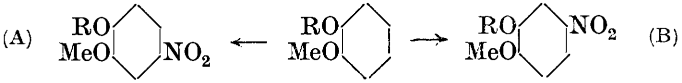
# XLIX.—*The Relative Directive Powers of Groups of the Forms* RO *and* RR′N *in Aromatic Substitution. Part I.*

By James Allan and Robert Robinson.

The nitration of veratrole in cold acetic acid solution proceeds extremely smoothly and 4-nitroveratrole is obtained in almost theoretical yield. Careful search reveals no trace of 3-nitroveratrole or of 4 : 5-dinitroveratrole in the product. An ether of guaiacol, other than veratrole, will naturally yield two nitro-derivatives in relative amounts which depend on the ratio of the directive powers of the groups RO and MeO.



Since the meta-directing influence of the alkyloxy-group is zero, we may assume that Directive Power of OR/Directive Power of OMe = % of (A) formed in the reaction/% of (B) formed in the reaction. In order to obtain numbers which can be compared, the directive power of MeO is taken to be 100. In every case nitration was carried out in cold glacial acetic acid solution, and the composition of the product determined by the method of thermal analysis with the aid of data derived from mixtures of substances of the types (A) and (B), which were prepared by appropriate alkylation of 4- and 5-nitroguaiacols, respectively. The directive powers found in this way were: MeO, 100; EtO, 135; $Pr^{\alpha}O$, 128; $Pr^{\beta}O$, 150; $n-C_4H_9{\cdot}O$, 123; $CH_2Ph{\cdot}O$, 113. It is interesting to note that Sonn and Patschke (*Ber.*, 1925, **58**, 1698) * have observed the order $CH_2{:}CH{\cdot}CH_2{\cdot}O > EtO > Pr^{\alpha}O > MeO$ for the orienting influence of these groups in the course of the preparation of ethers of β-resorcylaldehyde by the Gattermann synthesis.

## EXPERIMENTAL.

*Mixtures of 4-Nitro-2-ethoxyanisole and 5-Nitro-2-ethoxyanisole.*—5-Nitroguaiacol was prepared by the method of Pollecoff and Robinson (J., 1918, **113**, 648) and in the nitration of 2-methoxyphenyl carbonate it was found advantageous to continue stirring at 0° for 3·5 hours. The ethylation of 5-nitroguaiacol was carried out by Ludwig's method (*Monatsh.*, 1900, **21**, 100) and also by the xylene–ethyl sulphate–potassium carbonate process. The yield was 65% and the m. p. 102°. 5-Nitro-2-ethoxyanisole (Freyss, *Bull. Soc. ind. Mulhouse*, 1901, **70**, 375), m. p. 85°, was similarly obtained in 60% yield from 4-nitroguaiacol. The freezing points were determined in a double-jacketed glass tube with the usual precautions. Nucleation and stirring were practised and the thermometer was graduated in fifths of a degree, but could be read accurately to the nearest 0·1°. As in all subsequent cases, the entire range of composition was examined and a portion of the curve selected for closer study either because the readings

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* The work here described was carried out in 1922—1923 and the numerical results were disclosed when Part IV of this series was read at a meeting of the Society in June, 1925 (compare *J. Soc. Chem. Ind.*, 1925, **44**, 659T).

were more free from ambiguity in that region, or because the nitration mixture has a freezing point lying well inside the section.

The following data were employed in the present instance, the first number of each pair representing the percentage of 5-nitro-2-ethoxyanisole in the mixture: 31·5, 83·7°; 37·8, 79·5°; 42·4, 75·4°; 50·9, 66·3°; 54·1, 62·6°; 55·6, 60·1°.

*Nitration of 2-Ethoxyanisole.*—2-Ethoxyanisole, b. p. 213° (Tiemann and Koppe, *Ber.*, 1881, **14**, 2018) (10 g.) mixed with purified acetic acid (30 g.) was nitrated by the gradual addition of nitric acid (12·5 c.c.; *d* 1·42) in acetic acid (30 g.). The mixture was mechanically stirred and cooled in a freezing mixture; the highest temperature reached was 12°. After 45 minutes, the product crystallised and the temperature remained stationary at − 1°; water was then added, the solid collected, well washed and dried (yield 95%). The product (A) was crystallised from methyl alcohol (50 c.c.), and equilibrium ensured by keeping for 5 hours at 16°. The pale yellow crystals were collected, thoroughly drained under pressure, and dried (10·68 g.) (B). 7·1652 G. of (B) mixed with 0·5 g. of 4-nitro-2-ethoxyanisole froze at 66·0°. Hence from the graph, (B) contains 4·82 g. of 4-nitro-2-ethoxyanisole and 5·85 g. of 5-nitro-2-ethoxyanisole. In order to determine the composition of (A) it is necessary to estimate the solubilities of the isomerides in methyl alcohol at 16° and in presence of each other. 4-Nitro-2-ethoxyanisole (6·1860 g.) and 5-nitro-2-ethoxyanisole (3·8571 g.) were allowed to saturate methyl alcohol (25 c.c.) at 16°. The solid residue weighed 9·13 g. and its f. p. was 81·5°, corresponding to 34·9% of 5-nitro-2-ethoxyanisole. Combining these results, it appears that (A) contains 42·5% of 4-nitro-2-ethoxyanisole and 57·5% of 5-nitro-2-ethoxyanisole. That (B) contained the two isomerides only was shown by the fact that 7·1652 g. of (B) mixed with 1·0 g. of 4-nitro-2-ethoxyanisole froze at 68·9°. This corresponds to 51·4% of 4-nitro-2-ethoxyanisole, whereas the percentage calculated from the assumed composition of (B) is 51·9. This result and similar ones recorded below also guarantee the correct location of the points on the graph corresponding to the observed freezing points. The directive power of EtO relative to MeO (100) is therefore 135 in this series.

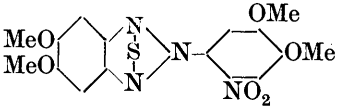
4 : 5-*Dinitro-2-ethoxyanisole.*—The mixture of mononitro-2-ethoxyanisoles was dissolved in cold nitric acid (*d* 1·42) and next day the product was precipitated by water and collected; it crystallised from alcohol in very pale yellow needles, m. p. 150° (yield almost quantitative) (Found: N, 11·6. $C_9H_{10}O_6N_2$ requires N, 11·6%). The m. p. of this methoxyethoxy-compound appears anomalous, since the related dimethoxy- and diethoxy-compounds melt at

132° and 113° respectively. By successive reduction with zinc dust in aqueous alcoholic hydrochloric acid solution, addition of sodium acetate and of a solution of phenanthraquinone in aqueous sodium bisulphite, and boiling, a flocculent, yellow precipitate of 3-*methoxy*-2-*ethoxyphenanthraphenazine* is obtained. Crystallised from xylene, the substance has m. p. 231°, gives a deep magenta solution in sulphuric acid, and fluoresces violet in benzene (Found : N, 8·2. $C_{23}H_{18}O_2N_2$ requires N, 7·9%).

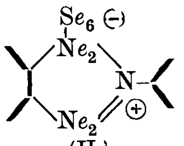
6′-*Nitro*-3′ (or 4′)-*methoxy*-4′ (or 3′)-*ethoxyphenyl*-4 : 5-*thiotriazo-catechol Methyl Ethyl Ether.*—Jones and Robinson (J., 1917, **111**, 910) obtained a compound, $C_{16}H_{16}O_6N_4S$, by the action of hydrogen sulphide on 4 : 5-dinitroveratrole in aqueous alcoholic ammonia. This substance was shown to be a nitro-derivative, reducible to a related diazotisable amine, and it was considered to be 6-nitroveratryl-4 : 5-thiotriazoveratrole (I).

We have applied the reaction under similar conditions to 4 : 5-dinitro-2-ethoxyanisole and have thus obtained a yellow compound which was crystallised by the addition of alcohol to its solution in nitrobenzene. The substance closely resembles nitroveratrylthiotriazoveratrole and appears to be homogeneous. The yellow, rectangular plates, m. p. 175°, are sparingly soluble in alcohol or ether and moderately readily soluble in benzene or chloroform (Found : C, 51·6; H, 4·4; S, 7·8. $C_{18}H_{20}O_6N_4S$ requires C, 51·4; H, 4·8; S, 7·6%).

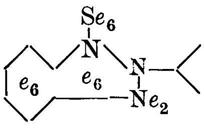
In these substances the $SN_3$ group is associated with 24 valency electrons and on the electronic theory of valency a reasonable assumption regarding the constitution of the thiotriazo-nucleus is that it contains the bipolar ion (II), where each straight line in thin type represents two electrons.



(I.)



(II.)



(III.)

It is very probable, however, that the nucleus has aromatic character and this requires a contribution of four electrons from the $SN_3$ group towards an aromatic sextet, two more being derived by fusion with the benzene nucleus. By analogy with glyoxaline these four electrons should be derived from the nitrogen atom joined to sulphur and from the double bond joining the other nitrogen atoms, giving the expression (III). Here, the sulphur atom is favourably situated for the purpose of increasing its covalency with the nitrogen atom and thus neutralising both its own electrical charge and that on the ring members. The formula (II) is derived from an *o*-thionitrosoazobenzene derivative by a process of internal addition precisely analogous to that assumed by Burkhardt and Lapworth (J., 1925, **127**, 1749) for the first stage of the reaction between nitrosobenzene and ethyl methylenemalonate. In the case we have discussed, the place of the unsaturated ester is taken by the thionitroso-group and the place of the nitroso-group by the azo-group.

4-*Nitro*-2-*propoxyanisole*, prismatic needles, m. p. 106° (Found : C, 56·6; H, 6·1. $C_{10}H_{13}O_4N$ requires C, 56·9; H, 6·2%) and 5-*nitro*-2-*propoxyanisole*, hexagonal tablets, m. p. 72° (Found : C, 56·9; H, 6·5%) were obtained in 70% and 65% yield, respectively, from 5-nitroguaiacol and 4-nitroguaiacol by the action of propyl iodide and potassium hydroxide in boiling alcoholic solution during 5—6 hours.

Mixtures of 4-nitro-2-propoxyanisole and 5-nitro-2-propoxyanisole had the following freezing points, the first number of each pair representing the percentage of 4-nitro-2-propoxyanisole in the mixture : 31·5, 55·5°; 34·2, 59·9°; 36·7, 63·5°; 41·0, 69·6°; 44·2, 73·4°; 50·5, 79·3°; 53·6, 82·4°; 57·0, 84·6°.

*Nitration of* 2-*Propoxyanisole*.—2-Propoxyanisole (10 g.), b. p. 220—225° (Cahours, *Compt. rend.*, 1877, **84**, 1195, gives 240—245°), dissolved in pure acetic acid (45 g.) was nitrated below 9° by the gradual addition with stirring of a mixture of nitric acid (15 c.c.; *d* 1·42) and acetic acid (35 g.). After one hour the product was precipitated by water, collected, washed and dried (A; 96% yield). This material was crystallised from 70 c.c. of 80% ethyl alcohol and after attaining equilibrium at 16° the solid was isolated (B) (10·79 g.). (B) froze at 75·2°, corresponding to 46·2% of 4-nitro-2-propoxyanisole. This was verified by adding 0·5213 g. of 4-nitro-2-propoxyanisole, when the f. p. was 77·6°, corresponding to 48·7% of 4-nitro-2-propoxyanisole (calc., 48·7%). A mixture of the isomerides (11·8861 g.), f. p. 78·5° (corresponding to 49·75% of 4-nitro-2-propoxyanisole) was allowed to reach equilibrium with 80% alcohol (40 c.c.) at 16°. The isolated solid froze at 80·0° (corresponding to 51·25% of 4-nitro-2-propoxyanisole) and the alcohol dissolved 0·5151 g. From these results it may be calculated that (A) contains 43·9% of 4-nitro-2-propoxyanisole and 56·1% of 5-nitro-2-propoxyanisole. The directive power of $Pr^{\alpha}O$ is, accordingly, 128.

4 : 5-*Dinitro*-2-*propoxyanisole*, obtained in theoretical yield from the mono-nitration product of 2-propoxyanisole by the action of nitric acid (*d* 1·42), crystallises from alcohol in needles, m. p. 143° (Found : C, 47·0; H, 5·0. $C_{10}H_{12}O_6N_2$ requires C, 46·9; H, 4·7%).

4-*Nitro*-2-iso*propoxyanisole*, pale yellow, prismatic needles, m. p. 83° (Found: C, 56·7; H, 6·1. $C_{10}H_{13}O_4N$ requires C, 56·9; H, 6·2%) and 5-*nitro*-2-iso*propoxyanisole*, yellow prisms, m. p. 53° (Found: C, 57·0; H, 6·3%), were obtained like the ethyl and propyl compounds previously described, but in this case the yields were only 30% and 15%, respectively. The freezing points of mixtures of the isomerides were the following, the first number of each pair giving the percentage of 5-nitro-2-*iso*propoxyanisole: 24·6, 69·7°; 30·4, 66·7°; 35, 63·7°; 39·5, 60·2°; 48·1, 53·8°.

*Nitration of* 2-iso*Propoxyanisole*.—Guaiacol was converted into its *iso*propyl ether by boiling in alcoholic solution with an equivalent of potassium hydroxide and *iso*propyl iodide. The yield of a colourless oil, b. p. 210—215°, was 90% (Found: C, 71·6, 71·6; H, 8·4, 8·2. $C_{10}H_{14}O_2$ requires C, 72·3; H, 8·4%). Somewhat low results in carbon estimations appear to be normal in the case of these ethers. Thus Cahours (*loc. cit.*) found C, 71·7 for 2-propoxyanisole. The nitration (of 8 g.) was carried out in the usual manner, giving a product (A) in 92% yield which was crystallised from 45 c.c. of 80% alcohol. After standing at 15°, the solids (B) were isolated (7·6978 g.). A mixture of 6·5663 g. of (B) with 2·4954 g. of 4-nitro-2-*iso*propoxyanisole froze at 57·0°, corresponding to 56·0% of 4-nitro-2-*iso*propoxyanisole. Hence (B) contains 39·3% of 4-nitro-2-*iso*propoxyanisole. A further 0·34 g. of 4-nitro-2-*iso*propoxyanisole was added and the f. p. was then 58·2°, corresponding to 57·8% (calc., 57·6%) of the 4-nitro-derivative. 60 C.c. of 80% alcohol dissolved 2·3089 g. of a mixture of 4-nitro-2-*iso*propoxyanisole (5·0 g.) and 5-nitro-2-*iso*propoxyanisole (4·641 g.) at 15° and the residue was isolated. 6·3365 G. of this product mixed with 4-nitro-2-*iso*propoxyanisole (1·1973 g.) had f. p. 61·3°, corresponding to 61·75% of the 4-nitro-derivative. From the above data it may be calculated that (A) contains 40·0% of 4-nitro-2-*iso*propoxyanisole and the directive power of $Pr^{\beta}O$ is 150.

4 : 5-*Dinitro*-2-iso*propoxyanisole*, prepared from the mixture of mononitro-derivatives of 2-*iso*propoxyanisole in the usual manner, is much more readily soluble in alcohol than the propoxy-isomeride and crystallises in rectangular plates, m. p. 129° (Found: C, 46·8; H, 5·0. $C_{10}H_{12}O_6N_2$ requires C, 46·9; H, 4·7%).

4-*Nitro*-2-n-*butoxyanisole*, m. p. 74° (Found: C, 58·3; H, 7·0. $C_{11}H_{15}O_4N$ requires C, 58·7; H, 6·7%), and 5-*nitro*-2-n-*butoxyanisole*, pale yellow prisms, m. p. 56° (Found: N, 6·6. $C_{11}H_{15}O_4N$ requires N, 6·2%), were obtained in the usual manner in 60% and 55% yield, respectively. The freezing points of mixtures of the isomerides are the following, the first number of each pair indicating the percentage of 4-nitro-2-*n*-butoxyanisole: 25·5, 39·8°; 28·3, 37·5°; 33·2, 32·6°; 36·5, 30·4°; 39·6, 33·2°; 42·7, 35·3°; 45·1, 35·7°; 46·9, 35·5°; 50·7, 39·6°; 52·2, 41·8°; 53·8, 44·1°.* A compound, f. p. 35—36°, appears to be formed containing 44% of the 4-nitro-isomeride. The eutectic on the side of the 4-nitro-isomeride is near 35° and on the side of the 5-nitro-isomeride it is near 30°.

*Nitration of* 2-n-*Butoxyanisole.*—The *n*-butyl ether of guaiacol was obtained in almost quantitative yield in the usual manner. It is a colourless oil, b. p. 236—239° (Found: C, 72·8; H, 8·8. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%), and, on nitration in acetic acid below 12°, gave a mixture of mononitro-derivatives (A) in 96% yield. This material was dissolved in 65 c.c. of 80% alcohol and, on cooling, an oil separated and subsequently crystallised. After keeping at 16°, the product (B) was collected, well drained, and pressed, and finally dried at 95° during an hour. (B) (8·5006 g.) mixed with 4-nitro-2-*n*-butoxyanisole (0·3088 g.) froze at 37·3°, corresponding to a mixture containing 49·0% of the 4-nitro-isomeride. On adding 0·3054 g. of the 4-nitro-isomeride, the f. p. observed was 39·6°, corresponding to 50·7% of the 4-nitro-isomeride (calc., 50·7%). Further addition of 4-nitro-2-*n*-butoxyanisole (0·2977 g.) gave a mixture found to contain 52·1% of the 4-nitro-isomeride (calc., 52·2%). A mixture of 4-nitro-2-*n*-butoxyanisole (6·0833 g.) and 5-nitro-2-*n*-butoxyanisole (6·5902 g.) was crystallised from 80% alcohol (50 c.c.) and, after standing at 16°, the solid was isolated and found to weigh 11·2734 g. and to freeze at 38·5°, corresponding to 49·75% of the 4-nitro-isomeride.

From the above data it follows that (A) contains 44·8% of 4-nitro-2-*n*-butoxyanisole and 55·2% of the 5-nitro-isomeride. Consequently the directive power of $n\text{-}C_4H_9\cdot O$ is 123.

4 : 5-*Dinitro*-2-n-*butoxyanisole,* obtained by further nitration of the mixed mononitro-derivatives in excellent yield, crystallises from alcohol in faintly yellow needles, m. p. 97° (Found: C, 48·7; H, 4·9. $C_{11}H_{14}O_6N_2$ requires C, 48·9; H, 5·2%).

4-*Nitro-2-benzyloxyanisole* was obtained in 75% yield from 5-nitroguaiacol by the action of benzyl chloride and potassium hydroxide in boiling alcoholic solution. It crystallises from alcohol in one of two forms, m. p. 93° and m. p. 98° (Found in material, m. p. 93°: C, 64·7; H, 5·2, and in material, m. p. 98°: C, 64·7; H, 5·1. $C_{14}H_{13}O_4N$ requires C, 64·9; H, 5·0%).

5-*Nitro-2-benzyloxyanisole,* m. p. 82°, was similarly obtained from 4-nitroguaiacol in 55% yield (Found: C, 64·9; H, 5·0%). The

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* In this case and also that of the benzyloxy-series, sharper and more consistent readings were obtained if, after thorough nucleation, stirring ceased when the cooling became very slow in the neighbourhood of the freezing point.

freezing points of mixtures of the isomerides were the following, the first number of each pair indicating the percentage of 5-nitro-2-benzyloxyanisole: 17·1, 85·0°; 23·7, 80·0°; 33·6, 72·9°; 37·2, 69·2°; 41·3, 65·2°; 46·0, 57·2°.

*Nitration of 2-Benzyloxyanisole.*—2-Benzyloxyanisole (9·766 g.) dissolved in acetic acid (65 c.c.) was nitrated by the gradual addition of a mixture of nitric acid (20 c.c.; *d* 1·42) and acetic acid (35 c.c.) with cooling in ice and stirring. The temperature rose momentarily to 18°, but quickly fell to 8°. After an hour, water was added and the product (A) collected, washed and dried (yield 98%). The material was crystallised from 80% alcohol (80 c.c.) at 16°, and the solid (B) completely freed from adherent mother-liquor and dried (11·1332 g.). A mixture of (B) (6·3452 g.) and 4-nitro-2-benzyloxyanisole (2·0015 g.) froze at 67·0° and therefore contained 39·5% of 5-nitro-2-benzyloxyanisole. On adding more 4-nitro-2-benzyloxyanisole (0·451 g.), the f. p. was 69·1°, corresponding to 37·3% of the 5-nitro-isomeride in the mixture (calc., 37·5%). Alcohol (50 c.c. of 80%) was saturated at 16° by the addition of 4-nitro-2-benzyloxyanisole (5·0 g.) and 4-nitro-2-benzylanisole (4·2528 g.). The solvent contained 0·3972 g. of the mixed isomerides, whilst the separated material had f. p. 59·5° and thus contained 44·8% of 5-nitro-2-benzyloxyanisole. From the above data it appears that (A) contained 53·0% of 5-nitro-2-benzyloxyanisole and 47·0% of the 4-nitro-isomeride and that the directive power of $CH_2Ph\cdot O$ is 113.

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