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A THESIS PRESENTED

FOR

THE DEGREE OF

DOCTOR OF PHILOSOPHY

OF

THE UNIVERSITY OF ST. ANDREWS

BY

MICHAEL G. BARTLE A.R.I.C.

1972



A SYNTHETIC STUDY IN THE

CHEMISTRY OF DIAZONIUM SALTS

Certificate

I certify that Michael Glover Bartle, A.R.I.C. has spent eleven terms at research work under my direction and that he has fulfilled the conditions of Ordinance No. 12 and Resolution of the University Court, 1967, No. 1, so that he is qualified to submit the following thesis for the degree of Doctor of Philosophy.

Professor Lord Tedder

DECLARATION

I hereby declare that the following thesis is of my own composition; that it is a record of the results of experiments performed by myself, and that it has not been submitted in any previous application for a Higher Degree.

Acknowledgements

The author wishes to express his sincere thanks to Professor Lord Tedder for his constant encouragement and advice.

Thanks are also due to Professors Lord Tedder and P.A.H. Wyatt for the facilities of the St. Andrews University Chemistry Department, to other members of the staff and research students for helpful discussion, to the technical staff for services rendered and to Mrs. K. Winton for typing the thesis.

Gratitude is expressed to the University of St. Andrews Purdie Fund for a grant to finance this work.

Research Training

The candidate was employed by I.C.I. Ltd., in the Process Development Section of the Terylene Works, Wilton, Teesside from September 1963 until October 1964. Then followed a four year sandwich course at Teesside Polytechnic, returning each summer to I.C.I., leading to Graduateship of the Royal Institute of Chemistry in 1968. The candidate joined Sketchley Ltd., a textile dyers, and was Chief Chemist when he left to undertake research into diazonium compounds.

The work described in this thesis was performed in the Chemistry Department of the University of St. Andrews between October 1969 and August 1972 under the supervision of Professor Lord Tedder.

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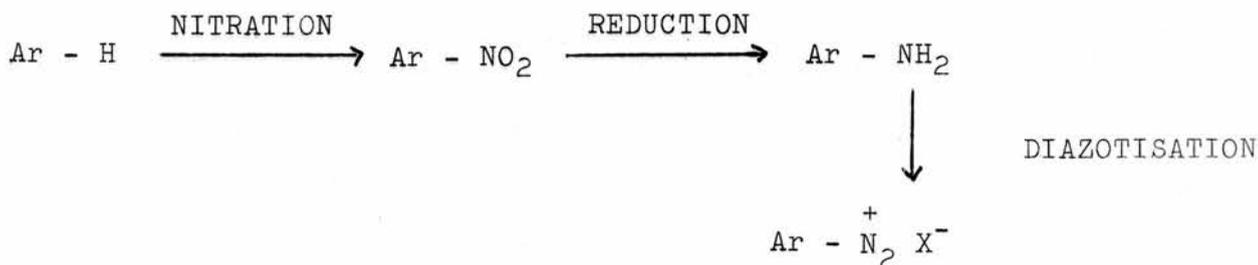
PART I

THE COUPLING OF DIAZONIUM SALTS WITH THIOPHEN AND FURAN

GENERAL INTRODUCTION

Aromatic diazonium salts are not only an extremely important class of compounds in the practical synthetic field of organic chemistry but through investigations of methods of their formation, their structures and their reactions, they are of academic importance and have been a means of extending the fundamental knowledge of organic chemistry.

The conventional method of formation is by diazotisation of the primary aromatic amine with cold, dilute, aqueous nitrous acid. This therefore requires a three stage process to convert an aromatic hydrocarbon into its diazonium salt viz: a) nitration of the nucleus followed by b) reduction of the nitro group to the amine and then c) diazotisation with nitrous acid:



Weselsky,¹ in the 1870's reported the formation of diazo-phenol and diazo-resorcinol as side reactions during preparations of nitrosophenol and nitrosoresorcinol using nitrous acid. Similar direct introductions of diazonium groups into aromatic nuclei have been reported since²⁻⁷ but, until Tedder and Theaker⁸ commenced a study in 1957, no one had attempted to develop this direct method although it offered great potential both industrially and academically. It was treated as a side-reaction although in some cases high yields of diazonium salt were found e.g. Morel and Sisley³ obtained 4-hydroxy-phenylazo-2-naphthol in 80% yield when they treated phenol with excess

hydrochloric acid and sodium nitrite and then added 2-naphthol.

Later still, Bourne and co-workers⁹ treated aromatic compounds with a solution of alkyl nitrite in trifluoroacetic anhydride in attempts to make nitroso-derivatives. In the case of non-activated aromatic compounds (e.g. benzene, naphthalene) nitration was the predominant reaction. However, with more reactive aromatic hydrocarbons, (e.g. mesitylene, anisole), diazonium salts were also obtained and were characterised by azo-coupling with 2-naphthol. It is believed that nitrosation occurred initially followed by reaction between the nitroso-group and nitric oxide (from dissociation of the alkyl nitrite) to give the diazonium nitrate, a reaction first reported by Bamberger.¹⁰

Tedder¹¹⁻¹³ has shown that these are examples of a general reaction by which diazonium salts can be prepared directly from aromatic compounds by the use of nitrous acid solutions or of solutions of nitrosyl derivatives of the type $\text{NO} - \text{X}$ (where $\text{X} = \text{Cl}^-$, HSO_4^- , CF_3COO^- , BF_3NO_2^- etc).

In the case of more reactive aromatic compounds such as phenols, diazonium salts were obtained in good yield (e.g. phenol, 80%) by the use of excess of aqueous sodium nitrite and hydrochloric acid or with excess of a solution of ethyl nitrite and hydrogen chloride in aqueous ethanol. With less reactive compounds such as polyalkylbenzenes and phenol ethers, it was found necessary to use more acidic media. Nitrosylsulphuric acid, prepared by dissolving sodium nitrite in concentrated sulphuric acid, reacts with anisole to give a 48% yield of diazonium salt. With mesitylene, a 78% yield is obtained and a 43% yield with m-xylene. Using toluene a negligible yield of diazonium salt was found and benzene itself was unaffected by these conditions.¹²

Pyrrole, thiophen and furan have been described as being

"super aromatic" compounds which is true only in so far as they are much more reactive to electrophilic reagents than benzene. Their heats of combustion and empirical resonance energies¹⁴ are considerably lower than benzene:

COMPOUND	HEAT OF COMBUSTION		EMPIRICAL RESONANCE ENERGY Kcal mole ⁻¹
	FOUND	CALC.	
Benzene	789.1	825.1	36.0
Pyrrrole	578.0	599.2	21.2
Thiophen	612.0	640.7	28.7
Furan	506.9	522.7	15.8

Tedder and Webster¹⁵ successfully applied the method of direct introduction of a diazonium group to hydrocarbon pyrroles and produced 2- and 3-diazopyrroles which were identified by coupling with 2-naphthol and isolating the azo dyes.

It was therefore expected that similar use of buffered nitrous acid or nitrosyl sulphuric acid should result in diazotisation of the nucleus of hydrocarbon thiophens and furans. In fact it was found impossible to diazotise the thiophen and furan derivatives available using these conditions or by use of nitrosyl chloride on 2-thiophenmercurichloride¹⁶ (cf Part II of this thesis).

There are several reports in the literature of the diazotisation of 2- and 3-aminothiophens^{17,18,19,20} to give a range of azo dyes but aminothiophens themselves are very unstable in the air.

Similarly, aminofurans are characterised by extreme instability to air unless the amino-group is protected by acylation or alkylation.²¹ The diazotisation of 3-aminofurans is said²² to proceed abnormally; the product couples with 2-naphthol to yield an azo dye but does not undergo any of the normal replacement reactions of diazonium salts. There are no reports concerning the behaviour of 2-aminofurans.

Since direct diazotisation of thiophens and furans seems to be inexplicably difficult it was decided to investigate these compounds by attempting to azo-couple a series of alkyl thiophens and alkyl furans with suitably reactive diazonium salts.

As established earlier, thiophen and furan are more reactive to electrophilic substitution than benzene and are of the order of reactivity of anisole or mesitylene. A literature search shows that although some substituted thiophens such as 2-amino-²³ and 2-acetamido-thiophens²⁴, have been coupled with diazonium salts to give azo dyes, attempts to couple hydrocarbon thiophens have resulted in "Gomberg" type arylation. Similarly no report could be found of the coupling of hydrocarbon furans although Eugster²⁵ has coupled the activated 3,4-dimethoxyfuran with diazonium salts derived from 4-nitro-aniline and benzidine.

The electrophilic nature of aromatic diazonium salts is increased by the presence of electron withdrawing groups in the aromatic nucleus so that for instance, the 2,4,6-trinitrobenzene diazonium salt is a powerful enough electrophile to substitute in weakly activated mesitylene²⁶ (though not in benzene). The diazonium salt derived from 2,4-dinitroaniline was known to couple readily with anisole²⁷ and was found during this work, to be also electrophilic enough to couple with mesitylene in the acidic conditions used during this investigation. This diazonium salt, 2,4-dinitrobenzene diazonium sulphate, was

therefore chosen as being fairly easily prepared and yet being a powerful enough electrophile for the coupling reagents to be used. Glacial acetic acid was picked as the reaction medium since the 2,4-dinitroaniline was to be diazotised in concentrated sulphuric acid solution, the thiophens and furans were all reasonably soluble in it and the acidic conditions should eliminate the possible Gomberg²⁸ free-radical arylation reaction which occurs in alkaline media.

The work described in this thesis (Part I) therefore comprises the coupling of diazonium salts, usually 2,4-dinitrobenzene diazonium sulphate, with a series of hydrocarbon thiophens (Section A) and a series of hydrocarbon furans (Section B).

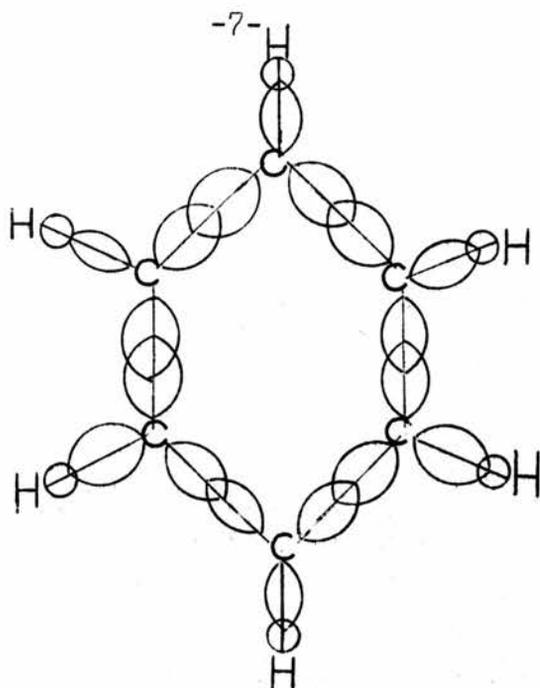
PART I SECTION A

THE COUPLING REACTIONS OF THIOPHENS

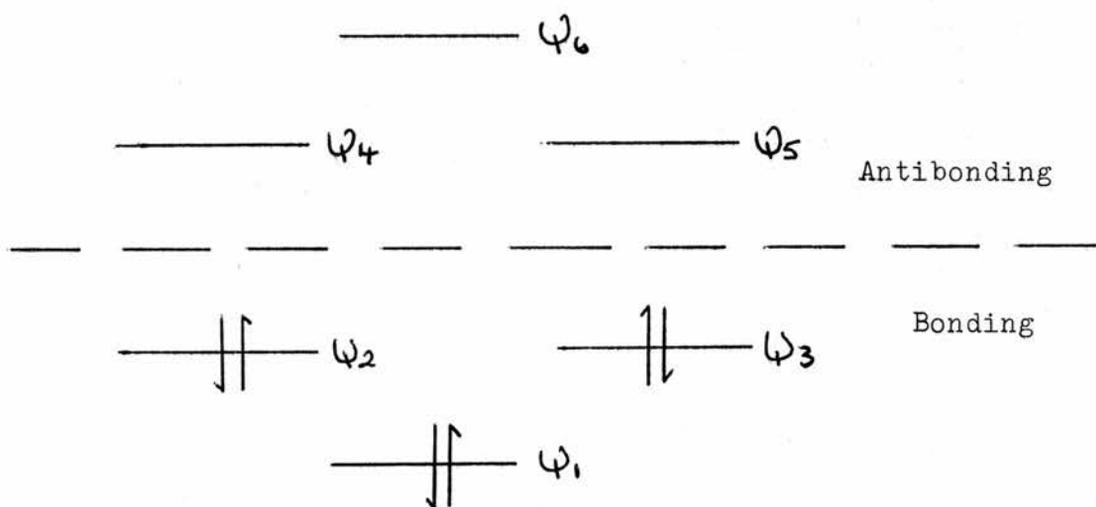
DISCUSSION

The problem of why certain cyclic polyolefins possess the properties of "reduced unsaturation and the tendency to retain type" i.e. are aromatic, when other cyclic polyolefins do not, was approached by Armit and Robinson²⁹ in 1925 when they formulated the concept of an "aromatic sextet" of electrons. Subsequently Hückel³⁰ proposed that "amongst fully conjugated, planar, monocyclic polyolefins, only those possessing $(4n + 2)$ π -electrons, where n is an integer, will have special aromatic stability." Thus benzene with six π -electrons ($n = 1$) shows aromatic character whereas cyclooctatetraene with eight π -electrons, behaves just as though it was a linear conjugated polyolefin.

Hückel's rule is concerned with the bonding of the atoms in the molecule. In the benzene molecule, the carbon s and $2p_x$ and $2p_y$ atomic orbitals are hybridised to give sp^2 hybridisation. The six carbon atoms are arranged in a regular hexagon which gives maximum overlap of two of the sp^2 hybrid orbitals of each carbon atom with those of the adjacent carbon atoms. This gives the σ -bonding of the benzene nucleus and the third sp^2 hybrid orbital points out from the centre of the planar molecule and overlaps with a $1s$ orbital of a hydrogen atom:



This leaves the non-hybridised $2p_z$ orbitals of the carbon atoms, containing one electron each, standing above and below the plane of the molecule. These are combined to form six molecular π -orbitals which have energy levels arranged symmetrically above and below the non-bonding level. The difference between these levels and those in a linear polyolefin is that the second and third levels are of equal energy:



The lowering of energy when the six electrons are delocalised into these π -orbitals is much greater than that achieved in a linear polyene and is known as the resonance energy. Thus the energy drop for the delocalisation of the π -electrons in buta-1,3,-diene is only $14.6 \text{ KJ. mole}^{-1}$ whereas in benzene it is about $148 \text{ KJ. mole}^{-1}$.

The resonance energy of a molecule can be correlated with its aromatic nature, since the greater the resonance energy is, the less likely is the compound to react in a manner which would destroy this stabilising π -orbital overlap (i.e. aromaticity) and so the more "aromatic" it is.

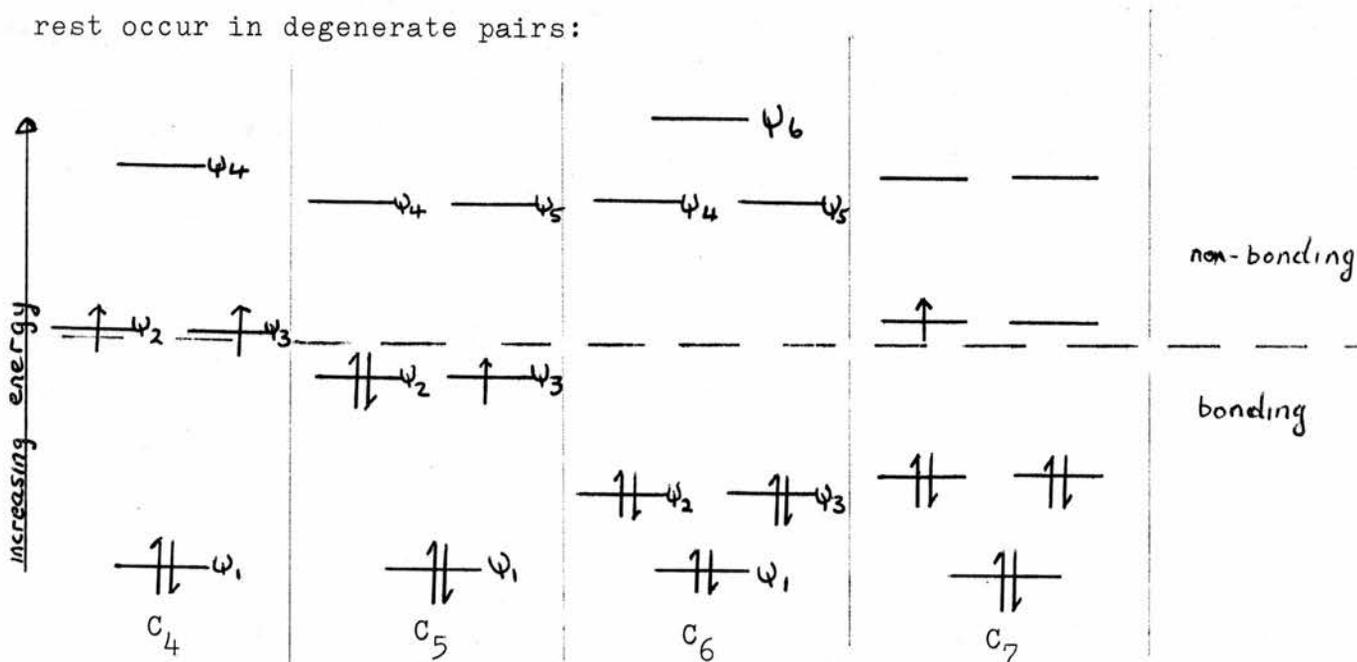
Although aromatic character is never absolute, an aromatic compound therefore does not exhibit the properties expected of its equivalent conjugated polyolefin. In general any compound which is considered to be aromatic will exhibit the following properties to some extent:

- a) high thermal stability
- b) reaction e.g. with HNO_3 , H_2SO_4 , Br_2 etc. occurs to give substitution rather than addition products (i.e. "retention of type")
- c) resistance to oxidation
- d) the properties of substituents are altered e.g. phenols are more acidic than alcohols and aniline is less basic than aliphatic amines and can be diazotised.

Benzene does not react immediately with bromine; it is difficult to hydrogenate; it is unaffected by ordinary oxidising agents and reacts with most electrophiles to give "addition with elimination" products i.e. substitution. A structural effect of the delocalised π -molecular orbitals is that all the carbon-carbon bonds are intermediate in length between carbon-carbon single and double bond lengths.

When considering other cyclic polyolefins with the general formula C_nH_n to see if they can be classified as aromatic or not, an important factor is the ring size. The molecule must be planar to allow for π -orbital interaction and also the sp^2 hybridised orbitals must exhibit a reasonable amount of overlap. In a five- or a seven-membered planar, cyclic polyolefin the overlap of the sp^2 orbitals is adequate though not as good as in a six-membered structure. The energy levels of the π -molecular orbitals also depend on the number of carbon atoms. In cyclic polyolefins with an even number of carbon atoms, the energy

levels of the lowest energy bonding orbital and the highest energy anti-bonding orbital are non-degenerate but all the remaining orbitals occur in pairs of equal energy. Where there is an odd number of carbon atoms however, the lowest bonding orbital only is non-degenerate and all the rest occur in degenerate pairs:

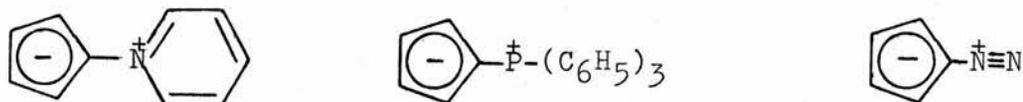


Hund's rule must be applied when assigning the π -electrons to their molecular orbitals and so, it can be seen that the C₄ molecule would be a diradical (i.e. triplet ground state). The C₅ and C₇ compounds each have an odd number of electrons in the ground state π -molecular orbitals and would therefore be free radicals. The C₆ compound (benzene), has all the bonding π -molecular orbitals filled with paired electrons.

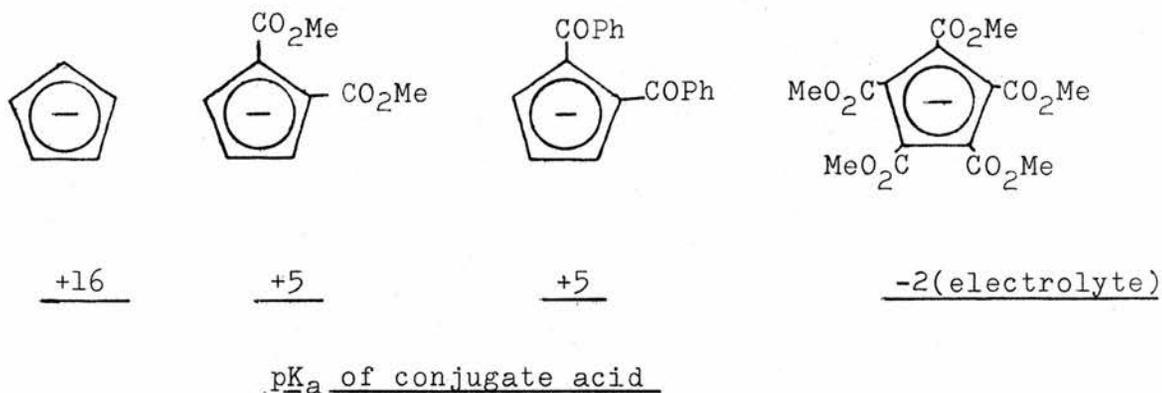
If the C₅ and C₇ cyclic polyolefins were to become iso-electronic with the C₆ compound they could reasonably be expected to be aromatic though probably to a lesser extent than benzene. If the C₇ compound lost an electron i.e. became a cation, it would become analogous to benzene and similarly, if the C₅ compound gained an electron by becoming an anion, the bonding π -molecular orbitals would be filled and the anion should be particularly stable.

Cyclopentadiene, C₅, has a $pK \approx 16^{31}$, which means that it is

more acidic than ethanol, and it readily forms an anion in presence of bases. The anion can be joined to some cationic centres to form ylids:



The phosphonium ylid couples with benzene diazonium chloride i.e. substitutes. Diazocyclopentadiene undergoes a series of addition with elimination reactions such as bromination, nitration, mercuration and also couples with diazonium salts. When carbonyl groups are introduced into the ring, the acidity increases considerably:

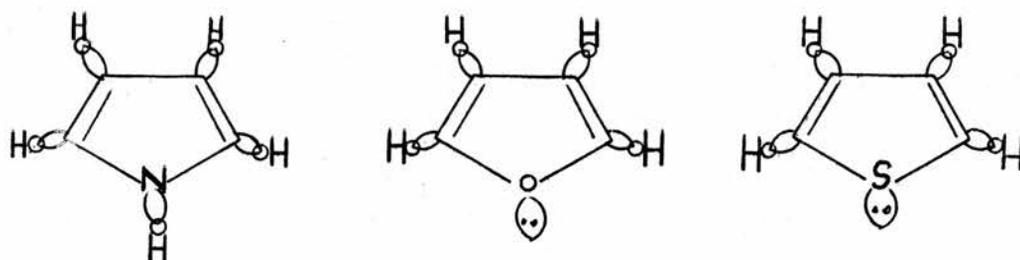


Therefore the cyclopentadienyl anion may be classified as an aromatic compound which leads to the possibility that the five-membered heterocyclic compounds, containing two double bonds and a hetero-atom capable of releasing electrons into a π -molecular orbital, may also be aromatic.

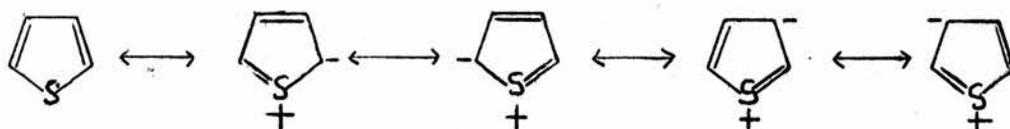
Pyrrole is a five-membered heterocyclic compound containing nitrogen in which all the ring atoms are sp^2 hybridised forming the σ -bond skeleton by overlap of two of the hybrid orbitals of each atom. The third sp^2 hybrid orbital of each atom, including nitrogen, overlaps with a hyd-

rogen atom $1s$ orbital. The unhybridised $2p_z$ orbitals of the carbon and nitrogen atoms can overlap to form π -molecular orbitals. Each carbon atom donates one electron, as in cyclopentadiene, but the nitrogen atom has two electrons in its $2p_z$ orbital so that the molecule is isoelectronic with the cyclopentadienyl anion. The nitrogen atom interferes with the relative energies of the π -molecular orbitals to the extent that they no longer occur in degenerate pairs. However, the first three orbitals into which the six π -electrons go, are all bonding molecular orbitals.

Furan can be treated similarly except that the third sp^2 hybridised orbital of the oxygen atom does not overlap with a hydrogen $1s$ orbital but contains a lone pair of electrons.



Thiophen, the sulphur containing heterocycle, is essentially similar to furan but with the complication that the valency electrons of sulphur have the principal quantum number 3 and therefore d-orbitals are available for bonding. If only the s- and p-orbitals are considered to be used, the molecular orbital picture of thiophen is the same as that of furan, with a lone pair of electrons in the third sp^2 hybridised sulphur orbital. Without d-orbitals, the following resonance hybrids can be constructed for thiophen:



However, Schomaker and Pauling³⁵ have suggested that the sulphur 3d-orbitals are involved in the bonding in thiophen. The energy difference between the 3p- and 3d-orbitals is small and Longuet-Higgins³⁶ proposed a pd hybridisation to give three pd^2 hybrid orbitals. Two of these hybridised orbitals are of the correct symmetry and energy to overlap with the carbon $2p_z$ orbitals to give the π -molecular orbital. The third hybridised orbital is of high energy and would be unoccupied in the ground state. If the 3d sulphur orbitals are involved, the following extra resonance hybrids for thiophen must also contribute:



Recently, Gerdil and Lucken³⁷ have used electron spin resonance spectroscopy on radical ions of dibenzothiophen and have compared the hyperfine splitting structure with that calculated for the two possible hybridisations and found that 3d-orbitals play no part in the bonding levels or the first unoccupied level of dibenzothiophen. This finding has been supported by polarographic reduction potentials and ultra-violet spectra³⁸ studies of dibenzothiophen.

Even if 3d-orbitals are involved in thiophen or the derivatives of thiophen used in this thesis, the canonical forms show that there is an excess negative charge on all the carbon atoms. Since sulphur is **less** electronegative than oxygen or nitrogen, it is more ready to release electrons into the π -molecular orbitals and there is good evidence to show that the electron delocalisation in thiophen is almost as complete as it is in benzene.

The electronic structure of thiophen is therefore similar to

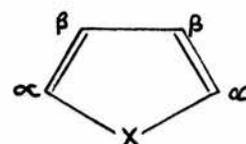
that of cyclopentadienyl anion and the physical and chemical properties support the belief that it is an aromatic compound. Thiophen is a colourless liquid^{with} an odour similar to benzene (when pure) and has a resonance energy¹³ of 120.1 KJ mole⁻¹. Although the physical properties of thiophen and benzene are of the same order in most instances, the marked divergence in freezing points is one example of dissimilarity³²:

	THIOPHEN	BENZENE
F.P. °C	-38.30	5.49
B.P. °C	84.12 (760mm)	80.10
n_D^{20}	1.5287	1.5014
d_4^{20}	1.0644	0.8791

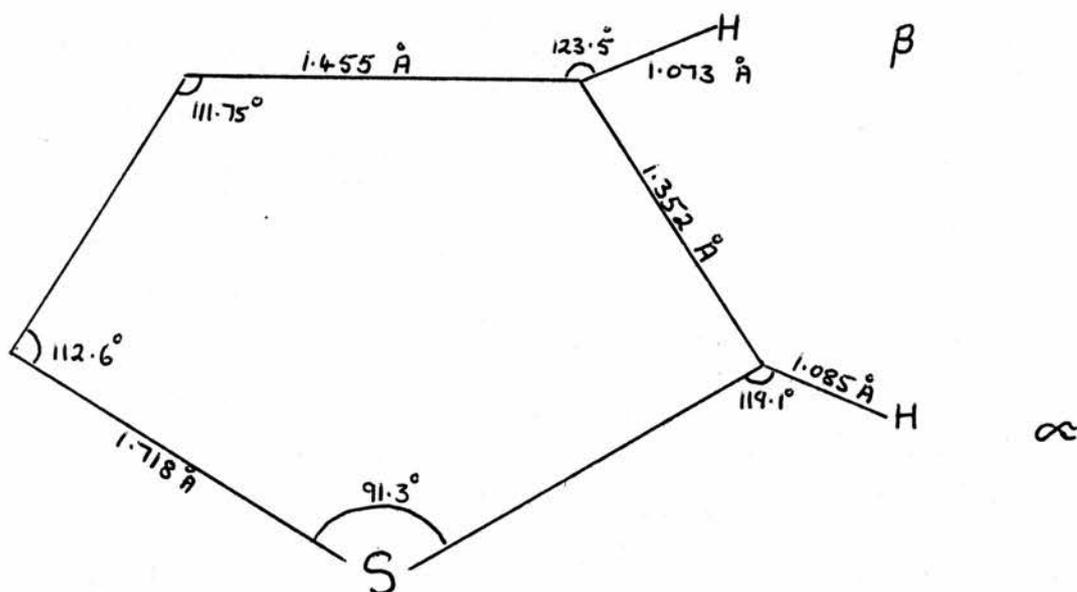
The ultra-violet absorption spectra are not closely related but thiophen is more similar to benzene than is pyrrole or furan. The nuclear magnetic resonance spectrum of a compound can give evidence of aromaticity. The magnetic field applied in determining these spectra induces circulation of the delocalised π -electrons setting up ring-currents which deshield the protons attached to the outside of the aromatic nucleus. In an aromatic compound this results in a large chemical shift in the n.m.r. spectra of these protons. From the following table³³ it would again seem that thiophen is more aromatic than pyrrole:

BENZENE	2.81 τ	
PYRROLE	α 3.47 τ	β 3.94 τ
THIOPHEN	α 2.84 τ	β 2.94 τ
FURAN	α 2.64 τ	β 3.72 τ

where



The dimensions of the thiophen molecule have been determined by a study of its microwave spectrum³⁴ and shows carbon-carbon bonds intermediate in length between double and single bond lengths:

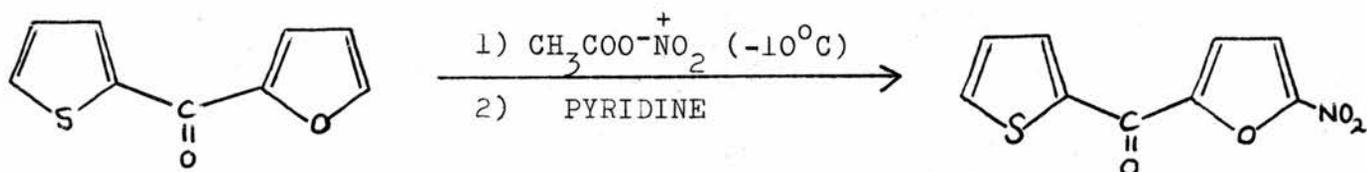


The carbon-sulphur bond length is shorter than a normal carbon-sulphur single bond (1.82 Å) and the carbon-sulphur-carbon bond angle is small, even less than the hydrogen-sulphur-hydrogen bond angle in hydrogen sulphide ($92.1^\circ \pm 0.2$).

All three five-membered heterocycles (pyrrole, thiophen and furan) are reduced more readily than benzene and can be oxidised although thiophen is the most stable. Furan readily undergoes Diels-Alder type addition and 1-methylpyrrole also does to a lesser extent but thiophen does not. Thiophen is also the most stable to acids and the least reactive to bromination.

Thiophen and its derivatives can be fairly described as aromatic compounds and should therefore be susceptible to substitution. In fact thiophen, furan and pyrrole are all more reactive to electrophilic reagents than benzene due to their unsymmetrical charge distributions resulting in the ring carbon atoms having a greater electron density

than those in benzene. Of the three systems, pyrrole is by far the most reactive while thiophen is the least. The following competitive reaction³⁹ exhibits the difference between thiophen and furan:



Substitution occurs preferentially at the 2- (5-) position in these compounds.

Furan shows only a limited aromatic character and thiophen is considered the most aromatic of the three heterocycles. Roughly, the reactivity to electrophilic substitution for pyrrole, furan and thiophen can be compared to the activated benzenoid compounds resorcinol, phenol and anisole respectively.

Aromatic diazonium salts are electrophilic reagents and will replace a hydrogen atom attached to a carbon atom when that atom is activated by an electron releasing group. A covalent N-C bond is formed and the diazonium salt is said to have coupled:



The resulting C-azo compound is strongly coloured due to the azo (-N=N-) linkage and the colour is intensified by increased conjugation.

The expectation that a sufficiently strongly-coupling diazonium compound would attack benzenoid hydrocarbons was realised when it was found that 2,4,6-trinitrobenzene diazonium salt reacts with mesitylene to form a crystalline azo-dye.²⁶

Benzene itself will not couple nor will durene⁴⁰ where the inductive effect of two ortho-methyl groups is insufficient to polarise either of the two coupling sites. It was noted by Saunders⁴¹ that only those benzenoid hydrocarbons having the mesitylene structure, where the three methyl groups are jointly able to polarise a hydrogen atom, are able to azo-couple. Similar results were found in the coupling of phenol ethers studied by Auwers^{42,43} in determining the effect of substituents in the ring and their effect on the point of attachment of the azo-link. He found that the para-position to the alkoxy group must be available and that coupling is most facile when a methyl group occupies both meta-positions i.e. when the configuration is that of mesitylene with one methyl group replaced by an alkoxy group (one characteristic of the azo-coupling of these compounds is that the alkoxy group is partially, or sometimes completely removed, depending on the diazonium salt used).

2,4-Dinitrobenzene diazonium sulphate was known to couple with anisole²⁷ but no report was found of it coupling with mesitylene. Experiments were carried out to test the reactivity of this diazonium salt with anisole and also with mesitylene.

2,4-Dinitroaniline was diazotised by the method of Saunders⁴⁴ and added to a solution of anisole in glacial acetic acid. Coupling reactions in highly acidic media are known to be slow and, although the solution became orange/red coloured on mixing, it was many hours before any precipitate appeared. About 70 hours reaction at 0°C was found to give a 26% yield of the azo-dye 4-(2',4'-dinitrobenzene)-azo-methoxybenzene. Extraction of the reaction mixture with chloroform followed by column chromatography of the washed and dried extract gave a small amount of a brown solid whose mass spectrum suggested the presence of the mono- (m/e 274) and di- (m/e 440) arylated anisoles but the sample could not be purified sufficiently to give a satisfactory analysis. Only 0.1%

yield of this impure material was found and no detectable amount of nitrogen was given off during the reaction.

In a similar reaction using mesitylene, a 5% yield of the azo dye 1-(2',4'-dinitrobenzene)-azo-2,4,6-trimethylbenzene was found. Surprisingly no report of this coupling reaction could be found in the literature. In addition to the deep red needles of the azo compound, a small yield (1%) of yellow needles of the arylated compound 1-(2',4'-dinitrophenyl)-2,4,6-trimethylbenzene was obtained by chromatography. In the reported coupling of diazotised picramide²⁶ with mesitylene, no mention is made of any arylated derivatives being isolated.

Under the conditions used in these experiments it would seem that the less activated the proposed coupling site is, the more likelihood there is of some arylation products being formed.

A literature search of the attempted azo coupling reactions of thiophen and its derivatives shows that some activated thiophens couple normally to give azo dyes. Friedländer⁴⁵ found that 3-hydroxy-thianaphthene couples with diazonium salts in a similar manner to 1-naphthol to form azo dyes. 2-Acetamido thiophenes were reported²⁴ to couple where the equivalent acetylated arylamines will not (e.g. acetanilide will not couple with a diazonium salt although aniline does readily). Quite a range of azo-dyes have been prepared by diazotisation of 2-^{17,18,19} and 3-²⁰ amino thiophens but all the reported attempts at coupling of diazonium salts with hydrocarbon thiophens have led to the formation of arylated products only. Gomberg and Bachmann²⁸ in 1924 noted that the formation of bi-aryl compounds through diazo reactions had been observed at various times by different investigators. Bamberger⁴⁷ developed the method employing what he termed "diazonium oxides" formed as precipitates by adding acetic acid to concentrated solutions of alkali aryl diazotate, RN_2OK . These compounds are very unstable and highly

explosive even when moist and this led to Gomberg and Bachmann developing the technique of adding aqueous sodium hydroxide solution dropwise, with cooling, to the mixture of the diazonium salt and the aromatic compound until the reaction was just alkaline. The bi-aryl derivatives were removed from the solution by steam distillation and the residue was found to contain polymers of chains of the aryl components coupled together. They concluded that alkali was essential to the formation of the bi-aryl compounds and assumed that the "diazo-oxide" was involved although it was not isolated.

Using this method, they succeeded in producing a large number of bi-aryls including several thiophen derivatives.

REAGENT	AMINE	PRODUCT	M.P. °C	YIELD %
Benzene	aniline	biphenyl	70.5	22
thiophen	aniline	phenylthiophen	42-43	11
benzene	4-bromoaniline	4-bromobiphenyl	91.2	40-46
thiophen	4-bromoaniline	4-bromophenylthiophen	100	20
benzene	4-chloroaniline	4-chlorobiphenyl	77.7	41
thiophen	4-chloroaniline	4-chlorophenylthiophen	83	24
benzene	4-nitroaniline	4-nitrobiphenyl	114	30
thiophen	4-nitroaniline	4-nitrophenylthiophen	137-138	23

Freund⁴⁸ coupled diazotised arsonilic acid with thiophen in sodium acetate buffered aqueous acetone and obtained the 2- or 3- arylated product only.

The homolytic aromatic arylation of thiophen has been studied systematically recently⁴⁹, including the Gomberg reaction, the thermal decomposition of N-nitroso-acetanilides and diaroyl peroxides. It was found that all the phenylating reagents tested gave 2- and 3-phenylthiophens in the ratio 90-95:10-5 except for phenylazotriphenylmethane which was identified as a special case. Another method of forming aryl thiophens was due to Mohlau and Berger⁵⁰ who added aluminium chloride to a suspension of a dry diazonium chloride in suspension in thiophen (also in other compounds). The yields were small.

The work recorded in section A of this thesis (Part I) involves the addition of a powerful diazonium salt, 2,4-dinitrobenzene diazonium sulphate, to a range of thiophen hydrocarbon compounds in glacial acetic solution. The glacial acetic acid specifically rules out the Gomberg free radical arylation mechanism since the necessary intermediates "diazo-oxides" or "diazo-anhydrides" are only formed above pH=7.

Equimolar proportions of diazonium salt to thiophen derivative were used in all the experiments and all recorded yields allow for any recovered starting material.

When diazotised 2,4-dinitroaniline was added to a solution of thiophen in glacial acetic acid, the solution immediately became orange coloured and darkened fairly quickly to a deep red. After a period of 70 hours, a red oil had separated out and was collected and chromatographed on an alumina column. The reaction mixture was also chloroform extracted to give more of the products found by chromatography of the oil. The first component eluted was a yellow oil which crystallised on standing but also decomposed to a sea-green coloured oil. Purification by chromatography on a silica column in the dark and recrystallisation from benzene/petrol 60/80 mixture gave yellow crystals of the mono-arylated compound 2-(2',4'-dinitrophenyl)thiophen. The 17% yield compares well with Gomberg's yield from 4-nitrobenzene diazonium chloride allowing

for loss on the column.

A second yellow component eluted by benzene was found to be the di-arylated compound 2,5-bis-(2',4'-dinitrophenyl)thiophen but only a 3% yield was obtained. Chloroform eluted a red oil which was recrystallised from benzene/petrol 60/80 and was found to be the 2,3,5-tris-(2',4'-dinitrophenyl)thiophen derivative. The compound could not be purified any further and only a 2% yield was found. All the results are tabulated in Table I.

No azo dye was found. In an attempt to discover what happened to the remainder of the reaction reagents, the experiment was repeated and the reaction mixture plus oil was chloroform extracted, as a whole. The chloroform extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. The solvent was removed and the resulting oil was boiled with first petrol 60/80 which was decanted off hot. The residue was boiled with benzene and the final residue was soluble in acetone. The three solutions were evaporated down to oils and studied by mass spectrometry. The petrol 60/80 and benzene solutions contained only the arylated derivatives as expected and the acetone solution gave a mass spectrum going up to only m/e 184 (probably unreacted 2,4-dinitroaniline^(P+1)). This was less than 1% of the starting material and certainly no high molecular weight polymers of thiophen were found. This probably eliminates any mechanism which involves ring-opening of thiophen since this would invariably lead to the formation of polymeric tars. This experiment also suggests that much higher yields of products are being formed than are found after chromatography.

An experiment was carried out using 4-nitrobenzene diazonium chloride instead of the more powerful diazonium salt, 2,4-dinitrobenzene diazonium sulphate, used above. The glacial acetic acid medium was used and the mono- and di-arylated derivatives were found in 11% yield and 5%

yields respectively (see Table I). The 2-(4'-nitrophenyl)thiophen was as light sensitive as the 2,4-dinitrobenzene diazonium salt equivalent.

The findings of these experiments were that not only were no azo compounds formed in conditions which produced dyes with anisole and mesitylene, but that arylated derivatives were found although highly acidic solutions were used. Under identical conditions, benzene did not arylate at all and anisole and mesitylene only did in trace amounts.

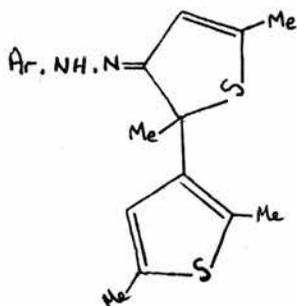
Since molecular nitrogen must be evolved in these arylations, the experiments were repeated and the volumes of nitrogen evolved were measured against time. With thiophen, after a small delay, nitrogen was rapidly given off so that after only $4\frac{1}{2}$ hours, 50% of the theoretical total amount was evolved and by the end of 70 hours, the normal reaction time, 92% of the theoretical volume was collected (it was found that the dilution of the thiophen in the glacial acetic acid affected the rate of nitrogen given off but, that the actual conditions chosen for the full scale experiments gave optimum results over the time the reactions were run). Using the 4-nitrobenzene diazonium chloride, the evolution of nitrogen gas was much slower and only one-sixth of the theoretical amount had been evolved after 24 hours.

In 2,5-dimethylthiophen, the 3-positions are so highly activated that they can be easily replaced by iodine on direct iodination⁵¹ or by nitro groups⁵² and on mixing with 2,4-dinitrobenzene diazonium sulphate the solution rapidly became dark red coloured. After 68 hours, the dark red gummy solid which had formed was collected, taken up in chloroform, washed with water, aqueous sodium bicarbonate solution, water and dried. Evaporation of the solvent gave a dark red oil which, under reduced pressure, filled the flask as a red "glassy" solid. The compound was very difficult to recrystallise and was purified by column chromatography. It was identified as the first azo-coupled hydrocarbon thiophen; 2,5-

dimethyl-3-(2',4'-dinitrobenzene)-azo-thiophen (see table I).

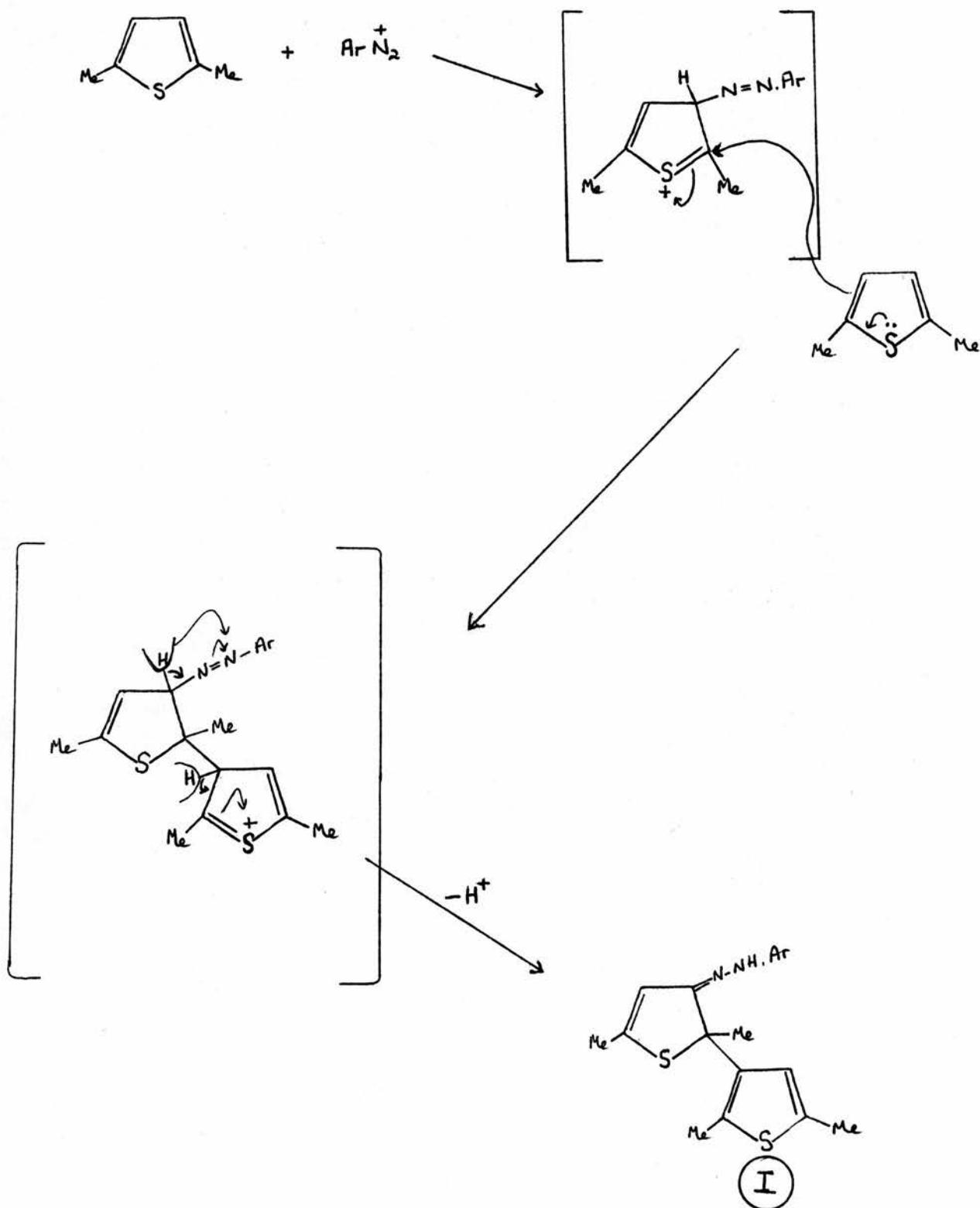
The reaction filtrate was chloroform extracted and gave more of the azo compound on chromatography together with another light sensitive compound found to be the mono-arylated derivative, 2,5-dimethyl-3-(2',4'-dinitrophenyl)-thiophen. A small amount of the di-arylated derivative, 2,5-dimethyl-3,4-bis-(2',4'-dinitrophenyl)-thiophen, was eluted by chloroform.

Between the two arylated compounds, two bright orange/red compounds were eluted in small yield, differing in m.p. by only 9°C. From the mass spectrum and analysis the lower melting compound was given the molecular formula $C_{18}H_{18}N_4S_2O_4$. The mass spectrum suggested that the molecule contains a 2,4-dinitrobenzene diazonium unit and two 2,5-dimethylthiophen units; also a strong peak at m/e 306 indicated the presence of the azo dye molecule; the infra-red spectrum had an N-H (O-H) absorption at 3300 cm^{-1} and this together with the light orange colour, suggested that the azo link had been altered although the N atoms were intact. The n.m.r. spectrum showed the 2,4-dinitrobenzene unit protons at $\tau(CDCl_3)$ 0.9 (d, 1H); 1.7-1.9 (m, 1H); 2.2-2.3 (d, 1H). Two thiophen nucleus protons were detected at 3.3 τ (s, 1H) and 3.7 τ (s, 1H). There were two doublets of six protons each at 7.6 τ and 7.9-8.0 τ and the undetected proton would be the N-H one. From this information the structure (I) was proposed for this compound:



(I)

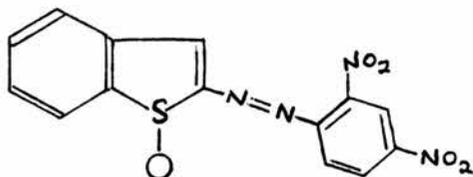
The following mechanism is proposed for the formation of compound (I):



The other red solid was similar in appearance to (I) but was found to have a mass 12 units higher; to contain the azo dye unit; to have a similar analysis, an infra-red absorption at 3280 cm^{-1} (v.s.) but to be insufficiently soluble even in D.M.S.O. to give an n.m.r. spectrum. No structure has been proposed for this compound which was obtained in too small a yield to pursue further.

2,5-Dimethylthiophen therefore is a case where both azo-coupling and arylation occur and it begins to look as if the thiophen reagent is of importance in the mechanism i.e. some coupled compound is formed between the thiophen and the diazonium salt, the decomposition of which depends on the thiophen substituents. The 2,5-dimethylthiophen is the only thiophen derivativetested to give an azo dye (cf. section B, 2,5-dimethylfuran).

Thianaphthene was reacted with 2,4-dinitrobenzene diazonium sulphate under the same conditions and three compounds were isolated. The first, which precipitated out of the reaction mixture, was a bright orange/red solid found to have a molecular formula $C_{14}H_8N_4O_5S$. The infra-red spectrum showed the lack of an -O-H (-N-H) absorption and the mass spectrum showed the presence of a 2,4-dinitrobenzene unit and a thianaphthene nucleus. From this evidence a possible structure is (II):



(II)

2-(2',4'-dinitrobenzene)-azo-thianaphthene-S-oxide.

This compound was obtained in very low yield and its structure and mechanism of formation were not pursued further.

From chloroform extraction of the reaction mixture, the mono- and di- arylated derivatives were isolated by chromatography. 2-(2',4'-Dinitrophenyl)-thianaphthene was found as yellow/orange needles, not sensitive to light, in 50% yield. The 2,3-bis-(2',4'-dinitrophenyl)-thianaphthene was found as a yellow solid in 13% yield. Although a high percentage of arylated compounds was found, the rate of evolution of nitrogen was found to be about the same as with thiophen.

From this it appears that extended delocalisation of the aromatic π -electrons has increased the amount of arylation and also the ratio of the di-aryl to the mono-aryl derivative formed. As some dibenzothiophen was available it was used in an experiment to see if any arylation would occur and if so, where. However, nearly all of the dibenzothiophen was recovered unreacted and the mass spectrum of the residue showed the highest peak at m/e 200 with no evidence of any aryl or azo compound.

Triphenylthiophen was prepared from desylacetophenone as white plates. These were found to be sparingly soluble in glacial acetic acid and the coupling reaction had to be carried out on a dilute scale. The major product isolated (65%) was 4-nitro-2,3,5-triphenylthiophen. About 10% yield of the impure arylated compound 4-(2',4'-dinitrophenyl)-2,3,5-triphenylthiophen was found which could not be recrystallised satisfactorily.

The experiment was repeated and the high yield of the nitro compound was confirmed. The low solubility of this thiophen is believed to be a factor in the poor yield of the arylated compound and the formation of the nitro compound was not found in any other thiophen tested.

The results of the coupling reactions with these thiophens are shown in table I below:

TABLE I: AZO COUPLING OF THIOPHENS IN GLACIAL ACETIC ACID SOLUTION

REAGENT	AMINE	DERIVATIVE	YIELD(%)	M.P. °C	COLOUR
Thiophen	4-Nitro-aniline	Mono-aryl	11	135	Yellow ^{L.S.}
		Di-aryl	5	148	Yellow
Thiophen	2,4-dinitro-aniline	Mono-aryl	17	60	Yellow ^{L.S.}
		Di-aryl	3	172	Yellow
		Tri-aryl	2	(126)	Red
2,5-Dimethyl-thiophen	2,4-dinitro-aniline	Azo	38	233	Dark red
		Mono-aryl	2	70	Yellow ^{L.S.}
		Di-aryl	2	(oil)	Red
		Compound I	2	197	Orange
Thianaphthene	2,4-dinitro-aniline	Mono-aryl	50	104	Yellow/orange
		Di-aryl	13	120	Yellow
		Compound II	1	290	Orange
2,3,5-Triphenyl-thiophen	2,4-Dinitro-aniline	4-Nitro-	65	168	Yellow
		4-Aryl-	10	76	Red
Dibenzo-thiophen	2,4-Dinitro-aniline	Recovered starting material			
Benzene	2,4-Dinitro-aniline	No aryl or azo products found			
Mesitylene	2,4-Dinitro-aniline	Azo	5	164	Deep red
		Mono-aryl	1.1	125	Yellow
Anisole	2,4-Dinitro-aniline	Azo	26	177	Orange/red
		(Mono-aryl)	(0.1)	(101)	Brown

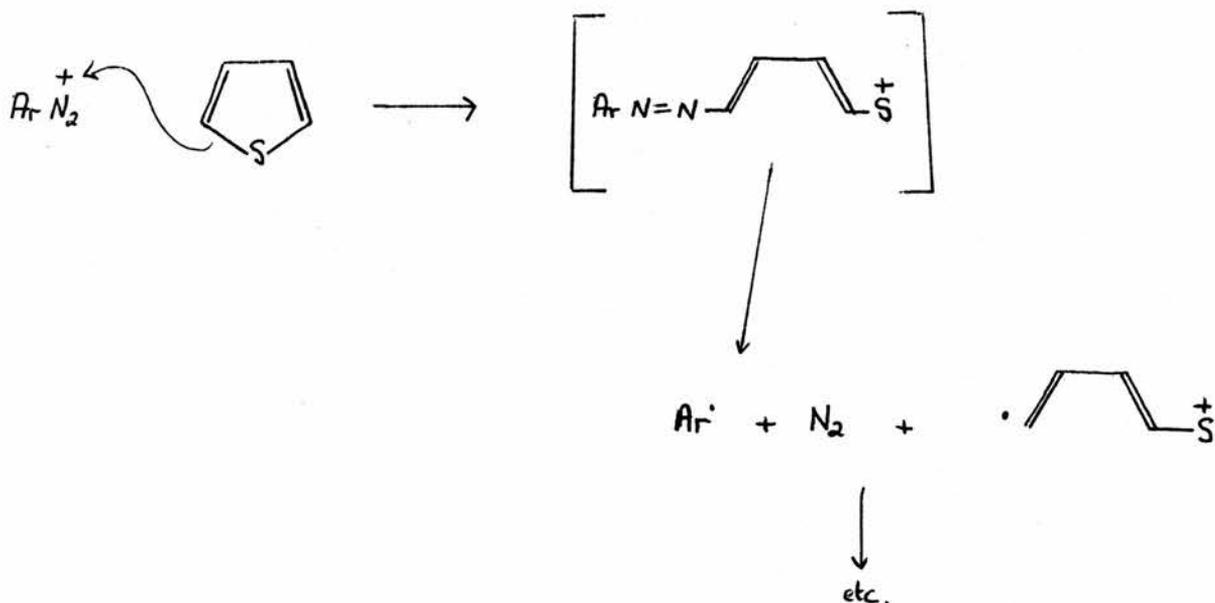
Thus the experiments have established that thiophen itself does not couple with a powerful diazonium salt to give an azo dye. If thiophen is compared to benzene which does not couple either, then, 2,5-dimethylthiophen should be compared to mesitylene and an azo dye is obtained. The methyl groups highly activate the 3-position coupling site protons^{51,52} and therefore we come back to the original finding that only activated thiophens couple to give azo dyes. Extension of the aromatic system by either ring fusion or conjugation does not activate the appropriate coupling site protons and azo dyes are not found. It is of note that there is no report of naphthalene azo coupling though 1-methylnaphthalene is reported²⁶ to couple with 2,4,6-trinitrobenzene diazonium salt but the azo compound was not isolated. It may be of interest to react naphthalene, 1,3,5-triphenylbenzene and similar compounds with 2,4-dinitrobenzene diazonium sulphate in glacial acetic acid solution.

The initial project has dealt with the azo coupling of a range of thiophens with a strongly coupling diazonium salt in acidic conditions. The fact that only the "activated" 2,5-dimethylthiophen yields the azo dye suggests that thiophen itself is not as reactive as mesitylene although it is known to be more reactive than benzene itself. However, the rapid evolution of nitrogen and the formation of arylated products, in fairly high yields, achieved with thiophen in these acidic conditions but not with benzene, mesitylene or anisole, indicates that some other factor is involved. The similarities and differences between thiophen and benzene have often been discussed so that Hartough⁵⁴ stated that thiophen and benzene ought to be compared as closely as a zoologist would compare the tortoise and the boa constrictor. Gronowitz⁵⁵ adds that it is thiophen which is the boa constrictor, but concludes that although he can demonstrate that many properties and reactions of thiophen derivatives are very dissimilar from

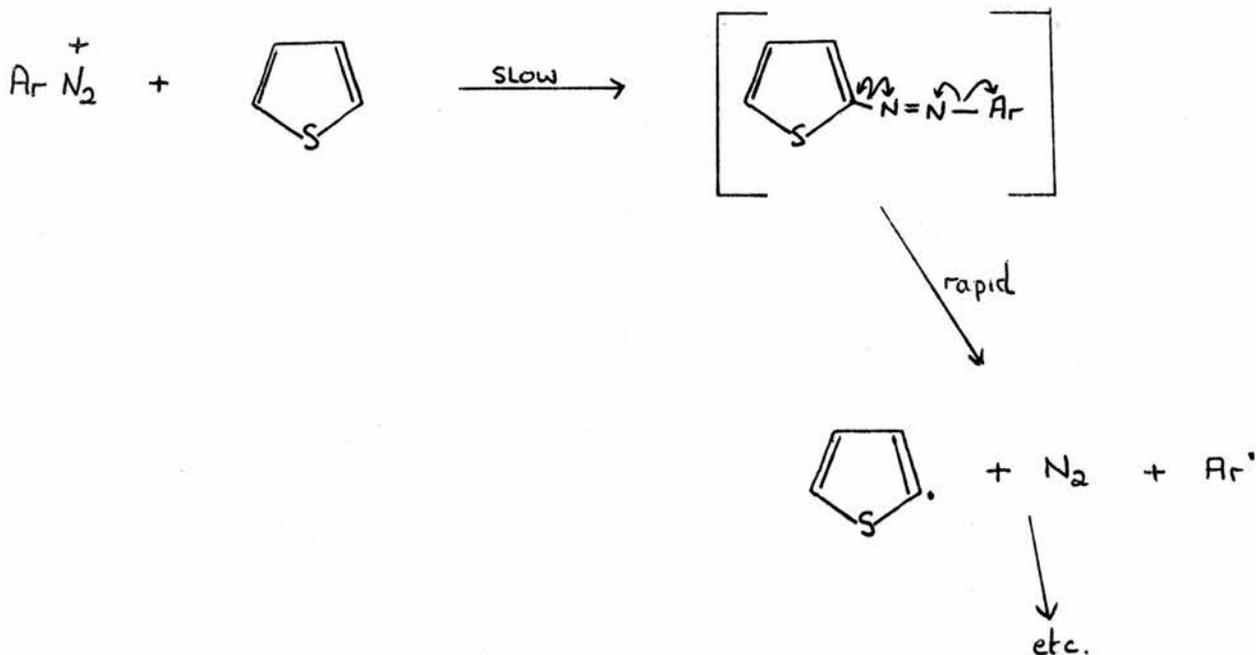
benzene he can give a longer discussion on the similarities.

This work has found another dissimilarity in that the thiophen derivatives induce the loss of nitrogen and the formation of arylated compounds when treated with diazonium salts, in acid solution. The Gomberg "diazo-anhydride" intermediates could not be formed at the low pH used and in any case, arylated benzene products would also be formed. The small time lag before the evolution of nitrogen occurs supports the belief that coupling of the diazonium salt and the thiophen derivative occurs initially.

If the coupling occurs at a ring carbon atom, one possibility is that of ring opening followed by decomposition into free radicals:

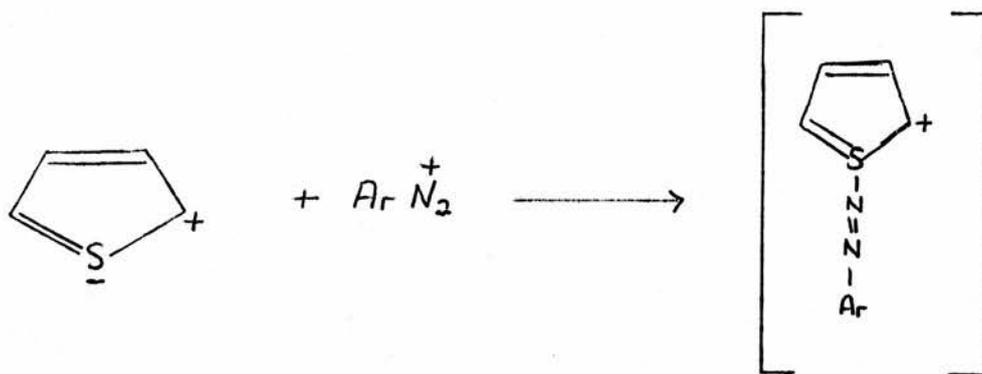


This mechanism should lead to the formation of some high molecular weight polymers of the thiophen fragment and none were found. An alternative of this mechanism would involve breakdown to radicals without ring opening:

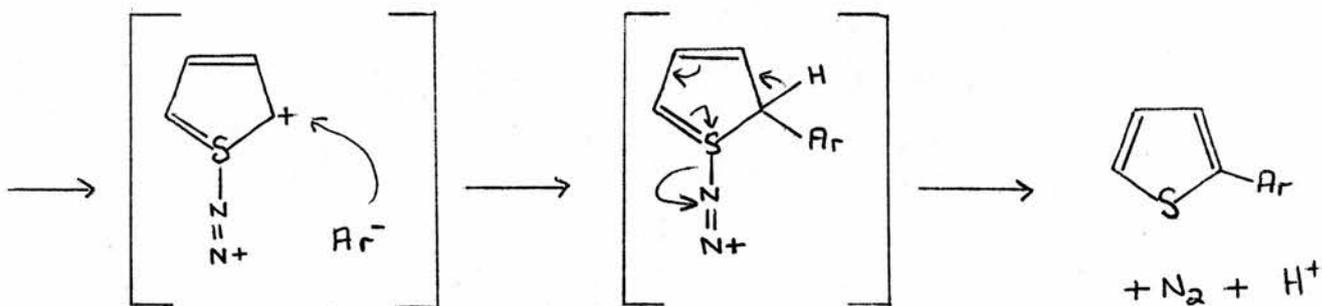


This infers that the thiophen nucleus, by some inherent property, presumably connected with the sulphur atom, is responsible for the breakdown of the azo compound. If this were so, the stability of the 2,5-dimethylthiophen azo compound is difficult to explain, since the methyl groups can have little effect on the overall electronic structure of the molecule. Again no bi-thiophens were found (except for compound I) although, in this case, the dilution of the reagents involved, may result in the re-coupling of the radicals, produced from any particular molecule breakdown.

E.C. Kooyman⁵⁶ recently stated ' the extreme ease of electrophilic substitution reactions with thiophen, is often attributed to the electron-donating properties of the sulphur atom, with respect to the 2- and 5- positions. In our opinion, the possibility of a primary attack on sulphur should not be excluded.' By the use of its 3d-orbitals, the sulphur atom can be shown to have a negative charge in some of its **canonical forms** (see page 12) and so initial coupling could occur at the sulphur atom:



This intermediate could breakdown into free radicals as before or could ionise:



(the mechanism could be either inter- or intramolecular)

Since no bi-thiophens were found, the latter mechanism is the better one. The formation of azo compounds with 2,5-dimethylthiophen also supports this mechanism since the methyl groups activate the 3- and 4- positions so that the primary electrophilic attack occurs at the 3- carbon atom preferentially.

Since pyrroles azo couple normally and, seemingly, only "activated" thiophens do, it was decided to repeat the reactions using a series of furan derivatives so that all three five membered heterocycles could be compared.

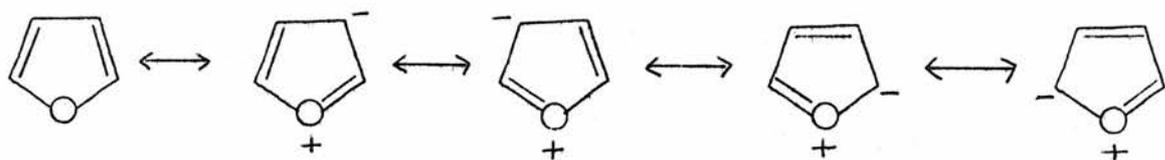
PART I SECTION B

THE COUPLING REACTIONS OF FURAN AND ITS DERIVATIVES

DISCUSSION

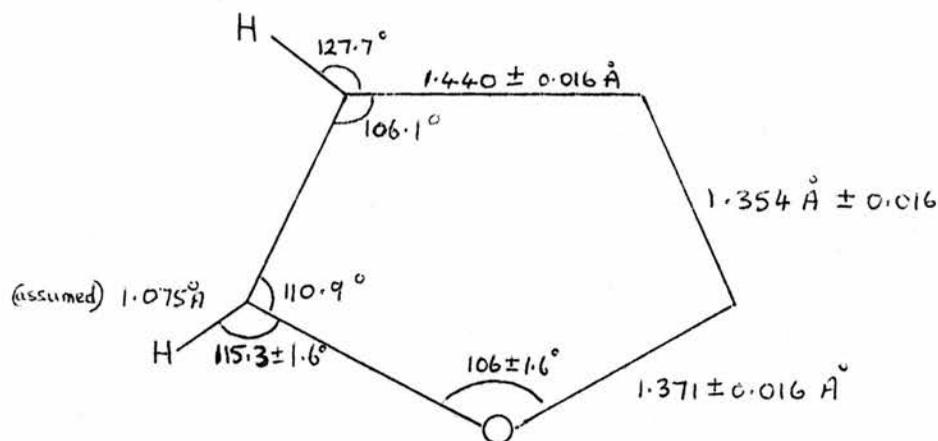
The earliest furan derivative reported was pyromucic acid (furan-2-carboxylic acid) which was obtained by Scheele, in 1780, from the dry distillation of mucic acid. Furan itself was not obtained until 1870 and in 1920, furfural (furan-2-aldehyde) became available in large quantities, from the acid hydrolysis of oat husks, so greatly stimulating searches for its uses and resulting in the development of the chemistry of furan.

Furan is the five-membered heterocyclic compound containing oxygen as the hetero-atom. The oxygen atom donates two electrons into the π -molecular orbitals, so making furan isoelectronic with benzene and thiophen. The oxygen atom has a lone pair of electrons in the third sp^2 hybrid orbital as does sulphur in thiophen but, unlike sulphur, it has no d-orbitals available for bonding. As a result, the **canonical forms** which can be constructed put excess negative charges on the carbon atoms, making electrophilic attack at the hetero atom unlikely. Some of the hybrids are illustrated below:



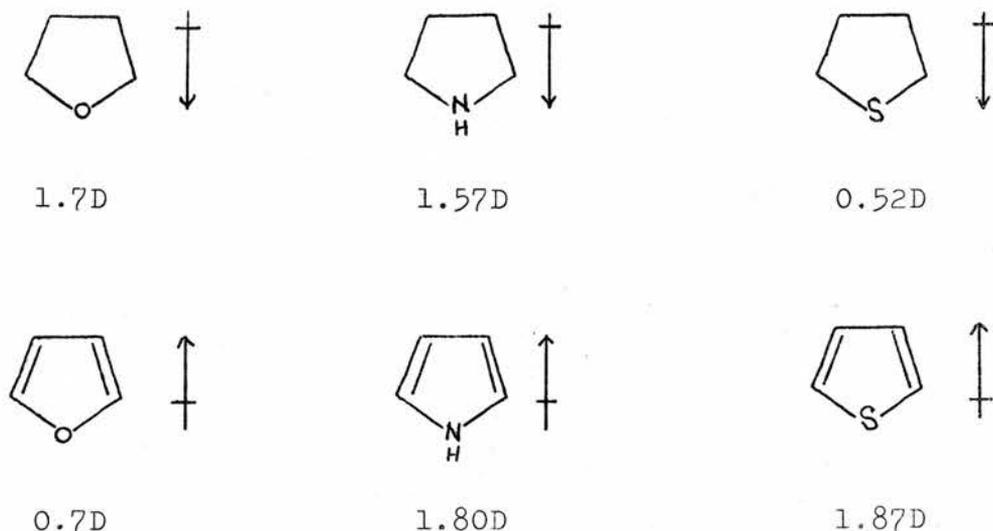
Furan is a colourless liquid b.p. 31.36°C with a chloroform

like odour. Microwave studies have shown that the furan molecule is planar⁵⁷ and have given the following molecular parameters⁵⁸:



When compared with 2,5-dihydro- and tetrahydrofuran parameters, furan shows shortened carbon-oxygen bond lengths and a contracted carbon-oxygen-carbon bond angle. However, the C₃-C₄ bond length is greater than a carbon-carbon bond length in benzene and the C₂-C₃ (C₅-C₄) bond length is very close to that of an ordinary ethylenic double bond.

This suggests that the "aromaticity" of furan is not as complete as that of thiophen and this is confirmed by reference to the comparative resonance energies and nuclear magnetic resonance spectra, illustrated in Section A. The fact that oxygen is more electronegative than sulphur or nitrogen is responsible for this since the oxygen atom will release its electrons less easily and delocalisation will be restricted. This tendency is seen by reference to the dipole moments of the three heterocycles and comparison with the dipoles of the tetrahydro- derivatives⁵⁹ (the arrow points to the negative end of the dipole):

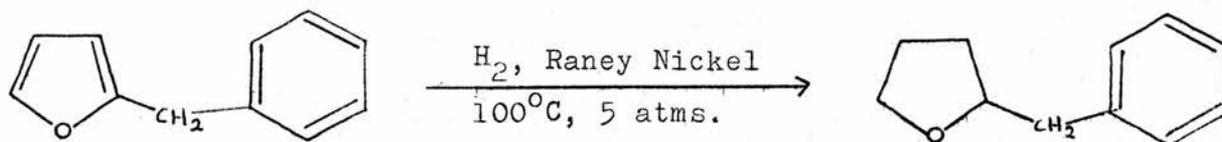


The physical data therefore suggests that furan should behave mainly as a diene ether which possesses a high degree of resonance stabilisation. It follows that suitable, electron-donating substituents will increase the "aromaticity" while other substituents will result in the development of the aliphatic chemical character.

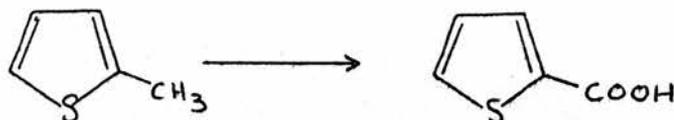
Although the aromatic stabilisation of furan, in terms of the physical factors discussed, is less than that of benzene, pyrrole or thiophen, the 2- (5-) carbon atom carries an excess negative charge which is greater than that in thiophen (assuming that the sulphur d-orbitals are involved, resulting in a less unsymmetrical charge distribution i.e. greater delocalisation). This means that furan is more susceptible to electrophilic attack than thiophen and can be compared with phenol for reactivity but, often, the attack leads to the formation of addition, rather than substitution, products.

Furan can be easily hydrogenated to tetrahydrofuran using a Raney nickel catalyst but thiophen poisons the catalyst, giving ring opened products (possibly indicating that the sulphur atom is the point of attack). Benzene is unaffected by these conditions as

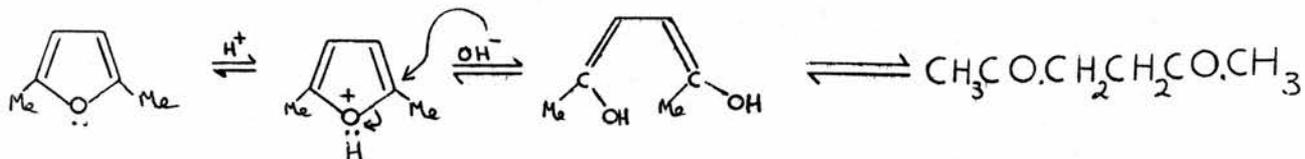
is shown by the following experiment:



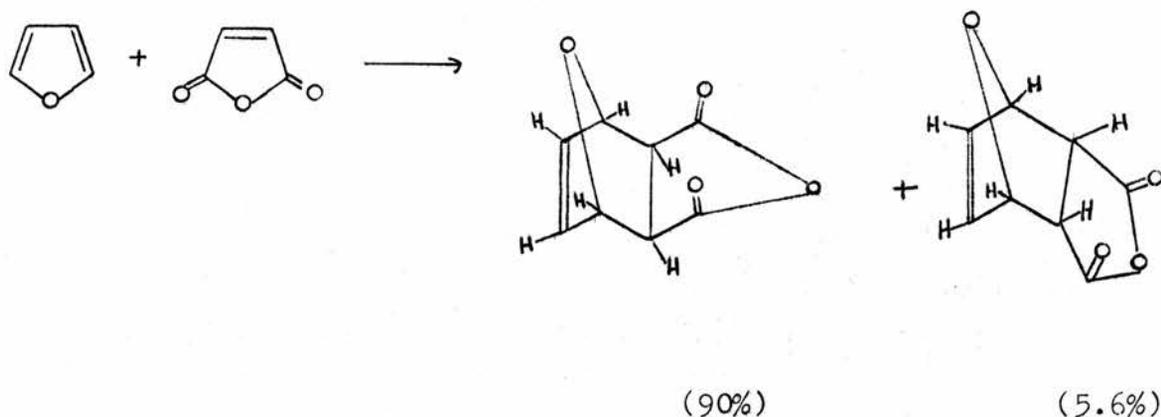
Furan is not as stable to oxidation as thiophen is and gives complex products (as does pyrrole) under conditions in which, for example, 2-methylthiophen can be oxidised with chromic acid to the corresponding 2-carboxylic acid:



Furan readily undergoes ring opening with mineral acids and with hydrochloric acid gives a mixture of succindialdehyde and polymer. With some 2,5-disubstituted furans, the ring opened compound can be obtained in quantitative yield.



Furan retains enough of its diene ether properties to enable it to undergo Diels-Alder type addition reactions. With maleic anhydride the expected adducts are found:



Furan can only be nitrated successfully at low temperatures and under anhydrous conditions. Furan cannot be sulphonated under ordinary conditions due to resonification, but with 1-proto-1-pyridinium sulphate in ethylene dichloride, an excellent yield of the 2-sulphonic acid is obtained, although these conditions do not attack toluene.

Furan normally gives a complex mixture of products on bromination but, under special conditions, the products of 2,5-addition can be isolated. Furan and pyrrole are so reactive that they can be acylated without using a catalyst where thiophen cannot. However, thiophen can undergo a Friedel-Crafts alkylation but furan and pyrrole undergo degradation due to the conditions used.

Thus, furan shows a limited aromatic character but is more reactive than thiophen. It often undergoes 2,5-addition in which cases it effectively behaves as a conjugated diene. Nevertheless, the higher reactivity to electrophilic reagents suggested that it would be worth reacting furan and its derivatives with a powerful diazonium salt even though ring opening could be expected from the use of the glacial acetic acid as the reaction medium.

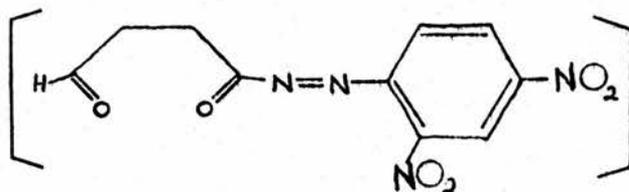
After a study of the condensation reactions of furans with

diazomethane, diazoacetic ester and related compounds it was reported⁶⁰ that the difficulty in preparing simple furan diazonium compounds is due, in part, to the ready coupling reaction of the diazonium group formed, with other furan nuclei. Amino-furans like amino-thiophens are unstable in the air and although 2,5-dimethyl-3-aminofuran is reported⁶¹ to diazotise and couple with 2-naphthol, little is known of the 2-aminofurans. A report of the preparation of nitroso-hydroxy-furans⁶², which could be useful in the preparation of some furan diazonium salts, seems dubious and Elderfield⁶³ states "that a re-investigation of the above compounds would be most welcome".

Hydroxy-dibenzofurans are reported⁶⁴ to couple readily with diazonium salts to give azo compounds. Johnson⁶⁵ has found 2- and 3-arylated furans from the coupling carried out in an alkaline solution i.e. under Gomberg conditions; and there are several other reports of arylations occurring under other conditions.^{66,67,48,49} Eugster²⁵ has successfully coupled activated 2,5-dimethoxyfuran but there are no reports of the coupling of simple furans with diazonium salts.

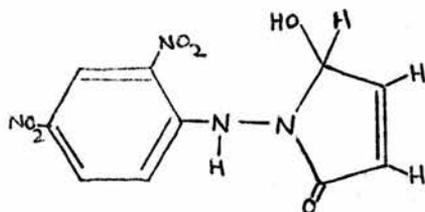
In the first reaction of the series, 2,4-dinitrobenzene-diazonium sulphate was added to an equimolar proportion of furan in glacial acetic acid and the mixture was stirred at room temperature for 70 hours. The precipitate that had formed was filtered off and recrystallised from acetone/benzene several times to give bright yellow crystals of compound **AI**. This was found to have a molecular weight of 280 and was assigned the molecular formula $C_{10}H_8N_4O_6$ from the elemental analysis. The infra-red spectrum showed the presence of an -OH (-NH) group (ν_{max} 3300 cm^{-1}) and a carbonyl group (ν_{max} 1680 cm^{-1}) and the mass spectrum and the nuclear magnetic resonance spectra confirmed the presence of a 2,4-dinitrophenyl unit. From

this evidence it seemed likely that an azo linkage had been initially formed between the diazonium salt and either furan, which then ring opened, or with the already ring opened furan to give structure (III).

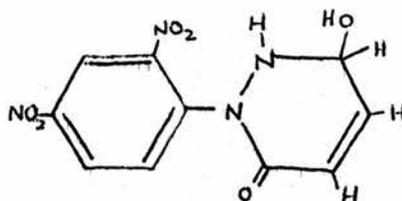


(III)

This then undergoes rearrangement since the compound showed the presence of two acidic protons (n.m.r.), had an -OH (-NH) absorption in the infra-red spectrum and was bright yellow coloured as opposed to the red colour expected for a compound of structure (III). Attempts to close the ring also failed and two possible structures for the rearranged compound are proposed:



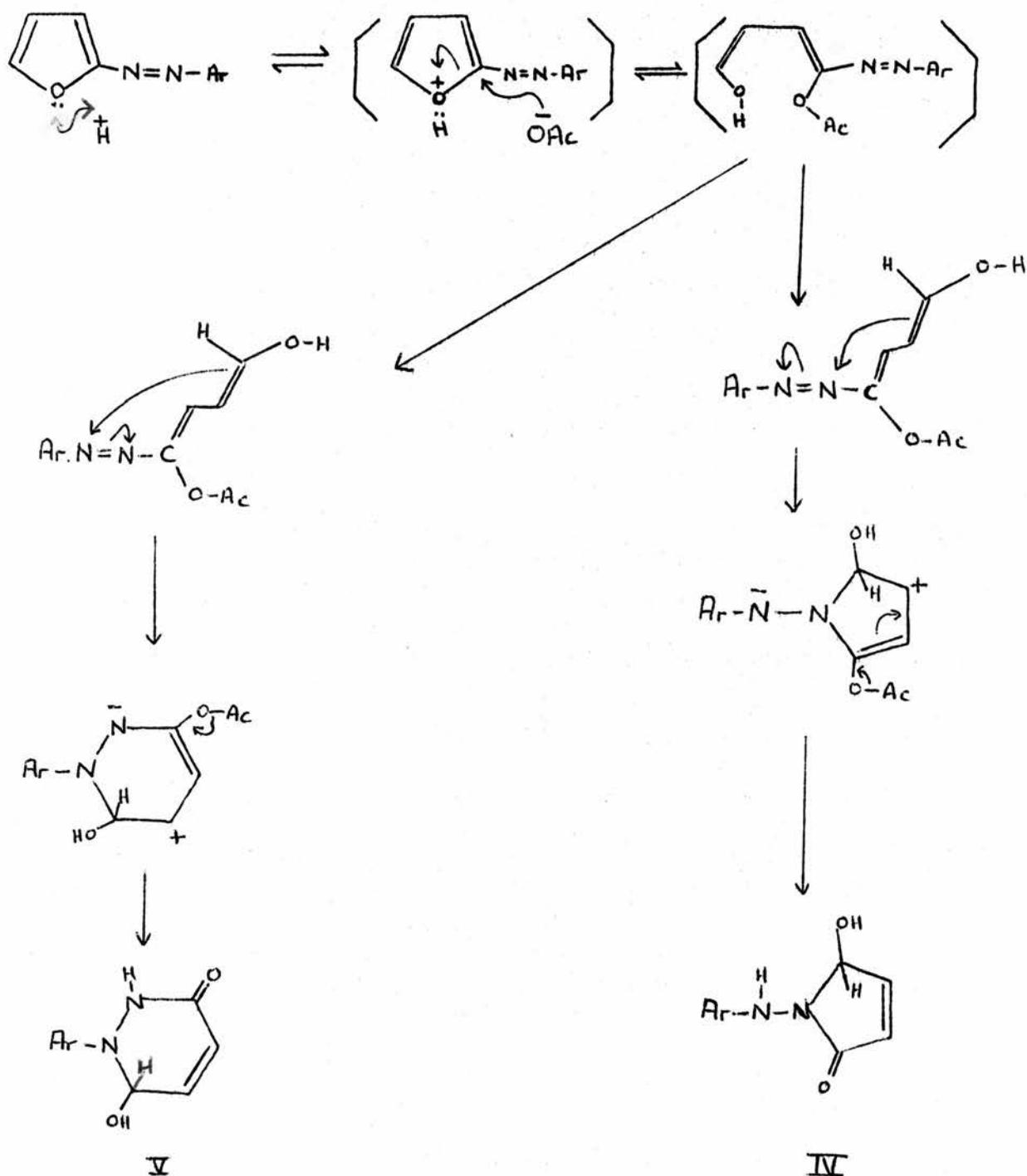
(IV)



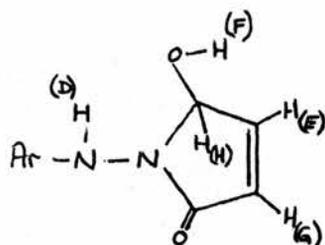
(V)

Both structures possess two acidic protons and six non-acidic protons and a study of the nuclear magnetic resonance spectra obtained by irradiating each proton could not readily distinguish

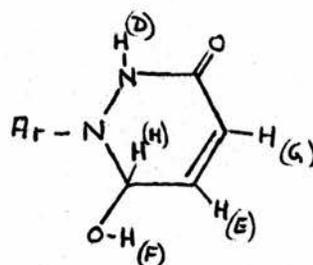
between the two structures. Benzoylation resulted in the formation of the dibenzoyl derivative and the loss of the acidic protons from the n.m.r. However, the benzoyl group protons crowded the n.m.r. too much for it to be of any value in determining the true structure. The proposed mechanism for the rearrangement is:



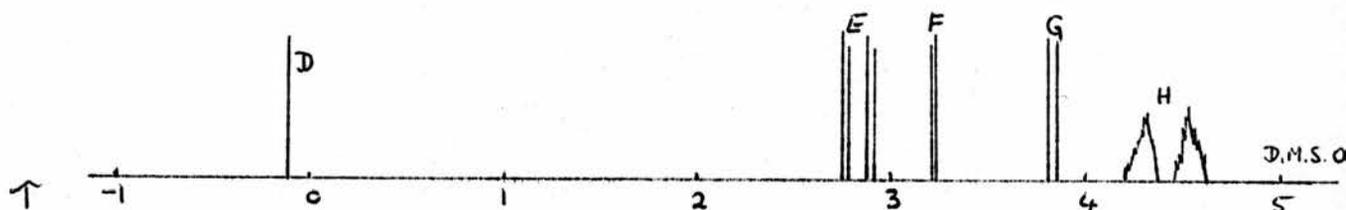
The protons of the structures (IV) and (V) are assigned to the nuclear magnetic resonance spectrum as follows (deleting the 2,4-dinitrophenyl unit protons):



(IV)



(V)



Protons D and F are lost on D_2O exchange and H becomes a singlet and is associated with F. Irradiation shows that protons H, E and G are all associated.

The effect of the 2,4-dinitrophenyl group on the proposed mechanisms suggests that the formation of the five-membered ring (IV) would be the most likely and work is proceeding to prepare this compound by another route.

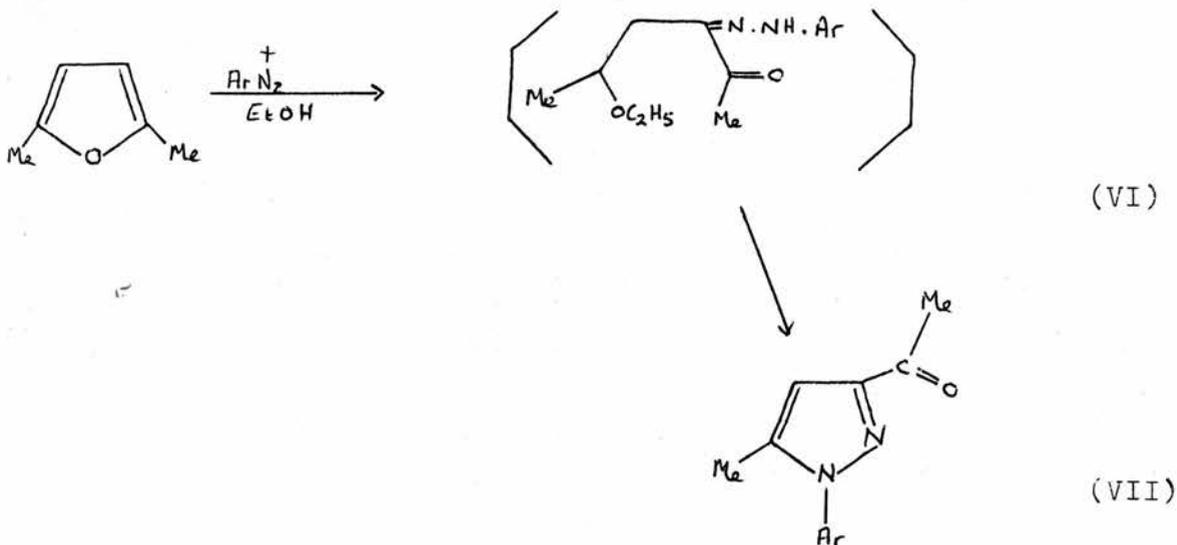
Furan was found to undergo a not altogether unexpected ring opening reaction but azo coupling does seem to be involved. Whether it occurred before ring opening of the furan happened or whether the coupling induced ring opening could perhaps best be investigated by trying a coupling reaction using succindialdehyde in glacial acetic acid.

While investigating compound (A1) (see experimental section), it was found that 2,4,6-trichlorobenzene diazonium sulphate was not a strong enough diazonium salt to couple with mesitylene but was found to couple with anisole although only in low yield.

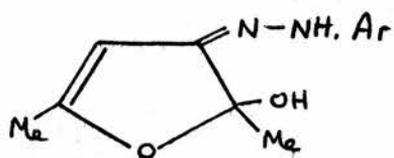
When 2,4-dinitrobenzenediazonium sulphate was added to a solution of 2,5-dimethylfuran in glacial acetic acid, a dark red, gummy precipitate was obtained which was very reminiscent of the one obtained with 2,5-dimethylthiophen. The dark red colour and the mass spectrum, (m/e 290), indicated that this was the azo compound (2',4'-dinitrobenzene)-3-azo-2,5-dimethylfuran and a molecular weight was determined under high resolution and found to be in extremely good agreement with the theoretical molecular formula (found m/e 290.0652, $C_{12}H_{10}N_4O_5$ requires m/e 290.0651). It was even more difficult to recrystallise this compound than the 2,5-dimethylthiophen azo compound and a pure crystalline solid could not be obtained. The best sample gave a micro analysis which agreed fairly well with the theoretical composition (found C, 50.11%; H, 3.61%; N, 18.42%, $C_{12}H_{10}N_4O_5$ requires C, 49.66%; H, 3.45%; N, 19.32%) and the infra-red spectrum showed an absence of -OH, -NH or -C=O groups. When the reaction was repeated using 2,4,6-trichlorobenzenediazonium sulphate a small yield of a similar compound was obtained which gave a highly resolved molecular weight in absolute agreement with that of (2',4',6'-trichlorobenzene)-3-azo-2,5-dimethylfuran (found m/e 301.9781, $C_{12}H_9N_2OCl_3$ requires m/e 301.9781). This was equally difficult to recrystallise satisfactorily and obtained in too small a yield to pursue further. No arylated derivatives were isolated in either reaction nor was there any evidence of ring opening having occurred.

That the azo compound had been isolated was further verified

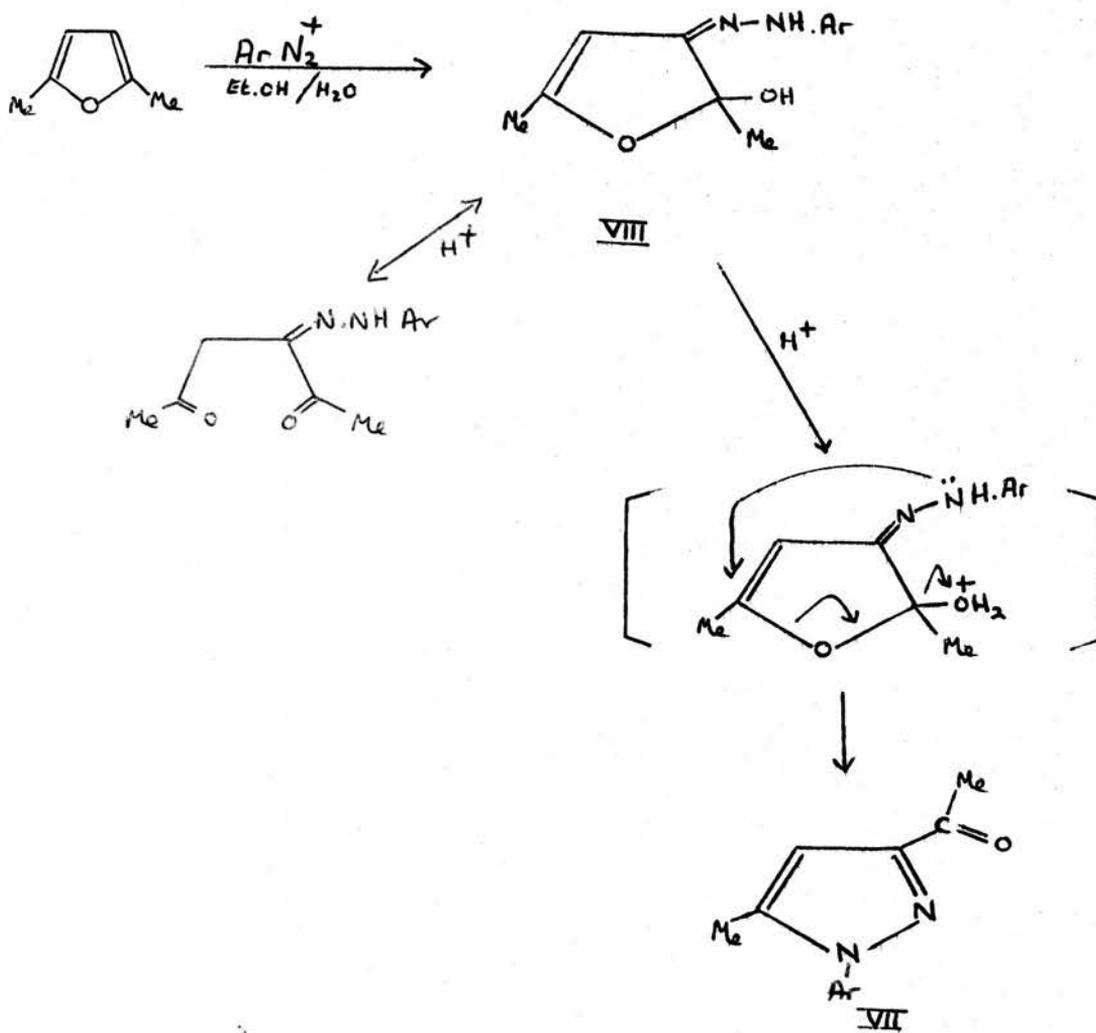
by checking a reaction reported ⁹⁶ to occur, between 4-nitrobenzene diazonium chloride and 2,5-dimethylfuran in ethanol, in which a ring opened product (VI) occurred initially which was readily rearranged in dilute hydrochloric acid to give compound (VII):



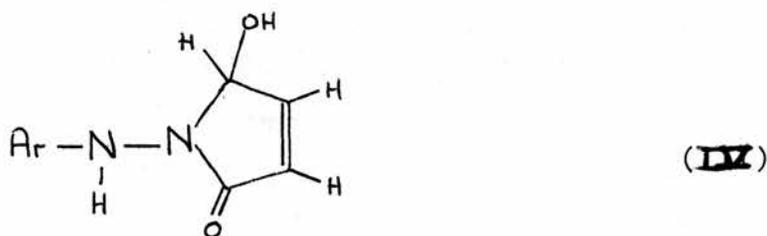
The experiment was repeated to confirm that the azo compound found in the glacial acetic acid reaction medium was not related to these compounds. The compound assigned (VI) was found as reported and gave (VII) on treatment with dilute hydrochloric acid in ethanol and the information obtained on (VII) confirmed the structure proposed in the report (infra-red ν_{max} 1680 cm^{-1} and no -NH or -OH absorption. Mass spectrum confirmed the molecular weight (m/e 245 (P^+))). However, the structure assigned to the intermediate (VI) was found to be incorrect from the evidence of the mass spectrum (m/e 263 (P^+)) and the infra-red spectrum (ν_{max} 3400 cm^{-1} (-NH, -OH) but no -C=O absorption). The mass spectrum suggested the presence of a molecule of water and not of ethanol so that the intermediate could be (VIII):



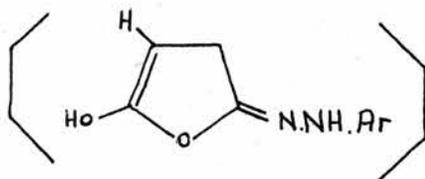
and the reaction mechanism becomes:



These low melting orange (VIII) and pale yellow (VII) solids were different from the azo compound (2',4'-dinitrobenzene)-3-azo-2,5-dimethylfuran in all respects and also from the compound (AI) obtained from the coupling reaction with furan in glacial acetic acid:



The equivalent from the above reaction would be:



which possesses no carbonyl group and would not give a similar nuclear magnetic resonance spectrum.

Further to this experiment, the reaction using 4-nitrobenzene diazonium chloride was repeated but using glacial acetic acid instead of ethanol. A dark red solid was obtained which was similar to the azo compound (2',4'-dinitrobenzene)-3-azo-2,5-dimethylfuran in appearance and in the difficulty of obtaining a pure crystalline solid. The compound had the same molecular weight as (VII) but melted 90°C higher and showed no carbonyl absorption in

its infra-red spectrum and is believed to be (4'-nitrobenzene)-3-azo-2,5-dimethylfuran (m.p. 222°C. Highly resolved molecular weight found m/e 245.0795, $C_{12}H_{11}N_3O_3$ requires m/e 245.0800).

A further experiment was carried out using 2,4-dinitrobenzene diazonium sulphate and 2,5-dimethylfuran in ethanolic solution. An orange solid, similar in nature to compound (VII) was found but which contained an extra molecule of water and also an infra-red absorption at 1680 cm^{-1} with no -NH, -OH absorptions. Refluxing in dilute hydrochloric acid/ethanol solution had no effect on this compound nor did drying in vacuo at 100°C. The compound bore no resemblance to the azo dye obtained in glacial acetic acid (work is proceeding to characterise it) and the solvent is concluded to be of great importance in the coupling reactions of furans.

The azo compound (2',4'-dinitrobenzene)-3-azo-2,5-dimethylfuran was obtained in 40% yield when glacial acetic acid was used as the solvent and no arylated derivatives were isolated. This reaction can be reasonably compared with that of 2,5-dimethylthiophen with 2,4-dinitrobenzene diazonium sulphate in glacial acetic acid when a similar yield of azo dye was found. As in the 2,5-dimethylthiophen, the two methyl groups exert a concerted effect on the 3-(4-) position, so that electrophilic substitution readily occurs. The methyl groups induce substitution at the 3-(4-) position and may also help to stabilise the azo compound formed.

In 2,5-diphenylfuran, the 3-(4-) positions will not be as reactive to substitution as those in the 2,5-dimethylfuran but they should be more reactive than those in furan itself. Also, the extended delocalisation should lead to an improved stability of the azo compound once formed. When 2,4-dinitrobenzene diazonium sulphate was added to a solution of 2,5-diphenylfuran in glacial acetic acid,

a deep green colour immediately occurred which gradually darkened to a deep red. Unlike in the 2,3,5-triphenylthiophen coupling reaction, which also gave a deep green colour on mixing, no nitro-furan derivative was isolated. Instead, the major product was the mono-arylated compound 3-(2',4'-dinitrophenyl)-2,5-diphenylfuran (57%). A lower yield (4%) of the di-arylated compound was found and a small amount of a red oil, believed to contain the azo compound, 3-(2',4'-dinitrobenzene)-azo-2,5-diphenylfuran.

The low yield of azo compound was expected but the high yield of the arylated compound was possibly caused as a result of the extended delocalisation since this is the major difference between this compound and the previous two, furan and 2,5-dimethylfuran. In order to pursue this idea, benzofuran was prepared.

Benzofuran was reacted with 2,4-dinitrobenzenediazonium sulphate in glacial acetic acid. Chloroform extraction of the reaction mixture and separation by column chromatography gave two components. The first was the mono-arylated compound, 2-(2',4'-dinitrophenyl)-benzofuran, obtained in 40% yield and the other was 2,3-bis-(2',4'-dinitrophenyl)-benzofuran, the di-arylated derivative, which was found in 6% yield. No azo compound was found which was again, not unexpected, and the high yields of arylated compounds supports the theory that extended delocalisation, without activation, plays an important part in the formation of arylated derivatives.

Apart from furan itself, the furans tested behave as aromatic compounds and give similar products to the thiophen derivatives used. Research has only been carried out on a small range of each group of compounds and absolute conclusions cannot be drawn. Activation seems to lead to coupling, even when the activation is provided by methyl groups only and a study of the 2-methyl,2,3,5-

trimethyl- and 2-(3-) methylbenzo- compounds would be of interest. Similarly, the theory that extended delocalisation leads to arylation, could be tested further by the use of the mono-, di- and tri-phenylated compounds.

What has been resolved is that these five-membered heterocyclic compounds, although generally behaving as aromatic species, yield very dissimilar products from the benzenoid compounds which they are compared with for reactivity, when they are reacted with a powerful diazonium salt in glacial acetic acid solution. It seems reasonable to assume that the hetero-atom is directly involved and yet the differences between sulphur in thiophen and oxygen in furan are great but the products and yields are comparable. The combined evidence of the thiophens and furans suggests that the initial attack of the diazonium compound must occur at a ring carbon atom and not at the hetero-atom, since oxygen possesses no suitable 3d-orbitals which are essential to the theory proposed in Section A.

PART I SECTION A

COUPLING REACTIONS OF THIOPHEN AND ITS DERIVATIVES

EXPERIMENTAL

General Experimental Procedure

Melting points were determined on a 'Gallenkamp' melting block and are uncorrected.

Infra-red spectra were run on a Perkin Elmer 137 (sodium chloride prism) or 257 (sodium chloride grating) instruments.

Ultra-violet spectra were obtained on a Unicam S.P. 800 spectrophotometer in methanol A.R.

Nuclear magnetic resonance spectra were recorded on a Perkin Elmer 60 MHz or a Varian HA 100, 100 MHz spectrometer and were measured with respect to internal tetramethylsilane.

Mass spectra were recorded on an A.E.I./G.E.C M.S. 902 instrument.

1. Diazotisation of 2,4-dinitroaniline

2,4-Dinitroaniline was diazotised according to the method of Saunders.⁴⁴ Sodium nitrite (7.0g) was gradually added with stirring to concentrated sulphuric acid (110 ml) and the mixture heated to 70°C to complete dissolution. When the temperature had fallen to 35°C, 2,4-dinitroaniline (18.3g) was added taking approximately twenty minutes. The dark red solution so obtained was stirred at room temperature for one and a half hours and then poured onto 200g of crushed ice. This solution, containing 0.1 mole of diazonium salt, was filtered into a cooled measuring cylinder and the calculated proportion used for each coupling reaction.

2. Comparative coupling of diazotised 2,4-dinitroaniline with anisole

This control experiment was carried out with each thiophen coupling, to check reproducibility. Diazotised 2,4-dinitroaniline (9.1g, 0.05 mole) was added to a solution of anisole (5.4g, 0.05 mole) in glacial acetic acid (200 ml) and stirred at 0°C for 68 hours. The precipitate (3.5g) was filtered off and recrystallised from acetone/petrol (60/80) to give orange needles of p-(2,4-dinitrobenzene)-azo-methoxybenzene (m.p. 177°C, lit⁶⁸ m.p. 177-178°C m/e 302 (P⁺). Found C = 51.51%; H = 3.21%; N = 18.35%, C₁₃H₁₀N₄O₅ required C, 51.65%; H, 3.31%; N, 18.55%). The filtrate was diluted with water, aqueous sodium bicarbonate solution until no longer acidic, water and dried over magnesium sulphate. The solvent was evaporated under reduced pressure to give a red oil (0.8g). Chromatography on an alumina column in benzene gave an orange compound which recrystallised from acetone/petrol 60/80 to give orange needles (0.4g) having the same melting point, alone or in admixture, as the p-2,4-dinitrobenzene-azo-methoxybenzene above. Chloroform eluted a small amount of brown solid (0.02g) which was

recrystallised from benzene/petrol 60/80. The mass spectrum showed a peak at m/e 440 corresponding to the parent ion for 2,4-bis-(2',4'-dinitrophenyl)-methoxybenzene and a large peak at m/e 274 corresponding to the mono-arylated derivative p-(2,4-dinitrophenyl)-methoxybenzene. (Analysis found C = 49.91%; H = 3.13%; N = 13.31%. $C_{19}H_{12}N_4O_9$ requires C, 51.81%; H, 2.73%; N, 12.73%.)

The total yield of p-(2,4-dinitrobenzene)-azo-methoxybenzene was 3.9g (26%). The yield of suspected diarylated compound was 0.02g (0.1%).

3. Reaction of 2,4-dinitrobenzene diazonium sulphate with thiophen

Diazotised 2,4-dinitroaniline (9.1g, 0.05 mole) was added to a solution of thiophen (4.2g, 0.05 mole) in glacial acetic acid (200 ml) and stirred at $0^{\circ}C$ for 70 hours. The mixture rapidly became orange and changed to deep red after several hours. The red oily precipitate, obtained on dilution with water, was collected (2.7g), taken up in chloroform, washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Removal of the solvent gave a red oil (1.8g) which was chromatographed on an alumina column with benzene. Eluted first was a yellow/orange oil (0.6g) which crystallised on standing and was found to be 2-(2',4'-dinitrophenyl)-thiophen. (m.p. $60^{\circ}C$. m/e 250 (P^+). Found C = 48.3%; H = 2.38%; N = 11.20%. $C_{10}H_6N_2O_4S$ requires C, 48.0%; H, 2.38%; N, 11.20%). This compound was found to be light sensitive and purification, by column chromatography in the dark, was needed immediately prior to analysis.

Chloroform eluted a red oil (0.6g) which was recrystallised from benzene/petrol 60/80 to give red crystals believed to be 2,3,5-tris-(2',4'-dinitrophenyl)-thiophen (m.p. $126^{\circ}C$. m/e 582 (P^+)).

Also large peak at m/e 416 corresponding to the diaryl derivative. Found C = 46.15%, H = 1.98%, N = 12.37%. $C_{22}H_{10}N_6O_{12}S$ requires C, 45.36%; H, 1.72%; N, 14.43%). The poor correlation of the elemental analysis and study of the mass spectrum suggests that this compound is contaminated by the diarylated thiophen derivative.

The reaction filtrate was extracted with chloroform and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent gave a red oil (3.7g) which was chromatographed on an alumina column. Benzene eluted a yellow oil (1.5g) which gave yellow crystals on standing and was found to be more of the 2-(2',4'-dinitrophenyl)-thiophen. A further yellow band eluted by benzene gave a yellow solid (0.4g) which was found to be 2,5-bis(2',4'-dinitrophenyl)-thiophen (m.p. 172°C m/e 416 (P⁺). Analysis found C = 46.44%, H = 1.88%, N = 13.31%. $C_{16}H_8N_4O_8S$ requires C, 46.15%; H, 1.92%; N, 13.46%). A red band eluted by chloroform was found, on subsequent purification, to be also mainly the diarylated product (0.2g). No azo compound was isolated.

The yield of the mono-arylated compound 2-(2',4'-dinitrophenyl)-thiophen was 2.1g (17%) and the yield of the di-arylated derivative was 0.58g (2.8%); 0.6g (2%) of the impure 2,3,5-tris(2',4'-dinitrophenyl)-thiophen was obtained. The reaction was repeated in an attempt to isolate the large percentage of unidentified products. The reaction mixture was extracted with chloroform and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent gave a red oil which was boiled with petrol 60/80 and decanted hot. Removal of the petrol 60/80 gave a red solid found to be a mixture of the mono- and di-arylated thiophen derivatives, by study of its mass spectrum

(m/e 250 and m/e 416). The remaining red oil was boiled with benzene, decanted hot and the benzene removed to give a red solid found by mass spectrometry to be mainly the 2,5-bis-(2',4'-dinitrophenyl)-thiophen m/e 416. The remaining red oil was found to be totally soluble in acetone and the mass spectrum showed it to be mainly unreacted 2,4-dinitroaniline m/e 184. ^(P+1) No high molecular weight polymers were found.

4. Reaction of p-nitrobenzene diazonium chloride with thiophen

p-Nitrobenzene diazonium chloride was prepared⁶⁹ from p-nitroaniline (7g) in water (15 ml) and sodium nitrite (3.6g). This mixture was poured on to ice (15g) and concentrated hydrochloric acid (15 ml) with stirring. After 10 minutes, the solution was filtered into a solution of thiophen (4.2g 0.05 mole) in glacial acetic acid (200 ml) and stirred at 0°C for 70 hours. The red solution was diluted with water and extracted with chloroform. The extract was washed with water, aqueous sodium bicarbonate solution, water and dried over magnesium sulphate. Evaporation of the solvent gave a red oil (2.2g) which was chromatographed on an alumina column. Benzene eluted a yellow oil (1.1g) which was recrystallised from benzene/petrol 40/60 to give a yellow solid found to be light sensitive. This was identified as 2-(4'-nitrophenyl)-thiophen (m.p. 135°C, lit⁷⁰ m.p. 137-8°C. m/e 205 (P⁺). Found C = 58.46%; H = 3.43%; N = 7.06%. C₁₀H₇NO₂S requires C, 58.53%; H, 3.42%; N, 6.83%).

Chloroform eluted a yellow component (0.7g) which was recrystallised from benzene/petrol 60/80 and was identified as 2,5-bis-(4'-nitrophenyl)-thiophen (m.p. 148°C m/e 326 (P⁺). Found C = 59.04%; H = 3.15%; N = 8.79%. C₁₆H₁₀N₂O₄S requires C, 58.89%; H, 3.07%; N, 8.59%).

The yield of the mono-arylated derivative was 1.1g (11%) and the di-arylated product was found in less than 5% yield but no tri-arylated compound was isolated.

6. Reaction of diazotised 2,4-dinitroaniline with 2,5-dimethylthiophen.

a) Preparation of 2,5-dimethylthiophen:

Acetyl acetone (35g) was diluted with dry benzene (200 ml) in a flask fitted with a powerful stirrer and a reflux condenser. Phosphorus pentasulphide (80g) was added slowly with stirring and the whole mixture was refluxed for 30 minutes. The liquid phase was distilled off and fractionated, giving 2,5-dimethylthiophen over the boiling range $133^{\circ}\text{C} - 136^{\circ}\text{C}$ (lit ⁷¹ b.p. $135 - 136^{\circ}\text{C}$. 23g (70%)).

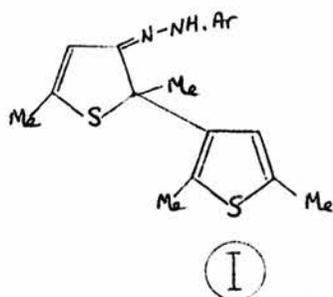
b) The coupling reaction:

Diazotised 2,4-dinitroaniline (9.1g. 0.05 mole) was added to a solution of 2,5-dimethylthiophen (5.6g. 0.05 mole) in glacial acetic acid (200 ml) and stirred at 0°C for 68 hours. A dark red oily precipitate formed which was collected, taken up in chloroform and washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent under reduced pressure gave a dark-red "glassy" solid (2.5g) which was characterised as 2,5-dimethyl-3-(2',4'-dinitrobenzene)-azo-thiophen. (m.p. 233°C . Measured molecular weight m/e 306.0428. $\text{C}_{12}\text{H}_{10}\text{N}_4\text{O}_8\text{S}$ requires 306.0423. Found C, 47.16%; H, 3.19%; N, 18.1%. $\text{C}_{12}\text{H}_{10}\text{N}_4\text{O}_8\text{S}$ requires C, 47.07%; H, 3.27%; N, 18.30%) This compound was found to be extremely difficult to recrystallise.

The reaction filtrate was diluted with water and chloroform extracted and the extract washed with water, aqueous sodium bi..

carbonate solution until no longer acidic, water and dried over magnesium sulphate. Removal of the solvent gave a dark-red oil (4.3g) which was chromatographed on an alumina column using benzene. A pale yellow component eluted first gave a yellow oil (0.2g) which crystallised on standing but rapidly turned dark green on exposure to light. It was purified on a silica column in the dark and was found to be 3-(2',4'-dinitrophenyl)-2,5-dimethylthiophen. (m.p. 70°C (d). m/e 278 (P⁺). Found C, 51.07%; H, 3.68%; N, 10.60%. C₁₂H₁₀N₂O₄S requires C, 51.80%; H, 3.61%; N, 10.10%).

A red band was eluted by benzene next which gave a red oil found to contain two similar compounds by T.L.C. These were separated by chromatography on a short silica column in benzene. The first red solid (0.2g) was recrystallised from acetone/petrol 60/80 to give bright red crystals m.p. 197°C. m/e 418 (P⁺). Elemental analysis suggested C₁₈H₁₈N₄. The apparent difference in molecular weight (96) can be represented by two sulphur atoms and four oxygen atoms to give C₁₈H₁₈N₄S₂O₄ as the most likely molecular formula. This molecule appears to be made up of one 2,4-dinitrobenzene diazonium unit linked to two 2,5-dimethylthiophen units. The above information, together with the N.M.R. spectrum supports the proposed structure I :



(Found C, 52.04%; H, 4.51%; N, 13.32%. C₁₈H₁₈N₄O₄S₂ requires C, 51.7%; H, 4.32%; N, 13.40%; I.R. ν_{\max} 3300 cm⁻¹ (broad. weak).

3100 cm^{-1} strong; N.M.R. (micro-cell) τ (CDCl_3) 0.9 (d, 1H), 1.7-1.9 (m, 1H), 2.2-2.3 (s, 1H), 3.7 (s, 1H), 7.6 (d, 6H), 7.9-8.0 (d, 6H).

The second red solid obtained was recrystallised from benzene/petrol 60/80 to give bright red crystals (0.1g) similar in appearance to compound (I). (m.p. 306°C ; m/e 430 (P^+), 416, 306; Found C, 53.40%; H, 4.25%; N, 13.20%; I.R. ν_{max} 3280 cm^{-1} v.s.; N.M.R. not soluble even in D.M.S.O.).

No structure could be assigned to this compound although the very strong ion at m/e 306 in the mass spectrum indicates the presence of a 2,5-dimethyl-3-(2',4'-dinitrobenzene)-azo-thiophen unit.

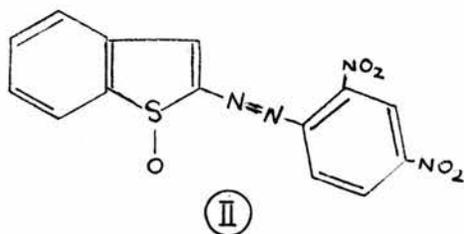
Chloroform eluted a red oil (0.3g) which could not be crystallised and was identified as the di-arylated derivative 3,4-bis(2',4'-dinitrophenyl)-2,5-dimethyl-thiophen (m/e 444 (P^+)). Found C, 49.15%; H, 2.82%; N, 12.48%. $\text{C}_{18}\text{H}_{12}\text{N}_4\text{O}_8\text{S}$ requires C, 48.72%; H, 2.71%; N, 12.60%).

Further elution with chloroform gave a red solid found to be more of the azo compound giving a total yield of 2,5-dimethyl-3-(2',4'-dinitrobenzene)-azo-thiophen of 5.75g (38%). Only 0.2g (1.5%) of the di-arylated derivative 3,4-bis(2',4'-dinitrophenyl)-2,5-dimethylthiophen was obtained and 0.21g (2%) of the red compound (I).

7) Reaction of diazotised 2,4-dinitroaniline with thianaphthene

Diazotised 2,4-dinitroaniline (9.1g. 0.05 mole) was added to a solution of thianaphthene (6.7g. 0.05 mole) in glacial acetic acid (200 ml) and stirred at 0°C for 52 hours. A small amount of precipitate formed which was filtered off and recrystallised from benzene/petrol 60/80 to give a bright orange compound (0.2g). (m.p. 290°C (d). m/e 344 (P^+); m/e 167 corresponding to 2,4-dinitrophenyl group; m/e 134 corresponding to a thianaphthene nucleus).

Elemental analysis suggested $C_{14}H_8N_4$ which required one sulphur atom and five oxygen atoms to make up the molecular weight to that of the parent: $C_{14}H_8N_4O_5S = 344$. From this information and the lack of an -OH absorption in the infra-red spectrum, the structure (II) below was assigned:



2-(2',4'-dinitrobenzene)-azo-thianaphthene-S-oxide (m.p. $290^{\circ}C$ (d). Found C, 48.72%; H, 2.35%; N, 16.25%. $C_{14}H_8N_4O_5S$ requires C, 48.83%; H, 2.33%; N, 16.28%).

The reaction liquor was diluted with water, chloroform extracted and the extract washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent under reduced pressure gave a red oil (9.2g) with a strong odour of thianaphthene and which crystallised on standing. This was chromatographed on an alumina column using benzene and after recovering unreacted thianaphthene (3.2g), benzene eluted a yellow component which gave an orange oil (3.9g). This was recrystallised from benzene and gave yellow/orange needles identified as 2-(2',4'-dinitrophenyl)-thianaphthene (m.p. $104^{\circ}C$. m/e 300 (P^+). Found C, 56.23%; H, 2.87%; N, 9.11%. $C_{14}H_8N_2O_4S$ requires C, 56.01%; H, 2.67%; N, 9.33%).

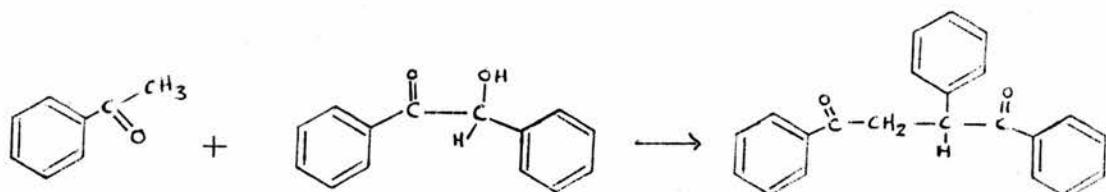
Chloroform eluted a yellow band which was recrystallised from benzene/petrol 60/80 to give a yellow solid (1.6g) identified as the di-arylated derivative 2,3-bis(2',4'-dinitrophenyl)-thianaphthene (m.p. $120^{\circ}C$. m/e 466 (P^+). Found C, 50.98%; H, 2.38%; N, 11.52%.

$C_{20}H_{10}N_4O_8S$ requires C, 51.5%; H, 2.15%; N, 12.01%).

The yield of 2-(2',4'-dinitrophenyl)-thianaphthene was 3.9g (49%) and the yield of the di-arylated compound was 1.55g (13%). The S-oxide derivative (II) was obtained in only about 1% yield.

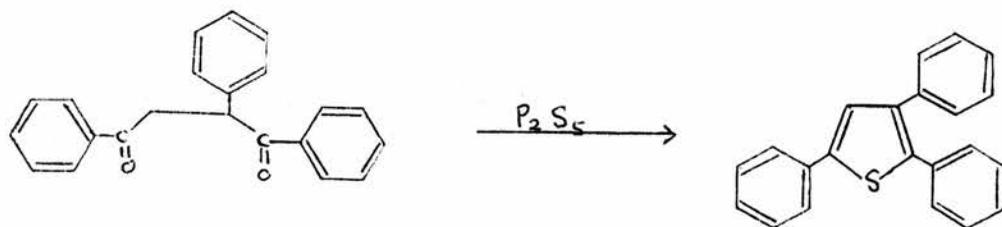
8. The reaction of diazotised 2,4-dinitroaniline with 2,3,5-triphenylthiophen

a) Preparation of desylacetophenone



Benzoin was prepared from benzaldehyde by the method of Adams and Marvel.⁷² (m.p. 133°C. 90% yield). A mixture of acetophenone (18g), benzoin (31g), potassium cyanide (4g) in 50% ethanol (150 ml) was refluxed for 1 hour 45 minutes, cooled and the organic layer was separated off and allowed to crystallise. The solid was recrystallised from ethanol to give yellow monoclinic crystals of desylacetophenone. (m.p. 125°C lit ⁷³ m.p. 126°C. 22g).

b) Preparation of 2,3,5-triphenylthiophen:⁷⁴



Desylacetophenone (5g) and phosphorus pentasulphide (2g) were heated together in a boiling tube to 150°C. The vigorous

reaction was allowed to subside and the mixture was boiled up with ethanol and filtered hot. The precipitate, which formed on cooling, was filtered off and recrystallised from ethanol to give white plates of 2,3,5-triphenylthiophen (m.p. 127°C lit⁷⁴ m.p. 127°C. Yield 3g (60%)).

c) The coupling reaction

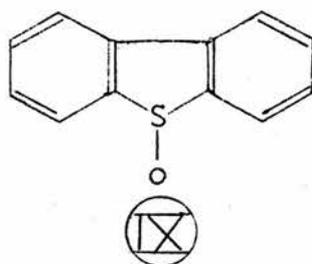
2,4-Dinitroaniline (0.6g) was diazotised and added to a solution of 2,3,5-triphenylthiophen (1.0g) in glacial acetic acid (400 ml required to dissolve the 2,3,5-triphenylthiophen) and stirred at 0°C for 70 hours. It was noted that shortly after mixing, the solution became a deep sea-green colour which darkened to red after several hours. (The electron spin resonance spectrum of this green solution showed an absence of free radicals). The reaction mixture was diluted and chloroform extracted and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent under reduced pressure gave a red oil (1.3g) which was chromatographed on a silica column with benzene. A yellow component was eluted first which gave a yellow oil (0.5g) which crystallised on standing. It was recrystallised from benzene/petrol 60/80 to give yellow needles found to be 4-nitro-2,3,5-triphenylthiophen (m.p. 168°C m/e 357 (P⁺) Found C, 73.80%; H, 4.14%; N, 3.87%; C₂₂H₁₅NO₂S requires C, 73.90%; H, 4.20%; N, 3.92%).

Chloroform eluted a red band giving a red solid (0.5g) found to contain unreacted 2,3,5-triphenylthiophen by mass spectral evidence. Chromatography on a short silica column in benzene gave unreacted 2,3,5-triphenylthiophen (0.3g) and a red oil (0.1g) which solidified on standing but could not be recrystallised satisfactorily. This was found to be 4-(2',4'-dinitrophenyl)-2,3,5-triphenylthiophen (m.p. 76°C m/e 478 (P⁺). Found C, 69.32%; H, 4.01%; N, 5.34%. C₂₈H₁₈N₂O₄S requires C, 70.3%; H, 3.8%; N, 5.86%).

The yield of 4-nitro-2,3,5-triphenylthiophen was 0.5g (65%) and 0.1g (10%) of the arylated derivative 4-(2',4'-dinitrophenyl)-2,3,5-triphenylthiophen was obtained.

9. The reaction of diazotised 2,4-dinitroaniline with dibenzothiophen

2,4-Dinitroaniline (3.0g) was diazotised and added to a solution of dibenzothiophen (3.0g) in glacialacetic acid (300 ml necessary to dissolve the dibenzothiophen). The mixture became dark brown coloured and was stirred for 52 hours. The solution was diluted with water and chloroform extracted and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent gave a dark red solid (4.1g) which was chromatographed on a silica column in benzene. A yellow component was eluted which gave a yellow solid (2.9g) which was found to be unreacted dibenzothiophen (m.p. 94°C lit⁷⁵ m.p. 96°C. m/e 184 (P⁺)) Chloroform eluted a small red band which solidified on standing to an impure red solid (0.1g). The mass spectrum of this component had very large peaks at m/e 184 (dibenzothiophen) and m/e 200 which could be compound (~~IX~~) by analogy with the thianaphthene reaction (see page 24).



The mass spectrum showed no arylated (m/e 350) or azo (m/e 378) compounds present and the reaction was not pursued.

10. Reaction of diazotised 2,4-dinitroaniline with mesitylene

2,4-Dinitroaniline (6.1g) was diazotised and added to a solution of mesitylene (4g) in glacial acetic acid (200 ml) and stirred for 72 hours. The red solution was diluted with water and chloroform extracted and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Removal of the solvent under reduced pressure gave a red oil (8.1g). This was chromatographed on a long alumina column in benzene and unreacted mesitylene (2.0g) was recovered first. A red band, slowly eluted, gave a solid (2.8g) composed of red and yellow crystals. Fractional crystallisation using benzene/petrol 60/80 mixtures gave deep red needles (0.5g) of 1-(2',4'-dinitrobenzene)-azo-2,4,6-trimethylbenzene (m.p. 164°C. m/e 314 (P⁺). Found C, 57.58%; H, 4.33%; N, 17.66%. C₁₅H₁₄N₂O₄ requires C, 57.33%; H, 4.46%; N, 17.83%).

The filtrate from the above recrystallisation gave a yellow solid (0.95g) which was recrystallised as yellow needles and found to be the mono-arylated derivative 1-(2',4'-dinitrophenyl)-2,4,6-trimethylbenzene (m.p. 125°C. m/e 286 (P⁺). Found C, 62.57%; H, 4.97%; N, 9.58%. C₁₅H₁₄N₂O₄ requires C, 62.94%; H, 4.90%; N, 9.79%).

Chloroform eluted an orange/red band which gave a red oil (0.2g) which could not be recrystallised and was not characterised.

The yield of azo compound was 0.5g (5%) and 0.95g (1.1%) of the mono-arylated derivative was obtained.

11. Measurement of the nitrogen evolved during the coupling reaction of thiophen with diazotised 2,4-dinitroaniline

Diazotised 2,4-dinitroaniline (1.0g) was added to a solution of thiophen (0.5g) in glacial acetic acid (40 ml) and the flask was connected to a gas-burette and stirred slowly (magnetically). The volume of gas evolved was recorded against time and compared with a series of controls under identical conditions: a) diazotised 2,4-dinitroaniline (1.0g) in glacial acetic acid (40 ml), b) diazotised 2,4-dinitroaniline (1.0g) in a solution of benzene (0.5g) in glacial acetic acid (40 ml), c) diazotised 2,4-dinitroaniline (1.0g) in a solution of anisole (0.5g) in ^{glacial} acetic acid (40 ml). All three controls gave identical results and in the latter case (c) the corresponding azo dye was isolated .

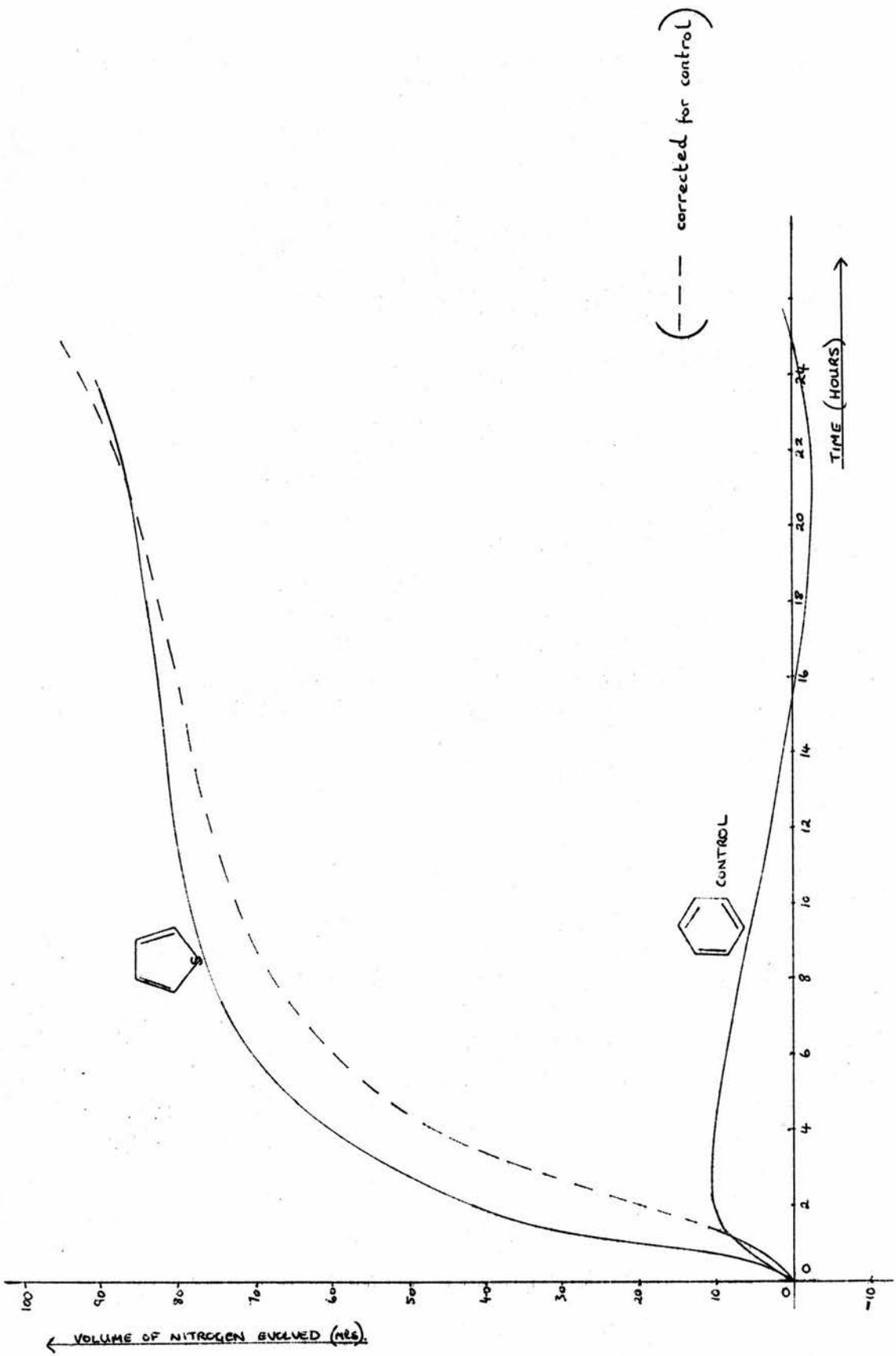
The readings obtained compared with the benzene control are tabulated below (Table II) and illustrated in diagram (I):

(Dilution with glacial acetic acid reduced the rate of loss of nitrogen from the thiophen reaction considerably and always the gas evolved initially in the control experiments was re-absorbed to zero or negative readings. One run was left for 70 hours and evolved 113 ml of nitrogen, almost the theoretical total (122 ml)).

Table II

TIME OF REACTION (hr)	THIOPHEN VOL N ₂ EVOLVED (ml)	BENZENE CONTROL VOL N ₂ EVOLVED (ml)
0	0.0	0.0
0.25	7.0	6.1
1.25	28.2	10.5
2.2	39.1	10.5
3.3	53.0	9.5
4.2	59.5	9.1
5.2	67.0	9.1
5.8	70.0	8.9
6.5	70.5	7.4
7.0	72.5	6.5
7.6	74.0	6.4
8.3	75.5	6.4
21.2	86.0	-2.5
22.2	87.1	-2.5
23.2	89.1	-1.5
23.5	90.0	-1.5
	Deep red coloured	Pale yellow-orange coloured

DIAGRAM I



Both reaction mixtures were diluted and chloroform extracted. The aqueous layers were added to alkaline solutions of 2-naphthol (1.0g) but the resulting azo dye could not be worked up quantitatively. The chloroform extractions were washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. The solvent was removed and the resulting oils chromatographed on alumina columns. The benzene control oil (0.7g) gave yellow crystals (0.05g) believed to be **1,3**-dinitrobenzene (m/e 168). Also a red oil (0.1g) was eluted by chloroform (m/e 218) which contained no azo or Gomberg products and was not characterised further. The thiophen reaction oil (1.5g) gave a yellow oil (0.8g) with benzene and a red oil (0.3g) with chloroform. These were recrystallised from benzene/petrol and identified as the mono- and di-arylated thiophen derivatives (see page 50). No tri-arylated derivative was obtained and a high yield (12%) of the 2,5-bis-(2',4'-dinitrophenyl)-thiophen compared with the large scale reaction was noted. A slightly increased yield (25%) of the mono-arylated product was found.

The experiment was repeated using diazotised 4-nitroaniline in the hope of being able to quantitatively couple the unreacted diazonium salt with 2-naphthol more successfully than with the 2,4-dinitroaniline diazonium salt but the rate of evolution of nitrogen was reduced to an unworkable speed (1/6 theoretical in 25 hours).

12. Measurement of the nitrogen evolved during the coupling reaction of thianaphthene with diazotised 2,4-dinitroaniline

Diazotised 2,4-dinitroaniline (1.0g) was added to a solution of thianaphthene (0.5g) in glacial acetic acid (40 ml) and the flask was connected to gas-burette and stirred slowly (magnetically). A control experiment of diazotised 2,4-dinitroaniline (1.0g) in a solution of benzene (0.5g) in glacial acetic acid (40 ml) was set up and the volume of gases evolved for each experiment with time was noted Table (III), diagram (II) .

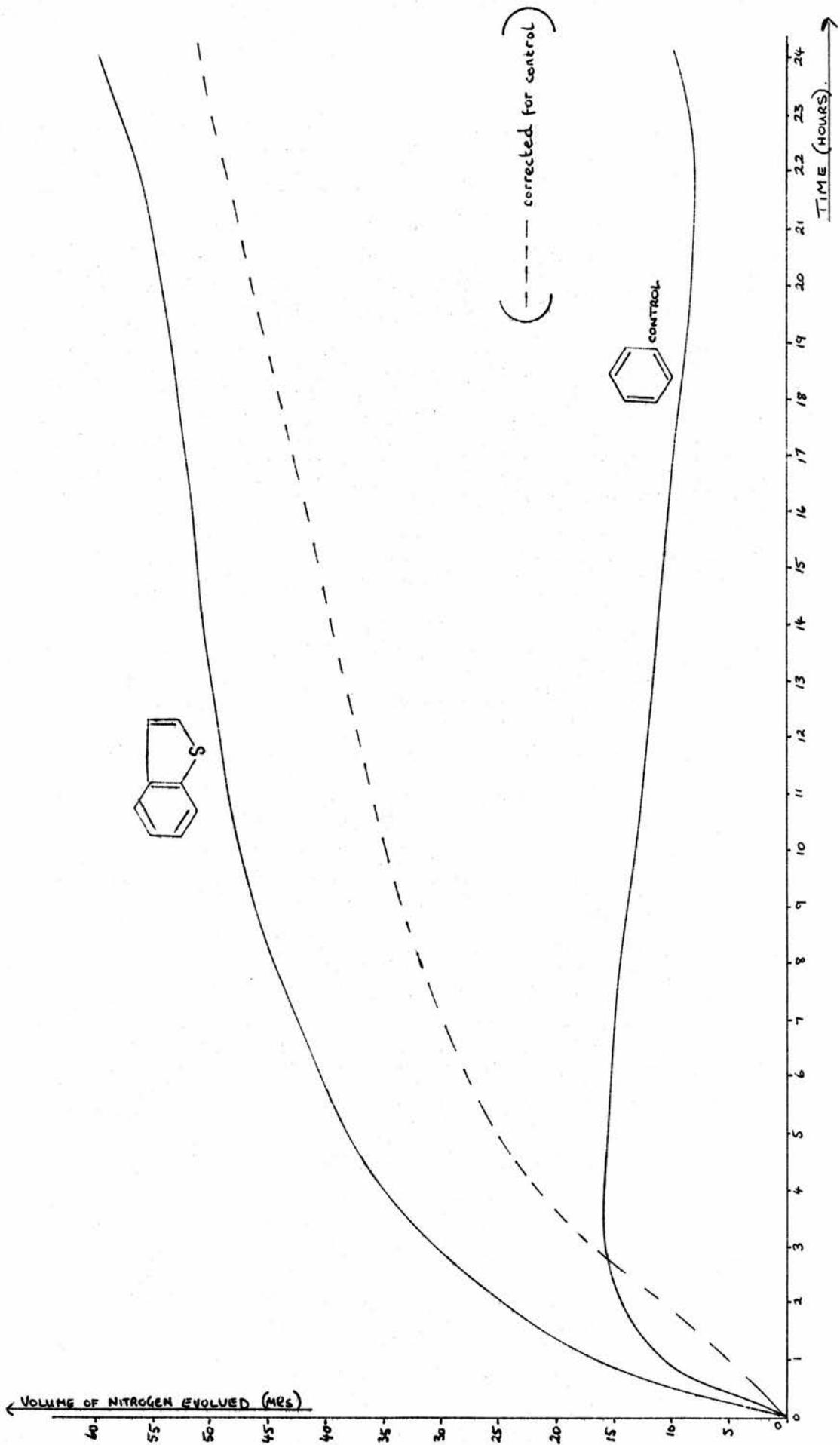
The solutions were diluted and chloroform extracted and attempts were made to couple the aqueous solutions with excess H-acid and back titrate with 4-nitrobenzenediazonium chloride solution. The end point using H-acid as an indicator was inconsistent and no meaningful results were obtained. The thianaphthene reaction extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent gave a red oil (1.0g) which crystallised on standing and smelled faintly of unreacted thianaphthene. Attempted recrystallisation from benzene/petrol 60/80 gave a red solid (0.1g) found to be identical to compound (II) (page 24) 2-(2',4'-dinitrobenzene)-azothianaphthene-S-oxide (m.p. 286°C, m/e 344 (P⁺)). The filtrate was chromatographed on a silica column in benzene and unreacted thianaphthene (0.1g) was recovered first followed by an orange band identified as 2-(2',4'-dinitrophenyl)-thianaphthene (0.2g see page 56). Chloroform eluted a red component (0.2g) which was recrystallised from benzene/petrol 60/80 and found to be the di-arylated compound 2,3-bis-(2',4'-dinitrophenyl)-thianaphthene (0.1g, see page 56).

The S-oxide (II) was found in 10% yield on this scale of reaction, the mono-arylated derivative 25% and the diarylated in 6% yield.

Table III

TIME OF REACTION (hr)	THIANAPHTHENE VOL N ₂ EVOLVED (ml)	BENZENE VOL N ₂ EVOLVED (ml)
0	0.0	0.0
0.5	10.1	8.0
1.5	21.0	13.5
2.5	27.5	15.2
3.5	34.0	15.2
4.5	37.0	15.2
5.5	39.2	14.6
6.5	42.0	14.3
7.5	44.0	14.0
8.5	45.5	13.1
9.5	46.0	12.3
10.0	46.5	12.0
22.0	57.0	8.5
23.0	59.0	9.0
24.0	60.0	9.8
	Deep red coloured	Pale yellow-roange coloured.

DIAGRAM II



13. Quantitative measurement of unreacted diazonium salt

Diazotised 2,4-dinitroaniline (1.0g) was added to a solution of thiophen (0.5g) in glacial acetic acid (40 ml) and the flask was connected to a gas-burette and stirred slowly (magnetically). A control experiment of diazotised 2,4-dinitroaniline (1.0g) in a solution of benzene (0.5g) in glacial acetic acid (40 ml) was set up and the volume of gases evolved for each experiment with time was noted (Table IV , diagram III):

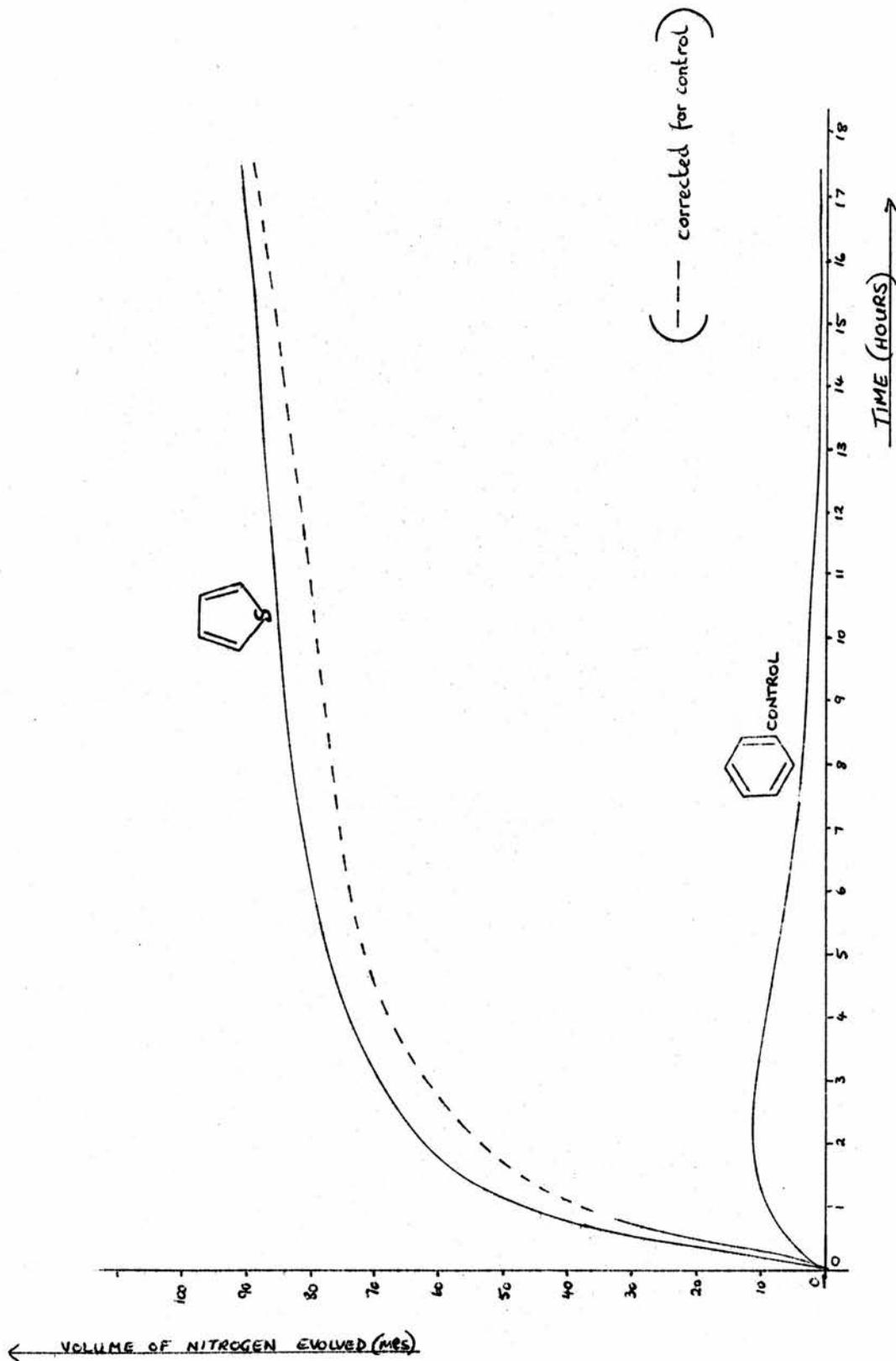
Table IV

TIME OF REACTION (hr)	THIOPHEN	BENZENE
	VOL N ₂ EVOLVED (ml)	VOL N ₂ EVOLVED (ml)
0	0.0	0.0
1.0	52.0	9.0
2.5	64.6	8.2
3.6	72.5	7.2
6.25	79.0	5.0
17.5	92.0	2.0
	red coloured	pale yellow-orange coloured

Both reaction mixtures were chloroform extracted and the following procedure⁷⁶ applied to the aqueous solutions:

Each was added to an aqueous solution of 1-(4'-sulpho-phenyl)-3-methyl-5-pyrazolone (1.5g) when the control reaction gave a dense orange precipitate and the thiophen solution gave only a small amount of orange precipitate. Each solution was buffered by excess sodium acetate after ten minutes and an aliquot (100 ml) was

DIAGRAM III



taken and the excess of pyrazolone was back titrated using ice-cold, standard 4-nitrobenzenediazonium chloride. The end point was determined using an aqueous solution of the sodium salt of H-acid (8-amino-1-hydroxy-naphthalene-3,6-disulphonic acid) as external indicator. (The end-point was reached when a faint permanent purple colouration was produced when a drop of the titrated mixture was spotted on to a filter paper and allowed to diffuse into an adjacent spot of H-acid solution). A high accuracy was not expected from this method and it was found that there was four to five times the amount of unreacted diazonium salt in the control than in the thiophen reaction mixture. Approximately 65% of the diazotised 2,4-dinitroaniline was found unreacted in the benzene control experiment.

Page No.	Compound	max μ	ϵ
52	2-(4'-nitrophenyl)-thiophen	342	19,000
50	2-(2',4'-dinitrophenyl)-thiophen	335	17,750
52	2,5-bis-(4'-nitrophenyl)-thiophen	335	16,080
51	2,5-bis-(2',4'-dinitrophenyl)-thiophen	352	12,890
50	2,3,5-tris-(2',4'-dinitrophenyl)-thiophen	354	21,534
53	3-(2',4'-dinitrobenzene)-azo-2,5-dimethylthiophen	394	8,400
54	3-(2',4'-dinitrophenyl)-2,5-dimethylthiophen	340	4,800
54	Compound (I)	400	64,100
56	2-(2',4'-dinitrophenyl)-thianaphthene	356	4,080
56	2,3-bis-(2',4'-dinitrophenyl)-thianaphthene	325	11,650
56	Compound (II)	438	680
58	4-(2',4'-dinitrophenyl)-2,3,5-triphenylthiophen	305	9,000
58	4-nitro-2,3,5-triphenylthiophen	376	21,400
60	1-(2',4'-dinitrobenzene)-azo-2,4,6-trimethylbenzene	480	6,280

PART I SECTION B

THE COUPLING REACTIONS OF FURAN AND ITS DERIVATIVES

EXPERIMENTAL

2,4-Dinitroaniline was diazotised using sodium nitrite in concentrated sulphuric acid as in the previous section (see page 49). Also, the results from the anisole control experiment in the thiophen series, apply to the conditions used in the series of furan derivatives coupled in this section.

1. Reaction of 2,4-dinitrobenzene diazonium sulphate with furan:

2,4-Dinitroaniline (9.1g, 0.05 mole) was diazotised and added to a solution of furan (3.4g, 0.05 mole) in glacial acetic acid (200 ml) and stirred at room temperature for 70 hours. A brown precipitate formed which was filtered off and recrystallised, several times, from an acetone/benzene mixture to give bright yellow crystals (8.4g). The mass spectrum showed this compound to have a molecular weight of 280 and elemental analysis gave the molecular formula $C_{10}H_8N_4$ which requires six oxygen atoms to make up to the found molecular weight. The work done in attempting to identify this compound (**AI**) is described below and discussed in the Section B Discussion (see page 38).

The filtrate from above was diluted with water, chloroform extracted and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent gave a yellow oil (1.0g) which was chromatographed on a silica column. Chloroform eluted a yellow oil (0.8g) which was identified as being more of the ring-opened compound (**AI**). No other components were eluted. The yield of compound (**AI**) was 9.2g (70%).

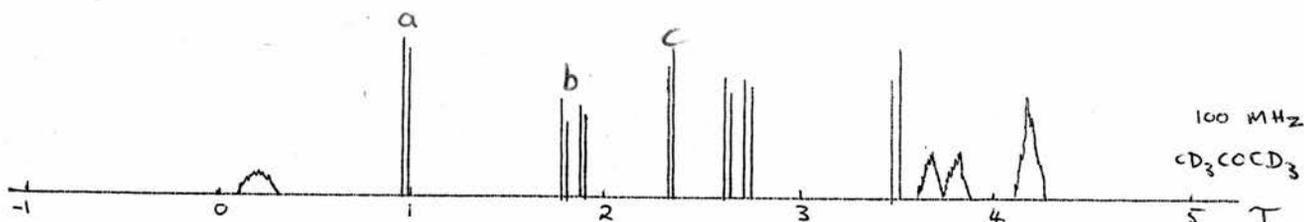
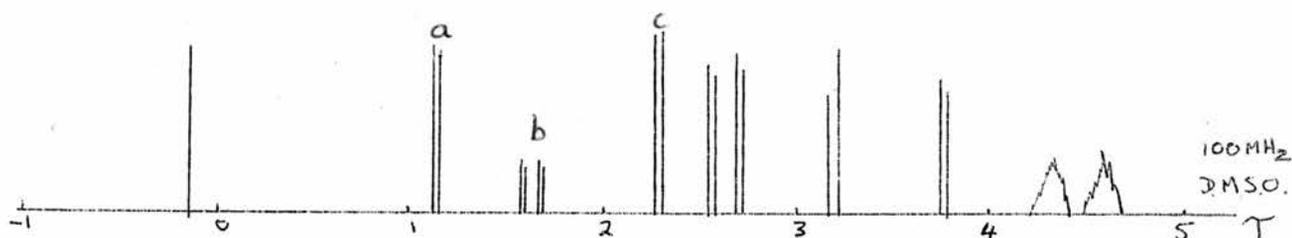
2. Attempts to characterise compound (III).

From the mass spectrum and the elemental analysis compound (AI) was formulated as $C_{10}H_8N_4O_6$ (m.p. $194^{\circ}C$. m/e 280 (P^+)). Found C, 42.96%; H, 2.71%; N, 20.03%. $C_{10}H_8N_4O_6$ requires C, 42.85%; H, 2.86%; N, 20.00%. Ultra-violet λ_{max} $332 m\mu$, $\epsilon = 15400$. Infra-red ν_{max} $3300 cm^{-1}$ (-OH, -NH); $1680 cm^{-1}$ (-C=O).

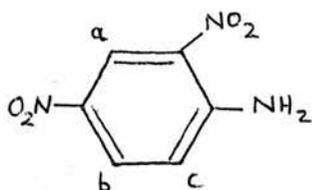
The substance was insoluble in dilute hydrochloric acid but gave a deep red solution when dissolved in 5N sodium hydroxide from which the yellow compound was re-precipitated on acidification with dilute hydrochloric acid.

a) Nuclear magnetic resonance spectra

The n.m.r. spectrum confirmed the presence of 8 protons but the spectrum changed with different solvents.

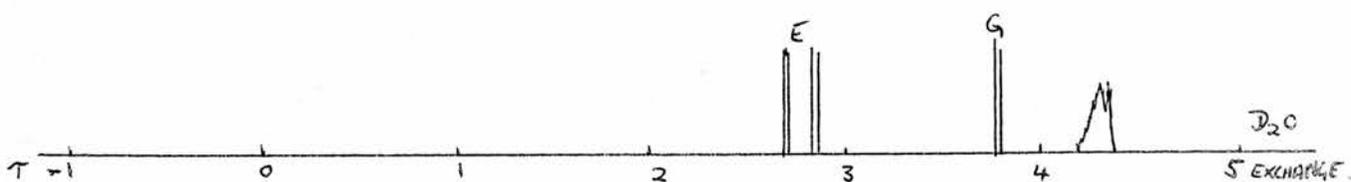
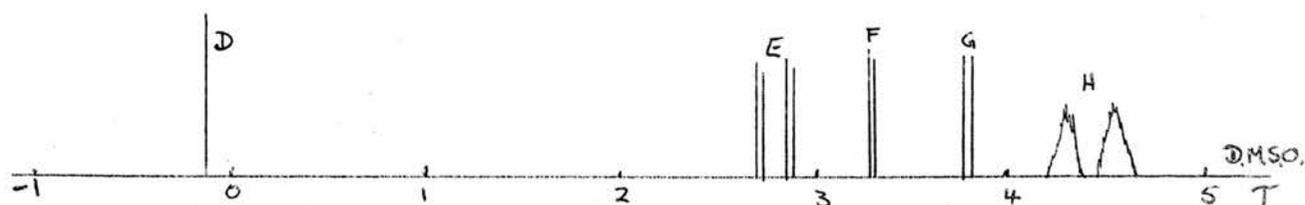


Signals a, b and c were found to belong to the 2,4-dinitrophenyl fragment by comparison with standard spectra:

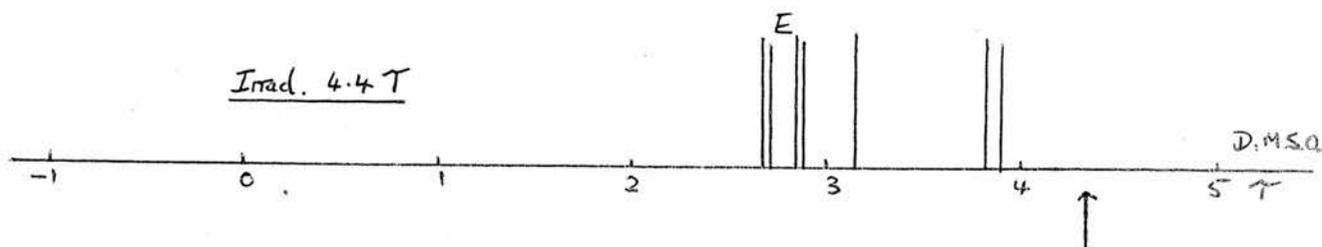


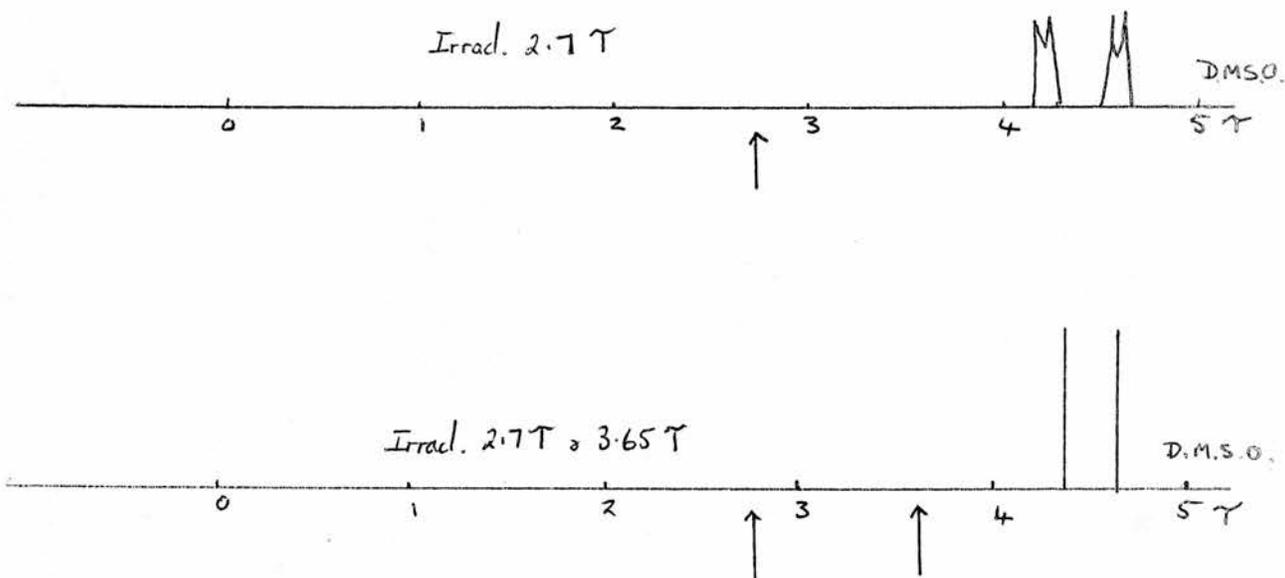
(These protons are eliminated from subsequent spectra).

D_2O exchange was carried out using D.M.S.O. as the solvent and showed that two protons exchange (D and F) and that a third proton signal (H) becomes a singlet:



The sample was then irradiated at 4.4τ ; 2.7τ ; 2.7τ and 3.65τ to give the following spectra:





b) Hydrogenation

Attempts to hydrogenate the material using Raney nickel catalyst at atmospheric pressure gave a fine black solid which was insoluble in boiling acetone and was too involatile to give a mass spectrum. The amount of hydrogen taken up suggested that the nitro groups were being reduced and the black powder was diazotised with sodium nitrite and dilute hydrochloric acid. Sulphamic acid was added to remove excess nitrous acid and the solution gave a red dye when added to alkaline 2-naphthol.

c) Ring closing attempt

On the assumption that compound (~~PI~~) had resulted from the ring opening of furan, it was refluxed with ammonium acetate solution in the hope of recycling it to a stable pyrrole derivative. The starting material was recovered intact and no reaction occurred when aniline was substituted for the ammonium acetate.

3. Reaction of 2,4,6-trichlorobenzene diazonium sulphate with furan

This experiment was carried out with the intention of forming a derivative of compound (AI) which could be easily hydrogenated and therefore help in establishing the structure.

2,4,6-Trichloroaniline (9.8g, 0.05 mole) was diazotised as for 2,4-dinitroaniline and added to a solution of furan (3.4g, 0.05 mole) in glacial acetic acid (200 ml) and stirred at room temperature for 48 hours. The solution was diluted with water and chloroform extracted and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Chromatography on an alumina column yielded only 0.2g of a brown solid believed to be the trichlorophenyl equivalent of compound (AI) (m.p. 150°C (d). m/e 290 (P⁺) with a pattern showing the presence of three chlorine atoms i.e. 9:9:3:1). The yield was too low to be of any assistance in determining the structure of compound (AI) and this experiment was not pursued further.

4. Reaction of 2,4,6-trichlorobenzene diazonium sulphate with mesitylene

2,4,6-Trichloroaniline (9.8g, 0.05 mole) was diazotised as for 2,4-dinitroaniline and was added to a solution of mesitylene (6.0g, 0.05 mole) in glacial acetic acid (200 ml) and stirred at room temperature for 48 hours. It was noted that the solution remained a pale orange colour throughout this period. The mixture was diluted with water and chloroform extracted and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent gave an orange liquid (7.1g) smelling of mesitylene. Subsequent

chromatography yielded mainly unreacted mesitylene and a trace amount (0.1g) of a red oil which had a mass spectrum indicating it to be the arylated compound 2,4,6-trichloro-2',4',6'-trimethylbi-phenyl. m/e 298 (P^+) with a three chlorine atom pattern. However, the oil still had an odour of mesitylene and since no azo compound was found, the reaction was not investigated further.

5. Reaction of 2,4,6-trichlorobenzene diazonium sulphate with anisole

2,4,6-Trichloroaniline (9.8g, 0.05 mole) was diazotised as for 2,4-dinitroaniline and added to a solution of anisole (5.4g, 0.05 mole) in glacial acetic acid (200 ml) and stirred at room temperature for 48 hours, during which time the solution became deep red coloured. The mixture was diluted with water and chloroform extracted and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. The orange oil produced on removal of the solvent smelled strongly of unreacted anisole and over 4.0g (80%) was recovered by vacuum distillation on a water bath. The remaining red oil was chromatographed on a silica column in benzene and two orange components were obtained in trace amounts. The first was purified on a silica column using petrol 60/80 and was obtained as a viscous red oil (0.11g) which could not be crystallised and was found to be the arylated compound 4-(2',4',6'-trichlorophenyl)-methoxybenzene (oil. m/e 286 (P^+) with a three chlorine atom pattern. Found C, 53.78%; H, 3.23%; N, 0.0%. $C_{13}H_9OCl_3$ requires C, 54.25%; H, 3.13%).

The second red oil was obtained in even less yield (0.1g) and could not be crystallised but was probably the azo compound (2',4',6'-trichlorobenzene)-4-azo-methoxybenzene on the evidence of a high resolution mass determination of the parent ion (found

m/e 313.9776; $C_{13}H_9N_2OCl_3$ requires m/e 313.9780).

The greatly reduced reactivity of 2,4,6-trichlorobenzene diazonium sulphate compared with the 2,4-dinitrobenzene diazonium salt was confirmed and was undoubtedly the reason for the poor yield of the ring opened furan derivative required.

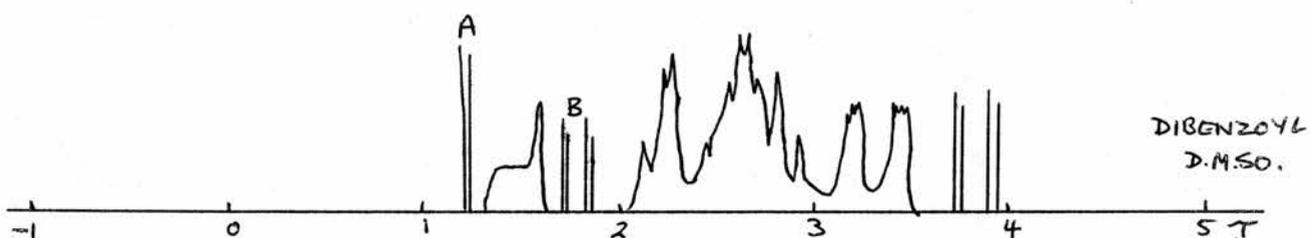
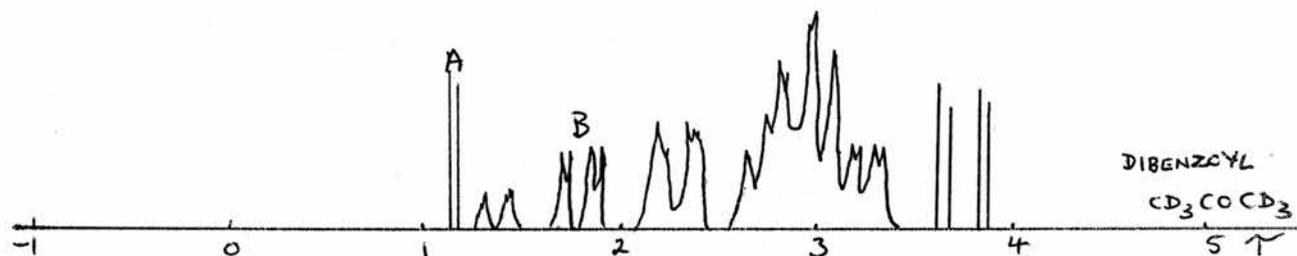
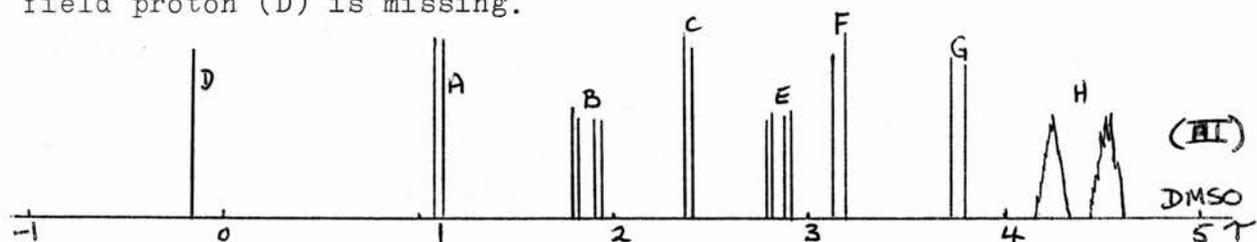
6. Benzoylation of compound (II)

Since the nuclear magnetic resonance spectrum of compound (III) showed it to have two acidic protons (from the D_2O exchange), benzoylation was attempted.

Compound (II) (1g) was dissolved in the minimum pyridine and benzoyl chloride (1g) was added to the yellow solution and the mixture was stirred overnight during which time it became deep red coloured. The solution was poured into water and chloroform extracted and the extract was washed with 5N hydrochloric acid, water and dried over magnesium sulphate. Evaporation of the solvent gave a red oil which was chromatographed on a silica column and gave an orange oil but not as a distinct component. This was recrystallised from benzene/petrol 60/80 to give a very pale yellow solid (0.4g). The mass spectrum and analysis suggest that this was the dibenzoylated derivative of compound (II) (m.p. $164^{\circ}C$. m/e 488 (P^+). Found C, 60.62%; H, 3.22%; N, 11.28%. $C_{24}H_{16}N_4O_8$ requires C, 59.27%; H, 3.28%; N, 11.48%).

As with the starting compound, the dibenzoyl derivative was found to be soluble in aqueous alkali to give a deep red coloured solution from which it was re-precipitated by acidification. The infra-red spectrum shows three carbonyl absorptions at 1690 cm^{-1} ; 1720 cm^{-1} and 1750 cm^{-1} and no evidence of any -OH or -NH absorptions as in the compound (II). The n.m.r. spectrum is too crowded by the

phenyl protons of the benzoyl groups to be of much use but the low field proton (D) is missing.



It seemed that the best way to characterise compound (II) would be to synthesise the proposed two possible compounds (see page 38.) by an unambiguous route. 2,4-Dinitrophenylhydrazine (1.5g) was dissolved in concentrated hydrochloric acid and furan (0.5g) was added. No reaction occurred in the cold so the mixture was heated to boiling, when dissolution was complete. The yellow solid (1.2g) which formed on cooling was filtered off and washed with water when it became deep red and was found to be recovered 2,4-dinitrophenylhydrazine (m.p. 196°C alone or in admixture with an authentic sample).

7. Reaction of 2,4-dinitrobenzene diazonium sulphate with
2,5-dimethylfuran

2,4-Dinitroaniline (9.1g, 0.05 mole) was diazotised and added to a solution of 2,5-dimethylfuran (4.8g, 0.05 mole) in glacial acetic acid (200 ml) and stirred at room temperature for 50 hours. Dilution with water produced a dark red gummy precipitate, which was collected. Attempts to purify the precipitate, by recrystallisation, failed and it was chromatographed on an alumina column using chloroform. A deep red "glassy" solid (3.8g) was obtained which was recrystallised from carbon tetrachloride and found to be (2',4'-dinitrobenzene)-3-azo-2,5-dimethylfuran (m.p. 172°C (d). Highly resolved mass ion m/e 290.0652. $C_{12}H_{10}N_4O_5$ requires m/e 290.0651. Found C, 50.11%; H, 3.61%; N, 18.42%. $C_{12}H_{10}N_4O_5$ requires C, 49.66%; H, 3.45%; N, 19.32%. Infra-red showed the absence of -OH, -C=O groups. Ultra-violet λ_{max} 340 m μ ; ϵ = 10,150, 470 m μ ; ϵ = 3,700.). The compound could not be purified further.

The filtrate was chloroform extracted and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent gave a red oil (3.8g) which was chromatographed on an alumina column. Chloroform eluted a deep red compound which was found to be more (1.8g) of the azo compound.

The only other compounds isolated were 1,3-dinitrobenzene (0.2g) and unreacted 2,4-dinitroaniline (0.7g). No arylated derivatives were found and the total yield of the (2',4'-dinitrobenzene)-3-azo-2,5-dimethylfuran was 5.6g (40%).

8. Reaction of 2,4,6-trichlorobenzene diazonium sulphate with
2,5-dimethylfuran

2,4,6-Trichloroaniline (9.8g, 0.05 mole) was diazotised as for 2,4-dinitroaniline and added to a solution of 2,5-dimethylfuran (4.0g) in glacial acetic acid (200 ml) and stirred at room temperature for 48 hours. The red/brown coloured solution was diluted with water and chloroform extracted and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Removal of the solvent gave a brown oil (5.8g) which was chromatographed on an alumina column. Petrol 60/80 eluted a colourless component which solidified to a white solid (1.7g) and was found to be 2,2'-4,4'-6,6'-hexachlorobiphenyl (m.p. 106°C. lit m.p. 112°C. m/e 358 with a six chlorine atom pattern. Found C, 38.99%; H, 1.17%; N, 0.0%. $C_{12}H_4Cl_6$ requires C, 39.89%; H, 1.11%). Benzene eluted an orange component (0.1g) which gave orange crystals believed to be 2,4,6-trichloronitrobenzene (m/e 225 (P⁺)).

Chloroform eluted a red oil (0.1g) which had a mass spectrum suggesting it to be the azo compound (2',4',6'-trichlorobenzene)-3-azo-2,5-dimethylfuran (m/e 302 (P⁺) with a three chlorine atom pattern. High resolution mass determination found m/e 301.9781. $C_{12}H_9N_2OCl_3$ requires m/e 301.9781). The sample could not be purified to give an acceptable analysis.

9. Reaction of 4-nitrobenzene diazonium chloride with 2,5-dimethyl-
furan in ethanol. (Eastman and Detert)⁹⁶

4-Nitroaniline (7.0g) was slurried with sodium nitrite (3.5g) in ice/water (100 ml) and concentrated hydrochloric acid (20 ml) was added with stirring and external cooling. This solution was added to a mixture of 2,5-dimethylfuran (4.8g) and sodium acetate

(15g) in ethanol (250 ml) and stirred at 0°C for three hours. The mixture was poured into water and the orange oil, which formed initially, solidified after several hours and was filtered off. It was recrystallised from benzene/petrol 60/80 to give the orange intermediate compound (VIII) (m.p. 125°C. m/e 263 (P⁺). Infra-red ν_{\max} 3400 cm⁻¹ (s) (-NH, -OH) but no -C=O absorption).

Some of the compound was refluxed in a mixture of 50:50 ethanol: 5N hydrochloric acid for five minutes and then poured into water. The orange solid was filtered off and recrystallised from ethanol/water as pale orange needles of compound (VII) (m.p. 133°C. m/e 245 (P⁺). Found C, 58.18%; H, 4.45%; N, 16.78%. C₁₂H₁₁N₃O₃ requires C, 58.78%; H, 4.49%; N, 17.14%. Infra-red ν_{\max} 1680 cm⁻¹ but no -NH (-OH) absorption. Ultra-violet λ_{\max} 295 m μ ; ϵ = 13,800).

10. Reaction of 4-nitrobenzene diazonium chloride with 2,5-dimethylfuran in glacial acetic acid

4-Nitroaniline (7.0g) was diazotised with sodium nitrite (3.5g) and concentrated hydrochloric acid (20 ml) as above and was added to a solution of 2,5-dimethylfuran (4.8g) in glacial acetic acid (150 ml) and stirred at 0°C for 20 hours during which time it became dark red coloured. The solution was diluted with water and chloroform extracted and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent gave a dark red oil (4.0g) which crystallised on standing. It was purified by chromatography on a silica column using chloroform. It was extremely difficult to recrystallise and was found to be the azo compound (4'-nitrobenzene)-3-azo-2,5-dimethylfuran. (m.p. 222°C. m/e 245 (P⁺).

Highly resolved molecular weight found m/e 245.0795. $C_{12}H_{11}N_3O_3$ requires m/e 245.0800. Found C, 59.02%; H, 4.56%; N, 14.89%.

$C_{12}H_{11}N_3O_3$ requires C, 58.78%; H, 4.49%; N, 17.14%. Ultra-violet $\lambda_{\max} 378 m\mu; \epsilon = 9,920$).

11. Reaction of 2,4-dinitrobenzene diazonium sulphate with 2,5-dimethylfuran in ethanol

2,4-Dinitroaniline (9.1g, 0.05 mole) was diazotised and added to a solution of 2,5-dimethylfuran (4.8g, 0.05 mole) in ethanol (600 ml required to maintain solution) and stirred at 0°C for three hours. The solution was diluted and allowed to stand overnight when the orange oil solidified and was filtered off (7.0g). It was recrystallised from benzene/petrol 60/80 and was found to be similar to compound (VI) except that it contains a molecule of water extra which could not be removed by drying at 100°C under vacuum. (m.p. 132°C, m/e 308 (P⁺). Infra-red $\nu_{\max} 1685 \text{ cm}^{-1}$ but no -NH (-OH) absorption. Found C, 46.96%; H, 4.00%; N, 17.87%. $C_{12}H_{12}N_4O_6$ requires C, 46.76%; H, 3.90%; N, 18.18%). Refluxing in ethanol/hydrochloric acid appeared to have no effect i.e. this was the equivalent of compound (VII) not (VI).

12. Reaction of 2,4-dinitrobenzenediazonium sulphate with 2,5-diphenylfuran

a) Preparation of 2,5-diphenylfuran

2,5-Diphenylfuran was prepared by the method of Lutz and Rowlett.¹¹⁹ Trans-dibenzoyl ethylene (50g) was added portionwise to a vigorously stirred, refluxing mixture of stannous chloride (150g), concentrated hydrochloric acid (100 ml) and glacial acetic acid (100 ml). The mixture was refluxed for 15 minutes, cooled to 50°C and poured into cold water. The precipitate was collected and re-crystallised from ethanol. The product was obtained as white plates, 31g (70%), m.p. 89-90°C (lit. m.p. 89.5-91°C).

b) Coupling reaction

2,4-Dinitroaniline (9.1g, 0.05 mole) was diazotised and added to a solution of 2,5-diphenylfuran (11g, 0.05 mole) in glacial acetic acid (400 ml). The solution immediately became deep green coloured and some precipitation of 2,5-diphenylfuran occurred, which was corrected by the addition of more glacial acetic acid, the green colour was similar to that found during the coupling reaction of 2,3,5-triphenylthiophen; (see page 58). After an hour or so the colour gradually turned to a dark red and the mixture was stirred for 70 hours. Although a slight precipitate had formed, the mixture was chloroform extracted without filtration and the extract was washed with water, aqueous sodium bicarbonate solution until no longer acidic, water and dried over magnesium sulphate. Evaporation of the solvent gave a dark red oil (16g) which was chromatographed on a silica column. Benzene eluted a yellow fraction which gave a red oil (11g). This was purified down a further silica column and re-crystallised from benzene/petrol 60/80 as orange needles. This compound was found to be 3-(2',4'-dinitrophenyl)-2,5-diphenylfuran

(m.p. 165°C. m/e 386 (P⁺). Found C, 68.25%; H, 3.70%; N, 7.00%.
C₂₂H₁₀N₂O₅ requires C, 68.39%; H, 3.63%; N, 7.25%. Infra-red shows
no -C=O. Ultra-violet λ_{\max} 322 m μ ; ϵ =28950, (376 m μ ; ϵ =17,370)).

A benzene/chloroform mixture eluted an orange component
which gave an orange solid (1.1g). This was found to be 3,4-bis-
(2',4'-dinitrophenyl)-2,5-diphenylfuran. (m.p. 114°C. m/e 552 (P⁺).
Found C, 59.36%; H, 2.92%; N, 9.79%. C₂₈H₁₆N₄O₉ requires C, 60.87%;
H, 2.90%; N, 10.15%. Infra-red shows no -C=O. Ultra-violet
 λ_{\max} 305 m μ ; ϵ =20400, 380 m μ ; ϵ =8800).

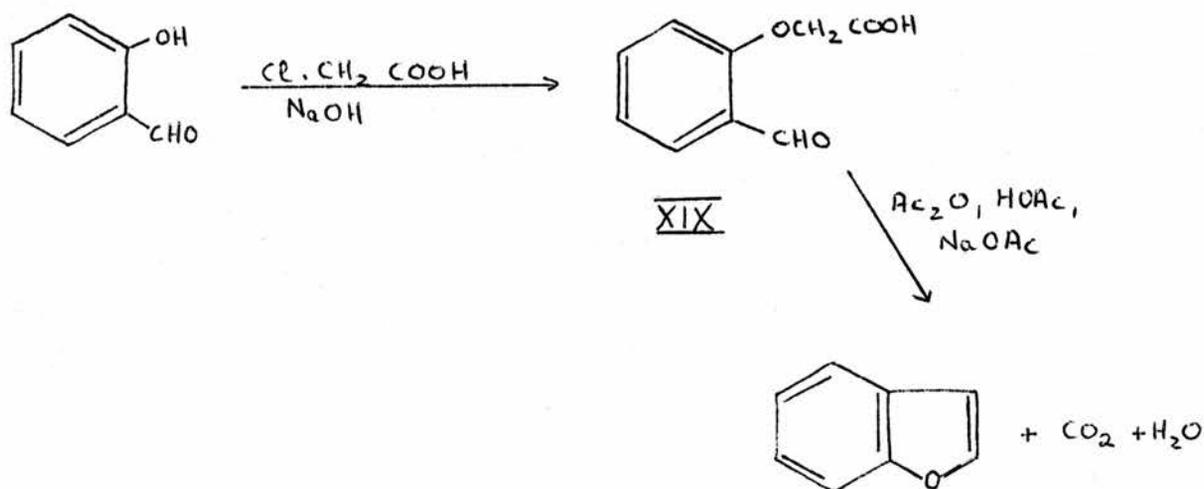
Chloroform eluted a small amount of a red oil (0.2g) which
could not be purified but appeared to contain 3-(2',4'-dinitrobenzene-
azo)-2,5-diphenylfuran. (Oil. High resolution m/e 414.0963.
C₂₂H₁₄N₄O₅ requires m/e 414.0964. Found C, 61.87%; H, 3.35%;
N, 12.16%. C₂₂H₁₄N₄O₅ requires C, 63.77%; H, 3.38%; N, 13.53%).

The reaction was not a clean one and several minor comp-
onents were isolated which could not be characterised. One red oil,
obtained from attempts to recrystallise the suspected azo compound,
gave a mass spectrum suggesting it to be the ring-opened mono-
arylated compound (m/e 402 (P⁺)) but the analysis could not be
correlated and too little was obtained to pursue further.

The yield of the mono-arylated compound 3-(2',4'-dinitro-
phenyl)-2,5-diphenylfuran was 11g (57%) and the di-arylated compound
3,4-bis-(2',4'-dinitrophenyl)-2,5-diphenylfuran was found in 1.1g
(4%) yield. The suspected azo compound was found in only 1% yield.

13. The reaction of 2,4-dinitrobenzenediazonium sulphate with benzofuran

a) The preparation of benzofuran:¹²⁰



o-Formylphenoxyacetic acid (XIX) was prepared by adding a solution of sodium hydroxide (80g, 2 mole) in water (200 ml) to a mixture of salicylaldehyde (106 ml, 1 mole) and chloroacetic acid (94.5g, 1 mole) in water (800 ml) and refluxing the mixture for three hours. Concentrated hydrochloric acid (approx. 190 ml) was added to acidify the solution and the unchanged salicylaldehyde was removed by steam distillation (approx. 40g. Distillate tested with 2,4-dinitrophenylhydrazine to ensure complete removal). The solution was cooled to 20°C and the light tan precipitate of o-formylphenoxyacetic acid was filtered and washed with water (yield 100g, 82% based on recovered salicylaldehyde). The material was dried without recrystallisation and 90g (0.5 mole) of it with anhydrous powdered sodium acetate (180g), acetic anhydride (450 ml) and glacial acetic acid (450 ml) was refluxed for eight hours. The cooled solution was poured into ice/water (2.5 l) and extracted with ether (1x600 ml). The ether layer was washed with water, cold 5%

sodium hydroxide solution (carefully) until basic (approx. 250 ml), water, saturated sodium chloride solution and dried over sodium sulphate. The solvent was removed under reduced pressure and the product was distilled at 166.5-168°C (or 97-99°C at 80 mm) and gave 40g (55% overall) of water-white benzofuran.

b) The coupling reaction:

2,4-Dinitroaniline (9.1g, 0.05 mole) was diazotised and added to a solution of benzofuran (5.9g, 0.05 mole) in glacial acetic acid (200 ml) and stirred at 0°C for 70 hours. The solution was diluted with water and chloroform extracted and the extract was washed with water, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Removal of the solvent gave a red oil (9.3g) which solidified in an unusual and characteristic manner. Some of this solid (2g) was dissolved in benzene and chromatographed on an alumina column, using benzene. A yellow component, which spread out on the column, was collected as a yellow solid (1.2g) and was recrystallised from benzene/petrol 60/80 as fine yellow needles of 2-(2',4'-dinitrophenyl)-benzofuran (m.p. 138°C, m/e 284 (P⁺)). Found C, 59.17%; H, 2.89%; N, 9.73%; C₁₄H₈N₂O₅ requires C, 59.16%; H, 2.82%; N, 9.86%. Infra-red showed absence of -OH, -C=O groups. Ultra-violet λ_{\max} 366 m μ ; ϵ = 16500).

Chloroform eluted a red oil (0.3g) which was recrystallised from benzene/petrol 60/80 and was found to be the di-arylated derivative 2,3-bis-(2',4'-dinitrophenyl)-benzofuran (m.p. 100°C. m/e 450 (P⁺)). Found C, 52.96%; H, 2.28%; N, 12.15%. C₂₀H₁₀N₄O₉ requires C, 53.30%; H, 2.22%; N, 12.45%. Infra-red showed absence of -OH, -C=O groups. Ultra-violet λ_{\max} 358 m μ ; ϵ = 15,750).

No azo compound was isolated and the total yield of the mono-arylated derivative was 5.6g (40%) and 1.4g (6%) of the di-arylated compound was obtained.

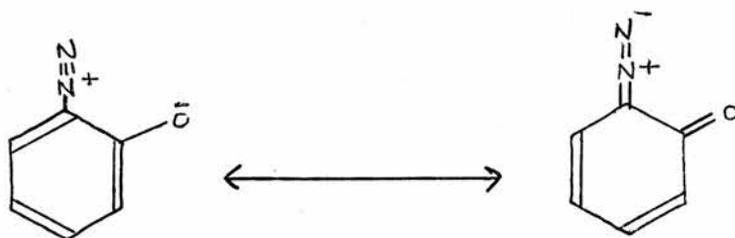
PART II

PART II

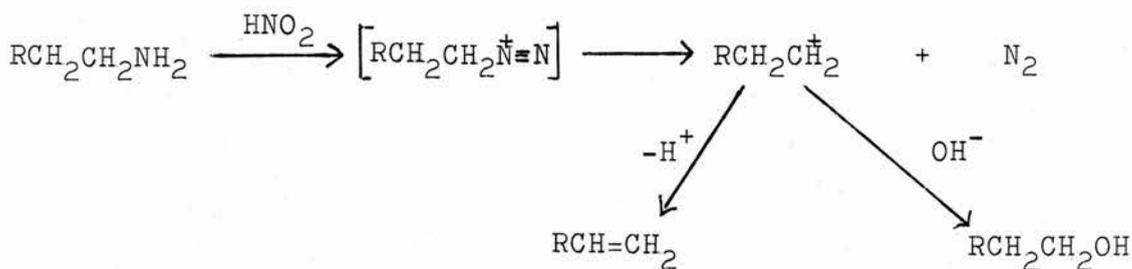
NITROSOACETYLENES AND ACETYLENIC DIAZONIUM SALTS

INTRODUCTION

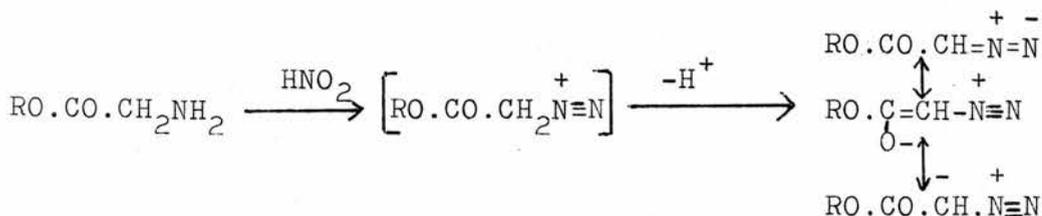
Since Greiss,⁴⁶ in 1860, reported the preparation of the first diazonium salt from picramic acid, diazonium salts have become an important class of organic intermediates in both synthetic and industrial chemistry.⁵³ Their usefulness comes in particular, from their electrophilic nature involving them in substitution (coupling) reactions and the ease with which the diazonium group can be replaced by other groups. Diazonium salts, the anions of which are derived from strong acids, give neutral solutions in water, which are completely dissociated.⁷⁷ The use of isotopic tracers has proved⁷⁸ that the two nitrogen atoms are not equivalent. The diazonium group exerts a very powerful -M effect roughly equivalent to two nitro residues.⁷⁹ Hence the dissociation constant of the p-hydroxybenzene diazonium ion (pK 3.4) is about 10^6 times greater than that of phenol itself.⁸⁰ In aromatic diazonium salts, the positive charge is delocalised through the π -electron system of the aromatic nucleus inferring a measure of stability and this stability can be increased by the presence of electron donating substituents in the aromatic nucleus.



With saturated aliphatic compounds, no such delocalisation can occur and attempts to produce such diazonium salts results in the loss of nitrogen to form a carbonium ion, which can react with the solvent, to give an alcohol, or lose a proton to give an olefin:



However, if the aliphatic primary amine has an electron withdrawing substituent in the 1-position, diazoalkane derivatives can be prepared via the diazonium salt, although these salts have not been isolated:



The first successful preparation of an aliphatic diazonium salt was in 1962 by Curtin et al, ⁸¹ who diazotised an aliphatic bridgehead amine (at -78°C) and isolated the 2-naphthol azo dye:



The possibility that an unsaturated aliphatic compound may stabilise, by delocalisation, a diazonium group introduced at the unsaturated centre, led to the work described in this thesis (Part II). The alkyne group, having π -orbitals of the same symmetry type as those associated with the diazonium group, should interact to give some delocalisation of the positive charge:



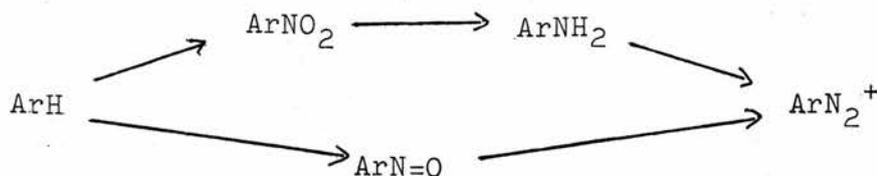
(only the \uparrow -orbitals in one direction are shown).

It can be argued that "sp" hybridisation in the triple carbon-carbon bond leads to tightly held electrons of relatively high "s" character compared to the equivalent double bond. This is indicated by their ionisation potentials of 11.41 and 10.5 eV for acetylene and ethylene respectively. As a result of this difference there is a reduction in delocalisation energy with the conjugation of triple bonds compared to the conjugation of double bonds:⁸²

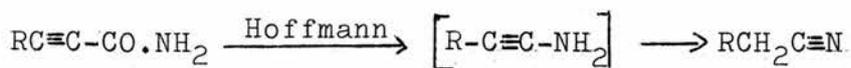
Hydrocarbon	Ionisation Potential	Conjugation energy difference
CH ₂ =CH ₂	10.5 eV	} 1.43 eV
CH ₂ =CH-CH=CH ₂	9.07 eV	
HC≡CH	11.41 eV	} 0.62 eV
HC≡C-CH	10.79 eV	

However this interaction should be increased by the powerful -M effect of the diazonium group and in fact Robson, Tedder and Woodcock^{92,83} have provided considerable evidence for the existence of acetylenic diazonium salts at -40°C, which suggests that some stabilisation is achieved relative to saturated aliphatic hydrocarbons.

Diazonium salts can generally be prepared by two routes:



The first is the conventional route by way of nitration of the hydrocarbon, reduction of the nitro group to an amino group, followed by diazotisation with nitrous acid. The second method involves nitrosation of the aromatic nucleus and subsequent diazotisation of the nitroso group, both steps usually by the same reagent and concurrently.⁸⁵ The conventional method is unsuitable for the synthesis of acetylenic diazonium salts since acetylenic amines are unknown and attempts to prepare them have resulted in the formation of the corresponding nitrile:⁸⁶

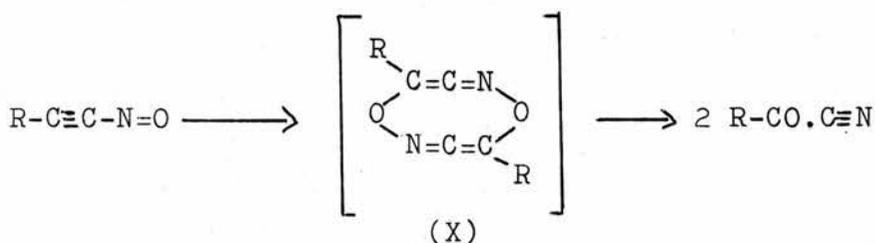


Thus the nitroso route was used although nitroso-acetylenes were also an unknown class of compounds. The main methods available for the preparation of C-nitroso compounds are:

1. oxidation of the amine or diethylketamine⁸⁷ by neutralised peracetic acid in methylene dichloride.
2. the action of nitrous acid on activated nuclei.
3. the reaction between nitrosyl chloride and (a) diaryl mercury⁸⁹ compounds, or (b) aryl mercuric or (c) magnesium halides.

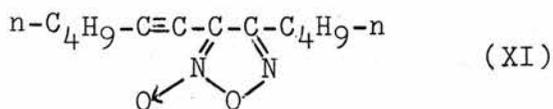
Since easily prepared mercury acetylides are known⁹⁰ the latter method (3) was used.⁹² The action of nitrosyl chloride on mercury acetylides in chloroform solution at -40°C produces dark green solutions which gave the following spectral data when dihex-1-ynyl mercury was used: in the infra-red strong bands at

2290 cm^{-1} and 1580 cm^{-1} attributed to conjugation of the carbon-carbon triple bond with the nitrogen-oxygen double bond. In the visible spectrum, the nitroso band $[n \rightarrow \pi^*]$ occurred at 640 $\text{m}\mu$. On warming to room temperature the green colour was lost and examination of the infra-red spectrum of the resulting oil showed that the above peaks had been replaced by peaks at 2210 cm^{-1} and 1710 cm^{-1} , a change due to the formation of the isomeric ketocyanide, believed to occur via an eight-membered ring intermediate ⁹² (X):



The ketocyanide was not isolated.

Treatment of the nitrosohex-1-yne with base did not produce the expected nitroso dimer but a compound containing a furoxan ring. ⁹² (XI):

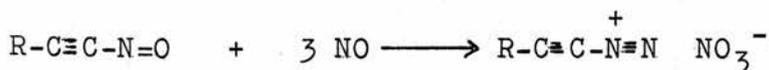


The mechanism of dimerisation must involve an initial condensation of the carbon-carbon triple bond across the carbon-nitrogen bond of a second molecule of the nitrosoacetylene, in the presence of base.

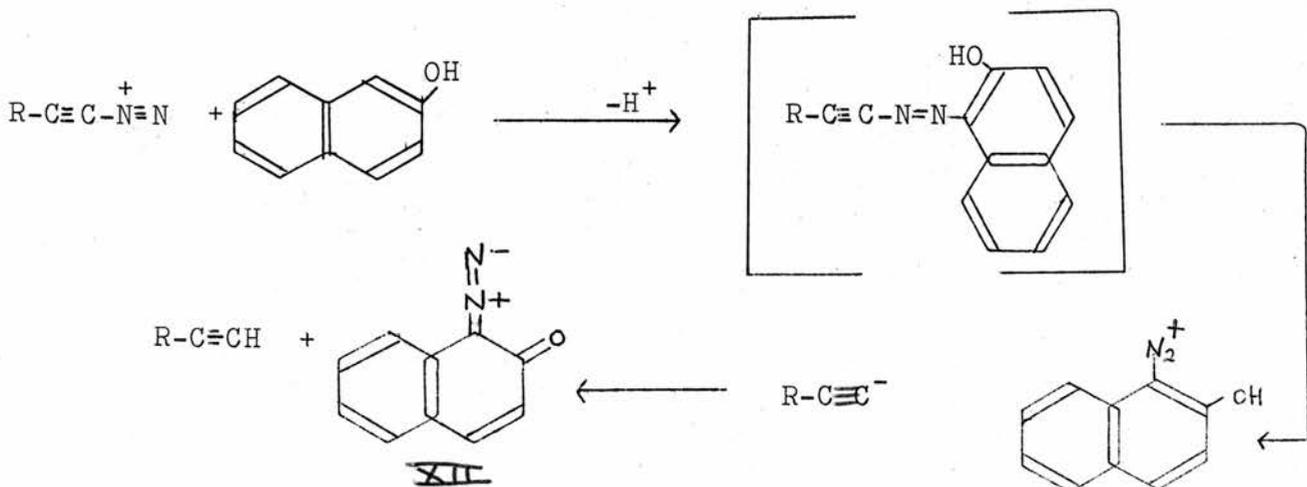
Attempts to perform the addition reaction between nitrosoacetylenes and aniline failed to leave the carbon-carbon triple bond intact and sydnone-oxime derivatives were isolated. ⁹² Hydrolysis of the nitrosoacetylenes occurs to give n-butyric acid and cyanide ions. Hydrogenation of nitrosoacetylenes does not

proceed with Raney nickel and with lithium aluminium hydride, it is not straightforward.⁸³

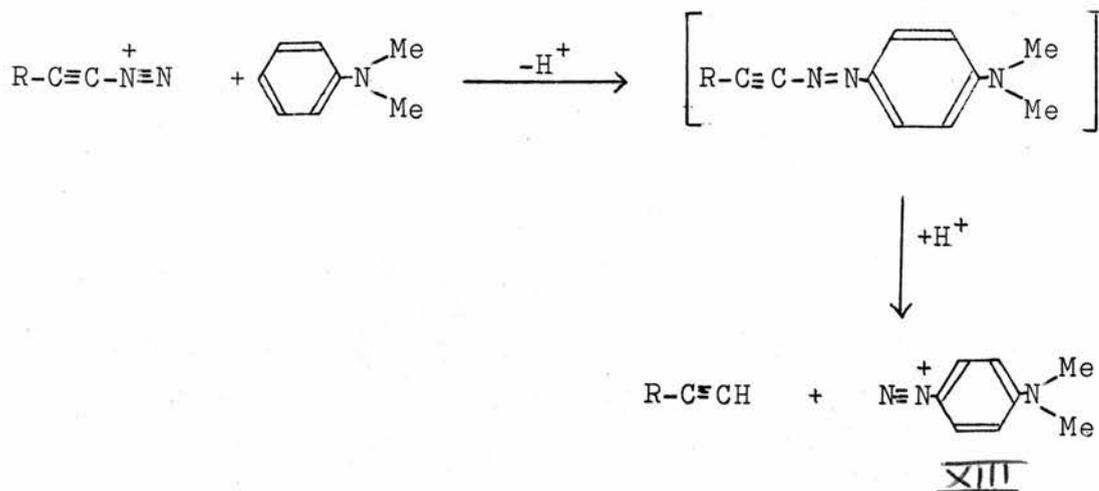
Nitric oxide reacts with the green solutions at -40°C to give golden-yellow solutions believed to be the diazonium salt:



Coupling reactions of this diazonium salt, to form acetylenic-azo derivatives, were attempted but, if these compounds are formed, they are unstable giving products indirectly supporting the formation of the diazonium salt. With 2-naphthol, naphthalene-1,2-diazo-oxide (XII) was isolated:

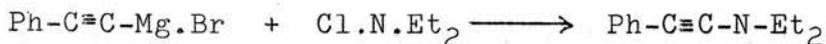


With dimethylaniline, N,N-dimethyl-4-amino-benzene diazonium ion (XIII) was identified by coupling with 2-naphthol:

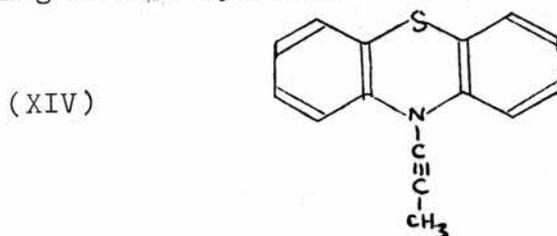


In these experiments great care was taken to remove the excess nitrosyl chloride and nitric oxide before the addition of the coupling reagent thus eliminating the possibility of direct introduction of the diazonium group into the aromatic nucleus.

Acetylenic compounds containing a hetero-atom adjacent to the carbon-carbon triple bond are well known; with non-metals such as sulphur, oxygen, silicon and halogens stable derivatives are formed but compounds containing nitrogen next to the triple bond are very rare. N,N-Diethylphenyl-ethynylamine is reported in a 1.7% yield⁹⁴ from the following reaction:



This compound gives a strong absorption in the infra-red at 2195 cm^{-1} . N-(1-Propynyl)-phenothiazine (XIV) has been reported⁹⁵ from the reaction of propargyl bromide with phenothiazine in dimethylformamide solution containing sodium hydride:



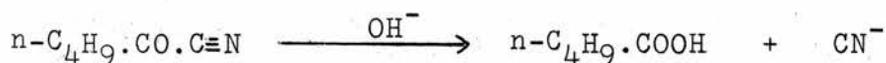
In section A of this thesis (Part II), the reactions and properties of the green solutions obtained from the reaction of dihex-1-ynyl mercury with nitrosyl chloride at -40°C are investigated further. Section B deals with attempts to unambiguously show that nitric oxide reacts at -40°C with the green nitrosohex-1-yne solutions to give the golden-yellow diazonium nitrate.

PART II SECTION A

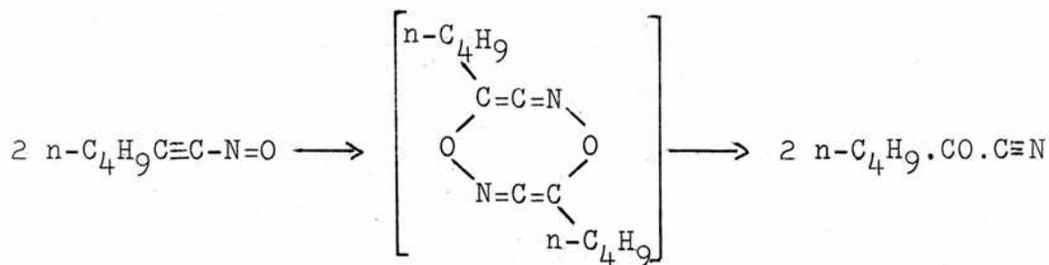
NITROSOACETYLENES

DISCUSSION

In 1963, Robson and Tedder⁸⁴ discovered that treatment of a solution of dihex-1-ynyl mercury in chloroform with nitrosyl chloride, at -40°C , gave a dark green solution believed to contain 1-nitrosohex-1-yne. The green solution decomposed slowly at room temperature but was stable indefinitely at -40°C and gave spectral data consistent with that expected of 1-nitrosohex-1-yne: infra-red absorptions at 2290 cm^{-1} ($-\text{C}\equiv\text{C}-$) and 1580 cm^{-1} ($-\text{N}=\text{O}$) and an ultra-violet absorption at $640\text{ m}\mu$ ($-\text{N}=\text{O}$ ($n\rightarrow\pi^*$)). After the green solution had been warmed to room temperature, the above peaks in the infra-red spectrum were replaced by absorptions at 2210 cm^{-1} and 1710 cm^{-1} due to n-butyrylcyanide. This was hydrolysed⁹² to give pentanoic acid and cyanide ions:

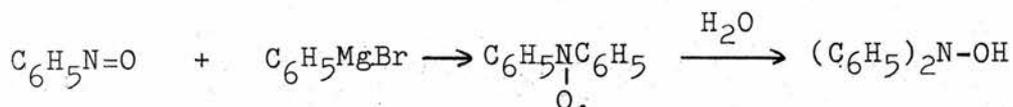


The proposed mechanism for the formation of the n-butyrylcyanide from 1-nitrosohex-1-yne involves an eight-membered cyclic dimer as an intermediate

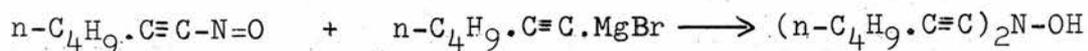


Attempts to isolate the keto-cyanide have not been successful but G.L.C. coupled mass spectrometry has provided strong evidence for its existence. Distillation always resulted in extensive polymerisation known to occur with butyryl- and isobutyryl- cyanides. The presence of mercury salts may catalyse this polymerisation

and is also believed to be a major factor in the failure to isolate any true nitrosoacetylene or acetylene diazonium salt derivative. Hydration of the acetylenic triple bond in the presence of catalytic quantities of mercuric salts is well established.⁸⁸ Tedder and Woodcock have investigated the use of other metal acetylides in the preparation of nitrosoacetylenes. Lithium acetylides and acetylenic Grignard reagents⁸³ were both found to give green solutions at -70°C if the nitrosyl chloride was added rapidly. However, if the nitrosyl chloride was added slowly, red/brown solutions were obtained. Wieland and Roseell⁹¹ reported red/brown mixtures from the reaction between nitrosobenzene and phenyl magnesium bromide, from which diphenylhydroxylamine was isolated and further studies⁹³ showed this to proceed via a free radical reaction:



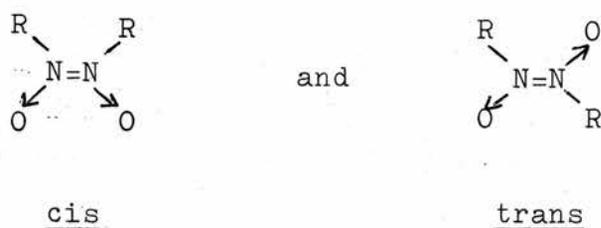
The slow addition of the nitrosyl chloride to the lithium acetylide or the acetylenic Grignard reagent is therefore believed to result in the rapid free radical reaction of the newly formed nitrosoacetylene with the unchanged metal acetylide:



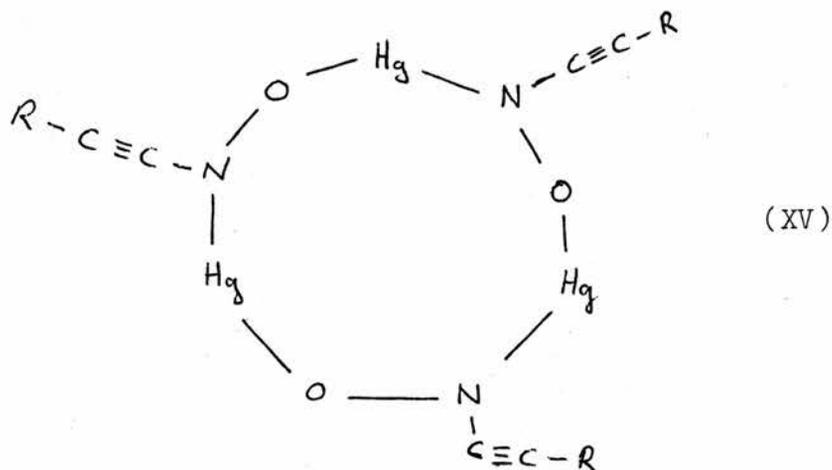
The infra-red spectra of these solutions did not show any $-\text{C}\equiv\text{C}-$ absorptions and such side reactions became a considerable drawback in the use of lithium or magnesium acetylide derivatives. Tedder and Woodcock concluded that the mercury acetylide preparation was

the most reliable.

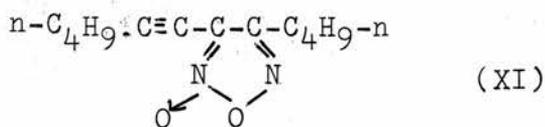
C-Nitroso compounds have been known for a long time, the first examples being 1-nitroso-4-(dimethylamino)-benzene⁹⁷ and nitrosobenzene.⁹⁸ They exist as blue-green solutions or colourless dimeric solids. The dimers exhibit cis and trans isomerism and may be formulated as:



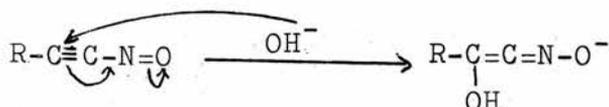
Robson and Tedder⁹² tried to isolate the dimer of 1-nitrosohex-1-yne but obtained a small amount of white solid whose analysis and infra-red data corresponded to $(n\text{-C}_4\text{H}_9\text{.C}\equiv\text{C-N=O.Hg})_n$ which may be a cyclic polymer (XV):



Tedder and Woodcock⁸³ treated 1-nitrosohex-1-yne with aqueous sodium hydroxide solution and, after warming to room temperature, obtained a colourless oil which was identified as the non-reversible dimer (XI):



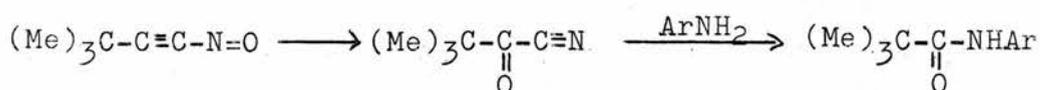
Similar dimers of 1-nitroso-3,3-dimethylbut-1-yne and 1'-nitroso-2,4,5-trimethylethynebenzene were not obtained suggesting that the base attacks the second carbon atom of the acetylenic triple bond which, in both of the above compounds, is protected by bulky methyl groups:



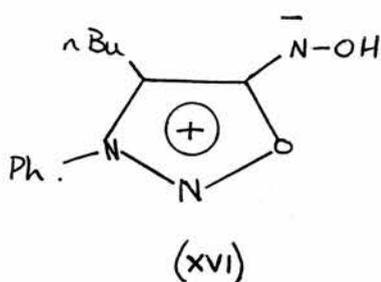
Both Robson and Woodcock have attempted to reduce the acetylenic triple bond of 1-nitrosohex-1-yne. Both found that Raney nickel failed to give any hydrogenation but that lithium aluminium hydride at $-10^{\circ}C$ gave reduced products. Although no pure products were isolated, n-hexylamine was detected by G.L.C. retention time analysis. In the present work attempts were also made to prepare derivatives of 1-nitrosohex-1-yne while maintaining the nitroso group intact; by attempting bromination of the $-C \equiv C-$ bond and by addition of cyclopentadiene across the $-C \equiv C-$ bond. In the case of bromination, no decolourisation of the bromine was observed, even at room temperature. With cyclopentadiene a colour change was noted on addition at $-40^{\circ}C$ but, when room temperature was reached, the solution smelled strongly of unreacted cyclopentadiene and evaporation of the solvent gave only a trace of an unidentified red oil.

When aniline was condensed with 1-nitrosohex-1-yne⁹² only red oils were isolated which did not contain $-C \equiv C-$ absorptions in their infra-red spectra. 1-Nitroso-3,3-dimethylbut-1-yne was

reacted with aniline and mesidine⁹² to give, in both cases, white crystalline solids identified as the products formed by the nucleophilic attack of the amine on the rearranged nitroso acetylene:



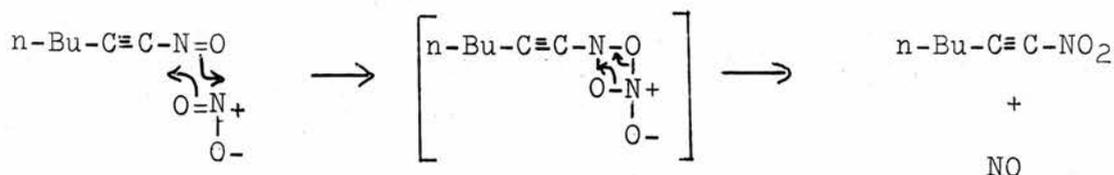
Tedder and Woodcock⁸³ identified a sydnone oxime (XVI) from the reaction of 1-nitrosohex-1-yne with aniline in the presence of excess nitrosyl chloride:



A mechanism was proposed. Steric hindrance was the cause of the failure of 1-nitroso-3,3-dimethylbut-1-yne and 1'-nitroso-2,4,6-trimethyl-ethynylbenzene to give similar sydnone oxime derivatives with aniline in the presence of excess nitrosyl chloride.

C-Nitroso compounds can be readily oxidised by nitric acid, hydrogen peroxide or permanganate, to give the corresponding nitro compound. Tedder and Woodcock⁸³ added hydrogen peroxide to a solution of 1-nitrosohex-1-yne at -40°C and obtained a pale yellow oil which gave an infra-red spectrum corresponding to that expected for a nitroacetylene (2270 cm^{-1} ($-\text{C}\equiv\text{C}-$) and 1575 cm^{-1} ($-\text{NO}_2$)). The carbon-carbon triple bond absorption was lost after a short while at room temperature and true characterisation was not achieved.

It was considered that the oxidation of 1-nitrosohex-1-yne to 1-nitrohex-1-yne could be carried out using either dinitrogen trioxide or nitrogen dioxide:

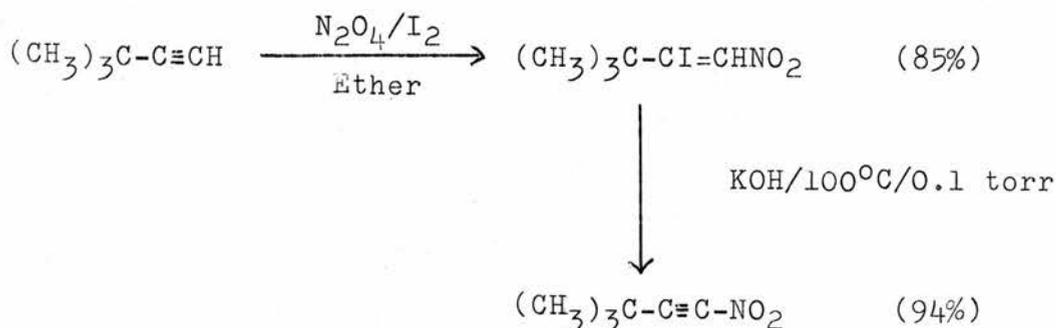


Dinitrogen tetroxide was prepared by heating lead nitrate in a steel tube and collected as a white solid using a receiver cooled in a solid carbon dioxide/acetone bath. The correct amount of this solid was weighed into dry, ethanol-free chloroform and added to a solution of 1-nitrosohex-1-yne at -40°C . The solution was allowed to reach room temperature, filtered from the precipitated mercury salts, washed and dried over magnesium sulphate. The infra-red spectrum showed no $\text{-C}\equiv\text{C-}$ absorptions and a G.L.C. trace showed it to contain similar products to those from the reaction using dinitrogen trioxide viz: hex-1-yne, n-butyryl cyanide and pentanoic acid.

Since the above work was completed, Jager and Viehe⁹⁹ have produced a series of nitroacetylenes by the dehydrohalogenation of the 2-iodo-1-nitroolefins. In this new class of compounds the strongly electronegative nitro-group polarises the carbon-carbon triple bond to produce a highly reactive electrophile:



These compounds would be expected to have a very high ground state energy and therefore to be of limited thermal stability. The first nitroacetylene synthesised, t-butylnitroacetylene was eventually obtained in almost quantitative yield from the reaction scheme below:



This nitroacetylene is a greenish-yellow, volatile, lachrymatory liquid (— b.p. $\approx 55^\circ\text{C}/15 \text{ Torr}$ (m.p. -3°C)). It does not detonate by shock, heating or glowing wire treatment and has a half-life of 2-3 days.¹⁰⁰ In the series of nitroacetylenes prepared by Jager and Viehe, the most stable was t-butylnitroacetylene (which was chosen as the representative for all the subsequent work¹⁰⁰) and the least stable was n-butylnitroacetylene. This was prepared from 2-iodo-1-nitrohex-1-ene and is a liquid with a half-life of only a few hours. The infra-red absorption (2265 cm^{-1} ($-\text{C}\equiv\text{C}-$)) and the thermal stability agree well with characteristics of the oil isolated by Woodcock (see page 100) in the attempted preparation of 1-nitrohex-1-yne. It would seem that the hydrogen peroxide oxidation of t-butylnitroacetylene should be attempted since the nitroacetylene obtained would be reasonably stable.

Tedder and Woodcock⁸³ have tried to prepare more stable nitroacetylenes by extending the delocalisation beyond the acetyl-

enic triple bond. However, with the addition of nitrosyl chloride to diphenylethynyl mercury and to ^{di-}2,4,6-trimethylphenylethynyl mercury, no green colour was observed even at -70°C . The marked increased stability (by steric protection) of the t-butyl group over the n-butyl group found by Jager and Viehe⁹⁹ in the nitroacetylenes was not found in the nitrosoacetylene solutions, both giving the corresponding acyl cyanide on warming to room temperature.

From the evidence in this section and in the acetylene diazonium salt section (Part II, Section B), there is little doubt that nitrosoacetylenes are produced by the action of nitrosyl chloride on mercury acetylides in solution at -40°C . That none have been isolated pure or as simple derivatives would point to an inherent instability, accentuated by the presence of mercuric ions. It appears that the nitroso group acts only as a single entity below -40°C (in the absence of base) but at above this temperature, 1,4-addition readily occurs. Nucleophilic attack of bases at the second acetylenic carbon atom is facile as is hydrolysis of the acetylenic triple bond in the presence of mercuric ions in an acidic solution. As a result of these factors, a vast number of products are produced of which only a few have been identified.

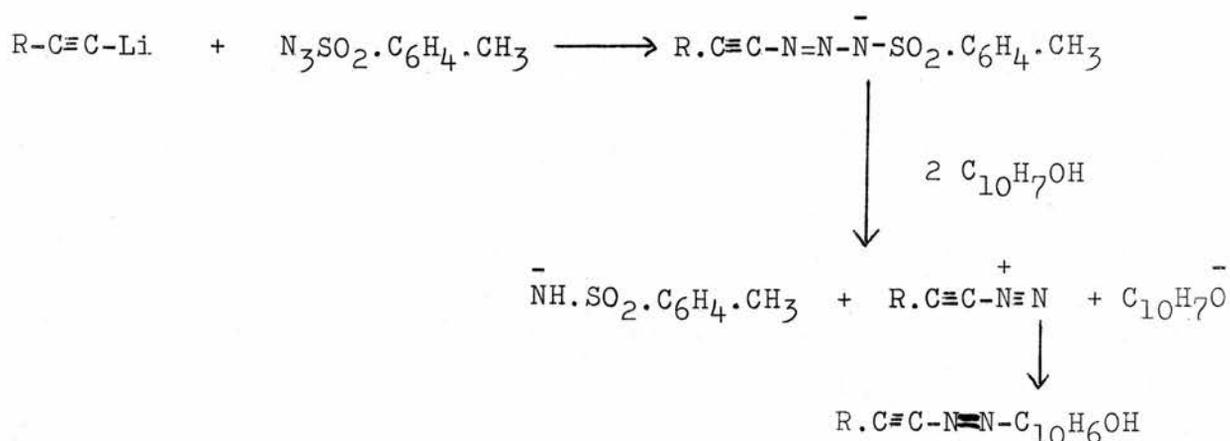
The potential of nitrosoacetylenes in synthetic organic chemistry cannot be realised until some or all of these difficulties can be overcome. Apart from the experiment to oxidise t-butyl-nitrosoacetylene to t-butyl-nitroacetylene, with hydrogen peroxide, mentioned in the text (see page 102) this line of research is severely limited. Since it is now possible to synthesise pure 1-nitroalkynes, reduction of these compounds may offer a route to forming nitrosoacetylenes without the damaging presence of metal ions.

PART II SECTION B

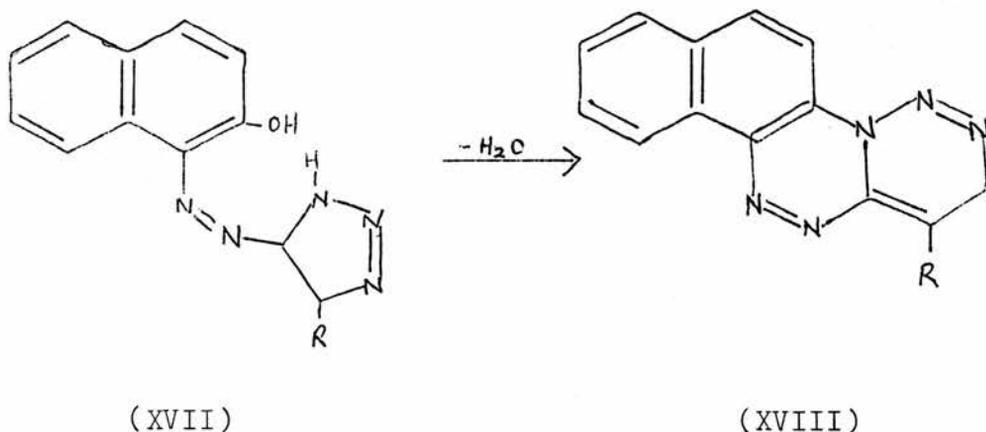
ACETYLENIC DIAZONIUM SALTS

DISCUSSION

The object of the work discussed in this section was to prepare stable acetylenic azo-compounds using acetylenic diazonium salts prepared by the reaction of nitric oxide with nitrosoacetylenes. Robson and Tedder⁹² had previously tried to couple toluene-p-sulphonyl azide with lithium acetylides; a reaction first observed by Curtius¹⁰¹ when he synthesised the diazonium derivative of malonic acid. More recently the reaction has been adapted to the preparation of diazo-oxides from phenols¹⁰² and the synthesis of diazocyclopentadiene.¹⁰³ The proposed reaction scheme is:

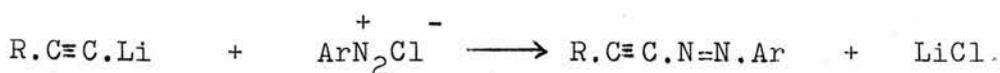


However, using the lithium acetylides of acetylene, hex-1-yne and phenylacetylene he found a compound identified as (XVII) in each case, which on warming ring closed to give (XVIII).

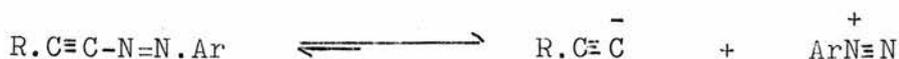


This was interpreted as evidence that initial coupling had taken place, but that the triazine formed had coupled with more azide. A mechanism was proposed.

Woodcock attempted to prepare acetylenic azo compounds by adding suspensions of aromatic diazonium salts in ether to lithium acetylides suspended in ether at 0°C.

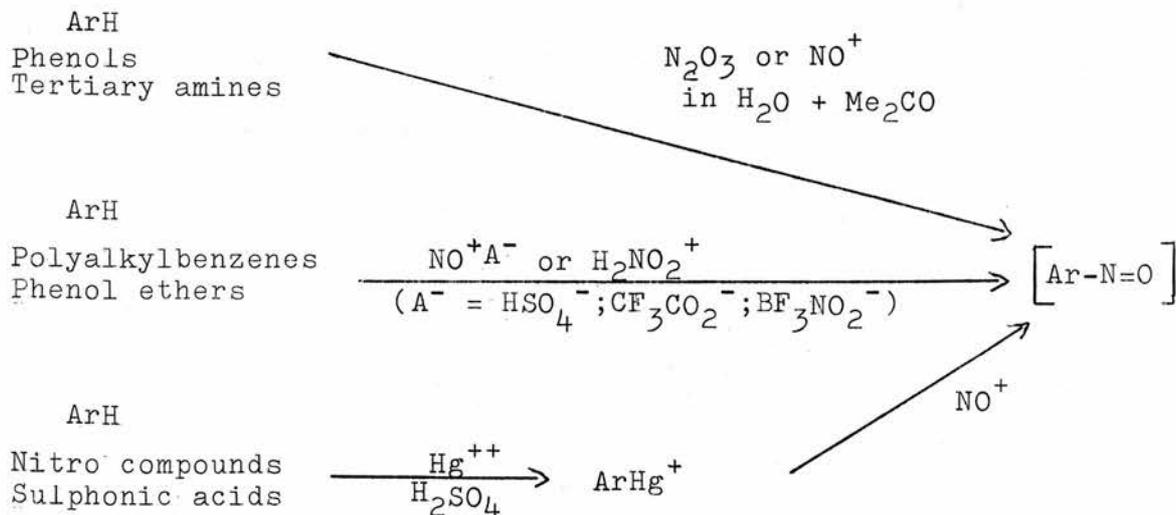


With benzene diazonium chloride and hex-1-ynyl lithium, a red solution was obtained over a period of one hour which gave a red oil with an absorption in the infra-red at 2200 cm^{-1} ($-\text{C}\equiv\text{C}-$) but column chromatography and thin layer techniques failed to isolate any components and the triple bond absorption was always lost. It was thought that a more stable azo compound would be obtained using p-nitrobenzene diazonium chloride but a vigorous reaction occurred with the loss of a colourless gas and the infra-red spectrum of the reaction products showed no $-\text{C}\equiv\text{C}-$ absorptions. The reaction with 4-N,N-dimethylaminobenzene diazonium chloride was extremely slow and again none of the isolated oils showed the presence of an acetylene group from their infra-red spectra. In the hope that conjugation throughout the molecule would increase stability, phenylethy~~ny~~lithium was used; again with no success. The evidence obtained in the reaction of aromatic diazonium salts with lithium acetylides suggests that any equilibrium between the diazonium cation and the acetylide anion would lie far to the right in the equation:



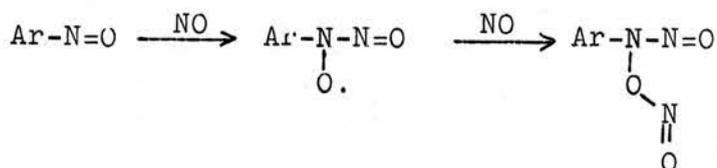
Woodcock's prediction from this work⁸³ that the coupling reaction of acetylenic diazonium salts is likely to give only indirect evidence for the formation of acetylenic diazonium salts has been confirmed by the work described in this section. The results obtained point to the formation of the required azo-compounds followed by dissociation to the acetylide ion.

Nitric oxide was shown⁹² to add to the green solution of 1-nitrosohex-1-yne at -40°C to give a golden-yellow solution believed to contain hex-1-yne diazonium nitrate. Where aromatic compounds can be converted into diazonium salts by the use of nitrous acid, there is little doubt that the aromatic nitroso compound is a necessary intermediate:¹⁰⁴

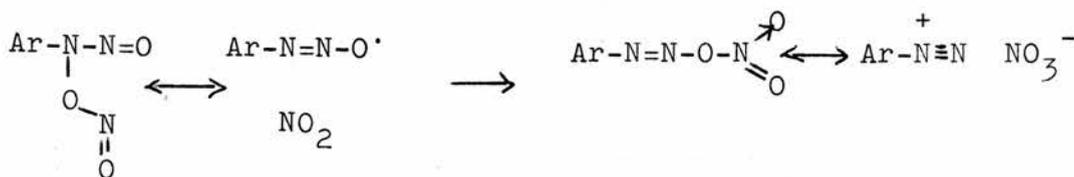


Bamberger was unable to establish the stoichiometry of the conversion of the nitroso group into the diazonium group. Havinga¹⁰⁵ has shown that 3 moles of nitrite in acetic acid are necessary and these results were confirmed by Tedder and Theaker¹⁰⁶ who found a 31% yield of azo dye with a 1:1 ratio of nitrosobenzene to nitrite but a 97% yield with a 1:3 ratio. Using nitric oxide, they found that nitrosobenzene in nitrobenzene solution absorbed two moles

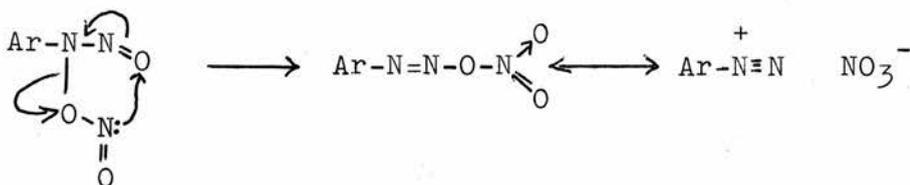
although the subsequent coupling reaction showed only a 75% yield of azo dye. However, assuming two moles of nitric oxide are required two possible mechanisms are proposed.¹⁰⁶ The initial simple addition



followed by (a) dissociation and readdition



or (b) an intramolecular rearrangement

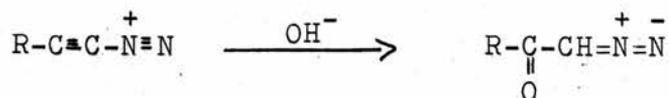


More information on the overall mechanism was sought using nitrosobenzene dissolved in benzene. Nitric oxide was bubbled through the green solution to give a red colour and a fluffy precipitate which was filtered off and identified as benzene diazonium nitrate by coupling with 2-naphthol. Nitrosobenzene in benzene was found to give no electron spin resonance spectrum. Attempts to carry out the nitric oxide addition in situ failed due to the turbulence caused by the passage of nitric oxide upsetting the balance of the machine.

Despite the fact that nitric oxide is one of the few stable inorganic radicals and its spin resonance has been extensively studied in the gas phase,¹⁰⁷ it has never been unambiguously detected in any condensed phase.¹⁰⁸ This was checked using nitric oxide dissolved in benzene: no resonance was found. To confirm that nitric oxide was sufficiently soluble in benzene to effect the conversion of a nitroso group to a diazonium group, an apparatus was set up in which the contents of one flask could be transferred to another by nitrogen pressure. The first flask contained benzene and the second nitrosobenzene dissolved in benzene. The system was purged with nitrogen and nitric oxide was bubbled through the benzene for ten minutes independently of the second flask. The flask was again purged with nitrogen to remove excess nitric oxide and the contents transferred to the nitrosobenzene flask. A white precipitate formed which proved to be benzene diazonium nitrate. By repeating the experiment but using a sample from each flask in an E.S.R. tube, it was found that mixing the two solutions outside the apparatus, a free radical intermediate was formed which gave a signal slowly increasing over a period of time, presumably due to the slow diffusion of the two solutions in the E.S.R. tube. The resonance signal was identified as a typical nitrogen triplet but due to breakdown of the machine, no further information was obtained. (It is hoped to pursue this study and to include the findings as an appendix).

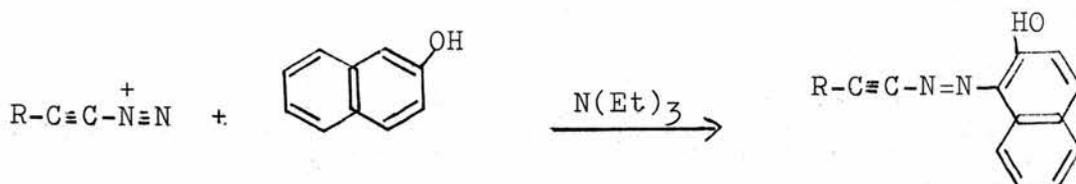
The golden-yellow solution obtained at -40°C by the reaction of 1-nitrosohex-1-yne with nitric oxide was investigated by Robson⁹² and Woodcock⁸³ to some extent. Woodcock decomposed the diazonium salt in the presence of CuCN in the hope of forming the nitrile. With hex-1-ynediazonium nitrate the infra-red spectrum showed the absence of a $-\text{C}\equiv\text{N}$ absorption and this reaction was not pursued.

Robson and Tedder⁹² attempted to couple hex-1-yne diazonium nitrate with phenyl lithium (cf page 104) and found an infra-red absorption at 2200 cm^{-1} ($\text{-C}\equiv\text{C-}$) in the reaction mixture but could not isolate any compound containing this group. In an attempt to hydrate the acetylenic triple bond while keeping the carbon-nitrogen bond intact:



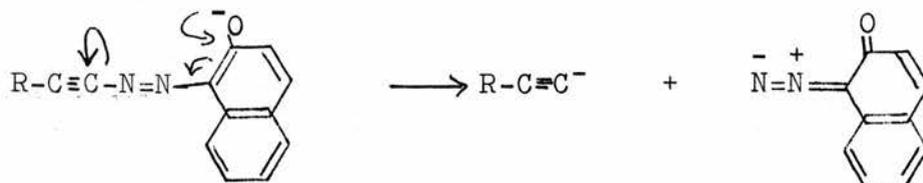
only a trace of a compound containing an infra-red absorption at 2090 cm^{-1} ($\text{=N}\equiv\text{N}^+ \text{ } ^-$) was found and that could not be identified. Decomposition of the diazonium group seems to occur faster than hydration of the $\text{-C}\equiv\text{C-}$ group.

The hex-1-yne diazonium nitrate solution was coupled with 2-naphthol in the presence of triethylamine in the hope of isolating the azo dye:



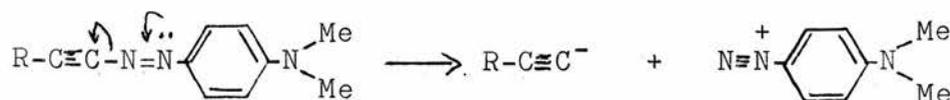
Chromatography of the reaction mixture gave a red oil with an infra-red absorption at 2100 cm^{-1} which was subsequently identified as containing naphthalene-1,2-diazo-oxide. A yellow crystalline solid obtained by chromatography was identified as 1-nitro-2-naphthol. Theaker¹⁰⁹ showed that reactions with nitrous acid and 2-naphthol do not proceed past the 1-nitroso-2-naphthol stage and care was taken to eliminate all excess nitric oxide before the addition of 2-naphthol. The mechanism of the formation of 1-nitro-2-naphthol is described later but the diazo oxide may well have been formed by dissociation

of the 1-(hex-1-yneylazo)-2-naphthol in the presence of base:

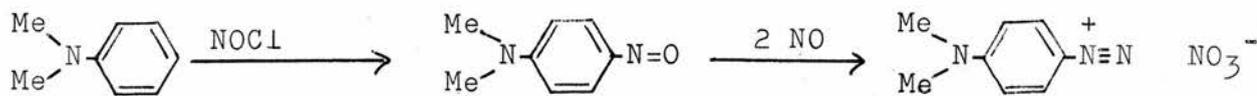


In the coupling reaction of *N,N*-dimethylaniline with hex-1-yne diazonium nitrate solution at -40°C , an orange-red colour was obtained immediately which turned yellow and gave a yellow precipitate on warming to room temperature. This precipitate was found to couple with alkaline 2-naphthol and was identified as the 4-(*N,N*-dimethylamino)-benzene diazonium salt. When the reaction mixture was chromatographed a yellow solid was eluted which was found to be 1-nitro-4-(*N,N*-dimethylamino)-benzene. As with the 2-naphthol coupling reaction above, care was taken to remove excess nitric oxide before the addition of the coupling reagent.

The explanation for the formation of these nitro compounds is that nitric acid is produced during the coupling of a diazonium nitrate and concurrent nitration of the coupling reagent occurs. The diazonium salt must have been formed by a similar dissociation of the azo-compound as in the 2-naphthol case although this was expected to be much less likely with *N,N*-dimethylaniline.



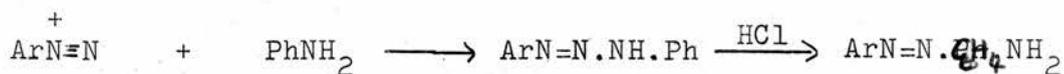
The reason for eliminating excess nitric oxide in these coupling reactions is that direct introduction of the diazonium group could occur:



No nitroso-compounds were isolated or detected by chelate formation with cupric acetate.⁹² It seems likely that the azo-compounds were formed, but readily dissociated into the acetylide anion and the diazonium cation. Robson and Tedder⁹² expecting greater stability of the azo compound if the diazonium cation was relatively unstable, treated hex-1-yne diazonium nitrate with anisole but were unable to isolate any acetylenic compound.

Similarly m-dimethoxybenzene and 1,3,5-trimethoxybenzene were used in the hope of forming a more stable azo derivative of the hex-1-yne diazonium nitrate. Reaction gave dark solutions in both cases but azo dyes were not isolated. Decomposition of the intermediates with hydrogen chloride and coupling of the aqueous layers with 2-naphthol led to the detection of small amounts of the dissociated diazonium salts. Gas-liquid chromatography of the organic layers showed the presence of n-butyryl cyanide.

Both Woodcock⁸³ and Robson⁹² attempted to couple hex-1-yne diazonium nitrate with aniline. Aniline couples with diazonium salts to give diazo-amino compounds which rearrange in the presence of strong acids to give amino-azo compounds:



Evidence¹¹⁰ shows that this rearrangement involves dissociation into the most stable diazonium salt followed by a coupling reaction. The reaction hoped for with hex-1-yne diazonium nitrate and aniline would be:

This conclusion is strengthened by Tedder and Woodcock's attempted preparation of hex-1-yne azo compounds using lithium acetylides and aromatic diazonium salts (see page 105). Attempts to stabilise the azo compounds by suitable substitution in the coupling reagent have so far failed.

PART II SECTION A

NITROSOACETYLENES

EXPERIMENTAL

1) Preparation of 1-Nitrosohex-1-yne

a) Dihex-1-ynyl mercury:

A solution of hex-1-yne (20g) in 95% ethanol (40g) was added dropwise with stirring to a cooled, dilute solution of alkaline mercuric iodide prepared by dissolving mercuric chloride (66g) in a solution of potassium iodide (163g) in water (163 ml) and adding 10% sodium hydroxide solution (125 ml). A white crystalline precipitate separated immediately. The mixture was stirred for two or three minutes, filtered, and the precipitate washed with 50% ethanol. Recrystallisation from 95% ethanol gave white plates of dihex-1-ynyl mercury (38g m.p. 95-96°C).

b) Nitrosation of the dihex-1-ynyl mercury

A stirred solution of dihex-1-ynyl mercury (6.0g) in dry, ethanol-free chloroform (50 ml) was cooled to -40°C using a dry carbon dioxide/acetone bath. Nitrosyl chloride was weighed into a known weight of dry, ethanol-free chloroform and a two molar weight (2.2g) of this solution, with respect to the dihex-1-ynyl mercury was cooled to -40°C and poured into the dihex-1-ynyl mercury solution at -40°C with stirring. The solution rapidly became dark green coloured. On warming to room temperature the solution became yellow. The green solution, believed to contain 1-nitrosohex-1-yne at -40°C, gave the following spectral data:

U.V. $\lambda_{\max} = 640 \text{ m}\mu$ in chloroform (-N=, N \rightarrow * π): I.R. $\nu_{\max} = 2280 \text{ v.s}$ (-C \equiv C-), 1580_{s} (N=O) cm^{-1} . In the yellow solution obtained at room temperature the infra-red absorption bands above were replaced by bands at 2210 cm^{-1} (-C \equiv N) and 1710 cm^{-1} (-C=O).

2) Attempted preparation of 1-nitrohex-1-yne

a) Reaction using dinitrogen trioxide

Dinitrogen trioxide was prepared by the dropwise addition of water to fuming nitric acid (200 ml) through which sulphur dioxide

had been passed. The gas evolved was collected as a deep blue solid in a tube cooled to -78°C with a solid carbon dioxide/acetone bath.

The dinitrogen ~~tri~~oxide was warmed gently and the gas bubbled through a solution of 1-nitrosohex-1-yne (prepared from dihex-1-ynyl mercury (6g)) in dry, ethanol-free chloroform under a nitrogen atmosphere. The solution became yellow and, when no more colour change occurred, was warmed to room temperature, the precipitated mercury salts filtered off and the chloroform solution washed with water and dried over magnesium sulphate. This solution showed an infra-red spectrum with absorptions at 2210 cm^{-1} ($-\text{C}\equiv\text{N}$) and 1710 cm^{-1} ($-\text{C}=\text{O}$) but no acetylenic absorptions. Analysis by gas-liquid chromatography using a $7' \times \frac{3}{8}"$ glass column packed with silicone oil (20%) on embacel (44-60 mesh) at a temperature of 85°C showed three major components: two identified by retention times as hexane and n-butyryl cyanide. Preparative gas-liquid chromatography isolated a trace of the third component having a very long retention time and an infra-red spectrum suggesting a carboxylic acid $\nu_{\text{max}} = 2700\text{-}3500\text{ cm}^{-1}$ (broad) ($-\text{OH}$), 1710 cm^{-1} ($-\text{C}=\text{O}$). The mass spectrum showed this to be pentanoic acid (M/e 116).

b) Reaction using nitrogen dioxide (as the dimer).

Dinitrogen tetroxide was prepared by heating lead nitrate in a steel tube and leading the gas evolved into a receiver cooled in dry carbon dioxide/acetone. Dinitrogen tetroxide (2g) was dissolved in dry, ethanol-free chloroform (50 ml) at -40°C and the solution added to 1-nitrosohex-1-yne (prepared from dihex-1-ynyl mercury (4g) in dry, ethanol-free chloroform (50 ml)) at -40°C). The mixture was allowed to reach room temperature and stirred overnight, filtered from the precipitated mercury salts, washed with

water and dried over magnesium sulphate. The infra-red spectrum of the filtered solution was little different from the solution obtained using dinitrogen trioxide. As there was no evidence of any intact acetylenic triple bond the solution was not investigated any further.

3) Reaction of bromine with 1-nitrosohex-1-yne

Bromine (2g) in dry, ethanol-free chloroform (30 ml) at -40°C was added to a solution of 1-nitrosohex-1-yne prepared from dihex-1-ynyl mercury (5.0g) in dry, ethanol-free chloroform (50 ml) at -40°C . The mixture took on the red colour of the bromine and was allowed to reach room temperature, filtered and washed with aqueous sodium bicarbonate solution when the red colour was replaced by a pale yellow-green colour. The organic layer was washed several times with water and dried over magnesium sulphate. Removal of the solvent gave a yellow oil (1.1g). Part of this oil was chromatographed on a silica column but no components could be isolated. Coupled gas chromatography mass spectrometry suggested only the presence of 1,2-dibromohex-1-ene. No other components could be identified.

4) Reaction of cyclopentadiene and 1-nitrosohex-1-yne

1-Nitrosohex-1-yne was prepared from dihex-1-ynyl mercury (5g) in dry, ethanol-free chloroform (50 ml), rapidly washed with aqueous sodium bicarbonate solution at room temperature, briefly dried over magnesium sulphate and cooled back to -40°C . Freshly distilled cyclopentadiene (2g) in dry, ethanol-free chloroform (25 ml) cooled to -40°C was added with stirring. The solution immediately turned a pale green colour and was allowed to warm up to room temperature slowly, with stirring, when it became orange/yellow coloured. The solution smelled strongly of dicyclopentadiene and evaporation of the solvent yielded a small amount of red oil (0.2g)

which was chromatographed on a silica column. Benzene eluted a brown oil (0.1g) which could not be identified. Other solvents eluted decomposition products which could not be separated into distinct components.

PART II SECTION B

ACETYLENIC DIAZONIUM SALTS

EXPERIMENTAL

1) Preparation of hex-1-yne diazonium nitrate

1-Nitrosohex-1-yne was prepared from dihex-1-ynyl mercury (6g) and nitrosyl chloride (2.2g) in dry, ethanol-free chloroform (100 ml) at -40°C (see page 115). The green nitroso solution was warmed to just above 0°C , rapidly washed with aqueous sodium bicarbonate solution, water, and then dried briefly over magnesium sulphate. It was quickly filtered at the pump and cooled back to -40°C . The apparatus was purged with dry nitrogen. Nitric oxide (prepared by the addition of 50% sulphuric acid (100 ml) to a solution of potassium nitrite (75g) and potassium iodide (38g) in water (200 ml)) was bubbled through two wash-bottles containing 10M sodium hydroxide and then dried by passage along a tube of phosphorus pentoxide. The gas was bubbled through the solution of 1-nitrosohex-1-yne at -40°C for about one and a half hours during which time the colour gradually changed to golden-yellow. When the colour change was complete, dry nitrogen was bubbled through the solution until the excess nitric oxide had been removed. When this solution of hex-1-yne diazonium nitrate was spotted onto a filter paper moistened with alkaline 2-naphthol an intense red colour was produced. (If air or moisture enter the system during the nitric oxide addition, the golden-yellow colour is not obtained).

2) Attempted preparation of 1-(hex-1-ynylazo)-2-naphthol

Hex-1-yne diazonium nitrate was prepared from dihex-1-ynyl mercury (6g) and nitrosyl chloride (2.2g) in dry, ethanol-free chloroform via the nitroso compound as previously described. Excess nitric oxide was removed by the passage of dry nitrogen for a few minutes. A solution of 2-naphthol (4.8g) in dry, ethanol-free chloroform (50 ml) was run in slowly from a dropping funnel with stirring maintaining the temperature below -40°C . As there was no significant colour change, triethylamine (5g) was added to give a

red colour which gradually darkened to brown. After half an hour the solution was allowed to warm to room temperature, washed with water, 5% sodium hydroxide solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent gave a red oil (1.1g) which was chromatographed on an activated alumina column. Petrol 40/60 eluted a yellow component over a period of several hours which gave a bright yellow crystalline solid (0.3g) on evaporation of the solvent. This substance, which gave a brilliant orange colour with alkali, was found to be 1-nitro-2-naphthol (m.p. 101°C (lit.¹¹¹ m.p. 103°C) m/e 189(P)). Benzene eluted a red compound (0.2g) which was found to be unreacted 2-naphthol. Chloroform eluted a red oil (0.2g) which was recrystallised from petrol 60/80 to give a red-brown solid identified as naphthalene -1,2-diazo-oxide (m.p. 94°C (lit.¹¹² m.p. 94-94.5°C) $\nu_{\max}(\text{KBr}) = 2100 \text{ cm}^{-1} (\text{N}=\text{N})$).

3) Reaction of hex-1-yne diazonium nitrate with aniline

Hex-1-yne diazonium nitrate was prepared from 1-nitrosohex-1-yne (from dihex-1-ynyl mercury (18g) and nitrosyl chloride (6.6g) in dry methylene dichloride (100 ml) by the passage of nitric oxide (see page 115)). Freshly redistilled aniline (18g) in dry methylene dichloride (50 ml) was added from a dropping funnel at -40°C giving a bright yellow precipitate. The reaction mixture was allowed to reach room temperature and hydrogen chloride was bubbled through to decompose the intermediate azo-compound. The red-brown solution was poured into ice-water and separated. The aqueous layer was added to an alkaline solution of 2-naphthol (2.0g) and the resulting red dye extracted with chloroform, washed with 5N sodium hydroxide, water and dried over magnesium sulphate. Removal of the solvent gave a red solid (2.6g) which was recrystallised from ethanol and found to be 1-benzeneazo-2-naphthol (m.p. 133°C (mixed m.p. with authentic

material also 133°C), m/e 248(P⁺)).

The organic layer was washed with 5N hydrochloric acid, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent gave a brown oil (15.3g) which was fractionally distilled. Hex-1-yne (0.7g) was recovered over the boiling range 60° - 80°C and a colourless oil (0.3g) over the range 85° - 110°C which had an infra-red spectrum showing a strong carbonyl absorption (1710 cm^{-1}) but only a weak cyanide band (2240 cm^{-1}). Further distillation over the range 110° - 125°C produced more colourless oil (0.1g) which had an infra-red spectrum showing a weak carbonyl absorption (1710 cm^{-1}) and a strong cyanide band (2240 cm^{-1}). Use of gas-liquid chromatography showed these oils to be a mixture of n-butyryl cyanide and n-capronitrile by comparison of retention times against authentic samples. Attempts to isolate the n-capronitrile by preparative gas-liquid chromatography failed to give a sufficiently pure sample.

4) Reaction of hex-1-yne diazonium nitrate with m-dimethoxybenzene

1-Nitrosohex-1-yne, prepared from dihex-1-ynyl mercury (20g) in dry, ethanol-free chloroform (100 ml) was converted to hex-1-yne-diazonium nitrate with nitric oxide (see page 115). Dry nitrogen was bubbled through the solution at -40°C for ten minutes to remove excess nitric oxide and then m-dimethoxybenzene (15g) in dry, ethanol-free chloroform (70 ml) at -40°C was added with stirring. A dark brown solution resulted through which hydrogen chloride was bubbled at room temperature for a few minutes. The mixture was poured on to crushed ice and separated. The aqueous layer was added to an alkaline solution of 2-naphthol (2g) to give a red-brown precipitate which was extracted with chloroform, washed with 10% sodium hydroxide, water and dried over magnesium sulphate. Removal of the solvent gave a red

dye (0.2g) which was found to be 1-(2',4'-dimethoxybenzene)-azo-2-naphthol (m.p. 119°C (lit.¹¹³ m.p. 121°C), m/e 308(P)).

The organic layer was washed with 5N hydrochloric acid, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Removal of the solvent gave a brown oil (12g) from which a white solid was precipitated on standing. This was identified as unreacted dihex-1-ynyl mercury (2g). Gas-liquid chromatography showed the presence of n-butyryl cyanide in the oil but distillation failed to separate any components and left a black tar, mainly mercury residues.

5) Reaction of hex-1-yne diazonium nitrate with 1,3,5-trimethoxybenzene

Hex-1-yne diazonium nitrate was prepared (see page 115) from dihex-1-ynyl mercury (6g) in dry, ethanol-free chloroform (100 ml) and dry nitrogen was bubbled through to remove excess nitric oxide. 1,3,5-Trimethoxybenzene (5g) in dry, ethanol-free chloroform (100 ml) at -40°C was added and the mixture stirred at -40°C for thirty minutes then warmed to room temperature. The suspected azo intermediate was decomposed with hydrogen chloride gas and poured on to crushed ice. The purple aqueous layer was added to 2-naphthol (2g) in 10% sodium hydroxide to give a red dye which was extracted with chloroform and found to be 1-(2',4',6'-trimethoxybenzene)-azo-2-naphthol (0.3g). (m.p. 162°C (lit.¹¹⁴ m.p. 165°C), m/e 338(P)). The organic layer was washed with 5N hydrochloric acid, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Removal of the solvent gave a brown oil from which 1,3,5-trimethoxybenzene (3.2g) was recovered by chromatography on an alumina column with benzene. No other components were isolated although gas-liquid chromatography indicated the presence of the keto cyanide, n-butyryl cyanide.

6) Reaction of hex-1-yne diazonium nitrate with N,N-dimethylaniline

Hex-1-yne diazonium nitrate was prepared in dry methylene dichloride (100 ml) from dihex-1-ynyl mercury (8g) (see page 115) and dry nitrogen was bubbled through the solution at -40°C to remove excess nitric oxide. N,N-Dimethylaniline (6g) was distilled and dissolved in dry methylene dichloride (50 ml) and added at -40°C to the diazonium salt solution. A red colour was obtained which turned yellow on warming to room temperature. A yellow solid was deposited which coupled with alkaline 2-naphthol and gave a red dye 1-(4'-dimethylaminobenzene)-azo-2-naphthol (m.p. 181°C (lit.¹¹⁵ m.p. 182°C)). The organic layer was washed with 2N hydrochloric acid, aqueous sodium bicarbonate solution until alkaline, water and dried over magnesium sulphate. Evaporation of the solvent gave a red oil (2.2g) which was chromatographed on an activated alumina column. Benzene eluted a yellow component (0.2g) found to be 1-nitro-4-dimethylaminobenzene (m.p. 160°C (lit.¹¹⁶ m.p. $162-3^{\circ}\text{C}$), m/e 166(P)). No other components were isolated.

7) Reaction of hex-1-yne diazonium nitrate with boron trifluoride diethyletherate

A solution of hex-1-yne diazonium nitrate was prepared in dry methylene dichloride (100 ml) from dihex-1-ynyl mercury (8g) and dry nitrogen was bubbled through the solution for ten minutes to remove excess nitric oxide. Boron trifluoride diethyletherate (6.3g) in dry methylene dichloride (50 ml) was cooled to -40°C and added dropwise to the diazonium salt solution at -40°C . The solution became pale yellow. A sample was removed and allowed to warm up to room temperature. The yellow colour remained but a fluffy white precipitate was deposited which started to effervesce vigorously. Another sample was removed and the gases given off at room temperature condensed into a liquid nitrogen trap to give a bright blue

solid, dinitrogen trioxide. More boron trifluoride diethyletherate (4g) was added and the mixture allowed to reach room temperature. Filtration gave a pale orange liquor and a white solid (3g) found to have a very high molecular weight, to contain mercury but to have no carbon-carbon triple bond absorption in the infra-red spectrum. Evaporation of the solvent produced more white solid (1.0g) and a red oil again showing no absorption in the carbon-carbon triple bond region of the infra-red. This material was shown to have several components by thin layer chromatography and was not characterised further. Throughout the experiment, attempts were made to couple the reaction mixture with alkaline 2-naphthol but only a deep green colour was obtained. Chloroform extraction gave a trace of a green solid which could not be characterised.

8) Study of the mechanism for the reaction of nitric oxide with a nitroso group producing a diazonium nitrate

a) Preparation of nitrosobenzene¹¹⁷

Nitrobenzene (25 ml) and ammonium chloride (15g) were stirred in water (500 ml) and zinc dust (37.2g) added in portions over five minutes. The temperature was maintained at 50-55°C with ice bath cooling. Twenty minutes after the start of the zinc dust addition, the solution was filtered, the residues washed with boiling water (200 ml) and the solution of 2-phenylhydroxylamine was cooled to 0°C. Concentrated sulphuric acid (75 ml) cooled to -5°C was added with stirring and a solution of sodium dichromate (17g) in water (70 ml) cooled to 0°C was added as rapidly as possible with vigorous stirring. After two or three minutes the precipitated straw-coloured crude nitrosobenzene was filtered and washed with water. The solid was steam distilled in an all glass apparatus until yellow oily globules appeared in the condenser. The green liquid condensed to a white solid in an ice-cooled receiver and was recrystallised.

from ethanol (m.p. 67°C (lit.¹¹⁷ m.p. 69°C), 6.5g (35%)).

b) Reaction of nitric oxide with nitrosobenzene

Nitrosobenzene (1g) was dissolved in benzene (50 ml) and nitric oxide was bubbled slowly through the green solution. Within minutes a white precipitate began to form which was filtered off carefully. This was dissolved in water and added to an alkaline solution of 2-naphthol. A red precipitate was obtained which was identified as 1-benzeneazo-2-naphthol (m.p. 133°C (lit.¹¹⁸ m.p. 133°C)).

c) Electron spin resonance spectroscopy on this reaction

Some freshly recrystallised nitrosobenzene was dissolved in the minimum amount of benzene and some of the solution was introduced into the E.S.R. cavity. No radical signal was found. The sample was removed and nitric oxide bubbled through it for a few seconds. The sample was replaced in the cavity but no signal could be found. Attempts were made to bubble nitric oxide through the sample while still in the cavity but the machine could not be balanced because of the turbulence in the solution.

Nitric oxide was bubbled through benzene for several minutes in an apparatus previously purged with nitrogen. A sample was rapidly removed by dropper, put in a sealed E.S.R. tube and introduced into the cavity of the machine. No free radical signal was recorded. Some of this nitric oxide in benzene solution was added to a dilute solution of nitrosobenzene dissolved in benzene in an E.S.R. tube which was then sealed and introduced to the cavity. The nitrogen triplet radical signal obtained increased in strength over a few minutes and was present for a long time probably due to the slow mixing by diffusion.

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APPENDIX I

This appendix is further to the work discussed in Part II, Section B (see page 108) on the electron spin resonance study of the addition of nitric oxide to nitrosobenzene. When the e.s.r. machine was repaired, the experiment was repeated and the same results were obtained, viz: nitrosobenzene in benzene solution and nitric oxide dissolved in benzene gave no e.s.r. radical signals but when mixed outside the cavity, and returned in a sealed tube, a nitrogen triplet radical signal was found (see diagram IV).

However, attempts to resolve the splitting pattern were completely unsuccessful. This is not uncommon with free radicals which have the lone electron on a nitrogen atom and, also, nitrogen radicals are susceptible to interference by atmospheric oxygen, resulting in broad lines which cannot be resolved.

The information required, that a free radical was involved in the addition of nitric oxide to a nitroso-group to produce a diazonium group, was obtained and it was decided not to pursue this work further at present.

DIAGRAM IV

