SOME REACTIONS OF ORGANIC PEROXIDES

by

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TABLE OF CONTENTS

-

General Introduction	l
Fart I	
INTRODUCTION OF OXYGEN FUNCTION INTO ARCHATIC	
NUCLEI USING FEROXIDES	
Historical Introduction	2
Reactions of Organometallic Compounds with	
Dialkyl Peroxides	2
Reactions of Organometallic Compounds with	
Alkyl Hydroperoxides	6
Reactions of Organometallic Compounds with	
Oxygen	8
Reactions of Organometallic Compounds with	
Dibenzoyl Feroxide	16
Friedel-Crafts Reactions of Aromatic Compounds	
with Diaroyl Peroxides	19
Mixed Aroyl Sulphonyl Peroxides	27
Experimental	
Materials	29
Infrared Spectra	30
Reactions of Organometallic Compounds with	
Dialkyl Peroxides	31
(a) Reactions of Dimethyl Peroxide with	
Fhenyllithium	32

(b) Reaction of Dimethyl Peroxide with	rage
Thenylmagnesium Bromide	33
(c) Reaction of Methyl <u>t</u> -Butyl Feroxide with	
Phenyllithium at 15-20°	34
(d) Reaction of Methyl <u>t</u> -Butyl Peroxide with	
Phenylmagnesium Bromide_at 15-200	35
(e) Reaction of Kethyl <u>t-Butyl Peroxide</u> with	
Phenyllithium at 35 ⁰ C	35
(f) Reaction of Methyl <u>t</u> -Butyl Peroxide with	
Phenylmagnesium Bromide at 35 ⁰	36
(g) Reaction of Diethyl Peroxide with Phenyl-	
lithium	36
(h) Reaction of Diethyl Peroxide with Phenyl-	
magnesium Bromide	37
(i) Reaction of Di-t-butyl Peroxide with Pheny-	
llium at 15-20°	37
(j) Reaction of Di- <u>t</u> -Butyl Feroxide with Fhenyl-	
lithium at 35 ⁰ C	3 9
(k) Reaction of Di- <u>t</u> -butyl Peroxide with	
Fhenyllithium at 0 ⁰ -5 ^o C	40
(1) Reaction of Di- <u>t</u> -Butyl Peroxide with	
Fhenyllithium at 80°C	41
Reaction of Oxygen or <u>t</u> -Butyl hydroperoxide	
with Organometallic Compounds	41

~

		rage
(a)	Reaction of Oxygen with	
	Phenyllithium	42
(b)	Reaction of Oxygen with Mixture of	
	Phenyllithium and <u>n</u> -Butyllithium	43
(c)	Reaction of Oxygen with 4-	
	Biphenylyllithium	44
(đ)	Reaction of Cxygen with Lixture of	
	4-Biphenylyllithium and <u>n</u> -Butyllithium.	45
(e)	Reaction of a Mixture of <u>t</u> -Butyl	
	hydroperoxide and Ethylmagnesium	
	Bromide with Phenyllithium	45
(f)	Reaction of <u>t</u> -Butyl hydroperoxide	
	with Phenyllithium	46
(g)	Reaction of Oxygen with 2-Methoxy-1-	
	Naphthyllithium	46
(h)	Reaction of <u>t</u> -Butyl hydroperoxide with	
	2-Methoxy-l-Naphthyllithium	48
2-Methox	y-l-Naphthyl Benzoate	49
Attempt	to Prepare $lpha$ -Hydroxyfurans	50
(a)	Reaction of oxygen with 2-Furyllithium.	50
(b)	Reaction of <u>t</u> -Butyl hydroperoxide with	
	2-Furyllithium	51
(c)	Reaction of <u>t</u> -Butyl hydroperoxide with	
	2-Methvl-5-furvllithium	51

iii

Page

	Fage
Reactions of Dibenzoyl Peroxide with	
Grignard Reagents: General Procedure	51
(a) <u>n</u> -Butylmagnesium Chloride	52
(b) Phenylmagnesium Chloride	53
(c) Fhenylmagnesium Iodide	53
Reactions of Benzoyl Peroxide in the Presence	
of Aluminum Chloride in Different Organic	
Solvents: General Procedure	54
(a) In Benzene	54
(b) In Nitrobenzene	55
(c) In Toluene	55
Reaction of Sodium Perbenzoate with Methane-	
sulphonyl and p-Toluene Sulphonyl Chloride	5 6
Results and Discussion	
Reactions of Organometallic Compounds with	
Dialkyl Peroxides	5 7
Reactions of Organolithium Compounds with	
t-Butyl Hydroperoxide and with Oxygen	62
Reactions of Grignard Reagents with Benzoyl	-
Peroxiãe	64
Aluminium Chloride - Catalysis of the	
Decomposition of Benzoyl Peroxide	65

i⊽

V	Demo
	rage
Reaction of Sodium Perbenzoate with	
Sulphonyl Chlorides	66
Bibliography	68
Part II	
PREFARATION OF α -METHCXYTHIOFHEMAS USING	
LETHYL t-BUTYL PEROXIDES	
Historical Introduction	73
2-Hydroxy- and 2- Alkoxythiophenes	74
3-Hydroxy- and 3-Alkoxythiophenes	82
3,4-Dihydroxy- and 5,4-Dialkoxythiophenes	86
Metalation of Thiophenes	88
Experimental	
Reaction of Methyl <u>t</u> -Butyl Peroxide with 2-	
Thienyllithium	96
Reaction of Dimethyl Peroxide with 2-	
Thienyllithium	97
Reaction of Methyl t-Butyl Peroxide with 5-	
Methoxy-2-thienyllithium	97
Reaction of Methyl t-Butyl Peroxide with 2-	
Nethyl_5-thienyllithium	98
Desetier of Mathul + Dutul Lemenics with 0	•••
Readeron of Meenyr <u>-</u> Bubyr reroxide with 2-	
Ithyl-5-thienyllithium	99

	Page
Reaction of Methyl <u>t</u> -Butyl Feroxide with 3-	
Methylthienyllium	100
Attempted Preparation of 2,5-Dimethoxy-3-	
thienyllithium	101
Diels-Alder Reaction	102
Results and Discussion	
Preparation of $lpha$ -Methoxythiophenes	103
Spectral Studies of α -Lethoxythiophenes	106
Bibliography	126
Summary and Claims to Original Research	131

vi

GENERAL INTRODUCTION

Unlike the hydroxy derivatives of benzene, which are comparatively stable, the hydroxy derivatives of furan are unstable and tautomerize more or less completely into keto forms. For this reason the preparation of ethers and esters of hydroxyfurans presents special problems. As part of a search for general routes to these compounds, Baramki (1) studied the reactions of arylithiums, including α -furyllithiums, with dialkyl peroxides as a means of forming ethers, and Samad (2) studied reactions of diaroyl peroxides which resulted in the introduction of aroyloxy groups into aromatic nuclei. In Part I of this thesis are described experiments designed to complete various aspects of the work initiated by Baramki and Samad. The most important result emerging from these studies was the discovery that good yields of methyl ethers could be obtained from the reaction of organolithium compounds with methyl t-butyl peroxide. In Part II this reaction was applied to the preparation of several α -methoxythiophenes, compounds which have hither to been, like α -methoxyfurans, relatively difficult to make; and the spectral properties of these compounds have been studied.

<u>Part I</u>

Introduction of Oxygen Functions into Aromatic Nuclei Using Peroxides

Historical Introduction

Reactions of organometallic compounds with dialkyl peroxides

In 1925 Gilman and Adams (3) reported the reaction between Grignard reagents and a number of organic peroxide including diethyl peroxide. They found that neither succinyl peroxide nor triphenylmethyl peroxide underwent a reaction with Grignard reagents, * but that both benzoyl peroxide and diethyl peroxide reacted according to the general equation:

 $R - 0 - 0 - R + R^{\dagger}MgX \longrightarrow R - 0 - R^{\dagger} + ROMgX$ (1)

In the reaction of diethyl peroxide with phenylmagnesium bromide, relatively large amounts of biphenyl (30%) were obtained along with phenetole (34%).

Campbell <u>et al.</u> (7) examined the reaction between di-t-butyl peroxide with phenylmagnesium bromide and some

^{**x**}For simplicity and convenience we shall usually represent the Grignard reagent conventionally as RMgX, although the work of Dessy <u>et al.</u> (4,5,6) shows that in diethyl ether it is most plausibly represented as R = -X

aliphatic Grignard reagents. They found that phenylmagnesium bromide and <u>t</u>-alkyl Grignard reagents failed to react with the peroxide, while <u>t</u>-butyl ethers were obtained with primary and secondary aliphatic bromomagnesium compounds.

Recently, Lawesson and Yang (8) described a rather similar reaction between \underline{t} -butyl perbenzoate and Grignard reagents from which \underline{t} -butyl ethers were obtained.

 $PhCO-O-O-But + RMgX \longrightarrow RO-But + PhCO-MgX$ (2)

R	R (a) With R Li		D D	(b) With RMgX		D D
	ROMe	(% Yield)	(% Yield)	ROMe	(% Yield)	(% Yield)
с ₆ н ₅ -		62	19		62	20
p-Me ⁰ .C ₆ H ₄ -	-	45	20		47	26
p-C6H5.C6H4	L -	65	11		53	trace
2-C ₁₀ H ₇ -		21	30		_¥	_X
2-furyl-		49 ^{**}	XXX			

Dimethyl Peroxide

TABLE I

Nature and Yields of Products from Reaction of

*Reaction not tried

Product showed slight contamination with aliphatic material * Product not isolated

Baramki (9) applied the reaction of Gilman and Adams, using dimethyl peroxide (10), to the preparation of various aromatic ethers. This peroxide gave higher yields of ethers, and lower yields of coupling products of the Grignard reagents, than did diethyl peroxide, as shown in Table I.

The reaction of organolithium in place of organomagnesium compounds with dimethylperoxide was studied by Baramki (9), since the former compounds are often more easily prepared. The yields of methyl ethers using organolithium compounds were virtually the same as when the Grignard reagents were used (Table I).

A mechanism of the reaction was proposed by Baramki. Although organometallic compounds are generally considered to react by ionic mechanisms (11, 12), free-radical mechanisms have occasionally been postulated (13). Hence, Baramki (9) tried to compare the reactivity of dimethyl peroxide towards a free radical and a carbanion, using triphenylmethyl radical and triphenylmethylsodium. Infrared examination of the products showed that only the latter gave methoxytriphenylmethane:

$$Ph_{3}C \xrightarrow{\phi} \rho \xrightarrow{\phi} OMe \longrightarrow Ph_{3}C - OMe + MeO \xrightarrow{\phi} (3)$$

although it proved impossible to isolate the ether in crystalline form. The reaction of organolithium and organomagnesium compounds also probably involves a nucleophilic attack on the peroxide linkage; many peroxide reactions involve such a mechanism. (3, 8, 9, 14a). This may involve a preliminary coordination of the metal atom by the unshared electrons of the oxygen as is well known to happen with ethers (14b).



Such a coordination would facilitate the formation of an ionpair (I) which then reacts as shown in eg. 4.

While the reaction of dimethyl peroxide with organomagnesium and organolithium compounds appears to be of general applicability, dimethyl peroxide is a very explosive and hazardous material to use.

Consequently, in this thesis the use of the relatively non-hazardous peroxides, methyl <u>t</u>-butyl peroxide and dit-butyl peroxide, was investigated.

Alkyl hydroperoxides have an active hydrogen atom, and so will react with one mole of Grignard reagent to form the magnesium salt of the hydroperoxide (II):

 $ROOH + R'MgX \longrightarrow R-O-O-MgX + R'H$ (5)

II

A second mole of Grignard reagent might be expected to attack the peroxide linkage of (II) to give either the ether (ROR') or the magnesium salt of the alcohol (R'OMgX), according to which oxygen of the peroxide is more susceptible to attack by a nucleophile. In the event, it is the oxygen attached to magnesium which, for electronic or steric reasons, is attacked:



This reaction gives a convenient method for converting a Grignard reagent to an alcohol. It was employed by Hurd (15) in 1953, who studied the reaction of tetralin hydroperoxide with the α -thienyl Grignard reagent. He included a suitable aliphatic Grignard reagent to convert the hydroperoxide to its magnesium salt. The reaction produced low yields (5%) of 2-thienol.

$$\underbrace{i-C_{3}H_{\eta}MgBr}_{S} + \underbrace{OOH}_{S} OMgBr}_{S} - \underbrace{Hydrolysis}_{S} OMgBr}_{S} + \underbrace{OH}_{S} OMgBr}_{S} + \underbrace{OH}_{S} OMgBr}_{S} + \underbrace{OH}_{S} OH}_{S} OH (7)$$

The reaction has also been studied by Walling and Buckler (16) and more recently by Lawesson and Yang(8), who used <u>t</u>-butyl hydroperoxide with aryl or alkyl Grignard reagents. Excellent yields of phenols or alcohols were obtained.

In order to achieve maximum utilization of the Grignard reagents, the magnesium salt of <u>t</u>-butyl hydroperoxide, prepared from equimolar quantities of ethylmagnesium bromide and <u>t</u>-butyl hydroperoxide, was employed as an oxidant and was found to be effective. Bromobenzene was converted to phenol by the method in 80% yield. A number of **ar**yl halides and neopentyl bromide were converted to phenols and neopentyl alcohol in this way. The reaction of Grignard reagents with <u>t</u>-butyl hydroperoxide

is particularly useful where direct hydrolysis of the halide is difficult or is complicated by side reactions such as elimination and rearrangement.

Reactions of organometallic compounds with oxygen

A familiar property of Grignard reagents is their rapid reaction with molecular oxygen, a reaction first investigated by Bodroux (17) and Bouveault (18) in 1903. The yield of alcohols from aliphatic Grignard reagents is generally good (60-90%) but yields of phenols from arylmagnesium halides are lower (10-22%).

The first information concerning the path of the Grignard reagent-oxygen reaction was obtained by Wuyts (19, 20), who found that oxidized solutions of ethylmagnesium bromide in ether-toluene solution liberated iodine from acidic KI solution and postulated an intermediate peroxide to explain his observation. Solutions oxidized at 0 and -70°, gave peroxide values of 0.7-6%, with the best results being obtained at -70° and relatively high dilution. Solutions of phenylmagnesium bromide gave less than 0.2% peroxide even under these optimum conditions. With this evidence in mind, Forter and Steele (21) have proposed magnesium salts of hydroperoxides as intermediates in the oxidation:

 $RM_g X + O_2 \longrightarrow ROOM_g X$ (8) $ROOM_g X + RM_g X \longrightarrow 2ROM_g X$ (9)

In 1953, Walling and Buckler (16) showed that by slowly adding a dilute ethereal solution of an alkyl Grignard reagent to ether saturated with oxygen at -75° ("inverse oxidation"), a high yield of peroxide could be obtained (e.g. <u>t</u>-C₄H₉MgCl: 91% yield by titration, 82% isolation of the hydroperoxide after hydrolysis).

The group R could typically be ethyl, benzyl, cyclohexyl, 2-octyl, <u>t</u>-butyl, or <u>t</u>-pentyl. The reaction has since been used for preparation of a number of other hydroperoxides and affords what is probably the easiest method for preparing small amounts of simple primary and secondary alkyl hydroperoxides.

Aryl Grignard reagents give evidence of the formation of peroxides at low temperature (a maximum of 9.3 per cent, from <u>p</u>-bromophenyl magnesium bromide); however, on warming, a deep colour develops at -20° , and from phenylmagnesium bromide, phenol (together with a little diphenyl and α -methyl benzyl alcohol) is isolated (16,22). It appears that an aryl peroxide, ArOOMgX, is initially formed, for which there is good reason to expect that an aryl

peroxide would be relatively unstable, since scission of the O-O linkage should yield a coloured phenoxy radical, $C_{6}H_{5}$ -O, which is stabilized by resonance with the π electron system of the aromatic ring. The resonancestabilized aryloxy radicals should then be the precursors of the observed products (16).

Walling and Buckler (16) suggested the following mechanism for the formation of the hydroperoxide:

Other mechanisms have been suggested for this step. Molecular oxygen is a diradical, and autoxidation processes in general appear to be radical reactions, involving either a chain process, yielding hydroperoxides, as in the autoxidation of hydrocarbons (23) (eq. 11), or electron transfer as in the autoxidation of the anions of hydroquinone (eq. 13), (24), in which oxygen is reduced to H_2O_2 .

$$R \cdot + O_2 \longrightarrow ROO \cdot$$
 (11)

$$ROO \bullet + RH \longrightarrow ROOH + R \bullet$$
 (12)

Grignard reagents participate in both polar and radical processes (11, 12, 13) (eq. 14).

$$R \cdot + \cdot MgX \iff RMgX \iff R^- + MgX^+$$
(14)

The autoxidation of the anion of 2-nitropropane has been studied by Russell (25), who postulated an intermediate hydroperoxide anion, formed by a chain process involving electron transfer and suggested a similar mechanism for the reaction of Grignard reagents with oxygen (eq. 11, 15). Doering and Haines have investigated

$$R-C-O \bullet + R^- \longrightarrow ROO^- + R \bullet$$
 (15)

the alkoxide ion catalyzed autoxidation of ketones and esters, concluding that the enolate ion is the reactive species, and that an intermediate hydroperoxide anion decomposes to the isolated products. However, they do not attempt to resolve the question whether the initial reaction follows a radical or polar path.

In the aryl Grignard reagent-oxygen reaction, the yield of phenol (at -20°) is increased from 47.0% to 74% if the phenyl magnesium halides is autoxidized in the presence of 1 or 2 mol. respectively of an alkyl Grignard reagent (16, 27). The function of the additional alkyl Grignard reagent is not certain, and two speculations have been postulated. Ivanoff (28), Lawesson and Yang (8) and Walling and Buckler (16) have suggested that the reaction follows the route shown in eq. 16.

 $RMgX + 02 \longrightarrow R0.0MgX \xrightarrow{ArMgX} R0.MgX + Ar0.MgX$ (16)

They believe that the alkyl Grignard reagent in the mixed reaction is peroxidized first to an alkyl hydroperoxide which is reduced subsequently by the aryl Grignard reagent. Alternatively, Wuyts (20) suggests that the aryl Grignard reagent is peroxidized first to an aryl hydroperoxide which is reduced later by "the more reductive" alkyl Grignard reagent in eq. 17.

 $\operatorname{ArMgX} + \operatorname{O}_{2} \longrightarrow \operatorname{ArO} \cdot \operatorname{OMgX} \xrightarrow{\operatorname{RMgX}} \operatorname{RO} \cdot \operatorname{MgX} + \operatorname{ArO} \cdot \operatorname{MgX}$ (17)

Although phenyl hydroperoxide has been postulated as an intermediate in the oxidation of phenyl magnesium bromide, as mentioned above, various attempts to isolate the apparently unstable aryl hydroperoxide have not been successful (16). Kharach and Reynolds(27) have extended Ivanoff's study on the oxidation of alkyl-aryl Grignard reagent mixtures, and have reached conclusions similar to those of Wuyts (20).

Simple alkyls of the alkali metals inflame in the air, but by controlled autoxidation good yields of alcohols can be obtained. Muller and Topel (29) assumed that the oxidation of organolithium compounds also proceeded through an intermediate peroxide. This was proved by Walling and Buckler (16) for the oxidation of <u>n</u>butyllithium.

They showed by titration that the "inverse oxidation" of n-butyllithium at -75° gave a 36% yield of peroxide.

Phenyllithium (like phenylmagnesium bromide) gave phenol in poor yeild, (29, 30) together with other products such as diphenyl. However, with an aliphatic peroxide, tetralin peroxide, phenyllithium gave phenol (95%) and tetralol practically quantitatively (15, 29).

Since the yield of phenol is increased when the phenylmagnesium halide is oxidized by molecular oxygen in the presence of 1 or 2 mol. of an alkyl Grignard reagent (16, 27), in this thesis the possibility of

increasing the yield of phenol by oxidation of a mixture of aliphatic lithium and aromatic lithium was investigated. α -Furanols

Hurd applied the Kharasch and Reynolds (27) method to make α -thienol. The synthesis of α -thienol involved the oxidation of a Grignard mixtures of 2-thienylmagnesium bromide and isopropylmagnesium bromide, the yield being about 25% of the theoretical.



In investigating the oxidation of aryllithium compounds, it seemed worthwhile to extend our studies to the oxidation of α -furyllithium (III), a compound readily available by metallation of furan with <u>n</u>-butyllithium. This would be expected to yield the lithium salt of α -furanol (IV),



which on acidification could yield the furanol (V) which would be expected to tautomerize to the more stable unsaturated butenolides (VI) (VII). The last compound (VII) has been prepared by Smith and Jones (31) as follows:



No OH band was found in I.R. spectrum, which makes doubtful the existence of the enolic form (V).

The synthesis of α -furanol (V) has been claimed by Hodgson and Davies (32), by heating 5-sulfo-2-furoic acid with concentrated, aqueous sodium hydroxide in the presence of a small amount of potassium chlorate (eq. 21). The product was described as a colorless crystalline solid, m.p. 80°, which turned brown on keeping and resinified with great ease. Hodgson and Davies (33) also claim to have nitrated the compound with a nitric-sulfuric acid mixture to obtain 5-nitro-2-furanol (VIII). This was



reduced to 5-amino-2-furanol (IX) by dissolving it in alkali, then adding the salt to zinc and hydrochloric acid.

The preparations claimed by Hodgson and Davies (32) are quite doubtful in view of the usual instability of furans in the reagents employed.

Reactions of organometallic compounds with dibenzoyl peroxide

Gilman and Adams (3) observed that the reaction of benzoyl peroxide with the Grignard reagent gave benzoate esters in about 30% yield. They put forward the following equation:

$$C_{6}H_{5}-C-O-C-C_{6}H_{5}+RMgX \longrightarrow C_{6}H_{5}-C-OR+C_{6}H_{5}-C-OMgX \quad (22)$$

Samad (34) investigated the reaction of four Grignard reagents with dibenzoyl peroxide and obtained 15-44% yields

of benzoate ester and 102-160% yields of benzoic acid. He found the yield of phenyl benzoate to be depressed by the addition of magnesium bromide to the Grignard reagent. Fhenyllithium reacted with dibenzoyl peroxide to give 71% of triphenyl carbinol and 10% of phenol (isolated as tribromophenol). These compounds are probably formed from phenyl benzoate initially produced:

PhCOOPh + PhLi
$$\longrightarrow$$
 PhCOPh + PhOLi
PhLi (23)
Ph₃COLi

The yields of benzoic acid were abnormally high in all reactions. Partial hydrolysis of the unreacted benzoyl peroxide had been suggested by Gilman and Adams to account for the formation of the excess benzoic acid. Lawesson and Yang (8), in a paper published after Samad's work, reinvestigated the reaction using purified benzoyl, peroxide and phenylmagnesium bromide prepared from sublimed magnesium, and found that benzoyl peroxide was completely consumed at the end of the reaction. Thus, the abnormally high yield of benzoic acid cannot be derived from the unreacted peroxide. In addition to phenyl benzoate (35%) and benzoic (127%) based on equation (22), which were obtained in

substantially the same yields as reported previously, a new product, bromobenzene (21%) was isolated. Since the Grignard used was free of bromobenzene, bromobenzene must be a subsidiary product during the reaction. Although the reaction of ethylmagnesium bromide with benzoyl peroxide yielded no gaseous product, but ethylbenzoate (35%) and benzoic acid (145%), it is possible that ethylbromide was produced likewise, and owing to its similar volatility with respect to ether, it escaped isolation. This possibility was substantiated as the ether recovered was shown to give a positive Beilstein test for halogen. Accordingly, a mechanism is postulated to account for the formation of these products which is in fair agreement with the observed stoichiometry.

 $\operatorname{RBr} + \operatorname{Mg} \longrightarrow \operatorname{R}_{2}\operatorname{Mg} \cdot \operatorname{MgBr}_{2}$ $\operatorname{MgBr}_{2} + (\operatorname{C}_{6}\operatorname{H}_{5}\operatorname{COO})_{2} \longrightarrow (\operatorname{C}_{6}\operatorname{H}_{5}\operatorname{COO})_{2}\operatorname{Mg} + \operatorname{Br}_{2} \quad (24)$ $\frac{1}{2}\operatorname{R}_{2}\operatorname{Mg} + (\operatorname{C}_{6}\operatorname{H}_{5}\operatorname{COO})_{2} \longrightarrow \operatorname{C}_{6}\operatorname{H}_{5}\operatorname{COOR} + \frac{1}{2}(\operatorname{C}_{6}\operatorname{H}_{5}\operatorname{-}\operatorname{COO})_{2}\operatorname{Mg} \quad (25)$ $\frac{1}{2}\operatorname{R}_{2}\operatorname{Mg} + \operatorname{Br}_{2} \longrightarrow \operatorname{RBr} + \frac{1}{2}\operatorname{MgBr}_{2} \quad (26)$

Equations 24 and 26 account for Samad's observation that addition of magnesium bromide depresses the yield of phenyl benzoate. They also suggest that the substitution of phenylmagnesium chloride for phenylmagnesium bromide might

conceivably result in higher yields of phenyl benzoate, since magnesium chloride is less likely than magnesium bromide to be oxidized by dibenzoyl peroxide to magnesium benzoate and free halogen. Consequently, in this thesis are discussed a few reactions of organomagnesium chlorides and iodides with benzoyl peroxide.

Friedel - Crafts Reactions of Aromatic Compounds with Diaroyl Peroxides

A general method for introducing the benzoyloxy group directly into an aromatic nuclei was suggested by the reported reaction of benzene with dibenzoyl peroxide in the presence of aluminium chloride. Reynhart (35) claimed that in the presence of aluminium chloride benzoyl peroxide reacted with benzene at 0°C to give a 90% yield of phenyl benzoate and 92% yield of benzoic acid: A possible mechanism for this reaction would be:

 $\begin{array}{c} \text{AlCl}_{3} \\ \text{Ph} - & \text{C} - & \text{O} - & \text{O} - & \text{C} - & \text{Ph} - & \text{C} - & \text{O} - & \text{Alcl}_{3}^{e} + & \overset{\text{COPh}}{+} \\ & & (H \\ & & & (H \\ & & & \text{O} - & \text{COPh} \\ & & & & \text{O} - & \text{COPh} \\ & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{COPh} \\ & & & & & \text{O} - & \text{O} - & \text{O} \\ & & & & & \text{O} - & \text{O} - & \text{O} \\ & & & & & \text{O} - & \text{O} - & \text{O} \\ & & & & & \text{O} - & \text{O} - & \text{O} \\ & & & & & \text{O} - & \text{O} - & \text{O} \\ & & & & & \text{O} - & \text{O} \\ & & & & & \text{O} \end{array}$

A similar mechanism has been postulated by Brown and coworkers (36) in the Friedel-Crafts benzoylation of benzene. At higher temperatures the yield of ester was said to drop and the amount of diphenyl formed to increase (35, 37). However, in carrying out this reaction at $0-5^{\circ}$, Samad (38) obtained much lower yields of phenyl benzoate which did not seem to be much affected by temperature. Furthermore, the compound was obtained when solvents other than benzene were used, seemingly from the overall reaction.

$$(\operatorname{ArcO}_2)_2 \longrightarrow \operatorname{ArcO}_2 \operatorname{Ar} + \operatorname{CO}_2$$
(28)

The investigations of Leffler (39) have shown that in the presence of $\mathbf{Br} \not on$ sted acid catalysts the ionic fission of the peroxide linkage in unsymmetrical diaroyl peroxides is favoured.



Denney (40) has shown that during bond breaking of the C-O linkage the p-methoxyphenyl group migrates specifically to that oxygen which is developing the positive charge i.e. a concerted process is taking place, and the free oxygen cation (X) is never formed as an intermediate in the reactions. This was done by using a compound labelled with O^{18} in the anisyl carbonyl group as shown:



The labelled peroxide(XII) was rearranged in thionyl chloride to the labelled carbonate (XIII). Basic hydrolysis of (XIII) provided p-methoxyphenol which contained no excess oxygen -18. The only conclusion that can be drawn out of this result is that the excess oxygen -18 never entered into the p-methoxyphenols. Since both oxygens of the cation (X) are equivalent, if it had existed one would expect 50% of the excess oxygen -18 to be in the pmethoxyphenol. An explanation which is consistent with these findings is that a concerted shift of the p-methoxyphenol occurred as the 0-0 bond broke (XIV XV).



It seems probable that in the presence of the much more powerful Lewis acid, aluminium chloride, promotes the ionic fission of the peroxide linkage of even symmetrical aroyl peroxides. The electron deficiency of the developing oxygen cation may then be relieved either by synchronous migration of an aryl group (40) (route a) to give the aryloxyformyl cation (XVIII), or by synchronous electron donation from an external aromatic nucleus (XVII) (route b), after the fashion of many Friedel-Crafts acylations (36). The latter route was found by Samad (38) to be possible only with highly reactive aromatic nuclei such as 1, 3-dimethoxybenzene.



Recently, Denney and Weiss (40) have reported an oxygen -18 tracer study of the formation of phenyl benzoate from benzoyl peroxide, benzene and aluminum chloride. The benzoyl peroxide was labelled with oxygen -18 in the carbonyl positions. The analytical data showed that practically none of the oxygen -18 was found in the ether oxygen and almost all in the carbonyl oxygen of the phenyl benzoate. These results coincide with the mechanism, given in Samad's thesis (38), as shown:



The heterolysis of the peroxide linkage leading to phenyl benzoate (route a) probably receives anchimeric assistance from the migrating phenyl group. In case of p, p'-dinitrobenzoyl peroxide, the p-nitrophenyl group has less migratory aptitude because of the electron withdrawing properties of the nitro group, so that in this case route (b) might compete successfully with route (a).

This expectation was realized when sufficiently reactive aromatic compounds were used as solvent in the reaction, direct substitution of the <u>p</u>-nitrobenzoyloxy groups into the solvent molecule taking place. These results were reported by Samad (38). It was obvious from the 54-77% yields of p-nitrobenzoic acid that competing reactions were taking place, since the maximum yield of this acid can be only 50% if the reaction path is defined by equation(37):

$$\operatorname{Ar-H} + (\operatorname{Ar} - \operatorname{CO}_2)_2 \longrightarrow \operatorname{Ar} - \operatorname{CO}_2 \operatorname{Ar} + \operatorname{Ar} \operatorname{CO}_2^{H}$$
(37)

Oxidation of solvent molecules to biaryls could give pnitrobenzoic acid in a maximum yield of 100%; however, in no case were biaryls isolated.

The aluminum-chloride-catalyzed decomposition of the unsymmetrical p-nitrobenzoyl peroxide was interesting. The reaction product should be determined by the rates of two competing reactions (a) and (b).

Reaction (a) should be favored by the greater basicity of the benzoyl carbonyl group, and hence by a greater concentration of the complex (XXIX) than of (XXX); on the other hand, the heterolysis of the latter should take place more readily because the anchimeric assistance of a phenyl group is superior to that of a p-nitrophenyl group. Inthe event, the latter effect is predominant, as evidenced by the isolation in 81% yield of phenyl p-nitrobenzoate (XXXII), but of no p-nitrophenyl benzoate (XXXI), when the reaction was carried out in methylene chloride. The aluminum-chloride-catalyzed decomposition thus follows the rearrangement pattern found by Leffler (39, 41) for the uncatalyzed decomposition of unsymmetrical peroxides. A small yield (12%) of p-nitrobenzoic acid probably came from the anhydride, produced by the reaction (39):

$$2Phc0.0.c0.0Ph \longrightarrow (Phc0)_2 0 + c0(0Ph)_2 + c0_2$$
(39)

In benzene and in nitrobenzene the catalyzed decomposition of this peroxide followed a less clear-cut path. The yield of p-nitrobenzoic acid was considerably larger, and of neutral material considerable smaller.
While the work of Samad (2) and later of Denney (40) (done after the work described in this thesis) has cleared up the main features of the reactions of diaroyl peroxides catalysed by aluminium chloride, various details remained to be settled. In particular, it was of interest to check the postulated evolution of carbon dioxide, as required in equation 28 and to see if the proportions of phenyl benzoate and diphenyl varied with the temperature of the reaction in the manner claimed by Reynhart (35).

Mixed Aroyl Sulphonyl Peroxides

Graf (42a)described the preparation of acetyl cyclohexanesulfonyl peroxide (XXXIII) by the autoxidation of a mixture of acetic anhydride, cyclohexane and sulphur dioxide. This preparation is rather laborious, and perhaps for this reason the reactions of this peroxide have been little investigated: it should be expected to have a large tendency to react by heterolysis of the peroxide linkage:

$$0 = 0 - 0 - 30_2 - 0_6H_{11}$$

XXXIII

Kirmse and Horner (42b) attempted to prepare benzoyl benzenesulphonyl peroxide, PhCO.O.O.SO₂Ph, from sodium perbenzoate with benzene sulphonyl chloride, and obtained benzoyl (99.2%) with evolution of oxygen. Consequently, it seemed of interest to investigate a simpler synthesis of such compounds. Samad studied the reaction of sodium perbenzoate with <u>p</u>-toluene sulphonyl chloride, and obtained benzoyl peroxide (76%), benzoic acid (19%) and phenol (1%, isolated as tribromophenol). In this thesis we describe a similar reaction using methane sulphonyl chloride.

EXPERIMENTAL

MATERIALS

Dimethyl peroxide, prepared according to the directions of Rieche (10), was not isolated as a pure liquid but was passed in a stream of nitrogen through a long column of Drierite and then into dry, peroxidefree ether cooled to -70° (yield, about 70%). This ether solution was reasonably safe to handle and could be stored in the refrigerator without apparent deterioration; however, once it exploded during the preparation. It was analyzed for peroxide by a modification of Rieche and Brumshagen's method (10). Ten milliliters of the solution were mixed with standard aqueous stannous chloride solution (5 ml.) in a tightly stoppered flask, and the mixture was stirred magnetically for 2 hours. The ether layer was then separated, washed quickly with two 10-ml. portions of water, and the washings were added to the stannous chloride solution. Excess standard iodine was added to this solution, which was then back-titrated with standard sodium thiosulphate solution.

Methyl <u>t</u>-butyl peroxide (b.p. 23°/119mm., d²⁰0.811, nD²⁴ 1.3770 (reported 1.3761) was prepared by the procedure

of Rust <u>et al.</u> (43). The compound is rather hazardous to handle since it may explode on impact and is highly in-flammable.

Diethyl peroxide (b. p. $22^{\circ}/90 \text{ mm., n}_D^{22}$ 1.3682 (reported 1.3698) was prepared by the method of Baeyer and Villiger (44) as modified by Harris and Egerton (46). (The organic layer, before vacuum distillation was dried with potassium carbonate).

Commercial grade di-<u>t</u>-butyl-peroxide, 4-bromobiphenyl, β -naphthyl methyl ether, and <u>t</u>-butyl hydroperoxide were used. The last was 84% pure by an iodometric method (46).

Commercial benzoyl peroxide was crystallized by addition of methanol to a concentrated solution of the peroxide in chloroform, and dried by several days standing at room temperature in an evacuated desiccator.

Infrared Absorption Spectra Determinations

A Perkin-Elmer Model 21 double beam recording infrared spectrophotometer and a Perkin-Elmer Infracord were used for the determination of infrared spectra. The spectra of liquid compounds were studied by preparing their contact films of liquids between two sodium chloride plates. The spectra of solid and some liquid compounds were determined in "spectral grade" carbon tetrachloride or chloroform (2% solution) or by using the potassium bromide technique (47, 48). In reporting the band intensities at the various frequencies, the following symbols are used: strong (s), medium (m), weak (w), shoulder (sh), and broad (bd).

A Nester and Faust (49) spinning-band column was used for the separation of liquid compounds.

Reaction of Dialkyl Peroxides with Organometallic

Compounds

The Grignard reagent and phenyllithium were prepared in the usual way in a three-necked flask equipped with an efficient reflux condenser, a nitrogen inlet tube, and a dropping funnel. The reaction mixture was stirred. The Grignard reagent and phenyllithium were filtered, and their respective concentrations were determined by the addition of a 2ml. aliquot to an excess of standard hydrochloric acid and back titration with standard sodium hydroxide. Aliquots of the organometallic compounds were used for the various reactions.

The organometallic compound was cooled to $15^{\circ}-20^{\circ}C$ and the dialkyl peroxide, diluted with an equal volume of anhydrous ether, was slowly added through the dropping funnel under a stream of nitrogen. The reaction mixture was kept overnight at room temperature.

In each case, the reaction mixture was acidified with dilute hydrochloric acid. The ether layer was separated, and the aqueous layer was extracted several times with The combined ether extracts were extracted with 3N ether. sodium hydroxide solution to remove the phenol which had formed during the preparation of the organometallic compound. The organic solution was then washed with water, dried, and the ether was removed by distillation. After removal of the organic solvent the mixture was fractionally distilled by using a Nester and Faust spinning-band column. The identification of the products of the reactions of the di-alkyl peroxides with the organometallic compounds is described below. The yields of products were based on the quantity of peroxide used, an excess of organometallic compound being used.

(a) Reactions of Dimethyl Peroxide with Phenylithium

The reagent prepared from 0.02 mole of bromobenzene and 0.04g. atoms of lithium reacted with 0.01 mole of dimethyl peroxide in ether solution (at 15° C). The remaining liquid after removal of the ether was distilled using the spinning-band column. The fraction boiling at $48^{\circ}-51^{\circ}/26$ mm. was collected and weighed 0.87g. On the basis of its refractive index (n_D^{22} 1.5152), and its infrared

spectrum ($\sqrt[4]{max}^{CCl\mu}$: 3040 (s), 2960 (s), 2840 (s), 2000-1680 (w, bd), 1600 (s), 1500-1450 (s, bd), 1300 (s), 1240 (s), 1175 (s), 1075 (m), 1040 (s), 880 (m), 690 (m) cm.⁻¹), the compound was identified as anisole (b.p. 154°, or 70°/40mm., n_D^{24} 1.5152 and infrared spectrum identical with above). The yield was 80%. The second fraction was collected at 152°/40mm. and solidified in the receiver to give white crystals melting at 68°-69°C, undepressed when mixed with an authentic sample of biphenyl. Yield 7.6%. This biphenyl was formed during the preparation of phenyllithium. When an aliquot of the same phenyllithium was hydrolyzed, an equivalent amount of biphenyl was found.

(b) <u>Reaction of Dimethyl Peroxide with Phenyl-</u> <u>magnesium Bromide</u>

The dimethyl peroxide (0.022 mole) in ether solution was added dropwise over a two hours interval to a stirred solution of phenyl magnesium bromide (0.03 mole in 15ml. of ether) which was maintained at $15^{\circ}-20^{\circ}$ C. Stirring was continued at the same temperature for two hours, then mixture was allowed to stand overnight at room temperature. The separation and identification of the products were the same as in (a). Yield of anisole: 1.83g. (77%). The yield of biphenyl (13%) was the same as that formed during the preparation of the Grignard reagent.

(c) <u>Reaction of Methyl t-Butyl Peroxide with</u> <u>Phenyllithium at 15-20⁰</u>

The methyl t-butyl peroxide (0.18 mole) in 25ml. of ether was added dropwise over a one hour interval to a stirred solution of phenyllithium (0.2 mole in 150ml. of ether) which was maintained at 15°-20°C. Stirring was continued at the same temperature for two hours, then the mixture was allowed to stand overnight at room temperature. The ether was removed from the organic layer and the remaining liquid was fractionally distilled using the spinningband column. The fraction boiling at 79°C was collected and weighed 6.1g. The compound gave an infrared spectrum identical with that of authentic <u>t</u>-butanol; $\gamma' \max_{\max}^{CCl} 4$; 3590 (m), 3300 (m), 2950 (s), 1470 (s), 1370 (s), 1330 (m), 1200 (s), 1140 (s), 910 (s) cm⁻¹. The yield was 46%. The second fraction was collected at 155°C and weighed 12.4g. (63.3%). On the basis of the refractive index $(n_{D}^{20}1.5153)$ and the infrared spectrum the compound was identified as anisole. The third fraction boiling at 1520/40mm. was collected, and was identified as biphenyl. The 6% yield of biphenyl was found to be the same as that formed during the preparation of the lithium reagent.

(d) <u>Reaction of Methyl t-Butyl Peroxide with</u> <u>Phenylmagnesium Bromide at 15-20^o</u>

The methyl <u>t</u>-butyl peroxide (0.15 mole) in 20ml. of ether was added dropwise over a one hour interval to a stirred solution of phenyl-magnesium bromide (0.18 mole in 95ml. of ether) which was maintained at 15-20°C. Stirring was continued at the same temperature for two hours, then the mixture was allowed to stand overnight at room temperature. The separation and identification of the products were the same as in (c). Yield of <u>t</u>-butanol: 4.3g (52%). (The <u>t</u>-butanol was contaminated by a small amount of unreacted methyl <u>t</u>-butyl peroxide. This was indicated by infrared spectrum; $\gamma \frac{\text{CCl}}{\text{max}}$ at: 875 (s), is the C-O absorption band of the peroxide (50). Yield of anisole: 3.3g (20.4%). The 13% yield of biphenyl was the same as that formed during the preparation of the Grignard reagent.

(e) <u>Reaction of Methyl t-Butyl Peroxide with</u> <u>Phenyllithium at 35^oC</u>

The methyl <u>t</u>-butyl peroxide (0.09) mole in 12ml. of ether was added dropwise over a one hour interval to a stirred solution of phenyllithium (0.10 mole in 86ml. of ether) which was maintained at $30^{\circ}-35^{\circ}$ C. The mixture was refluxed at 35° C for 16 hours. The separation and

identification of the products were the same as in (c). Yield of anisole 7.0g. (72.0%). The yield of biphenyl was 7.6% (1.169g).

(f) <u>Reaction of Nethyl t-Butyl Feroxide with Thenyl Magnesium</u> Bromide at 35°C.

The methyl <u>t</u>-butyl peroxide (0.12 mole) in 15 ml. of ether was added dropwise over a one hour interval to a stirred solution of phenyl magnesium bromide (0.14 mole in 80 ml. of ether) which was rainteined at $30^{\circ}-35^{\circ}$ C. The minture was refluxed at 35° C for 16 hours. The separation and identification of the products were the same as in (c). Yield of anisole was 5.01 g (38.0,3). The yeild of biphenyl was 2.94 g. (15.0,3). (g) Reaction of Diethyl Feroxide with lhenyllithium

Disthyl peroxide (0.1 mole) in 12 ml. of ether and 0.13 mole of phenyllithium in 110 ml. of ether were left overnight at room temperature. The reaction mixture was worked up in the usual way. The fraction boiling at $101^{\circ}/95$ mL, was collected and weighed 5.17g. On the basis of its refractive index $(n_D^{25}1.5089)$ and its infrared spectrum (γ) CCl4 at: 3020 (s), 2960 (s), 2000-1600 (w), bands, 1600 (s), 1490 (s), 1465 (s), 1430 (s), 1390 (s), 1340 (m), 1300 (s), 1220 (s), 1170 (s), 1160 (m), 1110 (s), 1075 (m), 1060 (s), 1040 (s), 925 (m), 898 (w), 875 (m), 689 (s) cm.⁻¹, the compound was identified as phenetole (b.p. 172°C, or 108°/100mm., $n_D^{21}1.5076$, and infrared spectrum identical with above). The yield was 38%. A second fraction collected at $152^{\circ}/40$ mm. had a m.p. 69°, and mixed m.p. with authentic biphenyl 70°-71°C. The 6.1% yield of biphenyl was the same as that formed during the preparation of the phenyllithium reagent.

(h) <u>Reaction of Dicthyl Peroxide with Phenyl Magnesium Bronide</u>

To 0.1C mole of phenyl-magnesium bromide in 50 ml. of ether, 0.07 mole of diethyl peroxide in 8 ml. of ether was added at $15^{\circ}-20^{\circ}$, and left overnight at room temperature. The separation and identification of the products were as in (g). Yield of phenetole: 2.56g. (30%). The 8.0% yield of biphenyl was the same as that formed during the preparation of the Grignard reagent.

(i) <u>Reaction of Di-t-butyl Peroxide with Phenyllithium</u> at 15-20⁰

At $15^{\circ}-20^{\circ}$ C, 0.11 mole of di-<u>t</u>-butyl peroxide in 10 ml. of ether was added to 0.12 mole of phenyllithium in 95 ml. of ether. The mixture was left overnight at room temperature. After removal of the ether, the liquid remaining was distilled using a Nester and Faust spinning-band column. The fraction boiling at $79^{\circ}-80^{\circ}$ was collected and weighed l.lg. The compound gave an infrared spectrum identical with that of a mixture of benzene and <u>t</u>-butanol; $\gamma' \frac{CCl}{MEX}$ 4 at: 3590 (m), 3300 (m), 2950 (s), 1470 (s), 1370 (s), 1330 (m), 1200 (s), 114C (s), 910 (s) cm⁻¹. The yield was 15%. (The <u>t</u>butanol was mixed with a small quantity of benzene which originated from the phenyllithium reagent). The second fraction was collected at $104^{\circ}-105^{\circ}$ and weighed 7.20 gm.

Its infrared spectrum was identical with that of authentic di-t-butyl peroxide. The third fraction was collected at 104°-106°C and weighed 2.50 g. The infrared spectrum was similar to that of authentic di-t-butyl peroxide, except that it had a strong absorption at 1725 cm^{-1} . (i.e. the characteristic frequency of the carbonyl absorption.) The 2, 4-dinitro-phenylhydrazone of this ketone was prepared, and had a m.p. 125°-126°C. The mixed m.p. with the 2. 4-dinitrophenylhydrazone of acetone was 125°-126°. The infrared spectra of both the 2. 4-dinitrophenylhydrazone of the ketone obtained and that of acetone were identical, and so the ketone was acetone. Hence the third fraction appeared to be a mixture. Separation by gas chromatography resulted in three fractions. On the basis of their infrared spectra in the gas phase, the three fractions were identified as acetone, di-t-butyl peroxide and toluene. (The ratio in this mixture was : 2:2:1). The yield of acetone was 15%, toluene 5%, and di-t-butyl peroxide 44%. (Total yield obtained in second and third fractions). The fourth fraction was collected at 80°-81°/22mm. and weighed 3.16g. On the basis of its refractive index $(n_D^{24}1.4880)$ and its infrared spectrum (γ $\frac{\text{CCl}}{\text{max}}$ 4 at 3040 (m), 2960 (s), 2000-1680 (w), bands, 1590 (s), 1490 (s), 1380 (s), 1360 (s),

1240 (s), 1160-1180 (s), 1069 (m), 1025 (m), 925 (s), 915 (s), 890 (s), 690 (s) cm⁻¹), the compound was identified as phenyl-<u>t</u>-butyl ether. (b.p. 70-71[°]/11mm., n_D^{20} 1.4880 (8). The yield was 19%. Biphenyl (9%) was obtained in the same amount as in the formation of phenyllithium reagent.

Since the acetone existed in the mixture which was collected at $104^{\circ}-105^{\circ}$, it was considered that the acetone might arise from thermal decomposition of di-<u>t</u>-butyl peroxide. Hence the experiment was repeated and the peroxide distilled under low pressure. The fraction was collected at $50^{\circ}-54^{\circ}/145$ mm. (n_D^{24} 1.3889) and weighed 7.30g. Its infrared spectrum was identical with that of authentic di-<u>t</u>-butyl peroxide. No carbonyl absorption appeared in the spectrum. The yield was 45%. Another fraction was collected at $80^{\circ}-81^{\circ}/22$ mm. and weighed 3.02g. On the basis of its refractive index (n_D^{24} 1.4879) and its infrared spectrum, the compound was identified as phenyl-<u>t</u>-butyl ether. The yield was 18.3%. The 5% yield of biphenyl was the same as that formed during the preparation of the phenyllithium reagent.

(j) <u>Reaction of Di-t-Butyl Peroxide with Phenyllithium</u> <u>at 35°C</u>

Di-t-butyl peroxide (0.12 mole) in 10ml. of ether was

added with stirring to an ethereal solution of phenyllithium (0.12 mole in 95 ml. of ether). The mixture was refluxed at 35° for 16 hours. After the usual working up, no di-<u>t</u>-butyl peroxide was recovered. The fraction boiling at 108° - $110^{\circ}/25$ nm. was collected and weighed 6.86g. The compound was identified by its refractive index $(n_D^{24}).4877$, and infrared spectrum as phenyl-<u>t</u>-butyl ether. The yield was 39.0%. The 9.9% yield of biphenyl was the same as that obtained during the preparation of the phenyllithium reagent.

(k) <u>Reaction of Di-t-butyl Peroxide with Phenyllithium</u> at 0⁰-5^oC

Di-<u>t</u>-butyl peroxide (0.11 mole) in 10ml. of ether was added with stirring to an ethereal solution of phenyllithium (0.12 mole in 95 ml. of ether) which was maintained at $0^{\circ}-5^{\circ}$ C. Stirring was continued at the same temperature for two hours, then the mixture was allowed to stand overnight 0°C. After usual working up, the liquid was distilled using a Nester and Faust spinning-band column. A fraction was collected at 50°-54°/145nm. (n²⁴_D1.3881) and weighed 14.4g. Its infrared spectrum was identified with that of authentic di-<u>t</u>-butyl peroxide. The yield was 89%. The next fraction was collected at 80°-82°C/22nm. and weighed 0.55g. On the

basis of its refractive index $(n_D^{24}1.4880)$ and its infrared spectrum, the compound was identified as phenyl-<u>t</u>-butyl ether. The yield was 3.3%. The 5% yield of biphenyl was the same as that formed during the preparation of the phenyllithium reagent.

(1) <u>Reaction of Di-t-butyl Peroxide with</u> <u>Phenyllithium at 80^oC</u>

Di-<u>t</u>-butyl peroxide (0.11 mole) in 10ml. of ether was added with stirring to an ethereal solution of phenyllithium (0.12 mole in 95 ml. of ether). The mixture was refluxed at 80° for 16 hours. After the usual working up, no di-<u>t</u>-butyl peroxide was recovered. The fraction boiling at 80° - $82^{\circ}/22$ mm. was collected and weighed 6.26g. The compound was identified by its refractive index ($n_{\rm D}^{24}$.4879) and infrared spectrum as phenyl <u>t</u>-butyl ether. The yield was 38.0%. The yield of biphenyl was 3.41g. (16%). <u>Reaction of Oxygen or t-butyl hydroperoxide with Organometallic Compounds</u>

Organometallic compounds were prepared in the usual way. Dry oxygen or <u>t</u>-butyl hydroperoxide was added into an agitated ether solution of organometallic compound. The oxidized organometallic compound was decomposed with aqueous sulfuric acid. The ether layer was separated and It was extracted with dilute sodium hydroxide. The phenol in the aqueous layer was worked up in the usual way. The identification of the products of the reaction with various organometallic compounds is described below.

(a) Reaction of oxygen with phenyllithium

Dry oxygen was bubbled into agitated phenyllithium (0.08 mole) in 70 ml. ether. The evolution of heat usually ceased after one and one-half to two hours. The oxidized phenyllithium was allowed to stand overnight. Then it was decomposed with aqueous sulfuric acid and worked up in the usual way. The aqueous layer which contained phenol was analysed according to Scott's Standard Methods of Chemical Analysis (51). The yield of phenol was 30.0% (lit. (30) 25%, 23.1% and 22.0%).

Additional experiments were carried out in which the amount of oxygen used was measured, in order to avoid possible over oxidation.

(I) 0.004 mole of dry oxygen was bubbled into an agitated solution of 0.004 mole phenyllithium in 15 ml. ether. The yield of phenol was 25%.

(II) 0.008 mole of dry oxygen was bubbled into an agitated solution of 0.004 mole phenyllithium in 15 ml. ether. The yield of phenol was 25%.

(III) 0.012 mole of dry oxygen was bubbled into an agitated solution of 0.004 mole phenyllithium in 15 ml. ether. The yield of phenol was 25%.

(IV) Dry oxygen was bubbled into an agitated solution of 0.04 mole phenyllithium in 15 ml. ether for four hours. The yield of phenol was 30%.

Since the yield of phenol was only 25% to 30% an attempt was made to isolate the other products of the reaction. The ether solution left after alkali extraction was washed, dried with magnesium sulfate and distilled using spinning-band column. The fraction boiling at $87^{\circ}/23$ mm. was collected and weighed 0.44g. (8.8%). The compound gave an infrared spectrum identical with that of authentic methyl phenyl carbinol. The methyl phenyl carbinol was formed during the preparation of the phenyllithium reagent. Mhen an aliquot of the same phenyllithium was hydrolyzed, an equivalent amount of methyl phenyl carbinol was formed. The other fraction $150^{\circ}-152^{\circ}/40$ mm. was collected and was identified as biphenyl. The yield was 5.5%. The residue from distillation contained a considerable amount of tars.

(b) Reaction of oxygen with mixture of Phenyllithium

and n-butyllithium

Dry oxygen was bubbled into an agitated mixture of

phenyllithium (0.08 mole) in 70 ml. ether and <u>n</u>-butyllithium (0.08 mole) in 75 ml. ether. The evolution of heat usually ceased after one and one-half to two hours. While the reaction proceeded, additional <u>n</u>-butyllithium (0.08 mole) in 75 ml. ether was added. The introduction of oxygen was discontinued after another hour. The oxidized mixture was allowed to stand overnight. The separation and identification of the phenol were the same as in (a). The yield of phenol was 30.0%.

(c) <u>Reaction of oxygen with 4-biphenylyllithium</u>

Dry oxygen was bubbled into an agitated solution of 4-biphenylylithium (0.014) mole in 50 ml. ether. The introduction of oxygen was discontinued after an additional hour. The oxidized mixture was allowed to stand overnight. Then it was decomposed with aqueous sulfuric acid and worked up in the usual way. To the aqueous layer which contained <u>p</u>-phenylphenol was added concentrated hydrochloric acid and this was extracted with ether. The ether layer was washed, dried and concentrated under reduced pressure. The residue which crystallized from dilute ethanol had m.p. 162° - 163° , identified as <u>p</u>-phenylphenol by mixed m.p. The yield of <u>p</u>-phenyl phenol was 0.469g. (19.0%) (Lit. (52) 3%).

(d) <u>Reaction of oxygen with mixture of 4-biphenylyl-</u> lithium and n-butyllithium

4-biphenylyllithium (52) was prepared from 4-bromobiphenyl (ll.6g., 0.05 mole) and lithium wire (0.85g., 0.12g. atom). Dry oxygen was bubbled into an agitated mixture of 4-biphenylylithium (0.038 mole) in 100 ml. ether and <u>n</u>-butyllithium (0.038 mole) in 40 ml. ether. While the reaction proceeded, an additional 0.038 mole of <u>n</u>butyllithium was added. The introduction of oxygen was discontinued after another hour. The oxidized mixture was allowed to stand overnight. The separation and identification of the <u>p</u>-phenyl phenol were the same as in (c). Yield 2.34g. (17.8%).

(e) <u>Reaction of a mixture of t-butyl hydroperoxide</u> and ethyl magnesium bromide with phenyllithium

The <u>t</u>-butyl hydroperoxide (0.084 mole) in 50 ml. of anhydrous ether was added during a one hour period to an etheral solution of ethyl-magnesium bromide (19) (0.10 mole in 70 ml. ether solution) which was stirred vigorously and cooled (-70° C) by means of a cooling mixture (acetone and dry ice). A solution of phenyllithium (0.10 mole in 60 ml. ether solution) was then added during the next 30 minutes into the cold suspension (-60° C) of magnesium <u>t</u>-butyl hydroperoxide. The mixture was stirred at -60° for an additional 30 minutes. It was allowed to warm to 0° and was maintained at this temperature for two hours. Vigorous stirring was required throughout the reaction in order to avoid caking. The reaction mixture was poured into ice-water, acidified, and the ether layer extracted with 2 N aqueous sodium hydroxide. The yield of phenol, determined according to Scott's Standard Methods of Chemical Analysis (51), was 9.1%.

(f) <u>Reaction of t-butyl hydroperoxide with phenyl-</u> lithium

<u>t</u>-Butyl hydroperoxide (0.042 mole) in 50 ml. of anhydrous ether was added slowly to a solution of phenyllithium (0.11 mole in 80 ml. ether solution) maintained at $0-5^{\circ}$ C. Stirring was continued at this temperature for 2-3 hours. The separation and identification of the phenol were the same as in (e). The yield of phenol was 92.8% (lit. (15) 75%).

(g) <u>Reaction of oxygen with 2-methoxy-l-naphthyl-</u> lithium

Lithium wire (0.28 g., 0.04 g. atom) in 15 ml. anhydrous ether was placed in a 100 ml. 3-necked flask. A solution of 1-bromo-2-methoxynaphthalene (4.7 g., 0.02 mole), which

was prepared according to the direction of Knapp (53), dissolved in 25 ml. anhydrous ether was introduced in a dropping funnel. Stirring was begun and about 4 ml. of the latter solution was added to the start the reaction. The remainder was added at such a rate that the solvent refluxed gently (solution turned grey color). Heat was applied at the beginning of the reaction and also near the end. The concentration was determined in the usual way. Yield of 2-methoxy-1-naphthyllithium was 80%.

Dry oxygen was bubbled into an agitated solution of 2-methoxy-l-naphthyllithium (0.014 mole) in 50 ml. ether. The introduction of oxygen was discontinued after three hours. The oxidized mixture was allowed to stand overnight. Then it was decomposed with dilute sulphuric acid. The ether layer was extracted with 3 N aqueous sodium hydroxide. The alkaline layer containing phenol was neutralized with 6 N hydrochloric acid and extracted with ether, dried and evaporated to give 0.585 gm. of a brown oily residue. The residue was chromatographed on alumina (Woelm, activity between II and III) in hexane. Elution with 4:1 hexane-benzene gave a semi-solid material which crystallized from hexane as colourless needless m.p.

53.5°-54.5°C of 2-methoxy-lnaphthol (0.174g), 14.2%. Infrared spectrum: γ $\stackrel{\text{CCl}}{\max}$ in cm⁻¹: 3530 (m), 3040 (m), 2940 (m), 2820 (m), 1650 (m), 1600 (m), 1490 (s), 1410 (m), 1380 (m), 1360 (s), 1280 (s), 1200 (m), 1180 (w), 1100 (s), 1060 (s), 905 (s). Calc. for C₁₁H₁₀O₂: C, 75.86%; H, 5.75%. Found: C, 75.70%, H, 5.78%.

(h) Reaction of t-butyl hydroperoxide with 2-

methoxy-l-naphthyllithium

<u>t</u>-butyl hydroperoxide (0.042 mole) in 50 ml. of anhydrous ether was added slowly with stirring into a solution of 2-methoxy-l-naphthyllithium (0.10 mole) in 200 ml. ether maintained at $0-5^{\circ}$ C. Stirring was continued at this temperature for 2-3 hours then at room temperature for 10 to 16 hours. Then the reaction mixture was poured into ice-water and acidified with 3 N hydrochloric acid. The separation of products was the same as in (g). The ether layer was evaporated to give 5.88 g. of brown oily residue.

The oily residue crystallized from hexane as a white solid (1.2 g., 7.2%), m.p. 285-290°C. This was recrystallized from acetone as colorless rods, m.p. 288-290°C. This substance was presumably slightly impure 4, 4'-dihydroxy-3, 3'-dimethoxy-1, l'-binaphthyl. Calc. for $C_{22}H_{18}O_4$: C, 76.30%; H, 5.20%. Found C, 75.39%; H, 5.02%. The compound was benzoylated in usual way to give a white solid, which was recrystallized from benzene as colorless rods, m.p. 346^O-348^OC. Calc. for $C_{36}H_{26}O_6$: C, 77.97%; H, 4.67%. Found : C, 77.98%; H, 4.88%.

The mother liquors from the isolation of 4,4'-dihydroxy-3,3'-dimethoxy-1,1'-binaphthyl were chromatographed on alumina (Woelm, activity between II and III) in hexane. Elution with 4:1 hexane-benzene gave a semi-solid material which crystallized from hexane as colorless needles of 2methoxy-1-naphthol, m.p. 53.5°-54.5°C. The infrared spectrum was the same as in (g). Yield 2.068 (23.1%).

2-Methoxy-l-Naphthyl Benzoate

2-methoxy-l-naphthol (0.20g.) was benzoylated with benzoyl chloride (0.5 ml.) in anhydrous pyridine (3 ml.) overnight. The reaction mixture was poured into 10 ml. of water. After a few hours a reddish oil deposited, and the supernatant liquid was decanted. The oil was dissolved in benzene and washed with 5% aqueous sodium carbonate solution, with 10% aqueous sodium hydroxide several times, and with water, and dried over magnesium sulfate. Evaporation to dryness left a brown oil which was chromatographed on alumina (Woelm, activity between II and III) in hexane. Elution with 4:1 hexane-benzene gave 2-methoxy-l-naphthyl benzoate, which crystallized from hexane as colourless rods, m.p. 104-105°C (lit. 110° (54)). γ ^{CCl}_{max} cm⁻¹: 3050 (w), 3020 (w), 2985 (w), 2860 (w), 1750 (v.s.), 1645 (m), 1609 (m), 1515 (w), 1485 (m), 1459 (m), 1385 (m), 1353 (w), 1318 (w), 1280 (v.s.), 1247 (v.s.), 1190 (m), 1175 (s), 1155 (m), 1150 (m), 1100 (v.s.), 1080 (s), 1067 (s), 1023 (s), 923 (w), 695 (m); Calc. for C₁₈H₁₄O₃: C, 77.69%; H, 5.03%. Found: C, 77.48%; H, 4.93%. Yield: 0.15g. (48%).

Attempt to Prepare \mathcal{X} -Hydroxyfurans

(a) Reaction of Oxygen with 2-Furyllithium

<u>n</u>-Butyllithium (55), prepared from 0.3 mole of <u>n</u>butyl bromide in ether (240 ml) was added with slight cooling to 0.3 mole of furan in ether (60 ml.) (59). The mixture was stirred and refluxed for six hours. Dry oxygen was then bubbled into the agitated 2-furyllithium solution. The evolution of heat usually ceased within one and a half to two hours. The mixture was kept at $0^{\circ}-5^{\circ}C$ overnight, and then worked up in the usual way. The ether layer was dried and evaporated. The remaining brown liquid was fractionally distilled using a spinningband column. A fraction (0.147g.) boiling at $85^{\circ}-90^{\circ}$

was collected and identified as <u>n</u>-butyl alcohol by formation of <u>n</u>-butyl 3, 5-dinitrobenzoate, m.p. $61^{\circ}-62^{\circ}$ C, undepressed by admixture with an authentic specimen. The residue from the distillation contained large amounts of involatile tars.

(b) Reaction of t-Butyl hydroperoxide with 2-

Furyllithium

<u>t</u>-Butyl hydroperoxide (0.05 mole) in 50 ml. of anhydrous ether was added slowly with stirring into a solution of 2-furyllithium (0.05 mole) in l00ml. of ether maintained at $0^{\circ}-5^{\circ}$ C. Stirring was continued at this temperature for 2-3 hours, then kept at $0^{\circ}-5^{\circ}$ C for sixteen hours. The separation and identification of the product were the same as in (a). A trace of <u>n</u>-butyl alcohol and a large amount of tar was obtained.

(c) <u>Reaction of t-Butyl hydroperoxide with 2-Methyl-</u> <u>5-Furyllithium</u>

Using the same method as in the reaction of \underline{t} -butyl hydroperoxide with 2-furyllithium, a large amount of tar and a trace of \underline{n} -butyl alcohol was obtained.

<u>Reactions of Dibenzoyl Peroxide with Grignard Reagents</u> General Procedure:

The Grignard reagents were prepared according to Kharasch and Reinmuth (57) by the addition of alkyl or aryl

bromide to a suspension of magnesium in ether under nitrogen, and estimated by titration of the base formed on addition of an aliquot of the solution to water. The solution of organometallic compound was then added under nitrogen, with stirring, to a suspension of peroxide in dry ether cooled to 0-4°. After addition, the reaction mixture was stirred an additional 30-60 minutes, followed by the addition of cold water and acidification by dilute hydrochloric acid. The ether layer was separated from the aqueous layer and extracted with sodium bicarbonate solution which on acidification gave benzoic acid. The ether layer was then extracted with 3-5% caustic potash solution to remove any phenol. After removal of acid and phenol, the ether layer was washed with water and dried by anhydrous sodium sulfate. The ether was removed by distillation and the residue was purified by recrystallization, absorption chromatography or vacuum distillation.

(a) <u>n-Butylmagnesium chloride</u>

From 9.86g. (0.04 mole) of benzoyl peroxide and 0.04 mole of n-butylmagnesium bromide were obtained benzoic

acid (4.55g., 47.3%) and 1.47g. of tar. No butyl benzoate was found in the reaction.

(b) Phenylmagnesium chloride

From 19.36g. (0.08 mole) of benzoyl peroxide and 0.08 mole of phenylmagnesium chloride were obtained 8.95g. (49.4%) of benzoic acid and 2.64g. (16.6%) of phenyl benzoate, which crystallized from ligroin, m.p. and mixed m.p. 68-69°C. Also 1.78g. (14.4%) of biphenyl were obtained, which crystallized from methanol, m.p. and mixed m.p. 68°C. No chlorobenzene was found in the product.

(c) Phenylmagnesium iodide

From 16.94g. (0.07 mole) of benzoyl peroxide and 0.07 mole of phenylmagnesium iodide were obtained benzoic acid 9.56g. (56%) and phenol (1.4%) characterized as tribromophenol.

No phenyl benzoate were found in the reaction. Biphenyl (0.38g., 3.5%) was obtained and crystallized from petroleum ether, m.p. and mixed m.p. 68°.

Reactions of Benzoyl Peroxide in the Presence of Aluminum Chloride in Different Organic Solvents

General Procedure:

Benzoyl peroxide dissolved in about four times its weight of organic solvent was slowly added under nitrogen with stirring, to an equimolar quantity of aluminum chloride suspended in about the same volume of the same solvent. Nitrogen was passed slowly over the reaction mixture and then led through a known volume of standard alkali, which was subsequently titrated for carbon dioxide (58). Reaction was allowed to proceed for 7 hours or more, except for the reaction in nitro-benzene (5 hours at 50°). The reaction mixture was then treated with dilute aqueous hydrochloric acid and filtered from a solid residue. The solid residue and the organic layer in the filtrate were both extracted with aqueous sodium bicarbonate to remove benzoic acid. The neutral organic solution was then washed with water. dried, and distilled: phenyl benzoate came over at 162° at 13 mm. and solidified, m.p. and mixed m.p. 69°.

(a) <u>In benzene</u>

To 6.75g. (0.05 mole) of aluminum chloride suspended in 50 ml. of benzene was added at 45-50°, 12.1g. (0.05 mole) of dibenzoyl peroxide dissdwed in 60 ml. of benzene. After

eight hours the reaction mixture was worked up to give 1.53g. (12.5%) of benzoic acid and 2.80g. (28.4%) of phenyl benzoate, b.p. 1629/13mm, m.p. and mixed m.p. 69°C; 0.037 mole (74%) of carbon dioxide was evolved.

(b) <u>In nitrobenzene</u>

To 6.75g. (0.05 mole) of aluminum chloride in 50 ml. of nitrobenzene 12.1g. (0.05 mole) of peroxide dissolved in the same volume of solvent was added and the reaction was allowed to take place for 5 hours at 45-50°C. The reaction mixture gave 2.23g. (18%) of benzoic acid, 2.31g. (23%) of phenyl benzoate, bp. 118-120°/15mm, m.p. 69°, alone or mixed with an authentic specimen, and 0.0154 mole (30.8%) of carbon dioxide.

(c) In toluene

To 6.75g. (0.05 mole) of aluminium chloride in 50 ml. of toluene, 12.1g. (0.05 mole) of benzoyl peroxide dissolved in the same volume of solvent was added and the reaction was allowed to take place for 5 hours at 45°-50°C. The reaction mixture gave 3.34g. (25.5%) of benzoic acid, 4.10g. (41.4%) of phenyl benzoate, b.p. 150-155°/10 mm, m.p. 69°, alone or mixed with an authentic specimen, and 0.022 mole (44%) of carbon dioxide. A trace of phenol (characterized as tribromophenol) was obtained.

Reaction of Sodium Perbenzoate with Methanesulphonyl and p-Toluene Sulphonyl Chloride

Methanesulphonyl chloride (9.16g.; 0.08 mole) in benzene (50 ml.) was added slowly with stirring to an aqueous solution of sodium perbenzoate (0.08 mole in 300 ml.), prepared according to Braun (59) and cooled in an ice-bath. The mixture was stirred a further six hours without cooling and then left overnight. The benzene layer was washed with water, and then extracted with aqueous sodium bicarbonate to remove benzoic acid (4.53g.; 47%) and with aqueous potassium hydroxide to remove phenol. The latter solution was acidified and extracted with ether. The oily residue after evaporation of ether was treated with bromine water to give tribromophenol (0.87g.; 3.2%) m.p. and mixed m.p. 94°. The benzene layer was cautiously concentrated to a small volume, and deposited dibenzoyl peroxide (2.42g.; 12%), m.p. and mixed m.p. 104°.

RESULTS AND DISCUSSION

Reactions of Organometallic Compounds with Dialkyl Peroxides

The results of studies of the reactions of various dialkyl peroxides with phenyllithium and phenylmagnesium bromide are shown in Table II.

TABLE II

Yields of ethers from reactions of dialkyl peroxides with phenyllithium and phenylmagnesium bromide

Peroxide	Reaction temp. (^o C)	Yield (%) from Ph Li	Yield (%) from PhMgBr
Dimethyl	15-20	80	77
Methyl <u>t</u> -butyl	15-20	63	20
Methyl <u>t</u> -butyl	35	72	38
Diethyl	15-20	38	30 [¥]
Di- <u>t</u> -butyl	0-5	3.3	
Di- <u>t</u> -butyl	15-20	19	
Di- <u>t</u> -butyl	35	39	o†
Di <u>-t</u> -butyl	80	38	oğ

*Gilman and Adams (3) report a 34% yield †Compare ref. (7) *Compare ref. (8)

Best yields were obtained with dimethyl peroxide, which reacted equally well with both lithium and magnesium compounds. However, the much safer methyl t-butyl peroxide gave with phenyllithium (but not with phenylmagnesium bromide) almost the same yields of anisole. No phenyl tbutyl ether was obtained from these reactions. With the more highly hindered di-t-butyl peroxide the superiority of phenyllithium was more marked (Table II), but even so the reaction was still incomplete after 12-14 hours at 15-20°, 45% of the peroxide being recovered. Reaction was complete in this time at 35°, but the yield was inferior to that obtained in the reaction of phenylmagnesium bromide with t-butyl perbenzoate, described by Lawesson and Yang (8). It would seem that the latter reaction will prove, in some instances, the method of choice for preparing tbutyl ethers, while the reaction of organolithium compounds with methyl-t-butyl peroxide will prove preferable for preparing methyl ethers.

Gilman and Adams (3) isolated a 30% yield of biphenyl, along with phenetole, from the reaction of diethyl peroxide with phenylmagnesium bromide. We also obtained 5-16% yields of biaryls from the mixtures after reaction of the peroxides. However, it was shown in several cases

(and seems likely for the others) that the biaryl was formed during the preparation of the organometallic compound.

Baramki (9) suggested that the reaction of organolithium compounds with a variety of alkyl peroxides may involve a preliminary coordination of the metal atom by the unshared electrons of a peroxide oxygen, as is well known to happen with ethers (9, 10).



Such a coordination would facilitate the formation of an ion-pair (XXXIV) which could then react as shown. The yields of ethers were decreased when there was an increase in the size of R. In case of dimethyl



peroxide and methyl <u>t</u>-butyl peroxide, there is less steric hindrance with organolithium compounds than with Grignard reagents and the reactions may be formulated as (39) and (40) respectively. In the equation (40), the inductive effects of three methyl groups should cause the oxygen (O_1) to be more negative, so that, the electropositive lithium can more easily attack O_1 than O_2 . This would account for the fact that phenyl-<u>t</u>-butyl ether was not formed during the reaction. On the other hand, the direction of attack may be due to the bulk of the phenyl group which prevents it from attacking the hindered O_1 . This idea could be tested by investigating the reaction of less hindered reagents (eg. CH_3Li) with methyl <u>t</u>-butyl peroxide.

From Table II the phenyllithium gives a lower yield of the ether with diethyl peroxide than with methyl <u>t</u>-butyl peroxide or dimethyl peroxide and gives the lowest yield of the ether with di<u>t</u>-butyl peroxide. The decreased yields and rates of reaction as the alkyl group on the peroxide oxygen being attached is changed from methyl to <u>t</u>-butyl finds a parallel in the decreasing facility of SN2 attacks on the carbon atom of alkyl halides as the neighboring alkyl group becomes more highly branched (60). The lesser effect of the nature of the alkyl group on the outgoing RC is also in harmony with this mechanism. On the other hand, the reactions of Grignard reagents show much greater sensitivity to the nature of <u>both</u> alkyl groups of

the peroxide. This effect is best explained by a fourcentre mechanism of the type generally postulated for the reactions of Grignard reagents (61, 62). The recent work of Dessy (4, 5, 6) indicates the phenyl Grignard reagent



to be a complex of $\operatorname{Ph}_2\operatorname{kg}$ and kgBr_2 , with only a negligible amount of PhkgBr. A four-center reaction of this complex with the peroxide linkage would require a conformational change (XXAV \longrightarrow XXXVI)^X of the peroxide which becomes progressively more difficult as the bulk of both R_1 , and R_2

^{*}It seems likely that neither I nor II are planar molecules (63, 64, 65) but that attainment of the transition state (XXAVII) requires the movement of R_1 and R_2 towards each other.

increases. The effect of such conformational equilibria on reaction rates is now well established (66). Further, it would be expected that the more stable transition state (XXXVII) would be that one in which the R_1 was the less bulky of the two alkyl groups, because of bulk of the phenyl group. This accords with the exclusive formation of anisole (IV; $R_1 = Ne$) from methyl <u>t</u>-butyl peroxide (I; $R_1 = Ne$, $R_2 = Bu^t$) (Table II).

Reactions of Organolithium Compounds with t-butyl Hydroperoxide and with Oxygen

We found that yields of phenols from the oxidation of aryllithium compounds with molecular oxygen are not improved by the presence of butyllithium. This is shown by the results in the Table III. Better yields were obtained where the oxidation was effected with a peroxide, such as commercially available <u>t</u>-butyl hydroperoxide, but were still sometimes very low.

2-Methoxy-l-naphthol, m.p. 53.5-54.5°, a new compound obtained from the oxidation of 2-methoxy-l-naphthyllithium, differed from a methoxynaphthol (m.p. 90°) obtained by Samad (2), which was thus proved to be l-methoxy-2-naphthol. (XXXIX). The latter methoxynaphthol was obtained by methylating with diazomethane the product obtained by oxidizing both α - and
TABLE III

Yields of Phenols from action of different oxidizing agents on aryllithium compounds

Compound	02	02+BuLi	ButOCH
	Yield (%)	Yield (%)	Yield [¥] (%)
Fhenyllithium	30 [†]	30	92.8 [‡]
p-Biphenylyllithium	184	19	
2-Methoxy-l-Naphthyllithiu	m 7.0		23.0
α -Furyllithium	0		0
5-Methyl-2-feryllithium			0

 β -naphthol with <u>p,p</u>,- dinitrobenzoyl peroxide, followed by hydrolytic removal of the p-nitrobenzoyl group. The oxidation product could have either the formula XL or XLL,

*Based on peroxide

[†]Gilman and Pacevitz (30) reported 22-25% yield [†]Maller and Topel (29), using 1,2,3,4-tetrahydro-1-naphthyl hydroperoxide, reported a 96% yield [§]Maller and Topel (29) reported a 3% yield but the present work shows the former structure to be correct, the initial product XLII from β -naphthol evidently rearranging by an acyl migration.



The oxidation of *X*-furyllithium and of 5-methyl-2furyllithium gave only intractable, high-boiling tars. Reactions of Grignard Reagents with Benzoyl Peroxide

Contrary to our expectations (p. 16), the reaction of phenylmagnesium chloride with benzoyl peroxide gave a <u>lower</u> yield of phenyl benzoate than did the reaction of phenylmagnesium bromide, while from the reaction of <u>n</u>-butylmagnesium chloride no <u>n</u>-butyl benzoate could be isolated. No phenyl benzoate was obtained from the reaction of benzoyl peroxide with phenylmagnesium iodide, but the small amount of phenol obtained may have come from the reaction of phenyl benzoate with the Grignard reagent:

$$PhCOOPh + PhMgI \longrightarrow PhCOPh + PhOMgI$$
(43)

No attempt was made at a complete analysis of the products of these reactions : enough was done to show that the poor yields of phenyl benzoate obtained using phenylmagnesium bromide were not improved by the use of the chloride or iodide.

Aluminium Chloride - catalysed Decomposition of Benzoyl Peroxide

The work described in the experimental section shows that 31-74% of the carbon dioxide expected from equation 28 (p. 20) is evolved during the aluminium chloride-catalysed decomposition of benzoyl peroxide to phenyl benzoate. The work also indicates that, contrary to Reynhart (35), the course of the reaction is not much affected by temperature. The trace of phenol obtained from the reaction in toluene may conceivably come from the hydrolysis during work-up of diphenyl carbonate produced by the reaction (equation 39, p. 26). Reaction of Sodium Perbenzoate with Sulphonyl Chlorides

The attempt by Samad (2) to obtain benzoyl <u>p</u>-toluenesulphonyl peroxide (XLIV; R=p - Me.C₆H₄) from the reaction of sodium perbenzoate with <u>p</u>-toluenesulphonyl chloride, and the attempt described in this thesis to obtain benzoyl methanesulphonyl peroxide (XLIV; $R=CH_3$) from the reaction with methanesulphonyl chloride gave only dibenzoyl peroxide (XLV) and a small quantity of phenol (XLVI) (isolated as the tribromo derivative).

	$1 \rightarrow \land$
Phco $CCNa + RSO_2 C1$ —	\rightarrow 0=C - O - OSO ₂ R + NaCl
XLIII	XLIV / Ph _
FhCO•ONa	$0 = \dot{C} - \dot{0} + 0SO_{2}R$
RSO2CI	\bigvee
$PhCO.OSO_R + NaCl$	Fh0.CO.OSOR
V FhCO-OONa	↓ H ₂ 0
$PhCO-OOCOPh + NaOSO_2R$	$PhOH + CO_2 + RSO_2OH$
XLV	(44) XLVI

Ph

The phenol was probably formed by heterolysis of the desired peroxides (XLIV) in the manner shown (29), the small yield of it is to be expected, in view of its susceptibility to oxidation in the reaction medium. A possible route to the dibenzoyl peroxide is shown and requires no comment.

The failure to prepare under these reaction conditions the mixed peroxides (XLIV; R = Me and $Me-C_6H_4$) contrasts with the successful preparation of acetyl cyclohexane sulphonyl peroxide by Graf (42), and may be due (inter alia) to the following reasons:

- 1. The latter peroxide was prepared in a relatively non-polar medium, while the preparation of the peroxides (XLIV; R=Me and Me-C₆H₄) was attempted in an aqueous medium which would favour ionic fission of the peroxide linkage.
- 2. The heterolysis of the peroxide linkage should receive more anchimeric assistance from a migrating phenyl group than from a migrating methyl group. (67).

Since this work was completed, Rasuwajew <u>et al.</u> (68) have described the reactions of compounds such as benzoyl methanesulphonyl peroxide, without giving the method of preparation of these compounds, which we have not been able to find in the literature. Benzoyl methanesulphonyl peroxide rearranges in the presence of methanesulphonic acid or Lewis acids to phenoxyformyl methanesulphonyl anhydride, which was isolated and characterized. This supports our mechanism (equation 44).

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Part II

Preparation of α -Methoxythiophenes Using

Methyl t-Butyl Peroxide

It is apparent from the results in Part I that methyl ethers may be conveniently prepared in high yield from the reaction of organolithium compounds, with methyl <u>t</u>-butyl peroxide. Baramki (1) applied a similar reaction to prepare 2-methoxyfurans. 2-Furyllithium (2) was prepared by the reaction of furan with <u>n</u>-butyllithium (3) and was allowed to react with dimethyl peroxide to get 2-methoxyfuran (eq. 1).

$$\frac{n-C_4H9Li}{0} \rightarrow 0 Li \xrightarrow{he_2O_2} 0 Le (1)$$

A liquid product boiling at 108.5°-111°, and having the same characteristics as the 2-methoxyfuran reported by Petfield and Amstutz (4), was obtained. The infrared spectrum of this compound showed characteristic furan bands as well as the band at 2850 cm⁻¹ for the methoxyl group. The structure of 2-methoxyfuran follows conclusively from its NAR spectrum, which, however, showed it to be contaminated with aliphatic impurities. Baramki also studied the metallation of 2-methylfuran, followed by treatment with dimethyl peroxide. A liquid product boiling at 128-130° was obtained. The NMR spectrum of this compound showed it to be made up of 2-methoxy-5-methylfuran, but again aliphatic



impurities were evident. Characteristic furan bands were obtained in the infrared spectrum of this compound, as well as the band at 2850 cm⁻¹ for the methoxyl group.

In Part II of this thesis we describe the preparation of 2-methoxythiophenes by a similar route, using the relatively safe methyl <u>t</u>-butyl peroxide in place of the treacherous dimethyl peroxide. In the historical introduction the work to date on hydroxy- and alkoxythiophenes will first be reviewed followed by a survey of the reactions by which thienyllithium compounds may be prepared.

Historical Introduction

2-Hydroxy- and 2-Alkoxythiophenes

In 1950 Hurd and Kreuz (5) reported the preparation of 2-hydroxythiophene (II) by the action of oxygen on 2-thienylmagnesium bromide in the presence of isopropyl magnesium bromide (eq. 3):



When isopropylmagnesium bromide was absent, no 2hydroxythiophene was obtained (5,6). The function of the isopropylmagnesium bromide has been discussed already in this thesis (p. 12).

While phenol, a simple aromatic enol, exists exclusively in the enolic form because of the high resonance energy of the benzene ring, the precise structure of 2-hydroxythiophene has been a matter of debate for some time. The recent NLR studies of Gronowitz and Hoffman (7) make it likely that the compound exists at room temperature almost exclusively as 3-thiolen-2-one (IV). This accords with its ultraviolet absorption ($\lambda_{max} 220 m\mu \xi_{max}$ 7940) in aqueous solution (5). However, some of its properties and reactions give evidence to the presence of the other tautomers (II and III) in equilibrium with IV (5). The compound is a weak acid, it gives a red ferric chloride colour, couples in alkaline solution with diazo-compounds, and forms an acetate, a benzoate, and a methyl ether (5). On the other hand, in the tautomeric keto-form it yields a benzylidene derivative and readily undergoes hydrolytic fission (the keto-form is of course a thiolactone), (5). The infrared spectrum of the liquid itself shows carbonyl and hydroxyl absorption and peaks corresponding to both aliphatic and aromatic C-H bonds (5).

2-Hydroxythiophene is unstable and decomposes in a few days even at low temperature. This characteristic may be due, in part, to the ability of the compound.to exist in different tautomeric forms.

2-Methoxythiophene was prepared by the action of dimethyl sulfate on 2-hydroxythiophene (5) showing the ability of the tautomeric compound in alkaline solution to form the anion corresponding to the enolic form II. On the other hand, no 2-methoxythiophene was formed by the action of methanolic hydrogen chloride on 2-hydroxythiophene or by treating 2-hydroxythiophene with methyl iodide and anhydrous potassium carbonate in refluxing acetone.

Sice (8) prepared 2-methoxythiophene and 2-ethoxythiophene by coppercatalyzed Williamson syntheses (eq. 4):

$$\begin{bmatrix} CH_3 ONa, CH_3 OH, CuO \\ S & -I & \\ \hline S & S & \\ \hline S & \\ \hline$$

5-Lethoxy-2-methyl thiophene (VL) was prepared by the reaction of 2-methoxythienyllithium and dimethylsulfate (8) (eq. 5).



The position of the lithium in the intermediate V was shown by treating the compound with carbon dioxide to form the carboxylic acid, which on Raney nickel desulphurization gave δ -methoxyvaleric acid (VIII) (8).

2-<u>t</u>-Butoxythiophene (IX) was prepared by the reaction of 2-thienylmagnesium bromide on <u>t</u>-butyl perbenzoate (eq. 6) (9).



Stadler (10) reported the synthesis of 5-nitro-2hydroxythiophene (X) by diazotization of 2-aminothiophene hydrochloride with potassium nitrite (eq. 7). Some doubt has been cast upon the existence of this compound since attempts to reproduce this synthesis were unsuccessful.

$$\bigcup_{S} -NH_2 \cdot HC1 \xrightarrow{KNO_2, H_2O} O_2N_{S} - OH$$
(7)

Kreuz and Hurd (11) have prepared 3,5-dinitro-2hydroxythiophene (XI) from nitrochlorothiophene (eq. 8).

Basic hydrolysis of the 3,5-dinitro-2-chlorothiophene gives rise to resinous materials, but the hydroxyl group could be introduced by the indirect route shown. 3,5-Dinitro-2-hydroxythiophene (XII) began to decompose within 5-10 minutes at 25°, but could be stored overnight at -20° without appreciable change. On rapid heating it decomposed violently at 50-52°. Like picric acid, it is an extremely



strong acid having an ionization constant of about 3 x 10^{-2} .

2-Methoxy-,2-ethoxy-, and 2-phenoxy-3,5-dinitrothiophenes have been made by Williamson syntheses using the halide XI, (11).

5-Acetyl-3-nitro-2-hydroxythiophene (XIV) has been prepared as shown in the reaction sequence below (11).



This compound was reported to be a somewhat weaker acid than 3, 5-dinitro-2-hydroxythiophene having an ionization constant of about 5 x 10^{-3} . 2-Methoxy-, 2-ethoxy- and 2phenoxy- 3-nitro - 5-acetothienones have been made by Williamson reactions of the chloride XIII (11).

The preparation of 5-methyl-2-hydroxythiophene (XV) has been claimed by Paal (12) through the action of phosphorus trior pentasulfide on levulinic acid (13,14,15) (eq. 10). A possible mechanism is as follows:



The compound is, in fact, most probably formulated as XV (cf. p. 75), although some evidence for the presence of XVI in equilibrium with it comes from the fact that it dissolves in alkali and forms an acetate and benzoate with acetic anhydride and with benzoyl chloride respectively. However,

it also reacts with benzaldehyde to yield a benzylidene derivative 3-benzylidene-5-methyl-4-thiolen-2-one (XVII), it is oxidized by ferric chloride to an indigoid dye, and it undergoes other reactions which support the assumption of a keto form (14,15).



Recently Gronowitz and Hörnfeldt (16) have reported the preparation of 4-methyl-2-hydroxythiophene (XVIII), contaminated with smaller amounts of the 3-methyl isomer (XIX), through metalation of 3-methylthiophene with <u>n</u>butyllithium, followed by reaction of the organolithium compound with butyl borate and subsequent peroxide oxidation (17).

It is possible that this might prove a more successful route to α -furances than that described in Part I of this thesis.

4, 5-Dimethyl-2-hydroxythiophene (XX) is obtained as a by-product in the preparation of 2,3-dimethylthiophene



from β -methyllevulinic acid and phosphorus trisulfide (eq. 12), (12).

$$CH_{3}CO-CH(CH_{3})-CH_{2}COCH \xrightarrow{\mathbb{T}_{2}S_{3}} CH_{3}- \bigcup_{S}OH + CH_{3}- \bigcup_{S}OH$$

3-Hydroxy- and 3-Alkoxythiophenes

3-Hydroxythiophene was prepared by Hurd and Kreuz from 3-thienyl magnesium bromide by oxidation with molecular oxygen in the presence of isopropylmagnesium bromide (5). Since this compound is even less stable than 2-hydroxythiophene, it could not be purified by Hurd and Kreuz. Later Ford and Mackay (18) repeated the same reaction and got pure 3-hydroxythiophene by two distillations. These authors confirmed the instability of the compound, reporting that it developed a reddish tinge and a disagreeable odour within a day, and finally resinified.

The infrared absorption spectrum of 3-hydroxythiophene in liquid film suggests that approximately equal amounts of bonded hydroxyl and unsaturated carbonyl groups are present. The absorption characteristic of an unsaturated carbonyl group clearly establishes the presence of the tautomeric 2, 3-dihydro-3-oxothiophene (XXII) in the liquid

$$\bigcup_{S}^{-OH} \Longrightarrow \qquad \bigcup_{S}^{0} \qquad (13)$$

and in solutions. The changes in the relative intensities of the carbonyl and hydroxyl bands suggests a shifting of equilibrium in favour of the oxo-form with increasing dilution, though a difference between the transition moments for the free and the hydrogen-bonded carbonyl

group could also be responsible for this effect. The compound is therefore best considered as a tautomeric mixture of XXI and XXII. However, the strength of the hydroxyl band in the spectrum of the liquid film, and the odour, suggest the pure 3-hydroxythiophene must be phenolic to a comparable extent.

There is thus a marked contrast between 2-hydroxythiophene, which probably exists largely in a keto form, and 3hydroxythiophene which, though also tautomeric, is nevertheless noticeably phenolic.

3-Methoxythiophene (XXIII) was prepared by a coppercatalyzed Williamson snythesis (eq. 14) (19).

 $3-\underline{t}$ -Butoxythiophene (XXIV) was prepared by the reaction of 3-thienyllithium and t-butyl perbenzoate (eq. 15) (20).



Baumann and Fronm (21) prepared 5-phenyl-3-hydroxythiophene from 5-phenyl-1, 2-dithiacyclopenten-3-one (XXV), obtained by the action of sulfur on ethyl cinnamate (eq. 16).

$$C_{6}H_{5}-CH = CHCOOC_{2}H_{5} + 2S \longrightarrow C_{6}H_{5} + C_{2}H_{5}OH$$
 (16)

This compound (XXV), when treated with chloroacetic acid in the presence of sodium sulfide, followed by treatment with acetic anhydride - sodium acetate, gives the acetate ester of 5-phenyl-3-hydroxythiophene (XXVI).



The tautomeric nature of this hydroxythiophene was first noted by Friedlander and Kielbasinski (22), who were able to obtain 2-isonitroso-5-phenyl-4-thiolen-3-one (XXVII) by the action of nitrous acid on it. (eq. 18).



86

5-Phenyl-3-hydroxythiophene was oxidized to an indigoid dye (XXVIII) by potassium ferricyanide, and was conversed



into 2-phenyl-3; 5, 5-tribromo-4-keto-4, 5-dihydrothiophene (XXIX) by bromine in cold acetic acid.

3, 4-Dihydroxy- and 3, 4-Dialkoxythiophenes

3, 4-Dihydroxythiophene (XXXI) is obtained in nearly quantitative yield by decarboxylation of 3,4-dihydroxy-2,5thiophene-dicarboxylic acid in refluxing pyridine. The synthesis of 3,4-dihydroxy-2,5-thiophenedicarboxylic acid is accomplished by the reaction of diethyl thiodiglycollate (23, 24) with methyl oxalate (eq. 21):



3,4-Dihydroxythiophene (XXXI) is found to be so reactive towards oxygen that it can be isolated only in the form of the dibenzoate (23).

3,4-Dimethoxythiophene was prepared by the reaction of diazomethane with 3,4-dihydroxythiophene (25) or alternatively by methylation of the dihydroxydicarboxylic ester XXX followed by the hydrolysis of the ester and decarboxylation (26).

Karrer and Kehrer (27) have prepared 3,4-dihydroxy-2thiophene propionic acid (XXXII).



The 3,4-dihydroxy-2-thiophene propionic acid gives a blue-green color with dilute ferric chloride. It will not react with hydroxylamine as a ketone, and it seems to exist solely in the dihydroxy form.

Metalation of Thiophenes

The metalation of an aromatic compound has been found to take place preferentially at a position ortho to a substituent having an unshared electron pair, independently whether the substituent is ortho, para, or meta directing in electrophilic arometic substitution. This is best accounted for by assuming that the reaction involves an initial coordination of the metallic atom of the metalating agent with the unshared electron pair of the substituent or in the case of heterocyclic aromatic compounds with the unshared electron pair of the heterocyclic atom. The subsequent reaction is best explained by the Roberts and Curtin (28), mechanism as follows:

$$\begin{array}{c} \begin{array}{c} \begin{array}{c} \mathbb{Y}: \text{Li}: \mathbb{C}_{4} \mathbb{H}_{9} \\ & \\ \end{array} \\ & -\mathbb{H} \end{array} \end{array} \end{array} \left(\begin{array}{c} \begin{array}{c} \mathbb{Y}: \text{Li} \\ & \\ \end{array} \right) + \mathbb{C}_{4} \mathbb{H}_{10} \longrightarrow \end{array} \right) + \mathbb{C}_{4} \mathbb{H}_{10} \end{array} \right)$$

Hartough and Schick (29) reported the metalation of thiophene and 2-halothiophenes with sodium amalgam to make 2-thienylsodium (XXXII) and 5-halo-2-thienylsodium (XXXIV). Subsequent carbonation and acidulation yielded the 2-thiophene carboxylic acid and 5-halo-2-thiophenecarboxylic acids, respectively. The alkylthiophenes (30) do not metalate directly with sodium. However, metalation was



accomplished via the transmetalation reaction by interaction of an alkylthiophene, metallic sodium, and an alkyl or aryl halide in a neutral solvent (eq. 24, eq. 25).

$$R'X \xrightarrow{Na(NaHg)} R!Na$$
(24)

$$\begin{array}{c} & & \\ & &$$

Schick and Hartough (30) did not observe the formation of isomers in the metalation of 2-methyl-thiophene. However, the presence of about 1% of a 3-isomer would not have been detected by the methods used. It appears, therefore, that a typical ortho-para-directing group in the 2-position, which would orient to the 3-and 5-positions, coupled with the tendency of the sulfur atom to orient to the 5-position, gives a directing factor of at least 100 to 1 in favor of the 5-position over the 3-position.

In 1949 Gilman and Shirley (31) reported the metalation of thiophene by organolithium compounds. The thiophene was treated with <u>n</u>-butyllithium in ether solution forming 2thienyllithium in 87% yield, as shown by conversion of the 2-thienyllithium to 2-thiophene carboxylic acid by treatment with solid carbon dioxide.

Gronowitz <u>et al.</u> (32) have shown that the metalation of 2-alkylthiophenes with <u>n</u>-butyllithium takes place exclusively at the 5-position, like the metalation of 2methoxythiophene (V; cf. p. 77).

Hartough and Schick (30) reported that 3-methylthiophene metalated (with sodium) exclusively in the 5-position. No trace of 3-methyl-2-thiophenecarboxylic acid could be detected. Since the yield of 4-methyl-2-thiophene carboxylic acid was 42%, it is possible that the existence of a small percentage of 3-methyl-2-thiophenecarboxylic acid could not be detected by the methods used. Gronowitz (33) suggested that the metalation in the 5-position was to be expected if the reaction was formulated as a nucleophilic attack of the butyl carbanion on hydrogen.



The inductive effect of the methyl group deactivates the whole thiophene nucleus towards nucleophilic attacked by making all the hydrogens less acidic. The 5-(meta) position was, however, affected to a lesser extent than the 2-(ortho) position, and thus the butyl carbanion attacked the most acidic hydrogen in the position meta to the methyl group.

It was found in a competitive experiment in which thiophene and 3-methylthiophene were metalated with insufficient amount of <u>n</u>-butyllithium, by analysis of the infrared absorption spectrum, that the acid mixture obtained after carbonation consisted of about 75% 2-thiophenecarboxylic acid and 25% 3-methyl-5-thiophenecarboxylic acid. This indicates that thiophene was metalated faster and hence was more acidic than 3-methylthiophene.

Sice (34) first produced evidence that <u>n</u>-butyllithium metalates 3-methylthiophene in the 5-position. 4-Methyl-2-

thiophene. The 4-methyl-2-thionyllithium reacted with dimethyl-formamide in other to obtain 4-methyl-2-thouadehyde. This aldehyde (XXXV) was converted upon oxidation by silver



oxide to the known 4-methyl-2-thiophenecarboxylic acid (XXXVI). The yield was 61%. The hydrazone of 4-methyl-2thenaldehyde decomposed at 120° in a solution of potassium hydroxide in ethylene glycol to give 2, 4-dimethylthiophene (XXXVII).



In 1954 Gronowitz (33) also reported that <u>n</u>-butyllithium metalates 3-methylthiophene in the 5-position. The carbonation of this reaction mixture gave 4-methyl-2thiophenecarboxylic acid in 68% yield.

However, more recently Ramanathan and Levine (35) reported that 3-methylthiophene on metalation with <u>n</u>butyllithium or phenyllithium and then carbonation gave 4methylthiophene-2-carboxylic acid (61-68%), and 3-methylthiophene-2-carboxylic acid (19%), while phenylsodium led to 4-methylthiophene-2-carboxylic acid (58%) and 3-methylthiophene-2,5-dicarboxylic acid (11%). Hence, metalation does not take place exclusively in the 5-position of 3methylthiophene (cf. ref. (30), (33), and (34)). It appears that since phenylsodium is probably a stronger base than the lithium reagents, it is able to dimetalate 3methylthiophene to some extent.

Similarly, Gronowitz (32) <u>et al.</u> recently reported that the metalation of 3-methylthiophene gave a mixture containing ca. 85% of the 3,5-and 15% of 2,3-isomer. The <u>n</u>-butyllithium was added to 3-methylthiophene and refluxed for half an hour. The reaction mixture was then added to N, N-dimethyl formamide, to give a mixture of aldehydes (eq. 28), (cf. ref. 34).



NMR-spectral analysis showed the mixture to consist of $83\pm3\%$ of 3-methyl-5-thiophenealdehyde and $17\pm3\%$ of 3-methyl-2-thiophene aldehyde.

EXPERIMENTAL

Reaction of Methyl t-Butyl Peroxide with 2-Thienyllithium

n-Butyllithium reagent (36), prepared from 0.2 mole of n-butyl bromide, was added with slight cooling to 0.2 mole of thiophene (2) and the mixture stirred and refluxed for six hours. The resulting 2-thienyllithium was cooled in an ice water bath to 20°C, and from a pre-cooled dropping funnel was added methyl-t-butyl peroxide (0.15 mole) diluted with 30 ml. anhydrous ether, with stirring under a nitrogen atmosphere. The reaction mixture was allowed to warm up slowly and refluxed for three hours. The reaction mixture was then decomposed with ice water and extracted with ether. The ether layer was dried. The ether was removed and the remaining liquid was fractionally distilled using a spinningband column. The fraction boiling at 760/65mm. was collected and weighed 6.16g. (Yield 36.0%). On the basis of its refractive index $(n_D^{24} \ 1.5243)$, and its infrared spectrum $(\frac{1}{max})^{\text{CCl}_4} \text{ cm}^{-1}$: 3050 (w), 3010 (m), 2950 (m), 2850 (w), 1750 (w), 1550 (m), 1475 (v.s.), 1430 (v.s.), 1370 (m), 1340 (m), 1225 (v.s.), 1200 (v.s.), 1155 (v.s.), 1080 (v.s.), 1040 (s), 1000 (s), 840 (s)) the compound was identified as 2-methoxythiophene. (lit. (8) b.p. $74^{\circ}-75^{\circ}/50$ mm., n_D^{25} l.5261; the infrared spectrum showed a band in the C-O-C region (1155 cm^{-1})).

Reaction of Dimethyl Peroxide with 2-Thienyllithium

Reagent <u>n</u>-butyllithium prepared from 0.1 mole of <u>n</u>butyl bromide, was added with slight cooling to 0.1 mole of thiophene. The mixture was refluxed for six hours. The resulting 2-thienyllithium was reacted with 0.08 mole of dimethyl peroxide in ether solution (at -10° C). The reaction mixture was allowed to warm up slowly and left at room temperature overnight. The separation and identification of the products were the same as before. Yield of 2-methoxythiophene was 3.5 g. (38%). Cacl. for C₅H₆SO : C, 52.64%; H, 5.26%. Found: C, 53.02%; H, 5.25%.

Reaction of Methyl t-Butyl Peroxide with

5-Methoxy-2-Thienyllithium

2-Lethoxythiophene (0.054 mole) was added with stirring to a solution of <u>n</u>-butyl lithium (30 ml. ether solution containing 0.06 mole <u>n</u>-butyl lithium). Then the addition was completed, the mixture was refluxed for 40 more minutes. To the resulting 5-methoxy-2-thienyllithium was added slowly, from a dropping funnel, methyl <u>t</u>-butyl peroxide (0.05 mole) diluted with 7 ml. anhydrous ether. Then addition was completed the mixture was refluxed for 12 hours. The reaction mixture was poured into ice-water and extracted with ether. The ether extract was dried. The ether was removed and the

remaining liquid was fractionally distilled using a spinningband column. The fraction boiling at $104^{\circ}-105^{\circ}/35$ mm was 2, 5-dimethoxy thiophene and weighed 3.16 g. (yield 44.0%); n_{D}^{24} 1.5168, d_{4}^{21} 1.1639. γ CCl₄ cm⁻¹: 3020 (w), 2950 (m), max. 2840 (w), 2000 (v.w.), 1570 (m), 1475 (s), 1440 (w), 1340 (m), 1220-1235 (v.s.bd.), 1150 (s), 1050 (m), 980-1000 (s.bd.), 700 (m), 685 (m). Calc. for $C_{6}H_{8}SO_{2}$: C, 50.0%; H, 5.55%; S, 22.2%. Found: C, 49.95%; H, 5.53%; S, 22.61%.

Reaction of Methyl t-Butyl Peroxide with 2-Methyl-5thienyllithium

2-Methylthiophene (0.05 mole) was added with stirring to a solution of n-butyllithium (30 ml. ether solution containing 0.06 mole n-butyllithium). The mixture was refluxed for five hours. To the 2-methyl-5-thienyllithium thus prepared was added slowly, from a dropping funnel, methyl \underline{t} butyl peroxide (0.05 mole) diluted with 7 ml. anhydrous ether. The reaction mixture was refluxed for three hours. The solution was left at room temperature overnight. The reaction mixture was poured into ice-water and extracted with ether. The ether layer was dried with magnesium sul-The ether was removed and the remaining liquid was fate. fractionally distilled using a spinning-band column. The fraction boiling at 70-71°/25mm. (lit. (8) b.p. 51-52°/10mm)
was collected and weighed 2.37g. (yield 37.0%). It was identified as 2-methyl-5-methoxythiophene on the basis of its refractive index, n_D^{24} 1.5171 (lit. (ll) n_D^{25} 1.5216) and its infrared spectrum ($\sqrt{\frac{CCl}{max}}$ cm⁻¹: 3000 (m), 2950 (s), 2820 (m), 2000 (v.w.), 1560 (m), 1495 (m), 1450 (s), 1430 (v.s.), 1340 (m), 1200-1235 (v.s.bd.), 1150 (s), 1140 (s), 1050 (v.s.), 1000 (s), 960 (w), 700 (v.w.)). Calc. for C₆H₈SC: C, 56.25%; H, 6.25%; S, 25.0%. Found: C, 56.59%; H, 6.33%; S, 24.6%.

Reaction of Methyl t-Butyl Peroxide with 2-Ethyl-5thienyllithium

2-Ethylthiophene (0.08 mole) was added with stirring to a solution of <u>n</u>-butyllithium (60 ml. ether solution containing 0.09 mole <u>n</u>-butyllithium). The mixture was refluxed for five hours. To the resulting 2-ethyl-5-thienyllithium was added slowly, from a dropping funnel, methyl <u>t</u>-butyl peroxide (0.08 mole) diluted with 9 ml. anhydrous ether. The reaction mixture was refluxed at 35° C for 16 hours. The reaction mixture was poured into ice-water and extracted with ether. The ether extract was dried. The ether was removed and the remaining liquid was fractionally distilled using the spinning-band column. The fraction boiling at $82.5^{\circ}-83^{\circ}/20$ mm. was 2-ethyl-5-methoxythiophene and weighed 7.88g. (yield 69.2%), n_D^{23} 1.5121, d_4^{23} 1.0467, $\bigwedge_{max.}^{iso-octane}$ 250 m/((€ 6890). $\gamma_{max.}^{CCl_4}$: 3020 (m), 2975 (s), 2840 (s), 2740 (m), 1510 (s), 1465 (s), 1438 (s), 1380 (w), 1350 (w), 1320 (w), 1225 (s), 1205 (v.s.), 1150 (s), 1060 (m), 1025 (s), 1000 (sh), 940 (w). Calc. for $C_{7^{H}10}$ OS: C, 59.15%; H, 7.04%; S, 22.53%. Found: C, 59.06%; H, 6.90%; S, 22.35%.

Reaction of Methyl t-Butyl Peroxide with 3-Methylthienyllithium

3-Lethylthiophene (0.05 mole) was added with stirring to a solution of <u>n</u>-butyl lithium (30 ml. ether solution containing 0.06 mole <u>n</u>-butyllithium). The mixture was refluxed for five hours. To the resulting mixture of methylthienyllithiums was added slowly, from a dropping funnel, methyl-<u>t</u>-butyl peroxide (0.05 mole) diluted with 7 ml. anhydrous ether. The color turned yellow while the mixture was refluxed for three hours. The solution was left at room temperature overnight. The reaction mixture was poured into ice-water and extracted with ether. The ether layer was dried with magnesium sulfate, the solvent removed and the remaining liquid fractionally distilled using the spinningband column. The fraction boiling at 74°-75°/25nm. was collected and weighed 1.80g. (yield 28%). n_D^{24} 1.5161, \bigwedge_{max} $237m\mu$ (ϵ 5840) γ $\frac{ccl_4}{max}$ cm⁻¹: 3000 (m), 2950 (s), 2860 (m), 2830 (m), 2000 (v.w.), 1560 (m), 1490 (v.s.), 1450 (v.s.), 1430 (v.s.), 1375 (s), 1370 (m), 1220 (v.s.), 1175 (m), 1150 (m), 1130 (v.s.), 1080 (m), 1000-1025 (s.bd.), 945 (w), 940 (m), 840 (m), 695 (s). Calc. for C₆H₈SO: C, 56.25%; H, 6.25%; S, 25.0%. Found: C, 56,53%; H, 6.56%; S, 24.61%.

From its NAR spectrum, this material was identified as a mixture of 3-methyl-2-methoxy thiophene and 4-methyl-2methoxy thiophene. (ratio 1:2.6) Separation by Beckman Gas Chromatograph: Model GC2A (column packed with polyethylene glycol (20%) on chromosorb W.) resulted in the two fractions in the ratio of 1 : 2.

Attempted Preparation of 2,5-Dimethoxy-3-Thienyllithium

2,5-Dimethoxy thiophene (1.40g. or 0.01 mole) was added with stirring to a solution of <u>n</u>-butyllithium (16 ml. ether solution containing 0.015 mole <u>n</u>-butyllithium). The mixture was refluxed at 35° C for 16 hours. The contents of the flask were poured into a slurry of dry ice in ether and the mixture was poured into ice water. The aqueous layer were acidified with 6N HCl and extracted by ether. Ether layer dried and evaporated. The thick black oily substance was obtained and weighed 1.20g. It was chromatographed on alumina. A brown oil was recovered 0.36g. It was identified as slightly impure 2,5-dimethoxy thiophene from its infrared spectrum.

Diels-Alder Reaction

Using the method of Diels and Alder (37), neither thiophene nor 2-methoxy thiophene would react with maleic anhydride to form an adduct.

RESULTS AND DISCUSSION

Preparation of 2-Methoxythiophenes

The reaction of 2-thienyllithium with methyl-<u>t</u>-butyl peroxide gave a 36% yield of 2-methoxythiophene. While with dimethyl peroxide it gave a 38% yield. Obviously the use of the highly dangerous dimethyl peroxide offers no significant advantage, and so all further experiments were done with the methyl <u>t</u>-butyl peroxide.

The yields obtained by this reaction compare very badly with those obtained by Sicé (80% for overall reaction in two steps from thiophene (8)), but the reaction has the great advantage of being effectively carried out in one step, since 2-thienyllithium is allowed to react without isolation. It can therefore be considered the most convenient method for preparing \mathcal{X} -methoxythiophenes.

Metalation of 2-methylthiophene (known to take place at the 5-position : p. 91), followed by treatment with methyl <u>t</u>-butyl peroxide gave 2-methyl-5-methoxy-thiophene in 37% yield. Similarly, 2-ethylthiophene gave 2-ethyl-5methoxythiophene in 69% yield, and 2-methoxythiophene gave 2,5-dimethoxythiophene in 44% yield. The two latter compounds are new. Metalation of 3-methylthiophene is known to give 4methyl-2-thienyllithium and 3-methyl-2-thienyllithium in a ratio of about 4:1 (pp. 81, 94). In the present work it was found that the metalation product reacted with methyl <u>t</u>-butyl peroxide to give a 28% yield of material analysing as a methylmethoxythiophene, but shown by NMR spectroscopy to be a mixture of two compounds. These are undoubtedly 4-methyl-2-methoxythiophene and (in smaller amount) 3methyl-2-methoxythiophene. The spectral properties of the mixture are discussed in the next section.

The various α -methoxythiophenes were colourless liquids, which changed to a yellowish color after standing overnight in the ice box. All were unstable, developing a dark brownish tinge and a disagreeable odour within two weeks and finally resinifying, even when kept sealed under nitrogen at 0°C.

Introduction of a methoxyl group into benzene causes a slight exaltation of the molecular refraction constant $[R]_{\mathcal{D}}$, the experimental value exceeding the calculated value by 0.54 (C.K. Ingold, <u>op. cit.</u>, p. 127) introduction of one and two methoxyls into thiophene causes no exaltation (Δ in Table IV), which, however, is observed when a methoxyl is introduced into the 5-position of 2-alkylthiophenes. It is difficult to account for this behaviour, though part of the variability may come from the fact that the densities and refractive indexes from which the observed $[R]_D$ values were calculated were not determined at 20°, the standard temperature for the atomic and bond constants used for obtaining the calculated $[R]_D$ of Table IV.

Molecular refraction cons	tants $[R]_{D}$	of thiophene	9S
Compound	Observed $\begin{bmatrix} R \end{bmatrix}_{D}$	Calc. ^a [R] _D	\bigtriangleup
Thiophene	24.79 ^b	(24.79)	
2-Lethoxythiophene	31.04 [°]	31.07	-0.03
2-Methoxy-5-methylthiophene	36.39 ⁰	35.71	+0.68
2-Methoxy-5-ethylthiophene	40.71 ^d	40.35	+0.36
2,5-Dimethoxythiophene	37.41 ^d	37.35	+0.06

	TA	BLE	IV
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^aCalc. from constants of Eisenlohr, given in C.K. Ingold, Structure and Mechanism in Organic Chemistry, Bell, London, 1953, p. 121, taking [R]_D of thiophene as 24.79.
^b[R]_D Calc. according to data in ref. (39a).
^c[R]_D Calc. according to date in ref. (8).
^d[R]_D Calc. according to data in this thesis. When the two α positions of thiophene are blocked, as in 2,5-dimethoxythiophene, it was thought that metalation would take place at the 3-position, which should be activated by the presence of the neighbouring 2-methoxyl group. In fact, no reaction took place. Presumably the mesomeric electron release illustrated in XXXVIII makes the acidity



XXXVIII

of the hydrogen at the 3-position too small for it to be removed by a <u>n</u>-butyl carbanion (cf. p. 89).

Spectral Studies of \mathcal{A} -Methoxythiophenes

The infrared, ultraviolet, and nuclear magnetic resonance spectra of the alkoxy thiophenes prepared in the course of this work have been studied and correlated with their structures. Certain empirical relationships between spectra and structure have been found which may prove useful in the elupidation of structures and characterization of new compounds.

(a) Infrared Absorption Spectra

The infrared spectra of thiophene and a number of its derivatives have been reported in the literature (38,39b,40). However, very little is known about the infrared absorptions of alkoxy thiophenes. The infrared spectra of the alkoxy thiophenes prepared in the present studies were examined using a Perkin-Elmer Model 21 double-beam recording spectrophotometer equipped with a rock-salt prism. Such a prism is not expected to have a high resolving power (41) in the region 4000-2000 cm.⁻¹, and furthermore, the relative intensities of bands will be low (41). However, all the mono-and disubstituted alkoxy thiophenes examined showed a relatively weak band between 3060-3020 cm.⁻¹ (see Table V). This is probably the =C-H stretching vibration (38). The intensity of the 3125 cm.⁻¹ band of thiophene decreased with increasing substitution on the thiophene nucleus as expected.

Neglecting some relatively weak bands between 2000 cm.⁻¹ and 1670 cm.⁻¹ which are probably overtone and combination tone vibrations, thiophenes generally absorb in the region 1600-1400 cm.⁻¹. Waddington <u>et al.</u> (42) assigned the bands in the region 1600-1400 cm.⁻¹ to a ring stretching (mode XXXIX and XL) apparently largely controlled by the carbon-carbon double bands.



XXXIX XL XII (Arrows indicate direction of motion in plane) Ring stretching modes XXXIX and XL are illustrated above.

TABLE V

Characteristic χ -Alkoxy Thiophenes

Frequencies

.

				TABLE V				
		Charac	teristic χ -A	lkoxy Thiophene	s Frequencie	S		
Compound	-C - H Stretching	Ring St:	retching	H In-plane Deformation		C-O-C Stretching	Ring Breathing	H Out- of- plane
S OLe	3050 (w)	1550(m)	1475(v.s.) 1430(v.s.)	1225(v.s.) 1200(v.s.)	1C80(v.s.) 1040(v.s.)	1155(v.s.)	1000(s)	840(s)
TeO SCLe	3060 (w)	1570(m) 1525(m)	1475(s) 1440(m)	1235- 1220(v.s.bd.)	1050(m)	1150(s)	1000- 980(s,bd,	700(m)
Leo	3060 (w)	1560(m)	1450(s) 1430(v.s.)	1235- 1200(v.s.bd.)	1050(v.s.)	1150(s) 1140(s)	1000(s)	960(w)
LeO S ±t	3020 (w)	1560(w) 1510(m)	1465(s) 1438(s)	1225(s) 1205(v.s.)	1060(m) 1025(s)	1150(s)	1000(sh)	940(w)
	3050 (w)	1560(m)	1490(v.s.) 1450(v.s.) 1430(v.s.)	1220(v.s.)	1080(m) 1025(s)	1150(m) 1130(v.s.)	1000(s)	940(w)

1.

FIGURE 1

Infrared Absorption Spectra of 2,5-Dimethoxythiophene (Fig.A) and 2-Ethyl-5-Methoxythiophene (Fig.B)



The hydrogen in-plane deformation frequencies appear between 1235 cm.-1 to 1200 cm.-1 and 1080 cm.-1 to 1025 cm.-1 (see Table V), according to Hartough (38).

A band that appeared between 1000 cm.⁻¹ to 980 cm.⁻¹ in all the compounds examined may be attributed to the ring breathing frequency (38) (mode XLI).

Absorption between 960 cm.⁻¹ and 700 cm.⁻¹ has been correlated with the C-H out-of-plane deformation vibration (38).

In all the alkoxy thiophenes (Table V), the -C-O-Cvibration frequencies corresponded to a very strong band at 1130 to 1155 cm.⁻¹. This is the region in which many alkyl ethers absorb, although usually aromatic ethers absorb at higher wavenumbers (43). In general the vibrations of the C-O-C system cannot be expected to differ very greatly from analogous vibrations of C-C-C systems since the masses of the atom and force constants of the bands are comparable; the fundamental vibrations of ethers accordingly fall into the same frequency ranges as those of aliphatic hydrocarbons (44), and the distinction of ether from C-C bands can be difficult. In the absence of symmetry restrictions, however, the dipole moment changes accompanying the vibrations in which oxygen atoms are involved are considerably greater than those where only saturated carbon atoms participate. Skeletal vibrations involving oxygen atoms may therefore be expected to give more intense infrared bands and the characterization of ether linkages depends very largely on the identification of such high intensity bands among other skeletal vibrations. However, in the present case thiophene has no band in the region between 1130 to 1155 cm.⁻¹, so that the assignment of the strong bands at 1130 to 1155 cm.⁻¹ to the -C-O-C- vibration can be made with confidence.

(b) Ultraviolet Absorption Spectra

Changes in electronic spectra due to individual groups are modified by interaction with other groups present in the same molecule. Such interaction may be of three kinds, vibrational, electronic, or steric. Vibrational interaction causes no profound changes in the ultraviolet light absorption properties, except for alterations in the vibrational fine-structure or in the shape of the band envelope. Electronic interaction, on the other hand, can result in marked changes in transition energy and in large wavelengthdisplacements of the bands. Such interaction is particularly strong in the case of adjacent groups containing highly polarizable π - or n- electrons, and the classical term

"conjugation" is given to such interaction. The term "chromophore" is given to unsaturated groups such as C=Cand C=O (π - electron groups), while the term "auxochrome" is given to such groups as $-NR_3$ and -OR (n- electron groups).

It is assumed that a molecule can absorb certain characteristic guanta of light energy which raise it to some electronically excited state. Absorption of light therefore brings about transition of the molecule from its ground state to an electronically excited state, and the difference in energy of these two states will determine the frequency of light absorbed. The more nearly the energy of the first excited state corresponds to the energy of the ground state, the longer is the wavelength of light absorption. Conjugation $(\pi - \pi \text{ conjugation or } \pi - n)$ conjugation) generally results in closing up of ground and excited electronic levels, i.e., a decrease in transition energy, and so results in a band displacement to longer wavelength, (bathochomic shift). If, on the other hand, resonance stabilizes the ground state more than it stabilizes the excited state, the difference between the two states increases and a shift towards shorter wavelength (hypsochromic shift) takes place. Steric interaction affects light absorption by influencing the stabilization of the

molecule in the ground or excited states. If steric factors interfere with resonance stabilization of the excited state, the energy difference between the two states increased and a hypsochromic shift occurs. The ultraviolet absorption data obtained in the course of this work are listed in Table VI. All samples were examined in solution in absolute alcohol and iso-octane at suitable concentrations for precise transmission measurements in a cell 1 cm. thick. Spectra were obtained using a Beckman DK-1 Recording Spectrophotometer which recorded absorbance (i.e., optical density) from which the molecular extinction coefficient in liters/mole-cm. was calculated in the usual manner (45).

Resonance within the thiophene ring gives rise to an ultraviolet absorption spectrum with a broad maximum (in ethanol) near 230 m,#, $\in_{max.}$ 7070 (46). Price and Walsh (47) conclude that the spectrum obtained is due to the excitation of a π -electron from the conjugated doublebond electrons. Hence, thiophene might be considered as a chromophore. However, only a very small bathchromic shift is observed when alkyl groups are substituted (effect of hyperconjugation) (48). Thus 2-methylthiophene has a maximum of **ab**sorption (46) at 232 m μ ($\in_{max.}$ 7410) (in ethanol).

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TABLE VI

Ultraviolet	absorption	of th	iophenes
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Compound	$\texttt{Solvent}^{f X}$	Λ_{\max} (mµ)	ϵ_{\max}	ref.
Thiophene	Ē	230	7070	46
11	I	231	7070	49
2-Methylthiophene	E	232	7410	46
**	I	234	7940	50
3-Methylthiophene	I	235	4780	51
2-Methoxythiophene	E	244	5380	٤
**	P	241	4300	8
2-Methyl-5-methoxythiophene	۲ <u>د</u>	249	6350	ę
**	P	249	5000	8
2-Ethyl-5-methoxythiophene	I	250	6890	ę
2,5-Dimethoxythiophene	ਜ਼	255	5660	ę
Lixture of 4-methyl-2-	E	234	5010	4
methoxythiophene and 3-methyl-	I	237	5840	ų
2-methoxythiophene				

*I =ethanol, I = iso octane, P = pentane.
{Present study.

In the present work the effect of substituting methoxyl group in the 2-position of thiophene was studied (Table VI). The methoxyl group is considered as an auxochrome and as such is expected to cause a bathochromic shift when attached directly to an aromatic system (52, 53). The bathochromic effect of the 2-methoxyl group may be explained on the basis of capability of such a group to conjugate (π -n-conjugation (54) with diene system of the thiophene nucleus as shown below (forms XLIII and XLIV).



The greater bathochromic shift in ethanol would then be expected because the more polarizable solvent should lower slightly the energy of the excited state made up mainly of XLIII and XLIV by solute-solvent interaction (55a).

It is difficult, however, to write plausible formulae (using the symbolism of resonance theory) for the excited states of 2-alkyl-5-methoxythiophenes and of 2,5-dimethoxythiophene which account for the additional bathochromic

shift produced by introducing a 5-alkyl- or 5-methoxyl group into 2-methoxythiophene. It is still more difficult to account for the strong <u>hypsochromic</u> shift produced by introducing a methyl group into the 3- and 4-positions (in the ratio of 1:2 in the mixture) of 2-methoxythiophene. These compounds obviously warrant more study, but in the meantime it can be said that it appears that the ultraviolet absorption spectrum allows one to differentiate between unsubstituted 2-alkoxythiophenes, those having alkyl substituents at the 5-position, and those having alkyl groups at the 3- or 4-positions.

(c) Nuclear Magnetic Resonance Spectra

The measurement of the nuclear magnetic resonance spectra of organic molecules has recently proved a powerful method for determining structure (55b, 56,57,58). The nuclei of certain atoms behave as if they were spinning, and generate a magnetic field. Then a compound containing such nuclei is placed in a magnetic pole gap, and subjected to the radiofrequency field of an oscillator, absorption of radiofrequency (rf) energy (resonance) occurs at particular combinations of the oscillator frequency and the magnetic field strength, and an rf signal is picked up by a detector.

For organic molecules, the resonance most generally measured is that of the various protons in the molecule. These will resonate at different applied fields because of the different degrees to which they are screened by their valency electrons. Protons from which the electrons are most removed by inductive, mesomeric, etc., effects resonate at the lowest fields. The difference in the field necessary for resonance of two different protons is termed the "Chemical shift."

The chemical shift (δ) is directly proportional to the magnetic field, and can be converted to the usual unit (parts per million = p.p.h.) by dividing by the value of the magnetic field.

The NLR spectra from monosubstituted benzenes are not readily subjected to a complete analysis and accurate quantitative data are rarely obtained (59, 60). As long as completely resolved NLR-spectra of monosubstituted benzenes cannot be obtained, it is difficult to relate proton chemical shifts to other substituent effects in benzene. The substituted furans and thiophenes give spectra which are more easily interpreted, and some NLR studies of these types of compounds have been undertaken (60,61,62,63,64,65). The discussion of substituent effects should evidently be

based on the chemical shifts for the unsubstituted compounds, but in case of thiophene this was initially not possible because its MLR spectrum is extremely complicated. Hoffman and Gronowitz have studied the NLR spectrum of thiophene (63) and they found the shift of the β -hydrogens to the α -hydrogens in the thiophene is 1.25 p.p.m. the β protons being at <u>higher</u> magnetic field (increased shielding). In furan and pyrrole (61) the resonances of the α - and β hydrogens are well separated and the shifts are 1.05 p.p.m.

The resonance of the α -hydrogens in furan (66) and in thiophene at lower applied field indicates that the electronattracting hetero atom unshields the α -hydrogens more than the β -hydrogens (Table VII). This general effect is modified by substituents (60,64,65).

The methoxyl group is of the (-I, +M) type, i.e., it is inductive electron-attracting but conjugative electrondonating. The following valence forms have been assumed (67) to contribute to the structure of 2-methoxythiophene (p. 116):



The resonances of all three protons occur at higher field than in thiophene, giving evidence of the shielding (60) (electron-donating) effect of the substituent. The largest shift to higher field is obtained for position 5, where through the conjugative effect the relative electrondensity is highest. In position 3, the conjugative effect is counteracted by the inductive electron-attracting effect, and resonance occurs at somewhat lower field. The effect of both the inductive and conjugative effect is small in position 4, and accordingly the proton resonance is only slightly displaced.

In the 3-methoxythiophene (60,67), the resonance structures like XLVII and XLVIII are of small importance



compared with XLV and XLVI, as they have decets around the sulfur as well as C = S double bonds. In other terms the mesomeric effect affects position 2 but not 4. This is

TABLE VII

Protons of thiophenes (τ values)

R₃ R₁ R₁ R₂ R₂

Comj	Compound		Substituent			Ring	Proton		Other	
		^R 1,	R ₂ ,	R ₃ ,	R_4	^H 2,	н _з ,	H ₄ ,	H 5	
l.	$\texttt{Thiophene}^{\texttt{X}}$	H	H	H	H	2.81	2.96	2.96	2.81	
2.	2-Me ⁹	Me	H	H	H	-	3.54	3.40	3.34	
3.	3-Ne ^{6†}	H	H	Me	H	3.40	-	3.26	3.01	
4.	2-01.e [±]	ОМе	H	H	H	-	3.89	3.41	4.14	
5.	2-0Me, 3-Me ⁽	O№e	H	Me	H	-	-	3.54	3.94	Me: 7.99 OMe: 6.30
6.	2-CMe, 4-Me ⁽	OMe	H	H	Me	-	3.49	-	4.00	Me: 7.92 OMe: 6.35
7.	2-0Me, 5-Me ^{(†}	OMe	ŗ⁻e	H	H	-	4.19	3.71	-	Me : 7.58 OMe: 6.36
8.	2-0Me, 5-Et ⁽	OMe	迅七	н	н	-	4.25	5.88	-	CLe: 6.42 CH ₃ :8.84 Lt (triplet) CH ₂ :7.37 (quartet)
9.	2-OMe, 5-OMe	Ole	OMe	H	H	-	4.47	4.47	-	OMe: 6.69
10.	3-0Me [≭]	H	H	OMe	H	3.92	-	3.34	3.06	
ref. c.f. c.f. This	(60,68) ref. (69) ref. (60,68) thesis	<u></u> 								

FIGURE 2

Nuclear Magnetic Resonance Spectra of 2,5-Dimethoxythiophene (Fig. A)

and 2-ethyl-5-methoxythiophene (Fig. B)



FIGURE 3

Nuclear Magnetic Resonance Spectrum of mixture of 4-Methyl-2-methoxythiophene and 3-methyl-2-methoxythiophene



completely verified by the NMR-spectra of these compounds. The shift for hydrogen 2(the "real" ortho position) in 3methoxythiophene is larger than that of hydrogen 5 and hydrogen 4. The shift for the 2-hydrogen is thus so large that although in thiophene the \mathcal{A} -resonance appears at the lowest applied field, it is here shifted to higher field than hydrogen 4. Gronowitz (40) found that the low field shift of the methyl group resonance in 2-methylthiophene is in agreement with the great electron-attracting property of 2thienyl over that of 3-thienyl.

The spectra of 5-methyl-2-methoxythiophene (69) and 5ethyl-2-methoxythiophene show the effect of the electronreleasing 2-methoxyl group in shifting the peak of 3-hydrogen to higher field than the effect of the 5-methyl group and 5ethyl group to the 4-hydrogen. In the spectrum of 2,5dimethoxythiophene, the spectrum shows one peak due to the ring protons and one peak due to the methoxyl groups. As expected, the peaks of the ring protons are shifted to much higher field.

The product from the metalation of 3-methylthiophene, followed by reaction with methyl <u>t</u>-butyl peroxide, would be expected to be a mixture of 4-methyl-2-methoxythiophene

(XLIX) and a lesser amount of 3-methyl-2-methoxythiophene (L); in fact, gas chromatography indicates (from relative areas of peaks) the ratio to be about 2:1. This is consistent with the NLR-spectrum which shows two peaks centred at about 6.35τ , for methoxyl, whose areas have a ratio of about 2:1. The same is true for methyl (τ 7.92), α -hydrogen (τ 4.00) and β hydrogen (τ 3.54). For reasons given earlier (p. 120), the α -hydrogen of 4-methyl-2-methoxythiophene would be expected to be more shielded than that of 3-methyl-2-methoxythiophene, and this agrees with the spectrum which shows the larger peak



at higher field. It is likely that the β -proton peak at higher field is also to be assigned to the proton of XLIX. Chemical shifts assigned to the separate compounds XLIX and L on the basis of these considerations are shown in Table VII.

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Summary And Claims to Original Research

- 1. The reactions of four dialkyl peroxides (dimethyl peroxide, methyl-<u>t</u>-butyl peroxide, diethyl peroxide and di-<u>t</u>-butyl peroxide) with phenyllithium and phenylmagnesium bromide were studied. Fhenyllithium reacted with all four per-oxides, although reaction with di-<u>t</u>-butyl peroxide was sluggish; phenylmagnesium bromide was less reactive. Good yields of anisole could be obtained from the reaction of phenyllithium with methyl <u>t</u>-butyl peroxide, which is a relatively safe peroxide to handle.
- 2. The yields of phenols from the oxidation of aryllithium compounds with molecular oxygen were not improved by the presence of butyllithium. Better yields were obtained when the oxidation was effected with t-butyl hydroperoxide. 2-Methoxy-l-naphthol was prepared in this way for the first time.
- 3. Attempts to prepare 2-hydroxyfuran and 2-methyl-5-hydroxyfuran through the oxidation of \mathcal{A} -furyllithium, gave only intractable, high boiling tars.
- 4. The use of phenylmagnesium chloride or iodide in place of phenylmagnesium bromide in reaction with dibenzoyl peroxide gave lower yields of phenyl benzoate.
- 5. The treatment of dibenzoyl peroxide with aluminum chloride gave phenyl benzoate and carbon dioxide. The yields of these two compounds were found not to vary greatly with temperature.
- 6. The attempt to obtain a mixed aroyl sulphonyl peroxide by the reaction of sodium perbenzoate with methane sulphonyl chloride, gave benzoyl peroxide, benzoic acid and phenol. The mechanism of the reaction is discussed.
- 7. 2-Methoxythiophene was obtained by treating thiophene with <u>n</u>-butyllithium to give 2-thienyllithium, followed by reaction of the latter with methyl <u>t</u>-butyl peroxide. By the same route 2-methyl-5-methoxythiophene, 2-ethyl-5methoxythiophene, and 2,5-dimethoxythiophene (the latter two new compounds) were prepared; while starting from 3methylthiophene a mixture of 4-methyl-2-methoxythiophene and 3-methyl-2-methoxythiophene was obtained.
- 8. The infrared, ultraviolet and n.m.r. spectra of the α methoxythiophenes were studied and discussed.