

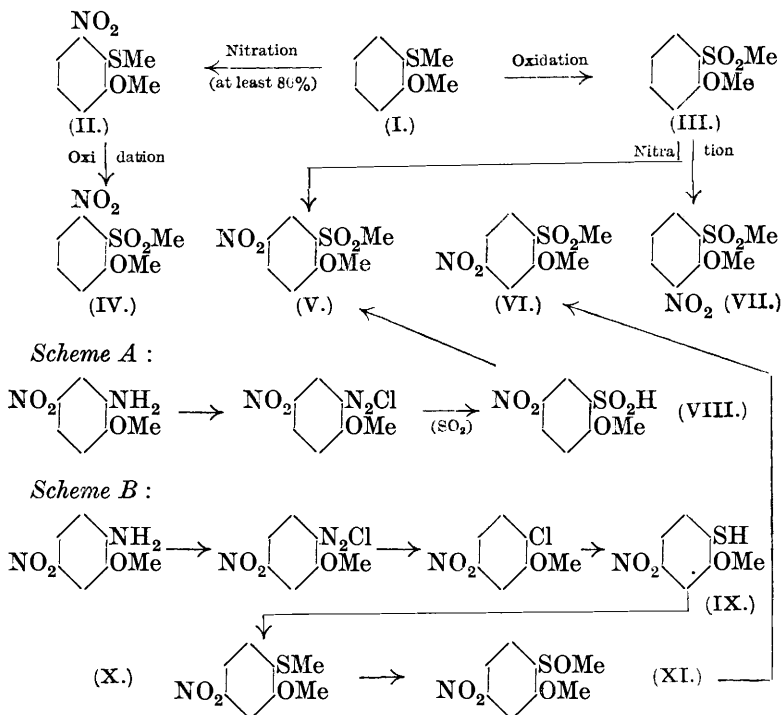
CCXX.—*The Nature of the Alternating Effect in Carbon Chains. Part VII. A Study of the Relative Directive Efficiencies of Oxygen and Sulphur in Aromatic Substitution.*

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IN previous parts of this series, the sequence $N > O > F$ has been established for the *op*-directive efficiencies of these atoms in the neutral state and directly attached to the benzene ring. In pursuance of a general scheme for ascertaining the relationship between the directive powers of atoms and their electronic structures and positions in the periodic classification of elements, an examination has now been commenced of certain sequences derived from vertical columns in the periodic table; and in this paper a study of the relative directive efficiencies of neutral oxygen and sulphur atoms is placed on record.

The nitration of *S*-methylthioguaiacol (I) was carried out under conditions similar to those used in previous parts of this investigation, and 80% of the product consisted of a single *mononitro*-derivative (II) in which the nitro-group had entered the nucleus in the ortho-position relative to the sulphur atom. The orientation of this product was effected by oxidising it to the *sulphone* (IV), which was different from each of the three isomeric sulphones (V),

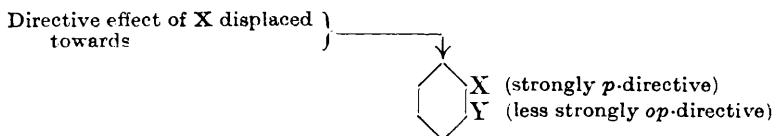
(VI), and (VII), all of which were synthesised by methods (see schemes A and B) which place their constitution beyond doubt. The simple sulphone (III), obtained by oxidising the methylthioguaiacol, yields on nitration a mixture of the isomerides (V) and (VII), the former in the larger quantity. The following table indicates the more important relationships :



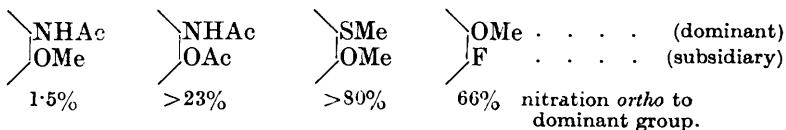
This result clearly establishes the sequence $S > O$ for the *op*-directive efficiencies of these atoms in the neutral state and directly attached to the benzene ring. Both atoms are under identical conditions of substitution in *S*-methylthioguaiacol, and any difference of activity which might arise through the greater stability of thionium than of oxonium salts (*e.g.*, nitrates, in nitration) is such as would handicap the sulphur atom.

The remarkable influence of the methoxyl group in causing the adjacent methylthiol group to direct so strongly to its *ortho*-position necessitates reference to analogous phenomena described by Ingold and Ingold (*this vol.*, p. 1310) and Holmes and Ingold (*ibid.*, p. 1328). Those cases may be summarised by the statement that if an *op*-directive group of relatively moderate strength be introduced

into the ortho-position to a group which, when acting independently, is powerfully *p*-directive, the latter, while still dominating, will have its directive action displaced in favour of ortho-substitution :—

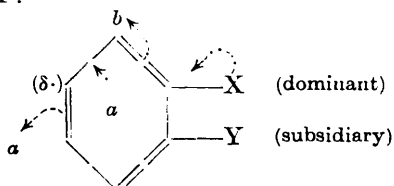


The following examples illustrate this rule :



The first pair (Ingold and Ingold, *loc. cit.*) are perhaps specially noteworthy, since the dominant group is the same in each case and the subsidiary group is changed only by the substitution of acetyl for methyl at the oxygen atom.*

These phenomena appear capable of explanation in terms of the hypothesis discussed by Ingold and Ingold if it be assumed that the small negative charge (δ^-) induced by Y (formula below) in its *p*-position is too weak to neutralise itself effectively by molecular addition with the reagent (leading to substitution at that point), but is, nevertheless, strong enough to divert the electrons from path (a) to path (b) at the bifurcation, thus favouring substitution in the *o*-position to X :



If this is the explanation, the phenomenon will be most pronounced at a certain optimum ratio of the directive strengths of X and Y ; for if Y is relatively *very* weak, it will have an inappreciable effect, whilst, if it is nearly as strong as X, the charges induced by it will become *externally* neutralised and substitution in both *p*-positions will occur. In the series formulated above, the optimum appears to be most closely approached by *S*-methylthioguaiacol. Veratrole and *o*-toluidine illustrate the two extremes.

The result $S > O$ agrees with Ingold and Ingold's theoretical generalisations (*loc. cit.*) according to which $Te > Se > S > O$ should

* This weakens the directive power of the oxygen atom (*loc. cit.*).

hold for the elements of Group VI. It is proposed to test these deductions further.

EXPERIMENTAL.

S-Methylthioguaiacol.—This was prepared from *o*-anisidine by the reactions $\text{MeO}\cdot\text{C}_6\text{H}_4\cdot\text{NH}_2 \rightarrow \text{MeO}\cdot\text{C}_6\text{H}_4\cdot\text{N}_2(\text{SO}_4)_{\frac{1}{2}} \xrightarrow{(\text{SO}_2)} \text{MeO}\cdot\text{C}_6\text{H}_4\cdot\text{SO}_2\text{H} \rightarrow \text{MeO}\cdot\text{C}_6\text{H}_4\cdot\text{SH} \rightarrow \text{MeO}\cdot\text{C}_6\text{H}_4\cdot\text{SMe}$, Gattermann's method (*Ber.*, 1899, **32**, 1147) being followed for the preparation of the sulphinic acid and mercaptan. The latter was methylated by two methods: (i) Thioguaiacol (5 g.) and methyl iodide (20 g.) were added to a solution of sodium methoxide prepared from 0.80 g. of sodium and 20 c.c. of methyl alcohol. After boiling for 6 hours, the solution was poured into water and the methylation product, isolated by means of ether, was distilled at the ordinary pressure. (ii) Thioguaiacol (14 g.) was boiled for 30 minutes with methyl sulphate (16 g.) and aqueous sodium hydroxide (10 g. in 60 c.c.); after cooling, the product was extracted with ether (yield 80%; b. p. 238°).

Mononitration. A solution of *S*-methylthioguaiacol (5 g.) in acetic anhydride (20 g.) was nitrated with a mixture of nitric acid (1.1 g.; *d* 1.5) and acetic anhydride (4.5 g.). After 12 hours, the product was shaken with water. From the solution, rendered faintly alkaline, ether extracted the mononitration product, which distilled as a pale yellow, rather viscous oil, b. p. 144—146°/2 mm. (yield, 6.0 g.; theory, 6.4 g.) (Found: C, 47.8; H, 4.4. $\text{C}_8\text{H}_9\text{O}_3\text{NS}$ requires C, 48.0; H, 4.5%).

Oxidation of the nitro-derivative. The mononitration product was oxidised with an equal weight of fuming nitric acid for 0.5 hour at 0°. After addition of water, the solid (m. p. 137—141°) was collected; from the filtrate, rendered alkaline, ether extracted a further quantity of the same substance, contaminated, however, by gummy impurities. The nitration and oxidation could be carried out without isolating the nitromethylthioguaiacol by slowly adding methylthioguaiacol to 1.5 times its weight of fuming nitric acid at -10°, and, after 1.5 hours, adding water and isolating the product as before.

6-Nitro-2-methoxyphenylmethylsulphone (IV).—The solid, m. p. 137—141°, on crystallisation from methyl alcohol, yielded stellate clusters of very pale yellow needles, m. p. 144—145° (Found: C, 41.2; H, 3.9. $\text{C}_8\text{H}_9\text{O}_5\text{NS}$ requires C, 41.5; H, 3.9%). On working up the mother-liquor, and the residues which had been extracted by ether, further quantities of the same substance were obtained, the total yield of purified material being, in the best experiment, 80% of the theoretical quantity, calculated on the *S*-methyl-

thioguaiacol taken. The ultimate residues were oily, however, and did not yield any other pure substance.

5-Nitro-2-methoxyphenylmethylsulphone (V).—This was obtained along with the 3-nitro-isomeride by nitrating 2-methoxyphenylmethylsulphone (III) (best prepared by methylating anisole-*o*-sulphinic acid with methyl sulphate and aqueous sodium hydroxide), and also by synthesis according to Scheme A (p. 1685).

(i) 2-Methoxyphenylmethylsulphone (2 g.) was added during 1 hour to nitric acid (4 c.c.; *d* 1.5) at 0°. Water was then added and the excess of acid neutralised. The solid product (yield, 3.0 g.; theory, 3.1 g.), m. p. 124—140°, crystallised from methyl alcohol in pale yellow, stout needles, m. p. 149° (Found: C, 41.2; H, 3.7. C₈H₉O₅NS requires C, 41.5; H, 3.9%). Mixed with the 6-nitro-compound, these melted at 126°.

(ii) 4-Nitro-*o*-anisidine (8.6 g., prepared by reducing 2:4-dinitro-anisole with ammonium sulphide) was dissolved in a mixture of sulphuric acid (20 c.c.) and water (150 c.c.), and diazotised with sodium nitrite (3.5 g.), also dissolved in a little water. A cooled mixture of sulphuric acid (25 c.c.) and water (40 c.c.) was then added, and the solution saturated at 0° with sulphur dioxide (about 40 g.). Copper powder (30 g.) was added and, after the evolution of gas had ceased, the solution was extracted with ether. The extract was shaken with aqueous sodium carbonate, and the alkaline solution acidified and again extracted with ether. The last extract was dried and evaporated, the partly solid residue rubbed with cold dilute aqueous potassium hydroxide, and the solution filtered from the oil. The 4-nitroanisole-2-sulphinic acid (VIII) precipitated on acidification crystallised from ethyl acetate in stout prisms (yield 0.6 g.; 4%), m. p. 134—136° (Found: C, 38.7; H, 3.2. C₇H₇O₅NS requires C, 38.9; H, 3.1%).

The sulphinic acid (0.3 g.) in 3*N*-aqueous potassium hydroxide (1.0 c.c.) was shaken with methyl sulphate (0.3 g.), and the solid product crystallised from methyl alcohol, 5-nitro-2-methoxyphenylmethylsulphone, m. p. 149°, being thus obtained.

4-Nitro-2-methoxyphenylmethylsulphone (VI).—(i. Scheme A) 5-Nitro-*o*-anisidine (Ingold and Ingold, *loc. cit.*) was diazotised in sulphuric acid solution, and the diazo-salt decomposed by sulphur dioxide in the presence of copper powder, as described above. Considerable difficulty was experienced in purifying the 5-nitro-anisole-2-sulphinic acid, but after several reprecipitations from alkaline solution, a product was obtained which crystallised from ethyl acetate in colourless needles, m. p. 127—129° (yield 2%).

The material was recovered mostly unchanged after treatment with methyl sulphate as in the preceding case. Its potassium salt was

therefore heated at 100° in a sealed tube with methyl iodide. Even so, some sulphinic acid was recovered, but a small quantity of a neutral product was isolated which crystallised from alcohol in very pale yellow leaflets, m. p. 163—164°. This was identified as 4-nitro-2-methoxyphenylmethylsulphone by comparison with the specimen prepared as described below.

(ii. Scheme B) 5-Nitro-*o*-anisidine (20 g.), dissolved in 32 c.c. of concentrated hydrochloric acid and 20 c.c. of water, was diazotised with 9 g. of sodium nitrite, and the solution treated with cuprous chloride prepared from 7.7 g. of cupric carbonate, 6 g. of copper, and 76 c.c. of hydrochloric acid. 2-Chloro-5-nitroanisole was isolated in a pure form, m. p. 83°, by distillation in steam (yield, 20 g.). This, covered with absolute alcohol, was treated with a solution of 26 g. of crystallised sodium sulphide in 27 c.c. of water and 16 c.c. of alcohol, added in three portions at 1-minute intervals, with vigorous shaking after each addition; the mixture was finally heated for 2—3 minutes on the steam-bath. After 5 minutes, much water was added and the mixture stirred until the precipitate became crystalline. The solid product was digested with cold 10% aqueous sodium hydroxide, and the filtered solution acidified with sulphurous acid. In this way, 5-nitrothioguaiacol (IX) was obtained as a yellow powder, m. p. 76—79°, giving a bright red solution in alkalis. The yield was 7.7 g., and 4—5 g. of unchanged chloro-nitroanisole were recovered by distilling the material insoluble in cold sodium hydroxide in a current of steam. By crystallisation from ether, large, deep orange-yellow prisms were obtained, m. p. 80—81° (Found: C, 45.3; H, 3.8. $C_7H_7O_3NS$ requires C, 45.4; H, 3.8%).

On treating the thiophenol (5 g.), dissolved in 22 c.c. of 5% aqueous sodium hydroxide, with 3 c.c. of methyl sulphate, heat was developed and the red colour of the alkali salt quickly disappeared. Further small quantities of methyl sulphate and alkali were added, and the mixture was boiled for a few minutes. The 5-nitro-*S*-methylthioguaiacol (X) crystallised from methyl alcohol in sulphur-yellow needles or prisms, m. p. about 95°.

This compound was dissolved in an equal weight of fuming nitric acid at 0°. Oxides of nitrogen were evolved and after 0.5 hour water was added. The precipitate, oily at first, became solid on rubbing, and was then crystallised from methyl alcohol, colourless prisms, m. p. 129—130°, of 4-nitro-2-methoxyphenylmethylsulphoxide (XI) being obtained (Found: C, 44.5; H, 4.2. $C_8H_9O_4NS$ requires C, 44.6; H, 4.2%).

The sulphoxide (0.14 g.) was covered with 2 c.c. of dilute sulphuric acid (1 : 3 by volume), a solution of 0.1 g. of potassium dichromate

in a little water added, and the mixture boiled for a few minutes. The solid product crystallised from ethyl alcohol in very pale yellow leaflets, m. p. 163° (Found : C, 41.4; H, 4.1. $C_8H_9O_5NS$ requires C, 41.5; H, 3.9%).

3-Nitro-2-methoxyphenylmethylsulphone (VII).—The methyl-alcoholic mother-liquor obtained in the crystallisation of the 5-nitro-compound was evaporated, a mixture of needles and tablets being obtained. The needles consisted of the 5-nitro-compound. The tablets were separated as far as possible mechanically and crystallised from methyl alcohol; large, pale yellow plates, m. p. 109° , were thus obtained (Found : C, 41.3; H, 4.2. $C_8H_9O_5NS$ requires C, 41.5; H, 3.9%).

Addendum. Bromination of S-Methylthioguaiacol.—The monobromination of *S*-methylthioguaiacol does not proceed quantitatively. Under a variety of conditions a considerable quantity of a dibromo-compound is formed. It crystallises from most organic solvents in colourless, silky needles, m. p. $88-90^{\circ}$ (Found : C, 31.1; H, 3.0. $C_8H_8OBr_2S$ requires C, 30.6; H, 2.7%). No definite proof of its constitution is offered, but the structure of 3 : 5-dibromo-*S*-methylthioguaiacol is suggested on grounds of analogy.

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