237. *The Nitrosation of Phenols. Part XVIII. The Synthesis of 3-Fluoro-4-nitrosophenol and of 3-Fluoro-6-nitrosophenol. A Comparison of the Stabilities of the 3-Halogeno-4-nitrosophenols.*

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The syntheses of 3-fluoro-4-nitrosophenol from 3-fluoro-4-nitrophenol and of 3-*fluoro*-6-*nitrosophenol* from 3-fluoro-6-nitrophenol are described. The direct nitrosation of *m*-fluorophenol to 3-fluoro-4-nitrosophenol has now been effected. 3-Fluoro-4-nitrosophenol does not appear to be convertible into 3-fluorobenzoquinone-4-oxime and moreover is an exceedingly stable substance compared with other 3-halogeno-4-nitrosophenols.

IT has previously been found that nitrous acid reacts with *m*-fluorophenol to form *mm'*-difluoro-*o*-indophenol, and that when the reagent is nitrosylsulphuric acid the main product is 4 : 2'-difluoro-4'-hydroxy-*o*-benzoquinone-1-phenylimine, a trace of 3-fluoro-4-nitrosophenol also being formed (Hodgson and Nicholson, J., 1939, 1405; this vol., p. 205). Attempts to nitrosate *m*-fluorophenol directly by almost every conceivable variation of procedure have always resulted in the production of one or both of the above *o*-quinonoid compounds owing to the immediate condensation of the initially nitrosated *m*-fluorophenol with *m*-fluorophenol. In this respect *m*-fluorophenol is far more reactive than the other *m*-halogenophenols.

The synthesis of 3-fluoro-4-nitrosophenol has now been achieved as follows : 3-Fluoro-4-nitrophenol ⟶ 3-fluoro-4-nitroanisole ⟶ 3-*fluoro*-4-*aminoanisole* ⟶ 3-*fluoro*-4-*nitrosoanisole* ⟶ 3-fluoro-4-nitrosophenol. The synthetic material is identical with the product obtained in traces by the action of nitrosylsulphuric acid in glacial acetic solution on *m*-fluorophenol.

Since only the last-named method, apart from the synthetic one, had afforded any 3-fluoro-4-nitrosophenol, many modifications of it were tried. Ultimately it was found that a solution of *m*-fluorophenol in pyridine, when added gradually to nitrosylsulphuric acid somewhat diluted with water (cf. the diazotisation procedure of de Milt and van Zandt, *J. Amer. Chem. Soc.*, 1936, **58**, 2044) and maintained below 10°, gave a mixture of compounds in which 3-fluoro-4-nitrosophenol predominated. At higher temperatures, red compounds were formed in increasing amounts. Recrystallisation from benzene gave the pure green 3-fluoro-4-nitrosophenol, the identity of which was confirmed by comparison with the synthetic product and by the formation of 3-fluoro-4-nitrophenol on oxidation.

The following evidence is in favour of the above green compound being a nitroso-compound rather than 3-fluorobenzoquinone-4-oxime :

(1) The other three 3-halogenobenzoquinoneoximes crystallise from benzene in colourless needles, whereas the 3-fluoro-compound crystallises in dark green, rectangular plates.

(2) When 3-chlorobenzoquinone-4-oxime is mixed in the cold with dimethylaniline and concentrated sulphuric acid, it gives immediately a blue condensation product; 3-chloro-4-nitrosophenol under the same conditions gives a blue colour only after a considerable time, indicating that conversion into the quinonoid form precedes condensation. 3-Fluoro-4-nitrosophenol gives, both with sulphuric acid alone and also with a mixture of dimethylaniline and sulphuric acid, an orange-brown colour, which remains unchanged after 12 hours.

(3) When mixed with cold *m*-fluorophenol and concentrated sulphuric acid, 3-chloro-4-

nitrosophenol and 3-chlorobenzoquinone-4-oxime develop deep green colours immediately, and 6-nitroso-3-methoxyphenol gives a deep red colour. 3-Fluoro-4-nitrosophenol, however, gives the orange-brown colour produced by sulphuric acid alone; this slowly changes to green, indicating gradual condensation with the *m*-fluorophenol.

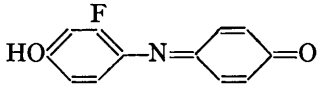
(4) 3-Fluoro-4-nitrosophenol does not form a silver salt, and dissolves in alkalis to form olive-green solutions, whereas all the authentic 3-halogenobenzoquinone-4-oximes form red solutions with alkalis.

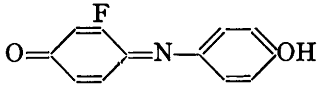
(5) Attempts to methylate 3-fluoro-4-nitrosophenol by the standard methods were unsuccessful. All the other 3-halogeno-4-nitrosophenols give some 3-halogenobenzoquinone-4-oxime methyl ether on treatment with diazomethane.

(6) The green 3-fluoro-4-nitrosophenol was recovered unchanged on acidification of its solution in alkali. The other greenish-yellow 3-halogeno-4-nitrosophenols are converted by alkali into the almost colourless 3-halogenobenzoquinone-4-oximes (Hodgson and Moore, J., 1923, **123**, 2499; 1925, **127**, 2260).

Although 3-fluoro-4-nitrosophenol gives a Liebermann reaction with phenol and concentrated sulphuric acid, this would not necessarily involve its conversion into the quinone-oxime form. Since no condensation takes place with dimethylaniline, it would appear that the formation of a blue colour with phenol is due to the tautomeric conversion of the phenol itself, so that the condensation product would have the constitution (I) rather than (II).

(I.)

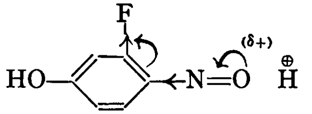




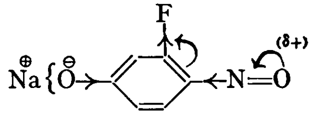
(II.)

Comparison of the Stabilities of the Four 3-Halogeno-4-nitrosophenols.—3-Fluoro-4-nitrosophenol cannot be converted into 3-fluorobenzoquinoneoxime, whereas 3-iodo-4-nitrosophenol is readily converted by solvents or even in the air into the quinoneoxime modification. 3-Chloro-4-nitrosophenol is stable in the air, but is slowly converted into 3-chlorobenzoquinone-4-oxime by acids. 3-Bromo-4-nitrosophenol is intermediate in stability between the 3-chloro- and the 3-iodo-analogue.

It follows that the powerful electron-attractive inductive effect (*—I*) of the fluorine atom has completely inhibited electron transfer from the hydroxyl oxygen to the nitroso-oxygen, either by the external attraction of hydrogen ions (acid conversion; III) (cf. Hodgson and Kershaw, J., 1929, 1553) or by alkaline conversion (IV).



(III. Repulsion instead of attraction.)



(IV.)

This inhibition by the fluorine atom in the case of *m*-fluorophenol itself is sufficient to reduce the activity of the neighbouring carbon atom in position 4, so that nitrosation in aqueous solution, and also condensation with 4-nitrosodimethylaniline, occur preferentially in position 6 (Hodgson and Nicholson, J., 1939, 1405). This inhibition is also shown by the fact that 3-fluoro-4-nitrosophenol is not attacked by diazomethane. This non-reactivity is in marked contrast with the almost quantitative formation of glyoxime *NN'*-di-2-chloro-4-methoxyphenol ether when 3-chloro-4-nitrosophenol is treated with diazomethane.

Synthesis of 3-Fluoro-6-nitrosophenol.—This *compound* was prepared from 3-fluoro-6-nitrophenol by successive methylation, reduction, oxidation, and demethylation, as in the case of 3-fluoro-4-nitrosophenol. It proved to be very stable, did not give a Liebermann reaction, and did not condense with dimethylaniline.

Cobalt Salts.—As would be expected, 3-fluoro-6-nitrosophenol forms a co-ordinated *cobalt* salt, whereas the *cobalt* salt of 3-fluoro-4-nitrosophenol is not co-ordinated.

EXPERIMENTAL.

Synthesis of 3-Fluoro-4-nitrosophenol.—An intimate mixture of 3-fluoro-4-nitrophenol (2 g.), potassium carbonate (2 g.), and methyl sulphate (1 c.c.) was heated on the water-bath for 5 minutes and then steam-distilled, the volume of liquid in the flask being kept as small as possible. 3-Fluoro-4-nitroanisole passed over, and a further quantity was obtained by adding more potassium carbonate (1 g.) and methyl sulphate (0·5 c.c.) to the residual liquor, which was then warmed and steam-distilled. 3-Fluoro-4-nitroanisole (1·5 g.) crystallised from light petroleum in colourless needles, m. p. 56·5° (Hodgson and Nixon, J., 1928, 1879, give m. p. 56·5°). This method is more convenient than treatment of the silver salt of 3-fluoro-4-nitrophenol with methyl iodide.

3-*Fluoro*-4-*aminoanisole* was obtained by reduction of 3-fluoro-4-nitroanisole with iron and alcoholic hydrochloric acid and isolated by steam distillation after the liquor had been made alkaline. It crystallised from water in long colourless needles, m. p. 50° (Found: N, 10·1. C_7H_8ONF requires N, 9·9%).

3-*Fluoro*-4-*nitrosoanisole* was prepared from 3-fluoro-4-aminoanisole by oxidation with Caro's acid (cf. Hodgson and Kershaw, J., 1929, 1553) for a few minutes. On steam-distillation it was obtained as a dark green oil, which solidified on cooling and then crystallised from light petroleum in long blue-green needles, m. p. 46° (Found: N, 9·3. $C_7H_6O_2NF$ requires N, 9·1%).

The emerald-green solution of 3-fluoro-4-nitrosoanisole in methyl alcohol (4 c.c.), when shaken with concentrated hydrochloric acid (1·5 c.c., *d* 1·16) for 5 minutes, became deep red and heat was evolved. The liquid was allowed to evaporate in the air, and the 3-fluoro-4-nitrosophenol crystallised from benzene, forming dark green, rectangular plates, m. p. 161° (Found: N, 9·9. Calc. for $C_6H_4O_2NF$: N, 9·9%).

Nitrosation of m-*Fluorophenol.*—Sodium nitrite (1·5 g.) was dissolved in concentrated sulphuric acid (15 c.c., *d* 1·84), the solution cooled to 0°, and ice (7 g.) added without stirring. When all the ice had dissolved, the whole was again cooled by an external freezing mixture, and a solution of *m*-fluorophenol (1 c.c.) in pyridine (7·5 c.c.) added dropwise with vigorous stirring during 30 minutes so that the temperature never rose above 10°. The mixture was stirred for a further 5 minutes and then poured into water (150 c.c.). The solid which separated was washed with water and dried in the air. It was a mixture of a red and a green compound; the latter was extracted with benzene, from which it separated in dark green crystals, m. p. 161° (Found: N, 10·0%; *M*, cryoscopic in phenol, 139. Calc.: *M*, 141), unchanged by synthetic 3-fluoro-4-nitrosophenol.

The 4-nitroso-structure was confirmed by comparison with 2-chloro,- 3-chloro-, and 3-bromo-4-nitrosophenols. In all cases a blue-green colour was obtained with cold *o*-chlorophenol and concentrated sulphuric acid, and a yellow-green colour with *m*-chlorophenol and concentrated sulphuric acid.

Synthesis of 3-*Fluoro*-6-*nitrosophenol.*—3-Fluoro-6-aminoanisole was obtained as a steam-volatile yellow-brown oil by the reduction of 3-fluoro-6-nitroanisole (Hodgson and Nixon, J., 1928, 1879). The *acetyl* derivative crystallised from water in colourless needles, m. p. 132° (Found: N, 7·9. $C_9H_{10}O_2NF$ requires N, 7·7%).

3-*Fluoro*-6-*nitrosoanisole* was obtained, by oxidation of 3-fluoro-6-aminoanisole with Caro's acid (*loc. cit.*), as a yellow-brown steam-volatile solid, m. p. 150° (Found: N, 8·9. $C_7H_6O_2NF$ requires N, 9·1%). With cold phenol and concentrated sulphuric acid it gave a dark blue colour.

3-*Fluoro*-6-*nitrosophenol* was obtained by demethylation of 3-fluoro-6-nitrosoanisole with concentrated sulphuric acid in methyl alcohol. On evaporation of the solution, it separated as a very dark micro-crystalline solid which had no m. p. (Found: N, 10·0. $C_6H_4O_2NF$ requires N, 9·9%). It gave with concentrated sulphuric acid a purple colour, which remained unaltered when phenol also was present.

The Cobalt Salts of 3-*Fluoro*-4-*nitroso- and* 3-*Fluoro*-6-*nitroso-phenol.*—(a) *Cobalt salt of* 3-*fluoro*-4-*nitrosophenol.* A solution of the phenol in methyl alcohol was diluted gradually with water until signs of precipitation appeared and was then added to a very dilute solution of cobalt nitrate in 50% aqueous methyl alcohol. The dark red-brown *cobalt* salt was immediately precipitated in micro-plates, m. p. 130—140° [Found: N, 8·7. $(C_6H_3O_2NF)_3Co$ requires N, 8·7%]. It gave the same Liebermann nitroso-reaction as the original substance, and was moderately easily soluble in chloroform, giving a red solution which was yellow in thin layers. It was decomposed by aqueous sodium hydroxide to give a red-brown mixture, from which cobalt sulphide was precipitated by hydrogen sulphide.

(b) *The co-ordinated cobalt salt of* 3-*fluoro*-6-*nitrosophenol.* *m*-Fluorophenol (1 g.), dissolved in water (200 c.c.) containing sulphuric acid (1 c.c., *d* 1·84), was shaken with finely powdered sodium cobaltinitrite (0·7 g.). The mixture turned red immediately and a dark maroon solid began to form after about an hour; after 3 hours this was filtered off. The *compound* was very soluble in chloroform, giving a deep red solution which was red in thin layers, and moderately easily soluble in benzene, ether, and methyl alcohol. It was unaltered by aqueous sodium hydroxide, and separated from chloroform in maroon plates, m. p. *ca.* 105° [Found: N, 8·7. $(C_6H_3O_2NF)_3Co$ requires N, 8·7%], which gave a purple colour with concentrated sulphuric acid, either alone or in the presence of phenol. This colour was identical with the purple colour given by 3-fluoro-6-nitrosophenol, which substance also gave an identical co-ordinated cobalt salt by procedure (a).

The authors desire to thank Imperial Chemical Industries Ltd. (Dyestuffs Group) for gifts of chemicals.

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[*Received, June* 19*th*, 1940.]