299. *The Nitrosation of Phenols. Part XVI.* m-*Fluorophenol. A New Red Indophenol.*

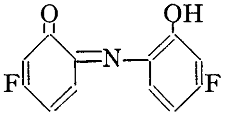
By HERBERT H. HODGSON and DONALD E. NICHOLSON.

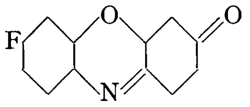
m-Fluorophenol behaves exceptionally towards nitrous acid in an aqueous medium in that reaction occurs in the 6-position instead of the normal 4-position, as in the case of the *m*-chloro-, *m*-bromo-, and *m*-iodo-analogues. Probably 5-fluoro-2-nitrosophenol is the first product formed, but this immediately condenses with unchanged *m*-fluorophenol to form a mm'-*difluoro*-o-*indophenol* which is red-brown and very stable to acids. The constitution of this new type of red indophenol has been established by a comprehensive scheme of colour reactions. This exceptional nitrosation of *m*-fluorophenol is compared with that of *m*-methoxyphenol, and both are explicable on electronic grounds.

THE action of nitrous acid on *m*-halogenophenols has been studied for the chloro-, bromo-, and iodo-derivatives (Hodgson and Moore, J., 1923, **123**, 2499; 1925, **127**, 2260; Hodgson and Kershaw, J., 1929, 1553; 1930, 967, 1969) and found to produce the *m*-halogeno-*p*-nitrosophenols as deep greenish-yellow, exceedingly reactive compounds which were immediately converted by alkalis, and less readily by hot mineral acids, into light greenish-yellow (almost colourless), very stable *m*-halogeno-*p*-benzoquinoneoximes, of which the m. p.'s were *ca.* 50° higher than those of their nitroso-isomerides. The absorption spectra of both sets of compounds exhibited marked differences (Hodgson, J., 1937, 520). The present paper now completes the series by a study of the action of nitrous acid on *m*-fluorophenol.

When an attempt was made to nitrosate *m*-fluorophenol directly, whether by nitrous acid alone, or in the presence of acetic acid and/or of mineral acids, the product was not a nitroso-compound, but a red-brown microcrystalline indophenol, which began to be formed immediately on admixture of the reactants, as shown by the rapid appearance of a red colour. When the reaction was conducted in 30% aqueous acetic acid at room temperature, precipitation of the red indophenol occurred continuously over several days, until an almost quantitative yield was obtained. At 100° the reaction was immediate, and it was also more rapid when carried out in sulphuric acid under Hodgson and Kershaw's conditions (*loc. cit.*). In all cases, a small amount of 5-fluoro-2-nitrophenol was obtained by a simultaneous reaction, as proved by its presence in the benzene extract of a mixture which had been kept for 48 hours.

When the above reaction mixture was repeatedly submitted to filtration at short intervals, the earlier precipitates gave the Liebermann nitroso-reaction. When extracted with ligroin or light petroleum, they afforded only red solutions with phenol and concentrated sulphuric acid. The later precipitates gave no Liebermann reaction. Microanalysis of the earlier precipitates gave decreasing nitrogen contents from 6·8 to 5·8%, showing the presence of small amounts of nitroso-compounds, which, however, could not be extracted in workable amounts. The later precipitates all had N, 6·0%. This red-brown compound was readily crystallised from 50% acetic acid, and then appeared to be homogeneous under the microscope as red microcrystalline plates. The following evidence indicates that it has the structure (I) of a mm'-*difluoro*-o-*indophenol*; if so, this would be the first representative of this class of compound.


(I.)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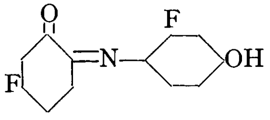
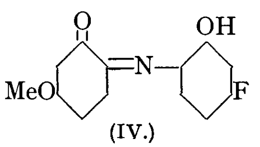
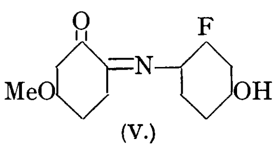
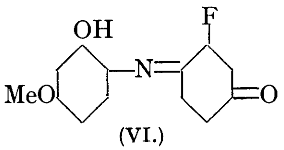

(III.)

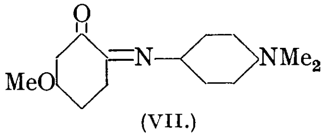
1. The red compound had the correct composition and molecular weight.
2. It was insoluble in cold benzene, light petroleum, ligroin, and ether; soluble in acetone and in ethyl and methyl alcohols; easily soluble in cold glacial acetic acid, and in hot 50% acetic acid; readily soluble in cold solutions of alkaline hydroxides and carbonates, from which it was precipitated unchanged by acids. These solubilities exclude the possibility that the compound is a red oxazone (II), for this contains two hydrogen atoms less than (I), and, since it contains no hydroxyl group, should not be readily soluble in the above solvents.
3. It formed no steam-volatile organic products when boiled with alkalis, with neutral, alkaline, or acid permanganate, alkaline potassium ferricyanide, or dilute nitric acid, but ammonia was evolved with boiling alkalis. This set of reactions excludes the structure (III), which would be expected to furnish a steam-volatile *p*-benzoquinone on oxidation.
4. The structure (I) is supported by the following colour reactions. (*a*) *p*-Nitrosodimethylaniline gives blue-green products when heated with phenol, *o*- and *m*-cresols, or *o*-chlorophenol, but red products are formed with *p*-cresol and *p*-chlorophenol, and with all the *m*-halogenophenols; all these colours persist unchanged for a reasonable period in cold concentrated sulphuric acid, and indicate that the *p*-indophenolic structures give rise to blue-green, and the *o*-indophenolic to red compounds. The oxazone structure is excluded in these reactions. (*b*) *m*-Chloro-*p*-nitrosophenol, when heated with phenol, the four *m*-halogenophenols, *p*-cresol, or *p*-chlorophenol, gives red products, but on heating it with *o*- or *m*-cresol or with *o*-chlorophenol, blue-green compounds are obtained; all these colours persist in cold concentrated sulphuric acid. (*c*) 2-Nitroso-5-methoxyphenol (Henrich and Eisenach, *J. pr. Chem.*, 1904, **70**, 332; Hodgson and Clay, J., 1929, 2775) condenses immediately when heated with *m*-fluorophenol, and also with *p*-cresol and *p*-chlorophenol but less readily, to give red products which remain red in cold concentrated sulphuric acid. If this compound is mixed with *m*-fluorophenol and treated in the cold with concentrated sulphuric acid, the condensation product is red, indicating the formation of a product of constitution (IV) or (V); moreover,

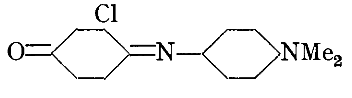

(IV.)

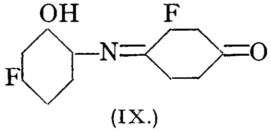

(V.)


(VI.)

if the product has structure (V), there is no isomerism into a blue-green compound of structure (VI). The red product is readily soluble in alkalis to give red solutions, a reaction which favours structure (IV). (*d*) Dimethylaniline condenses with 2-nitroso-5-methoxyphenol very slowly on warming, and very rapidly in the presence of concentrated sulphuric acid, to give a red compound. With 3-chloro-4-nitrosophenol, or 3-chlorobenzoquinone-4-oxime, however, blue compounds are obtained. Oxazone formation cannot occur in

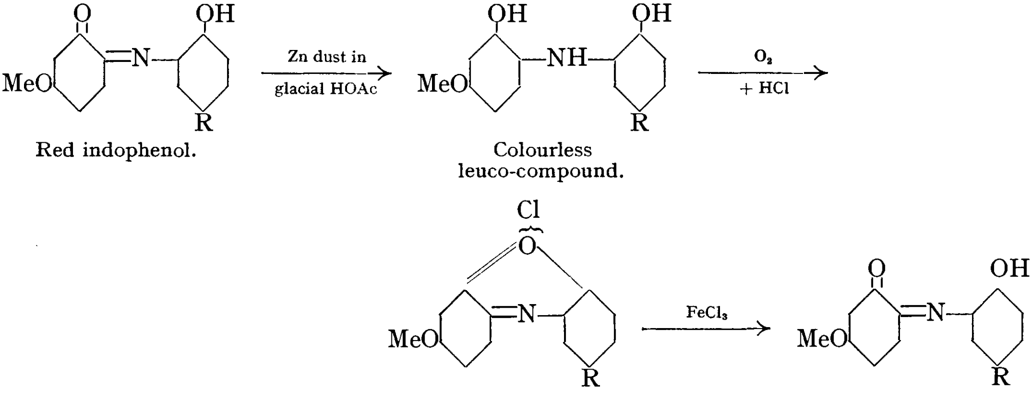

(VII.)


(VIII.)


(IX.)

these reactions, and structures (VII) and (VIII) would appear to represent the respective compounds formed. The red colour of the compound under discussion would therefore exclude the *p*-indophenolic structure (IX), since such compounds are blue.

5. The red compounds formed by 2-nitroso-5-methoxyphenol with *p*-cresol and *p*-chlorophenol when heated together, either without solvent or in glacial acetic acid solution, are reduced by zinc dust to leuco-compounds which, on atmospheric oxidation, particularly in the presence of hydrochloric acid, give blue solutions turned to red by ferric chloride. The following sequence of reactions has apparently taken place (R = Me or Cl, respectively) :



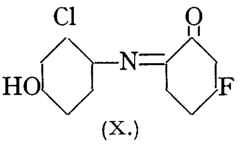
Red indophenol.

Colourless leuco-compound.

Blue oxazine.

Original red indo-phenol.

The assumed *mm'*-difluoro-*o*-indophenol under discussion, when submitted to this series of three reactions, gave successively a leuco-compound, a blue solution, and a red colour, thus affording support for the structure (I). If, however, *m*-chloro-*p*-nitrosophenol is condensed with *m*-fluorophenol in glacial acetic acid solution, the red indophenol formed is reduced to a leuco-compound which becomes red when treated with hydrochloric acid in air. The structure (X) which must be assigned to this compound would not admit of the formation of a blue oxazine. Whereas 2-nitroso-5-methoxyphenol condenses alone or in glacial acetic acid solution with phenol, *o*-cresol, and *o*-chlorophenol to give red compounds, the leuco-compounds of the first two give the above blue oxazine reaction, and the last a red solution with hydrochloric acid, showing that it has condensed in the *p*-position, as opposed to the *o*-position for the other two.



(X.)

Mechanism of the Nitrosation Reaction.—From the foregoing data, it would appear that the reaction of nitrous acid with *m*-fluorophenol takes place in two stages, *viz.*, (1) a slow nitrosation in the 6-position, accompanied by a small amount of nitration also in this position, and (2) a rapid consecutive condensation of the nitroso-compound with the unchanged *m*-fluorophenol to form the red compound (I) (cf. Schoutissen, *Rec. Trav. chim.*, 1921, **40**, 753).

When *m*-chlorophenol is treated similarly, a continuous yield of the *m*-chloro-*p*-nitrosophenol is formed, but if the reaction mixture is kept for several weeks, the final precipitates when extracted with light petroleum leave red-brown residues, which have no melting point, and are presumably similar to the main reaction product of the nitrosation of *m*-fluorophenol.

That the nitrosation of *m*-fluorophenol should occur in the 6-position is due to the powerful negative inductive (— *I*) effect of the fluorine atom on the 4-position, whereas in the other three *m*-halogenophenols, this effect is insufficient to inhibit nitrosation in the normal 4-position, as typified by the case of phenol itself. It is noteworthy that, whereas *o*-nitrosation in the case of *m*-fluorophenol is due to inhibition, that of *m*-methoxyphenol is due to enhanced reactivity of the 6-position due to the electromeric reactivity of the *m*-methoxy-group (Hodgson and Clay, *loc. cit.*).

EXPERIMENTAL.

Action of Nitrous Acid on m-*Fluorophenol.*—(a) *In aqueous acetic acid solution.* *m*-Fluorophenol (2 g.), dissolved in 50% aqueous acetic acid (25 c.c.), was treated with a solution of sodium nitrite (4 g.) in water (10 c.c.) either gradually or all at once. The resulting solution, which had now *ca.* 30% acetic acid content, immediately became deep red, and, after about 10 mins., a red-brown solid began to separate. This precipitation continued for several days until all the *m*-fluorophenol had reacted, and during the first 24 hours 0·5—1·0 g. could be filtered off. Steam-distillation, either of the original mixture, or of the solution after several precipitates had been removed, afforded 5-fluoro-2-nitrophenol in small quantity (m. p. and mixed m. p. with authentic specimen, 32°). Extraction of the reaction mixture with benzene after the reaction had lasted 24 hours, followed by steam-distillation of the extract, gave 5-fluoro-2-nitrophenol, thereby proving that it was formed by a slow reaction taking place simultaneously with the more rapid nitrosation. This nitration can be detected at almost all periods of the reaction. The early precipitates gave deep orange-brown colours with concentrated sulphuric acid, and the Liebermann reaction with cold phenol and concentrated sulphuric acid (see above). The precipitates collected after 24 hours gave either very poor colours or none at all in the Liebermann reaction, but dissolved gradually in the cold acid to give deep red-brown solutions. Extraction of the early precipitates with cold benzene gave negative results, and extraction with hot benzene, light petroleum, or ligroin afforded only traces of green products which gave the Liebermann reaction, the residues then dissolving slowly in cold phenol–sulphuric acid to give red-brown solutions; these, which were composed of red microcrystalline plates and appeared homogeneous, dissolved in cold glacial acetic and also in hot aqueous acetic acid as dilute as 50%, from which red-brown, microcrystalline plates separated which had no m. p. (Found: C, 61·2; H, 2·9; N, 6·0; *M*, cryoscopic in phenol, 236·5. $C_{12}H_7O_2NF_2$ requires C, 61·3; H, 3·0; N, 5·9%; *M*, 235), and were very stable towards hot concentrated or aqueous mineral acids. The other properties have been described above. When the nitrosation was conducted below 0°, products were formed which sintered from 100° to 130° owing to admixture with uncondensed nitroso-products.

(b) *In aqueous sulphuric acid solution.* *m*-Fluorophenol (4 g.), dissolved in a solution of sodium hydroxide (2 g.) and sodium nitrite (10 g.) in water (300 c.c.), was ice-cooled externally while a mixture of sulphuric acid (8 c.c.) and water (12 c.c.) was added with vigorous stirring during 2 hours. The colour of the solution immediately became orange-red and a copious tarry separation occurred. This tar was insoluble in light petroleum, and, when dissolved in alkali solution and reprecipitated at 0° with acids, afforded the red-brown *mm'*-difluoro-*o*-indophenol of reaction (a). When a solution of concentrated sulphuric acid (2 c.c.) in water (10 c.c.) was added to the nitrosation mixture (a), the red indophenol separated in a solid non-tarry condition. 5-Fluoro-2-nitrophenol was obtained by steam-distillation of all the reaction mixtures or of their benzene extracts.

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