# XLVIII.—*The Nitration of Benzaldoxime and Some of its Derivatives.*

By OSCAR L. BRADY and BRIAN E. M. MILLER.

THE orienting influence of the aldoximino-group has not been investigated, probably on account of its instability. With due precautions, however, it is possible to nitrate benzaldoxime, but the yield of nitro-derivative is poor owing to the difficulty of suppressing hydrolysis and oxidation leading to the formation of acid.

Vorländer (*Ber.*, 1919, **52**, 262) suggested that a positive pole attached to the benzene nucleus is meta-orienting and it has been shown that the introduction of successive saturated carbon atoms between a positive pole and the nucleus diminishes somewhat the meta-orienting effect (Flürscheim and Holmes, J., 1926, 1562; Ing and Robinson, *ibid.*, p. 1655; Goss, Ingold, and Wilson, *ibid.*, p. 2440; Goss, Hanhart, and Ingold, J., 1927, 250). Ingold (*Ann. Reports*, 1926, **23**, 131) suggests that the introduction of unsaturated carbon atoms between a positive pole and the benzene nucleus should cause a more rapid damping of the meta-orienting influence, but this is not borne out in the case of benzaldoxime and *N*-methylbenzaldoxime, which, in the presence of concentrated sulphuric acid, must be regarded as $\mathrm{CHPh{:}\overset{+}{N}{<}^{H}_{OH}}$ and $\mathrm{CHPh{:}\overset{+}{N}{<}^{Me}_{OH}}$ respectively. Both these compounds on nitration gave *m*-nitro-derivatives; the yields were poor and no indication of the production of *o*- and *p*-derivatives was obtained.

Since *O*-methylbenzaldoxime seems quite devoid of basic properties (Brady, Dunn, and Goldstein, J., 1926, 2388), its nitration is of particular interest. Although a monosubstituted benzene derivative, it resists the action of nitrating agents in an extraordinary manner: treatment with a mixture of fuming sulphuric acid and fuming nitric acid at room temperature gave about 10% of *O*-methyl-*m*-nitrobenzaldoxime, but a large amount of *O*-methylbenzaldoxime was recovered unchanged, and even after warming with the nitrating acid much *O*-methylbenzaldoxime was unacted upon. This abnormal behaviour is in line with the general unreactivity of *O*-methylbenzaldoxime (*e.g.*, its resistance to hydrolysis by acids or alkalis and its non-basic properties) and suggests that the $-\mathrm{CH{:}N{\cdot}OMe}$ group in conjunction with the benzene ring represents a system in which free affinity is reduced to a minimum. This may be sufficient to explain why the substitution that occurs is in the meta-position.

When other strongly directive groups are present, the orienting effect of the aldoximino-group is not apparent; *e.g.*, when *p*-methoxy-, 3 : 4-methylenedioxy-, and 3-methoxy-4-hydroxy-benzaldoximes are nitrated, the nitro-group enters in the 3-, 6-, and 5-positions, respectively, as in the case of the corresponding aldehydes. The *O*-methyl ethers of *p*-methoxy- and 3 : 4-methylenedioxybenzaldoximes are readily nitrated, the nitro-group entering in the 3- and 6-positions, respectively.

## EXPERIMENTAL.

*α-Benzaldoxime.*—The nitrating acid was prepared by adding 120 g. of fuming sulphuric acid (10% $SO_3$) to 12 c.c. of nitric acid (*d* 1·42), through which a current of air had been passed to remove nitrous acid as completely as possible.

α-Benzaldoxime (12 g.) was added with stirring to the above nitrating acid (54 g.), cooled in ice, at such a rate that the temperature did not rise above 0°; after a short time, the mixture was poured on ice. The red pasty mass thus obtained solidified after being washed with water. It was ground with 2*N*-sodium hydroxide, and to the yellow solution, filtered after dilution, an excess of a saturated solution of ammonium chloride was added. The precipitated oxime was collected, washed, dried, and crystallised from benzene–light petroleum, 4·5 g. (30% of the calculated amount) of *m*-nitrobenzaldoxime (m. p. 120°), identified by comparison with an authentic specimen, being obtained.

In a second experiment the precipitated oxime was collected and that dissolved in the mother-liquor was recovered by extraction with chloroform. The whole of the oxime so obtained was crystallised from benzene–light petroleum: the greater part of the *m*-nitrobenzaldoxime having thus been removed, the mother-liquor was examined for *o*- or *p*-derivative. It was evaporated to dryness, and the residue hydrolysed by heating under reflux with concentrated hydrochloric acid for 3 hours. After cooling, dilution, extraction with chloroform, and removal of the solvent 0·5 g. of aldehyde was obtained; this was converted into the phenylhydrazone, fractional crystallisation of which gave no indication of the presence of the *o*- or *p*-nitro-compound, the fractions melting at 120—121° and not depressing the melting point of *m*-nitrobenzaldehydephenylhydrazone (m. p. 122°) (compare Brady and Harris, J., 1923, **123**, 485).

*α-O-Methylbenzaldoxime.*—α-*O*-Methylbenzaldoxime (5 g.), dissolved in ice-cold concentrated sulphuric acid (10 g.), was added at 0° to 20 g. of a nitrating acid made by adding 85 g. of concentrated sulphuric acid to 10 c.c. of nitric acid (*d* 1·5). When the mixture had attained room temperature, a portion was poured on ice; the oil obtained was largely *O*-methylbenzaldoxime; other portions were warmed to various temperatures not exceeding 80°, but in no case was there any indication of nitration.

*O*-Methylbenzaldoxime (2 c.c.) was added cautiously to fuming nitric acid (5 c.c.) at room temperature: when about half had been added, a brisk effervescence occurred. At the end of the reaction the solution was poured on ice, the odour of benzaldehyde being then very perceptible. The benzaldehyde was extracted with ether, isolated in the form of the sodium bisulphite compound, regenerated, and identified by conversion into the semicarbazone.

*O*-Methylbenzaldoxime (5 g.) was added slowly to 10 c.c. of a nitrating acid (made by adding 78 g. of fuming sulphuric acid to 13·3 c.c. of fuming nitric acid), cooled in running water; considerable frothing occurred. After remaining at room temperature for 1½ hours, the mixture was poured on ice and then extracted with chloroform. The chloroform solution was shaken with 2*N*-sodium carbonate, and the reddish-yellow aqueous layer obtained, on being acidified and extracted with ether, gave about 0·1 g. of impure *m*-nitrobenzoic acid. The chloroform solution was then shaken with sodium bisulphite solution; no solid separated and the bisulphite solution, when distilled with sodium carbonate, gave no aldehyde. The chloroform solution was dried over anhydrous sodium sulphate, most of the solvent removed, and the residue fractionated, 1·1 g. of unchanged *O*-methylbenzaldoxime being collected at 180—200°. An ethereal solution of the residue in the flask was filtered from a small amount of tar and evaporated; the residual oil, which still had a strong odour of *O*-methylbenzaldoxime, was seeded with a minute trace of *O*-methyl-*m*-nitrobenzaldoxime and scratched vigorously, crystals beginning to separate after some minutes. The mixture was kept in a desiccator for 4 days and the crystals were then collected, pressed on a tile, and crystallised from dilute alcohol; the *O*-methyl-*m*-nitrobenzaldoxime (0·5 g.) obtained was identified in the usual way. The residual oil, probably mainly *O*-methylbenzaldoxime, weighed 0·76 g., and therefore about 50% of the *O*-ether was accounted for.

N-*Methylbenzaldoxime.*—Finely powdered *N*-methylbenzaldoxime (5 g.) was sprinkled cautiously with stirring into 7·5 c.c. of a nitrating acid (made from 78 g. of fuming sulphuric acid and 13·3 c.c. of fuming nitric acid and freed from nitrous acid by addition of urea), the temperature being kept below 5°. The mixture was poured on ice and extracted with chloroform several times and the combined extracts were dried over anhydrous sodium sulphate and saturated with hydrogen chloride. The precipitated hydrochloride was decomposed with 2*N*-sodium carbonate, the solid collected, and the solution extracted with chloroform. The solid (m. p. 109—110°) together with that obtained by evaporating the chloroform weighed 0·77 g. and after crystallisation from benzene gave *N*-methyl-*m*-nitrobenzaldoxime, m. p. 117°.

The mother-liquor from the crystallisation was evaporated, the residue hydrolysed by boiling with concentrated hydrochloric acid, and, after dilution, the aldehyde was extracted with ether and converted into the phenylhydrazone, which was fractionally crystallised; no indication of the presence of *o*- or *p*-nitro-derivative was obtained.

The filtrate from the hydrochloride precipitate was washed with sodium carbonate solution, dried, and evaporated and the residual oil was converted into a semicarbazone, 2·5 g., m. p. 209—210°, being obtained. This was apparently a mixture of the semicarbazones of benzaldehyde and *m*-nitrobenzaldehyde, repeated crystallisations from alcohol giving a fairly pure specimen of the latter.

In another experiment the chloroform solution, instead of being treated with hydrogen chloride, was thoroughly washed with water and distilled in a current of steam. The residual liquid, on extraction with chloroform, gave 1·14 g. of a mixture of *N*-methyl-*m*-nitrobenzaldoxime and *m*-nitrobenzaldehyde (m. p. 72—74°), from which 0·45 g. of *N*-methyl-*m*-nitrobenzaldoxime was isolated after several crystallisations from benzene. The chloroform layer in the distillate, after evaporating, gave 0·53 g. of an uncrystallisable oil with a strong odour of benzaldehyde.

A solution of *N*-methylbenzaldoxime in acetic acid, on treatment with nitric acid, slowly turned green and a copious evolution of gas occurred owing to oxidation; addition of water precipitated benzaldehyde.

α-p-*Methoxybenzaldoxime.*—The oxime (1 g.), dissolved in concentrated sulphuric acid (4 c.c.), was added to 2·5 c.c. of a nitrating acid (prepared from concentrated sulphuric acid, 85 g., and 70% nitric acid, 15 c.c.), the temperature being kept below 10°. The mixture was poured on ice and extracted with chloroform and the extract was shaken with *N*-sodium hydroxide to remove oxime. The aqueous layer, on being saturated with carbon dioxide, gave a pale yellow precipitate which, after two crystallisations from benzene, gave 3-nitro-4-methoxybenzaldoxime.

α-O-*Methyl*-p-*methoxybenzaldoxime.* — Preliminary experiments showed that when *O*-methyl-*p*-methoxybenzaldoxime was nitrated, a mixture of mono- and di-nitro-compounds was formed which was difficult to separate. The conditions were therefore chosen to favour the production of one or other of the compounds.

*O*-Methyl-*p*-methoxybenzaldoxime (2·6 g.), dissolved in concentrated sulphuric acid (15 c.c.), was added to 10 c.c. of a nitrating acid of the composition used in the case of *O*-methylbenzaldoxime, the temperature being kept below 30°. The solid obtained on pouring the mixture on ice was freed with difficulty from mononitro-compound by crystallising it four times from acetone and water; O-*methyl*-3 : 5-*dinitro*-4-*methoxybenzaldoxime* was then obtained in colourless needles, m. p. 129° (Found: N, 16·9. $C_9H_9O_6N_3$ requires N, 16·5%).

*O*-Methyl-*p*-methoxybenzaldoxime (0·5 g.), dissolved in concentrated sulphuric acid (5 c.c.), was added to 3 c.c. of a nitrating acid (prepared from 90 g. of concentrated sulphuric acid and 5·2 c.c. of 70% nitric acid), the mixture being cooled in running water. On pouring it on ice, 0·54 g. of crude product was obtained, m. p. 103—104°. Three crystallisations from alcohol gave slightly impure *O*-methyl-3-nitro-4-methoxybenzaldoxime, m. p. 116—117°, which, when mixed with a pure specimen (m. p. 120°), melted at 118—118·5°.

α-3 : 4-*Methylenedioxybenzaldoxime*.—A solution of the oxime (2 g.) in acetic anhydride (10 c.c.) was added at 0° to 10 c.c. of a nitrating mixture prepared by adding nitric acid (3 c.c., *d* 1·5) to acetic anhydride (45 c.c.). After being kept for a short time on ice, the reaction mixture was poured into water. The orange oil obtained (2·4 g.), consisting of a mixture of oxime and acetyl derivative, solidified when scratched. It was then finely powdered and suspended in cold 2*N*-sodium hydroxide, dissolving after 12 hours. Saturation of the solution with carbon dioxide precipitated 6-nitro-3 : 4-methylenedioxybenzaldoxime (1·1 g.), which was obtained pure after crystallisation from benzene.

α-O-*Methyl*-3 : 4-*methylenedioxybenzaldoxime*.—A solution of *O*-methyl-3 : 4-methylenedioxybenzaldoxime (1 g.) in glacial acetic acid (10 c.c.) was added to a 5% solution of fuming nitric acid in acetic acid (13 c.c.). No action occurred, but on heating on the water-bath for 5 minutes the solution turned brown; after cooling, it was poured on ice, 1·29 g. of a pale yellow precipitate, m. p. 143°, being obtained. One crystallisation from dilute alcohol gave 0·82 g. of pure *O*-methyl-6-nitro-3 : 4-methylenedioxybenzaldoxime, m. p. 147°.

α-3-*Methoxy*-4-*hydroxybenzaldoxime*.—The oxime (1 g.) was dissolved in glacial acetic acid (5 c.c.), and a 5% solution of fuming nitric acid in acetic acid (10 c.c.) added. The solution, which became dark, was immediately cooled in running water; 5-nitro-3-methoxy-4-hydroxybenzaldoxime then crystallised in almost quantitative yield. After being washed with a little acetic acid and with water and crystallised from alcohol, it gave the pure compound in excellent yield.

THE RALPH FORSTER LABORATORIES OF ORGANIC CHEMISTRY,
UNIVERSITY COLLEGE, LONDON. *[Received, December 5th, 1927.]*