# THE CATIONOID REACTIVITY OF NITRO-DIPHENYLSULPHONES.

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Thesis presented for the Degree of D.Sc.

by

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## Preface.

The Introduction and the section on General Conclusions in this thesis may be read together and provide a general outline of the scope, significance and salient features of the investigation. A description and detailed discussion of the experimental results are contained in Chapters I to VI wherein the order of presentation approximates to the order in which the experiments were made but, to minimise digression from the main theme, preliminary preparative work has largely been disposed of in Chapter I, whilst data, obtained from a different source yet confirmatory to a sub-section of Chapter II, have been carried over to the final chapter.

With the exception of those described in Chapter IV the experimental results have mostly been published (J.C.S., 1935, 537 and 896; 1936, 218; 1937, 242 and 246) and reprints of these publications are provided with the thesis. There are also submitted reprints of three additional papers dealing with a topic apart from the main thesis (J.C.S., 1933, 823; 1935, 535; 1937, 391).

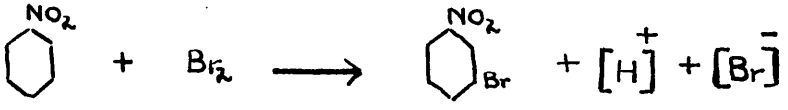
I gladly acknowledge here my indebtedness to several students, in particular to Mr. A. Livingston and Mr. T. D. Robson for assistance in the practical work; to Mr. J. M. L. Cameron for his care and reliability in carrying out micro- /

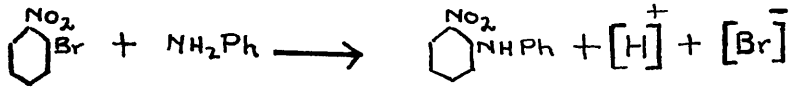
micro-analyses, and to The Chemical Society for grants towards purchase of materials. I am especially indebted to Professor T. S. Patterson whom I sincerely thank not only for the opportunity and facilities he provided for conducting research, but also for the encouraging interest he invariably displayed in the course of its development.

## CONTENTS

## Introduction.

The well-known mobility of a halogen atom situated ortho or para to a nitro group in the benzene ring has been the subject of many investigations and it has been recognised that not only halogen, but other atoms and groups may also be activated in these positions. It has further been established that activating influences of the same type - though markedly less in degree - may be supplied by such groups as :C=O, C:N, :$SO_2$, etc., that is, by other so-called <u>meta</u>- directing groups. The whole phenomenon is, in fact, an aspect of benzene substitution wherein the activating groups are those which in ordinary substitutions — halogenation, nitration, sulphonation etc. — commonly provide a retarding influence. The dual function of these groups implies a contrast in the types of substitution involved and the contrast is apparent from consideration of the character of the exchanges effected in two typical reactions:-

1. 

11. 

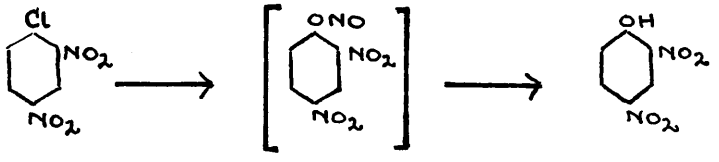
In reaction I, which proceeds much less readily than the bromination of benzene, a proton ($H^+$) has been displaced from the nucleus (cation exchange); in reaction II, which proceeds much more readily than the reaction between aniline and bromobenzene, an anion ($\bar{Br}$) has been displaced from the nucleus (anion exchange). The function of the nucleus - on the ionic double decomposition analogy - is described in type I as anionoid, and in type II as cationoid (1). To avoid confusion, substituents which promote anionoid reactivity in the ring (viz. $NH_2$, NHR, OH, OR etc.) are termed anionoid groups, and those which promote cationoid reactivity ($NO_2$, CO, CN, $SO_2$, etc.) are correspondingly cationoid groups. In each case, irrespective of the character of the substituent, the chief centres of actual <u>activation</u> are those situated <u>ortho</u> or <u>para</u> to the substituent. These centres are rendered anionoid by anionoid groups, and cationoid by cationoid groups. When, as in the bromination of nitrobenzene (reaction I), a reaction of the type not promoted by the substituent occurs, then the exchanges between nucleus and reagent take place at the centre least unfavourably affected, viz. at the <u>meta</u> position.

The /

The facile reactions undergone by benzene itself are all of the type promoted by anionoid groups. This, coupled with the fact that the halogen in mono, di, and tri-halogenobenzenes has little or no mobility (2), suggests that the intrinsic character of a benzene nucleus is to be regarded as anionoid. Moreover, hydrogen readily accepts and retains (as proton) a positive charge but, consistent with its rare occurrence as an anion, it is a reluctant participator in the anion exchanges found at cationoid centres. Consequently, cationoid reactivity is displayed in a benzene system only in presence of a cationoid substituent and generally requires the presence of a second substituent which, as a true potential anion situated ortho or para to the cationoid group, is capable of replacement.

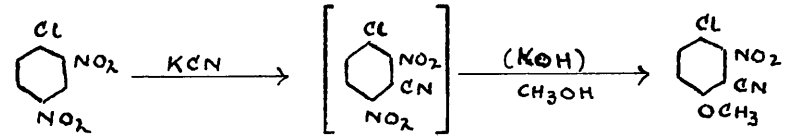
Since anionoid and cationoid groups have functions opposite in character, it is to be expected that their simultaneous presence in a benzene ring will result in at least partial neutralisation of their respective influences. It is therefore surprising that, almost without exception, the reagents used in the study of cationoid reactivity are precisely those which might be expected to paralyse the /

the cationoid system after the initial reaction. Thus the common reagents, amines, sodium alkyl and aryloxides etc., react to introduce substituents ($NH_2$, NHR, OH, OR etc.) which are vigorous promotors of anionoid reactivity and, the introduction effected, further reaction seldom ensues. When, however, the practical aspect of the problem is considered it becomes apparent that the choice of reagents suitable for the preservation or progressive development of a cationoid system is strictly limited. Silver nitrite — perhaps the most obvious reagent for the purpose — reacts in the metal-oxygen form yielding, untimately, phenols (3).

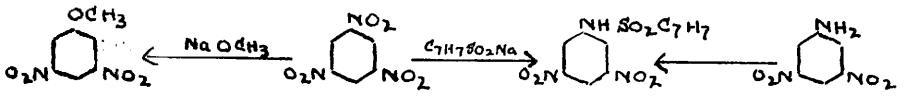



Potassium cyanide is probably too alkaline to be suitable and moreover has the disadvantage that it displays a preference for replacing hydrogen of the nucleus (formation of K H ?) and thereby initiates reduction processes. For example, 2:4-dinitrochlorobenzene reacts with potassium cyanide in methyl alcoholic solution to give (together with reduction products) 2-cyano-3-nitro-4 chloroanisole (4) which almost certainly results, as shown below, from the dinitrocyano /

dinitrocyano compound by reason of the alkaline nature of the reagent or because of alkali produced in the initial reaction.

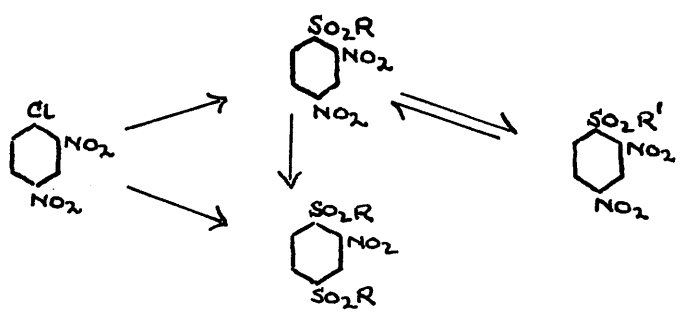



No information is at present available regarding the behaviour of cyanides derived from weaker bases. Sodium arsenite is definitely too alkaline (5) and sulphites would involve laborious practical work in isolating and purifying the very soluble sulphonic acid products. On that account sulphinates are preferable but both sulphites and sulphinates have the disadvantage of being reducing agents and, since their replacing powers are slight, they are worthless as reagents for the feebler cases of cationoid reactivity. For example, in the case of 1:3:5- trinitro-benzene, which with sodium methoxide yields 3:5- dinitro-anisole but which generally reacts very sluggishly in this type of reaction, the author found the sulphonamide (established as indicated) to be the chief product of reaction with sodium p-toluene sulphinate (cf. p. 84 Experimental).



This result may be compared with the production of sulphaminic acids ($RNHSO_3H$) from sodium bisulphite and nitrobenzene derivatives on the one hand (6), and with the formation of sulphonamides by the interaction of sulphinic acids and phenylhydroxylamines on the other (7).

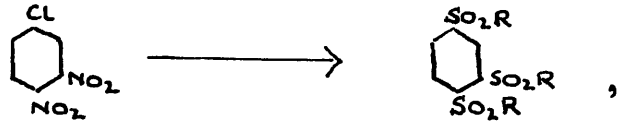
Despite these reducing properties sulphinates are capable of application as reagents for cationoid reactivity and, as the detailed considerations contained in the sequel show, they do conserve the cationoid character of the systems with which they react. For example, in the reaction with 2:4 dinitro-chlorobenzene they yield 2:4 dinitro-diphenylsulphone derivatives (p.13) in which the arylsulphonyl group is mobile and may be replaced by reaction with other sulphinates (sulphonyl exchange p. 24). At higher temperatures the reaction enters a second phase with formation of 2:5-bis-arylsulphonyl nitrobenzenes:-




(p. 27)

Advantage has been taken of the sulphonyl exchange phenomena to assess the effect of different sulphonyl anions on the facility of the replacement. Both in the case of dinitrodiphenylsulphones (p.25) and in related phenomena with thiolsulphonic esters (pp.70 and 73) the results indicate that the greater the stability of an anion, the more readily is it replaced and the less readily is it introduced (cf. also pp.13 ,30 and62 ), i.e. that the relative anionic stability of the actual and potential anions is a factor controlling cationoid reactivity.

The conservation of cationoid reactivity by sulphinate reagents is also illustrated by their reactions with 3:4-dinitrochlorobenzene (p.58) from which ultimately 1:2:4-tri-arylsulphonylbenzenes were obtained:-

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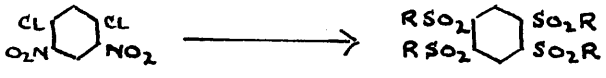
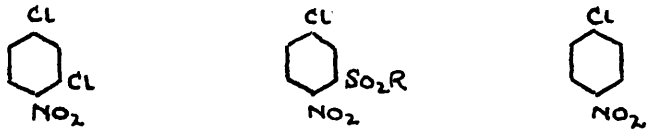
and by their reactions with 1:5-dichloro-2:4-dinitrobenzene (p.61) from which tetra-sulphones were produced:-



In these reactions with sulphinates it is not suggested that the introduction of the first sulphonyl group necessarily implies that a second sulphonyl group will thereafter be introduced more readily (though this may sometimes happen cf. p. 61), nor does it follow, in general, that the product of the first reaction will exhibit a greater cationoid reactivity than the parent substance from which it is derived. For example, in 2:4-dichloronitrobenzene the mobility of the o-chlorine exceeds by an unknown amount the mobility of the p-chlorine,

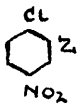



and the legitimate comparison is therefore between the reactivity of the mono-sulphonyl product and the corresponding compound (p-chloronitrobenzene) in which the sulphonyl group is formally replaced by hydrogen.

The search for a reagent calculated to preserve or augment cationoid reactivity in a system beyond the initial reaction is thus a particular aspect of a general inquiry into the effects produced in such a system by introducing — irrespective of the means adopted — new cationoid groups.

It /

It may be asked for instance how the new cationoid systems (e.g. A···F) formed by introducing another cationoid group Z into the isomeric chloronitrobenzenes compare with the parent compounds in degree of reactivity and in location of the centre or centres at which that reactivity is expressed.



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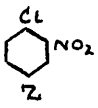

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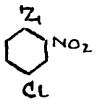

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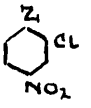

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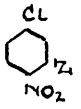

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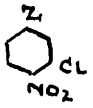


(F.)

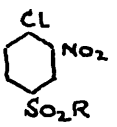
The literature of the subject, bulky though it is, supplies a very fragmentary answer; in a single case only viz., the dinitrochlorobenzenes ($Z = NO_2$) with sodium methoxide as reagent, has any aspect of completeness been achieved (8) and it is apparent that even here the effective cationoid group is always the nitro group. Other cationoid groups have almost completely been neglected except in so far as their influence is cumulative with that of a nitro group at one particular centre (types A and B). Again with the exception of the dinitrochlorobenzenes, no attempt has been made to study the reactivity of a system in which two dissimilar potential anions are simultaneously rendered mobile by a nitro group (types E and F). The impression is therefore created that in nitrobenzene derivatives cationoid /

cationoid reactivity is expressed only or, with all reagents, preferentially at one centre which is either ortho or para to the nitro group. How erroneous this impression is and how petrifying its effect on the study of cationoid reactivity has been, is shown, in the author's opinion, by the multiplicity of "unusual" reactions and the frequency of unparalleled contrasts found in investigating the reactivity of chloronitrodiphenylsulphones.

Benzene derivatives containing three substituents are most commonly encountered as variants of the 1:2:4 substitution pattern. Conforming to this pattern there are six possible chloronitrodiphenylsulphones and in the sequel a detailed account is given of the reactivity displayed by representatives of each of these chloronitro sulphone types. It will be noted that each substituent is a potential anion (Cl; $NO_2$; $SO_2R$) capable of being replaced when suitably activated, and two of them ($NO_2$ and $SO_2R$) are cationoid groups. The results obtained may be summarised with reference to the six types taken in pairs.

1. When the activating influences of the nitro and sulphonyl /

sulphonyl groups were cumulative as in the following compounds:-

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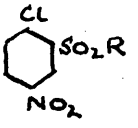
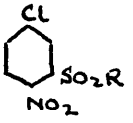



(B.)

only the chlorine atom underwent replacement (p.28).

2. The influence of the nitro group dominated the reactivity when the chlorine and sulphonyl groups were both present in the o:p-positions to it. In no reaction was the nitro group itself replaced although it occupied a position activated by sulphonyl (cf. p.53).

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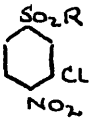
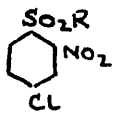



(F.)

The group replaced was not constant (p.54). Piperidine as reagent displayed a preference for replacing chlorine irrespective of whether it was situated o- or p- to the nitro group. In contrast, with the sodium salt of p-thiocresol as reagent the o-substituent with respect to nitro (i.e. $SO_2R$ in E, and Cl in F) underwent replacement.

3. The influence of the sulphonyl group dominated the reactivity in many of the reactions, when the chlorine and nitro groups both occupied positions o or p to it — Cl or $NO_2$ being replaced in reaction with piperidine, ammonia /

ammonia and sodium methoxide (pp. 39, 40 and 42). In other reactions— with mercaptide or sulphide reagents (pp.40 and 42)— the reactivity was controlled by the nitro group, the sulphonyl group being replaced.

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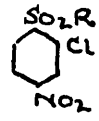



(C.)

In these last compounds (B and C) any one of the substituents may therefore be replaced according to the reagent selected.

In all of these reactions the general degree of reactivity displayed was noticeably high (p.44), chlorine in reaction with piperidine, for example, being readily replaced irrespective of whether it was present in an o:p- position to sulphonyl or to nitro. Nevertheless chlorine mobility in an unnitrated chloro sulphone was very markedly less than that in a (sulphonyl free) chloronitrobenzene (p.48).

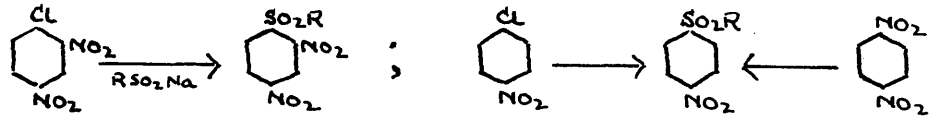
These facts and others referred to in the detailed discussions contained in Chapters II - VI lead to the general conclusions summarised in pages 75 - 77 .

## Chapter I.

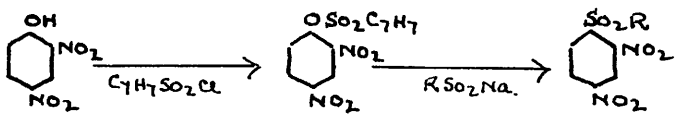
## General Preparative Methods.

### Mono and dinitrodiphenylsulphones.

Ullmann and Pasdermadjian (9) employed sodium benzene sulphinate to obtain nitrodiphenylsulphones from o- and p-chloronitrobenzene and from 2:4-dinitrochlorobenzene. In the last case the reaction proceeds readily in hot aqueous alcohol but with the mono-nitro compounds in the same medium it is necessary to heat the reagents in sealed tubes at 160°C. This inconvenience, however, is removed by conducting the reactions in hot ethylene glycol which is an excellent solvent for sulphinates and consequently has found extensive use in the present investigation. The method of preparation is not confined to reactions with sodium benzenesulphinate but has been successfully applied to a wide range of sulphinates of which the nitrobenzene and 2:5-dichlorobenzene sulphinates were found to be the least satisfactory in regard to the yields produced.



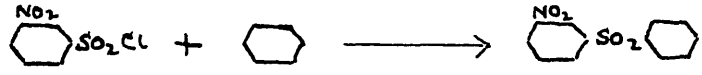
It was foreseen that in any extensive investigation, the preparation of sulphones from dinitro compounds or from nitrophenols would, on occasion, effect considerable economies both in time and materials, and hence in the preliminary work an examination was made of the action of sulphinates on o- and p- dinitrobenzene and on the p-toluenesulphonates of nitrophenols. Sulphones were readily obtained from o- and p- dinitrobenzene and from 2:4-dinitrophenyl p-toluene sulphonate but not from the p-toluene sulphonates derived from o- and p-nitrophenol (nor did these last compounds give a satisfactory yield of the sulphides — oxidisable to sulphones — by reaction with mercaptides).




Alkali mercaptides are much more efficient replacing agents than sulphinates, and oxidation of the sulphides produced affords an alternative method for the preparation of sulphones. The practical method adopted for the preparation of a particular o- or p- nitrodiphenylsulphone derivative is therefore decided by the accessibility and degree /

degree of reactivity of the starting material.

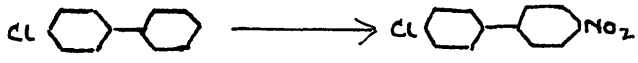
The m- mononitrodiphenylsulphones are not formed by anion exchange reactions and were generally prepared by a Friedel-Crafts condensation (cf. (10) e.g.:-



Chloronitrodiphenylsulphones

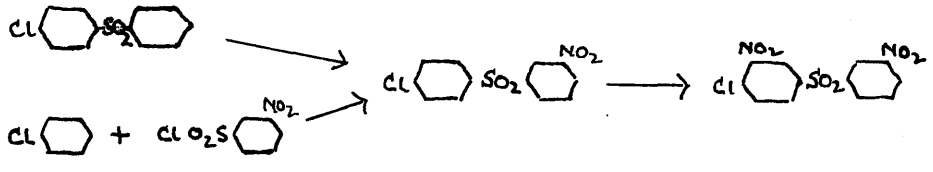
4-Chloro-3-nitrodiphenylsulphones - Type A.

It is an established fact that despite the ordinary op-directing character of chlorine, chlorobenzene nitrates less readily than benzene itself (11) and consequently nitration of monochlorodiphenyl results in heteronuclear substitution (12) e.g.



A phenyl or substituted phenyl nucleus, however, itself exerts an op-directing influence on a second nucleus to which it is attached and the analogy, therefore, scarcely suffices to predict the results of nitrating a system containing a phenyl and a chlorophenyl nucleus united by a m-directing radicle - moreover the nitration of monochlorobenzophenone /

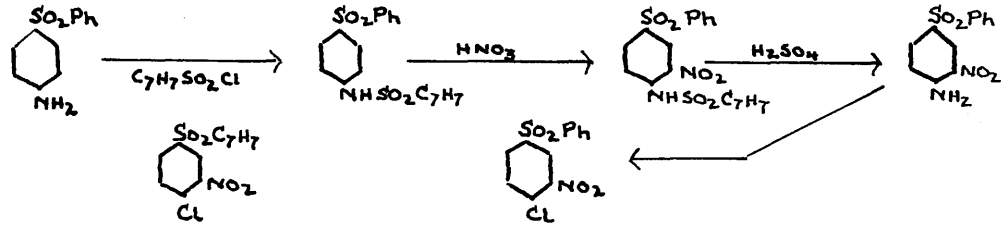
benzophenone does not appear to have been examined. Hence in the hope of preparing 4-chloro-3-nitrodiphenylsulphone the nitration of 4-chlorodiphenylsulphone was undertaken. The mononitrated product, obtained in good yield, did not, however, contain a mobile chlorine atom (piperidine test) and, by its preparation from m-nitrobenzenesulphonyl chloride and chlorobenzene (Friedel-Crafts reaction), was shown to be the heteronuclear substitution derivative viz., 4-chloro-3'-nitrodiphenylsulphone. Halogen mobility was demonstrated in the product of dinitration viz. 4-chloro-3-3'-dinitrodiphenylsulphone which was obtained either directly or via the mononitro compound from 4-chlorodiphenylsulphone.



This result is important as a demonstration of the co-operation between chlorine and sulphonyl groups in retarding anionoid reactivity in the disubstituted nucleus; the converse effect — joint promotion of nuclear cationoid reactivity — will be referred to later (p.47). Nitration of 4-chloro-4'-methyldiphenylsulphone /

methyldiphenylsulphone followed a course similar to that outlined above.

4-Chloro-3-nitrodiphenylsulphone was prepared by a series of reactions starting from 4-nitrodiphenylsulphone. The latter compound was reduced to the amine and this, in the form of its p-toluenesulphonyl derivative, was mono-nitrated. After hydrolysis the resulting 4-amino-3-nitro-diphenylsulphone was diazotised and the diazonium group replaced by chlorine (Sandmeyer).




The method or preparation coupled with the fact that the product contains a mobile halogen atom (p.28) is sufficient proof of the constitution. The corresponding 4-chloro-3-nitrophenyl p-tolylsulphone was prepared in exactly the same manner.

An alternative preparation, which was particularly useful as a source of the corresponding p-chlorophenyl-sulphone, was found in an application of the Friedel-Crafts reaction /

reaction as illustrated:-

Although with benzene and chlorobenzene this process gave satisfactory results the formation of unworkable tars rendered it useless in the case of toluene.

- - - - - - - - -

2-Chloro-5-nitrophenylsulphone - Type B.

The diphenylsulphone was the only representative of this type examined. Its preparation followed the lines of the last reaction viz:-

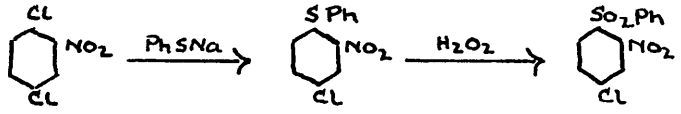
Here again attempts to prepare the p-tolyl analogue yielded only tars.

- - - - - - - - -

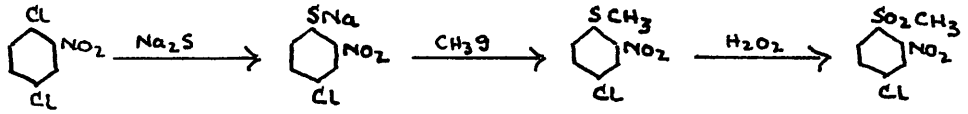
4-Chloro-2-nitrodiphenylsulphones - Type C.

2:5-Dichloronitrobenzene was found to react with sodium sulphinates to give the required sulphones, but, owing to complications in the reaction (p.38) these sulphones were best /

best prepared by oxidation of the corresponding sulphides. 4-Chloro-2-nitrodiphenylsulphide was readily obtained by adding the requisite quantity of thiophenol and sodium hydroxide to a warm alcoholic solution of 2:5-dichloro-nitrobenzene. The product was oxidised to the sulphone by warming with hydrogen peroxide in acetic acid solution.




Other aromatic sulphones of the class were prepared in the same way (p-tolyl and 2:5-dichlorophenyl instead of Ph) but for the methyl sulphone a modification of Blanksma's procedure (13) was preferred:-

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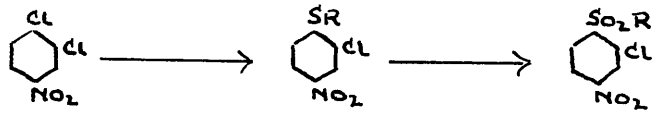
2-Chloro-4-nitrodiphenylsulphones - Type D.

Methods similar to those in Type C. were employed here, eg:-

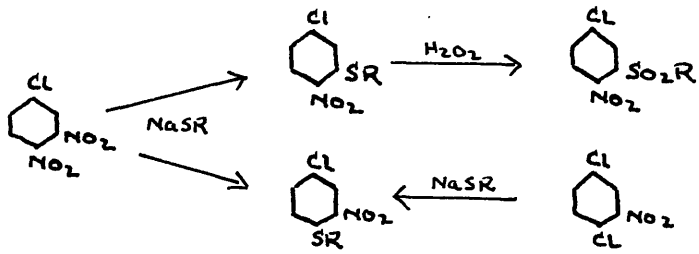



- - - - - - - - -

5-Chloro-2-nitrodiphenylsulphones - Type E.

The most convenient source of sulphones of this type was found in 3:4-dinitrochlorobenzene, which, although both of the nitro groups and the chlorine atom are potentially mobile, is known to react with amines and sodium alkyloxides with preferential replacement of the 3-nitro group (14).

Experiments showed that this preference was maintained in reactions with arylmercaptides but at the same time there were produced here considerable quantities of the p-isomerides which were identified by comparision with the sulphides obtained from 2:5 dichloronitrobenzene.



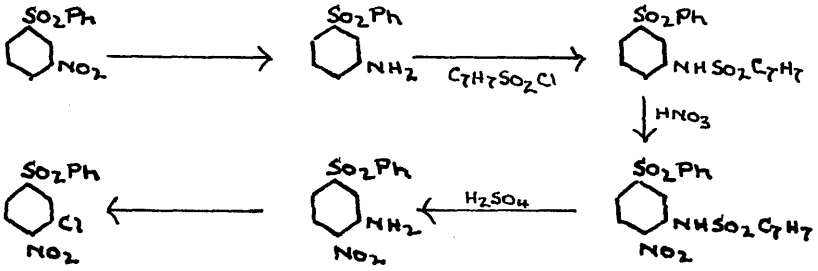

The preponderance of the required products, however, rendered their isolation and purification quite satisfactory and their oxidation to sulphones was effected in the usual way.

- - - - - - - -

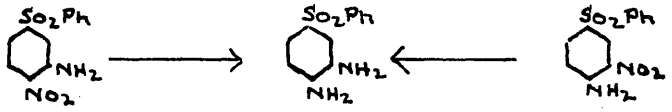
3-Chloro-4-nitrodiphenylsulphone - Type F.

There is no direct procedure for the preparation of a sulphone /

sulphone of this type. By analogy with their other reactions the dinitrochloro- and dichloronitro- benzenes which are potential sources would be expected to react with the sodium salt of thiophenol to give isomers of 3-chloro-4-nitrodiphenylsulphide. On that account the following preparative route was adopted:-




The nitration process involved gave, in addition to some dinitrated material, a mixture of mononitro derivatives from which, however, the required product was fairly easily obtained though the yield was small. Its constitution was established by reduction of the nitro-amine to a diamine which formed a quinoxaline derivative with benzil and by the fact that the same diamine and quinoxaline derivative were obtained from 3-nitro-4-aminodiphenylsulphone (cf. p. 17):-

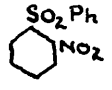



3-Chloro-4-nitrodiphenylsulphone was the only representative of the class which was prepared.

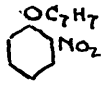
## Chapter II.

## The Reactions of 2:4-Dinitro-, 4-Chloro-3-nitro-, and 2-Chloro-5-nitro- diphenylsulphones.

When the experiments made in this section were commenced it was known that the phenylsulphonyl group in o-nitrodiphenylsulphone (I) is capable of replacement, Levi and Smiles already having shown (15) that with sodium p-tolyloxide and with aniline the diphenylether (II) and the diphenylamine (III) respectively are produced.

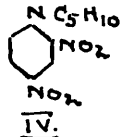



I.




II.

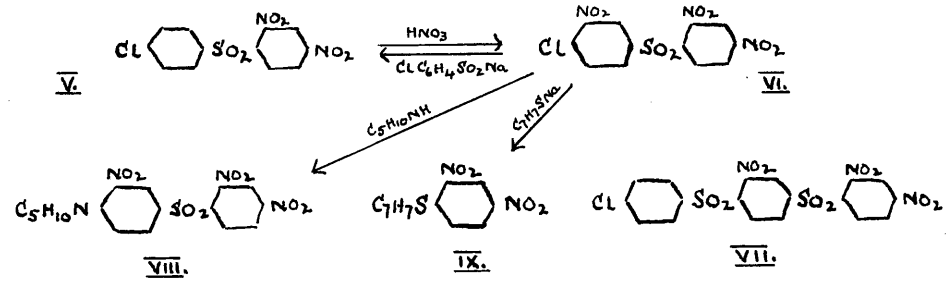

III.




IV.

It is, therefore, not surprising that similar replacements, occurring with greater rapidity, were found in the reactions of 2:4-dinitrodiphenylsulphones. In particular, the action of piperidine on a selection of these compounds was found to yield in all cases 2:4-dinitro-piperidino-benzene (IV). The facility with which these dinitro-sulphones were prepared from 2:4-dinitrochlorobenzene (p.13) suggested the possibility of obtaining polysulphones (e.g. VII) by nitration of the chlorophenyl derivative (V) followed /

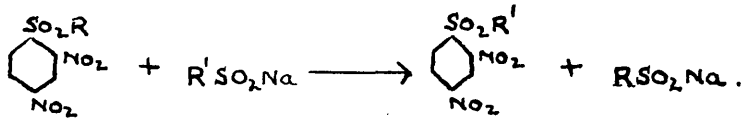
followed by condensation of the product (VI) with a second molecular proportion of sulphinate. The nitration (V⟶VI) was readily accomplished in sulphuric acid solution by the action of sodium nitrate.




Chain sulphones built up by an extension of such a process should be of interest in several directions and the project seemed all the more feasible when it was found that although excess of piperidine reacted with VI to yield 2:4-dinitropiperidinobenzene IV, yet with the theoretical quantity of the reagent only halogen (the bromo compound behaved similarly) was replaced, a piperidinotrinitrosulphone VIII being formed. In contrast with this preferential substitution of halogen, however, sulphinate reagents effected a rapid exchange of sulphonyl groups, for example, with sodium p-chlorobenzenesulphinate, V was rapidly regenerated from VI. Moreover, when instead of sulphinate, a molecular proportion of a mercaptide — viz. sodium salt of /

of p-thiocresol — was employed, 2:4-dinitrophenyl p-tolyl-sulphide IX was produced together with mere traces of ionised halogen. This selectivity in the point of attack by different reagents foreshadows the results of other experiments to be described later.

The capacity of 2:4-dinitrodiphenylsulphones to exchange sulphonyl groups in reaction with sulphinates was employed to determine the relative replacing powers of sulphonyl anions. The results of a number of experiments are summarised in Table I. The signs (+) and (-) respectively denote success and failure of the reaction:-




for which, with the exceptions noted, three molecular proportions of the sulphinate ($R^1SO_2Na$) were employed, the medium in all cases being aqueous dioxan and each solution being refluxed for ten minutes. The table includes only those examples in which the nature of the isolated substance was clearly established by melting point and mixed melting point determinations. In several other cases (e.g. R = phenyl, $R^1$ = p chlorophenyl) the product was a mixture (qualitative halogen test) which resisted fractionation.

TABLE I.

| R = | R¹ = | | R = | R¹ = | |
|---|---|---|---|---|---|
| Ethyl | Methyl* | + | Phenyl | 2:5-Dichloro-phenyl | - |
| Methyl | Ethyl | + | Phenyl | m-Nitrophenyl | - |
| Ethyl | p-Tolyl* | + | p-Chlorophenyl | Phenyl* | + |
| p-Tolyl | Ethyl | + | p-Chlorophenyl | p-Tolyl | + |
| p-Tolyl | Phenyl ‡ | + | p-Chloro-m-nitro | p-Chlorophenyl | + |
| Phenyl | p-Tolyl | + | p-Bromo-m-nitrophenyl | p-Bromophenyl | + |
| Phenyl | Methyl | + | m-Nitro-phenyl | p-Tolyl | + |
| Phenyl | Ethyl | + | p-Chloro-m-nitrophenyl | m-Nitrophenyl | - |

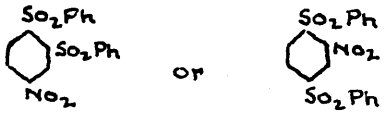
* Large excess ‡ 12 molecular proportions

These results suffice to indicate in a qualitative manner that the reaction is (a) reversible, being influenced by the concentration of free sulphinate ion and (b) dependent upon the relative stabilities of the competing sulphonyl anions (actual and potential) as inferred from the dissociation constants of the corresponding carboxylic /

carboxylic acids (the values of K for sulphinic acids have not been determined). The reaction may therefore be regarded as the establishment of an equilibrium in which the sulphone derived from the weaker sulphinic acid is formed in greater amount, and the order of replacing power for the sulphinates becomes:- $C_2H_5SO_2$ > $CH_3SO_2$ > p-$CH_3C_6H_4SO_2$ > $C_6H_5SO_2$ > p-$ClC_6H_4SO_2$ > 2:5-$Cl_2C_6H_3SO_2$ and 3-$NO_2C_6H_4SO_2$ (cf. also Tables II and III, pp. 70 and 73). The last two sulphinates, it will be recalled, were amongst those which gave the poorest yields in the finite reactions with 2:4-dinitrochlorobenzene (p.13).

These reactions resulting in sulphonyl exchange all occurred very rapidly in aqueous dioxan. When, however, the heating was prolonged or when the reaction was conducted in boiling ethylene glycol (i.e. circa 190°) further reaction ensued apparently arising from the continued action on the dinitrosulphones of sulphinate present in excess or produced during the exchange. To avoid unnecessary complications in investigating this second phase, the action of sodium benzenesulphinate on 2:4-dinitro-diphenylsulphone was examined. Analysis of the product indicated a bis-phenylsulphonyl-nitrobenzene structure and its reactions showed /

showed the presence of one mobile phenylsulphonyl group, which, with the appropriate reagent was replaced by a hydroxyl, ethoxyl, amino or piperidino group. Since the speed with which these replacements occurred was comparable with that in similar reactions with 2:4-dinitrodiphenylsulphone itself, it was inferred that the mobility of the ejected phenylsulphonyl radicle arose from the combined activating influences of both the residual nitro and the second phenylsulphonyl groups. Hence the formation of the disulphonyl compound from 2:4-dinitrodiphenylsulphone must involve replacement of one or other nitro group by phenylsulphonyl* and two structures are possible:-




The correctness of the p-disulphonyl structure follows from the syntheses of the compound and of its replacement products from 4-chloro-3-nitrodiphenylsulphone (p. 17) and the /

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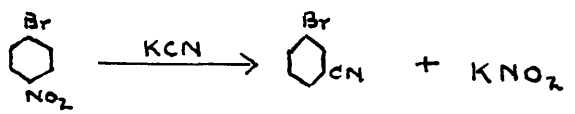
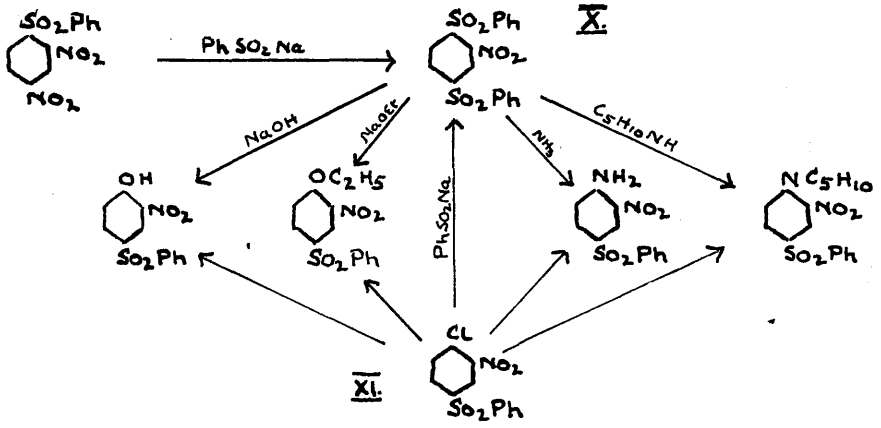
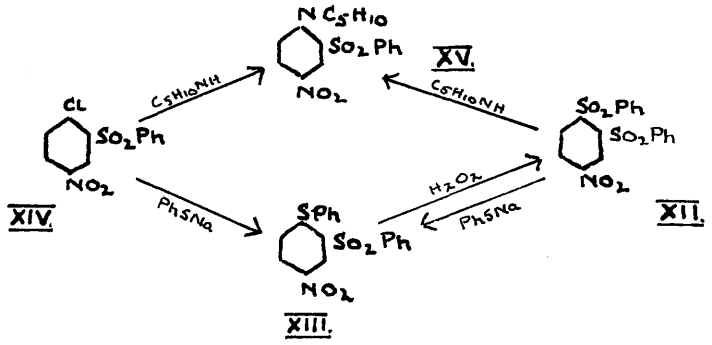
* The analytical data alone are not sufficient to show this. Contrast the behaviour of KCN with 2:4-dinitrochlorobenzene (p. 5 ) and in the following case (16);-



complete series of reactions may be represented as follows:-




The isomeric o-disulphonyl compound XII, prepared from 2-chloro-4-nitrodiphenylsulphone, was quite distinct from X and likewise gave a distinct replacement product XV with piperidine.



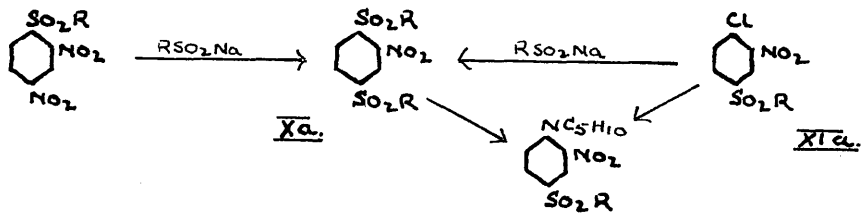

It was stated in the Introduction that systems in which a substituent chlorine atom was simultaneously activated by nitro and by a second cationoid group, had already received attention from numerous investigators. The /

The chloronitrosulphones XI and XIV come into this category and their pronounced reactivity, expressed in the high degree of chlorine mobility which they displayed, is in harmony with general experience in such cases [for $-SO_2R$ replaced by COOH cf. (17), by $SO_3H$ (18), by CN (19), by $-COCH_3$ and -COPh (20)]. It was noticeable, however, that XI was much more reactive towards sulphinates than was XIV — indeed the most satisfactory preparation of the o-disulphonyl compound XII was found in oxidation of the sulphide XIII. The sulphide itself and the piperidino compound XV were, on the other hand, very rapidly produced from XIV by reaction with the appropriate reagent. Borsche has expressed the view (20) that in isomeric pairs similar to XI : XIV the isomer nitrated ortho to the halogen is the more reactive. In the particular case of reaction with sulphinates these chloronitrosulphones therefore conform to Borsche's rule, but the rule is not generally acceptable since external conditions — especially the nature of reagents — exert a profound influence on the reactivity of the individual isomers. Moreover Baudet has shown (19) by quantitative measurements that of 2:4- and 4:2- nitrocyanochlorobenzenes it is definitely the para-nitrated isomer which reacts the more /

more readily with sodium alkyloxides.

Finally, it may be noted that these activating combinations of cationoid groups can not only confer mobility upon halogen substituents but also upon sulphonyl groups, as is shown by the reactions of the two disulphonylnitrobenzenes X and XII.

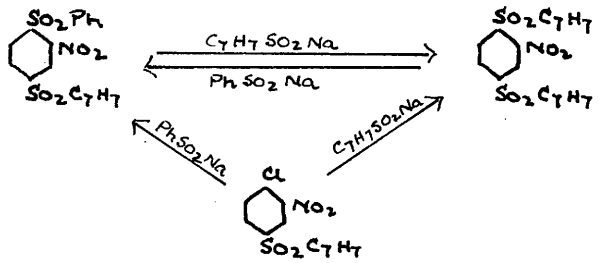
The replacement of the p- nitro group by the action of sodium benzenesulphinate on 2:4-dinitrodiphenylsulphone, resulting in the production of 2:5 bis phenylsulphonyl-nitrobenzene (X p.28), is a reaction of great interest. Further investigation showed that, within limits, it was capable of extension to other cases.




With sulphinate and sulphone derived from toluene (R=p-tolyl) the production of Xa and its synthesis from XIa followed exactly the lines described in detail for the bis-phenyl-sulphonylnitrobenzene X, and analogous products were obtained from its interaction with ammonia, piperidine, sodium hydroxide and sodium methoxide. Similarly the production and synthesis of Xa for the case R = p-chlorophenyl were equally /

equally successful but, with sulphinates and sulphones derived from the strongest sulphinic acids viz. R = 2:5-dichlorophenyl and R = 3-nitrophenyl, no reaction occurred — the corresponding dinitrodiphenylsulphone derivative employed as starting material being recovered unchanged — and, when more intense conditions were employed, complete destruction of the materials resulted. These observations show that the replacing power of the sulphinates (cf. pp. 13 and 26 ) is a controlling factor in the formation of 2:5-diarylsulphonylnitrobenzenes from 2:4-dinitrodiphenylsulphones.

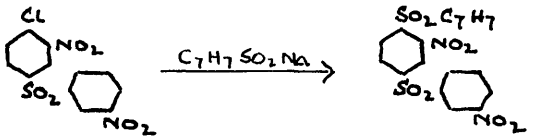
The capacity of the sulphonyl group in 2:4-dinitrodiphenylsulphones to undergo exchange in reaction with sulphinates was also observable though to a lesser extent in 2:5-diarylsulphonylnitrobenzenes.




The diagram shows the relationships established in one particular case from which it is evident that only the sulphonyl group ortho to the nitro group is affected.

The /

The possibility of sulphonyl exchange also arises in connection with the other, though less mobile sulphonyl group. In order to test this possibility the action of sodium p-toluene-sulphinate on the disulphonyl compound XVI was investigated.

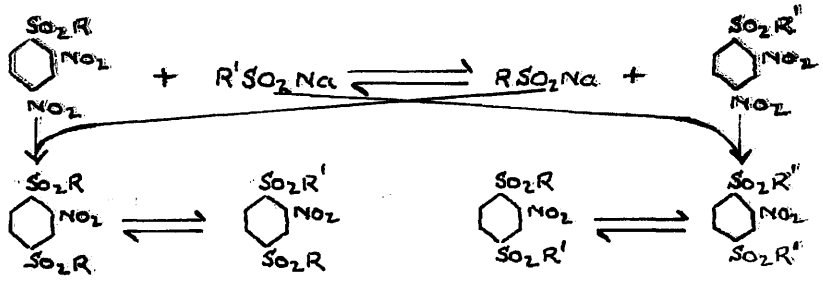



XVII. XVI.

The compound was obtained by the action of the sulphinate on the sulphone XVII (p. 16) in warm aqueous alcohol and was selected for study because the high replaceability of the m-nitrobenzenesulphonyl group (cf. p. 26) should favour the exchange in question. Nevertheless the continued action of the sulphinate on XVI even under extreme conditions yielded no trace of 2:5-di-p-tolylsulphonylnitrobenzene. The conclusion may, therefore, be drawn that in these 2:5-diaryl-sulphonylnitrobenzenes the sulphonyl group in the 5-position possesses practically no mobility towards sulphinate reagents.

To conclude this chapter the following scheme may be appended to show how the results obtained illuminate the /

the complexity of reactions which may arise from the action of a sulphinate on a 2:4-dinitro-diphenylsulphone:-



It may be added that reduction processes were apparent in several of the stages but were not investigated.

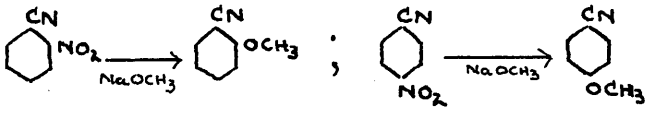
## Chapter III.

## The Reactions of 4-Chloro-2-nitro- and 2 Chloro-4-nitro-diphenylsulphone Types.

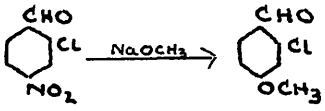
One very significant feature emerges from the reactions of 2:4-dinitrodiphenylsulphones examined in the preceding section. The reactivity of these compounds generally finds expression in replacement of the sulphonyl group, but when the reagent is so selected that this replacement results in reconstitution of an identical molecule i.e. when a sulphinate corresponding to the sulphonyl substituent is employed, a new centre of reactivity appears and the nitro group situated *para* to the sulphonyl undergoes replacement. It may be imagined that a virtual immobility is conferred upon the sulphonyl group which, in consequence, is able to exert its own activating influence and take advantage of the reactive state of the nucleus arising from the presence of nitro substituents. Moreover, the replaceability of a nitro group is very great and it has been shown (p.14) that sulphinates can replace it.

This interpretation of the reaction suggests that in nitrobenzene derivatives containing a second cationoid group the centres of reactivity will not always be found in the *o*:*p* positions /

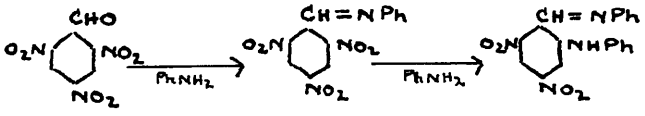
positions to the nitro group, its pre-eminence as an activating agent notwithstanding. An apparent transference of activation control from the nitro to the second cationoid group may be expected where these two groups occupy ortho or para positions to each other (and hence compete in directing activation at different centres) and when the second cationoid group, by reason of its own nature or as a result of superimposed circumstances, is itself not readily replaced under the influence of the nitro group. Although the lack of experimental data makes a general survey impossible, certain incidental observations recorded in the literature afford some confirmation of this view. The reactions in question are depicted here:-



(21)

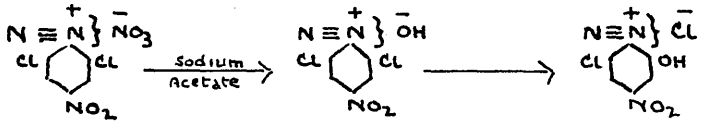


(22)



(23)

It will be seen that in each of these cases a nitro group has been replaced and that the second cationoid group is of such a nature that it does not readily form an anion and hence resists replacement. Although it has never been shown that "onium" substituents may induce anion mobility in the benzene ring (as for example in o- or p- chloro-aniline salts), nevertheless their ordinary meta- directing character classifies them with cationoid groups. It is, therefore, relevant to this thesis to note the frequent occurrence of anion exchange in benzene diazonium salts containing so-called "negative" (i.e. cationoid) substituents in the nucleus (24) and an example relating to the topic at present under discussion may be cited.*




(25)

One further example deserves consideration from this point of view. Nisbet and Goodlet (26) have recently found that in the reaction between piperidine and 1-chloro-4-nitro-acridone the nitro group, instead of activating the halogen atom /

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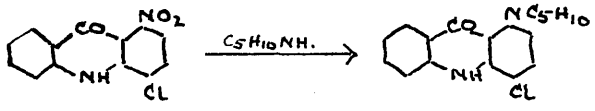
* The mechanism applied to this particular example, is the mechanism suggested by Orton (J.1903, 83, 797) and the one generally accepted in similar cases. The ultimate product is the "diazo-oxide."

atom and facilitating its replacement is itself replaced. The authors conclude that the reactivity of the molecule is preferentially directed towards removal of the heterogeneous polarity caused by the juxtaposition of two cationoid groups.




Now from the argument developed above, the replacement of the nitro group in the unchlorinated nitro-acridone would be anticipated and its replacement in preference to chlorine in the example quoted is more profitably correlated* with the presence of the amino group. Since the opposing effects of the nitro and amino groups are chiefly manifested in the respective ortho and para positions, it is clear that some neutralisation of these effects (at least in so far as they have permanence) must occur at $C_1$ with consequent reduction of chlorine mobility in 1-chloro-4-nitroacridone.

It has already been noted that the sulphonyl group in 2:4-dinitrodiphenylsulphones has a pronounced general mobility. This mobility, however, is not generally so great as that of a halogen atom similarly activated; moreover, it /

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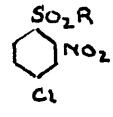
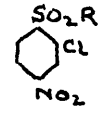
* The "removal of heterogeneous polarity" view does not accomodate the facts described on p. 39.

it is not solely dependent on active influences within the molecule but varies with the reagent employed (cf. pp. 23 - 24). Considerable reduction of the internal forces activating the sulphonyl must occur when a chlorine atom is substituted for either of the nitro groups yet, in the resulting molecule, the presence of three potential anions is still maintained. The next stage in the investigation was therefore the study of chloronitrodiphenylsulphones of types C and D.

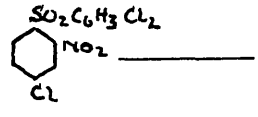


(C.)

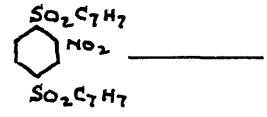


(D.)

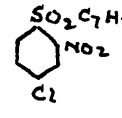
The capacity to exchange sulphonyl groups in sulphones of type C was very markedly diminished — indeed it was not established. For instance, with sodium p-toluene-sulphinate, whose replacing power is great (p.26 ), and the 2:5-dichlorophenyl derivative of C (viz. XVIII) in which maximum sulphonyl mobility should occur (ibidem), no reaction was observed under increasingly drastic conditions until finally, in boiling ethylene glycol with a slight excess of sulphinate, 2:5-di-p-tolylsulphonylnitrobenzene XIX was isolated.



XVIII.



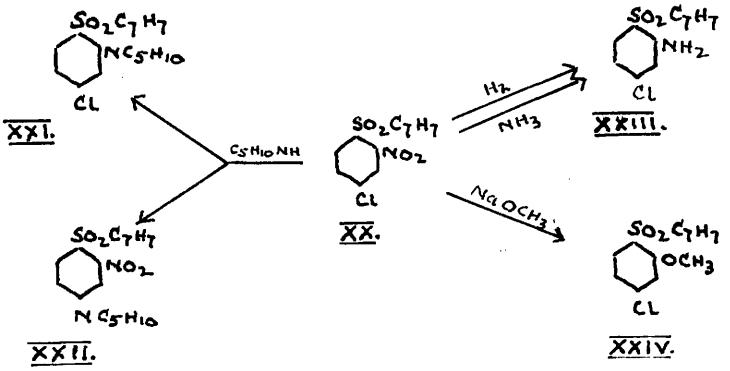
XIX.



XX.

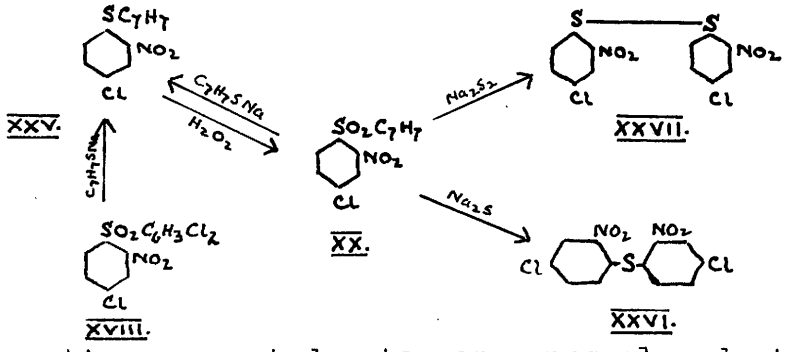
The evidence does not determine whether in the reaction with XVIII sulphonyl exchange precedes or is subsequent to replacement of chlorine. It is noteworthy, however, that formation of the disulphonyl XIX by the action of sodium p-toluenesulphinate on the p-tolylsulphone XX was found to occur under the same conditions and qualitatively with similar readiness as its formation from p-tolyl-2:4-dinitrophenyl-sulphone. This fact renders practical demonstration of sulphonyl exchange in compounds of type C exceedingly difficult in view of the experimental conditions required.

4-Chloro-2-nitrophenyl p-tolylsulphone XX was employed in reaction with certain other reagents and the results show in a most remarkable way the relative stability of the sulphonyl group combined with high reactivity in other centres in the molecule. With piperidine, a few minutes heating sufficed to complete the reaction which gave rise to two products XXI and XXII respectively formed by replacement of the nitro group and chlorine atom.



Methyl alcoholic ammonia effected replacement of the nitro group, the isolated amine XXIII being identical with the product of reduction. The nitro group was also replaced by methoxyl, XXIV, with sodium methoxide as reagent. It is possible that in all these replacement reactions more than one centre was simultaneously attacked — indeed the production of chloride and nitrite ions was generally observed — but only the products indicated could be isolated and it is certain that these were formed by far the most abundantly.

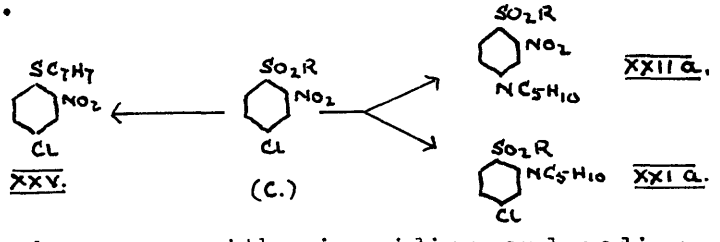
Experiments with another set of reagents, however, provide a striking contrast to the above results. When reagents of sulphide character were employed only the sulphonyl group underwent replacement. For example, XX rapidly reacted with p-thiocresol in alcoholic solution and in presence of alkali to yield the thioether XXV from which, by oxidation, it had been prepared (p.19 ).




This reaction was not due to some unusual reduction of the sulphone /

sulphone group for with p-tolyl mercaptide the same product XXV was formed from XVIII. Moreover sodium sulphide and sodium disulphide reacted with XX in a similar way, the sulphonyl group being replaced and the respective products, the sulphide XXVI and the disulphide XXVII, being identical with the known products obtained from 2:5-dichloronitrobenzene and these reagents (27).

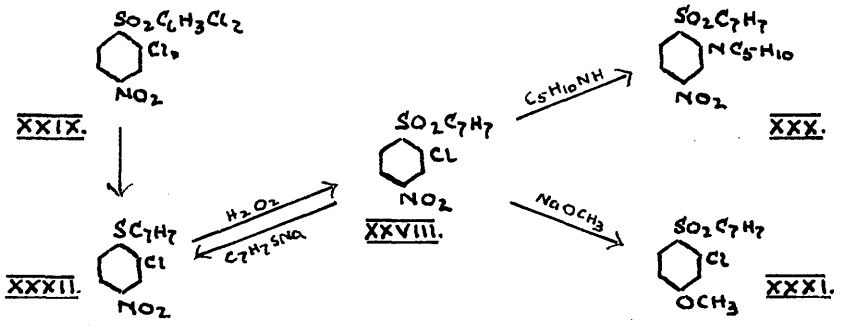
It seemed possible that alteration in the nature of the sulphonyl group itself might effect a change in the locus of reaction with a given reagent. For this purpose and on the basis of the results previously obtained (p. 26 ) the methyl sulphone ($\underline{\bar{C}}$ : R = $CH_3$) and the 2:5-dichlorophenylsulphone ($\underline{\bar{C}}$ : R = $C_6H_3Cl_2$) were selected as representing respectively the available extremes of sulphonyl stability and mobility.




In each case, however, with piperidine and sodium p-tolylmercaptide as reagents the replacements effected corresponded both in nature and qualitatively also in extent with those found for the p-tolylsulphone (C : R = $C_7H_7$. i.e. XX).

When /

When sulphones of the isomeric type D (e.g. XXVIII) were examined essentially similar results were obtained though differences emerged in points of detail. By the action of sodium p-toluenesulphinate on XXIX no sulphonyl exchange could be detected nor, indeed, could any di-sulphonyl derivatives be identified* either from XXVIII or from XXIX.




Only one piperidino derivative XXX was obtained from the interaction of XXVIII and piperidine, the chlorine atom having been replaced. The nitro group, on the other hand, was replaced in the reaction between XXVIII and methyl alcoholic sodium methoxide and the methyl ether XXXI so obtained was also formed, instead of an amine, when XXVIII was treated with methyl alcoholic ammonia. The resistance offered by this chloronitrosulphone to attack by ammonia is in contrast to the amine formation achieved with its isomer /

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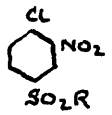
* Very small quantities of high melting products were occasionally obtained and these reactions require further investigation.

isomer (XX. p.39) and is further shown by recovery of the compound unchanged from boiling acetamide (procedure, cf. Kym, Ber., 1899, 32, 3539). The reaction with the sodium salt of p-thiocresol was analogous to that found in the isomeric sulphones (i.e. XX) both XXVIII and XXIX yielding the sulphide XXXII.

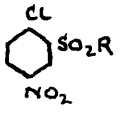
The remarkable fact is thus disclosed that any one of the three potential anions present in 4-chloro-2-nitro- or in 2-chloro-4-nitro-diphenylsulphone may preferentially be replaced according to the reagent selected. This must be attributed to some selective capacity in the reagent and is a striking demonstration of the important rôle played by the reagent in determining the reactivity of a cationoid system. How this selectivity is given effect — whether through the operation of a diversity of reaction mechanisms or through preferential energy exchanges in similarly constituted intermediates — must remain a problem for future research. Meanwhile the incidence of a powerful reagent factor may be recognised and, in the above reactions, a provisional distinction may be drawn between those reagents towards which the sulphonyl group has proved stable and the mercaptides and sulphides by which it has been replaced.

Now /

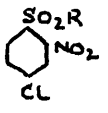
Now in the various reactions of these chloronitro-sulphones C and D, the general degree of reactivity displayed is very great and is comparable with that found in the isomers A and B wherein the o-p directive influences exerted by the nitro and sulphonyl groups co-operate at a common centre.



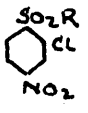
(A.)



(B.)



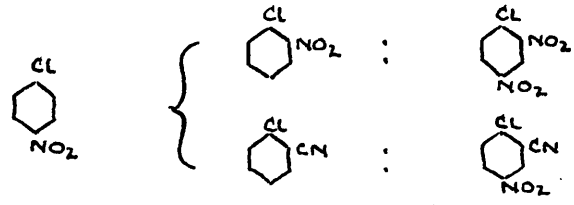
(C.)



(D.)

The reactivity shown in the reactions depicted on page 35 is also noticeably high and the facts therefore suggest that the activating and directive effects of cationoid groups need not be cumulative in order to produce a marked degree of anion mobility. The reactions of C and D in which the sulphonyl group survives, further illustrate the suggestion made on page 34 , viz. that an individually weak cationoid group ($-SO_2R$, CN, CHO etc.) may utilise nuclear activation proceeding from a nitro group to facilitate the operation of its own directive capacity. Activating effects are thus regarded as exerted on the nucleus and as finding their consummation in directive influences. The case of 1:3:5-trinitrobenzene (p. 5 ) may be cited in illustration /

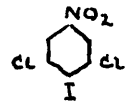
illustration of a cationoid system lacking a directive influence to translate activation into vigorous reactivity, and when this influence is supplied (cf. 2:4:6-trinitrobenzylideneaniline p. 35 ), pronounced reactivity results. Quantitative data recorded by Baudet (19) for the reactivity of 2-cyano-4-nitro-chlorobenzene may be adduced in support of these views in their application to a system in which directive influences are cumulative. It is known from various sources that the mobility of chlorine in o and in p-chloronitrobenzenes is overwhelmingly greater than in o-chlorocyanobenzene where, indeed, it is scarcely perceptible.



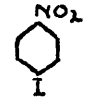
Nevertheless, with sodium methoxide as reagent 2:4 dinitrochlorobenzene reacts only between 5 and 6 times faster than 2-cyano-4-nitrochlorobenzene whose reactivity, incidentally, is about 7,500 times greater than that of p-chloronitrobenzene. Apparently, therefore, the cyano group in nitrocyanochlorobenzene finds itself in an environment in which, relatively, it can exert its influence to a far great extent than in the un-nitrated compound.

The /

The researches of Holleman and his co-workers have shown that an increase in general reactivity results from introducing a chlorine atom into the cationoid system formed by chloronitrobenzenes and by dinitrobenzenes. The compounds in question may be arranged in the following increasing order of reactivity (8):- Chloronitro- < dichloronitro- < dinitro- < dinitrochloro- benzenes. Chlorine is not, however, a true cationoid group for, although in common with cationoid groups it reduces the intrinsic anionoid reactivity of a phenyl nucleus (cf. p.15 ) and hence may be said to facilitate cationoid reactivity, it nevertheless retains its o:p-directing anionoid character.* While, therefore, its net effect on a cationoid system may be an increased general reactivity, that increased reactivity should be least pronounced in the positions situated ortho and para to the chlorine atom since it is in these positions (principally) that its anionoid characteristics will be displayed. Consequently the increased reactivity of XXXII compared with XXXIII (28) and of XXXIV compared with XXXV (8)




XXXII.




XXXIII.

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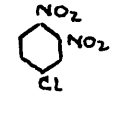
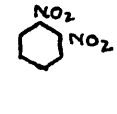



XXXIV.




XXXV.

is /

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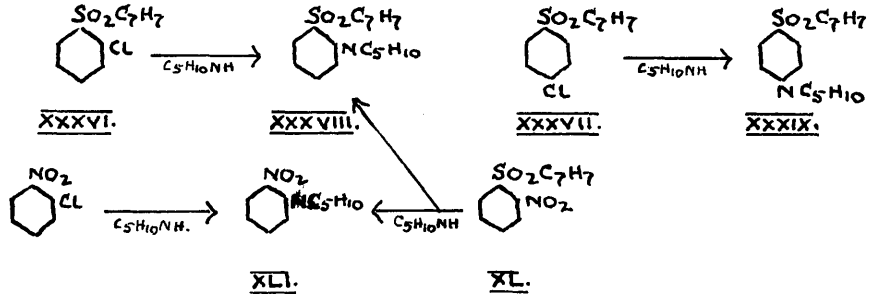
* i.e. Chlorobenzene (unlike nitrobenzene for example) is substituted (nitrated sulphonated etc.) in the op positions.

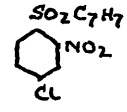
is attributed in each case to the directive power of the nitro group facilitated by the increased nuclear activation due to the presence of the chlorine atoms, whilst the preferential replacement (cf. p. 20 ) of the nitro group meta to chlorine in XXXIV illustrates the relative stabilising effect of chlorine on a p- substituent. On the basis of Flurscheim's theory of alternating affinity distribution, Kenner (29) regards the mobility of the m-nitro group in XXIV as the result of the loosening effect of an op directing (i.e. anionoid) group on a meta-substituent. This view, however, fails to recognise the unique character of halogen cf. later p. 49 ).

The considerations advanced in the preceding paragraphs indicate that in 2-chloro-4-nitro- and in 2-nitro-4-chlorophenyl p-toluenesulphones each of the substituents ($RSO_2$, Cl, $NO_2$) contributes to the general reactivity of the molecules, and, in fact, these chloronitro sulphones were found to be decidely more reactive than o- and p- chlorophenyl- or o- and p- nitrophenyl p-tolylsulphones. o-Chlorophenyl p-tolylsulphone XXXVI was obtained from the corresponding nitrosulphone by reduction followed by a Sandmeyer reaction. The p-isomer XXXVII was prepared by the Friedel-Crafts process from /

from chlorobenzene and p-toluenesulphonyl chloride. Each isomer reacted slowly with piperidine yielding the piperidino derivatives XXXVIII and XXXIX, the reactions requiring a longer time and more intense conditions than were necessary for similar reactions with o- and p- chloronitrobenzenes.




With piperidine, p-nitrophenyl p-tolylsulphone reacted very slowly with formation of tarry products which could not be purified. The reaction with the o-isomer XL however, was comparatively free from tar formation and two products, the piperidino-sulphone XXXVIII and o-nitro-piperidino-benzene XLI, were isolated. This concurrent replacement of the nitro and sulphonyl groups by piperidine raises the question why in a similar reaction with XX (p.39), the sulphonyl group has survived.

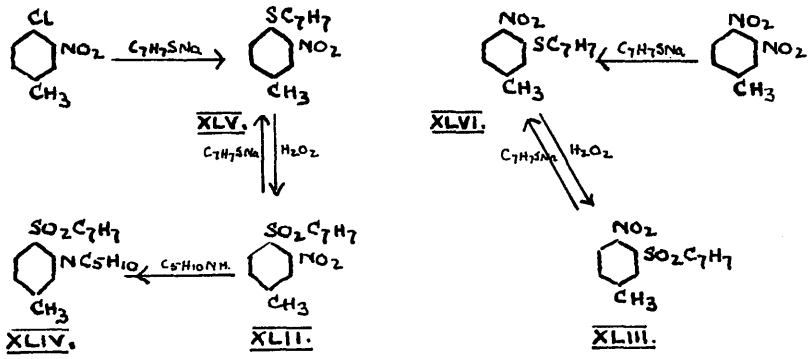


XX.

A partial answer may again be found in the effect of the chlorine atom present whereby, as in 3:4-dinitrochlorobenzene, a relative stabilisation of the p- substituent occurs.

As /

As has already been said the twofold effect of a sutstituent chlorine atom is peculiar to the halogens. If, instead of chlorine in XX, a true anionoid substituent (e.g. $CH_3$) were present, there should occur a general reduction of cationoid reactivity, the reduction being especially pronounced in the op-positions to that substituent. The sulphones XLII and XLIII were prepared by the reactions indicated and examined as test cases.




So markedly less was the reactivity found in these cases when compared with XX, that a fortyfold increase in the duration of reaction with piperidine resulted in recovery of fully 90°/$_o$ of XLIII unchanged whilst, under similar conditions, a slow and also very incomplete reaction with XLII yielded the piperidino-sulphone XLIV as the only product capable of isolation. To some extent, these qualitative results justify the views expressed but it will be noted that the relative /

relative op-retarding effect attributed to chlorine is not evident with mercaptide reagents in the chloronitrosulphones XX and XXVIII (pp.40 and 42), that it is less pronounced than with other reagents in the case of 3:4-dinitrochlorobenzene* (p.20) and correspondingly, in the reactions between XLII and XLIII and sodium p-tolyl mercaptide no discriminating effect could be referred to the methyl group since in both cases the respective sulphides XLV and XLVI were fairly rapidly regenerated.

The uncorrelated influence of the reagent occasions one further comment. The most marked discrepancies encountered in chloronitrosulphone reactivity have arisen from the contrast between reagents of the "sulphide" type on the one hand, and those of certain "oxide" or "amine" types on the other, and, as a whole, the results clearly show that mobility in nitrosulphones is not confined to the sulphonyl group. Now, Smiles and his colleagues (30) have investigated in an extensive series of researches the behaviour in alkaline media /

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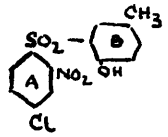
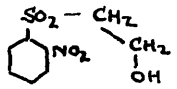
* The action of p-tolyl mercaptide on 3:4 dinitrotoluene (p.49) also gave a mixture in which the sulphide XLVI predominated.

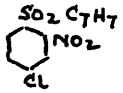
media of o-nitro-o -oxydiphenylsulphones e.g. XLVII.



XLVII.



XLVIII.

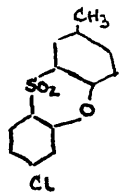


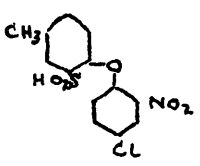
XX.

It is apparent in these compounds that the molecule carries its own reagent in the phenolic group of nucleus B. Modifications of the reactivity of the systems have been effected by varied substitution in the nuclei A and B and the hydroxyl group in B has been given an alcoholic character as in XLVIII, or has been replaced formally by $-NH_2$, $-NHCH_3$ etc.

These internal reagents are all of the "oxide" and "amine" types and, by analogy with the intermolecular reactions of XX (p.39) supplemented by the intrinsic suitability of the molecular structures, might be expected to react with elimination of sodium nitrite (in presence of alkali) and formation of ring products (e.g. XLIX, thioxin type). In practice however, the facile reaction in all cases consists in an isomeric change (e.g. XLVII⟶L) involving intramolecular replacement of the sulphonyl group.

XLIX.





L.

This contrast between inter- and intramolecular replacements strongly suggests the operation of some modifying influence upon the so-called reagent factor and may eventually provide a clue for interpreting the nature of this factor and the manner in which its effects are produced.

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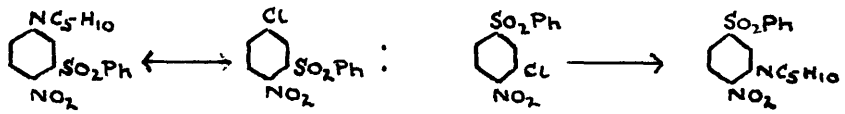
## Chapter IV.

## The Reactions of 3-Chloro-4-nitro and 5-Chloro-2-nitro-diphenylsulphones.

In the chloronitrosulphones described in this section the directive influences of the nitro and sulphonyl groups are again in competition with each other but there is an important difference between these and the isomeric sulphones which formed the main topic of discussion in the preceding chapter. This difference consists in the fact that here the chlorine as well as the sulphonyl group is subject to the activating and directive influence of the nitro group. Consequently if for any reason the effect of the nitro group is frustrated at one centre it may still operate at the other, and directive control in the molecule will, therefore, pass less frequently to the sulphonyl group. It follows that the chief interest in the present compounds lies in comparison of the groups replaced (i.e. the respective centres attacked) by different reagents. Unfortunately 3-chloro-4-nitro-diphenylsulphone is not only the sole representative of its type at present available but it is also rather inaccessible, and the comparison between it and 2-nitro-5-chlorodiphenylsulphone has of necessity been restricted to the reactions with a few selected /

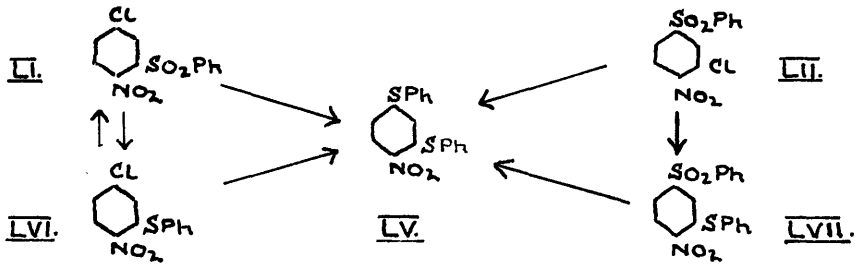
selected reagents.




LIII. LI. LII. LIV.

By reaction with piperidine each sulphone LI and LII, yielded only a monopiperidino derivative LIII and LIV respectively, the chlorine atom in both cases having been replaced and these replacements were more rapid than with o- or p- chloronitrobenzenes. A similar preference to replace chlorine rather than a sulphonyl group has been displayed by piperidine in all the reactions previously noted (pp. 23 , 39 and 42 ). To a lesser extent also this preference has included the nitro group (pp. 39 and 49 ) and, generally, the results suggest that towards this reagent a sulphonyl group is relatively stable. A striking contrast again emerged when the sulphones LI and LII were brought into reaction with a mercaptide. When sufficient thiophenol (and aqueous alcoholic sodium hydroxide) was employed a twofold replacement occurred, and same bis-thioether LV being formed from each isomer. This product was also obtained in a similar way directly from 3:4-dinitrochloro-benzene /

benzene - the source of the monothioether LVI (cf. p. 20 ).

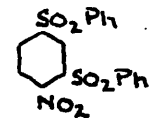



With the reactants in molecular proportions, however, a very important distinction emerged, for whereas LI underwent replacement of the sulphonyl group with regeneration of the sulphide LVI, the chlorine atom of LII was replaced and phenylthionitro-diphenylsulphone LVII was produced. The constitution of the last product follows from its analysis, its further reaction with mercaptide to yield LV and its oxidation to the disulphone LVIII (cf. below).

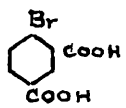
The reaction LII ⟶ LVII constitutes the first example of a sulphonyl group surviving reaction with a mercaptide when situated ortho or para to a nitro group. The result repudiates any hypothesis involving a specific interaction between sulphonyl substituent and "sulphide" reagent. The sole remaining consistency with regard to mercaptide reagents is contained in the observation that they replace, very rapidly, substituents rendered mobile by the influence of a nitro group. Mercaptides as reagents for cationoid reactivity have received very little attention, and in view of the obvious complexity of the topic it would be premature to /

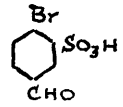
to press the observation further.

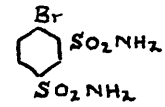
Oxidation of the 2:4-bis-phenylthio-nitrobenzene LV yielded the corresponding disulphone LVIII. In this compound each sulphonyl group is directly influenced by the nitro group whilst the latter is itself affected by the combined activating and directive influences of the two sulphonyl groups. Now although the cationoid effect of a single sulphonyl group in a phenyl nucleus is slight (in comparison with nitro) yet by analogy with similar cases examined by Schöpff and his co-workers (31), it is to be anticipated that the combined effects of two such groups situated meta to each other will be considerable (even when the potential anion to be rendered mobile is halogen and not nitro). For instance, it is known that halogen mobility is pronounced in the following compounds:-



LVIII.



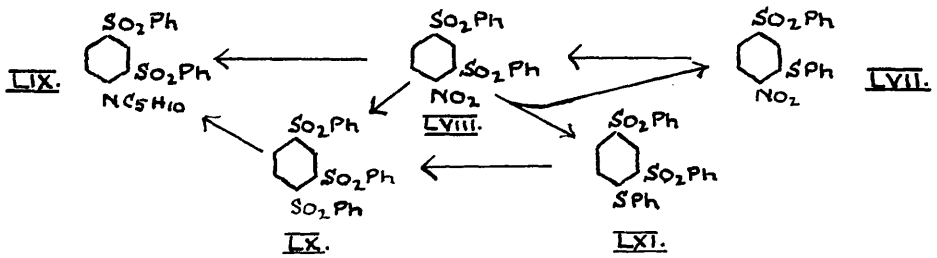





These facts, and others discussed on page 45 , strongly suggest that the development of cationoid reactivity in a benzene system becomes progressively easier with each added stimulus (cationoid group) after the initial resistance offered by the intrinsic anionoid character of the nucleus has been overcome.

The /

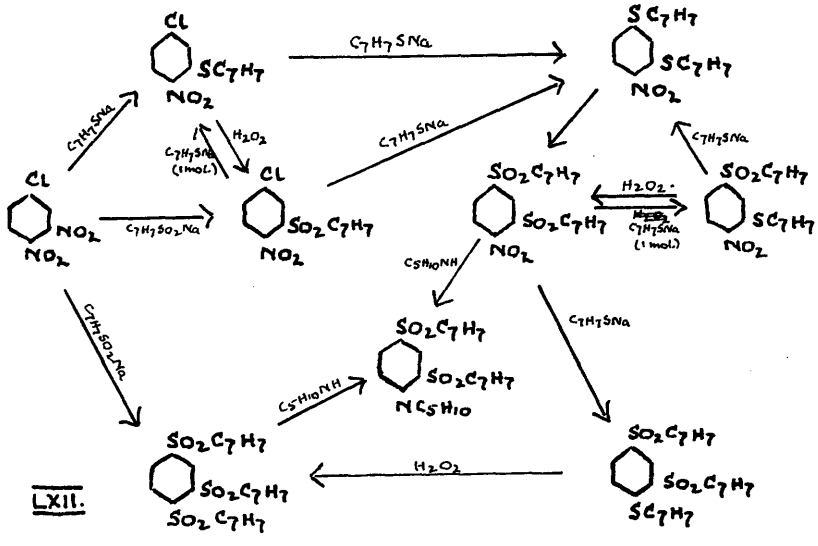
The analogy supplied by the activity of the disulphonamide example is sufficient warrant for the expectation of nitro mobility in 2:4-bis-phenylsulphonylnitrobenzene LVIII, and in practice this was demonstrated by replacement of the nitro group in reaction with piperidine LVIII→ LIX. Similarly by the action of sodium benzene sulphinate a trisulphone LX was formed and this compound also reacted with piperidine to give the piperidino product LIX.




When LVIII was treated with the sodium salt of thiophenol in aqueous alcoholic dioxan, two products were formed. One was identified as the phenylthionitro-diphenylsulphone LVII already encountered, whilst the other was nitrogen-free and, by oxidation to the trisulphone, was proved to be 2:4-bis-phenylsulphonyl-diphenylsulphide LXI. This partial replacement of the sulphonyl group once again illustrates the readiness with which mercaptides replace substituents activated by a nitro group.

Consideration of these results suggests the possibility of preparing the trisulphone directly from 3:4dinitrochloro-benzene /

benzene and sodium benzene sulphinate. In practice, however, the mixture of sulphones produced proved unexpectedly difficult to separate. On the other hand with sodium p-toluenesulphinate as reagent, 1:2:4-tri-p-tolylsulphonylbenzene LXII and 5-chloro-2-nitrophenyl p-tolylsulphone were isolated from the reaction mixture, so that the success of the reaction in the phenyl series would appear only to await the discovery of the most suitable reaction conditions. Since in the p-tolyl series the sulphones in all other respects closely resembled those derived from 5-chloro-2-nitrodiphenylsulphone, their reactions may be summarised without further comment in the following scheme:-




The /

The importance of the results obtained in this section consists in the demonstrated fact that two dissimilar potential anions (Cl and $SO_2R$) simultaneously subject to the influence of a nitro group, are dependent for the degree of mobility which they display not only on their positions relative to the nitro group (i.e. whether o or p to it) but also, in some uncorrelated way, on the nature of the reagent employed. The effect attributed to the reagent is apparently collateral with the character of the group (or groups) to be replaced for the accumulated evidence points to a resistance offered by the sulphonyl group to attack by piperidine but not offered, or not sustained in reactions with mercaptide. In this connection it is worthy of note that both piperidine (32) and sodium phenyl mercaptide (33) react more rapidly with o-chloro-nitrobenzene than with p-chloronitrobenzene.

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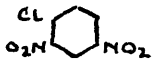
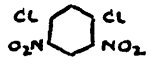
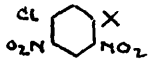
## Chapter V.

### The Reactions of Sulphones derived from 1:5-Dichloro-2:4-dinitrobenzene.

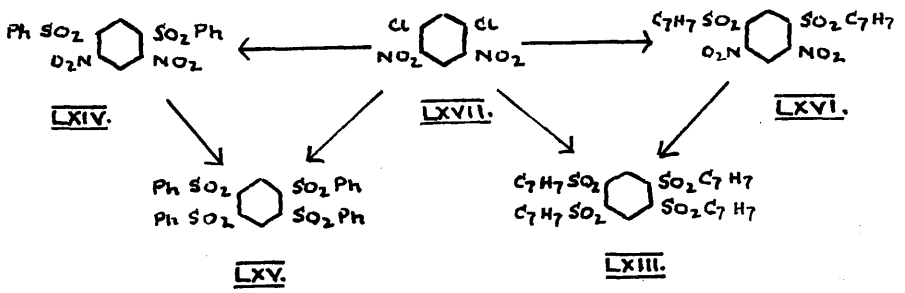
The 1:5-dichloro-2:4-dinitrobenzene structure may be regarded as a condensed duplication of the 2:4-dinitrochlorobenzene system, each chlorine atom being subject to the influence of an ortho and of a para nitro group.

The opportunity therefore arises to utilise the replaceability of the first chlorine atom in order to compare the halogen mobility in the derivative, with that of 2:4-dinitrochlorobenzene itself. In particular, it is the special province of the present investigation to ascertain how replacement of the first chlorine atom (a) by a sulphonyl (cationoid) group, and (b) by an anionoid group, affects the reactivity of the molecule both as a whole and as it is expressed in the mobility of the residual chlorine atom.

In the first place it is essential to note that the general reactivity of 1:5-dichloro-2:4-dinitrobenzene is greater than that of 2:4-dinitrochlorobenzene, as is shown by the quantitative measurements of Holleman and Hollander (8). Accordingly /

Accordingly, if this increased reactivity is maintained towards sulphinate reagents and if, as the results in previous chapters indicate, the replacement of one chlorine atom by a sulphonyl group yields a system still more reactive than 2:4-dinitrochlorobenzene, it should at least be a difficult matter to isolate a monosulphonyl derivative, by interaction with sulphinates. In practice, with sodium p-toluenesulphinate, it proved impossible (although mild conditions were used) to isolate pure even a disulphonyl derivative,— indeed gentle refluxing of a solution of the reactants in alcohol for quite a short period yielded a mixture of polysulphones from which the tetrasulphone was isolated. The isolation of this tetrasulphone LXIII, in view of the insoluble nature of the mixture and the slow crystallising power of the products, was best effected by reducing the nitro constituents to amines, removing these with acid and crystallising the residue.

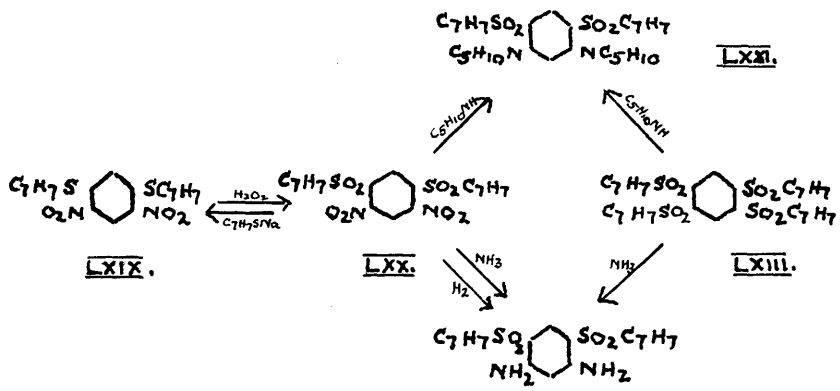


The smaller replacing power of sodium benzenesulphinate permitted isolation of the diphenylsulphone LXIV under the same reaction conditions, the tetraphenylsulphone LXV being formed to any great extent only at somewhat higher temperatures. Finally advantage was taken of the low replacing power of free sulphinic acids to prepare the di-sulphone LXVI directly by reacting on LXVII with p-toluene sulphinic acid.

The formation of these tetra-sulphones has features in common with the formation of 2:5-bis-arylsulphonylnitro-benzenes ultimately from 2:4-dinitrochlorobenzene (p. 28) and with the formation of 1:2:4-tri-p-tolylsulphonylbenzene from 3:4-dinitrochlorobenzene (p. 58). These reactions all illustrate the sustained reactivity of a cationoid system in reaction with sulphinates.

In contrast with the reaction of sulphinates and in harmony with the anionoid character of the introduced arylthio group, both mono- and di- thioethers, LXVIII and LXIX, were obtained by the action of mercaptide on LXVII though again the reaction was so rapid that both products were formed even with molecular proportions of mercaptide. 1:5-Di-p-tolylthio-2:4-dinitrobenzene LXIX on oxidation yielded the di-sulphonyl compound LXX and was regenerated from /

from this sulphone by reaction with mercaptide (2 mols). It will be recalled that the nitro group was partially replaced in the corresponding reaction with 2:4-di-p-tolylsulphonyl-nitrobenzene (p.57 cf. also p. 58).

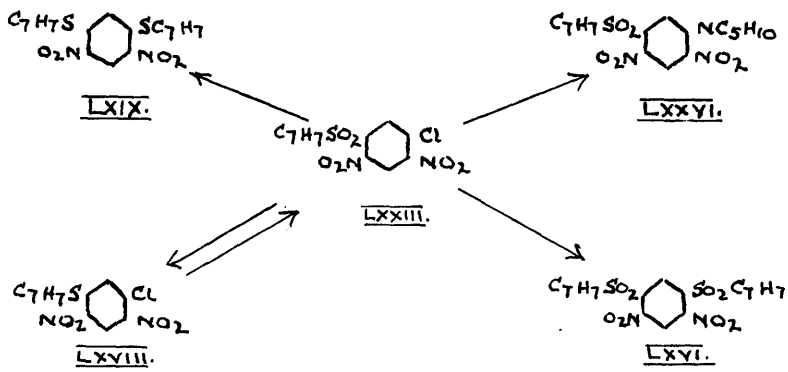


LXIX. LXX. LXXI. LXXII. LXXIII.

Piperidine (in excess) effected replacement of both nitro groups in LXX and the di-piperidino product LXXI was also formed from the tetrasulphone LXIII with this reagent. Likewise, when heated in sealed tubes with methyl alcoholic ammonia, LXX and LXIII each gave the di-sulphonyl-diamine LXXII, identical with the reduction product from LXX.

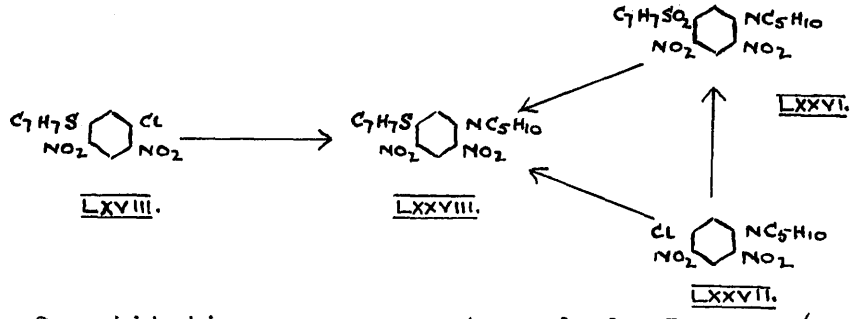
The mono tolylsulphone LXXIII was obtained by oxidation of the mono thioether LXVIII and in reaction with p-tolyl mercaptide this thioether was reformed together with /

with considerable quantities of the bis-thioether LXIX.

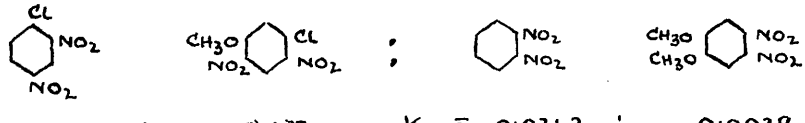



Certain other reactions of this mono-sulphonyl compound are of interest. For example, when heated with an excess of piperidine, the piperidino sulphone LXXVI was the only product which could be isolated. This result at once illustrates the comparative stability of a sulphonyl group to piperidine and the de-activating effect of the piperidino group on the cationoid system present in LXXVI, for it will be observed that the sulphonyl group here has survived the reaction conditions which occasioned its replacement in 2:4-dinitrophenyl p-tolylsulphone (p.22). Moreover 1:5-dichloro-2:4-dinitrobenzene itself forms a di-piperidino derivative with almost explosive violence (17). The piperidino-sulphone was also formed by reaction with sodium p-toluene sulphinate on the piperidino-chloro- compound LXXVII (17) and both LXXVI and LXXVII reacted with p-tolyl mercaptide to yield the tolylthio-piperidino derivative LXXVIII. This last compound /

compound was also produced from LXVIII by reaction with piperidine.




Quantitative measurements made by Lorang (34) show that the introduction of a methoxyl group in the 5- position in 2:4-dinitrochlorobenzene reduces chlorine mobility (towards sodium methoxide) to about one third and, similarly, Parijs (35) has found a marked reduction in nitro mobility in 4:5-dinitroveratrole compared with o-dinitrobenzene (the reaction constants are quoted here with the formulae).

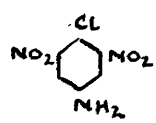


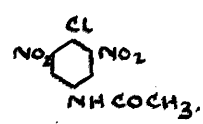
$K_o$ = 0·11 ; 0·037 . $K_{35}$ = 0·0242 ; 0·0029.

Lindemann and Pabst (36) in an investigation of great interest have further shown that the three methyl-2:4-dinitro-1-chlorobenzenes* (i.e. toluenes) are also less reactive than 2:4 /

* The position of the methyl with respect to the nitro groups also appears to be a controlling factor in the reactivity and this aspect of the subject has been carefully studied by Kenner and his collaborators. (37).

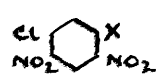
2:4-dinitrochlorobenzene. The reduction of cationoid reactivity due to the anionoid group may be contrasted with the increase in reactivity when the influence of the anionoid group is curtailed or is replaced by an actual cationoid influence. Thus it is significant that in a few recorded cases (38) halogen mobility, suppressed in the parent (chloro-nitro) aniline, has been demonstrated following acetylation (i.e. reduction of the anionoid effect) of the amino group, e.g. -




(non reactive) (reactive)

Again, comparative experiments on 5- substituted 2:4-dinitro-chlorobenzenes viz:-




showed that with p-toluenesulphinic acid as reagent (which requires for reaction a highly reactive second component cf. p. 62) reaction occurred only in the cases x = Cl, and x = $SO_2R$, and not in the cases x = H, SR, or $NC_5H_{10}$.

The /

The general evidence therefore indicates that the mobility of an atom (or group) is dependent not only on the cationoid groups in which, it may be considered, the directive control of the system is vested, but also on the enhanced or diminished cationoid environment occasioned in varying degrees according to the nature of other substituents present in the system.

## Chapter VI.

(Supplementary to Chapter II).

### Sulphonyl Exchange in Thiosulphonic Esters.

The exchange of sulphonyl groups in 2:4-dinitrodiphenylsulphones by the action of sulphinates (p. 24 ) is closely paralleled by the interconversions of 2:4-dinitrophenyl alkylethers (39) which, in turn, is related to the phenomena of alcoholysis (ester dismutation) exhibited by derivatives of carboxylic acids. It is therefore to be anticipated that sulphonyl exchange will be displayed in such compounds as acylsulphones, disulphones and thiolsulphonic esters. That the alkyl or arylthio groups in the last named compounds do provide the requisite centres of cationoid reactivity is indicated by the production of disulphides from these esters in reaction with mercaptides (40)

$$RS\cdot SO_2R + R'SNa \longrightarrow RS\cdot SR' + RSO_2Na.$$

Investigation confirmed the expected sulphonyl exchange in thiolsulphonic esters.* For example in reaction with sulphinates /

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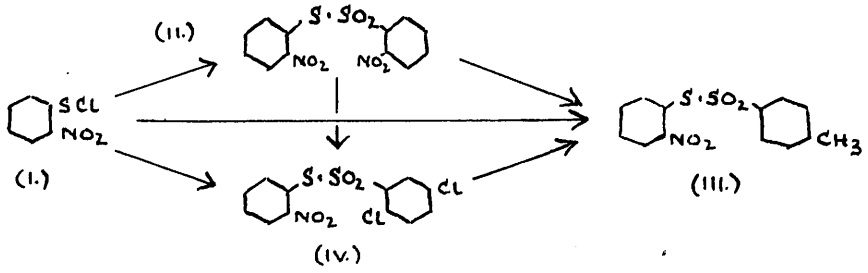
* The experimental data relevant to this investigation are contained in a reprint of the published work supplied with this thesis.

sulphinates the products of the sulphonyl exchanges II ⟶ III, II ⟶ IV, IV ⟶ III, were identical with those synthesised from the chlorothiol I. viz. I ⟶ II, I ⟶ III, I ⟶ IV.




For purposes of comparison with the 2:4-dinitrodiphenylsulphone series and employing the technique there described, an examination was made of the replacing powers of of different sulphinates in reaction with thiolsulphonic esters. The results are summarised in Table II in which, with reference to the following general reaction a successful case of sulphonyl exchange is denoted by (+) and an unsuccessful or restricted exchange by (-).

$$R^{I}S{\cdot}SO_2R^{II} + R^{III}SO_2Na \longrightarrow R^{I}SO_2R^{III} + R^{II}SO_2Na.$$

It will be seen from the table that, approximately, the sulphonyl group corresponding to the weaker sulphinic acid has the higher replacing power and that the sulphinate order is the same as was found in the 2:4dinitrodiphenylsulphone series. Further, the order is not apparently affected by alteration in the nature of the arylthio group (R.S.).

TABLE II.

$R^{I}S\cdot SO_2R^{II} + R^{III}SO_2Na \longrightarrow R^{I}S\cdot SO_2R^{III} + R^{II}SO_2Na$

| $R^{I} = R^{II}$ | $R^{III}$ | | $R^{I}$ | $R^{II}$ | $R^{III}$ | |
|---|---|---|---|---|---|---|
| Phenyl | p-Tolyl | + | Phenyl | p-Tolyl | p-Chloro-phenyl | - |
| p-Tolyl | Phenyl | - | do | do | p-bromo-phenyl | - |
| Benzyl | p-Tolyl | + | Benzyl | do | Phenyl | - |
| p-Chloro-phenyl | do | + | o-Nitro-phenyl | Phenyl | 2:5-Di-chloro-phenyl | - |
| p-Bromo-phenyl | do | + | do | p-Chloro-phenyl | p-tolyl | + |
| 2:5-Di-chloro-phenyl | do | + | do | do | p-Bromo-phenyl | + |
| do | m-Nitro-phenyl | + | do | p-Bromo-phenyl | Phenyl | + |
| do | o-Nitro-phenyl | - | do | do | p-Chloro-phenyl | - |
| o-Nitro-phenyl | phenyl | + | do | 2:5-Di-chloro-phenyl | p-Tolyl | + |
| do | p-Tolyl | + | do | do | Phenyl | + |
| do | p-Chloro-phenyl | + | do | do | p-Chloro-phenyl | + |
| do | p-Bromo-phenyl | + | | | | |
| do | 2:5-Di-chloro-phenyl | | | | | |

Sulphonyl exchange has also been recorded by Gibson in the reactions between thiolsulphonic esters and methylthio-acetonylsulphones conducted in presence of alkali (41).

$$RSO_2CH(SCH_3)\cdot COCH_3 \underset{RSO_2SCH_3}{\overset{R'SO_2SCH_3}{\rightleftharpoons}} R'SO_2CH(SCH_3)\cdot COCH_3$$

Since the thiolsulphonic ester may be replaced by sulphinate as reagent, the order of sulphonyl replacing powers might be expected to coincide with that found in the present investigations. Although the data available permitted a restricted comparison only, a contrast emerged in the failure of alkyl sulphinates to replace arylsulphonyl groups in the acetonylsulphone series (contrast Table I p. 25 ). In collaboration with Dr. Gibson this point was subsequently re-investigated and data of greater precision were obtained by measuring the change of rotation incurred in sulphonyl replacements with an optically active component. The results (published, J.C.S. March 1937) completely confirmed the conclusions already drawn from Tables I and II, and the anomaly mentioned in the acetonylsulphones was traced to hydrolysis of the acetyl group, which prevented sulphonyl exchange and was particularly noticeable with salts of the weaker sulphinic acids as reagents.

A /

A section of these results is quoted here to facilitate comparison with the sulphinate order already given. Table III contains the figures representing the percentage decomposition of methyl camphor-10-thiol-sulphonate V effected by various sodium sulphinates VI, the reaction being carried out with molecular proportions of the reagents in a fixed volume of aqueous alcohol. The values correspond to percentages of the maximum rotation change which would result from complete conversion of the active ester V into the active sulphinate VIII,

$$C_{10}H_{15}O\cdot SO_2\cdot SCH_3 + R\cdot SO_2Na \rightleftharpoons R\cdot SO_2\cdot SCH_3 + C_{10}H_{15}O\cdot SO_2Na$$

V. VI. VII. VIII.

control experiments having shown that the calculation is permissible and that the equilibria were instantaneously established at ordinary temperatures. In two cases (denoted in Table III by reversed arrows) the equilibria were also established by reacting on the inactive ester VII with the active sulphinate, and the concordance between the values suggests that the experimental error in the procedure is of the order of 5°/o.

$C_{10}H_{15}O \cdot SO_2 \cdot SMe + RSO_2Na \rightleftharpoons R \cdot SO_2 \cdot SMe + C_{10}H_{15}O \cdot SO_2Na.$

TABLE III

| R in $RSO_2Na$ | °/° Decomposition | Dissociation Constants for R·COOH ($\times 10^{-5}$) |
|---|---|---|
| n-Pentyl | 99 | 1·45 |
| Ethyl | 80 | 1·34 |
| p-Tolyl | 78 ⇌ 27 | 4·3 |
| p-Acetamido | 70 | 5·17 |
| Phenyl | 68 | 6·6 |
| 4-Methoxy-m-tolyl | 63 ⇌ 39 | |
| p-Fluorophenyl | 54 | 7·39 |
| α-Naphthyl | 53 | 20·4 |
| β-Naphthyl | 43 | 6·8 |
| p-Bromophenyl | 41·5 | 10·8 |
| p-Chlorophenyl | 41 | 9·3 |
| m-Nitrophenyl | 11 | 34·0 |
| o-Nitrophenyl | 2 | 630·0 |
| o-Tolyl | 1 | 12·5 |
| 2:5-Dichlorophenyl | 1 | |

The results show that, as a first approximation, the percentage /

percentage decomposition of the methyl camphor-10-thiol-sulphonate increases with the various sulphinates as the dissociation constants of the corresponding carboxylic acids decreases. It may be remarked that the order of the dissociation constants for the two naphthyl carboxylic acids appears to be ~~in~~ the inverse of that obtained from data given in International Critical Tables for the corresponding sulphonic acids. The actual order of sulphinate replacing power is the same in Tables I, II and III.

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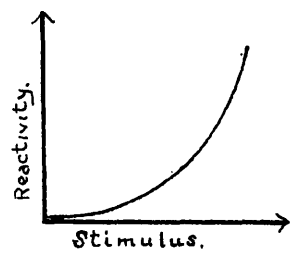
## General Conclusions

Aromatic cationoid reactivity is a phenomenon superimposed upon and contesting with the intrinsic anionoid reactivity of the nucleus (p. 3 ). It is pronounced only when the stimulus provided by a cationoid group is sufficiently powerful to overcome nuclear resistance and it is thereafter developed with increasing facility with each additional stimulus (pp. 56 and 66). A rough graphical representation of these effects is suggested in the accompanying diagram. Nuclear activation is chiefly "directed" by a cationoid group to the ortho and para positions, which are potentially the most reactive cationoid centres and, conversely, nuclear resistance which is increased by the presence of an anionoid group (halogen excepted, p. 46 ), is most pronounced in the o:p- positions with respect to the anionoid group. The activating and directive powers of cationoid groups undoubtedly vary from case to case and, individually, the nitro group is pre-eminently powerful.




These are factors which provide or oppose the provision of cationoid centres in the nucleus.

Reaction /

Reaction at a substituted cationoid centre involves anion exchange and it might be expected that the greater the tendency of the substituent to form an anion, the more readily would reaction take place. To some extent this expectation is fulfilled in sulphonyl exchanges where the competing anions are similar in type, but generally there appears to operate between substituent and reagent an uncorrelated selectivity factor which confuses the issue. Thus a substituent (e.g. $SO_2R$) which is readily replaced in reaction with one reagent (e.g. NaSR) may be sufficiently stable towards a second reagent (e.g. piperidine, pp.23 ,54 and63) to cause the reaction to be transferred to another centre*. The stability of substituents may cause a similar transfer of reaction centre even when there is involved simultaneous transfer of directive control from the stronger to the weaker of two cationoid groups present in the system (p.35). It may therefore arise in a given case that the only demonstrable reactivity is apparently controlled by the weaker directive agent.

These are factors which influence selection of the centre (or centres) /

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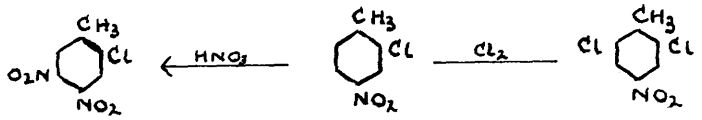
* The replacement of hydrogen in 2:4-dinitrochlorobenzene by reaction with potassium cyanide, compared with the usual chlorine replacement, is another case in point (cf. p. 5 ).

(or centres) involved in a reaction. Both sets of factors are regarded as contributory in the degree of mobility displayed.

In formulating these conclusions it is not suggested that the factors mentioned exhaust the influences governing aromatic cationoid reactivity. The present work has no claim to be a comprehensive examination of the general subject — it is exploratory, and its results show that the subject is neither simple nor even moderately developed. At the present stage therefore, no comprehensive generalisation is possible but the attempted recognition of contributory factors is both permissible and valuable, since thereby a progressive step is taken and a foundation for future research is laid. Ideally, the concept of anionoid and cationoid phases in aromatic reactivity contains the prospect of two co-extensive and mutually complementary aspects of nuclear substitution. In practice, the study of anionoid reactivity has advanced far beyond that of cationoid reactivity for which, experience shows, special conditions are necessary. Having regard to these conditions, considerable extension of the field of inquiry is involved in a conclusion which emerges from the study of nitrodiphenylsulphones, viz. that the nuclear activation arising from one cationoid group may /

may be harnessed to the independent directive influence of another. Moreover, in its general significance this conclusion is already supported by the examples gleaned from the literature (pp. 35 to 37 ). To the study of cationoid reactivity there is therefore enlisted not only the cumulative effects of two cationoid groups, but also the independent directive influences of sulphonyl, sulphinyl (sulphoxide), carbonyl, cyano and other relatively weak cationoid groups operating in a stimulated nuclear medium. The magnitude of the field which is thus disclosed for investigation is at once a comment on the restricted nature of present knowledge and a source of hope that its development will bear fruit in a closer correlation of the two aspects of aromatic reactivity.

The interaction of two chemical compounds involves the interplay of two sets of forces, and the study of nuclear cationoid reactivity must take into account the nature of the reagent. Again the problem is a general one. In anionoid reactivity the effects of different reagents are revealed in the variation of o:p- substitution ratios, and at least a few cases are known (42 ) in which a change of reagent simultaneously affects the position substituted together with the apparent directive control in the system, e.g:-




When /

When, therefore, in cationoid reactivity (as in nitrodiphenylsulphones) differences arising from competing directive influences are further accentuated by differences in the groups offered for replacement, it is scarcely surprising that somewhat spectacular reagent effects are encountered, Nevertheless, because of the wealth of reagents available, it is to cationoid reactivity that attention must be turned for a systematic study of these effects. Qualitative experiments such as those of the present investigation are the preliminaries necessary in defining the scope and character of the field to which eventually a quantitative survey must be applied.

In concluding this account of the cationoid reactivity of nitrodiphenylsulphones, emphasis has been laid on the general significance of the investigation rather than on the particular results obtained because, although these results undoubtedly have interest and value in themselves - as is shown in the discussions in Chapters II to VI - the author considers it is in their general significance that their real importance lies. Therefore it is with future research in view that these conclusions have been formulated and it is hoped that in this respect a justification, impetus and direction have been given to the development of an important subject which at present remains all too obscure.

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## EXPERIMENTAL

In this section the various compounds have been classified according to the methods used in their preparation. Formulae instead of names have been employed wherever possible.

| No. | Process. | Pages. | Class of Compounds. |
|---|---|---|---|
| 1. | The Action of Sulphinates. | 81 - 84 | Chlorosulphones, |
| 2. | Nitration of Sulphones. | 85 | nitrosulphones, |
| 3. | Friedel-Crafts Reaction. | 86 | and chloronitro- |
| 4. | Sandmeyer Reaction. | 87 | sulphones; |
| 5. | Reaction with Mercaptides. | | polysulphones, |
| 6. | Oxidation of Sulphides to Sulphones. | 87 - 91 | sulphides. |
| 7. | Reduction of Nitro groups. | 92 | Amines (sulphonamides) |
| 8. | Action of Methyl alcoholic Ammonia. | 93 - 94 | Nitroamines. |
| 9. | Nitration of Sulphonamides. | 94 - 95 | |
| 10. | Reaction of Piperidine. | 95 - 99 | Piperidino-Compounds. |
| 11. | Reaction with Sodium Methoxide. (ethoxide) | 99 - 100 | Ethers. |

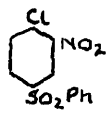
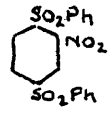
## Sulphones.

**Process 1.** The Action of Sulphinates on 2:4 Dinitrochlorobenzene etc.

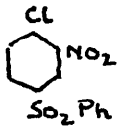
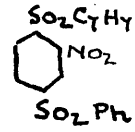
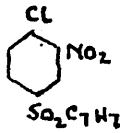
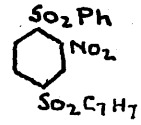
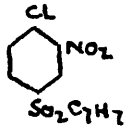
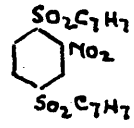
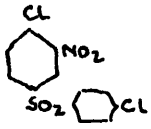
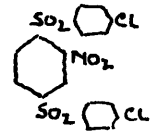
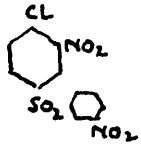
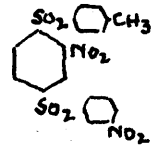
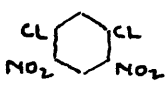
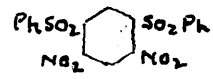
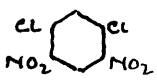
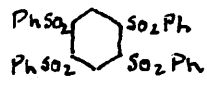
2:4-Dinitrochlorobenzene (1 mol.) or 2:4-dinitrophenyl p-toluenesulphonate (1 mol.) was refluxed with the requisite sodium sulphinate (1 mol.) for 10 - 20 minutes in aqueous alcoholic solution. The product was crystallised from acetic acid.

The compounds phenyl (160°), p-tolyl (187°), o-tolyl (154°), p-chlorophenyl (168°), p-bromophenyl (190°), methyl (187°) and ethyl (157°) - 2:4-dinitrophenylsulphones had the uncorrected melting points indicated, the values agreeing closely with data recorded for these substances prepared by oxidising the corresponding sulphides (43). 2:4:3'-Trinitrodiphenylsulphone had m.p. 197° (Found: N 11·8. $C_{12}H_7O_8N_3S$ requires N 11·9%) and 2':5'-dichloro-2:4-dinitrodiphenylsulphone, m.p. 178° (Found: N 7·5. $C_{12}H_6O_6N_2Cl_2S$ requires N, 7·4%).

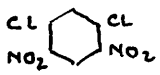
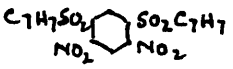
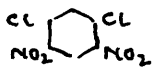
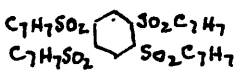
The following compounds were prepared by the same process from the sources indicated:-

| Source | Sulphinate | Compound | M.p. | Analysis Found | : Required % |
|---|---|---|---|---|---|
|  | phenyl |  | 158° | 53·5<br>3·5<br>3·8<br>16·1 | : 53·6, C.<br>: 3·3, H.<br>: 3·5, N.<br>: 15·9, S. |

Process I contd.

| Source | Sulphinate | Compound | M.p. | Analysis Found : Required % |
|---|---|---|---|---|
|  | p-tolyl |  | 180° | 3·6 : 3·4, N. |
|  | phenyl |  | 212° | 3·5 : 3·4, N. |
|  | p-tolyl |  | 221° | 56·1 : 55·7, C.<br>4·3 : 3·9, H.<br>3·4 : 3·3, N.<br>15·0 : 14·9, S. |
|  | p-chloro-phenyl |  | 231° | 14·9 : 15·1, Cl. |
|  | p-tolyl |  | 232° | 6·0 : 6·1, N. |
|  | phenyl (2 mols.) |  | 251° | 14·5 : 14·3, S. |
|  | phenyl (excess) |  | 305° | 19·8 : 20·0. S. |

Process I contd.

| Source | Sulphinate | Compound | M.p. | Analysis Found : Required % |
|---|---|---|---|---|
|  | p-tolyl (free acid) |  | 228° | 13·3 : 13·4,S. |
|  | p-tolyl (salt) |  | 315° | 18·1 : 18·4,S. |

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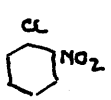
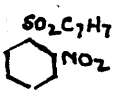
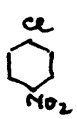
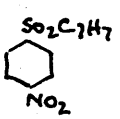
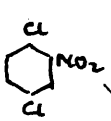
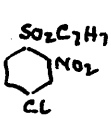
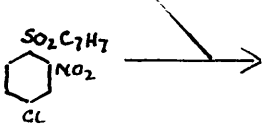
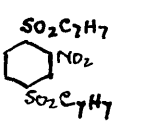
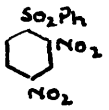
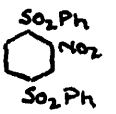
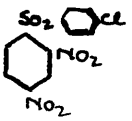
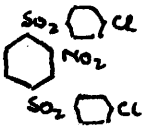
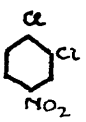
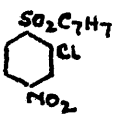
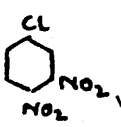
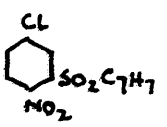
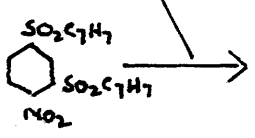
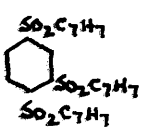
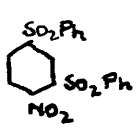
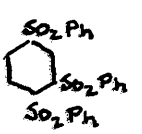
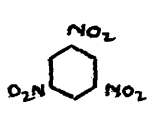
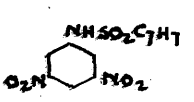
Process 1 A. An excess of the requisite sulphinate was refluxed for 1 - 3 hours in ethylene glycol solution with the chloronitro compound (source). The solid resulting from cooling or addition of water was fractionated from alcohol or acetic acid.

| Source | Sulphinate | Compound | M.p. | Analysis Found : Required % |
|---|---|---|---|---|
|  | p-tolyl |  | 156° | 5·2 : 5·1, N. |
|  | " |  | 170° | 5·2 : 5·1, N. |
|  | " |  | 124° | 4·4 : 4·5, N. |
|  | " |  | 220° | cf. process 1. |

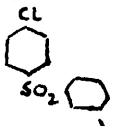
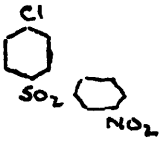
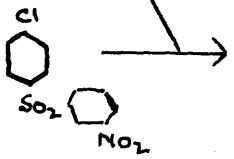
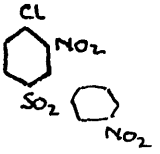
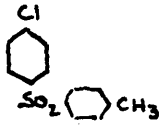
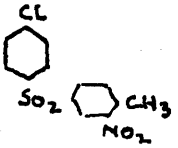
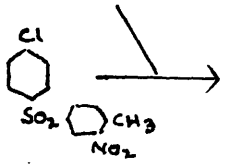
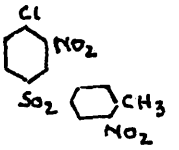
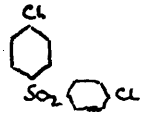
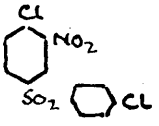
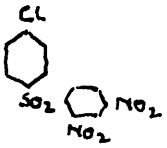
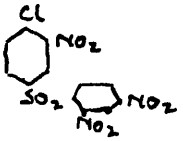
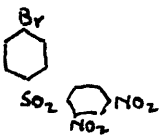
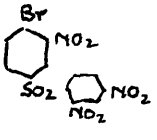
Process I A contd.

| Source | Sulphinate | Compound | M.p. | Analysis Found : Required % |
|---|---|---|---|---|
|  | phenyl |  | 158° | cf. process 1. |
|  | p-chloro-phenyl |  | 231° | cf. process 1. |
|  | p-tolyl |  | 125° | 4·4 : 5·0, N. |
|  | " |  | 189° | 4·8 : 4·5, N. |
|  | " |  | 185° | 17·6 : 17·8, S. |
|  | phenyl |  | 197° | 19·0 : 19·3, S. |
|  | p-tolyl |  | 221° | 12·5 : 12·5, N. |

- - - - - - - - - - -

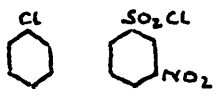
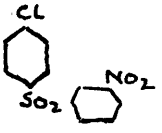
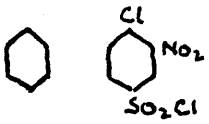
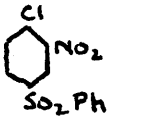
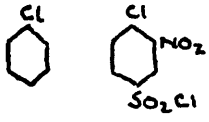
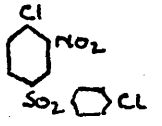
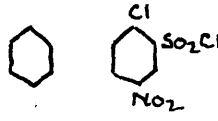
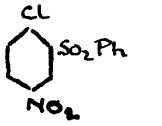
Process 2. Nitration of Sulphones.

Solutions of the sulphone (1 mol) and sodium nitrite (1 or 2 mol.) were gradually mixed and allowed to stand. The product either separated of its own accord or was precipitated by addition of the solution to water.

| Source | Product | M.p. | Analysis Found | Required |
|---|---|---|---|---|
|  |  | 140° | 4·9 | 4·7, N. % |
|  |  | 146° | 8·3 | 8·2, N. |
|  |  | 103° | 4·6 | 4·5, N. |
|  |  | 152° | 7·9 | 7·9, N. |
|  |  | 130° | 4·5 | 4·3, N. |
|  |  | 203° | 10·9 | 11·1, N. |
|  |  | 210° | 9·9 | 10·0, N. |

Process 3. Friedel-Crafts Reactions.

Equal weights of sulphonylchloride and aluminium chloride were refluxed (water bath) with an excess of the other reagent (e.g. benzene) as solvent. The semi-solid mass obtained after cooling and adding ice-water was extracted with hot acetic acid.

| Source | Compound | M.p. | Analysis Found | : Required |
|---|---|---|---|---|
|  |  | 140° | 4·9 | : 4·7, N. % |
|  |  | 127° | 4·8 | : 4·7, N. |
|  |  | 130° | 4·5 | : 4·3, N. |
|  |  | 174° | 8·1 | : 8·1, N. |

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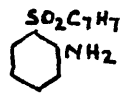
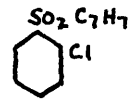
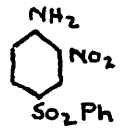
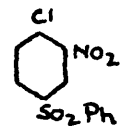
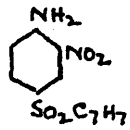
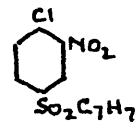
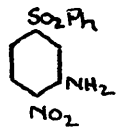
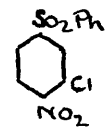
Process 4. Sandmeyer Reactions.

The procedure adopted was that described by Hodgson and Walker ( ref. 44 ) for use with nitrated anilines.

| Source | Compound | M.p. | Analysis Found : Required. |
|---|---|---|---|
|  |  | 113° | % 58·3 : 58·5, C. 4·4 : 4·1, H. |
|  |  | 127° | cf. process 3. |
|  |  | 120° | 4·6 : 4·5, N. |
|  |  | 133° | 4·8 : 4·7, N. |

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Process 5. Reaction with Mercaptides.

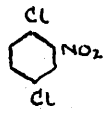
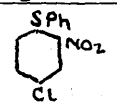
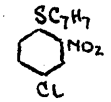
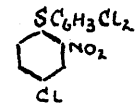
An alcoholic solution of the sodium mercaptide (1 mol) prepared /

Process 5 contd.

(prepared in situ from the mercaptan and sodium hydroxide) was slowly added to the second component of the reaction also dissolved in (hot) alcohol (or dioxan).

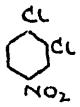
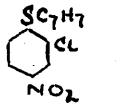
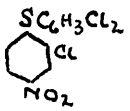
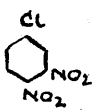
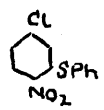
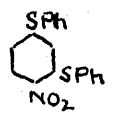
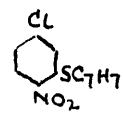
Process 6. Oxidation of Sulphides.

A large excess of hyperol was gradually added (2-4 hours) to a boiling solution of the thioether in acetic acid. The product separated on cooling or on addition of water and was crystallised from alcohol, acetic acid or dioxan.

| Source * | Thiol | Compound (a) Sulphide (b) Sulphone | M.p. | Analysis. Found : Required |
|---|---|---|---|---|
|  | Phenyl | (a)  | 87° | 5·3 : 5·5, N. % |
| " | p-tolyl | (a)  | 121° | 5·2 : 5·0, N. |
| | | (b) Sulphone | 124° | 4·4 : 4·5, N. |
| " | 2:5-dichloro phenyl |  | 107° | 4·4 : 4·2, N. |
| | | (b) Sulphone | 131° | 3·8 : 3·8, N. |

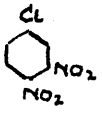
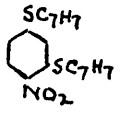
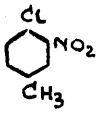
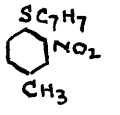
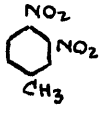
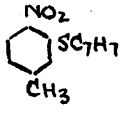
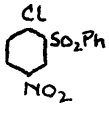
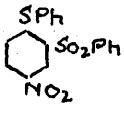
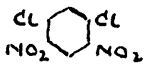
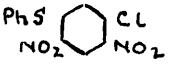
* Sulphones also yielded thioethers in similar reactions.

Process 6 contd.

| Source | Thiol | Compound | M.p. | Analysis Found : Required |
|---|---|---|---|---|
| | | (a) Sulphide<br>(b) Sulphone | | |
|  | p-tolyl | (a)  | 122° | % 5·0 : 5·0, N. |
| | | (b) Sulphone | 125° | 4·4 : 4·5, N. |
| " | 2:5-dichloro phenyl | (a)  | 112° | 4·0 : 4·2, N. |
| | | (b) Sulphone | 123° | 3·7 : 3·8, N. |
| *  | phenyl (1 mol) | (a)  | 127° | 5·4 : 5·3, N. |
| | | (b) Sulphone | 187° | 4·9 : 4·7, N. |
| " | phenyl (2 mol) | (a)  | 120° | 4·2 : 4·1, N. |
| | | (b) Sulphone (di) | 160° | 3·6 : 3·5, N. |
| * " | p-tolyl | (a)  | 126° | 5·2 : 5·0, N. |
| | | (b) Sulphone | 188° | 4·8 : 4·5, N. |

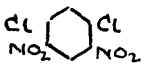
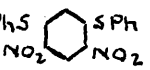
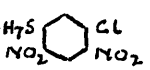
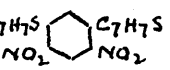
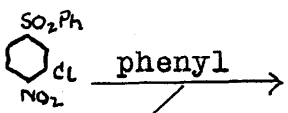
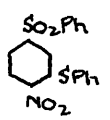
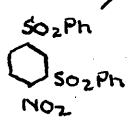
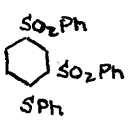
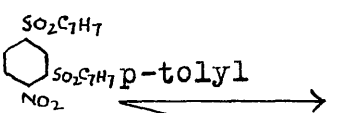
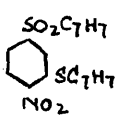
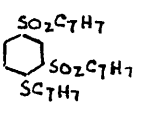
* In these cases quantities of the isomeric compounds (cf. p. 20 ) were also formed and were separated by fractional crystallisation.

Process 6 contd.

| Source | Thiol | Compound (a) Sulphide (b) Sulphone | M.p. | Analysis Found : Required |
|---|---|---|---|---|
|  | p-tolyl (2 mol) | (a)  | 105° | 4·0 : 3·8, N. |
| | | (b) Sulphone (di) | 158° | 3·4 : 3·3, N. |
|  | p-tolyl | (a)  | 116° | 5·5 : 5·4, N. |
| | | (b) Sulphone | 132° | 4·8 : 4·8, N. |
| *  | p-tolyl | (a)  | 124° | 5·5 : 5·4, N. |
| | | (b) Sulphone | 169° | 4·7 : 4·8, N. |
|  | phenyl | (a)  | 173° | 4·0 : 3·8, N. |
| | | (b) Sulphone | 209° | 3·7 : 3·5, N. |
|  | phenyl | (a)  | 108° | 9·0 : 9·0, N. |
| | | (b) Sulphone | 187° | 9·4 : 9·4, S. |

* In this case quantities of the isomeric compounds (cf. p. 50 ) were also formed and were separated by fractional crystallisation.

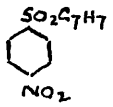
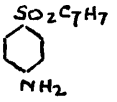
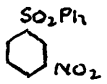
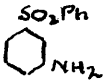
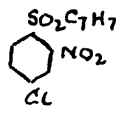
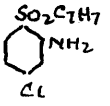
Process 6 contd.

| Source | | Compound | M.p. | Analysis Found : Required |
|---|---|---|---|---|
| | Thiol | (a) Sulphide<br>(b) Sulphone | | |
|  | phenyl | (a)  | 253° | 7·4 : 7·3, N. |
| | | (b) Sulphone (di) | 251° | 14·4 : 14·3, S. |
| " | p-tolyl | (a)  | 148° | 8·7 : 8·6, N. |
| | | (b) Sulphone | 198° | 8·0 : 7·9, N. |
| " | " | (a)  | 233° | 7·0 : 6·8, N. |
| | | (b) Sulphone (di) | 288° | 13·3 : 13·4, N. |
|  | phenyl | (a)  | 166° | 3·8 : 3·7, N. |
|  | " | (a)  | 221° | 20·3 : 20·6, S. |
| | | (b) Sulphone (tri) | 197° | cf. Process IA. |
|  | p-tolyl | (a)  | 124° | 3·6 : 3·5, N. |
| | | (a)  | 220° | 18·7 : 18·9, S. |
| | | (b) Sulphone (tri) | 185° | cf. Process IA. |

Process 7. Reduction of Nitro Groups.

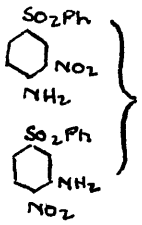
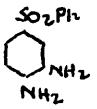
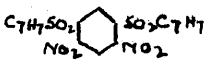
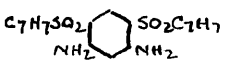
The nitro compound was gradually added to a boiling solution of excess stannous chloride in alcohol and the resulting solution after addition of concentrated hydrochloric acid (1cc. per 1 g. $SnCl_2$) was cooled and slowly stirred into a large volume of 20°/₀ caustic soda solution. The precipitated amine was purified from alcohol.

The p-toluene sulphonamides* (denoted by "amide" in the following list) were prepared from the amines by the action of p-toluenesulphonylchloride in pyridine.

| Source | Compound | M.p. | Analysis Found : Required |
|---|---|---|---|
|  |  | 181° | 5·6 : 5·7, N. |
| | amide | 214° | 3·8 : 3·5, N. |
|  |  | 115° | 6·2 : 6·0, N. |
| | amide | 152° | 3·8 : 3·6, N. |
|  |  | 136° | 5·2 : 5·0, N. |

* 3:4-Dinitrophenyl-p-toluenesulphonamide is described under process I A.

Process 7 contd.

| Source | Compound | M.p. | Analysis Found : Required % |
|---|---|---|---|
|  |  | 126° | 11·4 : 11·3, N. |
| | Quinoxaline derivative (cf. p. ) | 196° | 6·8 : 6·6, N. |
|  |  | 293° | 6·8 : 6·7, N. |

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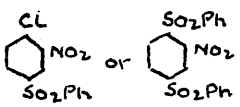
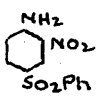
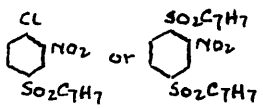
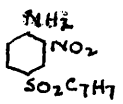
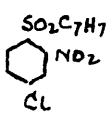
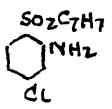
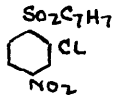
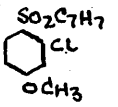
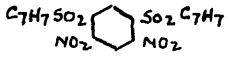
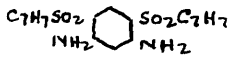
Process 8. Action of Methyl alcoholic Ammonia.

The Chloronitro compound or nitro sulphone was heated in a sealed tube with methyl alcohol (10cc. per 1 g.) amd comcentrated ammonia (10 mol.) at 150° for 3-5 hours.

| Source | Product | M.p. | Analysis Found : Required % |
|---|---|---|---|
|  |  | 170° | cf. Profess 9 |
|  |  | 184° | " " |
|  |  | 136° | cf. Process 7. |

Process 8 contd.

| Source | Product | M.p. | Analysis Found : Required |
|---|---|---|---|
|  |  | 118° | % 12·2 : 12·0, Cl. 11·1 : 10·8, S. |
|  or tetra-sulphone |  | 290° | cf. Process 7. |

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Process 9. Nitration of Sulphonamides.

3-Nitro-4-aminodiphenylsulphone - p- Aminodiphenylsulphone (9) was converted into the p-toluenesulphonamide, m.p. 190° (Found: N, 4·0. $C_{19}H_{17}O_4NS_2$ requires N, 3·6°/$_o$). The sulphonamide (6g.) was heated with nitric acid (6cc, d 1·4) in acetic acid (60cc.) for 1 hour; on cooling, 3-nitro-4-p-toluenesulphonamidodiphenylsulphone crystallised, m.p. 171° (from acetic) (Found: N, 6·8. $C_{19}H_{16}O_6N_2S_2$ required N, 6·5°/$_o$). Hydrolysis by warm concentrated sulphuric acid yielded the required amine, m.p. 170° (from acetic) (Found: N, 9·9. $C_{12}H_{10}O_4N_2S$ requires N, 10·1°/$_o$).

3-Nitro-4-amino-4'-methyldiphenylsulphone. - The p-toluene-sulphonamide from 4-amino-4'-methyldiphenylsulphone (process 7 6g.) was nitrated by feclyxing (1 hour) with nitric acid (6cc.; d, 1·4) and acetic acid (80cc.). Dinitrated material separated /

Process 9 contd.

separated on cooling (cf. publication J., 1936, 220 - Reprint). The mother liquor gave on dilution with water 3-nitro-4-p-toluenesulphonamido-4'-methyldiphenylsulphone, m.p. 130° (after purification from alcoholic dioxan) (Found: N, 6·4. $C_{20}H_{18}O_6N_2S_2$ requires N, 6·3%), hydrolysed by warm sulphuric acid to the required amine, m.p. 184° (from acetic) (Found: N, 9·7. $C_{13}H_{12}O_4N_2S$ requires N, 9·6%).

4-Nitro-3-aminodiphenylsulphone - The p-toluenesulphonamide from 3-amino diphenylsulphone (process 7. 7g.) was nitrated by refluxing (20 mins.) in a mixture of nitric acid (1·6cc.; d, 1·4) and acetic acid (50cc.). 3-p-Toluenesulphonamido-4-nitrodiphenylsulphone, m.p. 220° (from acetic) separated on cooling* (Found; N, 6·6. $C_{19}H_{16}O_6N_2S_2$ requires N, 6·5%) and was hydrolysed in the usual way to the required amine, m.p. 185° (Found: N, 10·1. $C_{12}H_{10}O_4N_2S$ requires N, 10·1%).

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Process 10. Reaction with Piperidine.

The compound was refluxed with piperidine for 2 - 5 minutes and, after cooling, the product was treated with water. The resulting /

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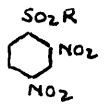
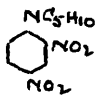
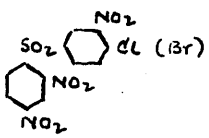
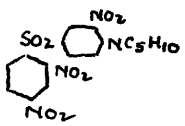
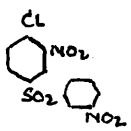
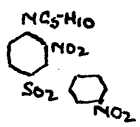
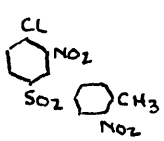
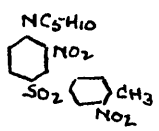
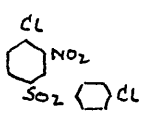
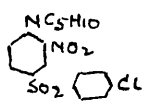
* The mother liquors contained at least one isomeric compound in addition to dinitrated material.

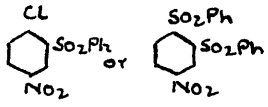
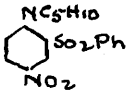
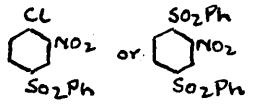
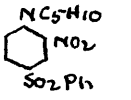
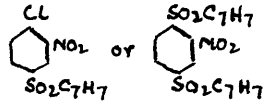
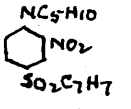
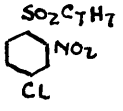
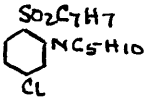
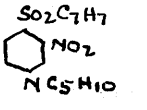
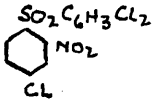
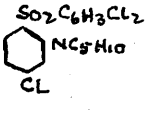
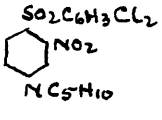
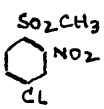
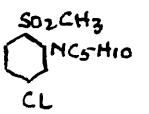
Process 10 contd.

resulting solid (or oil) was extracted with concentrated hydrochloric acid and after removing any insoluble portion (which was again extracted with acid and was sometimes an insoluble piperidinium hydrochloride) the base was liberated by addition of dilute ammonium hydroxide. Crystallisation (fractional where necessary) was effected from alcohol, dioxan, or acetic acid.

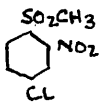
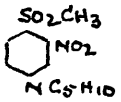
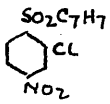
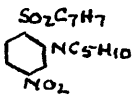
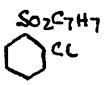
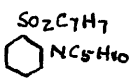
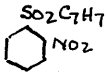
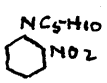
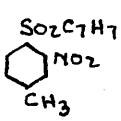
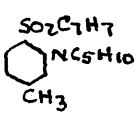
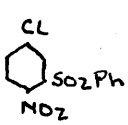
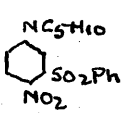
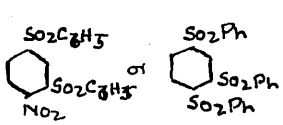
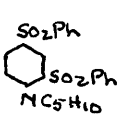
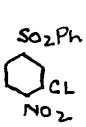
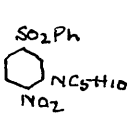
The compounds marked with an asterisk in the following list required an extended period for reaction.

| Source | Product | M.p. | Analysis Found : Required |
|---|---|---|---|
| | | | % |
|  |  | 92° | authentic specimen |
|  |  | 191° | 13 : 12·8, N. |
|  |  | 152° | 10·7 : 10·7, N. |
|  |  | 150° | 10·4 : 10·4, N. |
|  |  | 80° | 7·5 : 7·4, N. |

Process 10 contd.

| Source | Product | M.P. | Analysis Found : Required % |
|---|---|---|---|
|  |  | 178° | 8·1 : 8·1, N. |
|  |  | 133° | 7·9 : 8·1, N. |
|  |  | 108° | 7·9 : 7·8, N. |
|  |  | 121° | 4·3 : 4·0, N. |
| " |  | 183° | 7·8 : 7·8, N. |
|  |  | 153° | 3·5 : 3·5, N. |
| " |  | 172? | 7·0 : 6·8, N. |
|  |  | 134° | 5·1 : 5·2, N. |

Process 10 contd.

| Source | Compound | M.p. | Analysis Found : Required % |
|---|---|---|---|
|  |  | 126° | 10 : 9·9, N. |
|  |  | 171° | 7·7 : 7·8, N. |
| *  |  | 118° | 4·5 : 4·4, N. |
| *  |  | 75° | authentic specimen. |
| *  |  | 148° | 4·4 : 4·3, N. |
|  |  | 192° | 8·0 : 8·1, N. |
|  |  | 156° | 3·3 : 3·2, N. |
|  |  | 116° | 8·2 : 8·1, N. |

Process 10 contd.

| Source | Compound | M.p. | Analysis. Found : Required |
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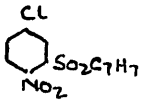
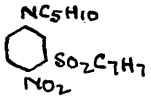
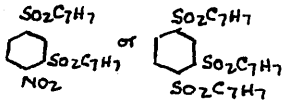
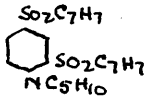
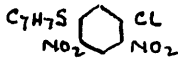
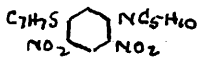
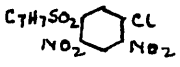
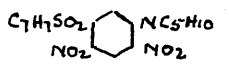
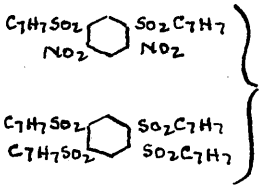
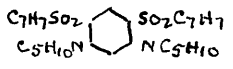
|  |  | 178° | % 7·9 : 7·8, N. |
|  |  | 163° | 3·2 : 3·0, N. |
|  |  | 192° | 11·2 : 11·3, N. |
|  |  | 180° | 10·3 : 10·4, N. |
|  |  | 228° | 5·0 : 5·0, N. |

Process 11. Reaction with Sodium Methoxide.

4-Chloro-2-methoxy-4'-methyldiphenylsulphone - 4-Chloro-2-nitro-4'-methyldiphenylsulphone was refluxed in a methyl alcoholic solution of sodium methoxide for 15 minutes. Addition of water yielded the required product, m.p. 117° (from alcohol) (Found: Cl, 12·1; S, 11·2. $C_{14}H_{13}O_3Cl_3$ requires Cl, 12·0; S, 10·8%).

2 Chloro-4-methoxy-4'-methyldiphenylsulphone was prepared in a similar fashion (cf. process 8).

Process 11 A. Reaction with Sodium Ethoxide.

4-Ethoxy-3-nitrodiphenylsulphone, m.p. 147° (Found: N, 4·65. $C_{14}H_{13}O_5NS$ requires N, 4·8%) and 4-Ethoxy-3-nitro-4'-methyldiphenylsulphone, m.p. 144°, (Found: N, 4·2. $C_{15}H_{15}O_5NS$ requires N, 4·4%) were prepared respectively from 4 Chloro-3 nitro- and 4-chloro-3-nitro-4'-methyl- diphenylsulphone by process 11, using sodium ethoxide in ethyl alcohol.

These ethers together with quantities of the corresponding phenols viz. 4 hydroxy-3-nitrodiphenylsulphone, m.p. 137° (Found: N, 5·1. $C_{12}H_9O_5NS$ requires N, 5·0%) and 4-hydroxy-3-nitro-4-methyldiphenylsulphone, m.p. 158° (Found: N, 4·9. $C_{13}H_{11}O_5NS$ 4·8%) were also prepared by refluxing suspensions of 2:5-diphenyl sulphonyl and 2:5-di-p-tolylsulphonyl- nitrobenzene respectively in aqueous alcoholic sodium hydroxide.

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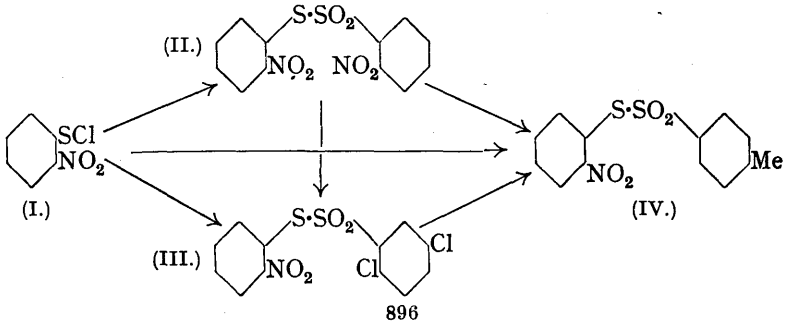
## 203. *Exchange of Sulphonyl Groups in Thiolsulphonic Esters.*

By J. D. Loudon and A. Livingston.

The exchange of sulphonyl groups in 2 : 4-dinitrodiphenylsulphones by the action of sulphinates (Loudon, this vol., p. 537) is closely paralleled by the interconversion of 2 : 4-dinitrophenyl alkyl ethers (Blanksma, *Centr.*, 1909, I, 1809), which, in turn, is related to the " Umesterung " phenomena exhibited by derivatives of carboxylic acids. It is therefore to be anticipated that sulphonyl exchange will be displayed in such compounds as acyl sulphones, disulphones, and in the so-called disulphoxides which Smiles and his co-workers have shown to be thiolsulphonic esters (J., 1924, **125**, 176; 1925, **127**, 224, 1821).

The following account is concerned chiefly with the behaviour of thiolsulphonic esters towards alkali sulphinates and the test case devised is illustrated in the diagram :



The identity of the products of the sulphonyl exchange (II ⟶ III; II ⟶ IV; III ⟶ IV) with those synthesised from the chlorothiol fully confirmed our expectations; moreover the fundamental similarity of the two preparative routes is obvious and this we have emphasised in condensations with the chlorothiol (I ⟶ II; I ⟶ III; I ⟶ IV) by substituting alkali sulphinates for the silver sulphinates employed by other workers (Zincke and Farr, *Annalen*, **1912**, **391**, 67; Smiles, *loc. cit.*). From the point of view of its synthetic value, however, the new process is subject to certain limitations, as is shown in the table, in which the success or failure of various instances of the following reaction is denoted by + or − respectively:

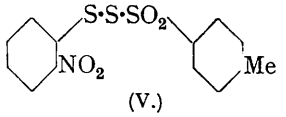
$$R'S{\cdot}SO_2{\cdot}R'' + R'''{\cdot}SO_2Na \longrightarrow R'S{\cdot}SO_2{\cdot}R''' + R''{\cdot}SO_2Na$$

| R′ = R″. | R‴. | | R′. | R″. | R‴. | |
|---|---|---|---|---|---|---|
| Phenyl | *p*-Tolyl | + | Phenyl | *p*-Tolyl | *p*-Chlorophenyl | − |
| *p*-Tolyl | Phenyl | − | ,, | ,, | *p*-Bromophenyl | − |
| Benzyl | *p*-Tolyl | + | Benzyl | ,, | Phenyl | − |
| *p*-Chlorophenyl | ,, | + | *o*-Nitrophenyl | Phenyl | 2 : 5-Dichloro-phenyl | − |
| *p*-Bromophenyl | ,, | + | | | | |
| 2 : 5-Dichloro-phenyl | ,, | + | ,, | *p*-Chlorophenyl | *p*-Tolyl | + |
| | | | ,, | ,, | *p*-Bromophenyl | + |
| ,, | *m*-Nitrophenyl | + | ,, | *p*-Bromophenyl | Phenyl | + |
| ,, | *o*-Nitrophenyl | − | ,, | ,, | *p*-Chlorophenyl | − |
| *o*-Nitrophenyl | Phenyl | + | ,, | 2 : 5-Dichloro-phenyl | *p*-Tolyl | + |
| ,, | *p*-Tolyl | + | | | | |
| ,, | *p*-Chlorophenyl | + | ,, | ,, | Phenyl | + |
| ,, | *p*-Bromophenyl | + | ,, | ,, | *p*-Chlorophenyl | + |
| ,, | 2 : 5-Dichloro-phenyl | + | | | | |

As a first approximation it may be concluded from these results that here, as with 2 : 4-dinitrodiphenylsulphones, facile exchange is only operative when the potential anion is of greater stability than the free sulphinate ion. It is further to be expected that the nature of the group R′S will also exert some influence on the reaction, but no clear evidence of this is available, although, in the sulphone series, it has now been found that no exchange occurs either with benzyl or with *p*-nitrobenzyl sulphones—a result which supports Smiles's conclusion (actually made with reference to the *o*-nitrobenzyl group; Kent and Smiles, J., 1934, 422) that the centres concerned are too feebly charged to engender pronounced sulphonyl mobility.

The action of potassium *p*-toluenethiolsulphonate ($C_7H_7{\cdot}SO_2{\cdot}SK$) on 2-nitro- and on 2 : 4-dinitro-chlorobenzene was examined as a possible source of the thiolsulphonic esters, but only the corresponding *p*-tolylsulphones were isolated. This behaviour recalls Fromm and Erfurt's suggestion (*Ber.*, **1909**, **42**, 3822) that the product of a similar action on benzyl chloride consists of an inseparable mixture of *p*-tolylbenzylsulphone and benzyl *p*-toluenethiolsulphonate. Reinvestigation of the point, however, established that the product was simply benzyl *p*-toluenethiolsulphonate, also prepared by the exchange process from benzyl benzylthiolsulphonate.

It was expected that vigorous treatment of *o*-nitrophenyl *p*-toluenethiolsulphonate (IV) by alkali sulphinates would result in production of *o*-nitrophenyl sulphones. This, however, has not been realised, but replacement of the thiolsulphonic group by sulphonyl in the analogous case of *p*-toluenesulphonyl *o*-nitrophenyl disulphide (V) was readily effected ($C_7H_7{\cdot}SO_2{\cdot}S$ replaced by *p*-toluenesulphonyl and by *p*-bromophenylsulphonyl but not by 2 : 5-dichlorophenylsulphonyl).



(V.)

Although, with alkali mercaptides, sodium benzylthiosulphate ($CH_2Ph{\cdot}S{\cdot}SO_3Na$) yields disulphides (Footner and Smiles, J., 1925, **127**, 2887) and sodium anthraquinone-1-sulphonate yields thio-ethers (Emmet Reid, Mackall, and Miller, *J. Amer. Chem. Soc.*, 1921, **43**, 2104), the corresponding replacements do not occur with alkali sulphinates.

## Experimental.

*Sulphonyl Exchange with Thiolsulphonic Esters.*—The general procedure adopted was to warm a homogeneous mixture of the sodium sulphinate (3 mols.) in water with the thiolsulphonic

ester (0·5 to 1 g.; 1 mol.) in a suitable solvent (alcohol, acetic acid, or dioxan) for 2 minutes and thereafter to cool and, where necessary, precipitate the product with water. The recrystallised products (alcohol or acetic acid) were identified by m. p. and mixed m. p. with synthetic specimens where these were known (Smiles and colleagues, *loc. cit.*) or alternatively characterised by analysis.

*Phenyl* p-*toluenethiolsulphonate*, obtained from phenyl benzenethiolsulphonate and sodium *p*-toluenesulphinate, had m. p. 74° (from alcohol) (Found: C, 58·9; H, 4·7. $C_{13}H_{12}O_2S_2$ requires C, 59·1; H, 4·5%).

*Benzyl* p-*Toluenethiolsulphonate.*—(1) A homogeneous mixture of potassium *p*-toluenethiolsulphonate (2 g.) in water and benzyl chloride (1 c.c.) in alcohol was gently refluxed for 1 hour and the oil precipitated on cooling was washed with water and placed in the ice-chest till it solidified. The product was obtained from alcohol in coarse crystals, m. p. 60° (Fromm and Erfurt, *loc. cit.*, give m. p. 55°).

(2) The same product resulted from treatment of benzyl benzylthiolsulphonate and sodium *p*-toluenesulphinate, in the usual way (Found: C, 60·5; H, 5·0. Calc. for $C_{14}H_{14}O_2S_2$: C, 60·4; H, 5·0%).

p-*Nitrobenzyl* p-*toluenethiolsulphonate*, prepared as in the previous case from *p*-nitrobenzyl bromide, melted at 120° after two crystallisations from acetic acid–alcohol (Found: N, 4·4. $C_{14}H_{13}O_4NS_2$ requires N, 4·3%).

p-*Chlorophenyl* p-*toluenethiolsulphonate*, obtained from *p*-chlorophenyl *p*-chlorobenzenethiolsulphonate, had m. p. 65° (from alcohol) (Found: Cl, 11·7. $C_{13}H_{11}O_2ClS_2$ requires Cl, 11·9%).

p-*Bromophenyl* p-*toluenethiolsulphonate*, by exchange (cf. Table), had m. p. 107° (from alcohol) (Found: Br, 23·6. $C_{13}H_{11}O_2BrS_2$ requires Br, 23·3%).

2 : 5-*Dichlorophenyl* p-*Toluenethiolsulphonate.*—The compound obtained from sodium *p*-toluenesulphinate and 2 : 5-dichlorophenyl 2 : 5-dichlorobenzenethiolsulphonate crystallised in two forms, which were separated by fractional extraction of the crude product with hot alcohol. The more soluble form, on slow heating, melted sharply at 86—87° and on continued heating resolidified, finally re-melting at the m. p. of the second form, *viz.*, 103° (Found: Cl, 21·2. $C_{13}H_{10}O_2Cl_2S_2$ requires Cl, 21·3%).

o-*Nitrophenyl benzenethiolsulphonate* was obtained (1) by sulphonyl exchange (cf. table) and (2) by interaction of *o*-nitrophenylsulphenyl chloride and sodium benzenesulphinate. In the latter process the sulphenyl chloride (5 g.), dissolved in ether (30 c.c.), was warmed with the dried powdered sulphinate (5 g.) in suspension for 15 minutes. After filtration the ether was evaporated, and the residue crystallised from alcohol; m. p. 87° (Found: N, 4·6. $C_{12}H_9O_4NS_2$ requires N, 4·7%).

o-*Nitrophenyl* p-*bromobenzenethiolsulphonate*, from *o*-nitrophenyl *o*-nitrobenzenethiolsulphonate, had m. p. 137° (from alcohol) (Found: N, 3·8. $C_{12}H_8O_4NBrS_2$ requires N, 3·7%).

2 : 5-Dichlorophenyl 3-nitrobenzenethiolsulphonate, from 2 : 5-dichlorophenyl 2 : 5-dichlorobenzenethiolsulphonate and sodium *m*-nitrobenzenesulphinate, had m. p. 116° after two crystallisations from alcohol (Found: N, 3·8. $C_{12}H_7O_4NCl_2S_2$ requires N, 3·8%).

*Replacement of Thiolsulphonic Group.*—When a dioxan solution of *p*-toluenesulphonyl *o*-nitrophenyl disulphide (V, m. p. 139°) was treated in the usual way with sodium *p*-toluenesulphinate, the product was identified as *o*-nitrophenyl *p*-toluenethiolsulphonate (m. p. and mixed m. p. 97—98°). Similarly, sodium *p*-bromobenzenesulphinate yielded *o*-nitrophenyl *p*-bromobenzenethiolsulphonate (m. p. 131°; mixed m. p. 132—133°; depressed by admixture with V to below 120°). Sodium 2 : 5-dichlorobenzenesulphinate, on the other hand, effected no replacement even when the reaction time was extended to 30 minutes (product had m. p. and mixed m. p. with V 138°).

*o*-Nitrophenyl *p*-toluenethiolsulphonate was refluxed for 45 minutes with sodium *p*-toluenesulphinate in ethylene glycol (neither reagent is separately affected by this treatment). The solution on cooling deposited a semi-solid mass, which crystallised from alcohol (charcoal) in colourless needles, m. p. 46°, unaffected by admixture with di-*p*-tolyl disulphide. In a second experiment, with the heating curtailed to 30 minutes, *p*-tolyl *p*-toluenethiolsulphonate was isolated (m. p. 74°; mixed m. p. 76°).

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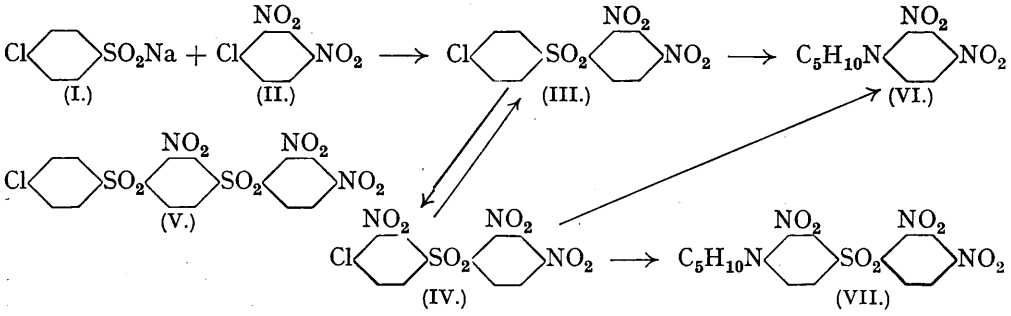
# 124. 2 : 4-*Dinitrodiphenylsulphones.*

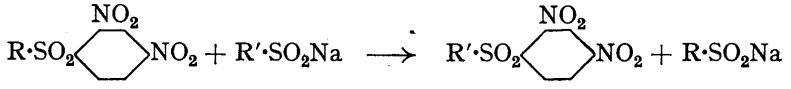
By James D. Loudon.

A study of the properties of 2 : 4-dinitrodiphenylsulphones has revealed some interesting examples of their reactivity, of which the following is a preliminary account. Their preparation has been effected by extension of Ullmann and Pasdermadjian's original procedure (*Ber.*, **1901**, **34**, 1150), *e.g.*, condensation of (I) and (II), or by the modification in which (II) is replaced by 2 : 4-dinitrophenyl-*p*-toluenesulphonate. The facility with which the reaction proceeds suggested the possibility of forming polysulphones, *e.g.*, (V) by nitration of (III), followed by condensation with a second molecule of (I).



The mononitration of (III) proceeded smoothly and the product was submitted to the piperidine test for reactive halogen, following the procedure of Le Fèvre and Turner (J., 1927, 1113). The difficulty of obtaining a homogeneous product, together with the ultimate isolation of (VI), showed that under these conditions (excess of piperidine) rapid scission of the sulphone linkage occurs. This was further demonstrated by the smooth conversion of other 2 : 4-dinitrodiphenylsulphone derivatives (*e.g.*, III) into (VI), the reaction being analogous to the slower replacement of the phenylsulphonyl group in *o*-nitrodiphenylsulphone by aniline (Levi and Smiles, J., 1932, 1488). That piperidine, however, exerts a preferential attack on the halogen of (IV) is shown by the isolation of (VII) from the reaction conducted in dioxan with the theoretical amount of base.

The mobility of the arylsulphonyl group in these compounds also frustrated the attempt to prepare (V) by interaction of (I) and (IV), the sole result being regeneration of (III), apparently by exchange of arylsulphonyl anions. The following table summarises the results obtained in other cases, the sign + denoting completion, and — failure of the reaction in which, with the exceptions noted, three molecular proportions of sulphinate were employed.



| R. | R′. | | R. | R′. | |
|---|---|---|---|---|---|
| Ethyl | Methyl * | + | Phenyl | Ethyl | + |
| Methyl | Ethyl | + | Phenyl | 2 : 5-Dichlorophenyl | — |
| Ethyl | *p*-Tolyl * | + | *p*-Chlorophenyl | Phenyl | + |
| *p*-Tolyl | Ethyl | + | *p*-Chloro-*m*-nitrophenyl | *p*-Chlorophenyl | + |
| *p*-Tolyl | Phenyl † | + | *p*-Bromo-*m*-nitrophenyl | *p*-Bromophenyl | + |
| Phenyl | *p*-Tolyl | + | *m*-Nitrophenyl | *p*-Tolyl | + |
| Phenyl | Methyl | + | *p*-Chloro-*m*-nitrophenyl | *m*-Nitrophenyl | — |

* Large excess. † 12 Molecules.

The table includes only those examples in which the nature of the isolated substance was clearly established by melting point and mixed melting point observations. In several other cases (*e.g.*, R = phenyl, R′ = *p*-chlorophenyl) the product was obviously a mixture (qualitative halogen test), which resisted fractionation from acetic acid.

The results recorded suffice to indicate in a qualitative manner that the reaction is

influenced (*a*) by the concentration of free sulphinate ion and (*b*) by the relative stabilities of the competing anions (actual and potential). They offer some points of contrast to the work of Gibson (J., 1931, 2637; 1932, 1819, *et seq.*), who has recently demonstrated sulphonyl mobility in the following case, and records failure of the exchange process (1)

$$R{\cdot}SO_2{\cdot}\underset{\displaystyle S{\cdot}CH_3}{\underset{|}{CH}}{\cdot}CO{\cdot}CH_3 \quad \underset{R{\cdot}SO_2{\cdot}S{\cdot}CH_3}{\overset{R'{\cdot}SO_2{\cdot}S{\cdot}CH_3}{\rightleftharpoons}} \quad R'{\cdot}SO_2{\cdot}\underset{\displaystyle S{\cdot}CH_3}{\underset{|}{CH}}{\cdot}CO{\cdot}CH_3$$

when purely aromatic thiolsulphonic esters (*e.g.*, $Ph{\cdot}SO_2{\cdot}SPh$ as distinct from $Ph{\cdot}SO_2{\cdot}S{\cdot}CH_3$) are employed and (2) where replacement of arylsulphonyl by alkylsulphonyl is attempted. With sulphones of the present series these limitations do not apply, for, on the one hand, both types of disulphoxide in presence of carbonate produced a facile exchange and, on the other, the effected replacement of arylsulphonyl by sodium alkylsulphinates was less readily reversed.

Experiments are in progress on the exchange of the sulphone group when attached to other cationoid centres, such as in thiolsulphonic esters.

## Experimental.

*Preparation of* 2 : 4-*Dinitrodiphenylsulphones.*—2 : 4-Dinitrochlorobenzene (or 2 : 4-dinitrophenyl *p*-toluenesulphonate) and the requisite sodium sulphinate in molecular proportion were heated in aqueous alcoholic solution for 10—20 minutes. After cooling, the solid was collected, washed with alcohol and water, and crystallised from acetic acid. The compounds, phenyl (159—160°), *p*-tolyl (187°), *o*-tolyl (154°), *p*-chlorophenyl (168°), *p*-bromophenyl (190°), methyl (187°), and ethyl (157°) -2 : 4-dinitrophenylsulphones, had the uncorrected melting points indicated, the values being in close agreement with those recorded for the same substances formed by oxidation of the corresponding sulphides (*J. Amer. Chem. Soc.*, 1932, **54**, 1985; 1933, **55**, 4956). 2 : 4 : 3′-*Trinitrodiphenylsulphone* had m. p. 196—197° (Found : N, 11·8. $C_{12}H_7O_8N_3S$ requires N, 11·9%), and 2′ : 5′-*dichloro*-2 : 4-*dinitrodiphenylsulphone*, m. p. 178° (Found : N, 7·5. $C_{12}H_6O_6N_2Cl_2S$ requires N, 7·4%).

4′-*Chloro*-2 : 4 : 3′-*Trinitrodiphenylsulphone.*—A solution of potassium nitrate (1·01 g.) in 20 c.c. of concentrated sulphuric acid was added to 4′-chloro-2 : 4-dinitrodiphenylsulphone (3·42 g.) in 60 c.c. of concentrated sulphuric acid. The crystals formed on standing were recrystallised from acetic acid and had m. p. 203° (Found : N, 10·9. $C_{12}H_6O_8N_3ClS$ requires N, 11·1%).

4′-*Bromo*-2 : 4 : 3′-*trinitrodiphenylsulphone.*—The product of the nitration of 4′-bromo-2 : 4-dinitrodiphenylsulphone, conducted as above, had m. p. 210° after several crystallisations from acetic acid (Found : N, 9·9. $C_{12}H_6O_8N_3BrS$ requires N, 10·0%).

*Action of Piperidine.*—The reaction (0·2 g. of sulphone and 2 c.c of piperidine) was rapid even in the cold. After being warmed for a few minutes, the solution was cooled and treated with dilute acid; the precipitated oil rapidly became solid except in the cases of 4′-chloro (and bromo)-2 : 4 : 3′-trinitrodiphenylsulphones, where partial solidification occurred only after several weeks. After crystallisation from alcohol the product in each case was identified as 2 : 4-dinitropiperidinobenzene, m. p. and mixed m. p. 92°.

2 : 4 : 3′-*Trinitro*-4′-*piperidinodiphenylsulphone.*—4′-Chloro-2 : 4 : 3′-trinitrodiphenylsulphone (0·5 g.; 1 mol.) in 5 c.c. of dioxan was treated with piperidine (0·22 g.; 2 mols.) in 2 c.c. of dioxan, and the resulting orange solution kept for 12 hours. The crystalline deposit was identified as piperidine hydrochloride (m. p. and mixed m. p. 236°). The oil formed by addition of water to the filtrate was extracted with concentrated hydrochloric acid. The extract on dilution with water yielded a solid which crystallised from acetone–alcohol in yellow plates, m. p. 190—191° (Found : N, 13·0. $C_{17}H_{16}O_8N_4S$ requires N, 12·8%). The same piperidine derivative was formed from the corresponding bromotrinitrodiphenylsulphone.

*Sulphonyl Exchange.*—The following example is typical of the procedure employed. Dinitrodiphenylsulphone (0·5 g.), dissolved in 6 c.c. of warm dioxan, was treated with a hot solution of sodium *p*-toluenesulphinate (0·9 g.) in 2 c.c. of water. The homogeneous mixture was heated for a few minutes and cooled (prolonged or more drastic treatment leads to complications which are under investigation). The solid which separated was washed with alcohol and then with water; it melted crude at 179—181°; crystallised from acetic acid, it had m. p. 187—188°, unaffected by admixture with 2 : 4-dinitrophenyl-*p*-tolylsulphone (m. p. 187°).

*Action of Disulphoxides.*—*p*-Tolyl *p*-toluenethiolsulphonate (0·3 g.) and 2 : 4-dinitrodiphenylsulphone (0·3 g.), dissolved in hot dioxan, were treated with a small amount of sodium carbonate and a few drops of water. The product, isolated as above, yielded 2 : 4-dinitrophenyl-*p*-tolylsulphone (m. p. and mixed m. p. 185—186°).

Methyl *p*-toluenethiolsulphonate gave the same result, but in the absence of alkali carbonate no reaction occurred in either case.

The author acknowledges his indebtedness to Mr. A. Naismith, B.Sc., who prepared some of the sulphones, and also to the Chemical Society for a grant.

GLASGOW UNIVERSITY. [*Received, February* 23*rd,* 1935.]

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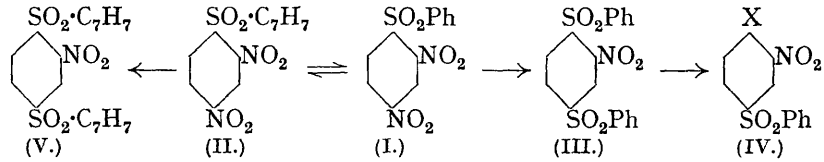
# 48. *The Action of Sulphinates on 2 : 4-Dinitrodiphenylsulphones.*

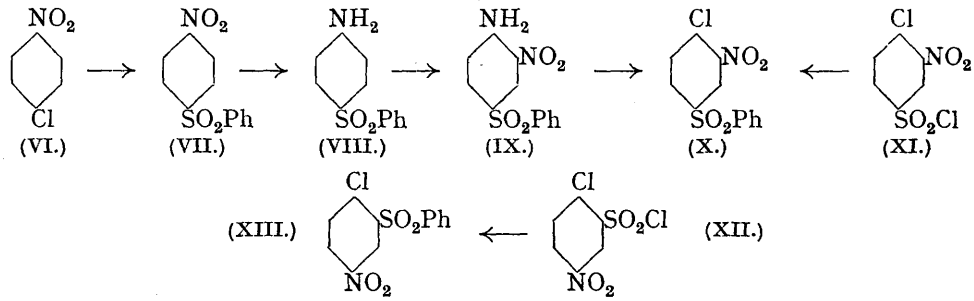
By James D. Loudon.

It has previously been shown (Loudon, J., 1935, 537) that the action of sodium *p*-toluenesulphinate on 2 : 4-dinitrodiphenylsulphone results in a rapid and reversible exchange of sulphonyl groups (I ⇌ II), accompanied by slower secondary reactions of unknown nature, apparently incurred by the continued action upon (I) and (II) of sulphinate present in excess or produced during the exchange. To avoid unnecessary complications in investigating this second phase, the action of sodium benzenesulphinate on 2 : 4-dinitrodiphenylsulphone (I) was first examined. Analysis of the isolated product indicated a nitrobis(phenylsulphonyl)benzene structure (*e.g.*, III), and its reactions showed the presence of one mobile phenylsulphonyl group. For instance, with alcoholic alkali a mixture of a *phenol* (IV; X = OH) and its *ethyl* ether (X = OEt) was readily produced, and alcoholic ammonia and piperidine gave an *amine* (X = $NH_2$) and a *piperidino*-derivative (X = $NC_5H_{10}$) respectively.



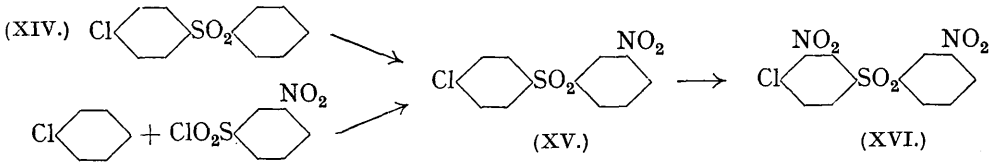

Since the mobility of this phenylsulphonyl group is comparable with that in (I), the inference may be drawn that it arises from the combined activating influences of both the residual nitro- and the second phenylsulphonyl group (for the activating effect of analogous combinations upon halogens, cf. *inter alia* Le Fèvre and Turner, J., 1927, 1113), and hence that the formation of the disulphonyl compound from (I) probably consists in replacement of one or other nitro-group by phenylsulphonyl (contrast the action of potassium cyanide on 2 : 4-dinitrochlorobenzene, where CN enters position 3; Van Heteren, *Rec. trav. chim.*, 1901, **20**, 107; Blanksma, *ibid.*, 1902, **21**, 424).

The selection of the *p*-nitro-group in (I) as the group actually concerned in the replacement follows from synthetic evidence, *viz.*, the mononitro-derivative (IX) of *p*-aminodiphenylsulphone was identical with the amine obtained from (III) with alcoholic ammonia, and was converted into the *chloronitro*-compound (X), from which (III) and its reaction products (IV) were produced by treatment with the appropriate reagents. Further, (X) was also obtained from the Friedel–Crafts condensation between 4-chloro-3-nitrobenzenesulphonyl chloride (XI) and benzene, whereas the isomeric *compound* (XIII), obtained in a similar way from (XII), yielded a *piperidino*-derivative quite distinct from (IV) (X = $NC_5H_{10}$).

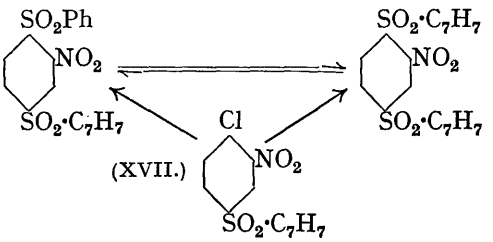



A parallel series of reactions and synthesis similarly identified the product of the action of sodium *p*-toluenesulphinate on (II) as 1-*nitro*-2 : 5-*di*-p-*tolylsulphonylbenzene* (V), but in this series the condensation between (XI) and toluene gave unworkable products. In both series the projected formation of the chloronitro-compounds by mononitration of

*p*-chlorodiphenylsulphone (XIV) and *p*-chlorophenyl-*p*-tolylsulphone was frustrated by entrance of the nitro-group into the non-halogenated nucleus, as shown by the absence of halogen mobility in the product (XV) (piperidine test) and by an independent preparation.




This result is analogous to the heteronuclear nitration of monohalogenated diphenyl derivatives, but the more closely related case of the benzophenone class does not appear to have been investigated. Dinitration of (XIV) yielded the active *chloro*-compound (XVI), from which a *piperidino*-derivative and the corresponding *amine* were readily obtainable. The disulphonyl derivatives obtained from (X), from its *p*-tolyl analogue (XVII), and from (XVI), all displayed the capacity to exchange sulphonyl groups adjacent to the nitro-group, but this capacity was less marked than in the case of the 2 : 4-dinitrodiphenylsulphones.




These results sufficiently indicate one aspect of the changes involved in the action of sulphinates on 2 : 4-dinitrodiphenylsulphones—others, which probably originate in the reducing powers of the sulphinates, have not been investigated. Whilst, as might be expected, replacement of the mobile nitro-group by arylsulphonyl was found to occur in both *o*- and *p*-dinitrobenzenes under the conditions employed for reaction with the corresponding chloronitro-compounds, the replacement of the *p*-nitro-groups in (I) and (II) involves some special features requiring further investigation. In this connexion, however, two points deserve mention : (1) in general, sulphinates may be expected to differ from the usual reagents (amines, hydroxides, etc.) employed to detect mobility in nitro-compounds, in that the latter, by introducing $NH_2$, OH, etc., tend to neutralise the effect of the nitro-group in facilitating further attack by anions, and (2) in particular, neither the nitro-group in (VII) nor that in the *o*-isomeride is replaced under the conditions sufficient to effect the replacements (I ⟶ III), (II ⟶ V).

## Experimental.

1-*Nitro*-2 : 5-*diphenylsulphonylbenzene* (III).—A solution of 2 : 4-dinitrodiphenylsulphone (5 g.) and sodium benzenesulphinate (10 g.) in hot aqueous dioxan was refluxed for 3—4 hours. The semi-solid mass which separated on cooling or on addition of water was washed with alcohol, then with water, and crystallised from acetic acid, forming colourless felted needles, m. p. 157—158°, soluble without decomposition in warm concentrated sulphuric acid and only very slowly attacked by aqueous alkali. The same *compound* was obtained by boiling the reagents for a few minutes in ethylene glycol solution (Found : C, 53·5; H, 3·5; N, 3·8; S, 16·1. $C_{18}H_{13}O_6NS_2$ requires C, 53·6; H, 3·3; N, 3·5; S, 15·9%).

3-*Nitro*-4-*piperidinodiphenylsulphone* (IV, X = $NC_5H_{10}$) was prepared by dissolving (III) in boiling piperidine, followed by dilution with water, extraction of the precipitate with hot concentrated hydrochloric acid, and reprecipitation with water. It formed salmon-coloured plates, m. p. 133°, from alcohol (Found : N, 7·9. $C_{17}H_{18}O_4N_2S$ requires N, 8·1%).

*Action of Aqueous-alcoholic Alkali on* (III).—A suspension of (III) (0·4 g.) in alcohol (15 c.c.)

and 3% aqueous caustic soda (4 c.c.) was refluxed till complete dissolution was effected. After partial removal of the alcohol, addition of water yielded an oil, which slowly solidified and was found to be 3-*nitro*-4-*ethoxydiphenylsulphone*; it formed needles, m. p. 147°, from alcohol (Found : N, 4·65. $C_{14}H_{13}O_5NS$ requires N, 4·8%). The filtrate from this substance gave on acidification with acetic acid 3-*nitro*-4-*hydroxydiphenylsulphone*, which crystallised from alcohol in almost colourless plates, m. p. 137° (Found : N, 5·1. $C_{12}H_9O_5NS$ requires N, 5·0%).

1-*Nitro*-2 : 5-*di*-p-*tolylsulphonylbenzene* (V), prepared in the same manner as (III), had similar appearance and properties. M. p. 220—221° (Found : C, 56·1; H, 4·3; N, 3·4; S, 15·0. $C_{20}H_{17}O_6NS_2$ requires C, 55·7; H, 3·9; N, 3·3; S, 14·85%).

3-*Nitro*-4-*piperidino*-4′-*methyldiphenylsulphone* was obtained in two forms—rapid crystallisation of the crude product [preparation similar to (IV) above] from hot alcohol yielding one form, m. p. 96—97°, which, kept in contact with the solvent, changed to the second form, m. p. 107—108°, also obtained directly by slower crystallisation (Found : N, 7·95. $C_{18}H_{20}O_4N_2S$ requires N, 7·8%).

3-*Nitro*-4-*hydroxy*-4′-*methyldiphenylsulphone*, m. p. 157—158° (Found : N, 4·9. $C_{13}H_{11}O_5NS$ requires N, 4·8%), and its *ethyl* ether, m. p. 143—144° (Found : N, 4·2. $C_{15}H_{15}O_5NS$ requires N, 4·4%), were prepared as in the cases of their lower homologues.

*Mononitrodiphenylsulphones.*—The following procedure dispenses with the sealed tubes employed in two instances by Ullmann and Pasdermadjian (*Ber.*, 1901, **34**, 1150). The requisite chloronitrobenzene and sodium sulphinate in molecular proportion were boiled in ethylene glycol for 3—4 hours. The product which separated on cooling (or on addition of water) was washed with alcohol and water and crystallised (charcoal) from alcohol or acetic acid. *o*-Nitrodiphenylsulphone had m. p. 147° (Found : N, 5·3. Calc. : N, 5·3%). *p*-Nitrodiphenylsulphone had m. p. 143° (Found : N, 5·4%). 2-Nitro-4′-methyldiphenylsulphone had m. p. 156° (*Chem. Abs.*, 1933, 998, patent, gives m. p. 156—157°) (Found : N, 5·2%).

4-*Nitro*-4′-*methyldiphenylsulphone* had m. p. 170° (Found : N, 5·2. $C_{13}H_{11}O_4NS$ requires N, 5·05). *o*- and *p*-Dinitrobenzenes (0·5 g.), treated in the same way for 30—40 minutes, gave the corresponding sulphones (m. p. and mixed m. p.).

4-*Amino*-4′-*methyldiphenylsulphone* (for indirect preparation, cf. Halberkmann, *Ber.*, 1922, **55**, 3074).—The nitro-sulphone (6 g.) was added in small quantities at a time to a boiling solution of stannous chloride (15 g.) in alcohol (15 c.c.) and the resulting solution after addition of concentrated hydrochloric acid (15 c.c.) was cooled and slowly stirred into 300 c.c. of 20% caustic soda solution. The precipitated amine was repeatedly extracted with alcohol and was crystallised from the same solvent; m. p. 181° (Found : N, 5·6. Calc. : N, 5·7%). 2-Amino-4′-methyldiphenylsulphone, similarly prepared, had m. p. 120—121° (Halberkmann, *loc. cit.*, gives m. p. 120—121°) (Found : N, 5·7%).

3-*Nitro*-4-*aminodiphenylsulphone* (IX).—(*A*) *p*-Aminodiphenylsulphone (Ullmann and Pasdermadjian, *loc. cit.*) was converted into the p-*toluenesulphonamide*, m. p. 190° (from acetic acid), by treatment with *p*-toluenesulphonyl chloride and pyridine (Found : N, 4·0. $C_{19}H_{17}O_4NS_2$ requires N, 3·6%). The sulphonamide (6 g.) was heated with nitric acid (6 c.c.; *d* 1·4) in acetic acid solution (60 c.c.) for 1 hour; on cooling, 3-*nitro*-4-p-*toluenesulphonamidodiphenylsulphone* crystallised, m. p. 171° (from acetic acid) (Found : N, 6·8. $C_{19}H_{16}O_6N_2S_2$ requires N, 6·5%). Hydrolysis by warm concentrated sulphuric acid yielded the required *amine*, m. p. 169—170° from acetic acid (Found : N, 9·9. $C_{12}H_{10}O_4N_2S$ requires N, 10·1%).

(*B*) 1-Nitro-2 : 5-diphenylsulphonylbenzene (0·5 g.), methyl alcohol (5 c.c.), and concentrated ammonia solution (0·6 c.c.) were heated in a sealed tube at 130° for 5 hours. The yellow crystalline product had m. p. 168—169° (from acetic acid), undepressed by admixture with the amine from (*A*).

3-*Nitro*-4-*amino*-4′-*methyldiphenylsulphone.*—(*A*) 4-Amino-4′-methyldiphenylsulphone yielded the p-*toluenesulphonamide*, m. p. 213—214° (from acetic acid) (Found : N, 3·8. $C_{20}H_{19}O_4NS_2$ requires N, 3·5%). From the nitration solution [the amide (8 g.), acetic acid (80 c.c.), and nitric acid (6 c.c.; *d* 1·4) after 1 hour's refluxing] there separated 3 : 5-*dinitro*-4-p-*toluenesulphonamido*-4′-*methyldiphenylsulphone* in colourless felted needles, m. p. 221° (Found : N, 8·25. $C_{20}H_{17}O_8N_3S_2$ requires N, 8·5%), which was hydrolysed to 3 : 5-*dinitro*-4-*amino*-4′-*methyldiphenylsulphone*, yellow needles (from acetic acid), m. p. 216° with previous softening at 205° (Found : N, 12·4. $C_{13}H_{11}O_6N_3S$ requires N, 12·5%). The constitution of this compound follows from its non-identity with 3 : 3′-dinitro-4-amino-4′-methyldiphenylsulphone (cf. below). The mother-liquor of the nitration solution after removal of the dinitro-compound gave on dilution with water 3-*nitro*-4-p-*toluenesulphonamido*-4′-*methyldiphenylsulphone*, m. p. 129—130° after repeated crystallisation from alcoholic dioxan (Found : N, 6·4. $C_{20}H_{18}O_6N_2S_2$

requires N, 6·3%). Hydrolysis of this product with concentrated sulphuric acid yielded the required *amine* (yellow needles, m. p. 184°, from acetic acid).

(*B*) The same amine (m. p. and mixed m. p. 184—185°) was obtained from (V) and alcoholic ammonia in the way already described for the phenyl homologue (Found: N, 9·7. $C_{13}H_{12}O_4N_2S$ requires N, 9·6%).

*4-Chloro-3-nitrodiphenylsulphone* (X).—(*A*) 3-Nitro-4-aminodiphenylsulphone was subjected to Hodgson and Walker's modification of the Sandmeyer reaction (J., 1933, 1620). The product formed pale yellow needles, m. p. 127°, from alcoholic dioxan. (*B*) 4-Chloro-3-nitrobenzenesulphonyl chloride, prepared by nitration of *p*-chlorobenzenesulphonyl chloride as described by Davies and Wood (J., 1928, 1125) but with the use of nitric acid (*d* 1·53), melted at 61—62° (from light petroleum) instead of 39—40° (*loc. cit.*). Fischer (*Ber.*, 1891, **24**, 3188) gives m. p. 40—41°, whereas Pollak and Katscher (*Monatsh.*, 1930, **55**, 371) find the value 59—60° (Found: N, 5·4. Calc.: N, 5·5%). The sulphonyl chloride (6 g.), aluminium chloride (6 g.), and benzene (10 c.c.) were heated on the water-bath for 1 hour. The semi-solid mass obtained on cooling and addition to water was extracted with hot acetic acid, from which the required product separated, m. p. and mixed m. p. with (*A*) 125—126° after purification (Found: N, 4·8. $C_{12}H_8O_4NClS$ requires N, 4·7%). Treatment with piperidine in the usual way gave the piperidino-derivative (IV; X = $NC_5H_{10}$), m. p. and mixed m. p. with the piperidino-compound prepared from (II) 132—133°. Digestion with aqueous alkali yielded the phenol, m. p. and mixed m. p. 137°, and with alcoholic sodium ethoxide, the ethyl ether, m. p. and mixed m. p. 147—148°.

*4-Chloro-3-nitro-4'-methyldiphenylsulphone* was prepared as described for (X, *A*) and gave corresponding halogen replacements; m. p. 120° (from alcohol) (Found: N, 4·6. $C_{13}H_{10}O_4NClS$ requires N, 4·5%).

*2-Chloro-5-nitrodiphenylsulphone* (XIII) was prepared from the sulphonyl chloride (XII) in the usual way (cf. X, *B*) and crystallised from dioxan in long silky needles, m. p. 174° (Found: N, 4·9. $C_{12}H_8O_4NClS$ requires N, 4·7%). Treatment with piperidine gave *5-nitro-2-piperidinodiphenylsulphone* in yellow plates, m. p. 178° (Found: N, 8·1. $C_{17}H_{18}O_4N_2S$ requires N, 8·1%).

*4-Chloro-3'-nitrodiphenylsulphone* (XV).—(*A*) Solutions of 4-chlorodiphenylsulphone (2·5 g.) and potassium nitrate (1 g.) in concentrated sulphuric acid (5 c.c. each) were mixed at 10° and, after 12 hours, poured into water. The solid was crystallised repeatedly from acetic acid. (*B*) *m*-Nitrobenzenesulphonyl chloride (2 g.), chlorobenzene (3 c.c.), and aluminium chloride (2 g.), treated in the usual way, gave the same *product* in colourless needles, m. p. 139—140° (Found: N, 4·9. $C_{12}H_8O_4NClS$ requires N, 4·7%).

*4-Chloro-3 : 3'-dinitrodiphenylsulphone* (XVI) was prepared in similar fashion from the mononitro-sulphone (XV) (3 g.), sulphuric acid (9 c.c.), and potassium nitrate (1 g.) or by direct dinitration; m. p. 146° (from acetic acid) (Found: N, 8·3. $C_{12}H_7O_6N_2ClS$ requires N, 8·2%). The *piperidino*-derivative was obtained in salmon-coloured leaflets, m. p. 151—152° (Found: N, 10·7. $C_{17}H_{17}O_6N_3S$ requires N, 10·7%).

*3 : 3'-Dinitro-4-aminodiphenylsulphone*, prepared from (XVI) and methyl-alcoholic ammonia (cf. IX, *B*), had m. p. 238° (from ethylene glycol) (Found: N, 13·2. $C_{12}H_9O_6N_3S$ requires N, 13·0%).

The following compounds were prepared in a similar way from 4-chloro-4'-methyldiphenylsulphone: *4-chloro-3'-nitro-4'-methyldiphenylsulphone*, m. p. 103° (Found: N, 4·6. $C_{13}H_{10}O_4NClS$ requires N, 4·5%); *4-chloro-3 : 3'-dinitro-4'-methyldiphenylsulphone*, m. p. 152° (Found: N, 7·9. $C_{13}H_9O_6N_2ClS$ requires N, 7·85%); *3 : 3'-dinitro-4-piperidino-4'-methyldiphenylsulphone*, m. p. 149—150° (Found: N, 10·4. $C_{18}H_{19}O_6N_3S$ requires N, 10·4%); and *3 : 3'-dinitro-4-amino-4'-methyldiphenylsulphone*, m. p. 231° (Found: N, 12·5. $C_{13}H_{11}O_6N_3S$ requires N, 12·5%).

By heating equimolecular proportions of sodium benzene- or *p*-toluene-sulphinate in aqueous alcohol (or dioxan) with the requisite chloronitro-compound (X, XVI, XVII) for 30—60 minutes, the following disulphones were prepared; they were purified by crystallisation from acetic acid: 1-nitro-2 : 5-diphenylsulphonyl- and -2 : 5-di-*p*-tolylsulphonyl-benzene; *1-nitro-5-phenylsulphonyl-2-p-tolylsulphonylbenzene*, m. p. 180° (Found: N, 3·6. $C_{19}H_{15}O_6NS_2$ requires N, 3·4%); *1-nitro-2-phenylsulphonyl-5-p-tolylsulphonylbenzene*, m. p. 212° (Found: N, 3·5. $C_{19}H_{15}O_6NS_2$ requires N, 3·4%); *1-nitro-2-phenylsulphonyl-5-m-nitrophenylsulphonylbenzene*, m. p. 233° (from *cyclo*hexanone) (Found: N, 6·4. $C_{18}H_{12}O_8N_2S_2$ requires N, 6·25%); and *1-nitro-5-m-nitrophenylsulphonyl-2-p-tolylsulphonylbenzene*, m. p. 232° (Found: N, 6·0. $C_{19}H_{14}O_8N_2S_2$ requires N, 6·1%).

Exchanges between the 2-arylsulphonyl groups were effected in dioxan solution as previously described (J., 1935, 537), the reactions here requiring 30 minutes' heating to attain equilibrium.

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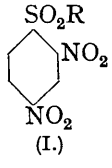
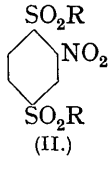
# 43. *The Mobility of Groups in Certain Nitrodiphenylsulphones.*

By James D. Loudon and Thomas D. Robson.

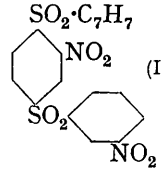
When cationoid reactivity is displayed by nitrobenzene derivatives the reactive centres are generally those situated *o*- or *p*- to the nitro-group which, among *m*-directing groups, is pre-eminent in its power to produce activation of this type. It has, nevertheless, been observed in certain isolated cases, where in the same molecule the effects of a nitro- and of a second activating group appear to be in competition with each other, that either the nitro-group itself (*e.g.*, *o*- and *p*-nitrocyanobenzenes, Reinders and Ringer, *Rec. trav. chim.*, 1899, **18**, 326, 330; 2-chloro-4-nitrobenzaldehyde, Tiemann, *Ber.*, 1891, **24**, 709; 2 : 4 : 6-trinitrobenzylideneaniline, Secareanu, *Ber.*, 1931, **64**, 837) or another substituent *o*- or *p*- to the second group (*e.g.*, 2 : 6-dichloro-4-nitrobenzenediazonium hydroxide; Witt, *Ber.*, 1909, **42**, 2957) undergoes replacement. This apparent transference of activation control or of activated centre is probably occasioned, in part at least, by reluctance of the second activating group itself to undergo replacement, and the point is aptly illustrated by the behaviour of 2 : 4-dinitrodiphenylsulphones (I), in which, by use of sulphinates as reagents, virtual immobility may be conferred on the otherwise labile sulphonyl group and production of (II) results (Loudon, J., 1936, 218; R = *p*-tolyl and phenyl). Other circumstances both internal and external to the molecule may be expected to contribute in determining the locus and degree of mobility displayed, and we have sought further information by extending the reaction (I ⟶ II), and by examining the effects produced on the mobility by certain modifications of the structure (I).



(I.)



(II.)

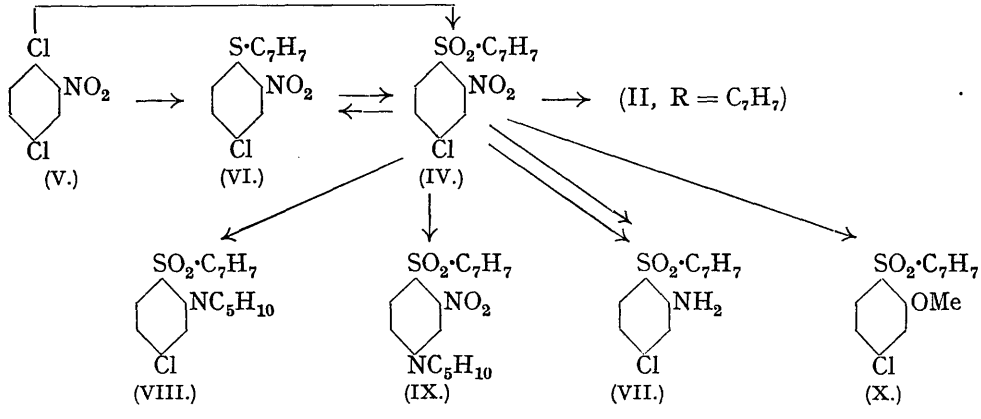


(III.)

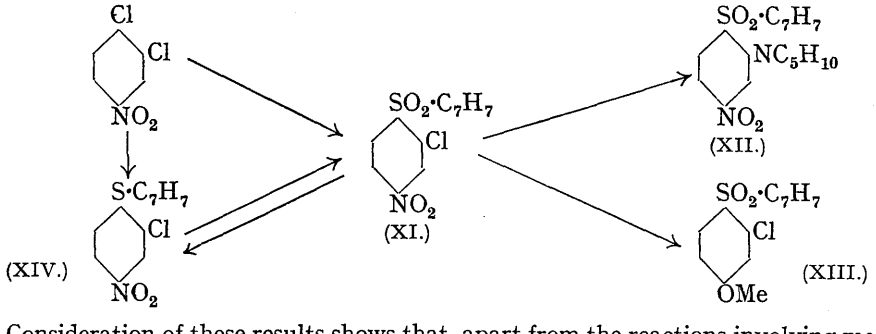
Under equilibrium conditions the ease with which sulphonyl groups replace each other may be represented by the order *p*-$CH_3 \cdot C_6H_4 \cdot SO_2 > C_6H_5 \cdot SO_2 > p$-$C_6H_4Cl \cdot SO_2 > m$-$NO_2 \cdot C_6H_4 \cdot SO_2$ $> 2 : 5$-$C_6H_3Cl_2 \cdot SO_2$ (J., 1935, 896), and we have found that the same qualitative order also represents the speeds of reactions (I ⟶ II). For instance, 4-chloro-2 : 4-dinitrodiphenylsulphone (I, R = $C_6H_4Cl$) with sodium *p*-chlorobenzenesulphinate yielded (II, R = $C_6H_4Cl$), identical with a specimen synthesised from chlorobenzene and 4-chloro-3-nitrobenzenesulphonyl chloride, followed by condensation with the sulphinate. On the other hand, with R = 2 : 5-dichlorophenyl, no disulphonyl compound (II) could be detected even under more intense reaction conditions. The reaction of sodium *p*-toluenesulphinate on (III) was selected as a favourable case for investigating the replacement of a sulphonyl group instead of a nitro-group as potential anion. Under comparable conditions, however, no reaction took place and prolonged treatment caused destruction of the materials.

Interesting results were obtained by extending the investigation to the *halogen* compound (IV), which was prepared either directly from (V) or *via* the *sulphide* (VI). It was found that, according to the reagent employed, any one of the three potential anions could be replaced. With sodium *p*-toluenesulphinate the chlorine atom was replaced, (II,

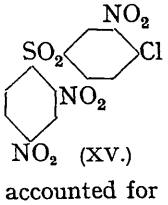
R = $C_7H_7$) being formed as readily as from (I). Methyl-alcoholic ammonia effected replacement of the nitro-group, the isolated *amine* (VII) being identical with the product of reduction. The sulphonyl group was replaced, with regeneration of (VI), by the action of *p*-thiocresol in presence of alkali. Further, brief treatment of (IV) with hot piperidine gave two separate *piperidino*-derivatives (VIII) and (IX)—4-chloro-2-nitropiperidinobenzene was obtained by Lellman and Geller (*Ber.*, 1888, **21**, 2283) from (V)—and finally, by the action of sodium methoxide on (IV), the nitrogen-free *ether* (X) was produced.




Slightly different results were obtained by the action of the same reagents on the isomeric *chloronitrosulphone* (XI). In this case no product could be isolated from the reaction with sodium *p*-toluenesulphinate, and with piperidine, only one *piperidino*-derivative (XII) was obtained, though here, as indeed in several other cases (cf. Experimental), indications were found that reaction was not confined to one centre. In contrast to the behaviour of (IV), treatment of (XI) with methyl-alcoholic ammonia yielded, instead of an amine, the *ether* (XIII), also obtained with sodium methoxide as reagent, and this resistance to attack by ammonia was further shown by recovery of the material (XI) unchanged from boiling acetamide (procedure, cf. Kym, *Ber.*, 1899, **32**, 3539). The reaction with *p*-thiocresol in presence of alkali was analogous to that found in the previous case, the *sulphide* (XIV) being formed.

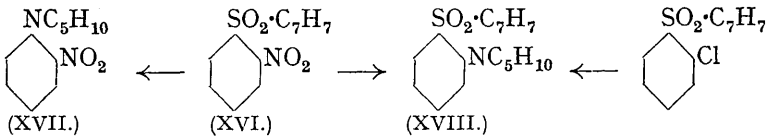



Consideration of these results shows that, apart from the reactions involving mercaptide (cf. also XX ⟶ XXI, below), the groups replaced are those situated *o*- and *p*- to the sulphonyl group. This differentiation between mercaptide and the other reagents is paralleled by work still unpublished and by experiments with (XV). Here with piperidine preferential replacement of chlorine occurs (J., 1935, 537), whereas with a slight deficiency of mercaptide there resulted only 2 : 4-dinitrophenyl *p*-tolyl sulphide (m. p. and mixed m. p.) with mere traces of ionisable halogen. In the other reactions it is important to note that the mobility is pronounced and is not adequately accounted for by the activating power of the sulphone group alone. Thus, quantitative

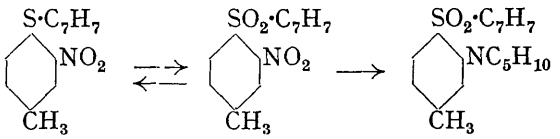


(XV.)

comparison of the mobilities displayed by chlorine in *o*-, *m*-, and *p*-chlorophenylmethylsulphones with those in the corresponding chloronitrobenzenes (Todd and Shriner, *J. Amer. Chem. Soc.*, 1934, **56**, 1382) shows that the former compounds are decidedly less reactive and, qualitatively, we have also found that formation of (IX) and (XII) occurs very much more readily than the reaction between piperidine and *o*- or *p*-chlorophenyl-*p*-tolylsulphone. The reaction between piperidine and *o*-nitrophenyl-*p*-tolylsulphone (XVI) was also relatively slow and, moreover, gave rise to two *products* (XVII) and (XVIII).

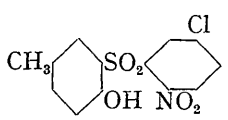



(XVII.) (XVI.) (XVIII.)




(XXI.) (XX.) (XIX.)

This concurrent replacement of sulphonyl and nitro-groups by piperidine raises the question why, in similar treatment of (IV), the sulphonyl group has survived. It seems probable that partial answers may be found in the activating influence of an *op*-directing group on a potential anion in the *m*-position (Kenner, J., 1914, **105**, 2728; 1922, **121**, 489), and also in the complementary stabilisation of substituents in the *o*- and *p*-positions. For example, we could isolate only one *product* (XIX) from the action of piperidine on the *sulphone* (XX), which differs from (IV) in having methyl in place of chlorine—an alteration, incidentally, causing here, as in other recorded cases (cf. Ibbotson and Kenner, J., 1923, **123**, 1265), marked decrease in the degree of mobility displayed. With alkaline *p*-thiocresol, (XX) gave the *thioether* (XXI), but was recovered unchanged from heating with sodium methoxide in methyl alcohol. It is obvious that the reactivity of these systems is sensitive to a variety of influences and it may be noted that replacement of the nitro- in preference to the sulphonyl group in the majority of the reactions with (IV) is in contrast to the behaviour of (XXII) and similar sulphones studied by Smiles and his co-workers (*e.g.*, J., 1932, 2774; 1934, 422; 1935, 181). In presence of alkali the facile reaction here is an intramolecular replacement of sulphonyl by the phenoxy-group, and thioxin ring formation is apparently of a secondary order.




(XXII).

It is hoped to make a more detailed study of certain aspects of the present work and further discussion is meantime postponed.

## Experimental.

**4 : 4′-*Dichloro*-3-*nitrodiphenysulphone*.**—(A) Aluminium chloride (3 g.) was added to a hot solution of 4-chloro-3-nitrobenzenesulphonyl chloride (4 g.) in chlorobenzene (2 c.c.), and the mixture heated (100°) for 1 hour. The product obtained after cooling and pouring into water crystallised from alcohol or acetone in colourless prisms, m. p. 130°. (B) The same *compound* was obtained together with dinitrated material (cf. Groves and Turner, J., 1929, 509) from 4 : 4′-dichlorodiphenylsulphone (1·5 g.) in sulphuric acid (20 c.c.) by cautious addition of potassium nitrate (0·53 g.) dissolved in sulphuric acid (10 c.c.), the resulting mixture being fractionally crystallised from acetone (Found : N, 4·5. $C_{12}H_7O_4NCl_2S$ requires N, 4·3%).

**4′-*Chloro*-3-*nitro*-4-*piperidinodiphenysulphone***, m. p. 80°, was prepared from the last compound in the usual way and was purified by slow cooling of its alcoholic solution from room temperature to 0° (Found : N, 7·5. $C_{17}H_{17}O_4N_2ClS$ requires N, 7·4%).

**1-*Nitro*-2 : 5-*di*-p-*chlorobenzenesulphonylbenzene***.—(A) 4 : 4′-Dichloro-3-nitrodiphenylsulphone (1 mol.) and sodium *p*-chlorobenzenesulphinate (1 mol.) were refluxed in aqueous alcohol for 1 hour. (B) 4′-Chloro-2 : 4-dinitrodiphenylsulphone (0·5 g.) and the sulphinate (2 g.) were boiled in ethylene glycol solution for a few minutes. In each case after precipitation of the product

with water and crystallisation from acetic acid the same *compound* was obtained in colourless felted needles, m. p. 231°, yielding the above piperidino-derivative on treatment with hot piperidine (Found : Cl, 14·9. $C_{18}H_{11}O_6NCl_2S_2$ requires Cl, 15·1%).

4-*Chloro*-2-*nitro*-4'-*methyldiphenyl Sulphide* (VI).—2 : 5-Dichloronitrobenzene (1·9 g.) in hot alcohol (10 c.c.) was treated with an alcoholic solution of *p*-thiocresol (1·24 g.) and sodium hydroxide (0·4 g.). Separation of the *product* commenced almost at once, but the mixture was warmed for some time before being allowed to cool. The resulting solid crystallised from acetic acid in large orange prisms, m. p. 121° (Found : N, 5·2. $C_{13}H_{10}O_2NClS$ requires N, 5·0%).

The same product was formed by similar treatment of the sulphone (IV).

4-*Chloro*-2-*nitro*-4'-*methyldiphenylsulphone* (IV).—(A) The sulphide (VI) was oxidised in acetic acid solution with an excess of hydrogen peroxide; the *product*, which partly separated on cooling, crystallised from alcohol in long needles, m. p. 124° (Found : N, 4·4. $C_{13}H_{10}O_4NClS$ requires N, 4·5%). (B) Molecular proportions of 2 : 5-dichloronitrobenzene and sodium *p*-toluenesulphinate were heated in the minimum quantity of ethylene glycol for 2 hours. The gummy solid which formed on cooling was fractionated from alcohol and yielded the soluble sulphone (IV) and the sparingly soluble 1-nitro-2 : 5-di-*p*-tolylsulphonylbenzene (II, R = $C_7H_7$; m. p. and mixed m. p. 220°). The latter compound was also formed by brief treatment of the sulphone (IV) with the sulphinate in boiling glycol.

2-*Chloro*-4-*nitro*-4'-*methyldiphenyl sulphide* (XIV), m. p. 122° (Found : N, 5·0. $C_{13}H_{10}O_2NClS$ requires N, 5·0%), and the corresponding *sulphone* (XI), m. p. 125° (Found : N, 4·4. $C_{13}H_{10}O_4NClS$ requires N, 4·5%), were produced by the methods described for their isomers.

2-*Nitro*-4-*piperidino*-4'-*methyldiphenylsulphone* (IX).—The sulphone (IV) was boiled for 3 minutes with excess of piperidine and, after cooling, addition of water yielded a solid which partly dissolved in cold concentrated hydrochloric acid and partly formed a colourless, sparingly soluble residue (hydrochloride?), readily hydrolysed by water to a yellow *solid*. The latter crystallised from alcohol in yellow plates, m. p. 183° (Found : N, 7·8. $C_{18}H_{20}O_4N_2S$ requires N, 7·8%).

4-*Chloro*-2-*piperidino*-4'-*methyldiphenylsulphone* (VIII).—The hydrochloric acid solution from the last experiment was neutralised with dilute aqueous ammonia and the precipitated solid was crystallised from alcohol. After removal of a small quantity of the yellow solid (IX, m. p. 180°) which separated first, the mother-liquor on dilution with water gave fine colourless needles, m. p. 121° after recrystallisation (Found : N, 4·3. $C_{18}H_{20}O_2NClS$ requires N, 4·0%).

4-*Nitro*-2-*piperidino*-4'-*methyldiphenylsulphone* (XII).—The sulphone (XI) was treated with piperidine in the usual way. The *product* crystallised from alcohol in lemon-yellow needles, m. p. 171°. Although no other product could be identified, both chloride and nitrite ions were formed in the reaction (Found : N, 7·7. $C_{18}H_{20}O_4N_2S$ requires N, 7·8%).

4-*Chloro*-2-*amino*-4'-*methyldiphenylsulphone* (VII).—(A) The sulphone (IV) was reduced with stannous chloride and hydrochloric acid in alcohol (cf. J., 1936, 220); the product crystallised from alcohol in colourless plates, m. p. 136°. (B) Treatment of the sulphone (2 g.) with methyl alcohol (10 c.c.) and concentrated aqueous ammonia (3 c.c.) at 150° for 10 hours gave the same *product*, m. p. and mixed m. p. 135—136°. Chloride and nitrite ions were formed in the process (Found : N, 5·2. $C_{13}H_{12}O_2NClS$ requires N, 5·0%).

2-*Chloro*-4-*amino*-4'-*methyldiphenylsulphone*, m. p. 165°, was obtained by reduction of the corresponding nitro-compound with stannous chloride and hydrochloric acid (Found : N, 5·1. $C_{13}H_{12}O_2NClS$ requires N, 5·0%).

4-*Chloro*-2-*methoxy*-4'-*methyldiphenysulphone* (X).—The sulphone (IV) was refluxed in a methyl-alcoholic solution of sodium methoxide for 15 minutes. Addition of water yielded a yellowish *solid*, which crystallised from alcohol (charcoal!) in colourless needles, m. p. 117°. Chloride ions were also formed in the reaction (Found : Cl, 12·1; S, 11·2. $C_{14}H_{13}O_3ClS$ requires Cl, 12·0; S, 10·8%).

2-*Chloro*-4-*methoxy*-4'-*methyldiphenylsulphone* (XIII) was similarly prepared from (XI) and was the only product which could be isolated from the action of methyl-alcoholic ammonia on (XI) (procedure as for VII B); m. p. 118° (Found : Cl, 12·2; S, 11·1. $C_{14}H_{13}O_3ClS$ requires Cl, 12·0; S, 10·8%).

2-*Chloro*-4'-*methyldiphenylsulphone*.—2-Amino-4'-methyldiphenylsulphone was subjected to Hodgson and Walker's modification of the Sandmeyer reaction (J., 1933, 1620). The *product*, which was rather difficult to purify, was repeatedly crystallised from alcohol, forming plates, m. p. 113° (Found : C, 58·3; H, 4·4. $C_{13}H_{11}O_2ClS$ requires C, 58·5; H, 4·1%).

2-*Piperidino*-4'-*methyldiphenylsulphone* (XVIII), m. p. 118° (from alcohol) (Found : N, 4·55. $C_{18}H_{21}O_2NS$ requires N, 4·4%), and 4-*piperidino*-4'-*methyldiphenylsulphone*, m. p. 134° (from

alcohol) (Found : N, 4·5%), were obtained by refluxing the corresponding chlorosulphones with piperidine (6 c.c. per 1 g.) for 2—3 hours (or by heating for shorter periods in sealed tubes at 160°), followed by extraction of the product with hydrochloric acid.

*Action of Piperidine on 2-Nitro-4′-methyldiphenylsulphone.*—The reagents were refluxed for 1½ hours, and the product extracted with concentrated hydrochloric acid. A quantity of unchanged sulphone was removed. The solid obtained by treating the extract with ammonia was slowly crystallised from alcohol, forming a mixture of red and pale yellow crystals which were separated by hand. The red variety after further purification melted at 73°, mixed m. p. 75° with authentic 2-nitropiperidinobenzene. The yellow crystals after several crystallisations from alcohol became colourless, m. p. 114°, and were identified (mixed m. p. 114—116°) as 2-piperidino-4′-methyldiphenylsulphone.

Similar treatment of 4-nitro-4′-methyldiphenylsulphone produced much tarry matter and very little acid-soluble material. The bulk of the sulphone was recovered unchanged.

*2-Nitrodi-*p*-tolyl sulphide* (XXI) was obtained in the usual way from 4-chloro-3-nitrotoluene (or the sulphone XX), *p*-thiocresol, and sodium hydroxide; it formed yellow plates, m. p. 116° (Found: N, 5·5. $C_{14}H_{13}O_2NS$ requires N, 5·4%).

*2-Nitrodi-*p*-tolylsulphone* (XX), m. p. 132°, was formed when (XXI) was oxidised with hydrogen peroxide in acetic acid (Found : N, 4·85. $C_{14}H_{13}O_4NS$ requires N, 4·8%).

*2-Piperidinodi-*p*-tolylsulphone* (XIX).—The sulphone (XX) was refluxed with excess of piperidine for 1½ hours. The *product*, obtained by the usual procedure, crystallised from aqueous alcohol in colourless prisms, m. p. 148° (Found : N, 4·4. $C_{19}H_{23}O_2NS$ requires N, 4·25%).

Our thanks are due to the Chemical Society for a grant and to Mr. J. M. L. Cameron, who carried out micro-nitrogen estimations on several of the compounds described.

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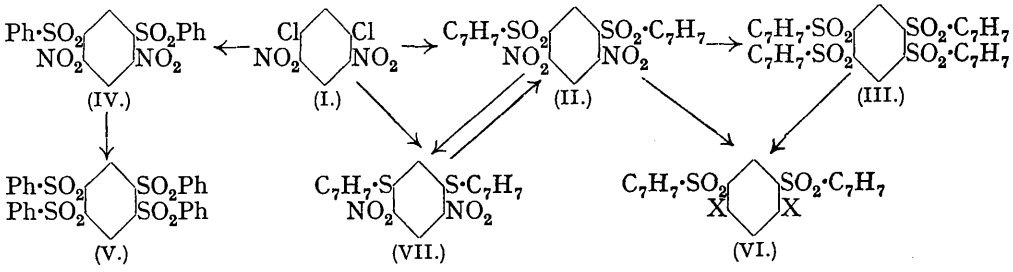
## 44. *The Action of Sulphinates on* 1 : 5-*Dichloro*-2 : 4-*dinitrobenzene.*

By A. Livingston and J. D. Loudon.

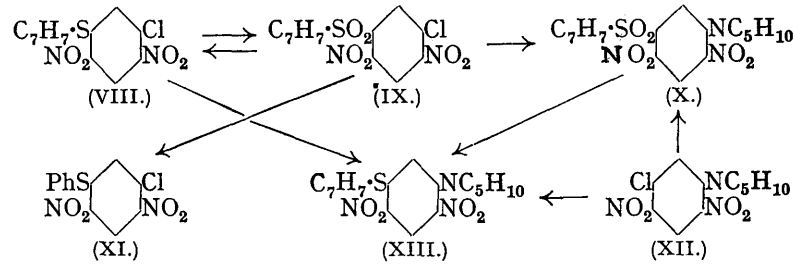
One interesting feature attending the use of sulphinates in displacing suitably activated substituents from a benzene nucleus consists in the fact that the sulphonyl groups so introduced may in turn activate new centres in the molecule and thus lead to further reaction. For instance, treatment of 2 : 4-dinitrochlorobenzene with sodium benzenesulphinate yields first 2 : 4-dinitrodiphenylsulphone and then 2 : 5-diphenylsulphonylnitrobenzene (Loudon, J., 1936, 218). Moreover, although the activating power of a single sulphonyl group may be slight (in comparison with nitro), yet by analogy with similar cases established by Schöpff and his co-workers (*Ber.*, 1891, **24**, 3771, 3785) it is to be anticipated that the combined effects of two such groups situated *meta* to each other will be considerable. From these points of view the action of sodium *p*-toluenesulphinate on 1 : 5-dichloro-2 : 4-dinitrobenzene (I) provides a case of particular interest, since here the arrangement of groups is such that ultimate production of tetra-*p*-tolylsulphonylbenzene may be expected. Experiment, in fact, showed that even under relatively mild conditions reaction proceeds beyond stage (II), yielding a mixture of sulphones from which the *tetrasulphone* (III) was isolated. The most interesting of the intermediate products, the *disulphonyl* compound (II), was obtained by employing in the reaction the free sulphinic acid instead of its salt—a modification which was unnecessary in the phenyl series (I $\longrightarrow$ IV $\longrightarrow$ V), since here under similar conditions the weaker replacing power of the benzenesulphinate (cf. J., 1935, 896) permitted isolation of (IV), the *tetrasulphone* (V) being formed only at higher temperatures.

The reactions of (II) with ammonia and piperidine also show the mobility of both nitro-groups. With the former reagent (II) and (III) each gave the *diamine* (VI, X = $NH_2$), also prepared from (II) by reduction, and similarly the *dipiperidino*-derivatives produced from (II) and (III) were identical (VI, X = $NC_5H_{10}$). On the other hand the sodium salt of *p*-thiocresol reacted with (II) to give the *dinitro-dithioether* (VII), directly obtained with this reagent from (I), thus providing another instance of the preferential replacement of

sulphonyl by mercaptide groups (cf. preceding paper). A similar selective action was also observed in the reactions of the *chlorodinitro-sulphone* (IX), which was obtained by oxidation of the *monothioether* (VIII) produced together with (VII) from (I). With theoretical




amounts of the reagents the chlorine atom was replaced by piperidine (IX ⟶ X), whereas alkaline *p*-thiocresol replaced the toluenesulphonyl group (IX ⟶ VIII). Since in reactions of the latter type the products might result from some unusual reduction of the sulphone group, we examined also the action of alkaline thiophenol on (IX) and, in harmony with the replacement view, obtained the *phenyl thioether* (XI), also directly prepared from (I). The other replacements depicted in the following scheme confirm the nature of the products referred to.




The results recorded here lend further support to the criticisms already advanced (Le Fèvre and Turner, J., 1927, 1114, and refs. given) against the conclusions of Borsche and Bahr (*Annalen*, 1913, **402**, 81), *viz.*, that there exists a fundamental difference in the mobilities of the two chlorine atoms in (I) [and correspondingly, in those of the nitro-groups in (II)]. Indeed, the ease with which both chlorine atoms are replaced renders difficult any qualitative assessment of the effect of the first replacement on the reactivity of the residual halogen. For this purpose, however, advantage was taken of the low replacing power of free *p*-toluenesulphinic acid as reagent and it was found that, of the compounds (IX) and (VIII or XII)—respectively derived from (I) by replacing one chlorine atom by a *m*-directing group on the one hand, and by a more powerful *op*-directing group (relative to Cl) on the other—the chlorine of (IX) alone underwent replacement This result may be compared with the reappearance of suppressed halogen mobility following acetylation of certain chloronitroanilines (Lindemann and Pabst, *Annalen*, 1928, **462**, 24), and also with the fact that in the formation of (X) from (IX) by the action of piperidine the sulphonyl group has survived reaction conditions which occasion its replacement in the corresponding dinitrodiphenylsulphones (X; $NC_5H_{10}$ replaced by H) (J., 1935, 537).

## Experimental.

2 : 4-*Dinitro*-1 : 5-*di*-p-*tolylthiobenzene* (VII).—*p*-Thiocresol (2 mols.) and 1 : 5-dichloro-2 : 4-dinitrobenzene (1 mol.), dissolved in alcohol, were treated with a 10% solution of sodium hydroxide (2 mols.). The solid *product*, after crystallisation from acetic acid, formed yellow plates, m. p. 233° (Found : N, 7·0. $C_{20}H_{16}O_4N_2S_2$ requires N, 6·8%).

5-*Chloro*-2 : 4-*dinitro*-4′-*methyldiphenyl sulphide* (VIII) was obtained, after removal of (VII), as the more soluble product of a similar experiment in which molecular proportions of the

reagents were used and the temperature was maintained below 10°. It formed yellow needles, m. p. 147—148° (from alcohol) (Found : N, 8·75. $C_{13}H_9O_4N_2ClS$ requires N, 8·6%).

2 : 4-*Dinitro*-1 : 5-*diphenylthiobenzene*, needles, m. p. 253° (Found : N, 7·4. $C_{18}H_{12}O_4N_2S_2$ requires N, 7·3%), and 5-*chloro*-2 : 4-*dinitrodiphenyl sulphide*, needles, m. p. 108° (Found : N, 9·0. $C_{12}H_7O_4N_2ClS$ requires N, 9·0%), were similarly prepared by means of thiophenol.

2 : 4-*Dinitro*-1 : 5-*di*-p-*tolylsulphonylbenzene* (II).—(A) The dithioether (VII) was oxidised by heating with excess of hydrogen peroxide in acetic acid solution for 2 hours at 100°. (B) *p*-Toluenesulphinic acid (2 g.) and 1 : 5-dichloro-2 : 4-dinitrobenzene (1·5 g.) were refluxed in alcohol (30 c.c.) for 30 minutes. In each case the *product*, after crystallisation from acetic acid, melted at 228° (Found : S, 13·3. $C_{20}H_{16}O_8N_2S_2$ requires S, 13·45%). Treatment of its alcoholic dioxan solution as described under (VII, above) gave the dithioether (VII), m. p. and mixed m. p. 233°.

2 : 4-*Dinitro*-1 : 5-*diphenylsulphonylbenzene* (IV), m. p. 251°, was obtained by similar methods (Found : S, 14·5. $C_{18}H_{12}O_8N_2S_2$ requires S, 14·3%).

1 : 2 : 4 : 5-*Tetra*-p-*tolylsulphonylbenzene* (III).—1 : 5-Dichloro-2 : 4-dinitrobenzene (2 g.) in warm alcohol (30 c.c.) and sodium *p*-toluenesulphinate (6 g.) in hot water (18 c.c.) were mixed and refluxed for 1 hour. The precipitate which rapidly formed melted indefinitely at 279° and was similar to that produced when (II) was heated (1 hour) with the sulphinate in acetic acid. Each product was partially purified (m. p. 306°) by crystallisation from methyl ethyl ketone, but residual nitro-compounds were best removed by reduction with stannous chloride and concentrated hydrochloric acid (9 g. and 100 c.c. respectively per 1·5 g. of material) in acetone (300 c.c.), followed by treatment with 20% sodium hydroxide solution (150 c.c.) and extraction of the solid with acetone. After crystallisation from methyl ethyl ketone the *product*, m. p. 315°, was free from nitrogen (micro-Dumas) (Found : S, 18·1. $C_{34}H_{30}O_8S_4$ requires S, 18·4%).

1 : 2 : 4 : 5-*Tetraphenylsulphonylbenzene* (V) was prepared by refluxing (IV) in acetic acid–ethylene glycol (1 : 1) with sodium benzenesulphinate (5 mols.) for a few minutes, heating being stopped when colour began to be developed. On cooling, the *product* separated; it crystallised from methyl ethyl ketone in colourless needles (nitrogen-free), m. p. 305° (Found : S, 19·8. $C_{30}H_{22}O_8S_4$ requires S, 20·0%).

2 : 4-*Diamino*-1 : 5-*di*-p-*tolylsulphonylbenzene* (VI, X = $NH_2$).—(A) Either (II) or (III) in methyl alcohol (20 c.c. per 2 g.) was heated in a sealed tube at 150° with concentrated aqueous ammonia (3 c.c., *d* 0·88) for 3 hours; cream-coloured needles were deposited on cooling. These were washed with boiling acetone and were obtained colourless by crystallisation from ethylene glycol; m. p. 293°. (B) The same *compound* was obtained by reduction of (II) (2 g.) with stannous chloride (18 g.) and hydrochloric acid (20 c.c.) in alcohol (20 c.c.), followed by treatment with 20% sodium hydroxide solution (300 c.c.) and extraction of the solid with acetic acid (Found : N, 6·8. $C_{20}H_{20}O_4N_2S_2$ requires N, 6·7%).

2 : 4-*Dipiperidino*-1 : 5-*di*-p-*tolylsulphonylbenzene* (VI, X = $NC_5H_{10}$) was prepared by heating (II) or (III) with excess of piperidine for 2 minutes. The solution was cooled, water added, and the precipitated solid extracted with concentrated hydrochloric acid, from which the compound was reprecipitated by addition of water. The product formed yellow plates, m. p. 228° (from alcohol) (Found : N, 4·95. $C_{30}H_{36}O_4N_2S_2$ requires N, 5·0%).

2 : 4-*Dipiperidino*-1 : 5-*diphenylsulphonylbenzene*, m. p. 221°, was prepared from (IV) in the same way (Found : N, 5·45. $C_{28}H_{32}O_4N_2S_2$ requires N, 5·3%).

5-*Chloro*-2 : 4-*dinitro*-4′-*methyldiphenylsulphone* (IX) was prepared by oxidation of the sulphide with hydrogen peroxide in acetic acid; m. p. 198° (from acetic acid) (Found : N, 8·0. $C_{13}H_9O_6N_2ClS$ requires N, 7·9%). Treatment of an alcoholic dioxan solution of the compound with *p*-thiocresol (1 mol.) and 10% sodium hydroxide solution gave a mixture of mono- and di-thioethers (VIII and VII, separated as under VIII), whilst with thiophenol the corresponding phenyl derivatives were produced.

5-*Chloro*-2 : 4-*dinitrodiphenylsulphone*, m. p. 187°, was similarly prepared (Found : S, 9·4. $C_{12}H_7O_6N_2ClS$ requires S, 9·4%).

2 : 4-*Dinitro*-5-*piperidino*-4′-*methyldiphenylsulphone* (X) was obtained in felted orange-yellow needles, m. p. 180° (from alcohol), by refluxing an aqueous alcoholic solution of 5-chloro-2 : 4-dinitropiperidinobenzene (Le Fèvre and Turner, *loc. cit.*) and sodium *p*-toluenesulphinate. The same compound was formed by heating (IX) with excess of piperidine (Found : N, 10·3. $C_{18}H_{19}O_6N_3S$ requires N, 10·4%).

2 : 4-*Dinitro*-5-*piperidino*-4′-*methyldiphenyl sulphide* (XIII) was prepared by refluxing (VIII) in piperidine (1 hour) and also by treating (X) or (XII) in alcohol with *p*-thiocresol and sodium hydroxide in the usual way; it formed yellow plates, m. p. 192°, from alcoholic dioxan (Found : N, 11·2. $C_{18}H_{19}O_4N_3S$ requires N, 11·3%).

Compounds (IX), (VIII), and (XII) were each heated in acetic acid solution with *p*-toluene-

sulphinic acid (1 mol.). (IX) yielded 2 : 4-dinitro-1 : 5-di-*p*-tolylsulphonylbenzene (m. p. and mixed m. p.) and (VIII) and (XII) were recovered unchanged.

The authors acknowledge the tenure by one of them (A. L.) of a Donaldson Scholarship from this University.

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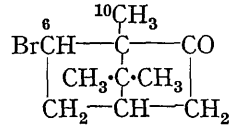
Additional Paper. I

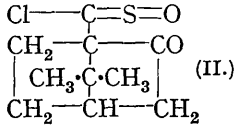
## 201. *Mercury Derivatives of Camphor. Part I. The Constitution of Reychler's Acid.*

By James D. Loudon.

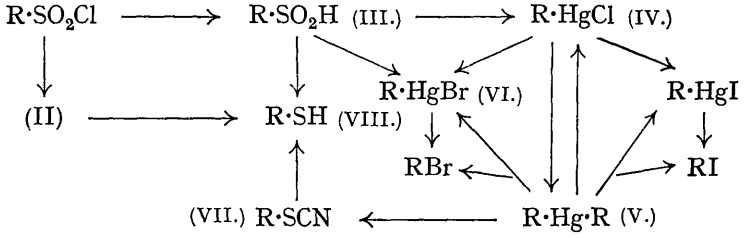
The sulpho-group of Reychler's camphorsulphonic acid has been assigned position 6 or 10 in the camphor nucleus. The evidence for the former rests upon the properties of "β"-bromocamphor obtained by thermal decomposition of the sulphonyl bromide and given the constitution (I) (Armstrong and Lowry, J., 1902, **81**, 1449; Forster, *ibid.*, p. 264; compare Burgess and Lowry, J., 1925, **127**, 271), whilst in support of the latter,

Wedekind, Schenk, and Stüsser (*Ber.*, 1923, **56**, 633) have shown that the chlorosulphoxide resulting from the action of pyridine on the sulphonyl chloride must have the structure (II).

(I.)



(II.)

In adopting these two compounds as criteria for the constitution of Reychler's acid, it has never been conclusively demonstrated that their formation from the parent acid is free from intramolecular change, for Wedekind, Schenk, and Stüsser (*loc. cit.*) were unable to characterise the reduction product of (II), and although Lipp and Lausberg (*Annalen*, 1924, **436**, 274) concluded that the bromine in (I) occupies the 10-position, their evidence depends on the validity of formulating the " dibromide " from camphene as 2 : 10-dibromocamphane.



R = camphor-10-radical.

It has now been found that mercury derivatives of camphor may be prepared from the sulphinic acids by the method devised by Peters in the aromatic series (*Ber.*, 1906, **39**, 3626), and the opportunity has been taken here to re-examine the constitutional relationships of the compounds mentioned above. Thus, as the diagram shows, the sulphinic acid (III) derived from Reychler's acid was converted into the mercurated camphors (IV) and (V), each of which on bromination yielded " β "-bromocamphor with intermediate formation of (VI). Iodination followed a similar course. Proof that the halogen occupies the same position as the original sulphur was obtained from the action of thiocyanogen on (V). Söderbäck (*Annalen*, 1919, **419**, 266) has shown that with diphenylmercury the products are phenyl mercurithiocyanate and phenyl thiocyanate; in the present case, without any attempt to isolate (VII), the product was reduced directly to the thiol (VIII) identical with that obtained from (III) (Drummond and Gibson, J., 1926, 3073). The same thiol resulted from the reduction of (II), thus establishing the constitutional similarity of the various compounds and, in conjunction with the oxidation of (II) to ketopinic acid (Wedekind, Schenk, and Stüsser, *loc. cit.*), also fixing position 10 in the camphor nucleus as the seat of substitution.

The misleading properties of " β "-bromocamphor must, therefore, be attributed to the peculiar position of the bromine atom in the molecule.

## Experimental.

Camphor-10-sulphinic acid was prepared either by the method of Hilditch (J., 1910, **97**, 1096) or by the more general procedure described by Krishna and Singh (*J. Amer. Chem. Soc.*, 1928, **50**, 792). In each case the product was an oil difficult to crystallise but directly applicable without disadvantage to the preparation of the mercury derivatives.

*Camphor-10-mercurichloride.*—Camphor-10-sulphinic acid (1 mol.) was heated for 4—5 hours with an alcoholic solution of mercuric chloride (2 mols.). The product was poured into water and after 12 hours the precipitate was collected, washed with alcohol, and extracted with hot chloroform. Concentration of the extract yielded *camphor-10-mercurichloride* contaminated with mercury salts, and a residue consisting of a variable quantity of oil containing some unchanged sulphinic acid and some disulphoxide. The mercurichloride was crystallised twice from alcohol to which a little chloroform had been added; m. p. 166°, $[\alpha]_{5461}^{18°}$ — 62·4° ($c$ = 10·32

in pyridine) (Found: Hg, 52·0; Cl, 9·0. $C_{10}H_{15}OClHg$ requires Hg, 51·8; Cl, 9·2%). The compound is slightly soluble in cold sodium hydroxide solution, is stable towards inorganic sulphides and cold dilute acids, but is decomposed by concentrated sulphuric acid.

*Biscamphor-10-mercury.*—The mercurichloride (12 g.), dissolved in hot acetone, was added to water (150 c.c.), and the suspension treated with alkaline stannous chloride (from 10 g. of sodium hydroxide, 8 g. of stannous chloride, and 200 c.c. of water). The mixture was stirred for 2 hours, and the solid was then collected and extracted with boiling acetone. On careful dilution with water and subsequent cooling, the product separated in crystalline form, m. p. 255—256°; $[\alpha]_{5461}^{18°}$ — 80·87° ($c$ = 10·14 in pyridine) (Found: Hg, 40·0. $C_{20}H_{30}O_2Hg$ requires Hg, 39·9%). When it was heated in alcoholic solution with mercuric halides (mol. proportions), the corresponding camphor mercurihalides resulted.

*Camphor-10-mercuribromide*, also prepared by the direct action of mercuric bromide on the sulphinic acid (compare above), had m. p. 156° (Found: Br, 18·5. $C_{10}H_{15}OBrHg$ requires Br, 18·5%). *Camphor-10-mercuri-iodide* had m. p. 146° (Found: I, 26·4. $C_{10}H_{15}OIHg$ requires I, 26·5%). The same compounds were formed together with the corresponding halogenated camphors (compare below) during bromination and iodination of biscamphor-10-mercury.

10-*Bromocamphor* (β-*Bromocamphor*).—Camphor-10-mercurichloride, suspended in an aqueous solution of bromine in potassium bromide, was shaken at 60° for 10 minutes. The resulting mixture was extracted with chloroform, and the extract washed with aqueous solutions of potassium sulphite and potassium carbonate, dried over calcium chloride, and concentrated. The crystalline product was recrystallised from alcohol; m. p. 77°; *oxime*, m. p. 156°, in accordance with the literature values. When the same reaction was conducted at the ordinary temperature, only camphor-10-mercuribromide resulted.

10-*Iodocamphor* was prepared by heating the mercurichloride (1 mol.) with iodine (1½ mols.) in benzene for 1 hour. The liquid was washed with potassium sulphite and carbonate solutions and, after drying, removal of the solvent yielded a crystalline product which was recrystallised from alcohol; m. p. 75° (Found: I, 45·6. $C_{10}H_{15}OI$ requires I, 45·7%). When the reaction was carried out in potassium iodide solution, the results were analogous to those in bromination, but the iodocamphor was less readily purified.

10-*Iodocamphoroxime* was prepared by the usual procedure and crystallised from alcohol; m. p. 158° (Found: I, 43·1. $C_{10}H_{16}ONI$ requires I, 43·3%).

*Camphor-10-thiol.*—(1) Biscamphor-10-mercury (5 g.) was kept for a week at room temperature with 40 c.c. of *N*-thiocyanogen in chloroform. After removal of the yellow precipitate, the filtrate was evaporated and the residual oil was dissolved in alcohol and reduced with zinc and hydrochloric acid for 1 hour. Thereafter the mixture was steam-distilled, the solid which collected in the receiver was shaken with sodium hydroxide, and after filtering from camphor (formed by reduction of camphor mercurithiocyanate) the thiol was precipitated with sulphuric acid. Crystallised from aqueous alcohol, the product had m. p. 66° (unaffected by admixture with an authentic specimen), gave the characteristic coloration (extracted by benzene) on treatment with aqueous-alcoholic nickel acetate (Drummond and Gibson, *loc. cit.*), and on titration with iodine yielded the disulphide, m. p. and mixed m. p. 225° (Lowry and Donnington, J., 1903, **83**, 479, give m. p. 224°). (2) 10-Chlorocamphor sulphoxide, prepared and purified as described by Wedekind, Schenk, and Stüsser (*loc. cit.*), was similarly reduced. Steam distillation yielded the same thiol, m. p. 65—66° after crystallisation; disulphide, m. p. 224°; nickel acetate test was positive.

The author acknowledges with gratitude his indebtedness to Professor T. S. Patterson and Dr. D. T. Gibson for their interest in this work, and to the latter also for the gift of a specimen of camphor-10-thiol.

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Additional Paper II.

# 123. *Mercury Derivatives of Camphor. Part II.*

By JAMES D. LOUDON.

THE successful application of Peters' reaction (*Ber.*, 1905, **38**, 2567), *viz.*,

$$R{\cdot}SO_2H + HgCl_2 \longrightarrow R{\cdot}HgCl + SO_2 + HCl$$

to the preparation of camphor-10-mercurichloride (Part I, J., 1933, 823) has led to investigation of other camphorsulphinic acids as sources of the related mercury derivatives. The results now obtained reveal marked differences in the reactivities of these acids towards mercuration. Thus, 3-chloro- and 3-bromo-camphor-10-sulphinic acids reacted with mercuric chloride to give yields of the corresponding mercury derivatives which were distinctly lower than that obtained from the unhalogenated acid under the same conditions. Considerable improvement has been effected by the use of pyridine as reaction medium or by employing the aqueous alkali sulphinates instead of the free acid (cf. " Organic Syntheses," III, p. 99)—both modifications being designed to protect the mercurated products from the attack of mineral acids formed in the reaction, and the former yielding slightly better results. On the other hand, 3-chloro- and 3-bromo-camphor-$\pi$-sulphinic acids, although much less stable than their " 10 " sulphinic analogues from the point of view of preservation, were so resistant to mercuration that evolution of sulphur dioxide was not perceptible and, at best, mere traces of mercurated products resulted. The investigation of these $\pi$-derivatives has consequently been abandoned.

The halogenated camphor-10-mercurichlorides were more stable than the parent substance to reduction by alkaline stannite solution, but their conversion into symmetrical mercury derivatives was readily accomplished by the action of copper gauze in pyridine (cf. Hein, Wagler, and Retter, *Ber.*, 1925, **58**, 1499).

## Experimental.

*3-Chlorocamphor-10-sulphinic Acid.*—3-Chlorocamphor-10-sulphonyl chloride (10 g.) was shaken for 3 hours with a concentrated solution of sodium sulphite (30 g. of the hydrate) and ice (20 g.). After precipitation by concentrated sulphuric acid the product separated from alcohol–chloroform in small compact crystals, m. p. 157° (decomp.) markedly affected by the rate of heating (Found: Cl, 14·3. $C_{10}H_{15}O_3ClS$ requires Cl, 14·2%).

*3-Bromocamphor-10-sulphinic acid* was prepared and purified in a similar way: m. p. 165° (decomp.) (Found: Br, 27·2. $C_{10}H_{15}O_3BrS$ requires Br, 27·1%).

*3-Chlorocamphor-π-sulphinic acid* was most conveniently prepared by adding the sulphonyl chloride in small quantities to a hot aqueous solution of sodium sulphite. After acidification of the cooled solution the product was obtained as a fine white powder, which melted with decomposition and could not be satisfactorily crystallised (Found: Cl, 14·0. $C_{10}H_{15}O_3ClS$ requires Cl, 14·2%).

*3-Bromocamphor-π-sulphinic acid*, prepared in the same way, had similar properties; m. p. 149° (decomp.) (Found: Br, 26·9. $C_{10}H_{15}O_3BrS$ requires Br, 27·1%).

*3-Chlorocamphor-10-mercurichloride.*—3-Chlorocamphor-10-sulphinic acid (9 g.) was refluxed with mercuric chloride (18 g.) in pyridine (30 c.c.) for 3 hours. The cooled solution, freed from metallic mercury, was cautiously added to an excess of dilute hydrochloric acid and the precipitate was collected, washed (finally with alcohol), dried, and extracted (Soxhlet) with chloroform, from which, on cooling, the pure compound separated in long needles, m. p. 218—219°. Yield, 40—50% of the theoretical $[\alpha]_{5461}^{16°} \pm 0·0°$ ($c = 1·24$ in pyridine), $+ 5·0°$ ($c = 1·00$ in chloroform) (Found: Hg, 47·3. $C_{10}H_{14}OCl_2Hg$ requires Hg, 47·5%).

*Bis-3-chlorocamphor-10-mercury.*—Copper gauze (5 g.) was kept in a solution of 3-chlorocamphor-10-mercurichloride (5 g.) in pyridine (30 c.c.) in a stoppered flask for 24 hours. After removal of the pyridine under reduced pressure, the semi-solid residue was shaken with concentrated aqueous ammonia and finally washed with water. The straw-coloured product was purified from alcohol–chloroform and then had m. p. 175°; $[\alpha]_{5461}^{16°} - 22·8°$ ($c = 1·14$ in pyridine) (Found: Hg, 35·2. $C_{20}H_{28}O_2Cl_2Hg$ requires Hg, 35·1%).

Treatment of acetone solutions of the compound with mercuric halides gave the corresponding mercurihalides, which were purified from alcohol–chloroform.

*3-Chlorocamphor-10-mercuribromide*, needles, m. p. 176° (Found: Hg, 43·1. $C_{10}H_{14}OClBrHg$ requires Hg, 43·1%), and *3-chlorocamphor-10-mercuri-iodide*, needles, m. p. 184° (Found: Hg, 39·1. $C_{10}H_{14}OClIHg$ requires Hg, 39·1%), were also prepared by shaking the mercurichloride at the ordinary temperature with bromine (iodine) in aqueous potassium bromide (iodide) solution.

Similar methods were employed for the corresponding 3-bromocamphor-10-mercury derivatives. *3-Bromocamphor-10-mercurichloride* was obtained from the sulphinic acid (pyridine) in 30—35% yields: m. p. 232°, $[\alpha]_{5461}^{16°} + 44·8°$ ($c = 1·07$ in pyridine) (Found: Hg, 43·3. $C_{10}H_{14}OBrClHg$ requires Hg, 43·1%). *Bis-3-bromocamphor-10-mercury* melted at 188—189° after crystallisation from acetone; $[\alpha]_{5461}^{16°} + 29·13°$ ($c = 1·03$ in pyridine) (Found: Hg, 30·4. $C_{20}H_{28}O_2Br_2Hg$ requires Hg, 30·4%). *3-Bromocamphor-10-mercuribromide* had m. p. 195° (Found: Hg, 39·5. $C_{10}H_{14}OBr_2Hg$ requires Hg, 39·3%), and *3-bromocamphor-10-mercuri-iodide* m. p. 173° (Found: Hg, 36·4. $C_{10}H_{14}OBrIHg$ requires Hg, 36·0%).

*Replacement of Mercury by Halogens.*—A suspension of 3-chlorocamphor-10-mercurichloride in an aqueous solution of bromine and potassium bromide was warmed until the solid was converted into a heavy oil. The latter was extracted with chloroform; after being freed from bromine, the concentrated extract yielded 3-chloro-10-bromocamphor, m. p. 98° (Armstrong and Lowry, J., 1902, **81**, 1452, give m. p. 98°).

3 : 10-Dibromocamphor (αβ-dibromocamphor), m. p. 114° (lit. 114°), was prepared in a similar way.

*3-Chloro-10-iodocamphor.*—The mercurichloride (1 g.) was refluxed for ½ hour with iodine (1 g.) in benzene (30 c.c.). After removal of the excess of iodine by washing with sulphite and carbonate solutions the crystalline deposit from the concentrate separated from alcohol in colourless needles, m. p. 89° (Found: C, 38·3; H, 4·6. $C_{10}H_{14}OClI$ requires C, 38·4; H, 4·5%).

*3-Bromo-10-iodocamphor*, similarly prepared, melted at 88—89° (Found: C, 33·7; H, 4·1. $C_{10}H_{14}OBrI$ requires C, 33·6; H, 3·9%).

The author acknowledges his indebtedness to Mr. P. Ross, B.Sc., who carried out the work on the π-acids, and to the Chemical Society for a grant.

Glasgow University. [*Received, March 9th*, 1935.]

Printed in Great Britain by Richard Clay & Sons, Limited, Bungay, Suffolk.

Additional Paper III.

Reprints of the following paper (J.C.S. 1937, 391.) are not yet available.

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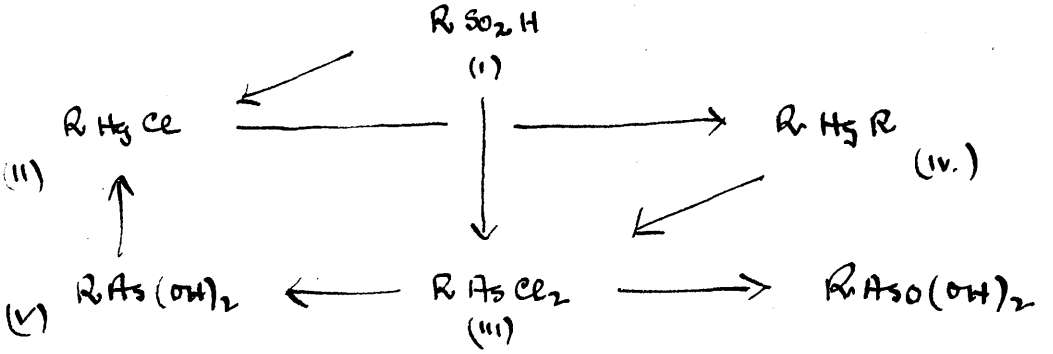
# The Preparation of Camphor-10-dichloroarsine from Camphor-10-sulphinic Acid.

By James D. Loudon.

The formation of organo-mercury compounds from sulphinic acids by the method discovered by Peters (Ber., 1905, 38, 2567) suggests the possibility of utilising these acids as a source of organic derivatives of certain other metals or metalloids which form with carbon a link of sufficient stability to survive the reaction conditions. It has previously been shown (Loudon, J. 1933, 823) that, with mercuric chloride, camphor-10-sulphinic acid (i) furnishes camphor-10-mercurichloride (ii) and it has been found that the corresponding dichloroarsine (iii) is readily produced by a similar process employing arsenic trichloride. The nature of the product is established by an alternative preparation from arsenic trichloride and bis-camphor-10-mercury (iv), and by the interesting observation that it is hydrolysed to a stable arsinic /

arsinic acid (v) from which, by treatment in aqueous solution with mercuric chloride, camphor-10-mercurichloride is quantitatively produced.




R = camphor-10-radical.

Although no other instance of this type of arsenuration has, to the author's knowledge, been published, Kharasch (J. Amer. Chem. Soc., 1921, 43, 610, footnote) also claims to have observed the same reaction in cases which are not specified. The reaction does not, however, appear to be of general application since with p-toluenesulphinic acid and naphthalene-2-sulphinic acid chiefly reduction products resulted.

## Experimental.

Camphor-10-dichloroarsine. - (A.) A mixture of camphor-10-sulphinic acid (10g. oil) and arsenic trichloride (9g.) was heated for 3 - 4 hours at 100°. The formation of sulphur dioxide was quickly perceptible. The excess of arsenic trichloride together with some water (which always appeared and was probably introduced with the sulphinic acid) were distilled off under reduced pressure and the residue, which solidified on cooling, was extracted with ether (charcoal). Concentration of the extract yielded a crystalline mass which, after repeated crystallisation from light petroleum, was obtained as long colourless needles, m.p. 89-90°.

(B.) Bis-camphor-10-mercury (5g.) and arsenic trichloride (20g.) were refluxed on an oil bath (190-200°) for 3 - 4 hours, and the product was worked up as in (A.). To separate the dichloroarsine from camphor-10-mercurichloride, the ether extract after evaporation was again extracted with small quantities of hot petroleum from which the dichloroarsine separated on cooling - m.p. and mixed m.p. 89-90°.

(Found: C, 40·2; H, 5·05; Cl, 23·6. $C_{10}H_{15}OCl_2As$ requires C, 40·4; H, 5·05; Cl, 23·9%).

Camphor-10-arsinic acid. - Camphor-10-dichloroarsine was shaken with /

with warm concentrated sodium hydroxide solution until complete dissolution was effected. The precipitate obtained by acidification (after cooling) was recrystallised from hot water and formed long needles, m.p. 100° (with decomposition). (Found: C, 43·4; H, 6·8. $C_{10}H_{17}O_3As.H_2O$ requires C, 43·2; H, 6·8%). When a suspension of the compound in benzene or light ether was gently warmed, it appeared first partly to dissolve and then suddenly to lose water. A white insoluble powder, melting indefinitely at 190°, was produced but could not be purified and had a somewhat variable composition.
(Found: C, 33·9 and 34·2; H, 4·9 and 5·7).

Camphor-10-mercurichloride was formed in excellent yield when an aqueous solution of the arsinic acid (0·5g.) and mercuric chloride (0·5g.) was heated for one hour. The solid formed was extracted with chloroform and the extract recrystallised from alcohol - m.p. and mixed m.p. with an authentic specimen, 166-167°.

Camphor-10-arsonic acid was obtained by concentrating the solutions produced (1) by passing chlorine into an aqueous suspension of the dichloroarsine and (2) by oxidising the same compound with hydrogen peroxide in acetic acid. The product crystallised from alcohol in massive prisms or in fine needles, melting in each case at 210°.

(Found /

(Found: C, 43·2; H, 6·3. $C_{10}H_{17}O_3As$ requires C, 43·5; H, 6·2%). The barium salt was more soluble in cold than in hot water.

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