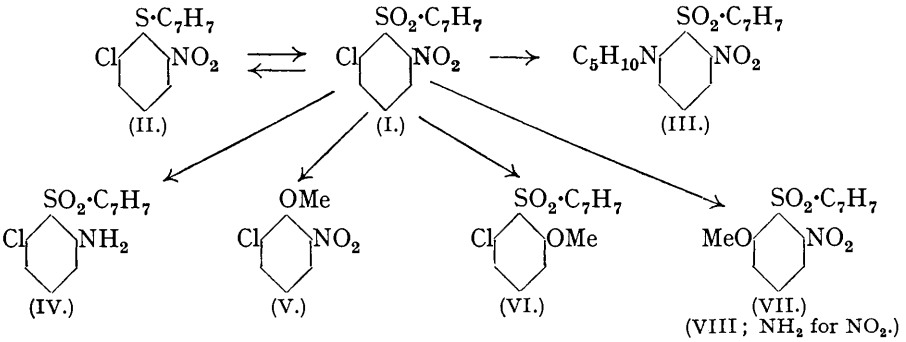
128. *The Mobility of Groups in Chloronitrodiphenylsulphones.*

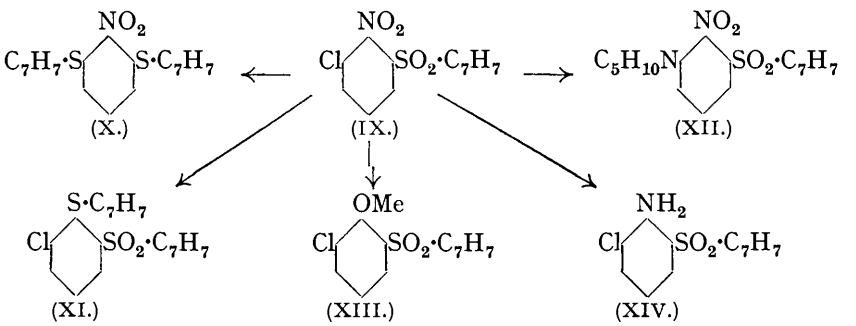
By James D. Loudon and Nathan Shulman.

In continuation of previous work the vicinally substituted sulphones (I) and (IX) have now been examined, and the table contains a general summary of the groups principally replaced by the action of four different reagents on the various sulphone types. The results show that the behaviour of these compounds is highly complex, the preferred centres of reaction varying with the arrangement of substituents and also with the reagent employed. It is suggested that steric inhibition of resonance is an important factor in reactions of this type and that it contributes to some of the contrasts encountered.

EACH of the three substituents in the main nucleus of homonuclear chloronitrodiphenylsulphones is potentially a stable anion and, when suitably activated, can be replaced in reactions with anionoid reagents. Two of the substituents (*viz.*, NO_2 and SO_2R) by their capacity to activate the respective *op*-positions supply the primary orienting influences for these reactions. In chlorodinitrobenzenes the mobility of substituents is similarly conditioned but considerably less complex, since the variety of substituents is smaller and the primary orienting influence is always vested in a nitro-group. It is of interest, therefore, to compare the reactions of the two sets of compounds and with this purpose we have examined the behaviour of the vicinally substituted sulphones (I) and (IX), thereby supplementing the results of previous work which is summarised in the table below.



The *sulphone* (I) was obtained by oxidising the corresponding *sulphide* (II), produced either from 2 : 3-dichloronitrobenzene or from 2 : 3-dinitrochlorobenzene in reaction with the sodium salt of thio-*p*-cresol; the sulphone itself was reconverted into the sulphide by the same reagent. Piperidine attacked the chlorinated centre in (I) yielding the *piperidino*-derivative (III), whereas ammonia replaced the nitro-group, giving the *amine* (IV), which was also obtained when (I) was reduced. All three possible products were formed by the action of sodium methoxide on (I); 2-chloro-6-nitroanisole (V) was isolated only in small yield, the bulk of material consisting of a difficultly separable mixture (VI and VII), from which, after reduction, 2-*amino*-6-*methoxy*-4′-*methyldiphenylsulphone* (VIII) and 2-*chloro*-6-*methoxy*-4′-*methyldiphenylsulphone* (VI), the chief product, were isolated.

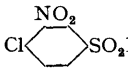
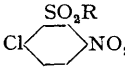
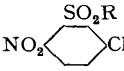
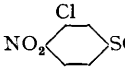
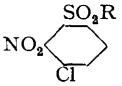
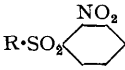
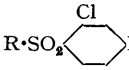
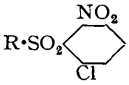
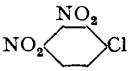
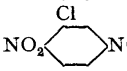
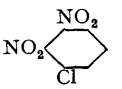


From the isomeric sulphone (IX) (Loudon, J., 1940, 1525) piperidine replaced the chlorine atom, forming (XII), the reaction being the slowest between this reagent and any sulphone of the series examined. Sodium methoxide and methyl-alcoholic ammonia brought about replacement of the nitro-group, giving the *products* (XIII) and (XIV) respectively, the latter being obtained also when (IX) was reduced. The *compound* (XI) was the chief product from the action of alkaline thio-*p*-cresol on (IX) and was accompanied by the dithio-ether (X). The production of the latter compound recalls its ready formation at the expense of 3-chloro-2-nitro-4′-methyldiphenyl sulphide in the reaction between 2 : 6-dinitrochlorobenzene and the mercaptide (*loc. cit.*), but we were unable to determine whether here, in the initial stage from (IX), the chloro- or the sulphonyl group

was preferentially replaced. The justification of the 2-nitro-3-aminodiphenylsulphone structure assigned to an amine previously reported (Loudon, J., 1939, 902; compound XV) consists in its conversion by the Sandmeyer reaction into 3-chloro-2-nitrodiphenylsulphone and in the analogous production of the dithio-ether (X) from the reaction of the latter compound with the sodium salt of thio-*p*-cresol.

Eight of the ten possible types of homonuclear chloronitrodiphenylsulphones have now been investigated. The missing types are 2-chloro-3-nitrodiphenylsulphone, in which only chlorine mobility is to be expected [cf. nos. (i) and (ii) of table], and 3-chloro-5-nitrodiphenylsulphone, the unique features of which adumbrate an order of reactivity quite distinct from that of its isomers. Although the compounds examined have not been strictly isomeric, the second aromatic nucleus (R in the table) comprising a phenyl or *p*-tolyl residue according to convenience in synthesis, yet the distinction is slight and may be ignored in comparing preferred centres of mobility, since these are very little affected even by profound modification of the sulphonyl component (Loudon and Shulman, J., 1938, 1618). The table contains a summary of the groups *principally* replaced by the action of four reagents on the different sulphone types (i)—(viii), a double entry denoting concurrent (formally bimolecular) reactions. The first two sulphones may be dismissed from further discussion, since they show exclusive replacement of halogen in normal consequence of the cumulative orienting effects of the nitro- and the sulphonyl group. In the other cases, (iii)—(viii), however, the orienting influences compete with each other and the results clearly show the capacity of sulphonyl to sustain its challenge to the nitro-group for control of the centre or centres of reaction. The significance of this fact—and of the high degree of reactivity displayed by the compounds in general—has already been discussed by Holmes and Loudon (J., 1940, 1521).

TABLE.

		NaSR.	NaOMe.	NH_3.	$C_5H_{10}NH$.	Ref.
(i)		Cl	Cl	Cl	Cl	J., 1936, 218
(ii)		Cl	Cl	Cl	Cl	,,
(iii)		SO_2R	SO_2R	SO_2R	Cl	§ J., 1939, 902
(iv)		Cl	NO_2	Cl(NO_2)	Cl	,,
(v)		NO_2(Cl or SO_2R)	NO_2	NO_2	Cl	This paper
(vi)		SO_2R	NO_2	NO_2	Cl(NO_2)	J., 1937, 242; 1939, 1618
(vii)		SO_2R	NO_2	‡	Cl	J., 1937, 242
(viii)		SO_2R	NO_2(Cl)	NO_2	Cl	This paper
(ix)		§2-NO_2 (1-NO_2)	*2-NO_2	—	—	
(x)		—	*1-NO_2	†1-NO_2(Cl)	—	
(xi)		1-NO_2	*1-NO_2	—	—	

‡ NO_2 replaced by OMe from solvent. Substituents numbered from the extreme left.

* Holleman and ter Weel, *Rec. Trav. chim.*, 1915, **35**, 44

† Korner and Contardi, *Atti R. Accad. Lincei*, 1914, **23**, i, 5a, 284

In so far as it exerts an electromeric effect, a chloro-substituent should oppose the influence of a *m*-situated cationoid group by causing a relative reduction of cationoid character at the *op*-centres, and hence should favour orientation by the nitro-group in (iii)—(v), and by the sulphonyl group in (vi)—(viii). This expectation is only fulfilled in a general sense, for although the sulphonyl group maintains a consistently high level of effectiveness in (vi)—(viii), the influence of the nitro-group declines from (iii) to (v) and a similar decline affects the corresponding 1-nitro-group in chlorodinitrobenzenes, (ix)—(xi). The most striking contrast between the two groups is furnished by the marked loss in relative power incurred by the nitro-group following the transfer of chlorine from the *p*-position in (iii) to the *o*-position in (v), and by the unimpaired efficiency of the sulphonyl group in the corresponding change from (vi) to (viii). It is apparent, however, that the reagent plays a very important part in determining the centres of reaction and, within the narrow compass of the present work, several different tendencies may be noted. For instance, with a single partial exception the mercaptide reagent attacks centres activated by the nitro-group, whereas piperidine, irrespective of the orienting influence, shows a consistent preference for replacing chlorine. Less consistently, the other two reagents tend to replace the nitro-group, the reactions being oriented by the sulphonyl substituent, but no general correlation of the reagent effects can be attempted with the data available.

Note on the Effect of Inhibited Resonance.—The contrast between the orienting powers of the nitro-group in (v) and the sulphonyl group in (viii) raises a point of general interest. Kenner has suggested that a nitro-group owes its pre-eminence as an activator to its capacity to form a preliminary union with the reagent, the process being subject to steric hindrance from *o*-substituents (J., 1914, **105**, 2717). Hampson and his collaborators have recently adduced evidence supporting the view that resonance between a nitro-group and a benzene nucleus is sterically inhibited by two *o*-methyl groups (J., 1937, 10; 1939, 981). Inhibited resonance arising from similar causes would account for the weaker orienting power, and hence for the preferred mobility of the nitro-group, marked (*), in such cases as 2* : 3-dinitrochlorobenzene, 2* : 3-dinitrotoluene (Kenner and Parkin, J., 1920, **117**, 852) and 2* : 3-dinitroanisole (Vermeulen, *Rec. Trav. chim.*, 1906, **25**, 12); and again, for the impaired power of the nitro-group as expressed by the reduced halogen mobility in 2 : 6-dichloronitrobenzene compared with its reactive isomers (Holleman and de Mooy, *ibid.*, 1915, **35**, 19), in 3-chloro-2 : 6-dinitro- compared with 2-chloro-3 : 5-dinitro- or 5-chloro-2 : 4-dinitro-toluene (Lindemann and Pabst, *Annalen*, 1928, **462**, 24) and in 3-chloro-2-nitro- compared with 3-chloro-4-nitro- or 3-chloro-6-nitro-anisole (Hodgson and Handley, J., 1926, 542). Since between the sulphonyl group and the nucleus only an inductive effect can operate if the sulphur octet is to be preserved, the argument also accommodates the efficiency of the sulphonyl group in (viii) contrasted with the weakness of the nitro-group in (v). Baddeley (*Nature*, 1939, **144**, 444) has applied the concept of inhibited resonance to a number of "ortho-phenomena" arising from a single *o*-substituent, and the present aspect may be illustrated by the preferred centres of mobility in 2* : 5-dinitrotoluene (Kenner and Parkin, *loc. cit.*) and in 2* : 5-dinitrochlorobenzene. Nevertheless, in such cases the inhibition must be considerably reduced in importance relative to other factors in the reactivity (cf. Lewis and Seaborg, *J. Amer. Chem. Soc.*, 1940, **62**, 2122) and is an insufficient guide for comparisons between molecules such as *o*- and *p*-chloronitrobenzenes, where the order of reactivity varies with the reagent (cf. de Mooy, *loc. cit.*; Brewin and Turner, J., 1928, 332), or for the Smiles rearrangement in which an *o*- is more effective than a *p*-nitro-group (Levi and Smiles, J., 1932, 1488).

Experimental.

2-Chloro-6-nitro-4'-methyldiphenyl Sulphide (II).—2 : 3-Dichloronitrobenzene (or 2 : 3-dinitrochlorobenzene) dissolved in warm alcohol was treated with a solution of the sodium salt of thio-*p*-cresol (1 mol.) in aqueous alcohol. The oil which was formed solidified and was crystallised from alcohol, giving yellow plates, m. p. 69—70° (Found : N, 5·2. $C_{13}H_{10}O_2NClS$ requires N, 5·0%). The corresponding *sulphone* (I), prepared by oxidation with hydrogen peroxide in acetic acid, formed colourless prisms, m. p. 139°, from acetic acid (Found : N, 4·6.

$C_{13}H_{10}O_4NClS$ requires N, 4·6%) and regenerated the sulphide (II) when treated with mercaptide in alcohol–dioxan.

6-*Nitro*-2-*piperidino*-4′-*methyldiphenylsulphone* (III), long yellow needles, m. p. 171°, was obtained when (I) was warmed for a few minutes with piperidine (Found : N, 7·75. $C_{18}H_{20}O_4N_2S$ requires N, 7·8%). Nitrite ions were also produced in the reaction.

2-*Chloro*-6-*amino*-4′-*methyldiphenylsulphone* (IV) was obtained from the sulphone (I), (*a*) by heating with ammonia in methyl alcohol at 160° for 5 hours, and (*b*) by reduction with stannous chloride–hydrochloric acid in acetic acid. The purified product in each case had m. p. and mixed m. p. 134—135° from alcohol (Found : C, 55·3; H, 4·3; N, 5·2. $C_{13}H_{12}O_2NClS$ requires C, 55·4; H, 4·3; N, 5·0%). The crude product from (*a*), after one crystallisation, was yellow and had a slightly higher nitrogen content (5·7%), which, together with the production of chloride ions during the reaction, suggests the formation of some 2-nitro-6-amino-4′-methyldiphenylsulphone.

Action of Sodium Methoxide on the Sulphone (I).—A solution of (I) and sodium methoxide in methyl alcohol–dioxan was heated for 1½ hours. Gradual addition of water gave a large fraction consisting of a colourless solid of m. p. 110° (from methyl alcohol), followed by a very soluble fraction, slender needles, from methyl alcohol, identified by m. p. and mixed m. p. 54—55° as 2-chloro-6-nitroanisole. Although the fraction of m. p. 110° had practically a constant m. p., its analysis suggested that it was a mixture (N, 1·5%) and consequently it was reduced by stannous chloride and anhydrous hydrogen chloride in acetic acid. The product obtained on pouring the reaction mixture into water was extracted with concentrated hydrochloric acid, and the insoluble residue was crystallised from benzene–ligroin, giving 2-*chloro*-6-*methoxy*-4′-*methyldiphenylsulphone*, m. p. 102° (Found : C, 56·7; H, 4·3. $C_{14}H_{13}O_3ClS$ requires C, 56·7; H, 4·4%). The combined mother-liquors from the reduction and the acid extract were made strongly alkaline and extracted with benzene, from which 2-*amino*-6-*methoxy*-4′-*methyldiphenylsulphone* was obtained by evaporation; it had m. p. 158°, from benzene–ligroin (Found : N, 5·0. $C_{14}H_{15}O_3NS$ requires N, 5·05%).

3-*Chloro*-2-*nitrodiphenylsulphone* was prepared from 2-nitro-3-aminodiphenylsulphone (J., 1939, 902) by Hodgson and Walker's modification of the Sandmeyer reaction (J., 1933, 1620). It formed small, compact crystals, m. p. 144°, from acetic acid (Found : N, 4·9. $C_{12}H_8O_4NClS$ requires N, 4·7%) and, when warmed in aqueous alcohol with 2 mols. each of thio-*p*-cresol and sodium hydroxide, gave a precipitate of 2 : 6-di-(*p*-tolylthio)nitrobenzene (X), m. p. and mixed m. p. 167—168° (other products, cf. below, were not examined).

3-*Chloro*-2-p-*tolylthio*-4′-*methyldiphenylsulphone* (XI).—A solution of 3-chloro-2-nitro-4′-methyldiphenylsulphone (IX), thio-*p*-cresol, and sodium methoxide (mol. propns.) in aqueous-alcoholic dioxan was kept for one week at room temperature. The crystalline deposit, consisting of a mixture of yellow needles and colourless cubes, was dissolved in warm alcohol–dioxan, and the solution was seeded with one of the colourless crystals, whereupon the *product* (XI) separated. It formed highly refractive cubes, m. p. 153—154° (Found : C, 61·9; H, 4·6. $C_{20}H_{17}O_2ClS_2$ requires C, 61·8; H, 4·4%). The yellow needles, recovered from the mother-liquor, were identified as (X). Repeated search disclosed no other product of the reaction, and similar results were obtained, but with slightly increased yield of (X), when 2 mols. of mercaptide were employed and the reaction solution was heated for 25 mins.

2 : 3-*Di*-p-*toluenesulphonylchlorobenzene*, m. p. 229° from acetic acid, was obtained by heating (XI) with hydrogen peroxide in acetic acid (Found : C, 57·3; H, 4·2. $C_{20}H_{17}O_4ClS_2$ requires C, 57·1; H, 4·0%).

2 : 6-*Di*-p-*toluenesulphonyl*-4′-*methyldiphenyl Sulphide*.—2 : 6-Di-*p*-toluenesulphonylnitrobenzene (J., 1940, 1525), thio-*p*-cresol, and sodium hydroxide were heated in alcohol–dioxan. The *product* crystallised from acetic acid in colourless flakes, m. p. 205° (Found : C, 63·7; H, 4·9. $C_{27}H_{24}O_4S_3$ requires C, 63·8; H, 4·7%). Oxidation with hydrogen peroxide in warm acetic acid, followed by precipitation with water, gave a colourless powder which could not be obtained crystalline, was very soluble in the usual solvents, and had no definite m. p. A sample dried over sulphuric acid gave analysis corresponding with 1 : 2 : 3-tri-*p*-toluenesulphonylbenzene (Found : C, 59·8; H, 4·5. Calc. for $C_{27}H_{24}O_6S_3$: C, 60·0; H, 4·4%), but its properties are unusual.

2 : 6-*Di*-p-*toluenesulphonylpiperidinobenzene* was obtained by refluxing 2 : 6-di-*p*-toluenesulphonylnitrobenzene in piperidine and had m. p. 143°, from alcohol (Found : C, 64·0; H, 5·8. $C_{25}H_{27}O_4NS_2$ requires C, 64·0; H, 5·75%).

2-*Nitro*-3-*piperidino*-4′-*methyldiphenylsulphone* (XII).—A solution of the sulphone (IX) in piperidine was heated under reflux for one hour during which piperidine hydrochloride

separated. The solid obtained by addition of water was crystallised from alcohol and formed pale yellow needles, m. p. 145°, no other product being detected (Found : C, 60·4; H, 5·8; N, 7·8. $C_{18}H_{20}O_4N_2S$ requires C, 60·0; H, 5·6; N, 7·8%).

3-*Chloro*-2-*methoxy*-4′-*methyldiphenylsulphone* (XIII).—The sulphone (IX) was heated with sodium methoxide in methyl alcohol and, after precipitation with water, the product crystallised from alcohol in colourless prisms, m. p. 108—109° (Found : C, 56·5; H, 4·25. $C_{14}H_{13}O_3ClS$ requires C, 56·7; H, 4·4%).

3-*Chloro*-2-*amino*-4′-*methyldiphenylsulphone* (XIV).—(*a*) The sulphone (IX) was heated with methyl-alcoholic ammonia at 160—170° for 6 hours. (*b*) The sulphone (IX) was reduced by stannous chloride and hydrochloric acid in acetic acid. In each case the *product* had m. p. and mixed m. p. 114° (Found : C, 55·5; H, 4·5; N, 4·8. $C_{13}H_{12}O_2NClS$ requires C, 55·4; H, 4·3; N, 5·0%).

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