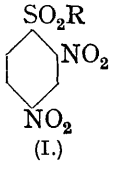
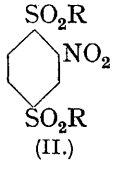
43. *The Mobility of Groups in Certain Nitrodiphenylsulphones.*

By James D. Loudon and Thomas D. Robson.

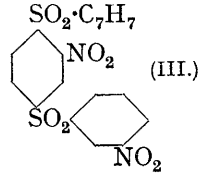
When cationoid reactivity is displayed by nitrobenzene derivatives the reactive centres are generally those situated *o*- or *p*- to the nitro-group which, among *m*-directing groups, is pre-eminent in its power to produce activation of this type. It has, nevertheless, been observed in certain isolated 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.)

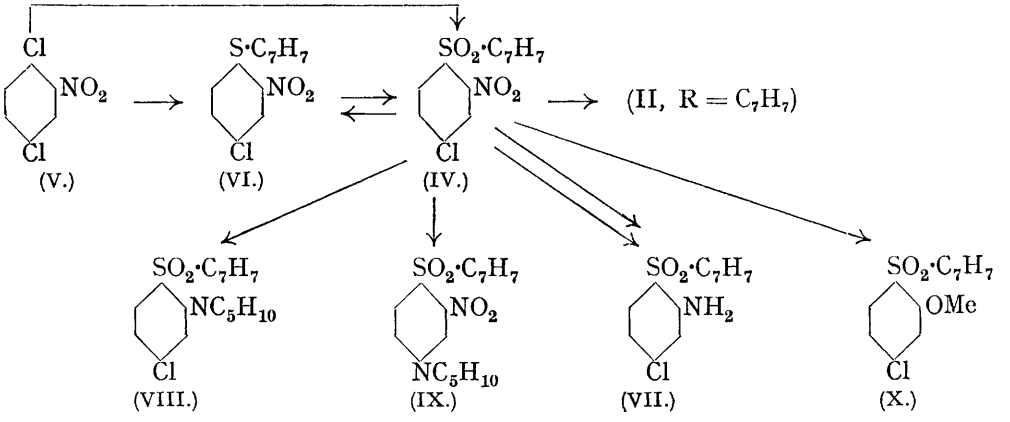


(III.)

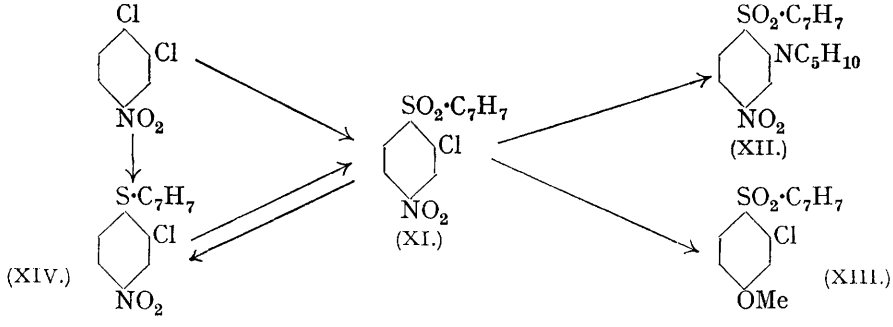
Under equilibrium conditions the ease with which sulphonyl groups replace each other may be represented by the order *p*-$CH_3 \cdot C_6H_4 \cdot SO_2 > C_6H_5 \cdot SO_2 > p$-$C_6H_4Cl \cdot SO_2 > m$-$NO_2 \cdot C_6H_4 \cdot SO_2 > 2 : 5$-$C_6H_3Cl_2 \cdot SO_2$ (J., 1935, 896), and we have found that 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,

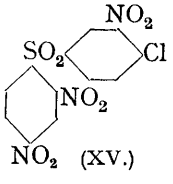
R = C_7H_7) being formed as readily as from (I). Methyl-alcoholic ammonia effected replacement of the nitro-group, the isolated *amine* (VII) being identical with the product of reduction. The sulphonyl group was replaced, with regeneration of (VI), by the action of *p*-thiocresol in presence of alkali. 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.



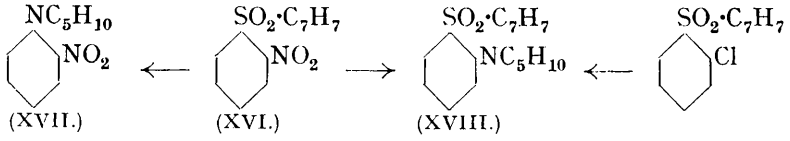
Slightly different results were obtained by the action of the same reagents on the isomeric *chloronitrosulphone* (XI). In this case no product could be isolated from the reaction with sodium *p*-toluenesulphinate, and with piperidine, only one *piperidino*-derivative (XII) was obtained, though here, 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.



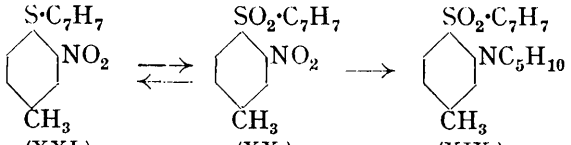
Consideration of these results shows that, apart from the reactions involving mercaptide (cf. also XX ⟶ XXI, below), the groups replaced are those situated *o*- and *p*- to the sulphonyl group. This differentiation between mercaptide and the other reagents is paralleled by work still unpublished and 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



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).

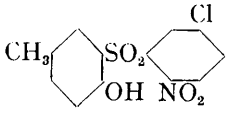


(XVII.) (XVI.) (XVIII.)



(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%).

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