193. *The Orienting Influence of Free and Bound Ionic Charges on Attached Simple or Conjugated Unsaturated Systems. Part VI. Nitration of Phenylalkylsulphones.*

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IN accordance with the theory first put forward by Allan, Oxford, Robinson, and Smith (J., 1926, 401) a side-chain group (A) * which, relatively to hydrogen, repels electrons must, when replacing hydrogen in the substance which is the standard of comparison, tend to increase the ratio of *op*-substitution to *m*-substitution.

A group (B) which, relatively to a hydrogen atom, is electron-attracting tends to promote *m*-substitution. When this hypothesis was originally propounded (*loc. cit.*; Ing and Robinson, *ibid.*, p. 1659) alternative mechanisms for the latter effect were suggested and, of these, the most simple and at present the most acceptable was the theory of " penultimate " substitution which allows the mechanisms associated with (A) type groups and (B) type groups to be identified in principle.

According to this view *inductive*, *general*, or *field* effects over the nucleus operate to differentiate the intensity of the electrical fields at the unsaturated carbon atoms. The carbon atom at which the density of electrons is greatest then becomes most readily the positive end of a simple or conjugated unsaturated system (enoid or

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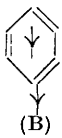
* Such groups have the effect of increasing the intensity of the negative electrical fields over the nucleus and clearly the inductive *effect* should be symbolised as $-I$ and not $+I$. Similarly, all the electrical polarity signs used in recent years in this *Journal* and the *Annual Reports* in connexion with inductive (general) and electromeric (tautomeric) effects should be reversed. —R. R.

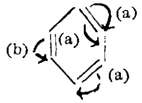
polyenoid). The next most probable polarisations are then easily identified on the same grounds.

These results can also be reached by considering the repulsion or attraction of electrons in the electromeric systems, as affected by the field developed by the substituent (A or B). In the annexed scheme (a), (b), (c) represent the possible polarisations (leading to anionoid reactivity) in order of probability, (a) being the most probable. In order to emphasise the identity of the theory for *op*- and *m*-substitutions a single expression serves for molecules containing (A) or (B) oriented as shown :

(A)



(B)



(c)—*all electromeric changes in a direction opposed to the field* (—).

Whatever view of the *mechanism* prevails, the general accuracy of the deductions to be made from these schemes in regard to the *results* of substitutions has been confirmed in a large series of substances. Only a few special cases remain for consideration and among these the arylalkylsulphones offer a feature of interest.

The nitration of phenylmethylsulphone was studied by Smiles and Twist (J., 1925, **127**, 1250), who found that the *m*-nitro-derivative was produced in 96—98% yield. Consequently, since it is possible to vary the alkyl group, the series affords an opportunity of observing the anticipated effect (promotion of *op*-attack) of substitution of methyl for hydrogen exerted by way of, through, or across an almost exclusively *m*-directive group.

Furthermore the (B) type character of the sulphone group is due to its co-ordinate links and consequent dipole and it is directly attached to the nucleus. It is thus a unique group, differing from $-NR_3^+$ in its total electrical neutrality and from –CO– in the lack of any conjugation with the nucleus.

The point to be determined by experiment was whether the electron repulsive (—*F*) properties of the higher alkyl groups can so modify the field of the sulphur atom (+*F*) that a perceptible diminution of *m*-orientation in $Ph\cdot SO_2\cdot R$ as compared with $Ph\cdot SO_2\cdot Me$ can be detected. It was obvious that the *op*-tendency must be present, but the magnitude of the effect relative to the *m*-direction by the sulphone group could not be forecast. The only known facts which appeared to bear on this problem were the results of nitration of *m*-nitrotoluene and *m*-tolyltrimethylammonium salts. In these cases the substitution occurs exclusively *op* to the nuclear methyl group.

In the present case the alkyl groups also *appear* to be comparable with the sulphone group, because, although comparatively remote from the nucleus, a small depression of *m*-substitution as the size of the alkyl group increases has been observed. The sulphones examined have given the following results on nitration. Phenylmethylsulphone (*m*-nitro, 98·5%); $Ph{\cdot}SO_2{\cdot}R$, R = Et (*m*, 96·0%), R = Pr^α (*m*, 93·1%), R = *n*-Bu (*m*, 85·7%); R = Pr^β (*m*, 80·0%).

It is very probable that in all cases where two opposing effects are present the existence of phases, due to the accidents of the approach of polarised molecules and perhaps other circumstances, must be contemplated. Thus the static condition, $Ph{\rightarrow}{-}SO_2{-}{\leftarrow}R$ may be temporarily disturbed so as to give in effect $Ph{\longrightarrow}SO_2{-}{\leftarrow}R$ and it must be remembered that such a molecule will have greatly enhanced anionoid reactivity.

The same view probably applies to the nitration of *m*-nitrotoluene and similar cases. The nitroxyl is temporarily electrically neutralised by solvent molecules and the molecule freed from the deactivating influence of the positive field is rapidly substituted and naturally in the *op*-positions to the methyl group.

The shares of static and dynamic conditions of the molecules in producing these effects can only be estimated after we have gained a far more intimate knowledge of molecular dipole moments and a clearer understanding of their interpretation.

The details of the experimental work call for little comment; the nitrations were effected by means of an excess of fuming nitric acid at room temperature and the products were examined by a modification of Francis and Hill's method of reduction and bromination. All the isomerides that might be produced were synthesised and the analytical procedure was controlled by the analysis of mixtures of known composition.

EXPERIMENTAL.

Preparation of the Sulphones.—The requisite phenylalkylsulphones were prepared by alkylation of sodium benzenesulphinate and the latter was obtained by a modification of Limpricht's method introduced for the preparation of sodium *m*-nitrobenzenesulphinate (*Ber.*, 1892, **25**, 75, 3477). Benzenesulphonyl chloride (35 g.) was gradually added (about 2 drops in a second) to a solution of crystallised sodium sulphite (95 g.) in water (90 c.c.) at 50° and mechanically stirred. The temperature usually rose to 70—80° and an alkaline reaction was maintained by the addition of sodium hydroxide when necessary. When the process was completed and the liquid had cooled to 25—30°, it was acidified with hydrochloric acid and the stirring continued for 3—4 hours; the white flocculent precipitate was then collected (yield of dry product, m. p. 82—83°, 27 g.).

Phenylmethylsulphone was prepared in the following manner. Benzenesulphinic acid (28 g.) and methyl sulphate (100 g.) were vigorously stirred and sodium hydroxide (50 g.) in water (200 c.c.) was added at such a rate that the temperature did not exceed 40°. Stirring was continued until the sulphone crystallised, the strongly alkaline mixture was then refluxed for 2 hours, and the product collected after cooling and recrystallised from water (yield, 24 g.; m. p. 87—88°).

The higher homologues were all prepared by interaction of sodium benzenesulphinate (1 mol.) with the corresponding alkyl halide (1·25 mols.) (ethyl iodide, *iso*propyl iodide, *n*-propyl bromide, *n*-butyl bromide) in boiling alcoholic solution and the yields were 80—85% in all cases.

Phenylethylsulphone crystallised from 70% alcohol in colourless plates, m. p. 42°.

Phenyl*iso*propylsulphone is a very pale yellow oil, b. p. 145—150°/1 mm. (Found : S, 17·3. Calc. for $C_9H_{12}O_2S$: S, 17·4%) (compare Otto and Otto, *Ber.*, 1888, **21**, 998).

Phenylpropylsulphone crystallised from 40% acetic acid in colourless hexagonal plates, m. p. 46° (Otto and Otto, *loc. cit.*).

*Phenyl-*n*-butylsulphone* is a faintly yellow, viscous oil, b. p 165—170°/1 mm. (Found : S, 16·0. $C_{10}H_{14}O_2S$ requires S, 16·2%).

Preparation of the o-, m-, *and* p-*Nitro-derivatives of the Phenylalkylsulphones*.—The *m*-nitro-compounds were obtained in the same way as the parent substances from sodium *m*-nitrobenzenesulphinate (Limpricht, *loc. cit.*).

m-Nitrophenylmethylsulphone crystallised from 30% acetic acid in colourless needles, m. p. 148° (compare Twist and Smiles, *loc. cit.*).

m-Nitrophenylethylsulphone crystallised from methyl alcohol in colourless rhombic plates, m. p. 101—102° (compare Limpricht, *Annalen*, 1893, **278**, 245).

m-*Nitrophenyl*iso*propylsulphone* crystallised from benzene–light petroleum (1 : 3) in colourless rhombic plates, m. p. 113° (Found : N, 6·2; S, 13·8. $C_9H_{11}O_4NS$ requires N, 6·1; S, 14·0%).

m-*Nitrophenyl-*n*-propylsulphone* crystallised from methyl alcohol in colourless prisms, m. p. 80° (Found : N, 6·2; S, 13·8%).

m-*Nitrophenyl-*n*-butylsulphone* was isolated from the reaction product by means of ether and distilled, b. p. 215°/3 mm., as a viscous, pale yellow oil (Found : N, 5·8; S, 13·3. $C_{10}H_{13}O_4NS$ requires N, 5·8; S, 13·2%).

In all the above cases the yields exceeded 80% of the theoretical and the crystalline products were identified with the substances obtained by the nitration of the phenylalkylsulphones (see below) by the undepressed melting points of mixtures.

The *p*-nitro-compounds were prepared by Waldron and Reid's method (*J. Amer. Chem. Soc.*, 1923, **45**, 2400) from the corresponding sulphides, but hydrogen peroxide was a more convenient oxidising agent than chromic acid. The substances agreed in properties with those described by Waldron and Reid (Found for the series of sulphones : N, 7·0, 6·6, 6·2, 6·2, 5·8. Calc.: N, 7·0, 6·5, 6·1, 6·1, 5·8%, respectively).

The *o*-nitrophenylalkylsulphones were likewise obtained from the sulphides by oxidation with hydrogen peroxide following the method of Claasz (*Ber.*, 1912, **45**, 1023).

o-Nitrothiophenol was methylated according to the method of Brand (*Ber.*, 1909, **42**, 3465) and converted into its ethyl and *n*-propyl ethers by the method of Foster and Reid (*J. Amer. Chem. Soc.*, 1924, **46**, 1936). The *iso*propyl and *n*-butyl ethers were obtained in a similar way.

o-Nitrophenylmethylsulphone (Brand, *loc. cit.*) sinters at 100° and then melts at 106°.

o-*Nitrophenylethylsulphone*, readily obtained from the corresponding sulphide by means of hydrogen peroxide (but not chromic acid; compare Foster and Reid, *loc. cit.*), crystallised from ethyl alcohol in colourless rectangular plates, m. p. 45·5° (Found : N, 6·6; S, 14·7. $C_8H_9O_4NS$ requires N, 6·5; S, 14·9%).

o-Nitrophenyl-*n*-propylsulphone crystallised from ethyl alcohol in colourless hexagonal tablets, m. p. 60·5° (Foster and Reid, *loc. cit.*, give m. p. 50°) (Found : N, 6·1; S, 13·8. Calc. for $C_9H_{11}O_4NS$: N, 6·1; S, 14·0%).

o-*Nitrophenyl*iso*propylsulphone* crystallised from alcohol in colourless needles, m. p. 59·5° (Found : N, 6·1; S, 14·0%).

o-*Nitrophenyl*-n-*butylsulphone* was a faintly yellow oil, b. p. 216—218°/3 mm. (Found : N, 5·8; S, 12·9. $C_{10}H_{13}O_4NS$ requires N, 5·8; S, 13·2%).

Method of Estimation of the m-*Isomeride in Mixtures of* o-, m-, *and* p-*Nitrophenylalkylsulphones.*—The method, essentially that of Francis and Hill (*J. Amer. Chem. Soc.*, 1924, **46**, 2494), depends on the reduction of the nitro-sulphones to amines, of which the *o*- and *p*-isomerides are dibrominated and the *m*-compound tribrominated.

Each stage, however, offered considerable difficulty and variable results were obtained; hence it was essential to investigate the behaviour of each of the possible products and also mixtures of them. After a number of trials of other processes, including the use of titanous chloride, the nitro-compounds were reduced by means of zinc dust and hydrochloric acid. Clean, colourless solutions were thus produced and consistent results were rendered possible. The major difficulty was, however, the separation of partly brominated amines during the addition of potassium bromate. This obstacle was overcome by raising the temperature of the solution, which could be done without loss of bromine.

Each product of nitration was first examined for the presence of nitrates and if these were absent the pure substance or mixture (*ca.* 0·1500 g.) was mixed with water (20 c.c.), glacial acetic acid (20 c.c.), and concentrated hydrochloric acid (15 c.c.) and reduced by means of titanous chloride (50 c.c. of a solution made from 160 c.c. of 20% titanous chloride and 400 c.c. of concentrated hydrochloric acid made up to 1000 c.c.) under the usual conditions (Knecht's method). Titration with a standard solution of ferric alum then gave the requisite information respecting the purity of the specimen (% of nitroxyl); this was used to control the homogeneity of the synthetical, supposedly individual nitro-sulphones and also to give the yield in the nitration processes.

In another experiment the substance or mixture under examination (*ca.* 0·2500 g.), mixed with zinc dust (20 g.) and water (20 c.c.), was treated with concentrated hydrochloric acid (60 c.c.), added in portions of about 15 c.c.; further equal amounts of zinc and hydrochloric acid were later introduced. The solution was filtered and the filtrate and washings were mixed with potassium bromide (15 c.c. of 20% solution) and concentrated hydrochloric acid (10 c.c.), making about 200 c.c. of liquid. After heating to 60—65° the solution was titrated with potassium bromate (1·245*N*), with starch–potassium iodide as the indicator; the temperature was not allowed to fall below 48°. Practice in judging the somewhat indefinite end-point was necessary and the end-point was not taken unless the clear blue ring on the indicator paper was obtainable after the solution had been kept for 10 minutes. The following results refer to the volume of bromate required (in c.c.) starting with 0·200 g. of each of the pure isomerides.

	Ortho.		Para.		Meta.	
R in $NO_2{\cdot}C_6H_4{\cdot}SO_2{\cdot}R$.	Found.	Theory.	Found.	Theory.	Found.	Theory.
Methyl	32·7	31·9	32·7	31·9	48·2	47·8
Ethyl	30·4	29·8	30·4	29·8	45·2	44·7
*iso*Propyl	29·0	28·0	29·0	28·0	45·3	42·0
n-Propyl	29·2	28·0	29·2	28·0	43·0	42·0
n-Butyl	27·2	26·4	27·2	26·4	41·7	39·6

It will be observed that in each case the disparity of the recorded results for the *o*- (or *p*-) and the *m*-isomerides is quite adequate and it should be stated that the experimental and not the theoretical values were adopted in the analyses of mixtures.

The results of such analyses of artificial mixtures were the following :

Mixture of isomeric nitro-phenylalkyl-sulphones.	Actual % of *m*-isomerides present.	*m*-Isomeride found, %.
Methyl	72·0	71·8
Ethyl................................	72·0	73·0
*iso*Propyl	72·0	72·5
n-Propyl	72·0	71·6
n-Butyl	67·2	67·4

The Nitration of the Sulphones.—The sulphone (4·0 g.) was carefully mixed with nitric acid (20 c.c., d^{16° 1·56, made by distilling fuming nitric acid over phosphoric oxide) at 0°, and the solution kept at room temperature. The mixture was added to ice, the nitric acid neutralised with sodium carbonate, and several hours allowed for complete separation of the product, which was collected, washed, and dried over sulphuric acid in a vacuum desiccator.

Phenylmethylsulphone gave a 98·6% yield of mononitro-derivatives (*m*-, 98·5%) in 72 hours at 18°.

Nitration of phenylethylsulphone without some loss was found to be impossible. At 18° for 8 hours a 95·5% yield was obtained (*m*-, 100%), but nitration at 10° for 4 hours gave only 93% (*m*-, 96·3%). The average result for the nitration of phenylethylsulphone was *m*-nitro-isomeride, 96%.

Phenyl-*n*-propylsulphone was nitrated at 18° for 4 hours (yield, 98·6%; *m*-, 93·1%).

Phenyl*iso*propylsulphone was nitrated at 7° for 6 hours (yield, 100%; *m*-, 80·0%).

Phenyl-*n*-butylsulphone was nitrated at 18° for 2 hours; the product was isolated by means of ether and chloroform extractions of the neutralised reaction mixture (yield, 98·3%; *m*-, 85·7%).

In considering these results we have assumed that the yields are quantitative and the *m*-isomeride found then corresponds to the percentage formed in the nitration. The results for *m*-nitration are then the following: $\mathrm{Ph{\cdot}SO_2{\cdot}Me}$ (98·5); $\mathrm{Ph{\cdot}SO_2{\cdot}Et}$ (96·0); $\mathrm{Ph{\cdot}SO_2{\cdot}Pr^{\alpha}}$ (93·1); $\mathrm{Ph{\cdot}SO_2{\cdot}Pr^{\beta}}$ (80·0) ; $\mathrm{Ph{\cdot}SO_2{\cdot}Bu}(n)$ (85·7%).

The detailed examination of the nitration of phenylethylsulphone indicated, however, that the *op*-isomerides were preferentially oxidised.

Hence, the more the yields fall short of 100% the more will the *op*-content of the product have been under-estimated. Making all such allowances, the extreme limits of the possible results are not very widely separated and the validity of the general conclusion to be drawn from the results of this investigation cannot be affected by varying the interpretation of the experiments.

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