

53. *The Nitrosation of Phenols. Part XIX. The Three Cresols and their Methyl Ethers. Some Semicarbazide Reactions.*

By HERBERT H. HODGSON and ERIC A. C. CROUCH.

Nitrous acid reacts normally with *o*- and *m*-cresol to give the 5- and the 6-nitroso-derivative respectively, but it nitrates *p*-cresol to form 3-nitro-*p*-cresol. Nitrosylsulphuric acid nitrosates or nitrates *o*- and *m*-tolyl methyl ethers according to conditions, but not *p*-tolyl methyl ether. 5-Nitroso-*o*-cresol and 5-nitroso-*o*-tolyl methyl ether are converted by dilute nitric acid into 3 : 5-dinitro-*o*-cresol and the *m*-tolyl isomerides are both oxidised to 6-nitro-*m*-cresol, *i.e.*, both nitrosotolyl methyl ethers lose the *O*-methyl group. Some analogy with the behaviour of the dialkylanilines towards nitrous acid is indicated. The differences between the nitroso-*o*- and -*m*-tolyl methyl ethers in their behaviour towards semicarbazide are discussed.

IN this investigation three nitrosation procedures have been used : (a) The standard process with sodium nitrite in dilute sulphuric acid (Bridge, *Annalen*, 1893, 277, 85); (b) the aqueous acetic acid method; and (c) the nitrosylsulphuric acid method of Hodgson and Nicholson (*J.*, 1939, 1808).

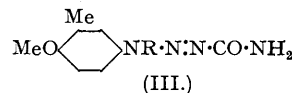
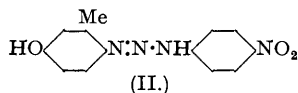
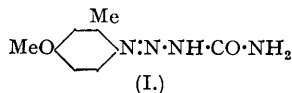
By (a) and (b), *o*- and *m*-cresol afforded 5-nitroso-*o*-cresol and 6-nitroso-*m*-cresol respectively, but *p*-cresol was nitrated to 3-nitro-*p*-cresol. Procedure (c) gave violent reactions with all three cresols and no useful products were obtained. All three tolyl methyl ethers were unaffected by (a) and (b), but (c) gave nitroso- or nitro-compounds with the *o*- and *m*-compounds according to the conditions, *viz.*, 5-nitroso-*o*-tolyl methyl ether or 3 : 5-dinitro-*o*-cresol from the *o*-ether, and 6-nitroso-*m*-tolyl methyl ether from the *m*-ether; *p*-tolyl methyl ether gave no useful product.

It will be noted that *p*-cresol is nitrated in the *o*-position to the hydroxyl group analogously to the *o*-nitration of dimethyl-*p*-toluidine (Hodgson and Kershaw, J., 1930, 277), whereas normal *p*-nitrosation occurs with *o*- and *m*-cresol. In the cases of the *o*- and the *m*-tolyl methyl ether, however, nitration, when it occurs, is accompanied by expulsion of the methyl from the methoxyl group as in analogous cases among the dialkyl-anilines (Hodgson and Nicholson, J., 1941, 470).

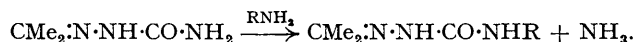
5-Nitroso-*o*- and 6-nitroso-*m*-cresol and 5-nitroso-*o*- and 6-nitroso-*m*-tolyl methyl ethers were readily oxidised by dilute nitric acid at 40° (cf. Robertson, J., 1902, 81, 1477), the *o*-compounds giving 3 : 5-dinitro-*o*-cresol, and the *m*-compounds 6-nitro-*m*-cresol. It would appear, therefore, that, under the experimental conditions used, the action of nitrosylsulphuric acid on the cresols and their methyl ethers proceeds by nitrosation and subsequent oxidation, with expulsion of the *O*-methyl group from the ethers.

The position of the nitroso-group in the nitrosotolyl methyl ethers was determined by oxidation of the *m*-tolyl compound to the corresponding nitro-compound and by conversion of the *o*-tolyl compound into *p*-toluquinone.

According to Bamberger (*Helv. Chim. Acta*, 1931, 14, 242), substituted hydrazines and aromatic nitroso-compounds react by initial addition of equimolecular amounts in a reaction of the aldol type, followed by oxidation of the resulting compound by another molecule of the nitroso-compound, which itself is reduced to a hydroxylamine. We find, however, that 6-nitroso-*m*-tolyl methyl ether condenses like a ketone with semicarbazide to form 4-methoxy-2-methylbenzenediazoaminocarbonamide (I), which crystallises unchanged from



boiling aniline, and reacts rapidly with cold *p*-nitrophenylhydrazine to form 4'-nitro-4-hydroxy-2-methyldiazoaminobenzene (II), the methoxyl group being demethylated. On the other hand, 5-nitroso-*o*-tolyl methyl ether reacts with semicarbazide according to the Bamberger generalisation; the product (III, R = OH) could not be crystallised and was identified by conversion by boiling aniline into 4-methoxy-3-methylhydrazobenzene-*N*-diazoaminocarbonamide (III, R = NPh). Since only one oxygen atom (exclusive of the methoxyl oxygen) remains in the final compound, the reaction takes place by substitution at the *N*-OH group rather than by condensation at the CO-NH₂ group, which was found by Borsche and his co-workers (*Ber.*, 1901, 34, 4299; 1904, 37, 3177; 1905, 38, 831; cf. also Wilson, Hopper, and Crawford, J., 1922, 121, 866) to be the main reaction between semicarbazones and amino-compounds on heating :



5-Nitroso-*o*-tolyl methyl ether condenses normally with *p*-nitrophenylhydrazine to form 4'-nitro-4-methoxy-3-methyldiazoaminobenzene.

This difference in reactivity between the nitroso-*o*- and -*m*-tolyl methyl ethers may be ascribed to the difference in anionoid character of the *N*-oxygen atoms. In the *o*-tolyl compound the anionoid character is mainly due to methoxyl, the *C*-methyl being in the *m*-position to the nitroso-group, but in the *m*-tolyl ether



both groups exercise their full effect. Consequently, both hydrogen atoms of semicarbazide react with the *N*-oxygen in the *m*-tolyl ether, but only one in the case of the *o*-tolyl ether. Both hydrogen atoms of *p*-nitrophenylhydrazine react with the *N*-oxygen in each ether, but the reaction is much more intense (as it should be) with 6-nitroso-*m*-tolyl methyl ether, not only taking place in the cold but also expelling the methyl group from the methoxyl group. The same reactivity of the *N*-oxygen in 6-nitroso-*m*-tolyl methyl ether is seen in its behaviour with hydroxylamine, a diazo-compound being formed as shown by subsequent coupling with β -naphthol (Hodgson, J., 1931, 1494), whereas the *N*-oxygen in 5-nitroso-*o*-tolyl methyl ether fails to react.

EXPERIMENTAL.

*Oxidation of 5-Nitroso-*o*-cresol and its Methyl Ether.*—The nitroso-compound (8 g.) was added in 30–40 minutes to well-stirred dilute nitric acid (60 c.c. of a solution of 50 c.c. of nitric acid, *d* 1.42, and 150 c.c. of water) at 40°. The precipitated 3 : 5-dinitro-*o*-cresol crystallised from dilute methyl alcohol (charcoal) in orange needles, m. p. 85–86° (Found: N, 14.1. Calc.: N, 14.1%).

*Action of Nitrosylsulphuric Acid on *o*-Tolyl Methyl Ether.*—(1) *Nitration.* A well-stirred solution of the ether (4 g.) in glacial acetic acid (25 c.c.) was maintained at 0° during the gradual addition of sodium nitrite (4 g.) in concentrated

sulphuric acid (10 c.c., d 1.84). The mixture was kept for 3 days at room temperature and then poured into water (600 c.c.). The precipitated 3 : 5-dinitro-*o*-cresol crystallised from dilute methyl alcohol (charcoal) in orange needles, m. p. and mixed m. p. 85.5—86°.

(2) *Nitrosation*. Sodium nitrite (8 g.) was slowly stirred into sulphuric acid (25 c.c., d 1.84) cooled in running water, and the mixture cautiously heated until the appearance of a yellow tinge (at 110°); it was then cooled rapidly to 0° with vigorous stirring. The thick paste was stirred gradually into a mixture of *o*-tolyl methyl ether (8 g.) and glacial acetic acid (25 c.c.) at -10° to -15° , the temperature not being allowed to rise above -5° ; the whole liquefied. (Nitrosation had occurred if a small quantity of the mixture gave a deep blue colour with cold water; a red colour indicated nitration, probably due to too rapid mixing.) After 10 minutes the mixture was run into ice-water. The precipitate of 5-nitroso-*o*-tolyl methyl ether crystallised from light petroleum in pin-cushion-like clusters of green needles, m. p. 53.5° (Found: N, 9.3. $C_8H_9O_2N$ requires N, 9.26%), which were only slightly soluble in water but very soluble in methyl and ethyl alcohols and were oxidised slowly in the air to a brown powder.

6-Nitroso-*m*-cresol is oxidised by dilute nitric acid, as described above, to 6-nitro-*m*-cresol, m. p. 125° after crystallisation from benzene (Found: N, 9.3. Calc.: N, 9.15%).

Action of Nitrosylsulphuric Acid on m-Tolyl Methyl Ether.—(1) Nitration under the conditions described for *o*-tolyl methyl ether gave 6-nitro-*m*-cresol, m. p. and mixed m. p. 124°.

(2) Nitrosation as described above afforded 6-nitroso-*m*-tolyl methyl ether, which crystallised from light petroleum in grass-green needles, m. p. 22° (Found: N, 9.4. $C_8H_9O_2N$ requires N, 9.3%), was very soluble in ethyl and methyl alcohols, but sparingly soluble in water, was oxidised by dilute nitric acid immediately to give 6-nitro-*m*-cresol, and gave an intense yellow-brown colour with concentrated sulphuric acid. The nitrosation mixture, when diluted with water, gave a red-violet colour.

4-Methoxy-2-methylbenzeneazo- β -naphthol was formed by heating a solution of 6-nitroso-*m*-tolyl methyl ether (2.5 g.), hydroxylamine hydrochloride (1.2 g.), sodium acetate (1.5 g.), and β -naphthol (2.4 g.) in ethyl alcohol (20 c.c.) and water (20 c.c.) for 30 minutes on the water-bath. It was precipitated with water at 0°, extracted with dilute sodium hydroxide solution, dissolved in hot ethyl alcohol, and the concentrated solution poured into water; the crystals that separated had m. p. 193° (Found: N, 9.3. $C_{18}H_{16}O_2N_2$ requires N, 9.6%).

Action of Nitrous Acid on p-Cresol.—A solution of *p*-cresol (4 g.), sodium nitrite (10 g.), and sodium hydroxide (2 g.) in water (100 c.c.) was treated gradually at 0° with dilute sulphuric acid (8 c.c., d 1.84, and 32 c.c. of water). After 30 minutes' stirring, the mixture was steam-distilled; 3-nitro-*p*-cresol crystallised from the distillate in yellow needles, m. p. 32.5° (Found: N, 9.3. Calc.: N, 9.15%). The same substance was obtained by the nitrosation method of Hodgson and Nicholson (J., 1939, 1808).

*Action of Semicarbazide on the Nitroso-*o*- and -*m*-tolyl Methyl Ethers*.—6-Nitroso-*m*-tolyl methyl ether (1.5 g.), semicarbazide hydrochloride (1.5 g.), sodium acetate (2 g.), and methyl alcohol (15 c.c.) were heated on the water-bath for 30 minutes. The resulting precipitate crystallised from pyridine in cream-yellow micro-plates of 4-methoxy-2-methylbenzenediazoaminocarbonamide, m. p. 224°, and then from boiling aniline in pale yellow, lenticular plates, m. p. 230° (Found: N, 27.1. $C_9H_{12}O_2N_4$ requires N, 26.9%).

5-Nitroso-*o*-tolyl methyl ether, treated in the same way, yielded a brown precipitate, from a solution of which in boiling aniline (15 c.c.) 4-methoxy-3-methylhydrazobenzene-*N*-diazocarbonamide separated in yellow needles, m. p. 238° (Found: N, 23.3. $C_{15}H_{17}O_2N_5$ requires N, 23.5%).

*Action of p-Nitrophenylhydrazine on the Nitroso-*o*- and -*m*-tolyl Methyl Ethers*.—5-Nitroso-*o*-tolyl methyl ether (2.5 g.), *p*-nitrophenylhydrazine hydrochloride (3.2 g.), and sodium acetate (2 g.) were heated with methyl alcohol (15 c.c.) and water (15 c.c.) on the water-bath for 15 minutes; the resulting 4'-nitro-4-methoxy-3-methyldiazoaminobenzene crystallised in khaki-coloured needles, m. p. 187.5° (Found: N, 19.8. $C_{14}H_{14}O_3N_4$ requires N, 19.6%), which gave a wine-red colour with alcoholic potassium hydroxide.

When 6-nitroso-*m*-tolyl methyl ether was treated with the same reagents in the cold, a strong aromatic odour was perceptible; the reaction was completed by 5 minutes' warming in the water-bath. The resulting 4'-nitro-4-hydroxy-2-methyldiazoaminobenzene crystallised from aniline in brick-red micro-plates, m. p. 205° (decomp. beginning at 185°) (Found: N, 20.8. $C_{13}H_{12}O_3N_4$ requires N, 20.65%), which were slightly soluble in alcoholic potassium hydroxide, giving a golden colour.

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TECHNICAL COLLEGE, HUDDERSFIELD.

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