THE MOBILITY OF GROUPS IN CHLORONITRODIPHENYLSULPHONES

THESIS

presented by

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Thanks are due also, to Mr.J.M.L.Cameron, who analysed many of the compounds described herein.

THE MOBILITY OF GROUPS IN CHLORONITRODIPHENYLSULPHONES

PAPERS

(A) The Mobility of Groups in 4-Chloro-2-nitrodiphenylsulphones.

(B) The Thermal Decomposition of Chloromercuric β- Ethoxyethanesulphinate.

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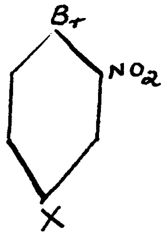
Section 1.

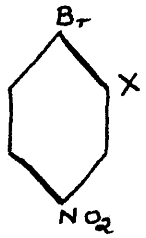
INTRODUCTION

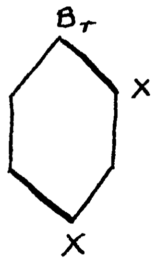
As early as 1854, Pisani(1) commented on the mobility of halogen atoms suitably placed with reference to nitro-groups in the benzene nucleus.

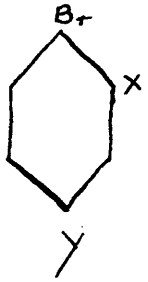
The classical example mentioned by him was that of picryl chloride.

Four decades elapsed however, before the mobility of halogens in presence of negative groups was studied in a comprehensive manner. In 1889 and subsequently, Schöpff and co-workers,(2) employing basic reagents such as alcoholic ammonia and aniline, demonstrated halogen mobility in the following types of compounds:-

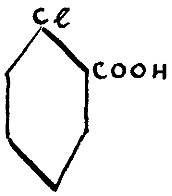




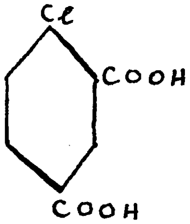




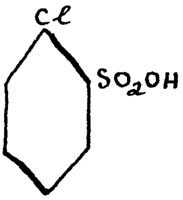
where x and y were meta-directing substituents such as:- -CN; $-CONH_2$; -COOH; -CHO; -COR; $-SO_2OH$. The results of this research led to the enunciation of Schöpff's rule:- "A halogen atom in the benzene nucleus is rendered active by the simultaneous presence in the ortho and para positions of two meta-directing substituents which may or may not be identical; if only one such group is present in the ortho or para position, no activation occurs unless that group is a nitro group". Thus, although a single carboxyl group in the ortho or para position could not activate a halogen atom, (without a catalyst*), two such groups did produce activation. This observation was found to apply to sulphonic acid groups also.



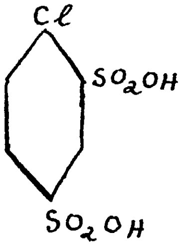
(A.)



(B.)



(C.)



(D.)

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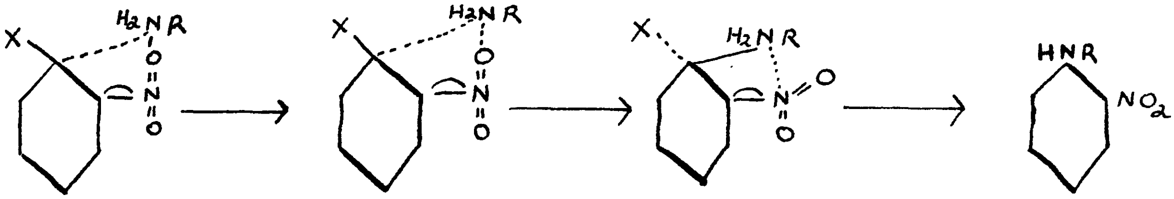
*Schöpff in these researches did not employ external catalysts.

i.e., in (B) and (D) the halogen was replaced by the amino or anilino groups. The general conclusion drawn from this work, was that meta-directing groups in the ortho and para positions of a halogenobenzene induced varying degrees of activity in the halogen atom, the nitro group being the most powerful in this respect.

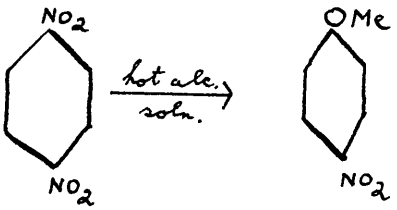
In 1914, Kenner(3) attributed this supremacy of the nitro group to the presence of a true double bond which permitted preliminary addition with reagents, and facilitated the replacement of the halogen by subsequent rearrangement.



where x = halogen (after Kenner)

Many other chemists have since then elaborated this concept which, in principle, is now generally accepted. Kenner himself however, mentions (loc.cit.) that in certain 2:4-dinitro and 2:4:6- trinitrophenyl derivatives, anomalous replacements occur, since a nitro group itself is replaced, and not the group subject to the combined influence of two (or three) nitro groups. His explanation was that under the effect of the nitro groups, the nucleus assumed a "negative" condition and thus became "somewhat different from that of the ordinary benzene nucleus".

A further important point in this publication by Kenner is the quotation of examples which imply that the activation by meta-directing groups, as studied by Schöpff, applies not only to halogen atoms, but to other groups, in fact, to all groups which can exist, even potentially, as anions:-



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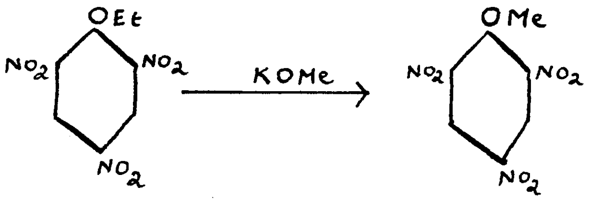
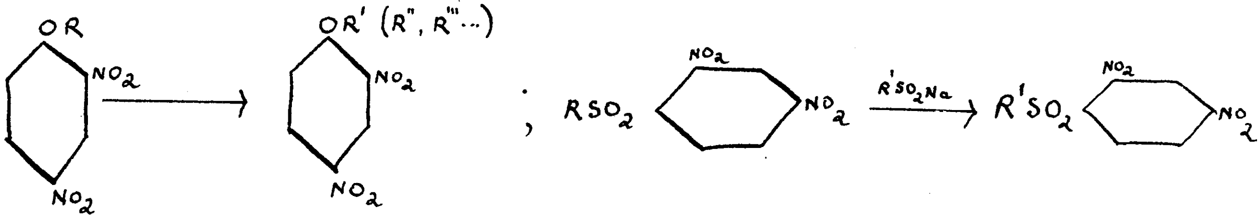


The following conclusions may now be drawn:-

(a) Schöpff's conception of the activation of favourably situated halogen atoms (with regard to meta-directing substituents) may be expanded to include the activation of all groups which can participate as anions in reactions of the replacement type.

(b) In certain 2:4- dinitro, and 2:4:6 – trinitrophenyl derivatives, anomalous replacements occur, in that a potential anion under the combined influence of two (or three) powerful meta-directing groups is unaffected while a nitro group itself is replaced.

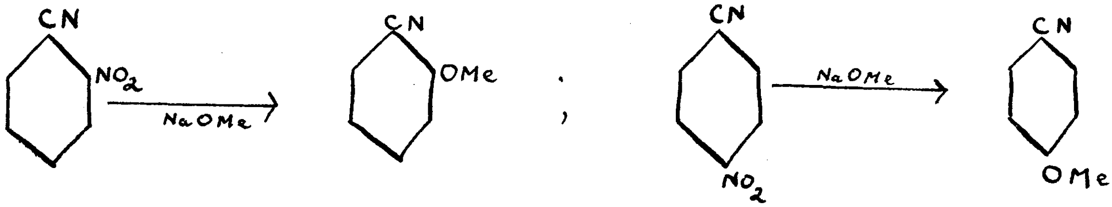
Many examples illustrating both these points have been noted. Typical of (a) are the interconversion of 2:4- dinitrophenylalkyl ethers studied by Blankama(4), and the work on 2:4- dinitrodiphenylsulphones by Loudon.(5)



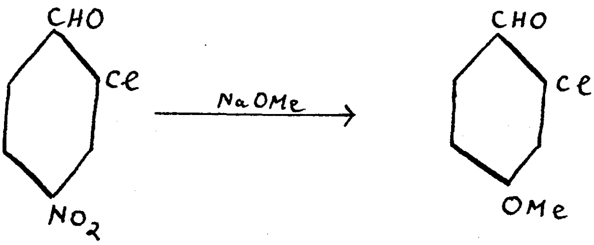
So many examples of (b) are now known that it is no longer satisfactory to dispose of them as "anomalies". In point of fact, these anomalous replacements can be classified into two groups, according to which substituent is replaced. These groups will be referred to as (α), where a nitro group is replaced, and (β) where a substituent situated in the ortho or para positions to a second meta directing group, is replaced.

A few examples of the first of the two groups (α) are:-

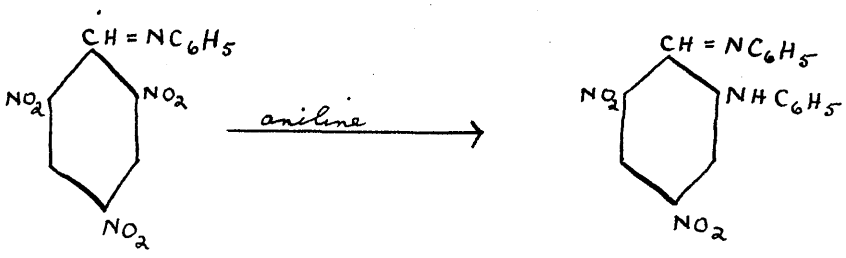
(1) The replacement of the nitro groups in ortho and para benzonitriles, Reinders and Ringer.(6)



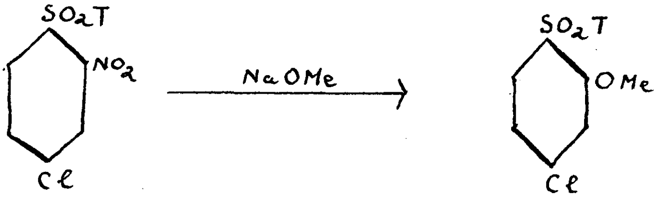
(2) Tiemann.(7)



(3) Secareanu.(8)



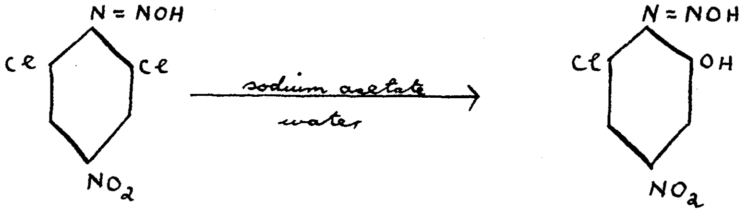
and many more examples, from chloronitrodiphenylsulphones, will be dealt with in the text. One such example is included for comparison with the foregoing, namely, Loudon and Robson.(9)



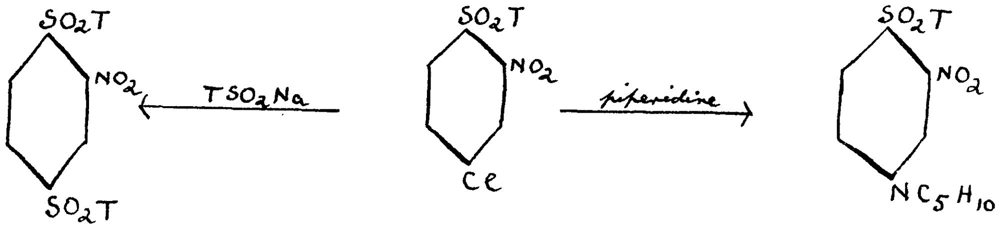
where T = p-tolyl

In all these examples it is apparent that the nitro group replaced was situated either in the ortho or para position to a second meta-directing substituent in the nucleus. By virtue of its position this second group not only resists the activating influence of the nitro group, but opposes it to an extent sufficiently powerful to effect the replacement of the nitro group as an anion.

The second group (β) deals with reactions in which both the nitro group and the second meta-directing group (situated as in α) are unaffected, but a substituent in the ortho or para position to the second group is replaced, e.g., Witt.(10)



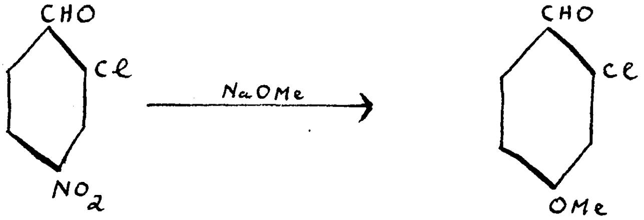
and again from chloronitrodiphenylsulphones, a single example (9) will suffice at present.



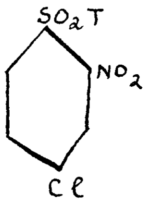
where T = p-tolyl.

From both groups (α and β) it is clear that the controlling directive influence has been withdrawn from the nitro group and transferred to the meta-directing group situated ortho or para to it.

A further point of interest is raised by Tiemann's example (7) which, while possessing all the factors permitting replacement of group (β) type, nevertheless undergoes replacement of group (α) type.



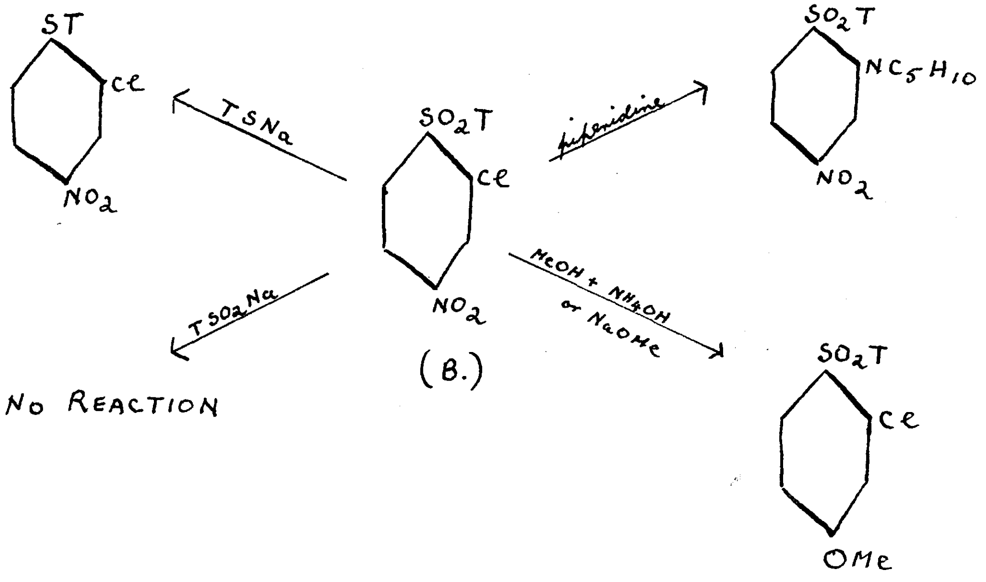
This indicates that other factors (in addition to the groups present and their relative positions) play a part in determining the location of centres of reactivity. That the choice of reagent has an important influence in this direction is borne out by the example (reference 9) already twice mentioned.

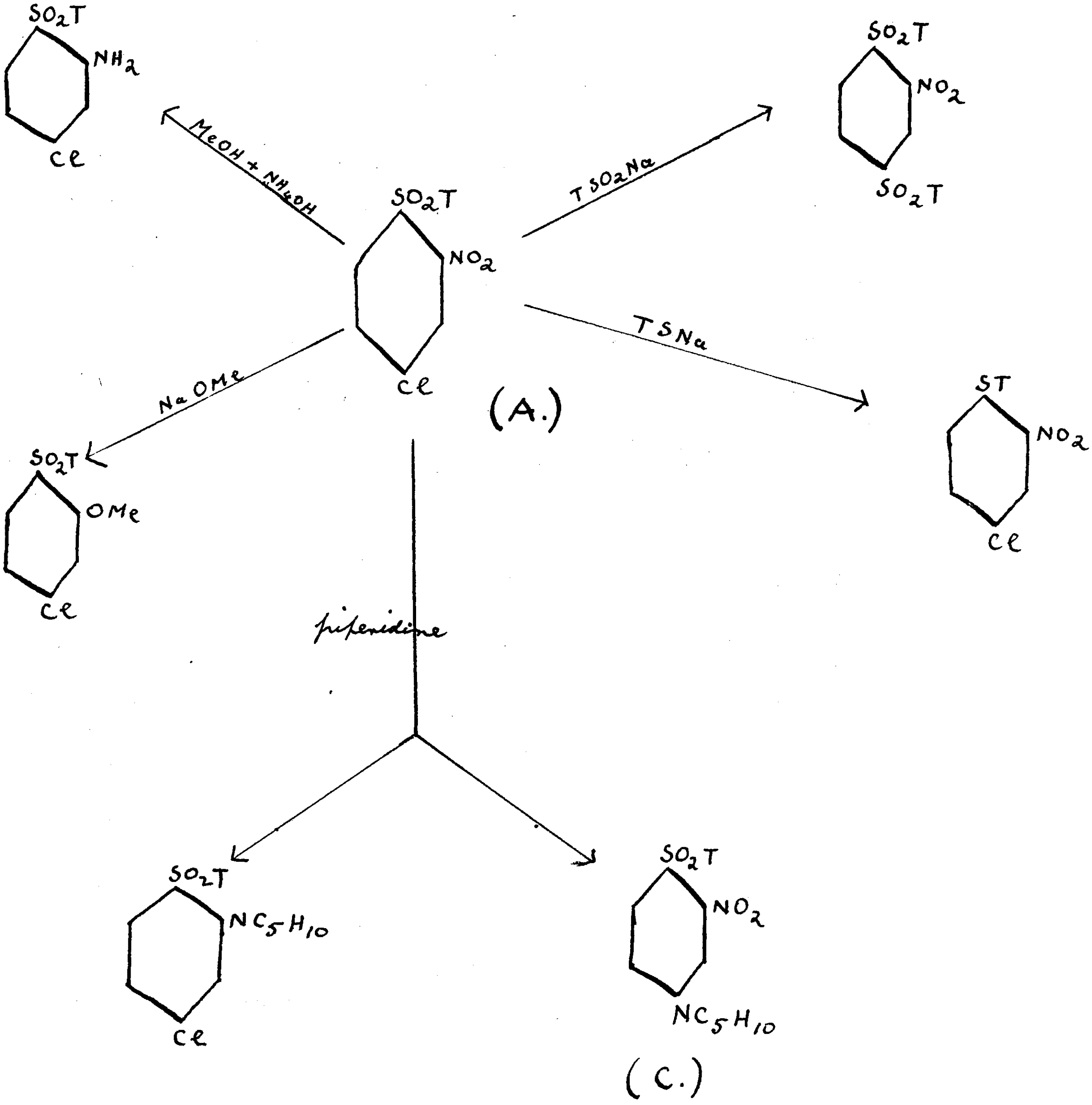


where T = p-tolyl

It has been shown that with sodium methoxide the nitro group was replaced (type α), with sodium p-tolylsulphinate and also with piperidine, the halogen was replaced (type β). Furthermore with alkaline mercaptide reagents, e.g. sodium p-tolylmercaptide, the sulphonyl group was replaced, a replacement which conforms to Schöpff's types.

Further instances of preferential replacements by various reagents are mentioned, (loc.cit.) and the influence of the other two factors (groups present and their relative positions) in determining the locus and also the degree of reactivity are illustrated by this example and that of the isomeric sulphone as follows:-




SO2T
NH2
Cl
MeOH + NH4OH
SO2T
NO2
SO2T
TSO2Na
SO2T
NO2
Cl
(A.)
TSNa
ST
NO2
Cl
NaOMe
SO2T
OMe
Cl
piperidine
SO2T
NC5H10
Cl
SO2T
NO2
NC5H10
(C.)

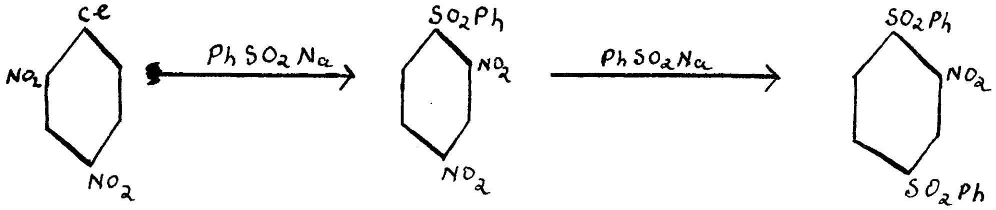
From (A.) two piperidino derivatives (mainly (C.)) were isolated, while from (B.) only one such derivative was isolated. Again, from (B.) no product was obtained with sodium p-tolylsulphinate although heating was carried on until the reagents decomposed. With methyl alcoholic ammonia (A.) gave the amine by nitro group replacement while (B.) gave the nitrogen free methyl ether.

It was decided consequently, to study further isomeric chloronitrodiphenylsulphones and observe the modifications in degree and loci of reactivity as well as relative speed of reactions at the centres of reactivity which the reagents mentioned would induce.

In addition to p-tolylphenylsulphones, it was decided also, to study other sulphones such as methyl, phenyl,and 2:5- dichlorophenylsulphones as well as sulphonamide and sulphonyl piperidide, in order to determine whether a change of R in the sulphonyl group of general form - SO_2R would have any effect on the above-mentioned themes.

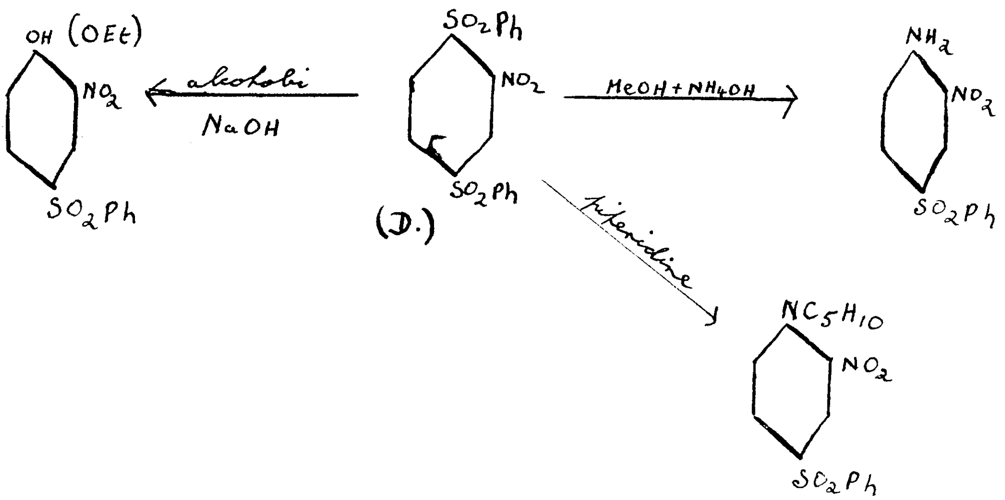
The choice of the sulphonyl group, in the subject of study, was not arbitrary. It was established by Loudon in 1936,(11) that the sulphonyl group had a marked effect on the nitro group as discussed under groups (α)

and (β). Furthermore, the sulphonyl group had this advantage; the usual reagents employed to detect mobility in aromatic nitro-compounds, (amines, hydroxides, etc.) by introducing amino or hydroxyl groups into the nucleus, tended to leave an inert molecule, while the former activated new centres in the molecule and led to further reactivity. These points were illustrated as follows:-



(D.)

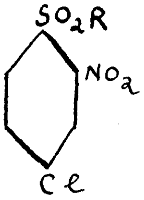
The product (D.) provides a further example of group (α) replacement and exhibits reactivity of the ortho sulphonyl group (except to sulphinate reagents), comparable with that of the halogen in 2:4- dinitrochlorobenzene, e.g.,



Section 2.

REPLACEMENT OF THE SULPHONYL GROUP BY REAGENTS OTHER THAN ALKALINE MERCAPTIDES

Previous work on the reactivity of the sulphone (I.) Loudon and Robson,(9) has shown that by selecting the reagent, the sulphonyl group, the nitro group, or the halogen atom could preferentially be replaced.

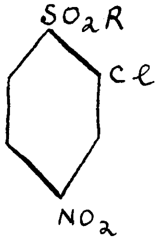


(I.)

where R = p-tolyl

It was found that the sulphonyl group was replaceable by mercaptide reagents, the nitro group by piperidine or by sodium methoxide, and the halogen atom by piperidine and also by sulphinate reagents. Although with sodium methoxide, only the nitrogen-free methyl ether was isolated, the presence of chloride ions indicated that reaction had not been confined to one centre.

Slightly modified results were obtained with the isomeric sulphone (II.) (loc.cit.)



(II.)

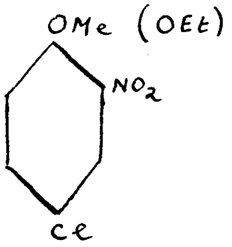
where R = p-tolyl

Here no product could be isolated after sulphinate treatment, and only one piperidine derivative was obtained. Furthermore, with methyl-alcoholic ammonia, the nitrogen-free methyl ether was obtained from (II.), whereas the nitro group was replaced by the amino group in (I.).

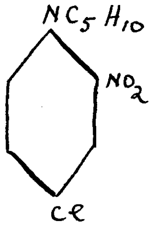
In both (I.) and (II.) mercaptide reagents only were found capable of replacing the sulphonyl group, although it was suspected that with other reagents also, replacement occurred at this centre.

It became of interest therefore, to determine whether all three substituents could be replaced by a single reagent. Piperidine and sodium methoxide (or ethoxide) were chosen as reagents, since the former had given two products with the sulphone (I.) where R = p-tolyl, and the latter gave strong indications that more than one centre had been attacked. Accordingly, the reaction between the sulphone (I.) where R = p-tolyl, and these reagents, was re-examined.

A modified process of separation (cf. experimental) was devised and this process enabled the isolation of products, proving that with sodium methoxide (or ethoxide), and also with piperidine, the sulphonyl group of (I.) had been replaced. By steam distillation of the reaction mixture in each case, the following product was obtained from the distillate:-



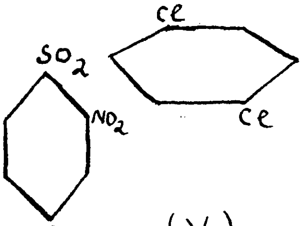
(III.)



(IV.)

These products agreed in m.pt. and mixed m.pt. with authentic samples of 4-chloro-2-nitrophenylmethyl (and ethyl) ether, and 4-chloro-2-nitropiperidinobenzene, respectively. The yields obtained were relatively low, however, being of the order of 5% of the methyl and ethyl ether derivatives, and 2% of the piperidine derivative.

Identical results were obtained from reaction of piperidine and of sodium methoxide on the sulphone (V.)

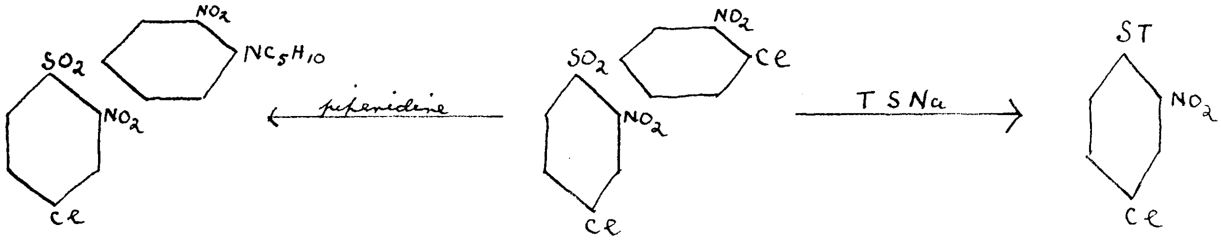


(V.)

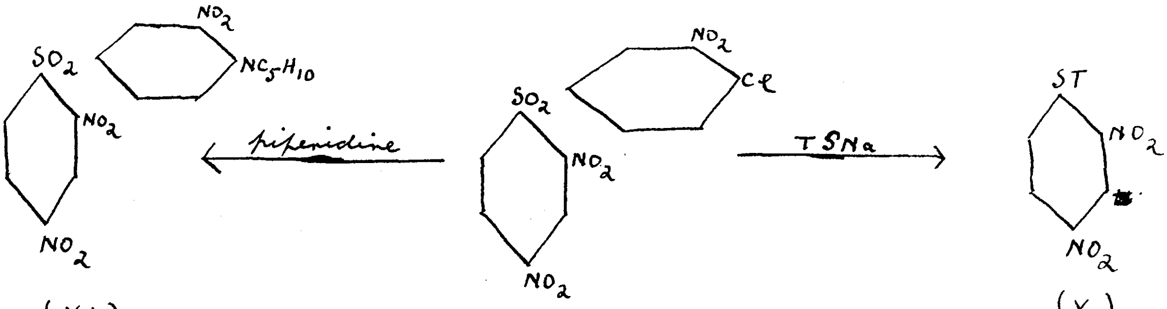
Thus, from the sulphone (1.), all three substituents were separately replaced by piperidine, and with sodium methoxide (and ethoxide) the sulphonyl and nitro groups were replaced, while the presence of chloride ions indicated the replacement of the halogen also.

Generally, however, most of the reagents employed attacked mainly one centre. One instance, is the preferential replacement of the sulphonyl groups in sulphones (I., II. and V.) by alkaline p-thiocresol and the confinement of the attack to the one centre.

The point is further illustrated by the behaviour of the sulphone (VI.) and a parallel example (VII.⟶ XI. and X.) is cited from Loudon and Robson.(9)



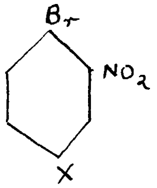
(IX.) (VI.) (VIII.)



(XI.) (VII.) (X.)

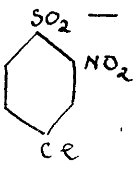
where T = p-tolyl

In both cases a halogen atom is activated by two powerful meta-directing groups (sulphonyl and nitro), but with a slight deficiency of mercaptide, the sulphonyl group is preferentially replaced, and mere traces of ionisable halogen were detected. With piperidine on the other hand, the halogen was readily replaced in both sulphones. In each case, also, the halogen provides a centre of reactivity closely related to Schöpff's types, i.e.,

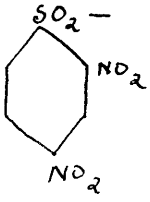


The only difference between Schöpff's type and (VI.) or (VII.) is that Schöpff had x = $-SO_2OH$ while here

x =

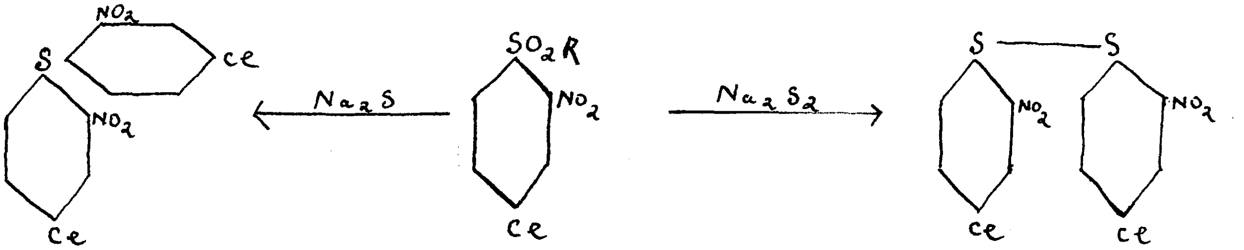


and



respectively. The change of the halogen from bromine to chlorine cannot be considered as having any effect in the alteration of the centre of reactivity.

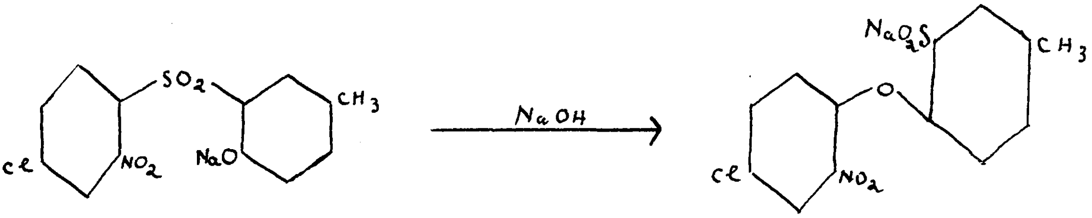
Since mercaptide reagents alone had, so far, proved capable of replacing the sulphonyl group quantitatively, (with sodium methoxide or ethoxide and with piperidine, as has been shown, the extent of sulphonyl replacement was comparatively slight), it seemed feasible that other reagents of sulphide character might also be effective in this respect. For this purpose, the action of (a) sodium sulphide, and (b) sodium di-sulphide on the sulphone (1.) was examined. The results proved that the sulphonyl group had been replaced by both reagents, and the products were obtained in yields comparable with those from mercaptide reactions.



(XII.) (I.) (XIII.)

The products (XII.) and (XIII.) agreed in m.pt. and mixed m.pt. with authentic specimens of bis-(4-chloro-2-nitrophenyl) sulphide and bis-(4-chloro-2 nitrophenyl)-disulphide respectively.

In course of their researches, Smiles and co-workers,(12) discovered that compounds such as 2-hydroxy- and 2-amino-2'-nitrodiphenylsulphones, underwent an intramolecular change in presence of alkali, during which the sulphonyl group was replaced by the phenolic or by the aniline group as follows:-



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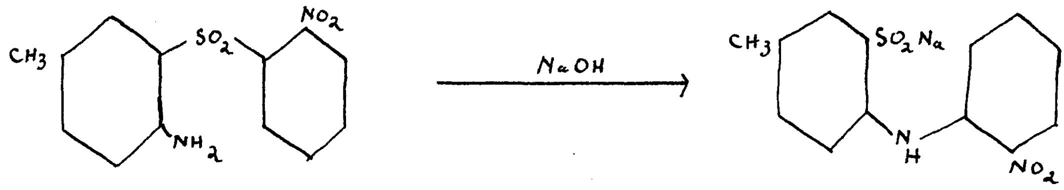
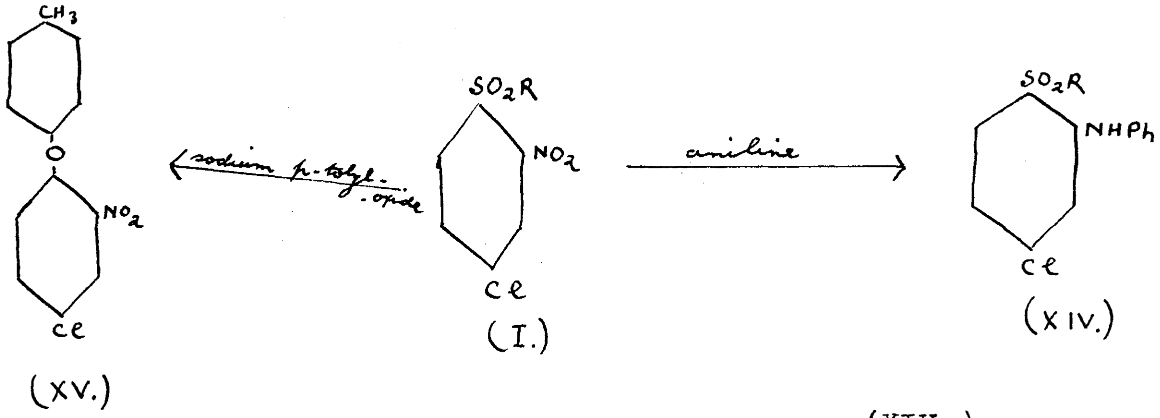


An attempt was made to parallel this work on an intermolecular basis by reacting on the sulphone (1.) where R = p-tolyl with sodium p-tolyloxide, and with aniline.

In contrast to normal intermolecular reactions with sulphones, wherein times for reactions generally varied from five to twenty minutes, the two reactions above required more intensive conditions. With aniline in particular, was this the case, as it was necessary to heat the reaction mixture at its boiling point for fully five hours, and the product (XIV.) was isolable only with great difficulty.



(XIV.)

The results showed that with sodium p-tolyloxide the sulphonyl group had indeed been replaced. The product (XV.) agreed in m.pt. and mixed m.pt. with an authentic sample of 4-chloro-2-nitrophenyl-p-tolyl ether. With aniline, however, the sulphonyl group remained intact, and the product (XIV.) analysed correctly for the formula ascribed it, (where R = p-tolyl).

Thus, alkaline phenols and inorganic sulphides and di-sulphides, may be added to alkaline mercaptides, as having a selective power favouring preferential replacement of the sulphonyl group in chloronitrodiphenylsulphones.

Section 3.

THE EFFECT OF CHANGES OF R in - SO_2R in 4-chloro-2-nitrodiphenylsulphones.

In addition to the three factors which have been described as exerting strong influences on the degree of activation and locus of reactive centres in chloronitrodiphenyl sulphones, namely, the groups present, their relative positions, and the reagent employed (c.f. introduction), a further possibility must now be considered.

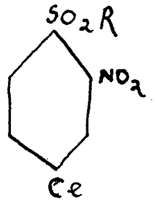
In the sulphones so far mentioned, (I., II., V., VI. and VII.) the radicle R in the sulphonyl group $-SO_2R$, has always been an aryl radicle, e.g. p-tolyl. It could not be assumed that a change of R to a radicle such as methyl or amino, would leave unaffected these conditions of reactivity. Accordingly, four sulphones in which R = Me, Ph, p- $C_6H_4M_e$, 2:5 - $C_6H_3Cl_2$, the sulphonyl piperidide and the sulphonamide, all of type (I.), were studied. The four sulphones have been shown by Loudon,(5) and Gibson and Loudon,(13) to represent a range of anionic stability of sulphonyl groups in the order mentioned, i.e. Me represents the most stable, and 2:5- $C_6H_3Cl_2$ the most mobile of these sulphonyl groups.

The methyl sulphone, (I.) R = Me, afforded a case of particular interest. The possibility existed, that with R = an aryl group, the sulphonyl group was immune from attack and quantitative replacement by non-mercaptide reagents, by virtue of the hindering action of R, due to its size. Where R = Me, however, this possible obstacle might be removed, as would be shown by high yields of products corresponding to sulphonyl replacement effected by non-mercaptide reagents.

The four sulphones, the sulphonyl piperidide and the sulphonamide were then treated with alkaline mercaptide and with piperidine.

A qualitative comparison was made, both of the times of reaction, and yields of purified products isolated.

The following table summarises the results obtained from these six compounds of general type (I.)



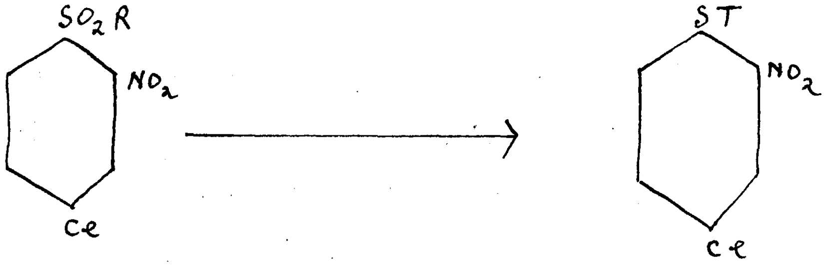
(I.)

In the case of piperidine, more than one product was isolated from the reaction mixtures, and the relative yields of different products are given as follows:-

(a) = product in which halogen atom was replaced.
(b) = " " " nitro group was "
(c) = " " " sulphonyl group was "

Value of R	Alkaline Mercaptide		Piperidine		Time Taken
	Group Replaced	Time Taken	Group Replaced	Relative Yields	
R = CH_3	$-SO_2R$	5 mins.	all three	$a > b > c$	5 mins.
R = Ph	$-SO_2R$	5 mins.	all three	$a > b > c$	5 mins.
R = p-$C_6H_4CH_3$	$-SO_2R$	5 mins.	all three	$a > b > c$	5 mins.
R= 2:5-$C_6H_3Cl_2$	$-SO_2R$	5 mins.	all three	$a > b > c$	5 mins.
R = $-NC_5H_{10}$	$-SO_2R$	5 mins.	all three	$a < b > c$	40 mins.
R - NH_2	$-SO_2R$	5 mins.	all three	$b \equiv a > c$	35 mins.

From the table it is evident that alkaline mercaptide exercised the selectivity already mentioned and in all the reactions replaced the sulphonyl group with uniform rapidity.



(I.) (VIII.)

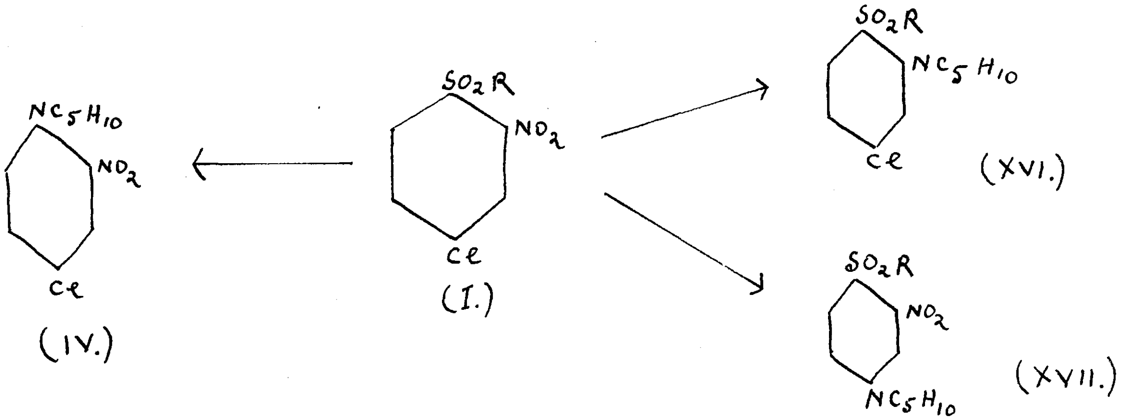
where T = p-tolyl.

With piperidine, uniform times of reaction, and relative quantities of products were observed for the four sulphones. With the sulphonyl piperidide and sulphonamide, however, the reactions were slower, and the relative yields of products were affected. These observations agree with the comments of Arndt and Martius,(14) in that the lesser reactivity of the sulphon-amide and -piperidide, may be attributed to the weaker "acidifying effects" of the two groups in question. This effect may here be considered as two-fold.

Firstly, it modifies the potential anionic stability of the sulphonyl group, and consequently the replaceability of that group.

Secondly, it influences the contribution of the sulphonyl group to the cationoid character of the nucleus as a whole, and thus has repercussions on the relative mobilities of all three substituents.

The reactions with piperidine, in general form were:-



The general conclusion from this work was that the reactivity of the system (I.) was much more sensitive to changes of the reagent employed, than it was to modifications of the radicle R, in the sulphonyl group - SO_2R.

Section 4.

FURTHER ISOMERIC CHLORONITRODIPHENYLSULPHONES

The study of the mobility of groups in chloronitrodiphenylsulphones was extended to include the examination of the vicinal isomers (XVIII.) and (XIX.)

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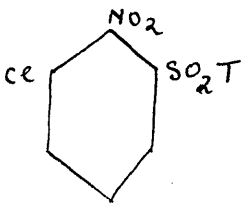
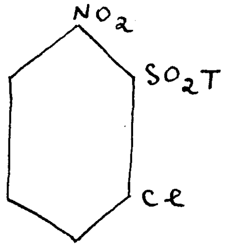


(XVIII.)



(XIX.)

where T = p-tolyl

The sulphones were treated with sodium methoxide, sodium p-tolyl mercaptide, piperidine, and methyl alcoholic ammonia.

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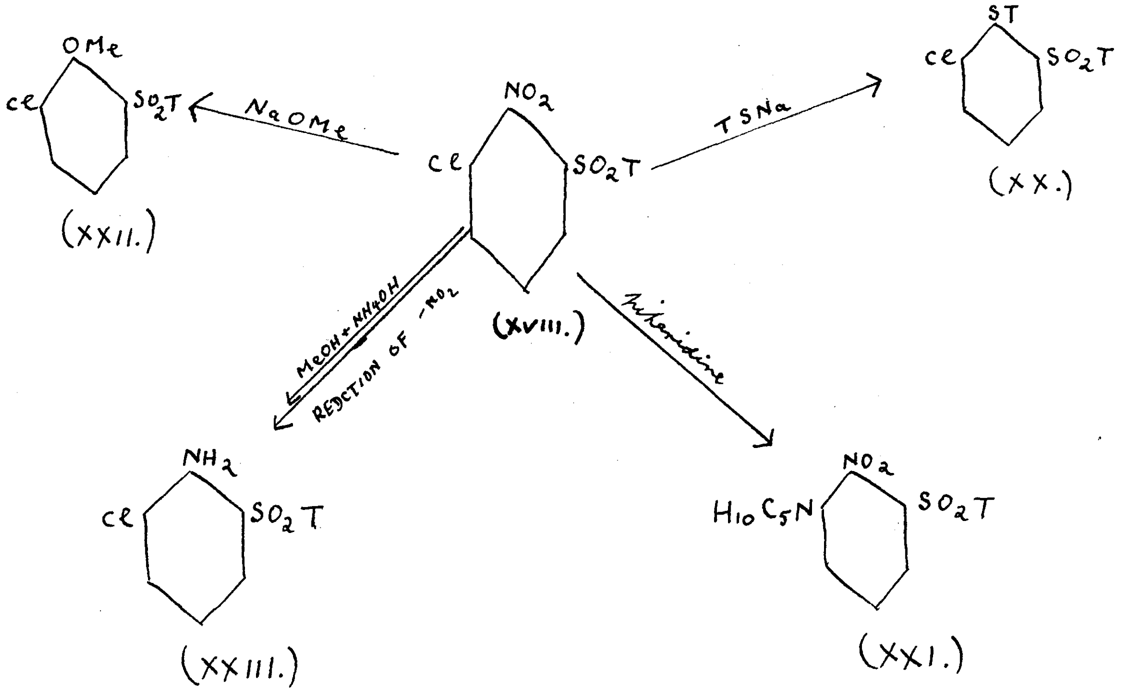
* Both the sulphones and the corresponding thio-ethers were made available by work as yet unpublished in Glasgow University.

With (XVIII.) the following results were obtained:-



Of these, the most notable reaction is that with mercaptide, resulting in the replacement of the nitro group (XVIII. ⟶ XX.), and not the sulphonyl group, towards which this reagent had in previous cases shown such marked preference.

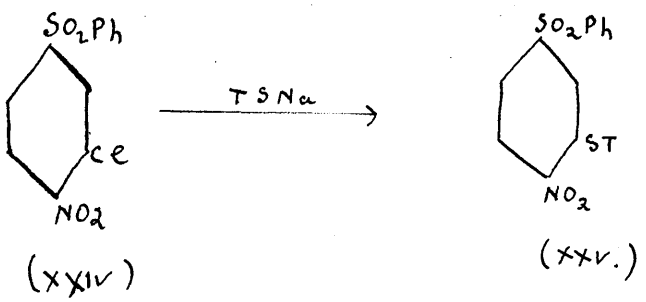
The other reactions agree with those previously observed with sulphones, except that only one product could be isolated from the piperidine reaction, (XVIII. → XXI.)

It is of some importance, that in this derivative (XXI.), the halogen atom had been replaced, for, with this exception, reactions with the sulphone (XVIII.), resulted in the replacement of the nitro group.

Assuming that the nitro group achieves the replacement of an activated anion by a preliminary addition mechanism (cf. introduction), the replacements of the nitro group may be explained by the suggestion that in the sulphone (XVIII.) such additions could occur only with difficulty, if at all, due to the "steric hindrance" (cf. Kenner (3)) offered by the two ortho substituents. The anomalous replacement of the nitro sulphonyl group by mercaptide may also be due to this cause.

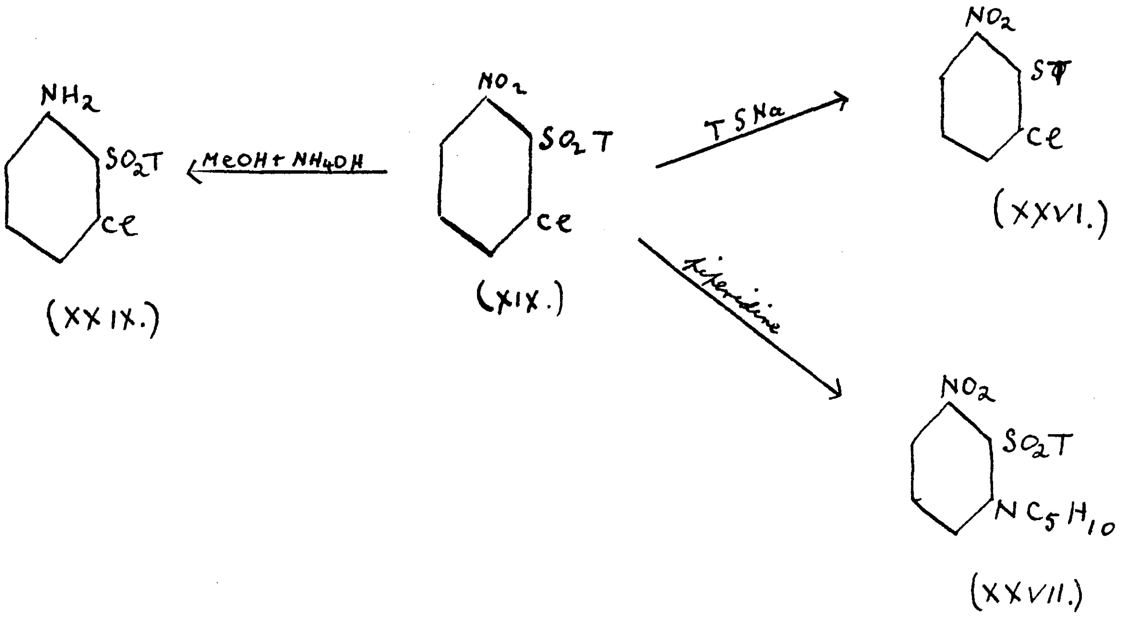
As for the piperidino product (XXI.) it has been observed that in all reactions between piperidine and sulphones, the halogen atom is always replaced. The two vicinal sulphones proved no exception to this rule.

Loudon,(21) described the only other example so far observed, of non-replacement of the sulphonyl group by mercaptide in chloronitrodiphenylsulphones:-



Here it seems that the sulphonyl group resists activation by the nitro group to such an extent, that the other centre influenced by the nitro group becomes the centre of reactivity.

The sulphone (XIX.) gave the following results:-



With sodium methoxide, a mixture, which could not be properly analysed, was obtained.

With piperidine again only one product (XXVII.) was isolated, though ionisable nitrite showed that the attack was not confined to the one centre.

Methyl alcoholic ammonia replaced the nitro group by the amino group, and mercaptide attacked the sulphonyl group.

Section 5.

GENERAL CONCLUSIONS FROM THE STUDY OF THE MOBILITY OF GROUPS IN CHLORONITRODIPHENYLSULPHONES

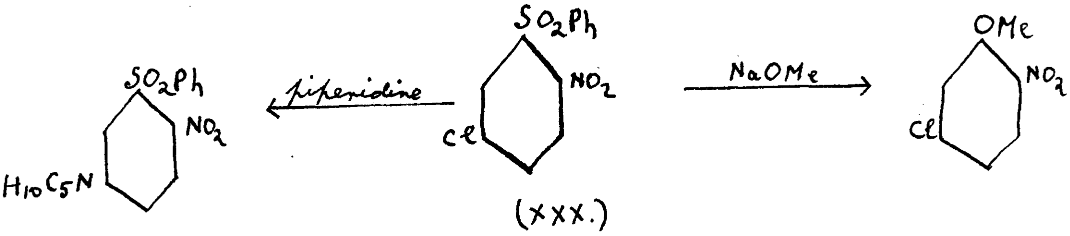
(a) The change of R in - SO_2R, where R is an alkyl or an aryl radicle, does not affect the locus or degree of reactivity in the molecule except in such cases where R is a group possessing alkaline properties not usually displayed by aromatic radicles. (e.g. sulphonamide, and sulphonyl piperidide). Even in these extreme cases, only minor changes occur, and it may be claimed as a general rule that changes of R in $-SO_2R$ do not affect the reactivity of the molecule.

(b) The relative changes in the positions of the substituents, in conjunction with the reagent employed, causes a much wider variation in the centres of reactivity. Even here, however, notable similarities occur throughout the series of sulphones studied. Mercaptide reagents, with one exceptional case, preferentially replace the sulphonyl group. With piperidine, a modification of the degree of reactivity occurs in different sulphones, but the halogen atom is consistently the substituent replaced, (in quantity, where more than one centre is attacked).

With methyl alcoholic ammonia, preferential replacement of the nitro group is exhibited.

Even where the nitro group is attacked, however, some modification in degree of reactivity occurs, since either the amino group (generally), or (less frequently), the methoxyl radicle, replaces the nitro group.

With sodium methoxide, the nitro group again generally suffers replacement. The one exception is that cited by Loudon,(15) in 5-chloro-2-nitrodiphenyl sulphone, (XXX.):-



In this sulphone, the sulphonyl group is jointly activated by the halogen atom and the nitro group. With piperidine the halogen atom is replaced, but with the other three reagents, the sulphonyl group is replaced. The sulphone (XXX.) therefore presents a close analogy with sulphone (XVIII.) in which piperidine has a similar result, while the other three reagents replace the nitro group.

With the exception of these two sulphones, which may be regarded as extreme cases, it may be stated that though changes in relative positions of the substituents produce variations of a wider character than a change of R in $-SO_2R$, the most notable variations occur as the result of selecting the reagents.

(c) In summarising the types of replacements in the sulphones studied (α, β, or Schöpff's types), the argument will be simplified by considering piperidine as replacing only the one centre, the halogen, in the sulphones studied. Replacements of Schöpff's 'modified' form, (nitro group activating a non-halogen group) are included. The following table shows the relative numbers of replacements, in the various sulphones, belonging to each type.

Sulphone	Schöpff's Type	Schöpff's Modified Type	α Type	β Type
(I.)	0.	1.	2.	2.
* (B.)	0.	1.	2.	1.
(XVIII.)	1.	0.	3.	0.
(XIX.)	0.	1.	1.	2.

* cf. Introduction.

It is evident that (α) and (β) type replacements greatly outnumber the other two types, and only one case of Schöpff's type occurs.

Moreover, if it is granted that all activations and replacements occur in Anionoid or Potential Anionoid forms, it becomes clear that there is no distinct line of demarcation between (α) and (β) type replacements, for the nitro group in all the sulphones mentioned, is situated either in the ortho, or para positions to the sulphonyl group, and can be rendered mobile with facility similar to the replacement of the halogen atom.

The method of subdivision into two group types (α and β) was employed to simplify the argument in face of the generally prevalent impression that the nitro group in aromatic compounds of the types studied, exerts a greater directing control as regards activation, than can be truly attributed to it.

Although it now appears that Schöpff's original conclusions have been almost completely reversed, (i.e. the nitro group, in presence of a favourably situated anion, is more often replaced than effecting replacement), it is hoped that the examples described herein, indicate that his conceptions have been expanded to cover a field much wider than with which he dealt.

Section 6

THE THERMAL DECOMPOSITION OF CHLOROMERCURIC-β-ETHOXYETHANESULPHINATE

A practical application of the mobility of groups was utilised in the preparation of a compound which might throw some decisive light on the disputed structure of the product obtained from the interaction of ethylene and mercuric chloride in aqueous or alcoholic solution, (for R = Et, Schoeller, Schrauth, Essers (15), general summary, Nesmajanow and Freidlina (16)).

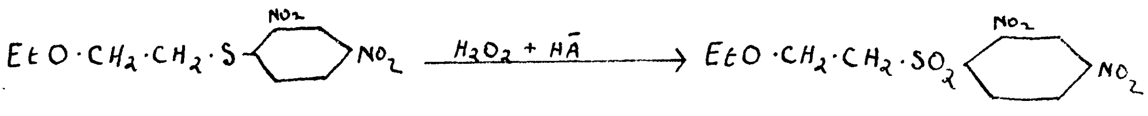
These structures were

$OR\ .\ CH_2\ .\ CH_2\ .\ HgCl$ and $(CH_2 : CH_2),\ HgCl\ (OR)$

(XXXI.) (XXXII.)

where R = Et.

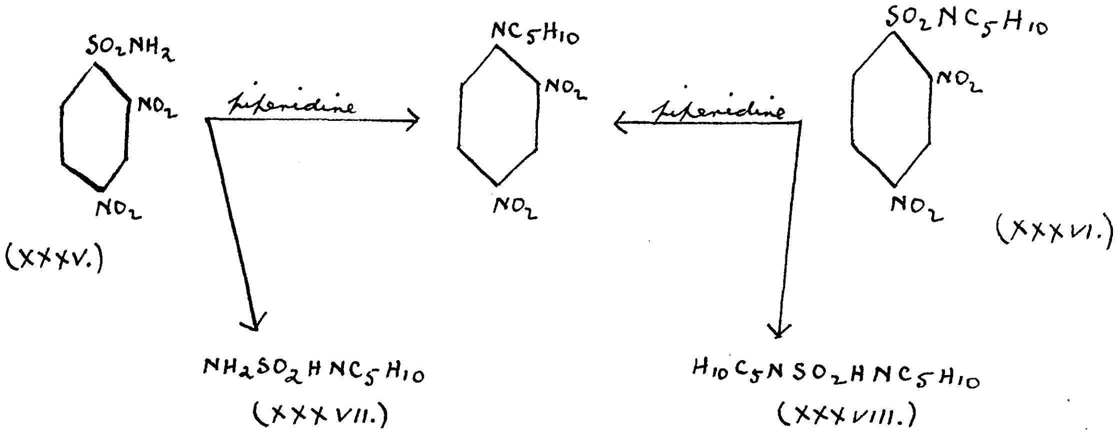
Sodium β-ethoxyethyl mercaptide, [Rojahn and Lemme (17)], was treated with the theoretical amount of 2:4 - dinitrochlorobenzene, yielding the sulphide (XXXIII.), which on oxidation with perhydrol in acetic acid solution, gave the sulphone (XXXIV.)



(XXXIII.) (XXXIV.)

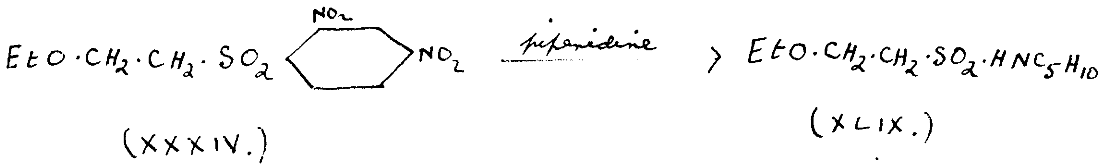
In this sulphone, the sulphonyl group is activated by the two nitro groups and therefore potentially became a centre of reactivity.

In 2:4-dinitrophenyl sulphonamide (XXXV.) and also in 2:4 - dinitrophenyl piperidide (XXXVI.), the sulphonyl group was found to be replaced on reaction with piperidine:-



The other products of the reactions were the piperidinium salts of aminosulphinic acid (XXXVII.) and piperidino-sulphinic acid (XXXVIII.) respectively.

The sulphone (XXXIV.) behaved in like manner on reaction with two molecules of piperidine, and gave rise to the piperidinium salt of β - ethoxyethyl sulphinic acid (XLIX.)



From this salt the sodium salt (XL.) was readily obtained.

$$EtO\cdot CH_2\cdot CH_2\cdot SO_2Na$$

(XL.)

This sulphinate was treated with mercuric chloride, and gave chloromercuric-β-ethoxyethanesulphinate, (XLI.)

$$EtO\cdot CH_2\cdot CH_2\cdot SO_2HgCl$$

(XLI.)

This investigation was undertaken in the hope that thermal decomposition of the sulphinate (XLI.) would result in the evolution of sulphur dioxide, leaving chloromercuric-β-ethoxyethane (XLII.)

$$EtO\cdot CH_2\cdot CH_2\cdot HgCl$$

(XLII.)

This product would have afforded an ideal basis for comparison with that of Schoeller, Schrauth and Esser's, (XXXI. or XXXII.).

Analgous decompositions have been described by Loudon (18).

Unfortunately, in this case the thermal treatment of (XLI.) caused the decomposition of the substance to a greater extent than was expected. In addition to sulphur dioxide, ethylene gas was also evolved, and no modification of conditions of treatment, such as buffering to p_H 7, altered this evolution. Indeed, the compound (XLI.) decomposed even on standing at room temperature, and gave rise to mercurous salts. Moreover, the decomposition was such that Schoeller's compound could not have been formed even as an intermediate product, as was shown by subjecting this compound to similar treatment, (in presence of mercurous and mercuric salts). Under these conditions, Schoeller's compound was quite stable and was recovered unchanged, and yielded ethylene, only at considerably higher temperatures.

This behaviour of the sulphinate can be compared to that shown by β-halogenoalkyl ethers, which on reaction with magnesium, evolve olefins instead of forming Grignard compounds. (Boord et al, (19), Tallman (20).

The procedure by which sodium-β-ethoxyethane-sulphinate was synthesised provides a new method of obtaining sulphinic acids. The method can be employed with advantage when the corresponding thiol is more readily available than the sulphonyl chloride, or when reduction of the latter is unsatisfactory.

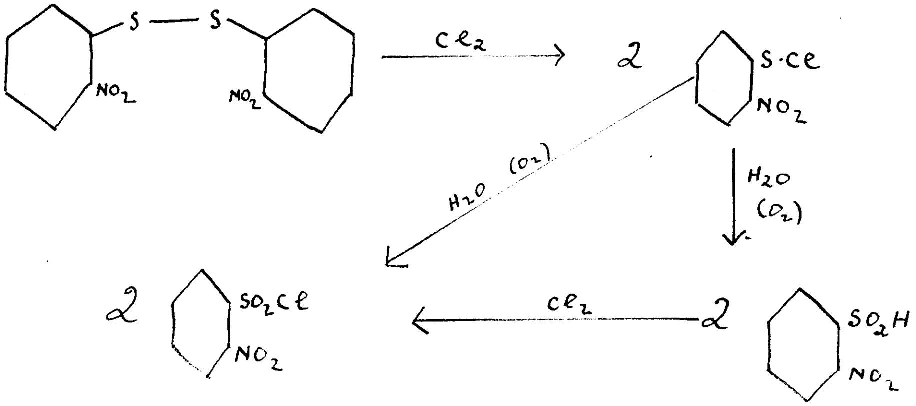
Section 7

THE PREPARATION OF SULPHONYL CHLORIDES BY CHLORINATION IN AQUEOUS ACETIC ACID.

In an earlier part of this research, certain nitrobenzenesulphonyl chlorides were required. Zincke (22) and Riesz (23) had developed a method of obtaining sulphonyl chlorides by chlorinating disulphides, dissolved or suspended, in acetic acid which had been slightly diluted with water.

The mechanism of this reaction, which requires but a single process, appears to be primarily, the formation of sulphenyl chloride, which reacts with water either to give the sulphonyl chloride directly, or through the sulphinic acid which is transformed to the sulphonyl chloride by the further action of chlorine.

The example of bis-orthronitrophenyl disulphide given below, illustrates this mechanism:-



Although this method failed with bis - 2:4 - dinitrophenyl disulphide, Fries (24) succeeded in obtaining 2:4 - dinitrobenzenesulphenyl chloride, by chlorinating 2:4 - dinitrophenyl thiolbenzoate.

A combination of the two procedures resulted in the successful preparation of the required sulphonyl chloride from the thioester in good yield.

This modified procedure had been successfully applied to other benzoylated thiols, thiolsulphonic esters (disulphoxides), and the ethyl ethylxanthate, when a publication by Douglass and Johnson (25), anticipated, in principle, these results.

The above authors, however, dealt with a development of their work an isothioureates only, as regards the preparation of sulphonyl chlorides.

Summarising this work, compounds containing the following groupings have successfully yielded sulphonyl chlorides on chlorination in aqueous acetic acid:-

$RS-SR$

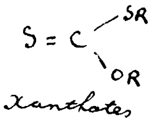
disulphides

$RSCOPh$

Benzoylated thiols

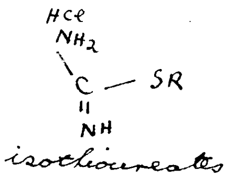
RSO_2SR

Thiolsulphonic esters



$S=C\begin{matrix}SR\\OR\end{matrix}$

Xanthates



$HCl\;NH_2-\underset{NH}{\overset{}{C}}-SR$

isothioureates

It may be concluded, from an examination of these types, that sulphonyl chlorides may be readily prepared from compounds, bearing the character of acylated thiols, by chlorination in an aqueous medium.

Section 8.

EXPERIMENTAL.

To avoid unnecessary repetition, the experimental procedure is largely referred to two processes A and B, and the formation by process A of 4-chloro-2-nitrophenyl p-tolyl sulphide (VIII.) found with all sulphones and sulphonamides of type (I.) in reaction with p-thiocresol is not further mentioned. Formation of the piperidino-compound (IV.) found in quantities indicating about 2% conversion is implied in referring to process B.

Process A. - A solution of the sulphone or chloronitro-compound (1 mol.) and the thiol (1 mol.) in alcohol or alcoholic dioxan was treated with sodium hydroxide (1 mol., 10% aqueous solution) and thereafter warmed for 5 minutes. The product which separated on cooling was crystallised from acetic acid.

Process B. - The compound was heated in excess of piperidine as solvent for 5 minutes (exceptions noted). After steam-distillation to remove 4-chloro-2-nitro-1-piperidinobenzene (IV.) (extracted from the distillate with benzene), the residue, which solidified on cooling or on stirring with dilute acid, was fractionally crystallised from alcohol.

For Section (2).

4:2':5' - Trichloro-2-nitrodiphenylsulphone (V.) - The corresponding sulphide, obtained from 2:5-dichloronitrobenzene and 2:5-dichlorothiophenol (process A), had m.p. 106-107° (Found: N, 4.4. $C_{12}H_6O_2NCl_3S$ requires N, 4.2%) and was oxidised with hydrogen peroxide and acetic acid to the sulphone, m.p. 131° (Found: N, 3.8 $C_{12}H_6O_4NCl_3S$ requires N, 3.8%). With piperidine (process B) the sulphone yielded 2':5'-dichloro-2-nitro-4-piperidinodiphenylsulphone, m.p. 172° (Found: N, 6.9. $C_{17}H_{16}O_4N_2Cl_2S$ requires N, 6.75%), and 4:2':5'-trichloro-2-piperidinodiphenylsulphone, m.p. 153° (Found: N, 3.5. $C_{17}H_{16}O_2NCl_3S$ requires N, 3.5%).

4:4'-Dichloro-2:3'-dinitrodiphenylsulphone (VI.) - 4:4'-Dichloro-2-nitrodiphenylsulphide, m.p. 158°, obtained from 2:5-dichloronitrobenzene and p-chlorothiophenol (process A) (Found: N, 4.8. $C_{12}H_7O_2NCl_2S$ requires N, 4.7%), was oxidised to 4:4'-dichloro-2-nitrodiphenylsulphone, m.p. 133° (Found: N, 4.3. $C_{12}H_7O_4NCl_2S$ requires

N, 4.2%). The latter compound nitrated in cold concentrated sulphuric acid solution by addition of potassium nitrate (1 mol.), yielded the required sulphone, m.p. 162° (Found: N, 7.6. $C_{12}H_6O_6N_2Cl_2S$ requires N, 7.4%). A solution of this sulphone in dioxan, when treated at room temperature with piperidine (2 mols.) and kept for a few hours, yielded, in addition to piperidine hydrochloride, only 4-chloro-2:3'-dinitro-4'-piperidinodiphenylsulphone, m.p. 140° (IX.) (Found: N, 9.9. $C_{17}H_{16}O_6N_3ClS$ requires N, 9.9%). The constitution of this piperidino-derivative was proved by the formation of the sulphide (VIII.) from it (process A).

Reactions of 4-Chloro-2-nitrophenyl-p-tolylsulphone with sodium sulphide and sodium disulphide.

1 Mol. of sodium sulphide was added to 2 mols. sulphone dissolved in hot alcohol and the mixture heated for 5 minutes. On cooling, the product separated out (XII.), and was recrystallised from acetic acid, m.p. 149-150°.

1 Mol. of sodium disulphide was added to a hot alcoholic solution of the sulphone (2 mols.) and the mixture heated for 5 minutes. On cooling, the product (XIII.) separated out and was recrystallised from acetic

acid, m.p. 212°.

5-Chloro-2-p-toluenesulphonyldiphenylamine (XIV.) was obtained by refluxing a solution of the above sulphone in aniline for 5 hours. The dark oil obtained by treatment with dilute acid solidified slowly and was repeatedly crystallised from acetic acid (charcoal). It formed colourless crystals, m.p. 121° (Found: N, 4.2. $C_{19}H_{16}O_2NClS$ requires N, 3.9%).

4-Chloro-2-nitrophenyl-p-tolyl ether (XV.) (m.p. and mixed m.p. 100°; cf. Fox and Turner (26)) was obtained when the above sulphone was heated with sodium p-tolyloxide dissolved in p-cresol.

For Section (3).

4-Chloro-2-nitrophenylmethylsulphone (Zincke, Ref. (22) p. 99), (he gives m.p. 143°; now found 155-156°) reacted with piperidine (process B) to give 2-nitro-4-piperidinophenylmethylsulphone, m.p. 126° (Found: N, 10.2. $C_{12}H_{16}O_4N_2S$ requires N, 9.9%), and 4-chloro-2-piperidinophenylmethylsulphone, m.p. 134°. (Found: N, 5.2. $C_{12}H_{16}O_2NClS$ requires N, 5.1%).

4-Chloro-2-nitrodiphenylsulphone. The corresponding sulphide, obtained from 2:5-dichloronitrobenzene and thiophenol (process A), had m.p. 86°. (Found: N, 5.35 $C_{12}H_8O_2NClS$ requires N, 5.3%) and was oxidised to the required sulphone, m.p. 121° (Found: N, 4.7. $C_{12}H_8O_4NClS$ requires N, 4.7%). The latter compound with piperidine (process B) gave 2-nitro-4-piperidinodiphenylsulphone, orange plates, M.P. 172°, (Found: N, 8.3. $C_{17}H_{18}O_4N_2S$ requires N, 8.1%), and 4-chloro-2-piperidinodiphenylsulphone, colourless needles, m.p. 121° (Found: N, 4.2. $C_{17}H_{18}O_2NClS$ requires N, 4.2%).

4-Chloro-2-nitrobenzenesulphonamide (Riesz, loc. cit.) treated with piperidine (45 mins., process B), yielded 4-chloro-2-piperidinobenzenesulphonamide, m.p. 152° (Found: N, 10.2. $C_{11}H_{15}O_2N_2ClS$ requires N, 10.2%), and 2-nitro-4-piperidinobenzenesulphonamide, m.p. 137° (Found: N, 14.9. $C_{11}H_{15}O_4N_3S$ requires N, 14.7%).

4-Chloro-2-nitrobenzenesulphonylpiperidide, obtained by slow addition of piperidine (2 mols.) to a well-cooled solution of the sulphonyl chloride (cf. section (7) experimental) in alcohol, formed colourless crystals, m.p. 138° (Found: N, 9.3. $C_{11}H_{13}O_4N_2ClS$ requires N, 9.2%). From it, 4-chloro-2-piperidinobenzenesulphonylpiperidide, m.p. 105° (Found: N, 7.9. $C_{16}H_{23}O_2N_2ClS$ requires N, 8.2%), and 2-nitro-4-piperidinobenzenesulphonylpiperidide, m.p.

121° (Found: N, 12.1. $C_{16}H_{23}O_4N_3S$ requires N, 11.9%), were obtained by the action of piperidine (45 mins., process B).

2:4-Dinitrobenzenesulphonylpiperidide (XXXVI.), m.p. 130° (Found: N, 13.5. $C_{11}H_{13}O_6N_3S$ requires N, 13.3%), prepared from the sulphonyl chloride and piperidine (2 mols.) in cold alcohol, and 2:4-dinitrobenzenesulphonamide (Willgerodt and Mohr (27)) each yielded (a) 2:4-dinitro-1-piperidino benzene (m.p. and mixed m.p. 92°) when heated for 35 minutes with excess of piperidine, and (b) 2:4-dinitrophenyl-p-tolylsulphide (m.p. and mixed m.p. 103°) when heated with alkaline p-thiocresol (process A).

<u>For Section (4)</u>.

3-Chloro-2-nitrophenyl-p-tolylsulphone (XVIII.) 2:6-Dichloronitrobenzene, (Holleman (29)), was dissolved in the minimum of cold alcohol and treated with alkaline p-thiocresol (1 mol.) in a few drops of water; the solution was allowed to stand for fourteen days. The mixture was filtered free from solid sodium chloride and 2:6-dithiotolylnitrobenzene. The filtrate was steam distilled to free from starting products, and the distillate was extracted with benzene. On evaporation, a yellow solid, m.pt. 83° was obtained. On oxidation this yielded the required sulphone, m.p. 151°. The m.pts. and mixed m.pts. of these compounds agreed with authentic samples of 3-chloro-2-nitrophenyl-p-tolyl thioether and 3-chloro-2-nitrophenyl-p-tolylsulphone respectively.

3-Piperidino-2-nitrophenyl-p-tolylsulphone (XXI.). The sulphone (XVIII.) was dissolved in excess piperidine and heated for 15 minutes. On cooling and addition of water, a solid (stirring) separated out. On crystallisation from alcohol this gave pale yellow needles m.p. 145° (Found: C, 60.4; H, 5.8; N, 7.8. $C_{18}H_{20}O_4N_2S$ requires C, 60.01; H, 5.8; N, 7.8%).

3-Chloro-2-p-tolylthiophenyl-p-tolylsulphone (XX.). The sulphone (XVIII.) in cold alcoholic dioxan, was treated with 1 mol. sodium p-thiocresol in a few drops of water, and allowed to stand for one week. The solid which separated was washed with alcohol and water, recrystallised from acetic acid, and gave white prismatic crystals, m.p. 156°. (Found: C, 61.9; H, 4.6. $C_{20}H_{17}O_2ClS_2$ requires C, 61.8; H, 4.4%).

3-Chloro-2-aminophenyl-p-tolylsulphone (XXIII.). One gm. of the sulphone (XVIII.) suspended in 12 cc. methyl alcohol and 3.2 cc. (10 mols.) of .88 ammonia, was heated in a Carius tube for six hours at 160-170°. On cooling, a faint yellow solid, which gave white needles on repeated crystallisations from acetic acid, separated out. M.pt. 114° (Found: C, 55.5; H, 4.5. $C_{13}H_{12}O_2NClS$ requires C, 55.4; H, 4.3%).

3-Chloro-2-methoxybenzene-p-tolylsulphone (XXII.) The sulphone (XVIII.) was heated for ten minutes with sodium methoxide ($1\frac{1}{2}$ mols.) in methyl alcohol and dioxan. On cooling the product separated out. On crystallisation from alcohol, white prismatic crystals were obtained, m.p. 108.5° (Found: C, 56.5; H, 4.2. $C_{14}H_{13}O_3ClS$ requires C, 56.7; H, 4.4%).

2-Chloro-6-nitrophenyl-p-tolylsulphone (XIX.). 2:3-Dichloronitrobenzene (Holleman (30)), was heated in alcohol with sodium p-thiocresol (1 mol.) for a few minutes. On cooling and recrystallising, orange-yellow rectangular crystals were obtained (XXVI.) (acetic acid) m.p. 69-70°. On oxidation, this compound yielded the required sulphone, m.p. 138-139°. Here also, m.p. and mixed m.pts. agreeing with authentic samples of the thioether and sulphone were obtained.

The reaction between the sulphone (XIX.) and alkaline p-thiocresol gave rise to the thio-ether (XXVI.).

The sulphone in alcoholic dioxan was heated for a few minutes with the reagent (1 mol.) and the product isolated as above.

2-Piperidino-6-nitrophenyl-p-tolylsulphone (XXVII.). The sulphone (XIX.) was heated for a few minutes in excess piperidine. On cooling, water was added and the resulting oil easily solidified (stirring). On crystallisation, firstly from alcohol, then acetic acid, light yellow needles, m.p. 169° were obtained. (Found: C, 56.2; H, 5.5; N, 8.0. $C_{18}H_{20}O_4N_2S$ requires C, 56.0; H, 5.6; N, 7.8%).

2-Chloro-6-aminophenyl-p-tolylsulphone (XXIX.). The sulphone (XIX.) was heated with methyl alcohol and ammonia (as for analogous reaction with sulphone (XVIII.)). The product, on crystallisation from alcohol giving faint yellow needles, m.p. 134-135° (Found: C, 55.2; H, 4.3. $C_{13}H_{12}O_2NClS$ requires C, 55.4; H, 4.3%).

<u>For Section (6).</u>

2:4-Dinitrophenyl β-ethoxyl sulphide (XXXIII.). An alcoholic solution (10.6 g. in 50 cc.) of β-ethoxyethylthiol, (Boord and Swallen (19)), was treated with an aqueous solution of sodium hydroxide (4 g. in 10 cc.) and added slowly to 2:4-dinitrochlorobenzene (20 g.) dissolved in cold dioxan. Sodium chloride, and some bis-2:4-dinitrophenyl disulphide separated, and after filtration, the filtrate deposited the required product, which crystallised from alcohol in yellow needles, m.p. 65-66° (Found: N, 10.1 $C_{10}H_{12}O_5N_2S$ requires N, 10.3%). The corresponding sulphone (XXXIV.), m.p. 97°, was obtained by oxidising the sulphide with hydrogen peroxide in acetic acid (Found: N, 9.2. $C_{10}H_{12}O_7N_2S$ requires N, 9.2%).

Chloromercuric β-ethoxyethanesulphinate (XLI.). The sulphone (XXXIV.) was heated with piperidine (2 mols.) in benzene solution for 5 minutes. After cooling, the solution was shaken with water containing just less than 1 mol. of sodium hydroxide, and the aqueous extract was concentrated somewhat to ensure removal of piperidine. At this stage the presence of the sodium salt of the required acid was demonstrated by heating a portion of the aqueous solution with 2:4-dinitrochlorobenzene in alcohol, whereby the sulphone (XXXIV.) was regenerated. The remainder of the sulphinate solution was treated hot with a solution of mercuric chloride in warm water, yielding the product as crystalline flakes, which were collected, washed, and dried in a vacuum desiccator (Found: Cl, 9.5;

Hg, 53.4. $C_4H_9O_3ClSHg$ requires Cl, 9.5; Hg, 53.75%).

The dry salt slowly decomposed at room temperature with formation of mercurous salts, and yielded sulphur dioxide on being heated. The formation of ethylene, when a suspension of the substance was refluxed in water or in an aqueous medium buffered to pH7, was shown by passing the evolved gases through a cold alcoholic solution of bromine, followed by addition of sodium hydroxide in slight excess, and by the formation of the bis-thioether (cf. below). No organic mercury derivative could be detected at any stage of the experiments. A very rapid evolution of ethylene occurred when the salt or Schoeller's compound was heated under reflux in ethylene glycol.

Bis-(2:5-dichlorophenylthio)ethane. An aqueous-alcoholic solution containing ethylene dibromide (1 mol.), 2:5-dichlorophenylthiol (2 mols.), and sodium hydroxide (2 mols.) was gently warmed for 5 minutes. On cooling, the product separated; it crystallised from acetic acid in colourless plates, m.p. 125°. The samples obtained from the decomposition experiments had the same m.p. and mixed m.p. (after being washed with alcohol to remove contaminating bis - 2:5-dichlorophenyl disulphide) (Found: C, 44.1; H, 2.5. $C_{14}H_{10}Cl_4S_2$ requires C, 43.75; H, 2.6%).

For Section (7).

The procedure, Riesz (23), consisted in saturating with chlorine a solution or suspension of the compound in acetic acid containing 10% of water (about 10 c.c. of liquid to 2 g. of solid). The product either separated on standing or was precipitated by cautious addition of water.

2:4-Dinitrobenzenesulphonyl chloride, m.p. 102°, was obtained in 50-60% yield from 2:4-dinitrophenyl thiolbenzoate, (Kym (28)), or from the disulphide by chlorinating a suspension in concentrated sulphuric acid, followed by dilution with acetic acid and water.

4-Chloro-2-nitrobenzenesulphonyl chloride (most conveniently prepared from the disulphide; Riesz (23)) was formed in 80-90% yield from 4-chloro-2-nitrophenyl thiolbenzoate. The latter, prepared by the Schotten-Baumann method from the thiol, had m.p. 124° (Found: N, 4.8. $C_{13}H_8O_3NClS$ requires N, 4.8%).

High yields of the corresponding sulphonyl chlorides were obtained from p-tolyl, o-nitrophenyl, and benzyl disulphoxides. Ethyl ethylxanthate gave a good yield of ethanesulphonyl chloride (fraction, b.p. 174-177°) which was extracted with benzene after dilution of the reaction solution with water.

Section 9.

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