydrochloric acid.

The free radical nature of the reaction was clearly demonstrated by the marked effect of oxygen on the reaction course. When it was repeated in glacial acetic acid containing oxygen, the new product LVI was formed, as well as benzil (LVIII) and three other products (t.l.c.).



The oxidation conducted in methylene chloride was complete with a half-mole equivalent of lead tetraacetate (as for fluorenone and benzophenone oximes), and led to benzil as the major product (see experimental).

Chapter 4

Geminal Dinitromethanes

4-1. Introduction

The unexpected* formation of gem-dinitromethanes in the lead tetraacetate oxidation of fluorenone oxime and benzophenone oxime probably resulted from secondary reactions caused by the production of nitric oxide in situ (Chapters 2 and 3). Since oxygen increased the yields of gem-dinitromethanes in the above oxidations, it appeared that nitrogen dioxide, formed from the reaction of nitric oxide and oxygen, might be responsible for the generation of the dinitromethanes. Since the latter compounds did not appear to be formed in the lead tetraacetate oxidations of indanone oxime (LII) and xanthone oxime (XLVII), it was of mechanistic interest to ascertain whether these oximes could react with nitrogen dioxide to form gem-dinitro derivatives. In this way, authentic samples might also be acquired.

The reaction of the forementioned aromatic ketoximes with nitrogen dioxide was therefore studied in detail. Before reviewing the results, a brief account of the methods available for the formation of gem-dinitromethanes of aromatic compounds will be presented.

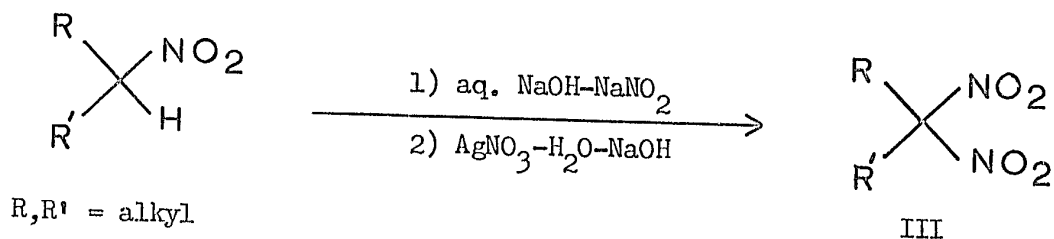
Ponzio (10), who studied the reaction of ketoximes with nitrogen dioxide, at the turn of the century, reported that aromatic ketoximes such as benzophenone oxime and acetophenone oxime did not lead to any gem-dinitro products (see Introduction). A conflicting report

* No geminal dinitromethane products had been observed in the lead tetraacetate, potassium ferricyanide or ceric ammonium sulfate (32) oxidations of any oximes (see Introduction).

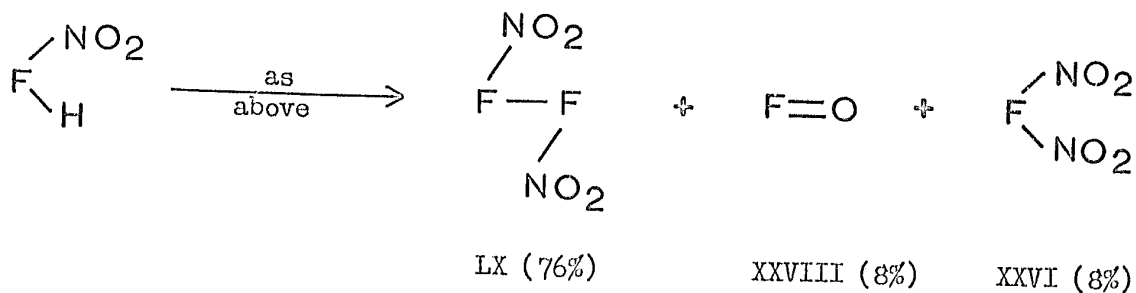
by R. Scholl (11), at about the same time, indicated that benzophenone oxime reacted with NO_2 to give high yields of a product which, in the light of our work, was definitely dinitrodiphenylmethane (XXXVIII).

Other methods available for formation of geminal dinitro compounds are of limited applicability or very inefficient (51).

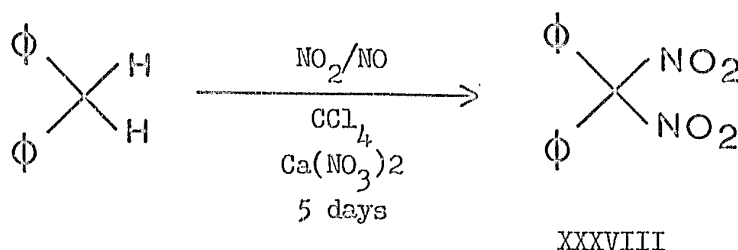
The most general method reported to date for the formation of gem-dinitro compounds involves the oxidative nitration of nitro-compounds by a silver nitrite-silver nitrate mixture (52). This method proved most useful for the preparation of aliphatic gem-dinitro compounds (III).



Aromatic gem-dinitromethanes, however, were formed in poor yield due to the predominance of oxidative dimerization, as typified by the oxidation of 9-nitrofluorene (LIX) which led mainly to the nitro dimer LX.

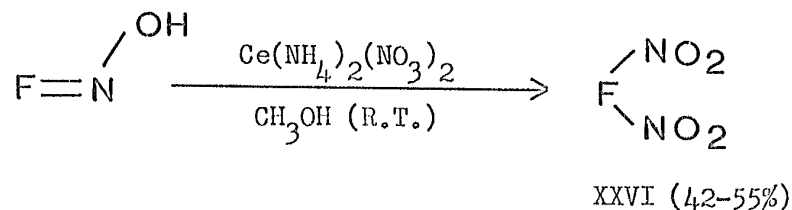


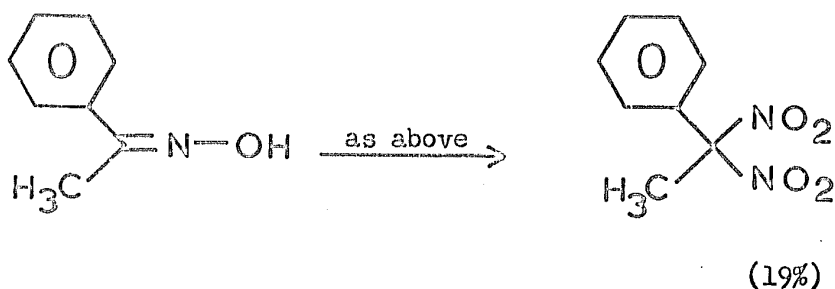
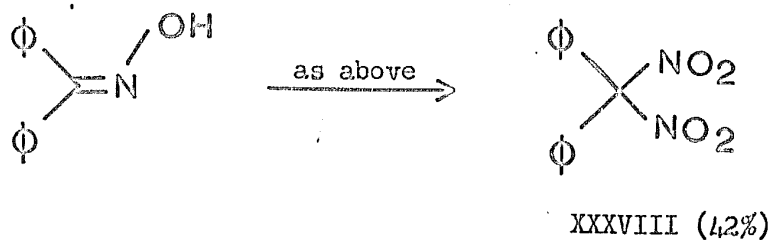
The nitration of active methylene groups leading to aromatic gem-dinitro products was also found to be an inefficient process (53). Dinitrodiphenylmethane (XXXVIII), for example, could only be formed in 30% yield from diphenylmethane under optimum conditions.



In summary, we have seen that methods exist for the preparation, in high yields, of aliphatic nitro compounds but none for the corresponding aromatic series. 9,9-Dinitrofluorene (XXVI) has been prepared in 8% yield (52) while dinitrodiphenylmethane (XXXVIII) was prepared in 30% yield by a slow and complicated method (53).

Just prior to the writing of this thesis, a private communication was received concerning the ceric ammonium nitrate oxidation of aromatic oximes (32). Chapman and Heckert discovered, to their surprise, that the oxidation of the oximes of fluorenone, benzophenone and acetophenone led to formation of the corresponding dinitromethane derivatives in the yields indicated below.





4-2. Geminal Dinitromethanes

The addition of fluorenone oxime to a green solution of nitrogen dioxide in glacial acetic acid or methylene chloride led to immediate reaction accompanied by the transient appearance of a yellow-brown colour. Work-up afforded pale yellow crystals of 9,9-dinitrofluorene (XXVI; see 4-3 for structure proof) in yields indicated in Table XIII. Only trace amounts of fluorenone were formed (t.l.c.) from the reaction carried out in glacial acetic acid.

The effect of temperature and mode of addition of the nitrogen dioxide on the yield of 9,9-dinitrofluorene was studied next. Nitrogen dioxide was slowly bubbled through a solution of fluorenone oxime in diethyl ether at 0°C. After a few minutes, the turquoise solution was worked-up to give in 86% yield pale yellow crystals of 9,9-dinitrofluorene, homogeneous by t.l.c. (Table XIII). The colour changes from the

initial reaction to the final isolation step did not indicate the formation of any intermediate(s) different from that appearing when the reaction was carried out in acetic acid or methylene chloride.

The addition of benzophenone oxime to a methylene chloride solution of nitrogen dioxide led to immediate reaction accompanied by the same colour changes observed for fluorenone oxime. However, work-up afforded dinitrodiphenylmethane (ca. 77%), contaminated by benzophenone (15%) and a minor amount of a polar impurity (t.l.c.)*. One crystallization from hexane afforded 57% of colourless crystals of dinitrodiphenylmethane (XXXVIII, for structure proof, see 4-3). The same product distribution was found when the above reaction was carried out by the addition of nitrogen dioxide to the oxime in methylene chloride.

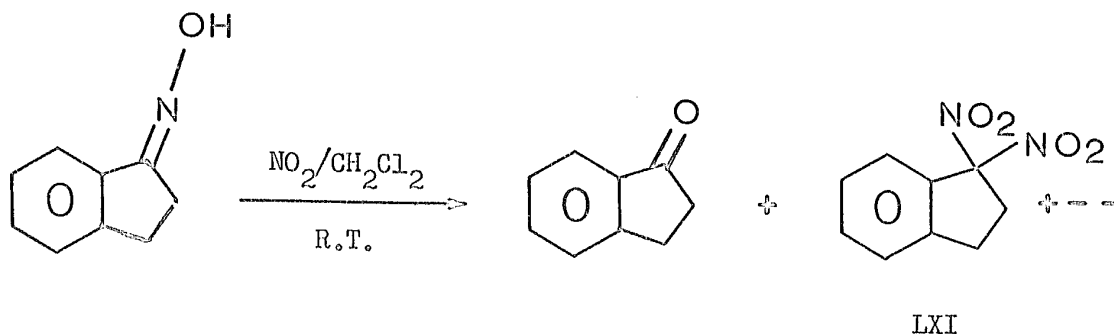
Xanthone oxime (XLVII) and indanone oxime (LII) both reacted immediately with nitrogen dioxide in methylene chloride in an analogous manner.

Work-up of the reaction solution from the xanthone oxime oxidation afforded an oil which readily crystallized from hexane to yield 70% of colourless crystals of dinitroxanthene (LI) (see Table XIII). The structure proof, given in 4-3, is not rigorous.

Work-up of the reaction solution from the indanone oxime oxidation gave a green oil which consisted mainly of indanone, but contained two other products (t.l.c.). Attempts to crystallize this oil were unsuccessful but chromatography on silica gel gave 75% of indanone

* The analysis was carried out by infrared spectroscopy.

and about 8% of an oil whose infrared spectrum and R_F value on t.l.c. strongly suggested a dinitromethane structure (LXI; Table XIII).



Thus, the formation of 1,1-dinitroindane (LXI) from the oxidative nitration of indanone oxime occurs in no more than 8% yield.

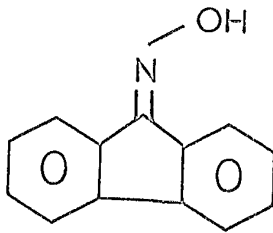
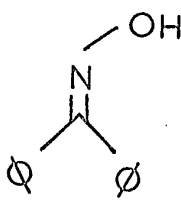
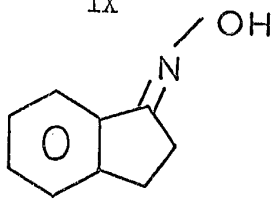
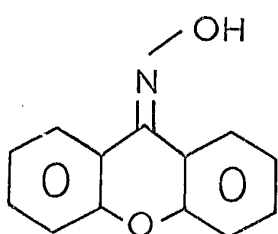
4-3. Structural Elucidation

9,9-Dinitrofluorene (XXVI)

The empirical formula for this new product was $\text{C}_{13}\text{H}_8\text{N}_2\text{O}_4$, (mass spectrometric M.W. 256). The broad peak appearing at $246 \text{ m}\mu$ (ϵ 26,000) could be assigned to absorption for the fluorenylidene aromatic skeleton (see UV data of fluorene in Table II, p. 17). The absorption band at $256 \text{ m}\mu$, characteristic of $\text{C}=\text{X}$ at the C-9 position (Table II), was absent. The nuclear magnetic resonance spectrum of compound XXVI contained only the complex splitting pattern for the aromatic protons of the fluorene skeleton at 7.2-8 p.p.m. The infrared spectrum of XXVI contained strong absorption peaks assigned to the asymmetric and symmetric $-\text{NO}_2$ stretching vibrations (Table XIV).

Compound XXVI was quantitatively converted to fluorenone with evolution of nitrogen dioxide when heated to its melting point. It was, however, stable in glacial acetic acid containing concentrated hydrochloric acid.

TABLE XIII
NITROGEN DIOXIDE OXIDATION OF AROMATIC KETOXIMES

Oxime	Solvent	Yield (mole %)		
		$\begin{array}{c} \diagup \text{NO}_2 \\ \diagdown \text{NO}_2 \end{array}$	$>=O$	Others
 XI	HOAc	1 ¹ 80%	1%	
	CH ₂ Cl ₂	82%	0%	None
	Ether (0°)	86%	0%	
 IX	CH ₂ Cl ₂	2 ² 57-77%	15%	ca. 5% product (R _f < R _f IX)
 LII	CH ₂ Cl ₂	8% ³	75%	14% oil (R _f < R _f LII)
 XLVII	CH ₂ Cl ₂	70% ⁴	0%	Product (R _f > R _f benzil)

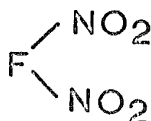
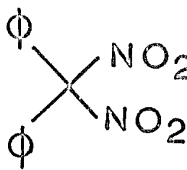
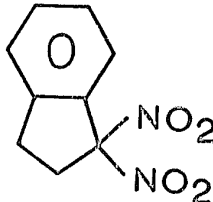
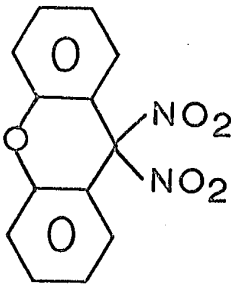
¹ Actual recovery from oxidation of 100 mg. of oxime.

² Crystalline product isolated in 57% yield. Remainder, including ketone present, determined by IR analysis.

³ Isolated as an oil and identified only by IR.

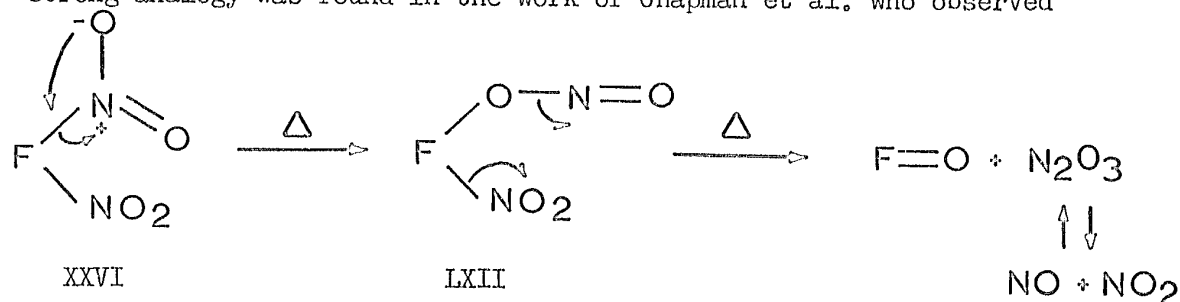
⁴ Only tentative assignment.

TABLE XIV
IR AND MELTING POINT DATA OF DINITROMETHANES

Dinitromethane	Melting point (°C.)		REF.	IR* ν_{NC_2} (cm ⁻¹)	
	Found	Reported		$\nu_{asym.}$	$\nu_{sym.}$
 XXVI	130-131	130-131.5	52	1567 (s)	1350 (m)
 XXXVIII	80.5-81	80	53	1570 (s)	1350 (m)
 LXI	-	-	-	** 1570 (s)	** 1360 (m)
 LI	74.5	-	-	1560 (s)	1345 (m)

* Spectra of pure samples in KBr were taken, unless otherwise indicated.
 ** Solution spectrum (CHCl₃) of reaction mixture was taken.

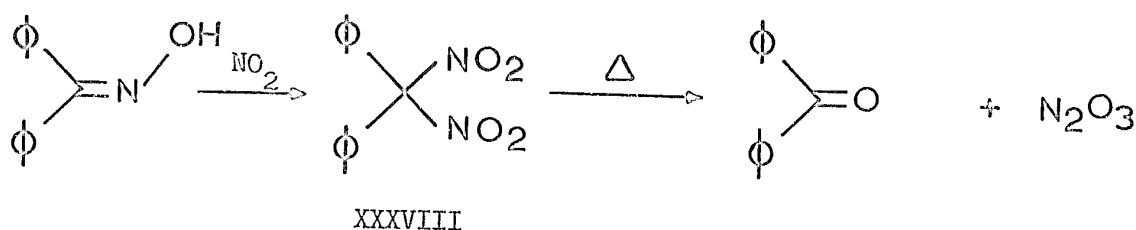
The foregoing results leave only 9,9-dinitrofluorene as the structure representing compound XXVI. The observed pyrolysis of this compound most probably proceeded by an initial rearrangement to the nitro-nitrito compound (LXII) which might then readily lose N_2O_3 . A strong analogy was found in the work of Chapman et al. who observed



that dinitromethanes were converted to the corresponding ketones on irradiation (48). In a previous paper, Chapman also showed the tendency for C-nitro to C-nitrite rearrangement under photolytic conditions (54). The photolysis results of Chapman may thus readily be explained as shown above.

Dinitrodiphenylmethane (XXXVIII)

Compound XXXVIII analysed for $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_4$ (osmometric M.W. 260). It decomposed to benzophenone on heating above its melting point. Its infrared spectrum contained the characteristic absorption bands for the $-\text{NO}_2$ group (Table XIV). Its ultraviolet spectrum had a strong absorption for the diphenylmethyldiene skeleton (214 $\text{m}\mu$), but was missing the absorptions characteristic of the $\text{C}=\text{N}$ functional group conjugated with the two phenyl groups (Table VII). These data paralleled those observed for 9,9-dinitrofluorene, and left only dinitrodiphenylmethane as the structure representing compound XXXVIII.



9,9-Dinitroxanthene (LI)

Reaction of xanthone oxime (XLVII) with nitrogen dioxide in methylene chloride gave colourless crystals of a compound LI, m.p.

74.5°, $C_{13}H_8N_2O_5$. Its osmometric molecular weight was 287.

The pyrolysis of this compound readily occurred ($>100^\circ$) with evolution of brown nitrous fumes, as had been observed for the previously discussed gem-dinitromethanes. Its infrared spectrum had absorption bands at 1560 and 1345 cm^{-1} , characteristic of the nitro group (see Table XIV). However, a strong band at 1685 cm^{-1} could not be assigned and did not occur in the spectra of the other gem-dinitro compounds.

The ultraviolet spectrum of compound LI in ethanol resembled that of xanthene (compare entries 2 and 1, Table XV) and lacked the intense absorption at 239 $m\mu$ found in xanthone (entry 3, Table XV). The very strong absorptions characteristic of quinoidal-type structures (entry 5, Table XV) were also missing.

In the light of the above evidence, compound LI was tentatively assigned the following structure.

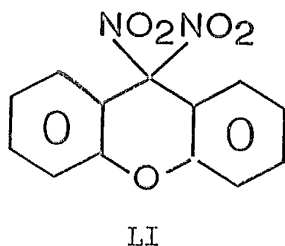


TABLE XV

UV DATA OF XANTHENE AND XANTHENE COMPOUNDS

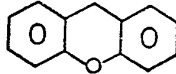
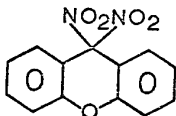
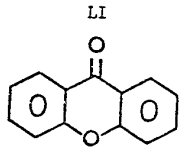
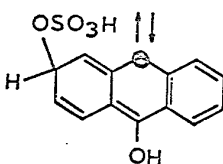
COMPOUND	SOLVENT	$\lambda_{\max}$ (m μ)		ϵ		REF.
	CYCLO- HEXANE	220 (10,000) 248 (9,452)	273 (sh) 284	(4,771) (6,021)		55
XANTHENE						
	ETHANOL	208 (12,880) 263 (11,000)	295	(1,570)		-
	ETHANOL	239 (39,000) 261 (12,600)	287	(4,200)		56a
XLIX						
	C ₂ H ₄ Cl ₂	261 (17,610)	276 286	(7,404) (8,751)	327 (3,452) 341 (9,452)	56b
XLIX						
	C ₂ H ₄ Cl ₂ + H ₂ SO ₄	251 (92,940) 268 (9,452)			334 (72,820) 392 (9,445) 406 (8,751)	56b

FIG. 11. The IR Spectrum of Dinitrodiphenylmethane.

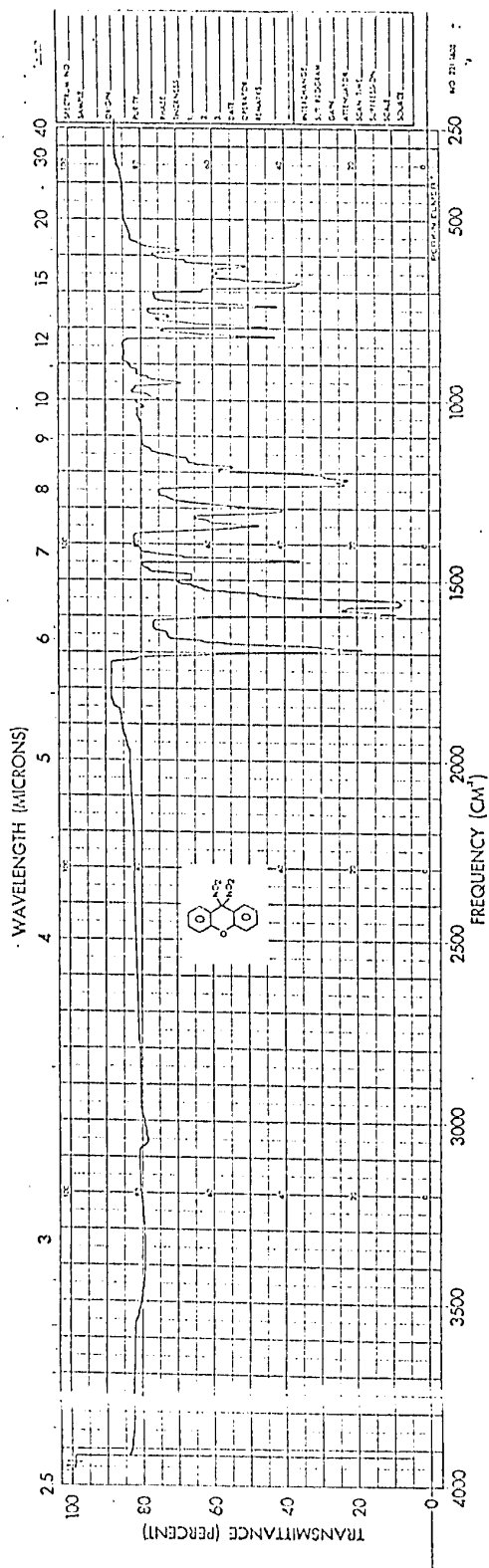


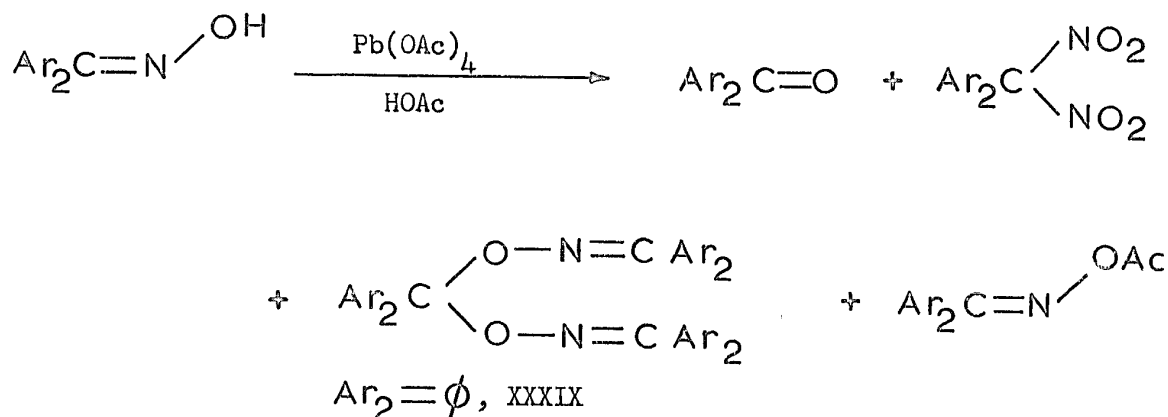
FIG. 12. The IR Spectrum of 9,9-Dinitroanthracene.

Chapter 5

Mechanistic Aspects of the Oxidations of Aromatic Ketoximes

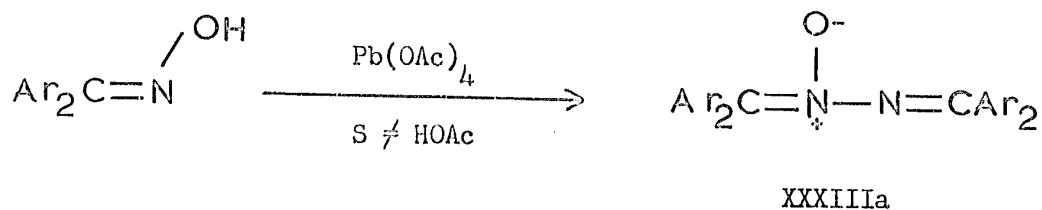
5-1. Brief Summary of Results

The lead tetraacetate oxidation of fluorenone oxime (XI) and benzophenone oxime (IX) in glacial acetic acid led to the formation of the corresponding parent ketones, gem-dinitromethanes, iminyl ketal derivatives (XXVII and XXXIX) and a minor amount of oxime acetates (see Table XVI).



It was found that when the fluorenone oxime oxidation was effected in the absence of oxygen, nitric oxide could be isolated. Moreover, the product distribution was markedly affected by the amount of oxygen available (see 2-1.1). Similar results were obtained from the oxidation of benzophenone oxime, since the nitrimine formation (XLI) was quenched and the dinitrodiphenylmethane (XXXVIII) yield increased when the lead tetraacetate oxidation was conducted in the presence of oxygen (Table XII). These results indicated the presence of free radicals and made probable secondary reactions involving nitric oxide, oxygen and nitrogen dioxide.

In contrast to these results, it was found that the lead tetraacetate oxidation of the above bis-aryl-ketoximes (IX and XI) conducted in solvents other than glacial acetic acid (dielectric constants ranging from ca. 2-100) led to a marked change in the products formed. In particular, a new product, azinemonoxide (XXXIII-a), was obtained. The product distribution studied quantitatively in methylene chloride was now insensitive to oxygen and complete oxidation of oxime



occurred with only a half-mole equivalent of lead tetraacetate (see Table XVI). Since negligible amounts of gem-dinitro derivatives were formed, it was apparent that any nitric oxide generated in situ had a rather different reaction fate from that observed in the oxidations conducted in glacial acetic acid.

This distinct difference found between oxidations conducted in glacial acetic acid and all other solvents investigated was not reflected in the ESR spectra of iminoxyl radicals, which, in the case of aromatic ketoximes, have been reported to be relatively solvent-independent (57). It should be noted that in the case of aliphatic ketoximes, some solvent dependency has been observed. Rassat (14), for instance, showed that iminoxyl radicals generated from the reaction of aliphatic ketoximes with lead tetraacetate in methylene chloride were very unstable; however, when the same radicals were formed by mixing lead tetraacetate (moist with

TABLE XVI

LEAD TETRAACETATE OXIDATIONS OF AROMATIC KETOXINES

OXIME		KETONE		GEM, -DINITRO PRODUCT		KETAL PRODUCT		AZINEOXONOXIDE		OXIME O-ACETATE	
		² HOAc	CH ₂ Cl ₂ ²	HOAc	CH ₂ Cl ₂	HOAc	CH ₂ Cl ₂	HOAc	CH ₂ Cl ₂	HOAc	CH ₂ Cl ₂
	(LV)	³ 0% (10%)	~50%	0%	-	0%	-	-	-	~10%	-
	(XI)	25% (~50%)	50%	20% (~25%)	~1%	~25% (0%)	2%		15%	~5%	~1%
	(IX)	50-60%	50%	9% (30%)	0%	3%	0%	0%	35%	~5%	~5%
	(XLVII)	⁴ ~90% (0%)	100% (~75%)	0%	0%	0%	0%		0%	~10%	0%
	(LII)	⁴ ~50% (75%)	75%	0%		0%	0%		0%	-	-

¹ Results for acetic acid (HOAc) as solvent are given for 1 mole equivalent of lead tetraacetate used.

² Results for methylene chloride (CH₂Cl₂) as solvent are given for a half-mole equivalent of lead tetraacetate used, unless otherwise specified. A star^(*) denotes 1 mole equivalent of Pb(OAc)₄ was used in both solvents.

³ Bracketed yields refer to yield obtained in the presence of oxygen. Otherwise, yields were unaffected by oxygen.

⁴ Nitrosoacetate, which readily decomposed to ketone, was present in ~50% yield.

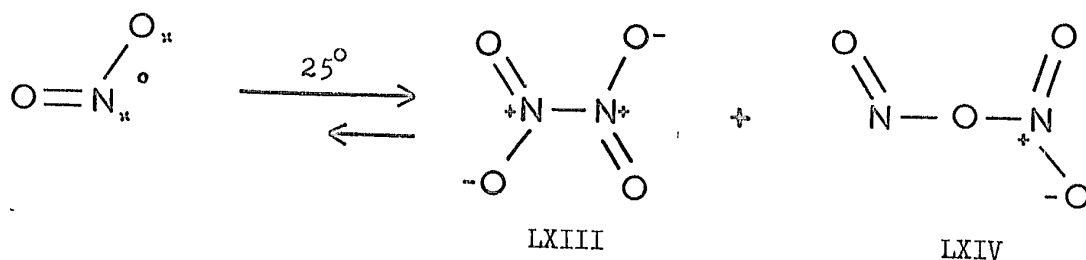
acetic acid) with aliphatic ketoximes, they were found to be much more stable.

The other model oximes studied displayed less complicated but different behaviour and will be dealt with later.

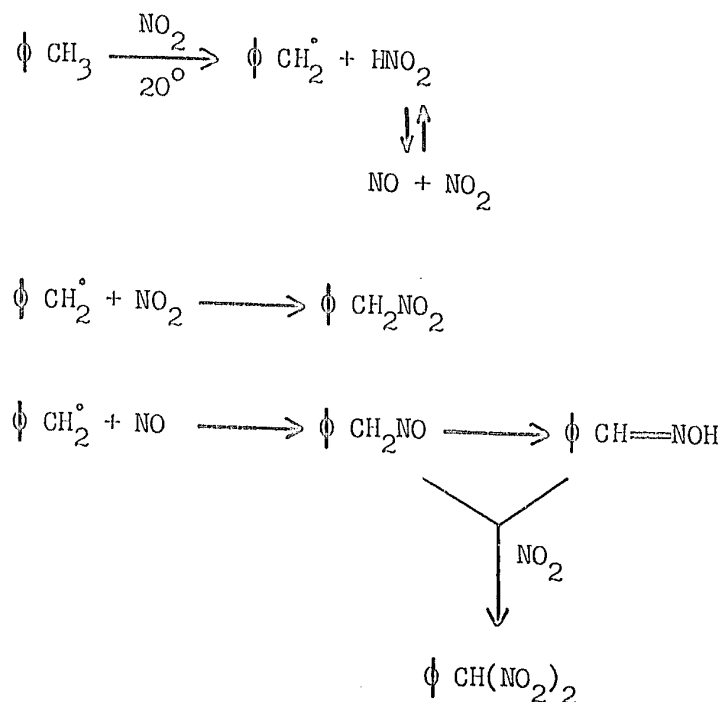
Before discussing the mechanism of the lead tetraacetate oxidation of aromatic ketoximes, we shall consider the mechanisms operating when nitrogen dioxide, oxygen, and nitric oxide are used as oxidizing agents. A direct correlation with the results obtained for the lead tetraacetate oxidations will then be made.

5-2. Oxidations with Nitrogen Dioxide: Gem-Dinitro Derivatives

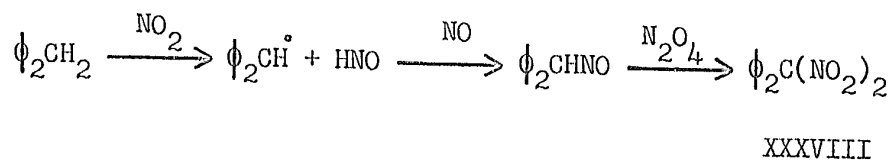
Gaseous nitrogen dioxide exists in rapid equilibrium with dinitrogen tetroxide (N_2O_4), the equilibrium at room temperature being mainly on the dimer side (7). The latter exists mainly as shown in structure LXIII but has been found to undergo ionic reactions usually attributed to structure LXIV, which has been identified by low-temperature infrared studies (58a).



Little is known of the mechanism of oxidative nitrations of organic compounds leading to gem-dinitro compounds (52,59). The most informative results were reported in a brief review article in 1963 (60). The mechanistic scheme presented was as follows:



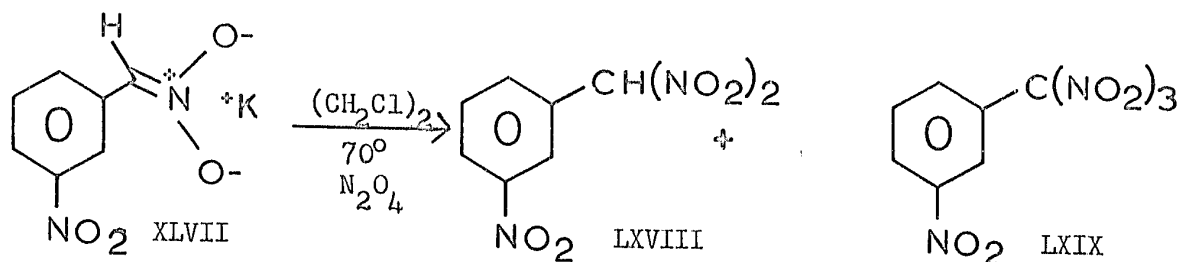
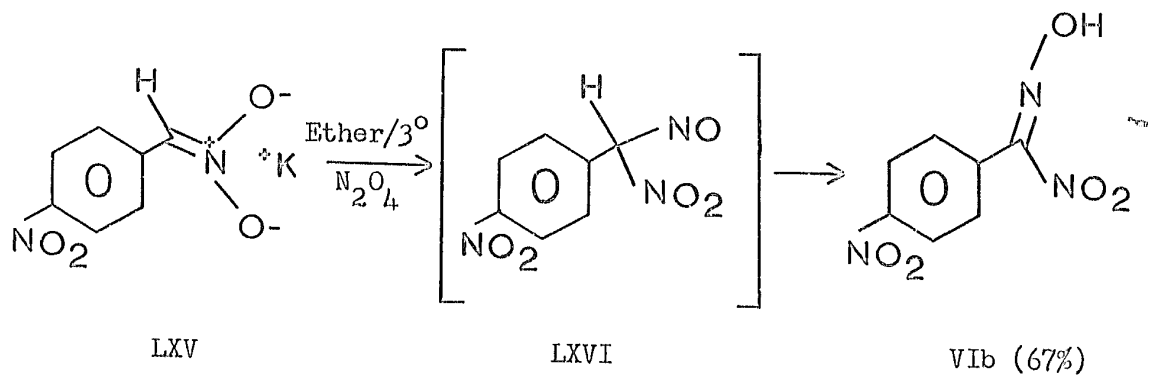
A similar scheme had been presented (53) for the conversion of diphenylmethane to dinitrodiphenylmethane (XXXVIII),



In both of these cases, however, no mechanism was described for the nitration of the intermediates leading directly to the gem-dinitro derivatives.

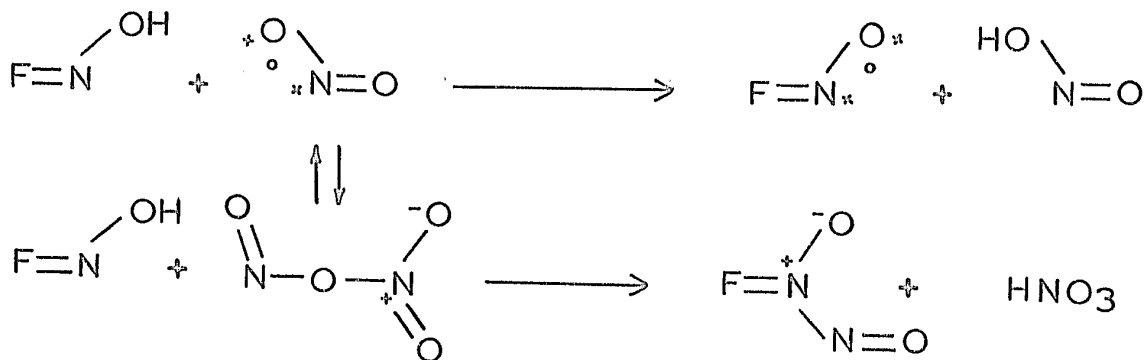
The behaviour of dinitrogen tetroxide as a nitrosating agent was well demonstrated by the work of Nokinov et al. (61) on the aci-nitro salt of p-nitrophenylnitromethane (LXV) which was converted to the benzonitrolic acid VIb, through intermediacy of the pseudonitrole LXVI.

Direct oxidation of a similar aci-nitrolate (XLVII) at 70° led to free



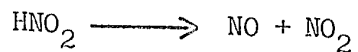
radical nitration products LXVIII and LXIX.

In the light of the above results, we may consider the following possibilities for the initiation step in the oxidation of fluorenone oxime.

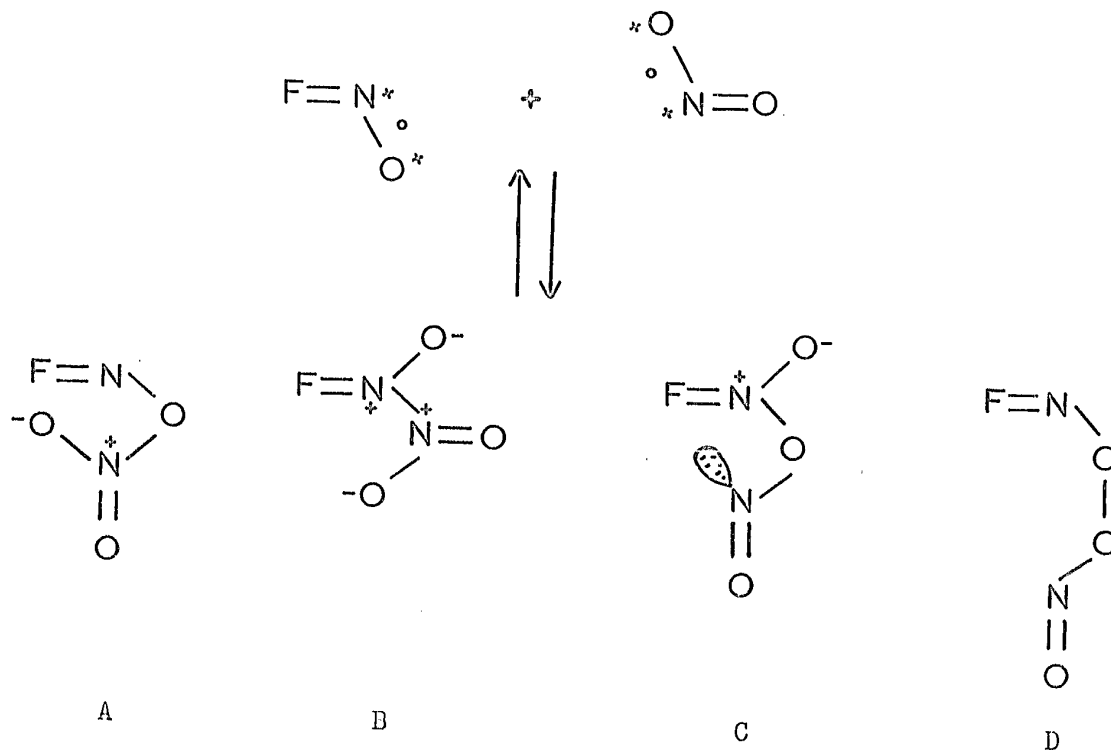


Reaction 2 can readily be ruled out since fluorenone oxime did not undergo any reaction with nitrous acid in glacial acetic acid which contains NO^+ (44). Moreover, the nitration of aldoximes (62) at 0° and at 55° always led to products corresponding to a free radical initiation as in reaction 1.

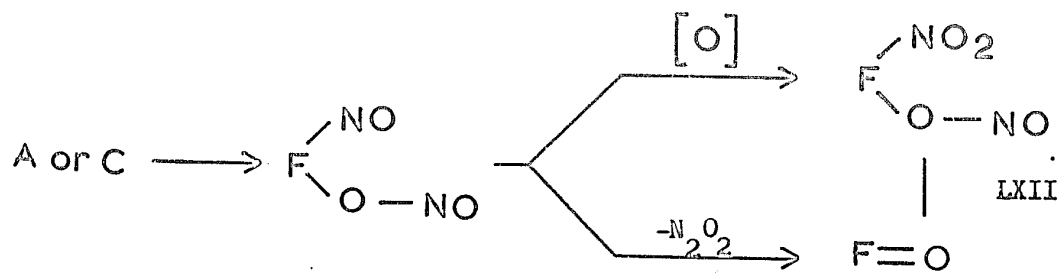
As previously shown (53,60), nitrous acid can decompose to nitric oxide and nitrogen dioxide, but in the presence of excess nitrogen dioxide we need only consider the latter.



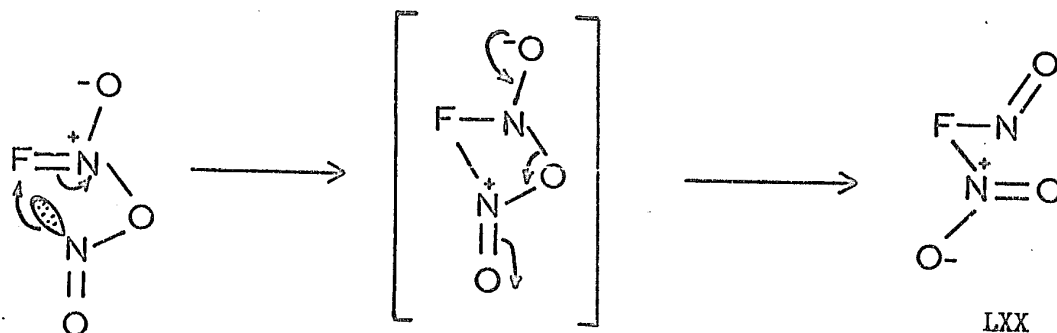
Dimerization between the iminoxyl radical XI_R and a nitrogen dioxide radical would be expected to be very facile since the electronic and geometric properties of these two radicals have been reported to be strikingly similar (20). Only three possible intermediates will be considered (A to C), since the fourth possibility (D) involves radical combination across the oxygens which has not been observed for nitrogen dioxide (58) or iminoxyl nitroxide (see introduction) dimerization.



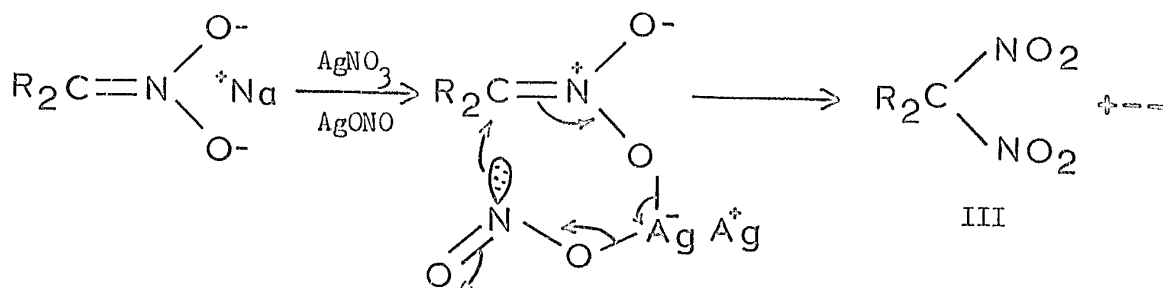
Intermediate B has a structure analogous to fluorenonazine-N-bis-oxide (XXXVII) and aldazine-N-bis-oxides (XVIII) which do not undergo spontaneous rearrangement. Intermediate B would be even less likely to rearrange due to the delocalization of the negative charge over the nitro group. Structures A and B can be further ruled out since rearrangement would lead to the 9-nitrito-9-nitro-fluorene (LXII) or fluorenone, neither of which was obtained in any significant yield.



Intermediate D would have a strong driving force for rearrangement created by the positively-charged nitronate nitrogen and the nucleophilicity of the nitrogen of the nitrite group. The gem-nitroso-nitro-derivative (LXX) would be an expected product.

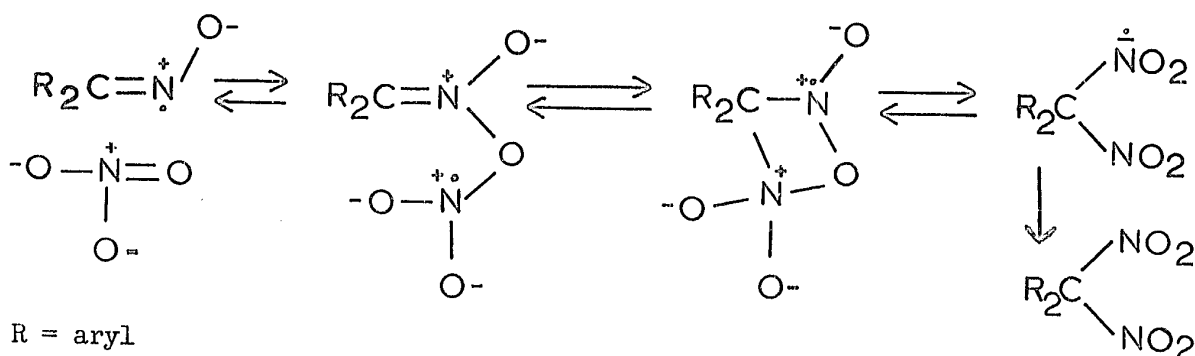


An intermediate similar to D has been postulated in the oxidative nitration of nitronates (LXXI) where a more favoured six-membered transition state was involved in gem-dinitrinomethane (III) formation (52).

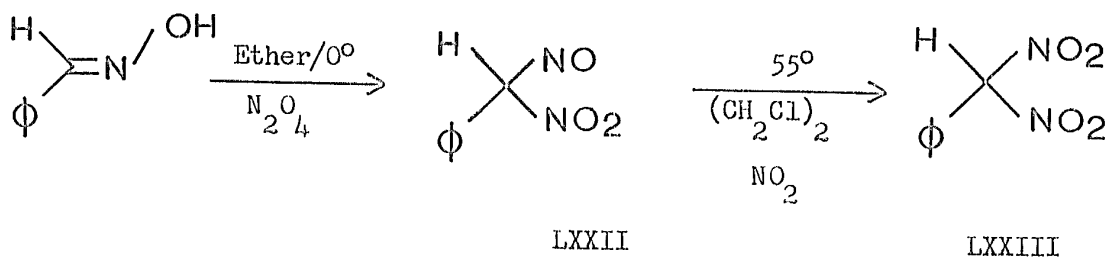


R = alkyl or aryl

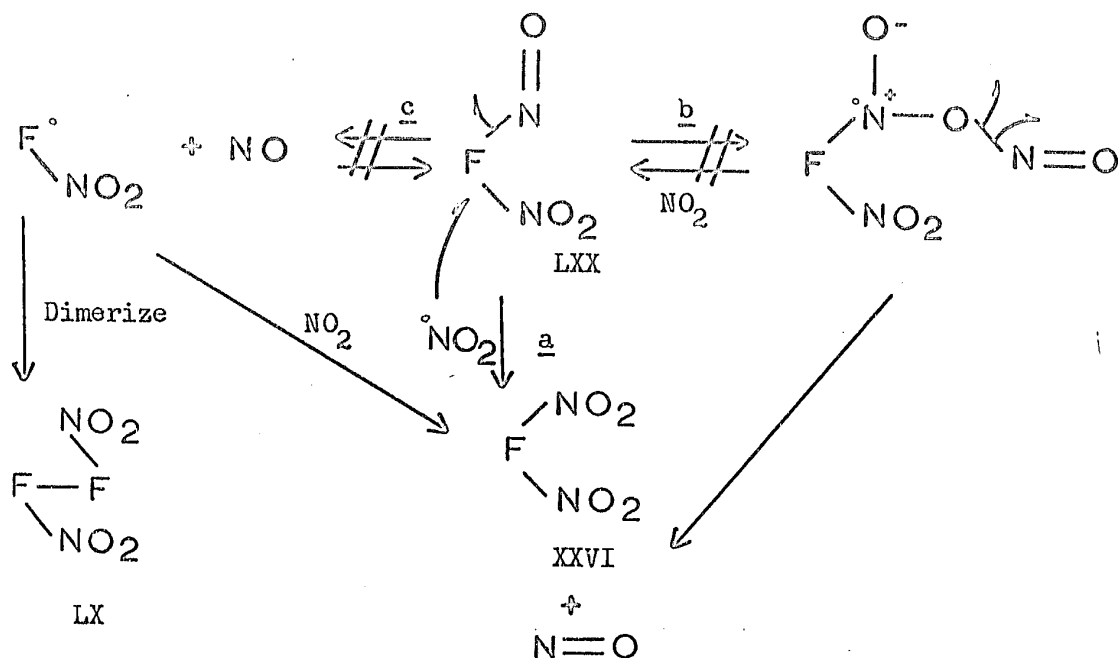
The same type of transition state was postulated for gem-dinitromethane product formation in the ceric ammonium nitrate oxidation of fluorenone, benzophenone, and acetophenone oximes (32).



The isolation of the gem-nitroso-nitro product (LXX) from the fluorenone oxime oxidation was not possible when the reaction was carried out at 0°, under which conditions the similar derivative of benzaldoxime (LXXII) was isolated (62). Since nitration of this pseudo-nitrole LXXII to gem-dinitrophenylmethane (LXXIII) readily occurred at



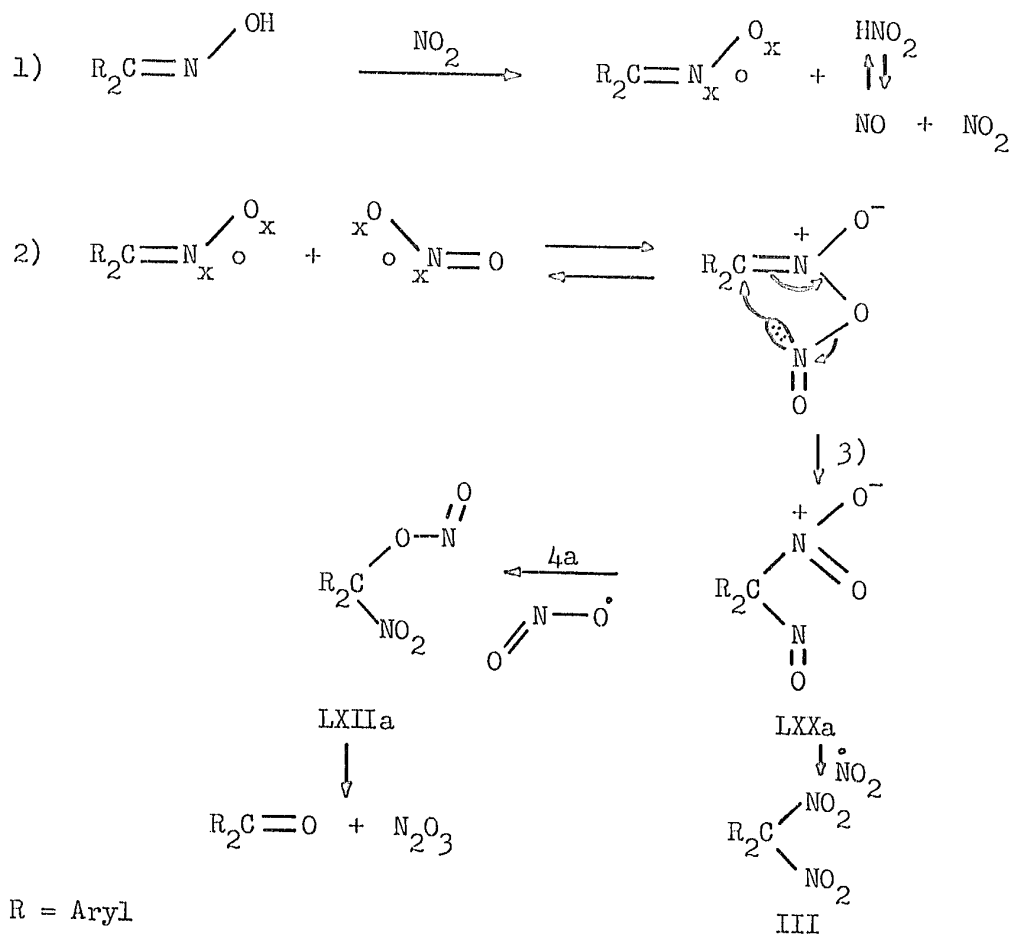
higher temperatures and since stable blue pseudonitroles were obtained in the similar oxidation of aliphatic ketoximes (63), it may be postulated that rapid oxidation of intermediate LXX occurred in one of the following ways to form 9,9-dinitrofluorene (XXVI).



A radical displacement mechanism is postulated (path a). Path b can be ruled out from the results stated above. Path c does not exist to any significant extent since no 9-nitrofluorenyl dimer LX was obtained even when a very dilute solution of nitrogen dioxide was slowly added to fluorenone oxime (2-1.3).

Summing up, we have the following probable mechanistic path for formation of 9,9-dinitrofluorene (XXVI) from the reaction of oxime with nitrogen dioxide.

Scheme I - Gem-Dinitromethane Formation

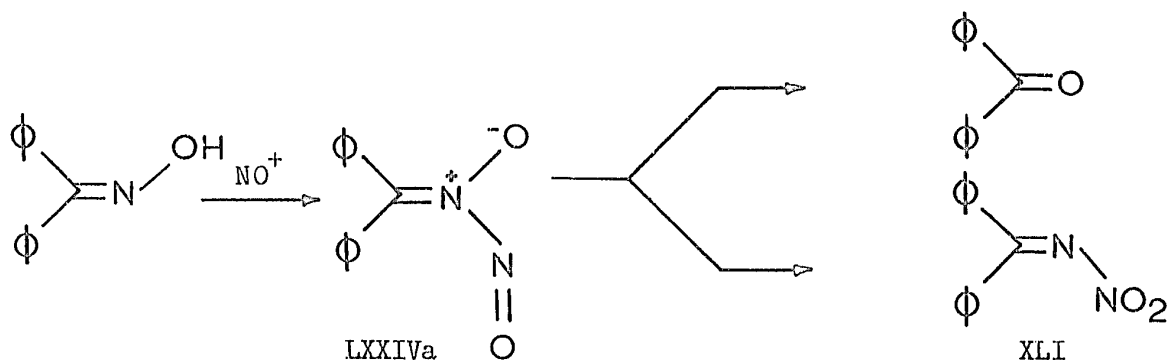


Scheme I will readily explain the formation of pseudonitroles for aliphatic ketoximes (63) and aromatic aldoximes (62). The aromatic stabilization of a fluorenyl free radical in the transition state readily leads to spontaneous oxidation of the postulated pseudonitrole (LXX) in the oxidative nitration of fluorenone oxime to 9,9-dinitrofluorene (XXVI). The same scheme may be used to explain the formation of gem-dinitromethanes from benzophenone oxime and xanthone oxime where similar aromatic stabilization is present.

The formation of traces of parent ketone from the oxidative

nitration of fluorenone oxime and a minor amount of benzophenone from the similar oxidation of benzophenone oxime may be explained by postulating radical displacement of nitric oxide in intermediate LXXa by NO_2 over its oxygen atom (reaction 4a in Scheme I). The resulting gem-nitronitrite LXXIIa, not as yet isolated, might then decompose to N_2O_3 and ketone, either homo- or heterolytically. Not enough work has been done on this aspect of the problem to warrant further speculation.

The formation of parent ketone from the initial nitrosation of the benzophenone oxime is highly unlikely because the expected (64) N-nitroso-nitrone LXXIVa was found (see 5-5) to lead to benzophenone as well as the nitrimine derivative (XLI). The latter was not obtained at all.

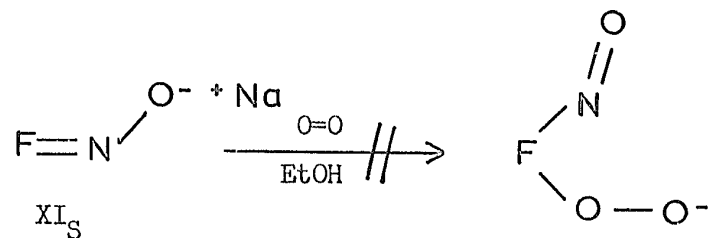


In the case of indanone oxime (LII), the major product formed was the parent ketone (LIII) while minor amounts of nitration products were observed. A different route has obviously been followed which may be due to the known lesser stability of iminoxyl radicals of the oxime compared to the radicals from the above bis-aryl ketoximes (Table I). Further work was not conducted in this area since no nitration products had been observed from the lead tetraacetate oxidation of indanone oxime.

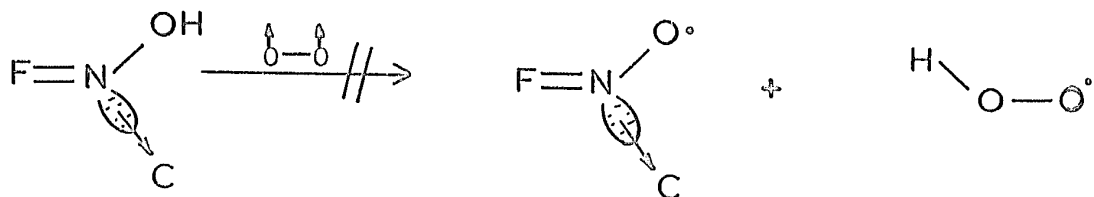
5-3. Autoxidations of Aromatic Ketoximes

Few reactions have received more attention than autoxidation, the reaction of molecular oxygen with organic materials (65). However, a survey of the chemical literature to date indicated that oximes had not been included in these studies.

Fluorenone oxime was oxidized by oxygen in glacial acetic acid. The initiation step probably led to the formation of the iminoxyl radical of the oxime as shown in reaction 1 of Scheme II (p. 114). Although ionic reactions of organic compounds with oxygen have been reported (65b), this type of mechanism may be ruled out since the salt of fluorenone oxime (XI_S) was inert to oxygen.



The iminoxyl radical (XI_R) formed in the initial step is stabilized, at least in part, by the delocalization of the lone electron over the orbital including the lone pair of the nitrogen (Introduction). Any complexing of this lone pair in the oxime might therefore lead to a quenching of the initiation step.



C = complexing agent

This process was probably operative in the oxidation of fluorenone oxime carried out in aqueous acetic acid or trifluoroacetic acid through protonation of the oxime nitrogen*, since no reaction occurred in these acidic solvents.

The use of dry benzene as solvent probably led to a lowering of the oxidation potential of molecular oxygen since no oxidation occurred in this solvent. Although very little is known about the redox potentials of compounds in non-aqueous solvents, it seems likely that these potentials are a function of the dielectric constants of the solvents being used (67).

Benzophenone oxime behaved similarly to fluorenone oxime in its oxidation with molecular oxygen. In contrast to these results, indanone oxime and aliphatic oximes such as cyclohexanone oxime, 2,2,6,6-tetramethylcyclohexanone oxime and pregnenolone-20-oxime-3 β -acetate were completely unreactive under the above conditions. This lack of reactivity may be due to the fact that the iminoxyl nitroxides of aliphatic oximes are much less stable than those of bis-aryl ketoximes (see Table I).

Xanthone oxime (XLVII) did not undergo any oxidation with molecular oxygen. This may be due to the + - mesomeric effect of the bridged oxygen which may give the OH bond ionic character.

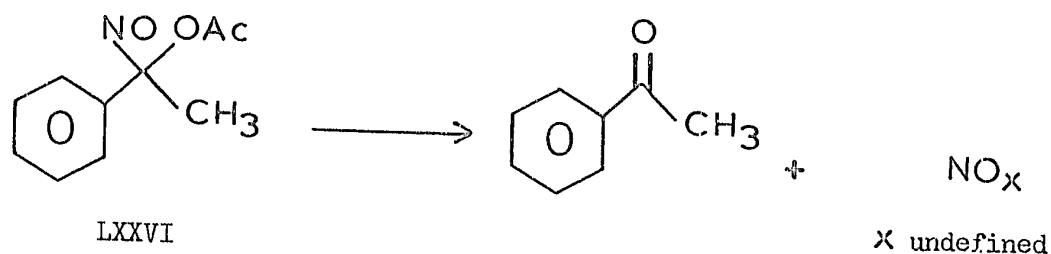
Although the iminoxyl radicals from benzil antimonoxime (IX_R; see 3-4) and biacetyl monoxime (XIII_R) are more stable (Table I) than

* Spectral studies conducted on oxime hydrochlorides have indicated that protonation takes place at the nitrogen of oximes (66). Fluorenone oxime hydrochloride precipitated from acetic acid containing conc. HCl.

the fluorenoniminoxyl radical (XI_R), the oximes were found to be stable to oxygen. The internal hydrogen bonding in these oximes was therefore probably the cause for the lack of reactivity.

Once iminoxyl radicals have been formed (reaction 1, Scheme II), they may react with molecular oxygen or combine with the hydroperoxy radicals formed in the initial step. Reaction will occur preferentially at the nitrogen of the iminoxyl radicals. The reaction paths leading to the observed ketone and dinitro products are shown in Scheme II (2 and 3).

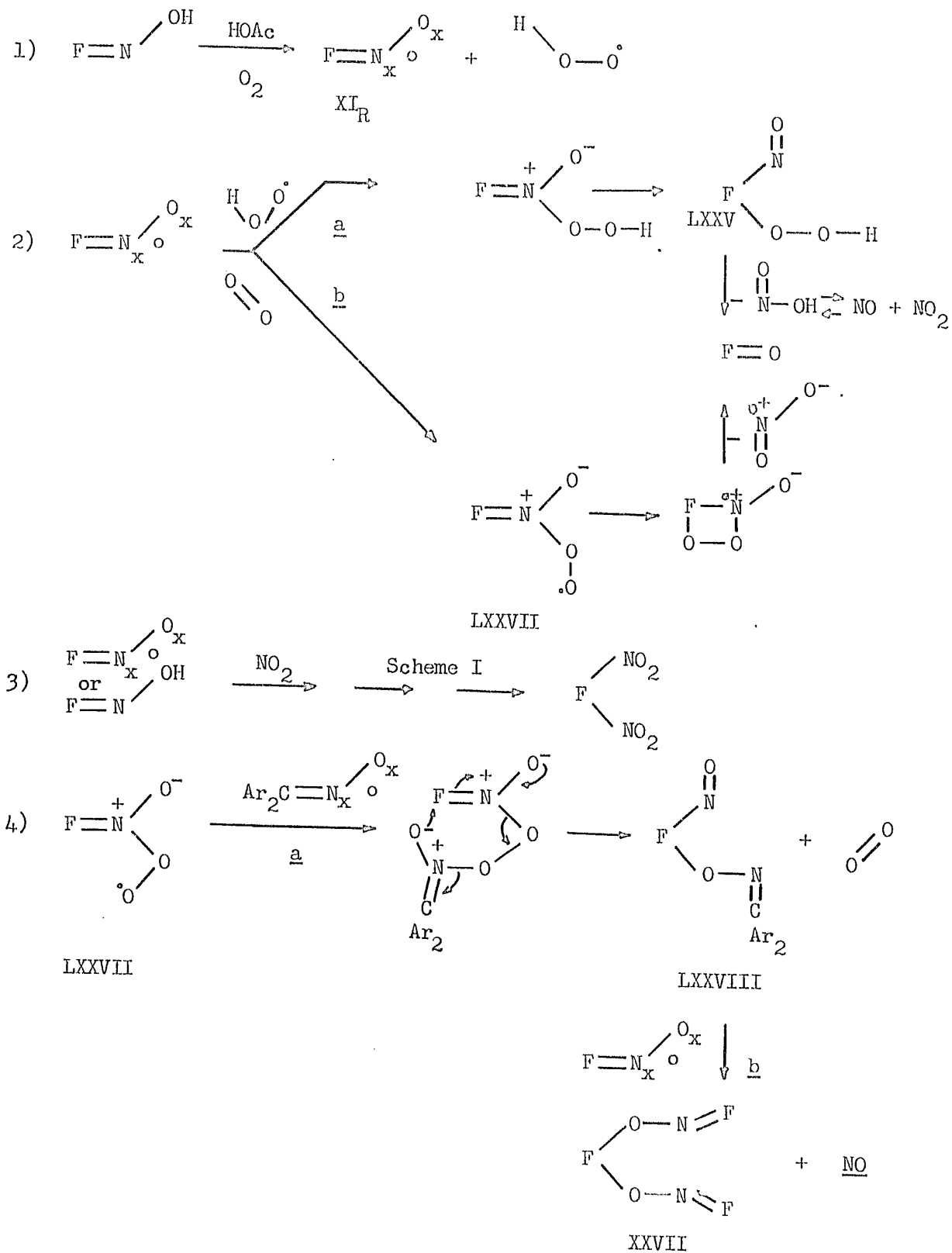
The type of rearrangements shown in reaction 2 (Scheme II) have been previously discussed in the reactions of aromatic oximes with nitrogen dioxide. In the presence of excess oxygen, path 2b would be expected to be the main route. The decomposition of the gem-nitroso-peroxide LXXV in reaction 2a finds precedent in the known instability of gem-nitrosoacetates from aliphatic ketoximes (27). In the case of acetophenone oxime, the blue nitrosoacetate LXXVI could not be isolated because it decomposed with evolution of nitrous fumes (24b).



The nitrogen dioxide formed in reaction 2 may react with oxime and with iminoxyl radicals to form the observed gem-dinitromethanes (reaction 3).

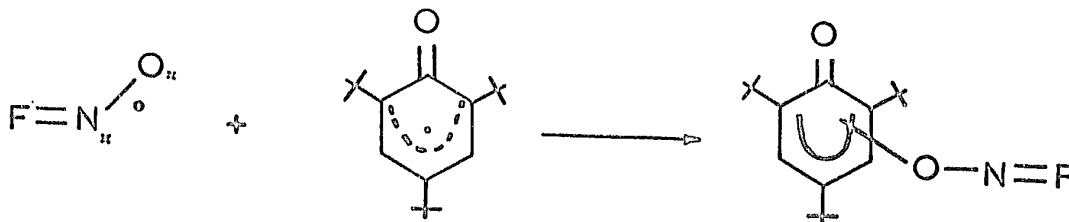
When the autoxidation of fluorenone oxime was carried out in

Scheme II - Autoxidation of Fluorenone Oxime



acetic acid saturated with oxygen, there was formed, in 13% yield, 9,9-difluorenylideneiminoxylfluorene (XXVII). When oxygen was bubbled through the solution, none of it was formed. This suggested that iminoxyl radicals of fluorenone oxime (XI_R) were probably involved in the formation of ketal XXVII but were quenched in the presence of sufficient oxygen (path 2b, Scheme II).

The ketal XXVII may have formed via the reactions shown in step 4 of Scheme II. Recombination of iminoxyl radicals with the N-peroxy radicals LXXVII could lead to the gem-nitrosoiminoxyl compound LXXVIII. An iminoxyl radical might then displace nitric oxide from intermediate LXXVIII to form the ketal XXVI (4b, Scheme II). The new bond would be formed at the oxygen of the iminoxyl radical since minimum crowding would thereby be obtained in the transition state. This type of addition has been described for the free radical reaction of fluorenone oxime with aroxyl free radicals (68).

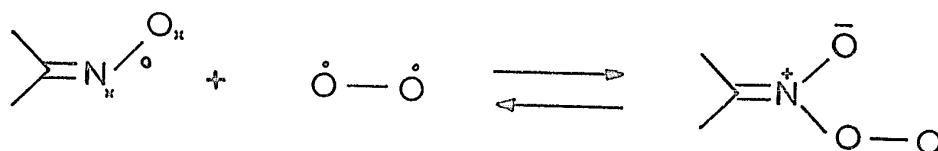


Any mechanisms leading to formation of ketal XXVII through ionic reaction of oxime may be ruled out since the reaction was carried out in glacial acetic acid.

The formation of intermediate LXXVIII by a free radical path involving iminoxyl radicals and nitric oxide (see 5-4) seemed unlikely since the ketal was formed in glacial acetic acid saturated with oxygen.

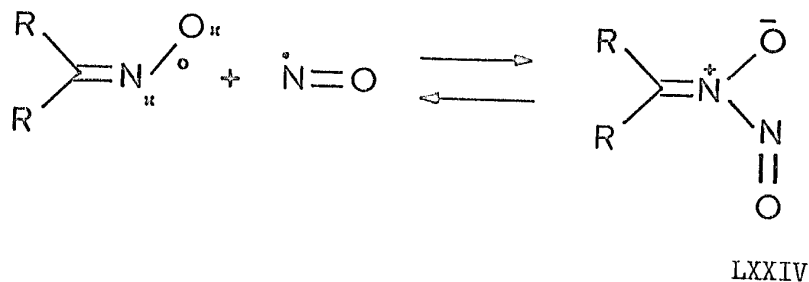
The nitric oxide would probably be rapidly consumed before it could combine with iminoxyl radicals.

Product formation from the autoxidation of benzophenone oxime can also be rationalized with Scheme II. However, not a trace of ketal XXXIX had been formed. This was probably a reflection of the shorter half-life of the iminoxyl radical of this oxime compared to that of fluorenone oxime. The ability of iminoxyl radicals to exist in the presence of oxygen long enough to undergo reactions with species other than oxygen may be explained by the following equilibrium, made possible by the long half-lives of these radicals (Table I; IX_R and XI_R).



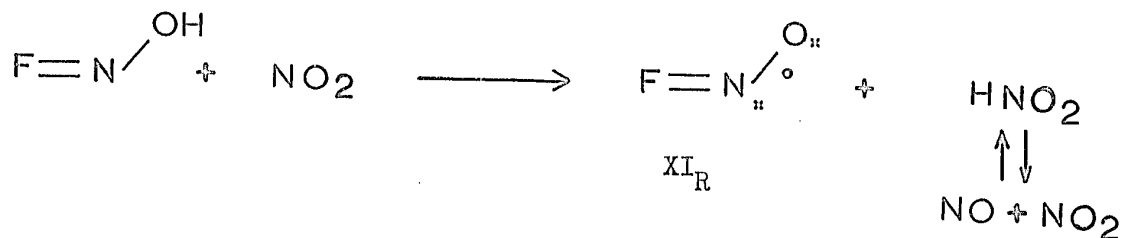
This type of equilibrium has been suggested for other autoxidation reactions (65b).

The detection by ESR of fluorenone and benzophenone iminoxyl radicals in acetone solutions saturated with nitric oxide (69) may also be rationalized by the above-type of equilibrium:



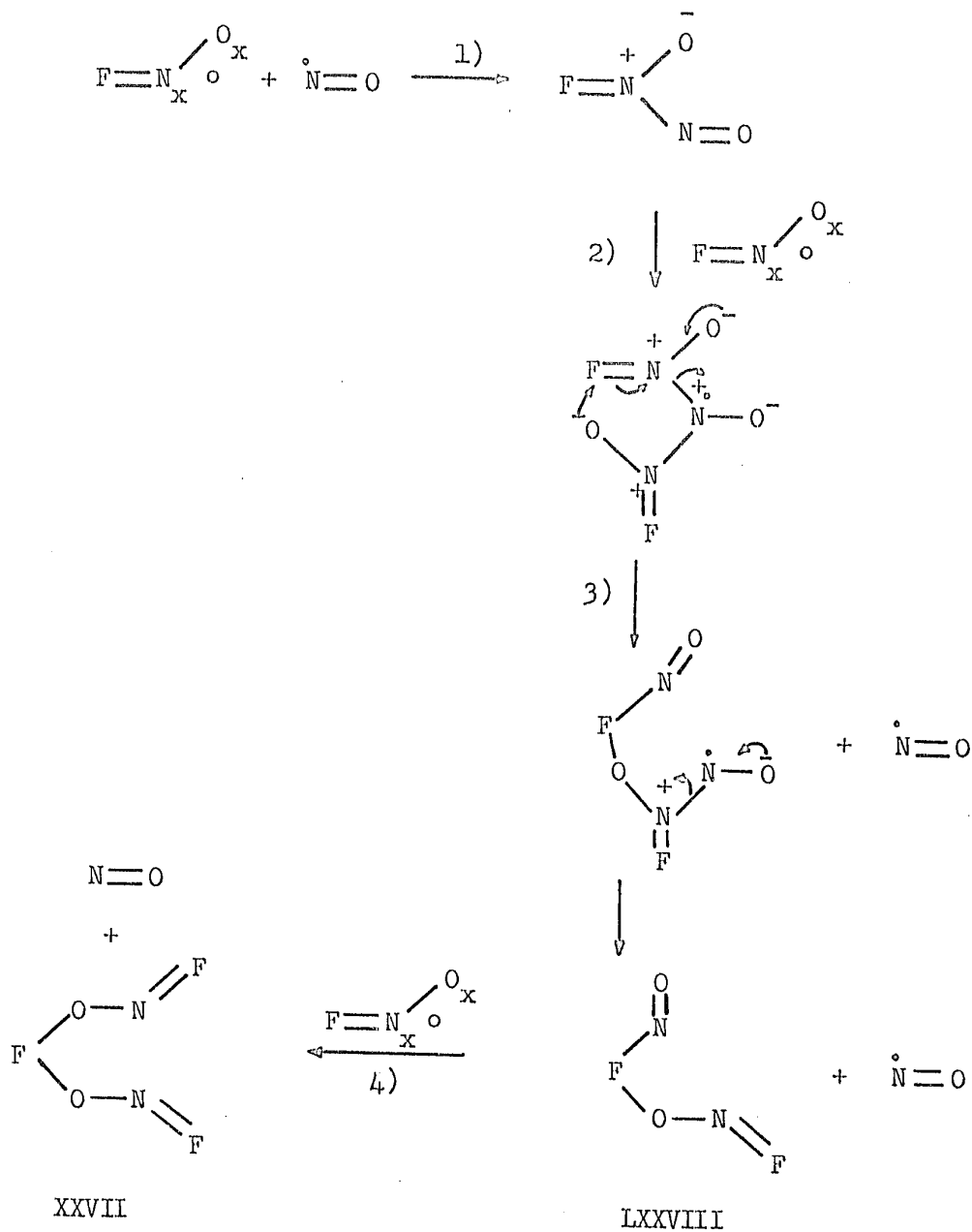
5-4. Nitrogen Dioxide as a One-Electron Oxidizing Agent

It was shown (5-2) that the reaction of nitrogen dioxide (NO_2) with fluorenone oxime led to iminoxyl radicals (XI_R) which rapidly reacted with the excess NO_2 present to form 9,9-dinitrofluorene (XXVI). The slow addition of a one mole equivalent of nitrogen dioxide to fluorenone oxime in glacial acetic acid led to this dinitro product (XXVI), but fluorenone and a minor amount of ketal XXVII were also formed.



Dimerization of iminoxyl radicals (XI_R) could lead to fluorenon-azine-N-bis-oxide (XXXVII). This was not obtained as a product nor as an intermediate. A free radical reaction leading to ketal formation, as shown in Scheme II (reaction 3) cannot be rationalized for the above conditions. It, therefore, seems probable that ketal formation arose by the following path involving the nitric oxide generated in situ (Scheme III).

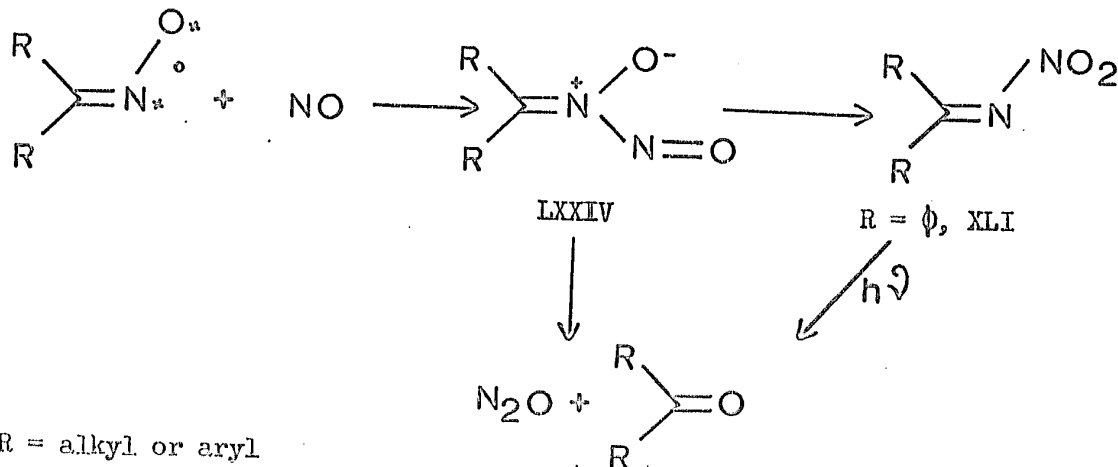
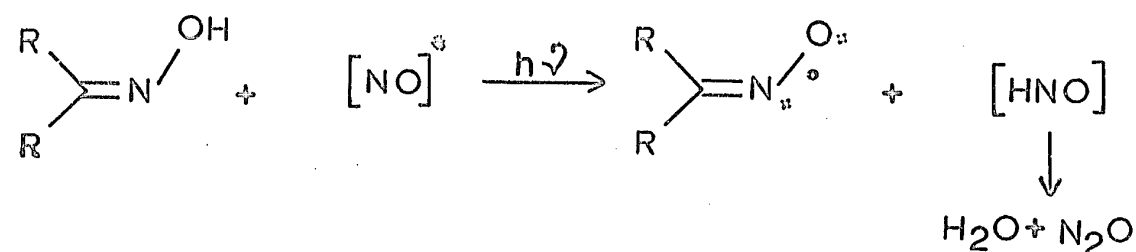
Scheme III - Iminyl Ketal Formation



The N-nitrosnitron LXXIVb may behave as a trap for iminoxyl radicals in analogy to the similar behaviour of nitroso compounds (70). The resulting intermediate LXXVIII can react further with iminoxyl radicals to form ketal XXVII (step 4 above; also Scheme II - 4b).

5-5. Reactions of Aromatic Ketoximes with Nitric Oxide

There have been no reports to date in the chemical literature of the reaction of oximes with nitric oxide. The reactions of salts of oximes with nitric oxide, the latter behaving as a Lewis acid, have been described (71). A cursory report on the free radical oxidation of oximes by nitric oxide was communicated to us by O.L. Chapman et al. (48). They found that certain oximes (e.g. cyclohexanone and pinacolone oximes) gave a modest yield of carbonyl product on treatment with nitric oxide in the dark in acetone via the corresponding iminoxyl radical (ESR). In other cases, such as benzophenone oxime, formation of the iminoxyl radical could be observed only when the solution was irradiated in the presence of nitric oxide. The initial intermediates formed were postulated as the following:



R = alkyl or aryl

The reaction of fluorenone and benzophenone iminoxyl radicals with nitric oxide, in the absence of ultraviolet radiation, has been shown to lead to approximately 50% parent ketone and 30% nitrimine derivative (30,69). Different results were obtained in the above study due to side reactions arising from the photochemistry of products such as the nitrimine XLI.

In our investigation on the reactions of aromatic ketoximes with nitric oxide, we found that oxidations in the dark did occur but were markedly influenced by solvent. Thus fluorenone oxime did not react with nitric oxide in glacial acetic acid* but rapidly reacted in benzene to form fluorenone. In methylene chloride, immediate conversion to ketone, fluorenonazinemonoxide (XXX) and other minor products occurred.

In summary, we note that

- (i) aromatic ketoximes may react with nitric oxide without UV irradiation to yield products whose formation are very solvent dependent;
- (ii) iminoxyl radicals may be generated from the reaction of oximes with nitric oxide, but other reaction paths, directed by the solvent used, may also exist.

5-6. Lead Tetraacetate Oxidations of Aromatic Ketoximes

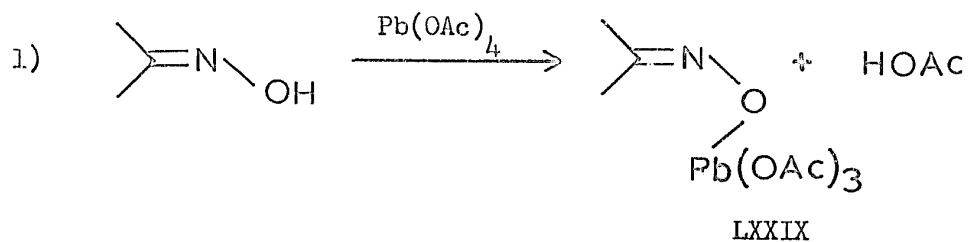
5-6.1. Initiation steps and parent ketone formation

Fluorenone oxime O-acetate (XXXV) and O-ether did not undergo any reaction with lead tetraacetate in methylene chloride or in acetic

* Benzophenone oxime underwent rapid reaction but the products formed were not studied.

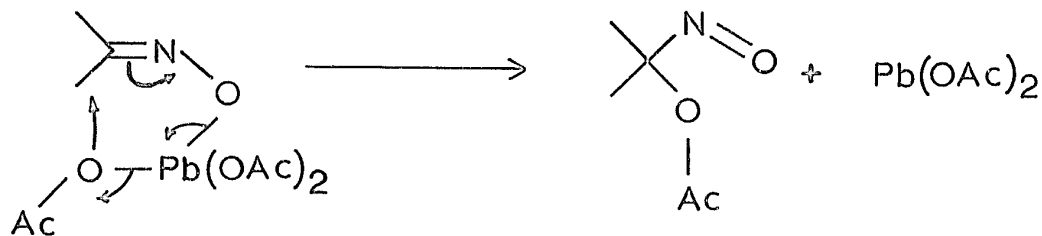
acid. It was shown that acetic acid was a by-product in the oxidations of aromatic ketoximes conducted in methylene chloride.

In the light of these results, it appeared that the initiation step in the lead tetraacetate oxidations of aromatic ketoximes occurred as follows.



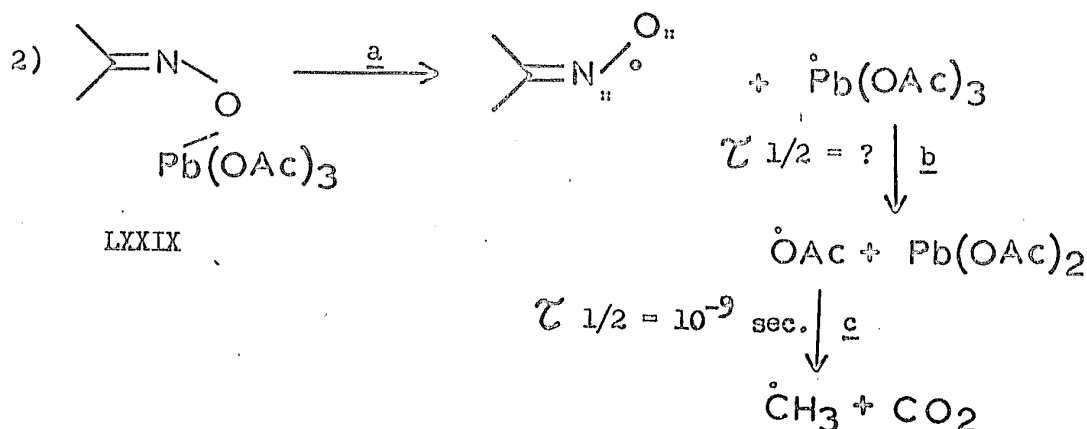
The formation of organometallic intermediates, as represented by structure LXXIX, has been reported in other reactions of lead tetraacetate (33).

A concerted rearrangement of the organolead intermediate could lead to gem-nitrosoacetate formation as follows.



This process was highly unlikely in the oxidation of bis-aryl-ketoximes since very stable iminoxyl radicals derived from these were observed (ESR). Moreover, the free radical nature of the lead tetraacetate oxidation of aromatic ketoximes has been clearly demonstrated (Chapters 2 and 3).

Homolysis of the iminoxyl-lead triacetate intermediate (LXXIX) would lead to the iminoxyl radicals which have been reported for aromatic ketoximes, as well as other oximes* (Introduction).



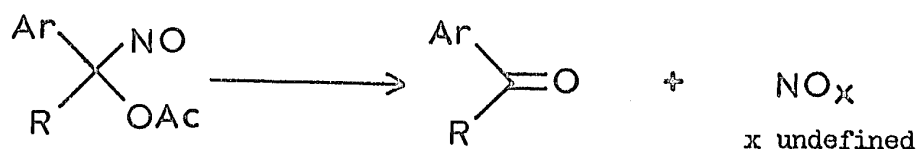
The lead triacetate radical, formed in reaction 2a, can decompose to lead diacetate and acetoxy radicals (2b). The latter have been reported to have a half-life of about 10^{-9} seconds (71). If the lead triacetate radicals had a half-life similar to that of acetoxy radicals, no recombination with iminoxyl radicals from bis-aryl-ketoximes would occur once these had escaped from the solvent cage. The lead triacetate radical may however be sufficiently long-lived to undergo recombination with iminoxyl radicals to form intermediate LXXX (Scheme IV-3, p. 126), which can rearrange to the gem-nitrosoacetate XV in a manner previously described for gem-dinitro product formation (Scheme I, p. 109).

The recombination of iminoxyl radicals with acetoxy radicals,

* This same scheme (reactions 1 and 2) has been presented for aliphatic oximes and aromatic aldoximes (20b).

formed from reaction 2b shown above, is highly unlikely since it has been reported that the acetoxylation of organic compounds with lead tetraacetate has never involved free acetoxy radicals (72).

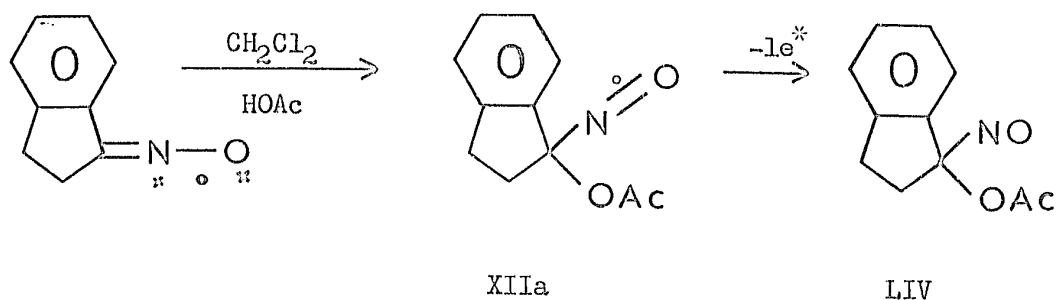
A gem-nitrosoacetate was observed only in the lead tetraacetate oxidation of indanone oxime (LIV). This product was stable in solution but it readily decomposed to parent ketone when concentrated. A similar observation had been reported by Lown (24b) on the lead tetraacetate oxidation of acetophenone oxime. The blue nitrosoacetate (LXXVI) from the latter could not be isolated because it decomposed with evolution of nitrous fumes. The instability of aromatic gem-nitrosoacetates was further shown by the work of Kropf et al. (28) on the oxidation of aldoximes. They reported that a blue solution, attributed to the nitrosoacetate intermediate LXXVIa, formed from the reaction of benzaldoxime with lead tetraacetate in protic solvents, rapidly discoloured with the formation of nitrous fumes and benzaldehyde.



R = CH₃, LXXVI

R = H, LXXVIa

The formation of nitrosoacetate LIV from the lead tetraacetate oxidation of indanone oxime (see 3-3) in analogy with the studies reported for acetophenone oxime (24b) probably arose, at least in part, through the radical anion XIIa, and not via the iminoxyl radical as shown in reaction 3 of this section.



Since no such radical anions have yet been detected (ESR; introduction) for bis-aryl-ketoximes, the mechanism leading to gem-nitrosoacetates would best be represented by reactions 1-3 (Scheme IV).

In the light of the observed instability of the gem-nitrosoacetates of aromatic ketoximes and aldoximes described above, it was not surprising that no gem-nitrosoacetates** could be detected from the lead tetraacetate oxidation of the bis-aryl-ketoximes; fluorenone oxime, benzophenone oxime and xanthone oxime.

The formation of parent ketones from gem-nitrosoacetates, whose intermediacy was suggested for xanthone oxime (3-2), will next be described in the light of the mechanism proposed above.

The yields of parent ketone obtained from the lead tetraacetate oxidations of aromatic ketoximes are shown in Table XVI (5-1). The results obtained with glacial acetic acid as solvent indicate that Scheme IV may be used to represent the formation of parent ketone, at least in part. The iminoxyl radical from benzil anti-monoxide (LV_R) has such a high stability (3-4) that reaction 3 (Scheme IV) probably does not occur

* A more detailed mechanism had not been provided by Lown (44).

** Not even a transient blue or turquoise colour, characteristic of aliphatic and aromatic nitrosoacetates, could be detected in any of these reactions.

and no ketone formation can therefore result. The formation of a minor amount of ketone in the presence of oxygen may be explained in analogy to ketone formation from the autoxidation of fluorenone oxime (Scheme II).

In the case of fluorenone oxime, reaction 3 most likely takes place, leading to the formation of minor amounts of nitrosoacetate XV. This intermediate might spontaneously decompose to acetyl radicals, observed fluorenone and observed nitric oxide* (Scheme IV - 4).

The formation of fluorenone oxime O-acetate (XXXV), which was experimentally observed, could arise through recombination of the above acetyl radicals with fluorenone iminoxyl radicals.

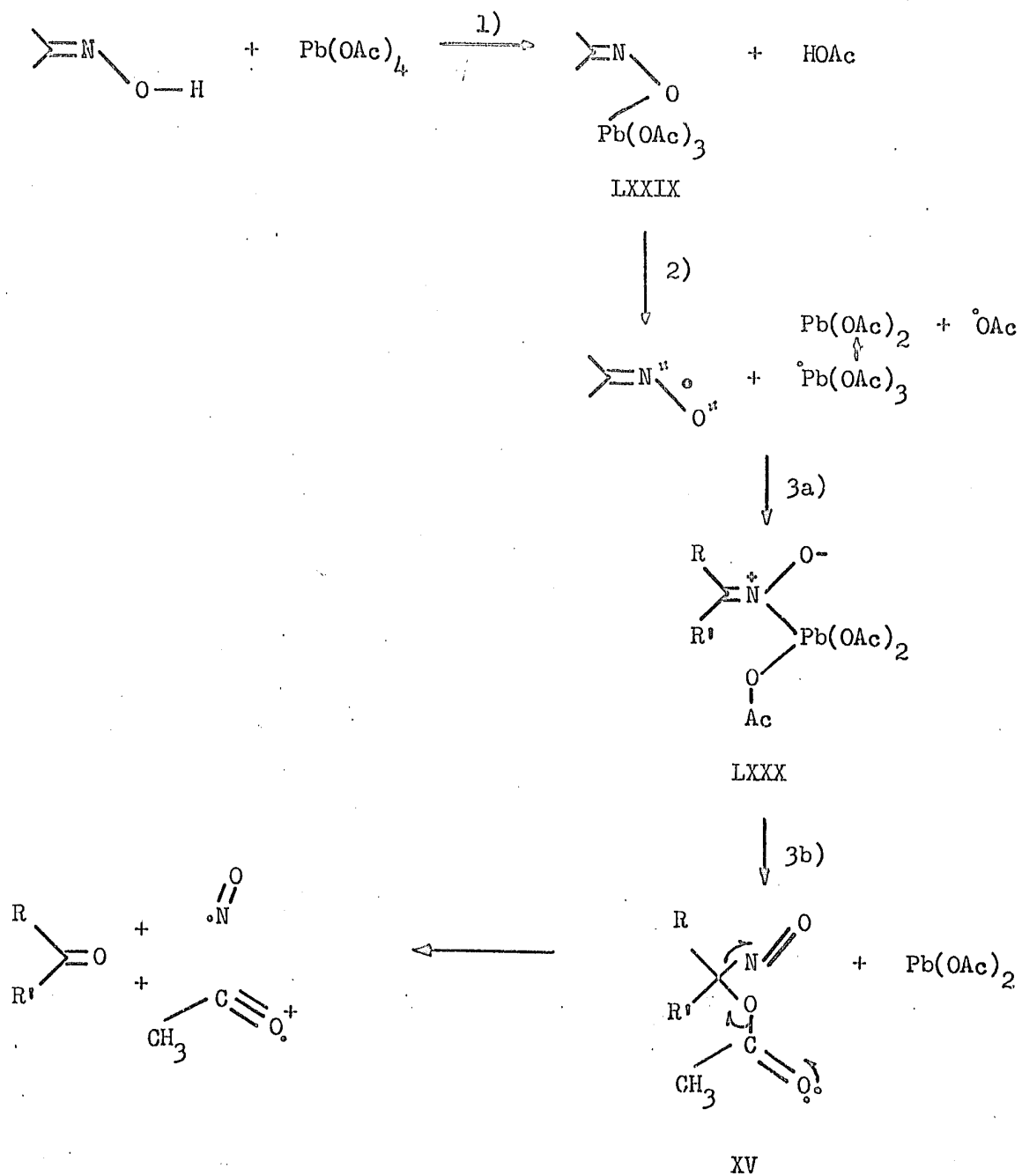
The life-time of the iminoxyl radical from benzophenone oxime (IX_R) is 10 times shorter than that of the fluorenone iminoxyl radical (XI_R). Since these life-times were measured in lead tetraacetate solutions and since no secondary radicals were observed due to solvent participation (see introduction), it seemed likely that the difference in life-times was a reflection of the recombination of iminoxyl radicals with lead triacetate radicals (reaction 3 of Scheme IV). A higher yield of nitrosoacetate resulting from the lead tetraacetate oxidation of benzophenone oxime might therefore be expected, which in turn might lead to the observed higher yield of parent ketone**.

While the yield of fluorenone increased in the lead tetraacetate oxidation of fluorenone oxime in acetic acid when oxygen was introduced,

* This represents a gross overall mechanism for nitrosoacetate decomposition. Other free radicals, such as fluorenone iminoxyl radicals (XI_R) may be involved in the product formation.

** Other reaction paths leading to parent ketone, resulting from secondary reactions (e.g. NO reactions, 5-5) may also exist.

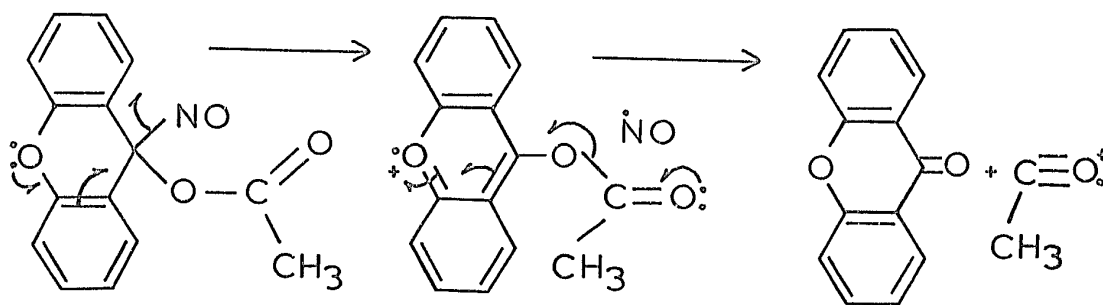
Scheme IV - Lead Tetraacetate Oxidations of Aromatic Ketoximes



R = Aryl; R' = Aryl or alkyl

the amount of benzophenone produced in the comparable reaction was unaffected. The reaction of the iminoxyl radicals from fluorenone oxime and benzophenone oxime with oxygen leading to parent ketone has previously been described (5-3). Apparently the recombination of benzophenone iminoxyl radicals with lead triacetate radicals (and other radicals such as NO) is sufficiently rapid to exclude any reaction with oxygen. This is consistent with the argument that greater recombination of lead triacetate radicals occurs with iminoxyl radicals from benzophenone oxime than with those from fluorenone oxime.

The high yield of xanthone resulting from the lead tetraacetate oxidation of xanthone oxime (XLVII) probably arose via the reaction steps shown in Scheme IV. Since no nitrosoacetate intermediate could be detected (no blue or turquoise colour had formed), the latter may have decomposed as rapidly as it formed. This decomposition would be more facile than that for the nitrosoacetate of fluorenone oxime due to the electromeric effect of the bridged oxygen.



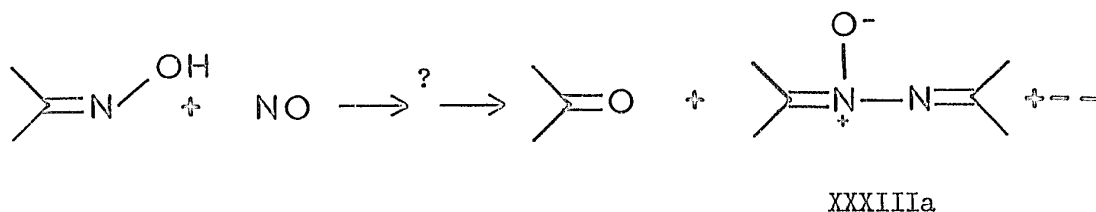
A minor amount of xanthone oxime O-acetate (L, IR only) may have formed by recombination of iminoxyl radicals from xanthone oxime with acetyl radicals, as previously described for fluorenone oxime.

Solvent effect

The lead tetraacetate oxidations of benzil anti-monoxime (LV), fluorenone oxime and benzophenone oxime conducted in methylene chloride led to parent ketone formation in about 50% yield. It was unaffected by oxygen and required only a half-mole equivalent of the oxidizing agent (see Table XVI). In contrast to the results obtained in glacial acetic acid, the stabilities of the iminoxyl radicals of these oximes (Table I) no longer reflected the amounts of parent ketone formed.

The detection (ESR) of iminoxyl radicals from the lead tetraacetate oxidation of aromatic ketoximes in methylene chloride was described in the introduction. Parent ketones were probably formed in these oxidations through the reactions shown in Scheme IV (p. 126). The cage effect of the methylene chloride solvent was probably responsible for a higher recombination of iminoxyl radicals with lead triacetate radicals (step 3a) with subsequent formation of intermediate gem-nitrosoacetates (XV) in step 3b, leading to parent ketone in step 4 (Scheme IV). Nitric oxide would be formed along with the ketone.

The formation of minor amounts of 9,9-dinitrofluorene in the oxidation of fluorenone oxime in methylene chloride provided evidence for the presence of nitric oxide in situ (see 5-2). It has previously been shown that nitric oxide reacts rapidly with fluorenone oxime in methylene chloride but not in glacial acetic acid (5-5). It is therefore probable that only half a mole equivalent of lead tetraacetate was required in the oxidations conducted in methylene chloride because the nitric oxide could rapidly react with the oxime.



The final products resulting from the reaction of nitric oxide with fluorenone oxime were found to be the same as those obtained from the lead tetraacetate oxidation of this oxime (see 5-5). A mechanism accounting for this reaction cannot be given with the present knowledge.

The reaction of xanthone oxime in methylene chloride with one mole equivalent of lead tetraacetate led to quantitative and instantaneous formation of parent ketone, whose yield was little affected by molecular oxygen. The reaction may have proceeded through a concerted mechanism leading to nitrosoacetate XLVIII (see 3-2) which could spontaneously decompose to parent ketone.

Indanone oxime behaved very similarly to xanthone oxime. Recombination of lead triacetate radicals to form the gem-nitrosoacetate product (step 3, Scheme II) probably did not occur since the blue colour observed for the oxidation conducted in glacial acetic acid had not formed. A different mechanism had previously been postulated from the results of ESR studies (p. 123).

5-6.2. Ketal formation

The formation of ketals XXVII and XXXIX from the lead tetraacetate oxidations of fluorenone oxime and benzophenone oxime respectively

has never been reported. The oxidation of these oximes with ceric ammonium nitrate (32) and with potassium ferricyanide ((8) and 2-3.1) did not lead to the ketal derivatives.

The most likely mechanism for ketal formation is that proposed in section 5-4 for the oxidation of fluorenone oxime with a mole equivalent of nitrogen dioxide (Scheme III). This mechanism is consistent with the results given in 2-1.1 and 3-1.1 for the formation of 9,9-difluorenylideneiminoxylfluorene (XXVII) and 1,1-bis(diphenylmethylen-iminoxyl)-diphenylmethane (XXXIX).

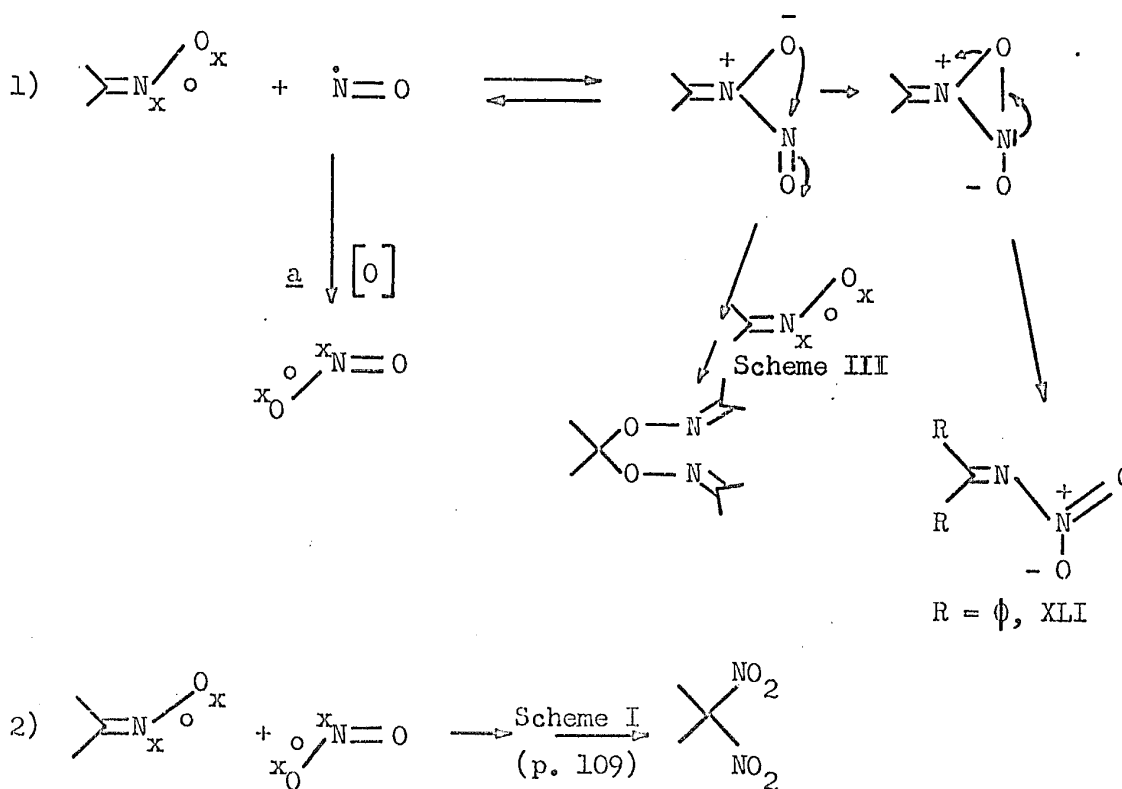
The iminoxyl radical of benzophenone oxime (IX_R) is about ten times more reactive than that of fluorenone oxime (XI_R) (Table I). This difference in reactivity was displayed by the observed change in reaction time from about one-half hour for fluorenone oxime oxidation to less than a minute for benzophenone oxime oxidation. It may account for the very low yield of ketal XXXIX obtained from benzophenone oxime since long-lived iminoxyl radicals are required for recombination as shown in reaction 4 of Scheme III (p. 118).

When the lead tetraacetate oxidation of fluorenone oxime was conducted in methylene chloride, the yield of ketal XXVII dropped to 1-3% and was insensitive to air. Dropwise addition of the lead tetraacetate to the oxime in methylene chloride led to an increase in the yield of the ketal to 8-10%. These results suggested that the following ionic mechanism was probably responsible for formation of intermediate LXXVIII, which could then further react, as shown in Scheme III, in a free radical step. (See 5-6.2 in Fig. 13, p. 129).

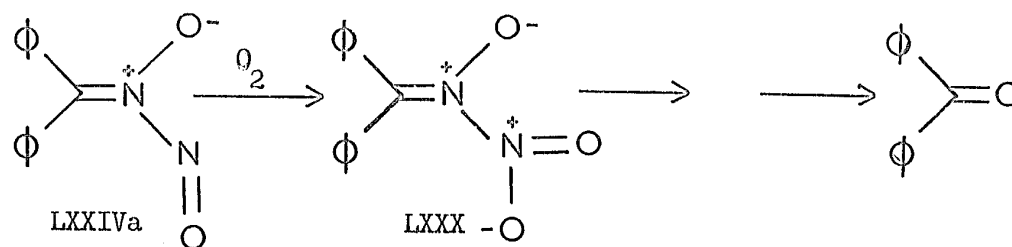
5-6.3. Formation of nitro products

The reaction of the iminoxyl radicals of fluorenone oxime and of benzophenone oxime with nitric oxide has been shown to lead to about 50% of parent ketone and 35% of the nitrimine derivative (5-5). The formation of the nitrimine product (XLI) from the oxidation of benzophenone oxime in oxygen-free acetic acid most likely arose in the same manner (Scheme V - 1). The concurrent formation of dinitrodiphenylmethane (XXXVIII) may readily be explained by assuming that free nitric oxide may readily be oxidized to nitrogen dioxide (Scheme V - 1a; later discussed). The subsequent rapid reaction of NO_2 and iminoxyl radicals (reaction 2) leads mainly to dinitrodiphenylmethane.

Scheme V - Nitration Products from Lead Tetraacetate Oxidations



When the lead tetraacetate oxidation of benzophenone oxime was conducted in the presence of oxygen, there was an increase in the yield of the gem-dinitro product XXXVIII, accompanied by the disappearance of the nitrimine XLI. The rapid* reaction of oxygen with nitric oxide probably led to complete quenching of nitrimine formation (step 1a). This might also have occurred through oxidation of the N-nitrosnitron LXXIVa which might be expected to lead to the N-nitronitron LXXX, whose decomposition to parent ketone has previously been described (5-2, p. 102).



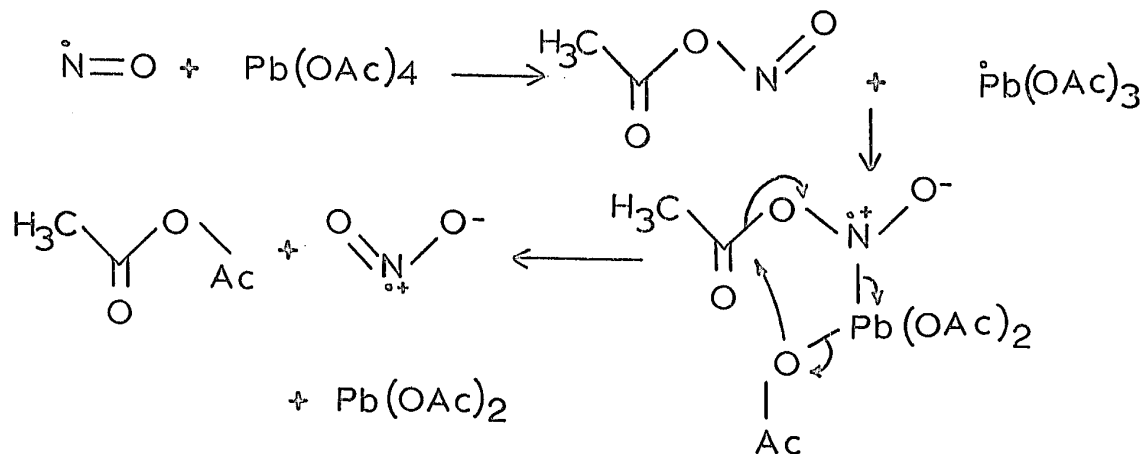
However, this process did not occur since there was no increase in the yield of ketone when the reaction was conducted in the presence of oxygen.

The same Scheme V may be used to explain the formation of 9,9-dinitrofluorene (XXVI) from the lead tetraacetate oxidation of fluorenone oxime in glacial acetic acid. However, the life-time of the fluorenone iminoxyl radicals is about 10 times greater than that for the benzophenone iminoxyl radicals (Table I). The equilibrium in step 1 of Scheme V would be shifted to a higher concentration of nitric oxide, which might be oxidized to nitrogen dioxide by lead tetraacetate. Moreover, the

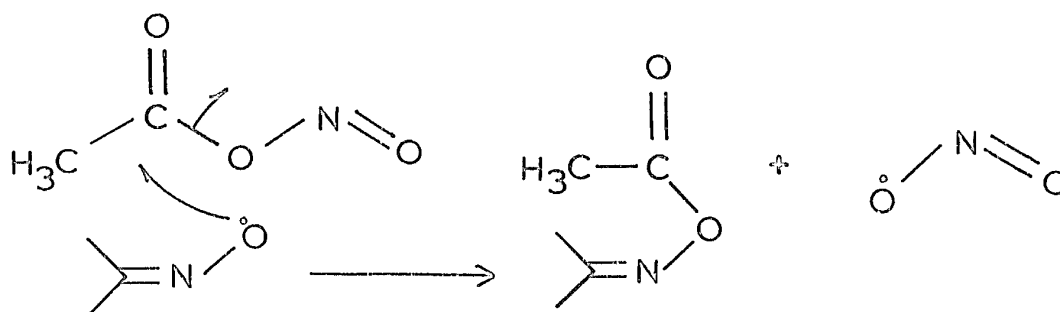
* Fluorenone oxime was instantaneously converted to 9,9-dinitrofluorene (2-1.3) when its acetic acid-nitric oxide solution was exposed to oxygen.

longer-lived fluorenone iminoxyl radicals may react with the N-nitroso-nitrone LXXIVb to lead to ketal formation (see 5-6.2). Both these processes might be responsible for the absence of any nitrimine product.

The participation of lead tetraacetate in the oxidation of nitric oxide leading to gem-dinitro compound formation was clearly demonstrated in the study of the oxidation of fluorenone oxime. Whereas only 4% of 9,9-dinitrofluorene (XXVI) was formed in the oxidation of fluorenone oxime in oxygen-free acetic acid with a half-mole equivalent of lead tetraacetate, a yield of about 20% was obtained when a one mole equivalent of oxidizing agent was used. The oxidation of nitric oxide may have proceeded through the intermediacy of acetyl nitrite which would be expected to scavenge free radicals, in analogy with nitroso compounds (70).



It is interesting to note that the formation of minor amounts of oxime acetate may readily be explained by the attack of an iminoxyl radical onto the intermediate acetyl nitrite.

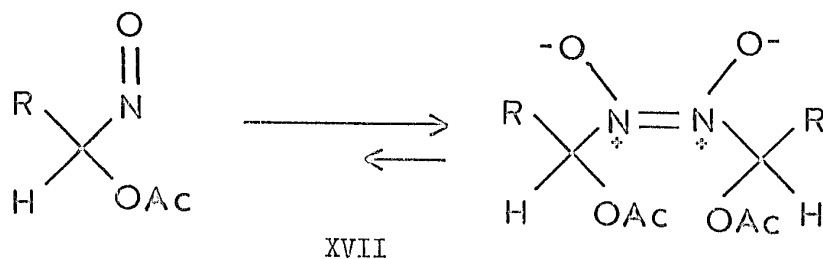
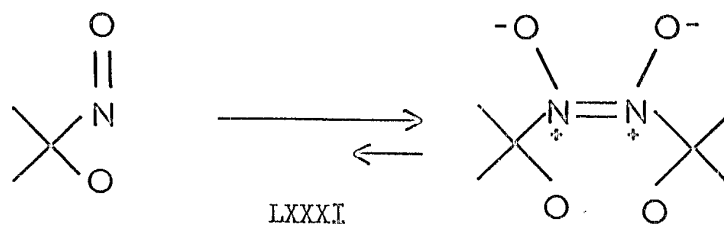


5-6.4. Azine-N-bis-oxides

Azine-N-bis-oxide formation from the oxidation of ketoximes has never been reported. Fluorenonazine-N-bis-oxide (XXXVII) was, however, obtained from the potassium ferricyanide oxidation of fluorenone oxime (2-3.1)*.

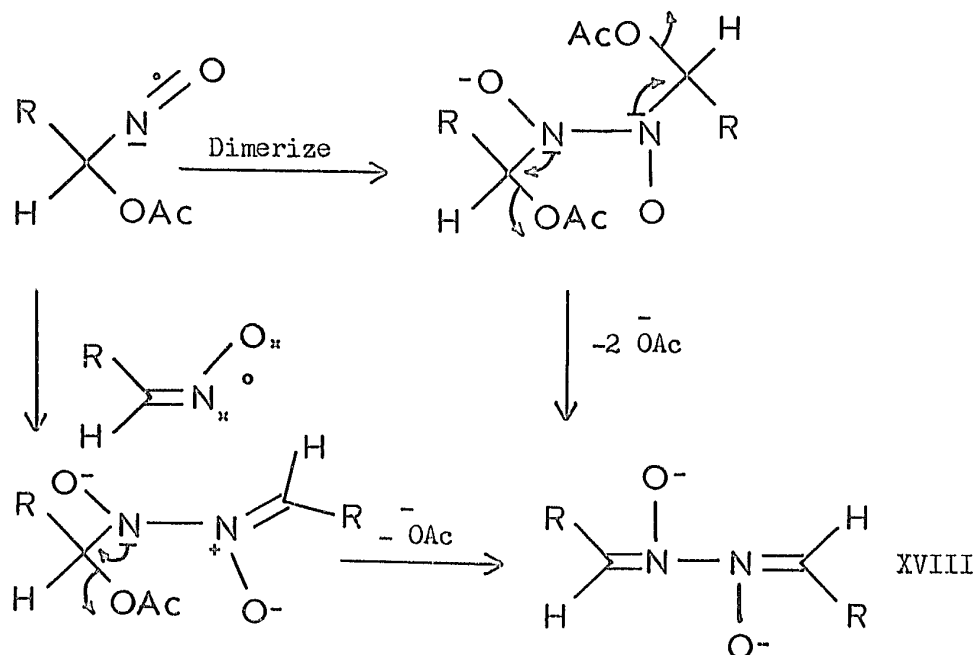
The oxidations of aromatic aldoximes have been found (26,28,32) to lead, in high yield, to the corresponding aldazine-N-bis-oxides (XVIII). The simplest possible mechanism might involve dimerization of two iminoxyl radicals. This was highly improbable since (i) the ESR spectra of solutions of aldoximes and lead tetraacetate (14) indicated the appearance of secondary radicals with the corresponding rapid disappearance of the iminoxyl radicals, (ii) ketoximes afforded iminoxyl radicals covering a wide range of stabilities (see Introduction and Table I) and yet no azine-bis-oxides have generally been isolated. Steric hindrance was probably not responsible for this difference since both the nitrosobenzoates (LXXXI) of alicyclic ketoximes and the nitrosoacetates (XVII) from aliphatic benzaldoximes readily existed as dimers.

* By analogy with the comparable reactions of benzophenone oxime (31), it is felt that the reported anhydride N-oxide structure XXII is also really the azine-N-bis-oxide (XXIII).

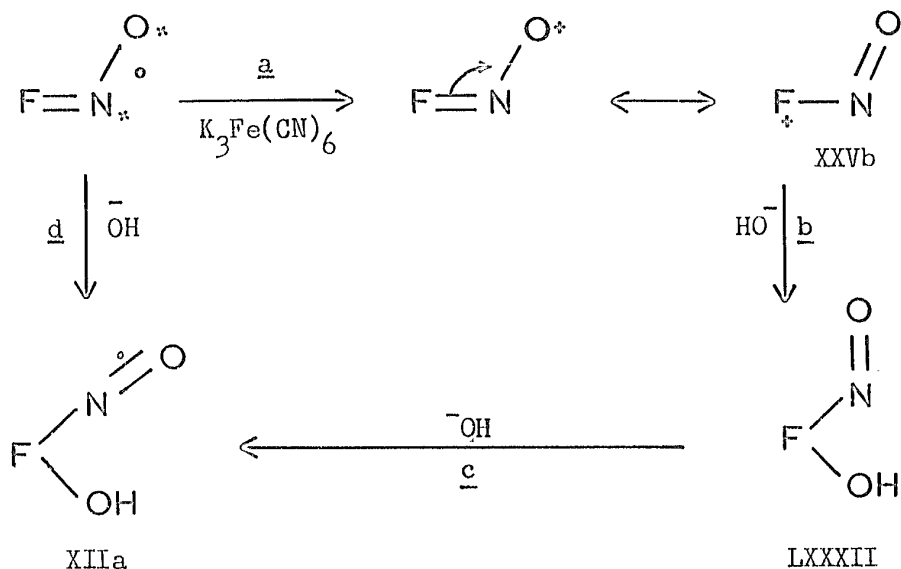


R = alkyl

The mechanism operative in the formation of aldazine-N-bis-oxides (XVIII) from the lead tetraacetate oxidation of aldoximes may involve the recombination of the observed secondary radicals XII (Introduction) or their reactions with iminoxyl radicals.



It is possible that the known reaction of potassium ferri-cyanide with free radicals to form cations (73) occurs in the ferri-cyanide oxidation of fluorenone oxime as follows (path a).



Since the oxime was slowly added to an alkaline ferricyanide solution, the iminoxyl cation XXVb could readily be attacked by hydroxyl ions to form the gem-nitroso-hydroxy compound LXXXII (path 2b). The formation of radical anions XIIa might arise from this intermediate LXXXII* (path 2c) or could be formed directly from the iminoxyl radical (path 2d). Further reactions of these radical anions might lead to fluorenazone-bis-N-oxide (XXXVII), as described for aldazine-N-bis-oxide formation (p. 13).

The radical ions XII have not yet been reported for bis-aryl ketoximes oxidized with lead tetraacetate; we have found that no azine-bis-oxides were formed in the oxidations of these oximes in glacial acetic acid or in methylene chloride.

* The formation of radical anions from nitroso compounds in basic media has been well characterized (74).

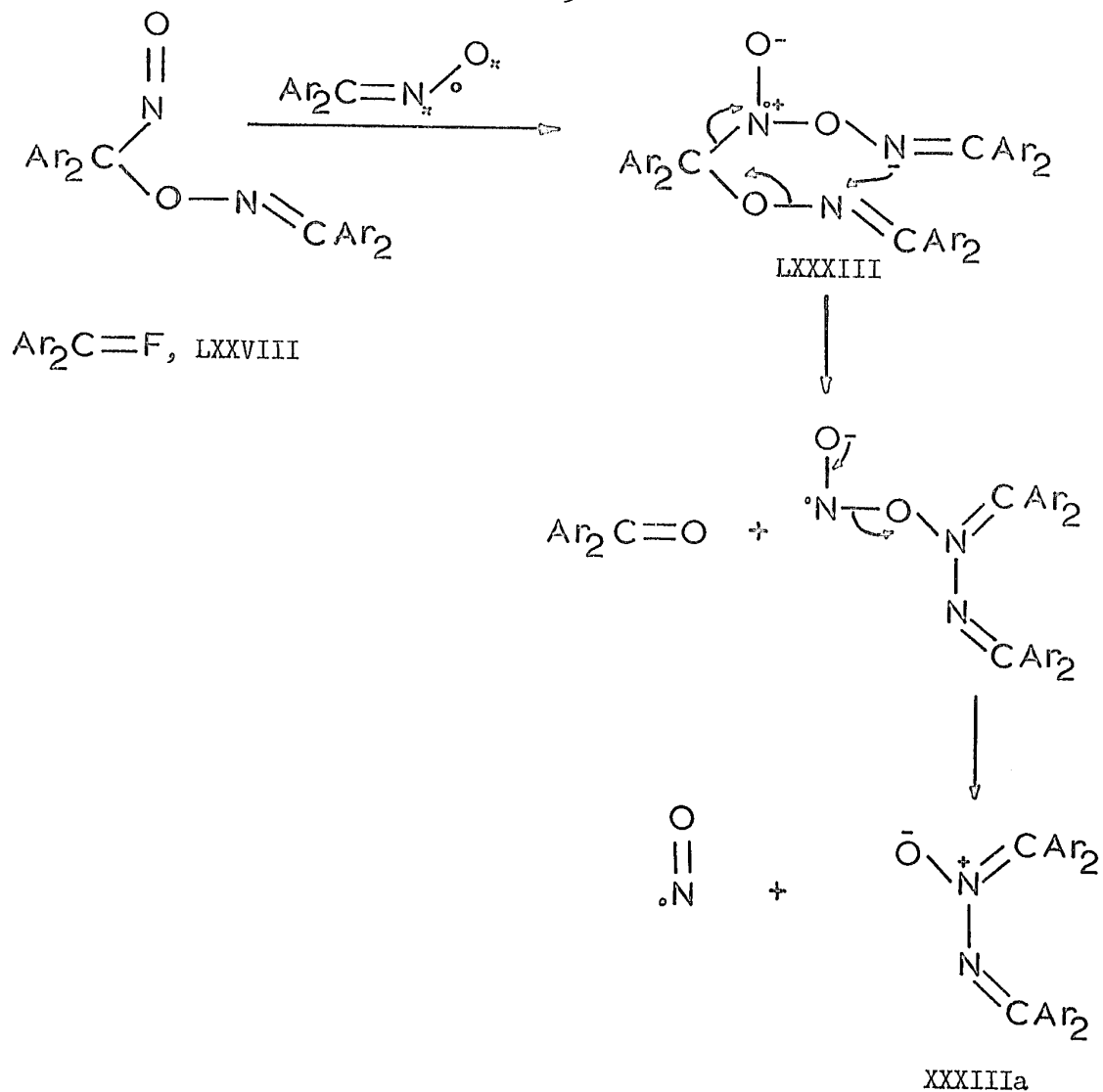
5-6.5. Azinemonoxides

Fluorenonazinemonoxide (XXX) has been prepared in 6% yield from the ceric ammonium nitrate oxidation of fluorenone oxime. Under these conditions, no such product was obtained from benzophenone oxime (32). Benzophenonazinemonoxide (XLIII) has been prepared in 25% yield from the peracetic acid oxidation of benzophenoneketazine (36) and in similar yield from the potassium ferricyanide oxidation of benzophenone oxime (31).

We have found that the lead tetraacetate oxidation of fluorenone oxime and benzophenone oxime in solvents other than glacial acetic acid gave rise to the corresponding azinemonoxide in about 15 and 35% yields respectively.

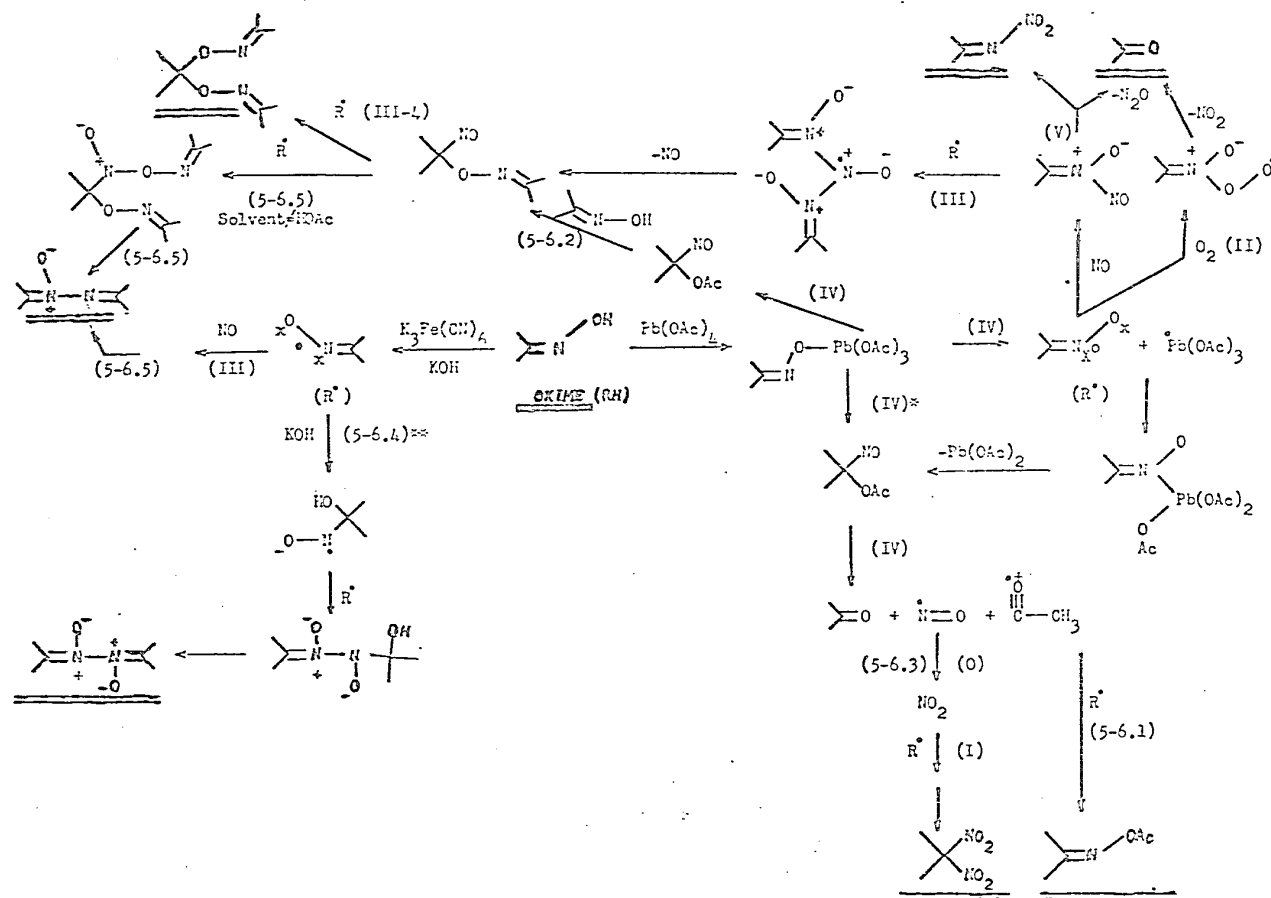
The intermediacy of the azine-bis-oxide (XXXVII) leading to ketazinemonoxide from the lead tetraacetate oxidation of fluorenone oxime has been ruled out (2-3.2).

It was previously shown that the lead tetraacetate oxidation of fluorenone oxime in methylene chloride probably led to the gem-nitrosoiminoxy intermediate LXXVIII (5-6.2). This nitroso compound could act as a radical scavenger to lead to intermediate LXXXIII which could then rearrange to the observed azinemonoxide (XXXIIIa). This suggested mechanism, shown below, does not account for the observation that no azinemonoxide was formed in glacial acetic acid, while addition of sodium acetate did lead to formation of this product. The role of the solvent is still very poorly understood (see 5-5).



5-7. General Mechanistic Scheme for the Oxidation of Aromatic Ketoximes

In the light of the foregoing discussion, the following scheme (Fig. 13) is presented to indicate the various reaction paths which aromatic ketoximes can follow when oxidized with various reagents. The bis-aryl ketoximes follow nearly all the reaction paths shown, while less conjugated oximes such as indanone oxime or oximes containing substituents conjugated with the iminoxyl group, such as xanthone oxime, mainly follow the reaction paths leading to gem-nitrosoacetates and ketones.



* Roman numerals refer to Schemes in Chapter 5.

** These numbers refer to section describing reaction shown.

FIG. 13. General Mechanistic Scheme for the Oxidations of Aromatic Ketoximes.

Experimental

General

The melting points were determined on a Gallenkamp melting point apparatus in open capillaries, and are corrected. The analyses were carried out by Dr. C. Daessle, Montreal and Beller Microanalytical Laboratory, Germany. The infrared spectra were determined on the Perkin-Elmer 337 (qualitative) and 521 (quantitative) grating spectrophotometers, using 1 mm sodium chloride cells or potassium bromide pellets. Low temperature spectra and spectra of solutions containing water were taken in 0.1 mm Amalgam FT cells (IRT-2) from Barnes Engineering Co. The ultraviolet spectra were measured with a Beckman recording spectrophotometer model DK1. Nuclear magnetic resonance spectra were recorded on a Varian A60 instrument (tetramethylsilane = 0 p.p.m.). Woelm alumina and Davidson No. 923 silica gel were used for column chromatography. Merck A.G. silica gel was used for thin layer chromatography (t.l.c.). The mass spectra were taken on a Hitachi Perkin-Elmer RMU6D mass spectrometer by Morgan and Schaffer Corporation, Montreal. The ionization potential was 70 eV. and the inlet temperature for indirect introduction of a sample was 250°.

Lead Tetraacetate

The lead tetraacetate used in all experiments was purchased in 100 g amounts from Fisher Scientific (Matheson, Coleman and Bell). It was freshly crystallized from glacial acetic acid, filtered, covered with a sheet of polystyrene and briefly sucked dry. It was then dried for

five minutes in an Abderhalden (refluxing methanol and 0.1 mm pressure). This acid-free crystalline lead tetraacetate could be stored in the dark in vacuo for a few days, with no decomposition.

Solvents

Glacial acetic acid used was 99.7% pure (Anachemia), while methylene chloride was Certified Fisher Scientific grade. These solvents were obtained oxygen-free by distilling the contents of freshly-opened bottles under a stream of helium. The receiving flasks were filled with bone-dry nitrogen and well stoppered. They were flushed with bone-dry nitrogen whenever solvents were pipetted out.

Apparatus

Reactions were carried out in oxygen-free solvents in an inert atmosphere in a one side-armed (with stopcock) two-necked reaction flask (125 or 50 ml, depending on total amounts of solvents used). One neck contained a rotatable cup for addition of lead tetraacetate and the second neck contained a three-hole two-way stopcock for evacuating the system and readily filling with inert gas. The side-arm containing a stopcock led to a manometer when initially evacuating and filling the system with inert gas or to a set of liquid air traps and/or mercury trap when actually carrying out the reaction under a positive pressure of inert gas. Dropwise addition of reagents was made by replacing the rotatable cup by a dropping funnel with pressure-equalizing side-arm. Inert gases were bubbled through the reaction solution via a polystyrene tube attached to the three-hole, two-way stopcock. Stirring

was effected magnetically. Cooling was provided by an isopropanol bath to which was added the desired amounts of dry ice. .

Preparation of Oximes

The preparation of each oxime is described in the section where it is first mentioned. If no modification was made for the procedure found in the literature, the m.p. and reference were simply stated.

Chapter 1

Structural Elucidation of the Oxidation Products from Bis-Aryl Ketoximes

1-1. Oxidation Products from Fluorenone Oxime

9,9-Dinitrofluorene (XXVI)

A. Addition of fluorenone oxime (XI) to lead tetraacetate in glacial acetic acid

To a stirred solution of lead tetraacetate (5.22 g, 1 me) in glacial acetic acid (100 ml) was added 3.16 g XI, m.p. 195-196° (reported m.p. 192-3° (75)). After two minutes, the brown solution contained very little starting material (t.l.c., benzene-ether (95.5:2.5)). After three hours, the solution was filtered from the lead diacetate (identified by t.l.c. of its DMSO solution and mixed m.p.) which had precipitated.

Addition of water to the mother liquor gave a yellow precipitate which was dissolved in methylene chloride, washed with saline water and sodium bicarbonate solution (5%) and dried (MgSO_4). Crystallization from methylene chloride-hexane at 6° overnight gave 454 mg of 9,9-dinitrofluorene (XXVI) as pale yellow needles, m.p. 129.5-131° (dec. with NO_2 evolution). Recrystallization from hexane gave an analytic sample with m.p. 131-3° (dec.) (reported m.p. 130-1.5° (dec.) (52)).

Anal. Calcd. for $\text{C}_{13}\text{H}_8\text{NO}_2$: C, 60.94; H, 3.15; N, 10.93; O, 24.98

Mol. Weight 256

Found: C, 60.76; H, 3.53; N, 10.47; O, 25.20

Mol. Weight (mass spec.) 256.

B. Addition of lead tetraacetate to fluorenone oxime (XI) in glacial acetic acid

A solution of lead tetraacetate (1.4 g, 1 me) in glacial acetic acid (35 ml) was added, in twenty minutes, to a stirred solution of XI (585 mg) in glacial acetic acid (25 ml). During the addition, the solution colour gradually turned yellow-orange and then returned to yellow. Reaction was complete at the end of the addition¹. Work-up was carried out as described in part A.

Two crystallizations of the crude product (524 mg) from hexane gave 70 mg of pure XXVI (t.l.c. and mixed m.p.). Alternatively, chromatography on silica gel (10 g; dry method²) with hexane-benzene (95:5) gave 150 mg of XXVI, m.p. 130-132.5° (dec.), homogeneous by t.l.c. Further elution with hexane-benzene (3:2) gave 200 mg of fluorenone (t.l.c., IR, mixed m.p.). Elution with ether gave 50 mg of starting oxime XI (t.l.c. only). No further products were obtained (CH₃OH was finally used).

9,9-Difluorenylideneiminoxylfluorene (XXVII)

A. From reaction of fluorenone oxime (XI) with lead tetraacetate in the absence of air

Lead tetraacetate (1.2 g, 1 me) was added to glacial acetic acid (50 ml) which was purged with bone-dry nitrogen for one hour. To this vigorously stirred solution was added fluorenone oxime (1 g). After about one half hour precipitation occurred. The brown suspension slowly

¹ An aliquot (0.5 ml) was shaken with 0.1 N potassium iodide solution (2 drops). Addition of starch solution gave a purple colour only when unreacted lead tetraacetate remained.

² The hexane insoluble crude product was dissolved in methylene chloride to which was added a little silica gel and MgSO₄. Evaporation left a solid mixture which was ground with a mortar and pestle, suspended in hexane and poured onto the silica gel-hexane column.

faded to yellow as the reaction proceeded to completion. After four hours, the suspension was filtered to give 290 mg of a light yellow precipitate of XXVII, slightly contaminated by XI (t.l.c.), m.p. 264.5-5.5° (dec.). One crystallization from methylene chloride-ethyl acetate afforded yellow microcrystals of pure XXVII with unchanged m.p. Variations in the melting point of compound XXVII between 260 and 265° over a one degree range were obtained according to the solvents used. Three recrystallizations from methylene chloride-ethanol gave an analytical sample of XXVII, m.p. 267° (dec.).

Anal. Calcd. for $C_{39}H_{24}N_2O_2$: C, 84.60; H, 4.34; N, 5.06; O, 5.78

Mol. Weight 552

Found: C, 84.46; H, 4.26; N, 5.16; O, 5.96

Mol. Weight (osmometric- $CHCl_3$) 597.

When the reaction was repeated with half amounts of all reagents indicated above, only a 16% yield of ketal XXVII was obtained.

B. From 9,9-Dichlorofluorene

1. 9,9-Dichlorofluorene (XXIX)

The procedure described by Schmidt and Wagner (75) was used, except that a shorter reaction time (15 minutes) was allowed, giving 10 g of XXIX, m.p. 102-104° (reported 103°), from fluorenone (10 g) and phosphorus pentachloride (20 g). It was found that correspondingly shorter reaction times must be used with smaller amounts of reactants, otherwise intractable mixtures resulted.

2. Fluorenone oxime (975 mg) was added to a solution of sodium hydride (480 mg of 50% NaH-oil suspension) in dimethyl sulfoxide. A

deep red solution immediately resulted. After 10 minutes, 9,9-dichloro-fluorene was added. The solution was stirred overnight, in a nitrogen atmosphere.

Addition of water gave a precipitate which was filtered. This yellow compound (150 mg) was identified as ketal XXVII from its m.p., mixed m.p., IR spectrum and R_f value on t.l.c.

Hydrolysis of ketal XXVII

Ketal XXVII (200 mg) in spectral grade chloroform (20 ml) containing 3 drops of acid (conc. HCl) was refluxed for 1 minute. The solution was neutralized and dried by shaking with NaHCO_3 and MgSO_4 . A quantitative IR of the solution showed that oxime XI and fluorenone (XXVIII) were present in the ratio of 2 to 1. No other products were detected (t.l.c.).

Alternatively, the solution was washed with sodium bicarbonate solution (10%) and saline water, dried (MgSO_4), evaporated to dryness and chromatographed on silica gel (10 g; dry method²). Elution with hexane-benzene (4:1) gave 13 mg of a compound with $R_f \gg R_f$ XXVII. Elution with hexane-benzene (1:1) gave fluorenone (XXVIII, 70 mg), m.p. 83-85°. Finally, elution with benzene gave fluorenone oxime (120 mg), m.p. 195°.

	<u>Hydrolysis Product:</u>	<u>XXVIII</u>	<u>XI</u>
Yield	Calculated	65 mg	141 mg
	Obtained	70 mg	120 mg + 13 mg "decomposition"

Stability of oxime XI and its O-acetate (XXXV) to acid

When XI was subjected to the same hydrolysis conditions as XXVII, very minor decomposition to the product with $R_f \gg R_f$ XXVII, described above, took place (t.l.c.).

Fluorenone oxime O-acetate (XXXV) m.p. 74° (reported m.p. 79° (77)), prepared by acetylation of XI at room temperature, was stable to the above hydrolysis conditions.

Fluorenone oxime O-acetate (XXXV)

The infrared spectra (CHCl_3) of the crude mixtures from the reactions described in 2-1.1 and 2-2.2 generally contained a weak absorption peak at 1765 cm^{-1} . NMR spectra of some of these crudes were taken and contained an absorption at 2.35 p.p.m. (CDCl_3). Authentic XXXV gave identical absorptions in its IR and NMR spectra. A typical analysis follows.

Entry 6 to Table II

The reaction was conducted as described in section 2-1.1 for entry 6.

Infrared analysis carried out with 40 mg of crude oil dissolved in 10 ml spectral grade chloroform gave 7% absorption at 1765 cm^{-1} . Authentic XXXV (4 mg) dissolved in 10 ml spectral grade chloroform also gave 7% absorption at 1765 cm^{-1} . The crude oil therefore contained ca. 10% (by weight) of compound XXXV. Addition of conc. HCl to the crude oil in CHCl_3 (40 mg/10 ml) did not alter the IR spectrum of this solution.

The NMR spectrum of 100 mg of crude oil in 0.3 ml COCl_3 gave a sharp absorption peak at 2.35 p.p.m. whose peak height was ca. 70 units. An NMR spectrum of 14 mg of authentic XXXV in 0.3 ml COCl_3 gave identical absorption with a peak height of about 103 units. Thus, about 10% (by weight) of XXXV was present in the crude. Addition of authentic XXXV to the crude gave a superimposable peak at 2.35 p.p.m. of increased intensity.

Isolation of XXXV

Attempts to isolate compound XXXV by chromatography always led to a mixture of XXXV and fluorenone oxime, since these two compounds had identical R_f values. Examples are provided in the experimental section in Chapter 2.

Fluorenonazinemonoxide (XXX)

A. Preparation

Lead tetraacetate (1.4 g, 1 me) was added all at once to a stirred solution of oxime XI (1.17 g) in oxygen-free methylene chloride (200 ml). An opaque chocolate brown suspension immediately formed. The reaction was complete after four and a half hours.

The precipitate which had formed was filtered, dissolved in dimethyl sulfoxide, and shown to be lead acetate by t.l.c. comparison with an authentic sample.

The methylene chloride filtrate was washed with water (4 x 25 ml), dried (MgSO_4) and evaporated in vacuo to give a red oil (1.55 g). Elution on silica gel (30 g; dry method²) gave the products shown in the

following table. Twenty ml fractions were collected and recombined if identical (t.l.c.).

Solvent	Volume (ml)	Compound Eluted	Amount	
			mg	mole %
Hexane (H)	100	Oil (R_f R_f XXVII)	39	-
Hexane-benzene (B)(4:1)	50	-	-	-
H-B (3:2)	50	-	-	-
H-B (5.5:4.5)	150	-	-	-
H-B (1:1)	50	XXVII	36	3
	50	XXVI	20	1
	100	Red compound (?)	31	-
	200			
H-B (3:7)	100	XXVIII	525	50
H-B (1:9)	200	-	-	-
Benzene	200	XXX	141	12
		XXX + XI	{ 40 + 100	{ 4 + 8
Ether	200	Orange residue	38	-

Crystallizations of initial benzene fractions from methanol gave red rosettes of XXX (141 mg), homogeneous by t.l.c. A recrystallization from methylene chloride-petroleum ether (90-120°) gave an analytical sample with m.p. 178°.

Anal. Calcd. for $C_{26}H_{16}N_2O$: C, 83.85; H, 4.33; N, 7.52; O, 4.30
Found: C, 83.60; H, 4.43; N, 7.80; O, 4.38.

Alternatively, ketal XXVII was first precipitated (3% yield) from the crude oil by addition of methanol-ether (5 ml). Evaporation left a red oil which was crystallized overnight from methylene chloride-petroleum ether (90-120°) at 10° to give dark red crystals of XXX (3%), m.p. 164.5-165.5°, homogeneous by t.l.c.

B. Hydrolysis of fluorenonazinemonoxide (XXX) to 9-chlorofluorene (XXXII)

Compound XXX (100 mg) was dissolved in glacial acetic acid (5 ml) and methylene chloride (0.5 ml) containing concentrated hydrochloric acid (3 drops). This dark orange solution was shaken for 13 hours. The yellow solution now contained only traces of unreacted XXX (t.l.c.). After addition of methylene chloride (50 ml), the solution was neutralized with 5% NaHCO₃ solution (5 x 25 ml), washed with brine (2 x 25 ml), dried (MgSO₄) and evaporated to give an orange-yellow residue (136 mg). The crude hydrolysis product was dissolved in hot hexane, eluted through silica gel (3 g) to give 34 mg of XXXII, m.p. 88.5-91.5°, homogeneous by t.l.c. (benzene). Further elution gave fluorenone (XXVIII, 60 mg), along with a few mg of oxime XI and other more minor impurities.

<u>Hydrolysis Product:</u>		<u>XXVIII</u>	<u>XXXII</u>
Yield	Calculated:	48 mg	+ 54 mg
	Found:	60 mg (62%)	+ 34 mg (33%) + minor impurities

An analytic sample of XXXII was obtained by overnight sublimation of the chromatographic product at R.T. and 0.2 mm pressure. It melted at $33.5-34^{\circ}$ and had $\sqrt{\text{CCl}_4}$ 640 (s), 680 (s) cm^{-1} (Cl).

Anal. Calcd. for $\text{C}_{13}\text{H}_9\text{Cl}$: C, 77.81; H, 4.49; Cl, 17.71

Found: C, 77.45; H, 4.70; Cl (by diff.) 17.8₅.

Synthesis of 9-chlorofluorene (XXXII)

Excess lithium aluminum hydride was added to fluorenone (500 mg) in ether (10 ml). Vigorous reaction occurred to give a pale yellow solution which turned pink upon refluxing for a few minutes. Sodium hydroxide solution (1N) was added to just neutralize excess reducing agent. The suspension was filtered, the ethereal solution was dried (MgSO_4) and evaporated to leave 9-fluorenol. Thionyl chloride was added to the latter till vigorous reaction stopped. After a few minutes, addition of water precipitated out light yellow flaky crystals. Crystallization from methanol (-10° overnight) gave colourless flakes (60 mg) of XXXII, m.p. 86° (reported m.p. 90° (78)). This compound was identical to XXXII obtained from the acid hydrolysis of XXX (mixed m.p., IR, and t.l.c.).

Solvolysis of 9-diazofluorene (XXXIVa)

1. Preparation of XXXIVa

Fluorenone hydrazone (XLIV), prepared from reaction of fluorenone and hydrazine hydrate in refluxing ethanol (37), was vigorously shaken with yellow mercuric oxide at R.T. as described by

Nenitzesau and Solomonian (79) to give compound XXXIVa, m.p. 93.5-94.5° (reported m.p. 94-95° (79)).

2. Solvolysis to 9-chlorofluorene (XXXII)

Compound XXXIVa (15 mg) was added to glacial acetic acid (2 ml) containing concentrated hydrochloric acid (1 drop). Immediate and quantitative hydrolysis to compound XXXII occurred (t.l.c.). Addition of water gave pale yellow crystals of XXXII, identical with an authentic sample (t.l.c. and mixed m.p.).

3. Solvolysis to 9-fluorenyl acetate

The above procedure was repeated in glacial acetic acid (2 ml). Instantaneous solvolysis occurred to yield one product (t.l.c.). A drop of concentrated hydrochloric acid was added to the solution which was left standing overnight. No new products were formed (t.l.c.). Saline water (20 ml) and ether (20 ml) were added. The ether extract was washed with alkaline solution (10% NaHCO₃) and saline water, dried (MgSO₄) and evaporated to a yellow oil which had an identical R_f value with that of 9-fluorenyl acetate, prepared by lithium aluminum hydride reduction of fluorenone and subsequent acetylation at room temperature.

C. Reduction of fluorenonazinemonoxide (XXX) to fluorenonazine (XXXI)

1. Reduction with triphenylphosphine

Petroleum ether (90-120°, 10 ml), containing compound XXX (40 mg) and triphenylphosphine (P₃) (17.5 mg, 1 me) was refluxed for 24 hours. Only partial reduction to a single product had occurred. An

excess of ϕ_3P (50 mg) was therefore used and overnight refluxing was effected in a nitrogen atmosphere. Upon cooling, red needles crystallized out (24 mg). A recrystallization from methylene chloride-ethanol gave dark-brown crystals of XXXI (20 mg), m.p. $270.5-271^\circ$ (reported m.p. 265° (37)), homogeneous by t.l.c., undepressed upon admixture of synthetic XXXI (see 3).

The mother liquor was evaporated to dryness. Addition of ether left colourless crystals of $\phi_3P \rightarrow O$ (5 mg), m.p. $151-152^\circ$ (undepressed mixed m.p.) while the ether solution contained XXXI and unreacted XXX.

2. Reduction with lithium aluminum hydride ($LiAlH_4$)

To compound XXX (10 mg) suspended in anhydrous ether (2 ml) was added excess $LiAlH_4$ (1 mg). An opaque green solution was obtained after a few minutes, which was quenched with 1N sodium hydroxide solution. Analysis of the ethereal solution obtained by filtration showed the presence of XXXI, along with minor amounts of products arising from reduction of this product (compared to a similar run using XXXI instead of XXX). Reduction of product XXXI occurred even when equimolar amounts of XXX and $LiAlH_4$ were used.

3. Synthesis of fluorenonazine (XXXI)

The procedure of Curtius (37) was mainly followed. A steel bomb containing fluorenone (2 g), hydrazine hydrate (0.23 ml of 35% +) and ethanol (0.4 ml) was kept in an oil bath at 150° for five hours. The glistening violet-brown crystals obtained upon cooling of the bomb

were ground, dissolved in methylene chloride-benzene, diluted with absolute ethanol and left at 6°. Glistening red needles (427 mg) of fluorenonazine, m.p. 269.5-270° (reported 265° (37)) were obtained.

Fluorenonazine-N-bis-oxide (XXXVII)

A. Preparation

Fluorenone oxime (2.34 g) and potassium hydroxide (KOH, 680 mg) in ethanol (40 ml) were added (16 mins) to a vigorously stirred solution of potassium ferricyanide (6.8 g, 1.7 me) and KOH (13.6 g) in distilled water (300 ml) kept at -3 to -7° with a dry ice-isopropanol bath. The resulting suspension was allowed to warm up overnight to give a red oily precipitate which was readily filtered (extraction of the mother liquor with methylene chloride gave negligible amounts of red oil). Addition of ether to the red oil gave 410 mg of light yellow microcrystals of compound XXXVII, homogeneous by t.l.c., m.p. 210° (dec.). This compound was dissolved in hot benzene which was dried (MgSO_4). Absolute ethanol was then added so that crystallization occurred at R.T. to give crystals with m.p. 212.5° (dec.). Recrystallization from benzene-methylene chloride (7.5:1; ca. 20 ml) at 10° (a few days) gave an analytic sample of XXXVII (70 mg from 300 mg crude crystals) m.p. 212.5° (dec.).

Anal. Calcd. for $\text{C}_{26}\text{H}_{16}\text{N}_2\text{O}_2$: C, 80.4; H, 4.15; N, 7.21; O, 8.24
Found: C, 81.8; H, 3.18; N, 7.00; O, 8.08.

B. Acid hydrolysis

Azine-bis-oxide XXXVII (5 mg) in methylene chloride (5 ml) was

readily precipitated out of solution, unchanged (t.l.c.) by the addition of glacial acetic acid (1 ml). However, addition of 1 drop of concentrated hydrochloric acid to this methylene chloride solution immediately gave a deep yellow solution containing about equimolar amounts of fluorenone and its oxime (t.l.c.).

C. Pyrolysis

Compound XXXVII melted with decomposition to a red oil whose thin layer chromatogram was identical to that obtained for the pyrolysis melt of fluorenonazinemonoxide (XXX).

D. Attempted reduction

Triphenylphosphine (60 mg) and XXXVII (40 mg) stirred in tetrahydrofuran for three days remained unreacted. When refluxing dioxane was used in a nitrogen atmosphere (7 hr) about five products were formed in minor amounts. No fluorenonazinemonoxide (XXX) nor fluorenonazine (XXXI) could be detected (t.l.c.).

E. Lead tetraacetate stability

To azine-bis-oxide XXXVII (5 mg) in methylene chloride (3 ml) was added lead tetraacetate (50 mg). No reaction occurred. Addition of acetic acid (1 ml) did not lead to any reaction either (t.l.c.).

1-2. Oxidation Products from Benzophenone Oxime

Dinitrodiphenylmethane (XXXVIII), 1,1-bis(diphenylmethylideniminoxyl)-diphenylmethane (XXXIX), and benzophenone nitrimine (XLI)

A. Preparation from lead tetraacetate oxidation of benzophenone oxime (IX)

Solid lead tetraacetate (4.48 g, 1 me) was added to a rapidly stirred solution of IX (2 g) (m.p. 143-144°, reported 142° (80)) in oxygen-free acetic acid in a nitrogen atmosphere. After five minutes, the solution was a light orange-brown. After another 15 minutes, a yellow suspension had formed. Reaction was complete¹.

The acetic acid solution was evaporated at 30° in vacuo and 10 ml of methylene chloride was added. The undissolved lead acetate (2.59 g) was filtered off, and the solution evaporated. The resulting oil (1.84 g) was crystallized from methanol at -10° overnight to give colourless flakes (60 mg). One recrystallization from methanol-methylene chloride gave 48 mg of XXXIX, m.p. 169.5-171.5°. Recrystallization from the same solvent mixture gave a pure analytic sample (t.l.c.), m.p. 170.5-171.5°.

Anal. Calcd. for $C_{39}H_{30}N_2O_2$: C, 83.84; H, 5.41; N, 5.01; O, 5.73

Mol. Weight 558.65

Found: C, 84.05; H, 4.93; N, 5.29; O, 6.07

Mol. Weight (osmometric- $CHCl_3$) 547.

The mother liquor from the above reaction was evaporated. The resulting yellow oil was dissolved in hexane and poured onto a column of silica gel (60 g). Elution with hexane-benzene (7:3) gave 226 mg of colourless crystals of XXXVIII, m.p. 78.5-79°, homogeneous by t.l.c. One crystallization from hexane gave colourless plates of dinitrodiphenyl-

methane (XXXVIII), m.p. 80.5-81° (dec. 100°, with evolution of NO₂).

Anal. Calcd. for C₁₃H₁₀N₂O₄: C, 60.46; H, 3.90; N, 10.85; O, 24.78

Mol. Weight 258.2

Found: C, 60.22; H, 4.79; N, 10.60; O, 24.58

Mol. Weight (osmometric-CHCl₃) 260.

Further elution with hexane-benzene (7:3) gave pale yellow crystals of XLI (245 mg), m.p. 62-66°, homogeneous by t.l.c. Crystallization from hexane at 6° overnight gave colourless plates of benzophenone nitrimine (XLI), m.p. 70-71° (dec. 165°, with NO₂ evolution).

Anal. Calcd. for C₃₉H₁₀N₂O₂: C, 69.01; H, 4.46; N, 12.38; O, 14.14

Mol. Weight 226

Found: C, 69.15; H, 4.55; N, 12.37; O, 14.16

Mol. Weight (osmometric-CHCl₃) 233.

Further elution with benzene afforded 1.15 g of benzophenone (XL) as pale yellow crystals (identified by t.l.c., IR and mixed m.p.).

Elution with ether gave 35 mg of an oil having an R_f value (t.l.c.) equal to that of benzophenone oxime. An infrared spectrum of this oil in chloroform contained a peak at 1765 cm⁻¹ which remained constant upon addition of concentrated hydrochloric acid to the solution. This absorption suggested that the oil might consist mainly of benzophenone oxime O-acetate (XLVI), in analogy with the observations made for fluorenone oxime O-acetate (XXXV, p.147).

B. Syntheses and reactions of these oxidation products

Dinitrodiphenylmethane (XXXVIII)

See Chapter 4 for synthesis from oxidative nitration of

benzophenone oxime. Compound XXXVIII was found to be stable to concentrated hydrochloric acid.

Benzophenone nitrimine (XLI) from diphenyldiazomethane (XLII)

Diphenyldiazomethane (XLII) was prepared according to a reported method (81) with some modifications. The hydrazone of benzophenone (10 g, m.p. 96-98° (Aldrich Chemical)) was finely ground with yellow mercuric oxide (11.2 g) and shaken in 50 ml of petroleum ether (30-60°) at R.T. for 24 hours. Filtering and evaporating left a red oil (2.6 g), which turned to red crystals of diphenyldiazomethane (XLII) on cooling below R.T. (homogeneous by t.l.c.).

Compound XLII (2.6 g) was vigorously shaken in benzene-cyclohexane (120 ml. 1:1, spectral grade) and kept under a positive nitric oxide gas pressure. The reaction proceeded as described by Horner et al. (30). Crystallization of the crude product from methanol (5 ml) at -6° overnight gave 600 mg of a mixture of nitrimine XLI and benzophenone (t.l.c.). Recrystallization from 10% aqueous acetic acid at -6° for 2 hours gave colourless plates of benzophenone nitrimine, m.p. 70.5-71°. The melting point was undepressed upon admixture with XLI (from the lead tetraacetate oxidation of benzophenone oxime) and had an identical IR spectrum (KBr matrix).

Acid hydrolysis: A solution of compound XLI (20 mg) in ethanol (4 ml) containing concentrated hydrochloric acid (3 drops) was heated under reflux for one hour. Quantitative hydrolysis to benzophenone took place (t.l.c.).

Benzophenonazinemonoxide (XLIII)

Lead tetraacetate (560 mg) was added to a rapidly stirred solution of benzophenone oxime (500 mg) in methylene chloride (15 ml). The reaction was complete in less than a minute¹. The green suspension was filtered, giving 340 mg of lead acetate. The filtrate was diluted with methylene chloride to 50 ml and an aliquot examined with the infrared spectrometer. The solution was then evaporated to a small volume (ca. 5 ml) and chromatographed by t.l.c. using ether-benzene (2.5:77.5) as solvent system. The products were spotted with an ultraviolet lamp and extracted with ether and methylene chloride, successively. In order of decreasing R_f values, the following products were obtained: benzophenone (272 mg), an oil (39 mg) ($R_f = R_f$ oxime IX) and compound XLIII (150 mg). One crystallization of XLIII from ethanol (2 hours at 10°) gave yellow microcrystals, m.p. 153-154.5° (dec.), ν KBr 1510 and 1439 cm^{-1} (N $\longrightarrow$ O). This compound was identified as benzophenonazine-monoxide (reported m.p. 151-3° (31)) by m.p., mixed m.p., t.l.c. and comparison of the infrared spectra.

Chapter 2

Oxidation of Fluorenone Oxime

2-1.1. Lead tetraacetate oxidation in glacial acetic acid

Entries to Table I

As previously described in the experimental section (1-1), a column chromatography was initially carried out to determine the product distribution obtained in the lead tetraacetate oxidation of fluorenone oxime (XI) in glacial acetic acid in the presence of air (entry 1).

Any changes in ketal formation were readily detected by filtration of this precipitate. Attention was focussed on changes in 9,9-dinitrofluorene (XXVI) formation, which were recorded as shown in the following representative example.

Fluorenone oxime (585 mg) and lead tetraacetate (700 mg, 1 me) were mixed in glacial acetic acid (25 ml) purged with nitrogen. Filtering the resulting suspension afforded 28 mg of ketal XXVII, slightly contaminated by starting oxime. To the acetic acid solution was added water. The precipitated solid was filtered, dissolved in methylene chloride and worked up as previously described (1-1, part A, p. 143). The oil, remaining upon evaporation of the methylene chloride solution, crystallized from hexane to give 84 mg (11%) of 9,9-dinitrofluorene (XXVI). The mother liquor was evaporated and the crude residue was analysed by infrared spectroscopy.

Extinction coefficients were measured for the oxime (XI), oxime acetate (XXXV) and 9,9-dinitrofluorene (XXVI) in the ranges of absorption obtained for the analyses of crude products. Only small

variations (2-3%) were found in measurements of extinction coefficients. The settings used on the Perkin-Elmer 521 infrared spectrometer for analysis of standard solutions of synthetic samples were used for all analyses.

Entries to Table II

The experimental runs were conducted as shown in the following example. The apparatus has been described in the General section. All solids used in these oxygen-free experiments (e.g. lead tetraacetate and fluorenone oxime) were degassed in the reaction flask prior to reaction. In order to simplify analysis of the crude reaction mixtures, a graphical technique using IR spectroscopy was used (Appendix B). The following entries are representative examples.

Entry 1

Fluorenone oxime (585 mg) was degassed in the 50 ml reaction flask which was filled with helium. Oxygen-free glacial acetic acid (25 ml) was pipetted into the flask kept under positive helium pressure. Lead tetraacetate (700 mg, 1/2 me) was weighed into the rotatable cup which was inserted into the reaction flask. After evacuating and filling (with helium) the flask a few times, the lead tetraacetate was added all at once to the vigorously stirred oxime solution. The former completely dissolved within 2-4 minutes. After five minutes, a dark brown suspension had formed which gradually faded to a yellow colour in about one hour. Reaction was now complete¹.

The suspension was filtered to give 233 mg of a solid which

was refluxed in methylene chloride. Evaporation of the methylene chloride solution left 80 mg of ketal XXVII (14%), slightly contaminated by oxime XI and fluorenone (XXVIII). One crystallization from acetic acid-methylene chloride gave 63 mg (11%) of pure XXVII (t.l.c.).

Addition of water to the acetic acid mother liquor gave a solid mixture which was filtered, washed with water, air-dried and finally dried in a vacuum oven (0.1 mm and 80°). This crude solid (440 mg) was then analysed by infrared spectroscopy as described in Appendix B. The aqueous acetic acid mother liquor was shaken with methylene chloride. The methylene chloride solution was then washed with saline water and 5% sodium bicarbonate solution. It was dried (MgSO₄), and evaporated to give 60 mg of fluorenone (XXVIII).

The above experiment was repeated to test reproducibility. The results are shown below.

<u>Compound</u>	<u>XXVI</u>	<u>XXVIII</u>	<u>XI</u>
Run 1	4%	22%	40%
Run 2	3%	20%	43%

Different work-up conditions

The acetic acid reaction solution was filtered from the precipitated ketal XXVII (233 mg). It was then concentrated to a small volume at 50° in vacuo and finally brought to dryness at 40° and under vacuum (0.1 mm). Methylene chloride was added to this oil. Lead acetate was filtered from the resulting solution. Evaporation to dryness gave an oily residue which was analysed as described above. The

same results were obtained (within the experimental error $\pm 3\%$).

Entry 2 - Trapping of nitric oxide gas

In a separate run, the same procedure was used as described in entry 1, except that helium gas was flushed through the reaction solution and led through two carbon tetrachloride-dry ice baths and then two liquid air traps containing silica gel.³

The first liquid air trap contained a blue solid contaminated by trace amounts of a green-blue solid. The latter might be dinitrogen tetroxide. The trap was evacuated with an oil pump (0.1 mm) and allowed to warm up by immersing it in a CCl_4 -dry ice bath. The very faint brown gas was transferred to an infrared gas cell. The IR spectrum of this gas contained a strong doublet at 5.5_5 and 5.6_0 microns, which might be due to N-O stretches (reported $\nu_{\text{NO}} = 5.25$ and 5.4 microns (82), but variance exists in the literature). No absorptions corresponding to the presence of nitrous oxide (82) were observed in the above IR spectrum. Exposure of this sample to air gave a dark brown gas having an irritating smell, characteristic of nitrogen dioxide.

Entry 6 - Reaction of fluorenone oxime with one mole equivalent of lead tetraacetate

The same experimental conditions were used as described in entry 1. However, the lead tetraacetate (1.348 g) was degassed in a flask filled with nitrogen, dissolved in oxygen-free methylene chloride-acetic acid (4:5, 18 ml), and transferred to a dropping funnel (with side arm for equalizing pressures) fitted to the reaction flask kept under positive

³ Nitric oxide is adsorbed by silica gel (Dr. C. Winkler's students, Chem. Dept., McGill University).

nitrogen pressure. The lead tetraacetate solution was added in ten minutes. A fluorescent yellow colour immediately appeared and remained ten minutes after the addition. After a total of 20 minutes, a yellow-brown colour appeared. After 15 minutes longer, the solution had turned clear yellow and contained no oxidizing agents¹. The solution was evaporated to about 20 millilitre volume at room temperature in vacuo. The suspension which had formed was filtered to give 100 mg of ketal XXVII, containing only traces of oxime (t.l.c.). Further evaporation to near dryness and filtering did not yield any more ketal.

The mother liquor was worked up as previously described (both methods gave approximately the same results).

2-1.2 Molecular oxygen

Autoxidation of fluorenone oxime (XI)

A. Glacial acetic acid

When XI (50 mg) was left in dry* glacial acetic acid (3 ml) in a stoppered flask for ten hours, a minor amount of fluorenone (XXVIII) and 9,9-dinitrofluorene (XXVI) was formed (t.l.c.). After another ten hours, reaction was complete (t.l.c.). The suspension which had formed was filtered to give 6 mg (13% yield) of compound XXVII, identical with 9,9-difluorenylideneiminoxyfluorene (t.l.c. and mixed m.p.). The mother liquor was evaporated in vacuo at room temperature. The solid mixture (44 mg) was dissolved in spectral grade chloroform (10 ml). The solution was shown to consist of 25% XXVI and 60% XXVIII (IR analysis - Appendix B).

* The use of acetic acid from a bottle opened a large number of times greatly reduced the oxidation rate.

B. Glacial acetic acid saturated with oxygen

Glacial acetic acid was purged overnight with oxygen under a small positive pressure and stored in a stoppered flask. This solution was used in the experiment described in (A) above. The same results were obtained.

C. Glacial acetic acid-sodium acetate

When the reaction in (A) was repeated with anhydrous sodium acetate (1 g) added to the acetic acid solution, no reaction occurred.

Relative basicities of fluorenone oxime sodium salt (XI₅) and sodium acetate

A solution of sodium acetate (1 g) in water was shaken with fluorenone oxime (50 mg). The oxime was quantitatively recovered by extraction with methylene chloride (t.l.c.).

D. Benzene-oxygen

Fluorenone oxime (25 mg) in benzene (5 ml) dried over sodium and saturated with oxygen was shaken in a stoppered flask for two days on a mechanical vibrator. Only starting oxime was recovered after evaporation of the solvent (t.l.c.).

E. Ethanol-potassium hydroxide

Fluorenone oxime (25 mg) was dissolved in ethanol (10 ml) containing potassium hydroxide (25 mg). Oxygen was bubbled through this solution for two days. No reaction occurred (t.l.c.).

Autoxidation of fluorenone hydrazone (XLIV) to fluorenonazine (XXXI)

The same procedure for oxidation of XLIV (50 mg; prepared on p. 151) was used as described for the autoxidation of fluorenone oxime (XI) in glacial acetic acid. A quantitative yield (50 mg) of red crystals of XXXI, m.p. 269° was obtained. This product was identified as fluorenonazine by comparison with an authentic sample (t.l.c. and mixed m.p.).

2-1.3. Nitrogen oxides

Addition of fluorenone oxime (XI) to nitrogen dioxide-acetic acid solution

To a magnetically stirred turquoise glacial acetic acid solution of nitrogen dioxide (compressed gas from Matheson Co.) was added, all at once, fluorenone oxime (100 mg). A dark yellow-brown solution immediately formed and spontaneously turned turquoise again. Degassing with the water pump left a pale yellow solution which was brought to dryness on the water bath (60°) with a flash evaporator. Hexane (5 ml) was added to the pale yellow residue which contained a trace amount of fluorenone (t.l.c.). Colourless crystals (95 mg) of pure 9,9-dinitrofluorene (XXVI), m.p. 130-133° (dec.) were obtained (t.l.c. and mixed m.p.). Compound XXVI was found to be stable under the above work-up conditions. Repeat of this oxidation in other solvents gave similar results (see 4-2).

Reaction of XI with nitric oxide and nitric oxide-air

Nitric oxide (compressed gas from Matheson Co.) was bubbled through oxygen-free glacial acetic acid (5 ml) containing oxime XI (100

mg) in the 50 ml reaction flask (described in the General section), containing polystyrene inlet tubing dipped into the reaction solution. No reaction occurred since oxime XI was recovered when the solution was brought to dryness in vacuo. However, if the reaction was repeated with air allowed to enter the system, instantaneous reaction occurred. The solution was evaporated in vacuo to a smaller volume, water was added and the precipitate was filtered to give colourless crystals of XXVI (80 mg), m.p. 131-133° (dec.), identical with authentic XXVI (t.l.c. and mixed m.p.).

Formation of 9,9-difluorenylideneiminoxyfluorene (XXVII) from reaction of nitrogen dioxide (1 mole equivalent = 1 me) with fluorenone oxime (XI)

Nitrogen dioxide (11 ml, 1 me with respect to XI) was transferred from a dibutyl phthalate-containing gas burette into a partly evacuated flask (initially flushed with nitrogen) containing oxygen-free glacial acetic acid (20 ml). The stoppered flask (containing a stopcock) was vigorously shaken to give a pale yellow solution which was transferred to a dropping funnel being flushed with nitrogen. This solution was added dropwise to a stirred solution of XI (97.5 mg) in oxygen-free glacial acetic acid (20 ml) kept in a nitrogen atmosphere. The light yellow oxime solution turned deeper yellow and turbid as the addition proceeded to completion. After two hours, addition was complete. The suspension was evaporated in vacuo to dryness. Addition of ether (5 ml) left 4 mg of ketal XXVII, identified by t.l.c. and mixed m.p. with an authentic sample. The mother liquor was evaporated. The crude solid (92 mg) was dissolved in chloroform (20 ml). IR analysis (Appendix B)

indicated the presence of fluorenone (ca. 15%), 9,9-dinitrofluorene (ca. 40%) and unreacted oxime XI (ca. 40%). These results were qualitatively confirmed by t.l.c.

2-1.4. Ionic-type oxidizing agents

Nitrous acid

A. Properties of nitrous acid in acetic acid

a. Sodium nitrite (50 mg) added all at once to glacial acetic acid (3 ml) gave a blue solution and caused vigorous bubbling of N-oxides. Exposure of the solution to air led to brown nitrous fumes.

b. Slow addition of sodium nitrite (25 mg) in water (0.5 ml) to acetic acid (3 ml) gave a colourless solution which gave a positive starch-iodide test.

B. Fluorenone oxime (XI) stability to nitrous acid

Sodium nitrite (22.5 mg, 1.5 me) in distilled water purged with nitrogen (0.5 ml) was added, in 15 minutes, to an oxygen-free acetic acid solution (3 ml) of XI (50 mg). Vigorous magnetic stirring was effected during the addition. The solution was stirred overnight in a nitrogen atmosphere. Only trace amounts of fluorenone (XXVIII) and 9,9-dinitrofluorene (XXVI) had formed (t.l.c.).

When the procedure was carried out with rapid addition of sodium nitrite as in (a) above, XXVI and XXVIII were formed as major and very minor products, respectively (t.l.c.)

2-2. Oxidation in Methylene Chloride

2-2.1. General solvent effect

Benzene

Lead tetraacetate (113 mg, 1 me) was added to a magnetically stirred solution of fluorenone oxime (50 mg) in benzene (2 ml). Instantaneous reaction occurred to give an orange solution, which contained mainly fluorenone (XXVIII), fluorenonazinemonoxide (XXX) and a minor amount of 9,9-dinitrofluorene (XXVI).

Similar oxidations conducted in tetrahydrofuran, wet ether, methylene chloride and dimethylsulfoxide led mainly to ketone XXVIII and azinemonoxide XXX.

Methanol

The reaction was conducted as above using 1.13 g of lead tetraacetate and 500 mg of fluorenone oxime in absolute methanol (wet methanol gave the same results). Instantaneous reaction occurred. The solution was evaporated to dryness. The crude residue was extracted with methylene chloride. This solution was washed with water, dried (MgSO_4), and evaporated. One crystallization from hexane (1 hour at 5°) gave 133 mg of fluorenone oxime, m.p. $194\text{--}196^\circ$. The mother liquor contained mainly fluorenone, some fluorenonazinemonoxide (XXX) and about four very minor products (t.l.c.).

2-2.2. Methylene chloride as solvent

Entries to Table X

In all of these experiments, the methylene chloride solutions were analysed by infrared spectroscopy before and after work-up. All

the absorption bands found in these spectra could be accounted for once the components were all isolated. The strong bands at 1765 and 1720 cm^{-1} , observed for all the reactions studied, disappeared when the solutions were washed with water, except for a weak band at 1765 cm^{-1} assigned to the oxime O-acetate XXXV. These same bands were obtained when a spectrum of glacial acetic acid in methylene chloride was taken. No bands for acetic anhydride were ever observed.

The entries in Table X were obtained as shown by the following representative examples.

Entry 2

The experimental procedure was described in 1-1, p. 143.

Entry 3

Lead tetraacetate (694 mg, 1/2 me) in oxygen-free methylene chloride (25 ml) was added in 10 minutes to fluorenone oxime (585 mg) in methylene chloride (50 ml) in a nitrogen atmosphere. A dark brown suspension formed as the addition was made. After another 10 minutes, reaction was complete¹. The orange suspension was concentrated to ca. 10 ml by blowing nitrogen through it. An aliquot was removed (0.1 ml) and analysed in the 0.1 mm IRT cells. Bands at 3565 cm^{-1} (5%), 1765 cm^{-1} (27%), 1720 cm^{-1} (67%), 1570 cm^{-1} (10%) could be assigned to oxime, oxime O-acetate and/or acetic acid, fluorenone and acetic acid, and azinemonoxide (XXX), respectively.

The suspension was filtered to give lead acetate (518 mg). The solution was washed with water and NaHCO_3 solution (5%), dried (MgSO_4),

and evaporated to a red oil (585 mg). IR analysis of this oil in methylene chloride indicated the absence of the 1765 and 1720 cm^{-1} bands, assigned to acetic acid. Addition of ether (5 ml) gave 57 mg of 9,9-difluorenylideneiminoxyfluorene (XXVII), containing traces of fluorenone oxime (t.l.c.). The mother liquor was chromatographed on four silica gel plates (20 x 20 cm) with ether-benzene (2.5: 87.5) as eluting solvent. The components were spotted with an ultraviolet lamp and extracted with methylene chloride. Fluorenone oxime (30 mg) containing minor amounts of the oxime O-acetate ($\leq 1\%$, IR) and fluorenonazinemonoxide (XXX) contaminated with fluorenone were isolated. One crystallization of the latter mixture from ethanol gave 82 mg (14%) of XXX, t.l.c. pure. The mother liquor consisted mainly of fluorenone, with a few minor impurities (t.l.c.). It was evaporated to dryness and dissolved in chloroform. Infrared analysis of this mixture indicated that 50-60% of fluorenone (based on the starting oxime) had been formed.

Entry 4

The reaction in entry 3 was repeated with the reaction temperature kept at about -15° with an isopropanol-dry ice bath. After a half-hour at -15° , a deep orange-brown suspension had formed. An aliquot (0.5 ml) was syringed into a vial kept at -20° and analysed in the IRT cells (0.1 mm) at -20° and at R.T. The infrared spectra at these two temperatures were identical.

Even after two hours at -15° , unreacted lead tetraacetate remained. On warming up to R.T., the reaction was completed within 30

minutes¹. Work-up was conducted as previously described to give 40 mg of lead acetate and 35 mg of ketal XXVII.

The methylene chloride solution (mother liquor) was extracted with sodium hydroxide solution (2N). Acidification of the alkaline aqueous extracts gave only 3 mg of fluorenone oxime.

Since difficulties had previously been encountered in the isolation of fluorenonazinemonoxide XXX, a different method of isolation was attempted in the light of the tested stability of fluorenonazine-monoxide to basic conditions.

The evaporated solution was dissolved in tetrahydrofuran (5 ml) containing 2 ml aqueous ethanol (30% H₂O) and 200 mg hydroxylamine hydrochloride. This solution was refluxed for one half hour and evaporated. The residue was taken up in methylene chloride, washed with water and acid (10% HCl) and extracted with base (2N NaOH solution).

The methylene chloride solution was evaporated to give a red oil (100 mg) containing XXX and 3 very minor impurities (t.l.c.). Attempts to crystallize the oil were unsuccessful.

The alkaline extract was neutralized with acid (conc. HCl) to give 354 mg of fluorenone oxime, equivalent to a 60% yield of fluorenone.

Entry 5

The experiment in entry 2 was repeated, but glacial acetic acid (1 ml) was added to the methylene chloride (25 ml) solution. The dark brown suspension formed after four minutes of reaction turned lighter brown and finally light orange (25 minutes). The reaction was now complete¹. The suspension was concentrated and filtered to give

482 mg of lead acetate. The solution was washed with water and sodium bicarbonate solution (5%), dried (MgSO_4) and evaporated to an orange oil (556 mg). The addition of ether to this oil did not give any ketal XXVII. Evaporation and drying with the oil pump at 50° (0.1 mm) gave back the above oil (556 mg). An NMR spectrum of 100 mg of this crude in 0.3 ml deuterated chloroform contained a small absorption at 2.25 p.p.m. corresponding to ~4.5 mg fluorenone oxime O-acetate (ca. 1% of total crude).

The above oil was also partly dissolved in chloroform (40 mg/ml). The infrared spectrum of this solution was compared to that obtained from a similar solution for the crude obtained in entry 2. The product distribution was thus estimated by a comparison of peak heights. A comparison of these solutions on t.l.c. was also made.

2-3. Oxidation of Fluorenone Oxime with Potassium Ferricyanide

2-3.1. Formation of fluorenonazinemonoxide (XXX) and fluorenonazine-N-bis-oxide (XXXVII)

A. Reaction at room temperature

The same procedure was used as described for the low temperature reaction on p. 154. A red oil (487 mg) was obtained. An IR spectrum of this oil (15 mg) in chloroform (2 ml) was taken. Addition of ether left a yellow-orange precipitate (22 mg) which contained trace amounts of compound XXX (t.l.c.). One crystallization from methylene chloride-benzene gave yellow microcrystals of pure XXXVII, m.p. 213° (dec.), undepressed upon admixture with an authentic sample (see 1-1).

The ether solution was evaporated to dryness. The resulting oil was crystallized from petroleum ether (90-120 $^\circ$ fraction) at 10°

overnight. Red crystals (25 mg) were obtained, slightly contaminated by fluorenone oxime and an unknown impurity (t.l.c.). Recrystallization from petroleum ether (overnight at R.T.) gave red rosettes of XXX, m.p. 166-167°, identical with authentic fluorenonazinemonoxide (mixed m.p. and IR).

B. Reaction at ca. -5°: formation of intermediate XLV

The reaction was conducted as previously described on p. The yellow suspension which had formed was warmed up to -2° (to dissolve frozen solution) and filtered to give a light yellow precipitate (XLV).

(i) On standing at room temperature, XLV spontaneously decomposed to a red oil with evolution of brown nitrous fumes. Work-up was then effected as previously described to give a red oil. An infrared spectrum of a standard aliquot of this oil (15 mg/2 ml CHCl₃) was compared to that obtained in part A and was found to be almost identical. A t.l.c. comparison qualitatively confirmed this observation.

(ii) Alternatively, XLV could be quickly transferred to a vial and stored at -10° with no resulting decomposition. It readily dissolved in chloroform (-20°) and partly in ether (-20°) to give yellow solutions which turned orange on warming to R.T. (due to azinemonoxide XXX formation), even when these cold solutions were initially dried (MgSO₄).

(iii) XLV was washed with ether at -20° to remove water present. It was then allowed to warm up to R.T. Spontaneous decomposition to a

red oil still occurred.

(iv) A few mg of XLV in chloroform at -20° was dried with MgSO_4 and analysed by infrared spectroscopy at this temperature and at R.T. A strong transient peak at 2340 cm^{-1} was noted, which disappeared as the solution was left standing at R.T. A similar transient absorption peak at 2340 cm^{-1} had been observed in the IR spectrum of a solution of ketal XXVII containing a drop of concentrated hydrochloric acid. No assignment could be made.

Absorption bands at 1712 cm^{-1} ($\nu_{\text{C=O}}$ for fluorenone), and at 1550 and 1565 cm^{-1} ($\nu_{\text{N}} \longrightarrow 0$ for azinemonoxide) increased in intensity as the chloroform solution of XLV was warmed up to R.T.

2-3.2. Comparative study of the lead tetraacetate oxidations of fluorenone oxime

Low temperature oxidation of fluorenone oxime (XI) in oxygen-free methylene chloride-ether

The experiment was conducted as described for entry 4 in 2-2.1. To oxime XI in oxygen-free ether (45 ml) at -80° was added lead tetraacetate in methylene chloride-ether (1:3.3, 26 ml). A pale yellow suspension immediately formed with addition of the lead tetraacetate. No colour changes occurred after two hours at this temperature. On warming to -30° (1/2 hour) the suspension turned to a light brown colour. A yellow-orange colour, indicative of formation of fluorenonazinemonoxide (XXX), only appeared when the suspension was warmed up to -10° . After 12 hours at this temperature, the suspension was filtered to give unreacted lead tetraacetate (30%). An aliquot (0.2 ml) was syringed

from the mother liquor at -10° and immediately analysed in 0.1 mm IRT cells cooled down by flushing with methylene chloride at -80° . No change in the resulting spectrum was noted as the cells warmed up to R.T.

The mother liquor (-10°) was washed with water. The precipitated black lead oxide (due to unreacted lead tetraacetate) was filtered. The filtrate was dried (MgSO_4) and evaporated to an orange residue (328 mg). Ether (5 ml) was added but no precipitate was formed. Analysis of this crude by t.l.c. and IR indicated that mainly oxime XI was present, with lesser amounts of fluorenone and its azinemonoxide (XXX). Not a trace of fluorenonazine-N-bis-oxide (XXXVII) could be detected (t.l.c.).

Oxidation of oxime XI in methylene chloride in the presence of fluorenonazine-N-bis-oxide (XXXVII)

The oxidation was conducted as described for fluorenonazine-monoxide formation (XXX) in section 1-1. One hundred milligrams of oxime XI and corresponding amounts of other reagents were used. Compound XXXVII (50 mg) was added before addition of the lead tetraacetate. Addition of ether to the crude residue obtained after work-up gave 51 mg of crystals consisting of XXXVII (t.l.c. and mixed m.p.) contaminated with trace amounts of ketal XXVII (t.l.c.).

Chapter 3

Oxidation of Other Aromatic Ketoximes

3-1. Oxidation of Benzophenone Oxime (IX)

3-1.1. and 1.2. Lead tetraacetate oxidations in glacial acetic acid and in methylene chloride

The products in the various experimental runs (results entered in Table XII) were generally isolated as described in section 1-2. Infrared spectra of crude reaction mixtures were taken before and after work-up, as in the studies on the oxidation of fluorenone oxime. These spectra were identical except for the bands at 1765 and 1720 cm^{-1} which were mainly due to acetic acid. Comparison of these spectra with individual spectra of isolated products indicated that no significant decomposition had occurred during the isolation steps.

3-1.3. Molecular oxygen

Oxime IX (50 mg) was oxidized as described in part B of section 2-1.2. After 24 hours, t.l.c. indicated the absence of IX and the presence of benzophenone (XL) and dinitrodiphenylmethane (XXXVIII).

Addition of water gave a colourless oil which was dissolved in ether, washed with water and sodium bicarbonate solution (10%), dried (MgSO_4), and evaporated to a pale yellow oil (43 mg). A t.l.c. of this oil in methylene chloride showed compounds XL and XXXVIII, in a ratio of about 4:1 (determined by t.l.c. comparison with a solution of authentic samples).

3-1.4. Nitrogen dioxide

See section 4-2.

3-2. Oxidation of Xanthone Oxime

Preparation of xanthone oxime (XLVII)

Xanthione was prepared by the following modified method (83). Xanthone (4.39 g) and phosphorus pentasulfide (5.28 g) were intimately ground and heated to 140°. Heating above this temperature leads to decomposition to xanthone and other products. After a half-hour, the green-brown cake which had formed was crystallized from ethanol (ca. 400 ml). Xanthione was obtained as green-brown needles (4.5 g), homogeneous by t.l.c.

The procedure of Graeber and Roder (83) was followed for conversion of xanthione to xanthone oxime. Xanthione (2.08 g) was refluxed in absolute ethanol (150 ml) containing hydroxylamine hydrochloride (12.5 g) and sodium carbonate (100 mg). Addition of water gave pale pink crystals which were air-dried to give 2 g of pure (t.l.c.) XLII, m.p. 160-161° (reported m.p. 161°).

Oxidation of xanthone oxime (XLVII) with lead tetraacetate in oxygen-free glacial acetic acid

Lead tetraacetate (210 mg, 1 me) was added all at once to XLVII (102 mg) in oxygen-free glacial acetic acid (10 ml). A dark brown colour immediately formed which began to fade after one minute of magnetic stirring. After three minutes, all the lead tetraacetate was consumed¹. After 10 minutes, a pale yellow solution had formed. Addition of water gave colourless crystals (70 mg) which consisted mainly of xanthone and a

very minor product (t.l.c.). An infrared spectrum of these crystals (5 mg/ml CHCl_3) was almost identical to a spectrum of xanthone (5 mg/ml CHCl_3), except for a peak at 1765 cm^{-1} .

	<u>(cm^{-1})</u>	<u>1765</u>	<u>1740</u>	<u>1660</u>	<u>1620</u>	<u>1460</u>	<u>1350</u>	<u>1340</u>
Isolated crude	(5 mg/ml):	40%	15%	80%	79%	45%	65%	65%
Xanthone	(5 mg/ml):	0%	10%	84%	79%	40%	65%	68%

Oxidation in oxygen-free methylene chloride

Upon addition of a one mole equivalent of lead tetraacetate to xanthone oxime in oxygen-free methylene chloride, a dark chocolate-brown solution formed and lead acetate precipitated out. After five minutes, reaction was complete¹. The solution gradually faded to a pale yellow colour (1/2 hour). A t.l.c. of this solution indicated mainly the presence of xanthone, with traces of three other products. The lead acetate (705 mg) was filtered. Light yellow fluffy crystals (552 mg) were obtained after neutralizing (5% NaHCO_3), washing, drying (MgSO_4) and evaporating the methylene chloride solution. Although trace amounts of impurities were present (nitrous fumes given off on standing), the product was identified as xanthone (XLIX) by t.l.c., infrared and mixed m.p.

Oxygen present

When the above reaction was repeated in the presence of oxygen, a pale yellow solution was immediately formed. Xanthone was formed as the major product (ca. 75%, determined by IR and t.l.c. only). A minor

amount of a product with $R_f > R_f$ xanthone was also present (t.l.c.).

Repeat in the presence of oxygen

A repeat of the above experiment in glacial acetic acid containing oxygen immediately gave a light yellow solution. Addition of water gave an oil which was extracted with ether. This solution was neutralized (5% NaHCO_3 solution), washed with saline water, dried (MgSO_4) and evaporated to a pale yellow oil (50 mg). Analysis (t.l.c.) of this oil in methylene chloride showed the presence of about three major and seven minor products. No xanthone nor 9,9-dinitroxanthene (LI, see 4-2) was present (t.l.c.).

3-3. Oxidation of Indanone Oxime (LII)

Oxidation in oxygen-free glacial acetic acid

Indanone oxime (LII, 500 mg), m.p. $144-146^\circ$ (lit. $144-146^\circ$ (85)), prepared exactly as for benzophenone oxime (1-2), was dissolved in oxygen-free glacial acetic acid (25 ml). Lead tetraacetate (1.51 g, 1 me) was added to this vigorously stirred solution to give immediately a yellow solution which turned to a fluorescent green after one minute. Reaction was complete¹ after 15 minutes. The green solution contained mainly a product with $R_f > R_f$ indanone (LIII) (turquoise spot on t.l.c.) and a minor amount of indanone (LIII). The solution was evaporated in vacuo at room temperature to give a green-brown viscous oil. Analysis (t.l.c.) of an aliquot of this oil in methylene chloride indicated that the turquoise product had decomposed mainly to indanone. Only three other very minor products could be detected, with R_f values smaller than

that of indanone oxime (t.l.c.). Infrared analysis of the crude oil in chloroform also confirmed the predominant presence of indanone (ca. 90%).

Oxidation in presence of oxygen

The above procedure was repeated. The reaction time was the same. The dark turquoise solution was worked up as previously described to give mainly indanone (LIII) and a product with R_f smaller than that of indanone oxime (t.l.c.). Infrared analysis indicated that ca. 75% of indanone had been formed.

Oxidation in methylene chloride

The above procedure was repeated with methylene chloride.

3-4. Oxidation of Benzil Anti-Monoxime (LV)

A. Lead tetraacetate oxidation of LV in oxygen-free glacial acetic acid

Lead tetraacetate (1.97 g, 1 me) was added to a stirred solution of LV (1 g; Eastman (25 g bottle)) in oxygen-free glacial acetic acid (50 ml) in a nitrogen atmosphere. A light yellow solution immediately formed. Addition of water (after 2 minutes) to a few drops of the reaction solution gave a colourless precipitate but no lead oxide. A positive starch-iodide test was nevertheless obtained even after one hour of reaction time but the same crude precipitate (t.l.c.) was obtained whether work-up was effected after 10 minutes or after 24 hours after mixing the reagents.

Water was added to the reaction solution to give a colourless

oily precipitate which aggregated to a yellow solid as the suspension was stirred. This solid was filtered, washed with water and air dried (930 mg). It consisted mainly of a new product LVI and a minor amount of a compound with R_f less than that of oxime LV (t.l.c.). Infrared analysis of this crude product showed bands at 1760 cm^{-1} (m) assigned to the oxime O-acetate compound LVII, and at 1710 (s), 1680 (s), 1605 (s), 1570 (s) and 1350 (m) cm^{-1} .

Purification of crude LVI

Attempts to crystallize the crude product from hexane-methylene chloride, methanol, and aqueous methanol were unsuccessful.

Chromatography of this crude product (1.175 g) on silica gel (60 g) with hexane-benzene (1:1) gave 100 mg of an oil ($R_f > R_f$ benzil (t.l.c.)) whose IR spectrum (CHCl_3) contained strong bands at 1710 and 1580 cm^{-1} . Elution with benzene gave 450 mg of yellow crystals of benzil (t.l.c., IR and mixed m.p.). Further elution with benzene-ether (49:1) gave 130 mg of a mixture of benzil and compound LVI. Elution with benzene-ether (93:7) gave 173 mg of benzil, contaminated by four minor impurities. Finally, elution with benzene-ether (3:1) gave 200 mg of an oil ($R_f < R_f$ oxime LV) whose IR spectrum (CHCl_3) contained a strong band at 1700 cm^{-1} .

Similar results were obtained when purification of crude LVI was attempted on silica gel plates, using benzene-ether (49:1) as eluting solvent.

B. Lead tetraacetate oxidation of LV in oxygen-free methylene chloride

The same procedure was followed as described in (A). Addition of lead tetraacetate (1.97 g, 1 me) immediately gave a yellow-orange solution which turned to yellow-green suspension within a minute. After one hour, the suspension had gone from a green to a yellow colour. Unreacted lead tetraacetate remained even after 24 hours. Addition of water gave a brown precipitate corresponding to greater than 25% of unreacted lead tetraacetate (~400 mg of lead oxide was actually isolated). The methylene chloride solution was washed with water and 5% sodium bicarbonate solution. It was dried (MgSO_4) and evaporated to a yellow oil containing mainly benzil (t.l.c. and IR) and about five minor products (t.l.c.).

Chapter 4

Geminal Dinitromethanes

- 4-2. } Preparation and Characterization of Gem-Dinitromethanes from
and
4-3. } Reaction of Aromatic Ketoximes with Nitrogen Dioxide

The following general method was used. Methylene chloride (25 ml) was briefly purged with nitrogen dioxide (compressed gas from the Matheson Co.) to give a light brown solution. The oxime (ca. 100 mg) was added all at once to the magnetically stirred solution. Immediate reaction occurred. After five minutes, the light green solution was evaporated at R.T. in vacuo. Work-up was continued as follows.

9,9-Dinitrofluorene (XXVI) from fluorenone oxime (XI)

Pale yellow crystals were obtained from the oxidation of XI (100 mg) which consisted of pure XXVI (107 mg), m.p. 129.5-131° (dec., with evolution of NO₂), identical with authentic XXVI (t.l.c. and mixed m.p.; see 1-1).

Similar results were obtained when the reaction was carried out by bubbling NO₂ gas through a solution of oxime XI in ether (25 ml) kept at 0°. Compound XXVI was obtained (112 mg), m.p. 129.5-131° (identified by t.l.c. and mixed m.p.).

Dinitrodiphenylmethane (XXXVIII) from benzophenone oxime (IX)

Pale yellow crystals (174 mg) were obtained from the oxidation of oxime IX (150 mg) which consisted of a mixture of XXXVIII, benzophenone,

and a minor impurity ($R_f < R_f$ IX). A crystallization from hexane (6°) gave colourless, flaky crystals of pure XXXVIII (115 mg), m.p. $79-79.5^\circ$, identical with authentic dinitrodiphenylmethane (t.l.c. and IR; see 1-2).

The mother liquor was evaporated (59 mg) and dissolved in spectral grade chloroform (10 ml). The infrared spectrum of this solution was compared with a standard solution of benzophenone (XL) and dinitrodiphenylmethane (XXXVIII). The comparison indicated that the mother liquor consisted of ca. 40% of XL and ca. 60% of XXXVIII.

9,9-Dinitroxanthene (LI) from xanthone oxime (XLVII)

A yellow oil was obtained from the oxidation of XLVII (250 mg) which consisted of one major and one minor product (t.l.c.). Crystallization from hexane (6° overnight) gave colourless crystals of LI (227 mg), m.p. $72.5-73^\circ$ (dec. 108° , evolution of NO_2 observed at 128°), homogeneous by t.l.c. Recrystallization from hexane (R.T.) gave colourless plates of LI, m.p. 74.5° , ν^{KBr} 1560 and 1345 cm^{-1} (NO_2).

Anal. Calcd. for $\text{C}_{13}\text{H}_8\text{N}_2\text{O}_5$: C, 57.36; H, 2.96; N, 10.29; O, 29.39

Mol. Weight 272

Found: 1) C, 58.48; H, 4.22; N, 9.68; O, 27.62

2) C, 58.33; H, 4.42; N, 9.82; O, 27.43

Mol. Weight (osmometric- CHCl_3) 287.

Chemical properties of LI

(i) Compound LI (5 mg) was stable when left 24 hours in methylene chloride or in glacial acetic acid, containing concentrated hydrochloric

acid.

(ii) Pyrolysis (128°) of LI led to evolution of nitrous fumes but no xanthone was detected in the product mixture (t.l.c.).

(iii) Reaction of LI (5 mg) in ether (1 ml) with lithium aluminum hydride (2 mg) readily occurred but no xanthone or xanthhydrol were formed.

Mass spectral properties of LI compared to 9,9-dinitro-fluorene (XXVI)

The mass spectra of LI and XXVI were taken under the conditions shown below. Probable fragmentations of interest are included.

<u>Compound XXVI (M.W. 256)</u>	<u>Compound LI (M.W. 272)</u>
Direct inlet temp. = 90°	Direct inlet temp. = R.T.
$I_v = 70$ eV.	$I_v = 70$ eV.
$256^{+} \longrightarrow 210^{+} + NO_2$ (0.2%) (10%)	$240^{+} \longrightarrow 223^{+} + OH \quad m^{*} 207.3$
$210^{+} \longrightarrow 180^{+} + NO$ (100%)	$223^{+} \longrightarrow 195^{+} + 28 \quad m^{*} 170.5$
	$195^{+} \longrightarrow 165^{+} + NO \quad ?$

The fragmentation pattern of LI could not be rationalized. This is probably due to the known complicating effect of the bridged-oxygen on the overall fragmentation pattern (86).

1,1-Dinitroindane (LXI) from indanone oxime (LII)

A yellow oil (277 mg) was obtained from the oxidation of LII (250 mg), consisting mainly of indanone (LIII) and three minor products (t.l.c.). The predominant presence of LIII was also confirmed by IR analysis of the crude oil. Attempts to crystallize this oil from hexane-methylene chloride were unsuccessful.

The oil was taken up in methylene chloride and evaporated in the presence of silica gel (200 mg). This residue was added to a column of silica gel (10 g) in hexane. Elution with hexane-benzene (1:1) gave a yellow oil (31 mg) whose infrared spectrum (CHCl_3) contained bands characteristic of gem-dinitromethanes at 1570 cm^{-1} (s) and 1360 cm^{-1} (m). These absorption bands and the R_f value (t.l.c.) suggested that this product might be compound LXI (8%). Further elution gave an oil (15 mg, ca. 4%) whose IR spectrum contained a strong carbonyl band at 1680 cm^{-1} , in addition to bands at 1590 (s), 1570 (vs) and 1370 cm^{-1} (m). No definite assignment could be made. Elution with benzene-ether (7:3) gave a yellow oil (170 mg) consisting of indanone (75%; t.l.c, and IR), contaminated by trace impurities. Elution with methanol gave an oily residue (14% by weight) of undetermined composition.

Chapter 5

5-3. Autoxidations of Aromatic Ketoximes

The same procedure for the following oximes was used as described in part B of section 2-1.2: xanthone oxime (XLVII), indanone oxime (LII), benzil anti-monoxime (LV), biacetyl monoxime (Eastman Chemical (10 g bottle)), cyclohexanone oxime (m.p. 85-87°, Fisher (100 g bottle)), 2,2,6,6-tetramethylcyclohexanone oxime⁴ (m.p. 151.5°), and prègnenolone-20-oxime-3 β acetate⁵.

5-5. Oxidations with Nitric Oxide

Fluorenone oxime (XI)

Oxidation of XI with nitric oxide in oxygen-free benzene was conducted as described in 2-1.3 and led instantaneously to a deep yellow solution. Analysis (t.l.c.) showed fluorenone as the only product.

The reaction was repeated in oxygen-free methylene. An orange solution immediately formed. Analysis (t.l.c.) showed fluorenone and fluorenonazinemonoxide (XXX) as major products, along with a number of minor products (t.l.c.). When the reaction was repeated in methylene chloride in the presence of air, instantaneous reaction occurred to give a yellow solution. Analysis (t.l.c.) showed the presence of mainly 9,9-dinitrofluorene (XXVI), but also minor amounts of compound XXX.

⁴ and ⁵ These samples were gratefully received from K. Dahl⁴ and Y.C. Lin⁵; colleagues in this laboratory.

Conclusions and Contributions to Knowledge

1. The oxidation of bis-aryl ketoximes with nitrogen dioxide leads to high yields of geminal dinitromethanes through radical reactions involving iminoxyl nitroxides. This very facile method is not useful for less conjugated ketoximes, such as indanone oxime, since high yields of parent ketone are formed. This method had been used at the turn of the century but conflicting and uncertain reports had then been made on the products formed (10,63). No other comparatively simple and useful procedure has been reported to date.
2. The bis-aryl ketoximes, fluorenone and benzophenone oximes, undergo slow autoxidation only in glacial acetic acid to form parent ketone and geminal dinitromethanes. In the case of fluorenone oxime, 9,9-difluorenylideneiminoxylfluorene is also formed. Xanthone oxime, benzil anti-monoxime, and less conjugated ketoximes such as indanone oxime and aliphatic oximes, are not oxidized by molecular oxygen.

Oxygen abstracts a hydrogen radical from oximes to form the corresponding iminoxyl radical which further reacts with oxygen to form nitrogen dioxide and observed products. The lack of reactivity of the above oximes has been qualitatively correlated with the ionicity of the O-H bonds and stabilities of iminoxyl nitroxides.
3. The autoxidation of fluorenone hydrazone in glacial acetic acid leads to quantitative formation of fluorenonazine, previously prepared under vigorous conditions (37).
4. Nitric oxide oxidation of bis-aryl ketoximes has been reported to occur in acetone only under ultraviolet irradiation (48). However,

the solvent plays a key role in these reactions. Fluorenone oxime, for example, is stable to nitric oxide in glacial acetic acid, but is spontaneously converted to fluorenone in benzene and to the ketone and fluorenonazinemonoxide in methylene chloride. The nature of the interaction of the solvent in this oxidation is as yet unknown.

5. a(i) Lead tetraacetate oxidation of the bis-aryl ketoximes, fluorenone and benzophenone oximes, in glacial acetic acid leads to parent ketones, geminal dinitromethanes, iminyl ketal derivatives, and oxime O-acetates. Molecular oxygen quenches the formation of benzophenone nitrimine and 9,9-difluorenylideneiminoxyfluorene and markedly affects the product distribution. Side reactions due to nitric oxide, oxygen, and nitrogen dioxide have been rationalized from the results obtained from separate studies conducted with these oxidizing agents.

(ii) Lead tetraacetate oxidation of the forementioned bis-aryl ketoximes in solvents other than glacial acetic acid leads mainly to parent ketones and ketazinemonoxides. A quantitative study conducted in methylene chloride shows that the product distribution is insensitive to oxygen and that a half-mole equivalent of lead tetraacetate suffices for complete oxidation of these oximes. The formation of parent ketone in high yield is attributed to efficient radical-radical recombinations caused by the cage effect of the solvent. Gem-nitrosoacetates are postulated as intermediates. Iminyl ketal formation, observed in this solvent only for the oxidation of fluorenone oxime, appears to occur through successive ionic and free radical reaction steps. All other products seem to be formed through free radical reactions.

b. The lead tetraacetate oxidation of benzil anti-monoxime, whose iminoxyl radical is more stable than that of the bis-aryl ketoximes in a (15), leads to a major unidentified product when conducted in oxygen-free glacial acetic acid and to the parent ketone as major product when conducted in methylene chloride. The results suggested that long-lived iminoxyl radicals (15) are initially formed and react further to give observed products. The cage effect of methylene chloride on the reaction was again invoked to explain the high yield of parent ketone observed in the oxidation conducted in this solvent.

c. The oxidation of xanthone oxime in both methylene chloride and glacial acetic acid is complete with a one mole equivalent of lead tetraacetate and leads essentially to parent ketone. The free radical nature of this reaction in glacial acetic acid was demonstrated by the marked change in products formed when oxygen was not excluded. The results can be rationalized in terms of the electron-feeding effect of the bridged-oxygen.

d. Indanone oxime behaves similarly to aliphatic ketoximes (25,26) when oxidized with lead tetraacetate. The oxidation conducted in glacial acetic acid leads mainly to the gem-nitrosoacetate, which decomposes readily to parent ketone. The oxidation is not as sensitive to solvent as bis-aryl ketoximes and requires a 1 mole equivalent of lead tetraacetate in both acetic acid and methylene chloride. Secondary nitroxides, detected by ESR (14,24) are invoked to explain nitroso-acetate formation. The radical-radical recombinations involving iminoxyl and lead triacetate radicals, occurring in the lead

tetraacetate oxidations of the oximes in 5a, b and c, may also be taking place.

6. The potassium ferricyanide oxidation of fluorenone oxime leads to mainly fluorenone, fluorenonazine-N-bis-oxide, fluorenon-azinemonoxide, and nitrogen oxides; the latter two are formed from a transient intermediate only stable below 0°C.

The pyrolytic and hydrolytic modes of decomposition of fluorenonazine-N-bis-oxide have been rationalized in terms of the known behaviour of azinemonoxides (36).

The anhydride N-oxide structure proposed for the analogous oxidation product of benzophenone oxime (31) is most likely the azine-N-bis-oxide. These compounds are not formed in the lead tetraacetate oxidations of the aromatic ketoximes studied. Secondary nitroxides, whose formation in lead tetraacetate oxidations was reported only for acetophenone oxime and aliphatic ketoximes (24), are invoked to explain the formation of azine-N-bis-oxides from the oxidations of both ket- and ald-oximes.

7. No evidence for formation of iminoxyl cations was obtained in any of the oxidations studied. Benzisoxazoles, whose formation might be expected by intramolecular reactions of these cations, could not be detected.

The iminoxyl radicals generated in the oxidations of ketoximes may react over nitrogens or oxygens, since it has been shown that the unpaired electron is about equally delocalized over the iminoxyl oxygen and nitrogen (20). The actual mode of reaction is markedly determined by electronic factors. Dimerization of the long-lived

iminoxyl radicals from bis-aryl ketoximes to form azine-N-bis-oxides apparently does not occur. The shorter lived radicals from aceto-phenone oxime (24b) and indanone oxime do not undergo any dimerization either. The variation in product formation in the lead tetraacetate oxidations of ketoximes can be qualitatively correlated with the reported (15) stabilities of the corresponding iminoxyl radicals.

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APPENDIX A

Comparison of Mass Spectral Data of Some Fluorenone Derivatives

The mass spectral data of 9,9-difluorenylideneiminoxyfluorene (XXVII), fluorenonazinemonoxide (XXX), and fluorenonazine-N-bis-oxide (XXXVII) is compared in the table shown below. All the mass peaks which could be related to the molecular ion peak are shown below. Some minor mass peaks (1%) in the higher mass range have been omitted. Peaks due to skeletal fragmentation (in the lower mass range) have also generally been omitted.

Mass-Charge Ratio (m/e)	<u>Relative Intensity</u>				
	XXVII		XXX		XXXVII
	70 eV.	10 eV.	70 eV.	12 eV.	70 eV.
372					0.2
359	1.3	1.0			0.3
358	7.3	4.2	0.3	0.9	1.0
357	25.9	13.0	1.7	6.4	2.7
356	9.0	3.0	6.2	20.0	4.4
355	4.0	0.6	5.5		3.7
343	0.6		0.1		2.3
342	0.8		0.2		3.6
341	0.3		0.6	0.9	0.6
340	0.6		0.2		1.1
329	5.0	1.2	0.7	0.2	0.7
328	11.6	4.0	2.4	1.3	1.9
327	7.1		4.0	4.0	2.3
326	4.0		2.9		1.9
325	2.0		0.5		0.4
324	5.3		0.7		0.4

(continued)

Relative Intensity (cont'd.)

Mass-Charge Ratio (m/e)	XXVII		XXX		XXXVII
	70 eV.	10 eV.	70 eV.	12 eV.	70 eV.
196	1.5	0.1	0.2		0.9
195	10.0	0.6	0.5		1.4
182	2.5	2%	0.4	0.5	1.0
181	33.2	26%	3.2	9.0	16.0
180	51.2	100.0	78.2	70.0	100.0
179	45.1	96.0	100.0	100.0	28.6
178	43.6		6.8		7.1
177	22.6		3.6		5.7
176	4.7		1.5		1.4
165	4.6		2.0		2.9
164	10.0		3.3		2.9
163	7.2		3.3		2.7
162	2.0		1.4		0.9
153	22.0		9.9		8.6
152	100.0		41.7		51.5
151	65.0		28.8		23.0
150	36.5		16.5		2.9
145	5.8		2.1		0.4
78	2.4		1.4		4.4
77	9.2		5.5		3.9
76	72.4		29.7		21.8
64	2.4		1.4		8.4
63	32.2		14.6		11.0
52	0.8		4.6		1.5
51	16.8		12.8		4.1
50	16.8		12.8		4.6
49	4.0		0.9		16.1
30	4.9		17.7		6.1
29	1.6		2.0		1.7
28	15.5		29.2		24.5
18	14.3		9.0		7.7

(continued)

Relative Intensity (cont'd.)

ADDITIONAL INFORMATION					
Vapour Temp. (°C.)	200 (Direct		250 (Indirect)		200 (Direct)
V_A	1750 v.		1750 v.		1750 v.
V_M	2400 v.		2000 v.		2000 v.
	70 eV.	10 eV.	70 eV.	10 eV.	70 eV.
Metastable			354.5	-	354.5
Peaks			326	-	326
(m/e values)	178.5	-	177.5 (v.w.)*	-	178.5
	150.5	-	150.5 (v.w.)	-	150.5
	128.5	-	128.5 (v.w.)	-	128.5

* v.w. = very weak intensity.

APPENDIX B

Graphical Analysis for Product Distribution

Fluorenone oxime (XI), fluorenone (XXVIII), and 9,9-dinitrofluorene (XXVI) have characteristic and distinct absorptions in their infrared spectra at 3565 cm^{-1} , 1712 cm^{-1} , and 1565 cm^{-1} respectively. Standard solutions of these compounds were prepared. A graphical plot of percent absorption versus concentration was then obtained, as shown on the following page.

A sample (40-50 mg) from the reaction mixtures obtained in the oxidations of fluorenone oxime was dissolved in 10 ml spectral grade chloroform. Absorptions were recorded at the above wavelengths on the Perkin-Elmer "521" spectrophotometer with the same settings as those used for the initial analysis of standard solutions. The product distribution of compounds XI, XXVIII, and XXVI in these mixtures could thus be directly determined from the graph.

The results obtained by this method were reproducible within ca. $\pm 3\%$.

