CXXIX.—*The Isomerism of the Oximes. Part XXX. The Preparation of* o-*Methoxybenzaldoxime from Bisnitrosyl-*o-*methoxybenzyl.*

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The preparation of the two isomeric forms of a substituted benzaldoxime is not always possible (Brady and Dunn, J., 1916, **109**, 666) and in no case is this more remarkable than in that of *o*-methoxybenzaldoxime, which exists only in the α-form, many attempts to obtain the isomeric β-compound through the hydrochloride in various ways, or by the action of light, having been completely unsuccessful (Brady and Dunn, J., 1923, **123**, 1787; Brady and McHugh, J., 1924, **125**, 584). For a summary of the facts bearing

on this problem, see Brady, Cosson, and Roper (J., 1925, **127**, 2427). An attempt has now been made to prepare β-*o*-methoxybenzaldoxime by the method by which Behrend and Nissen (*Annalen*, 1892, **269**, 390) first obtained β-*o*-chlorobenzaldoxime (compare also Behrend and König, *Annalen*, 1891, **263**, 216, 348). The latter compound has now been prepared from the α-oxime by the action of ultra-violet light (Brady and McHugh, *loc. cit.*) and through the hydrochloride by a special method (Brady, Cosson, and Roper, *loc. cit.*), but at the time of Behrend and Nissen's work the hydrochloride method had not been successfully applied (Dollfus, *Ber.*, 1892, **25**, 1923).

The method involves the preparation of N-o-*methoxybenzyl*-p-*methoxybenzaldoxime* (I) from *o*-methoxybenzyl chloride and β-*p*-methoxybenzaldoxime, its hydrolysis to N-o-*methoxybenzylhydroxylamine hydrochloride* (II), the conversion of this into *nitroso*-N-o-*methoxybenzylhydroxylamine* (III), which with a trace of nitric acid yields *bisnitrosyl*-o-*methoxybenzyl* (IV); the last compound, on treatment with alkali, gives *o*-methoxybenzaldoxime.

$$(o)\ MeO\cdot C_6H_4\cdot CH_2Cl + (p)\ MeO\cdot C_6H_4\cdot CH{:}NOH \longrightarrow$$
$$(I.)\ (p)\ MeO\cdot C_6H_4\cdot CH{:}N(:O)\cdot CH_2\cdot C_6H_4\cdot OMe\ (o) \longrightarrow$$
$$(II.)\ (o)\ MeO\cdot C_6H_4\cdot CH_2\cdot NH\cdot OH,HCl \longrightarrow$$
$$(III.)\ (o)\ MeO\cdot C_6H_4\cdot CH_2\cdot N(NO)\cdot OH \longrightarrow$$
$$(IV.)\ [(o)\ MeO\cdot C_6H_4\cdot CH_2\cdot NO]_2 \longrightarrow MeO\cdot C_6H_4\cdot CH{:}NOH$$

β-*p*-Methoxybenzaldoxime was chosen as the means of obtaining the *N*-ether, because this β-oxime is comparatively stable and is one of the easiest to prepare in the pure state. This method of obtaining the necessary *N*-substituted hydroxylamine was not used by Behrend and Nissen, but their method would have involved considerable loss of the valuable *o*-methoxybenzyl chloride.

Behrend and König, by decomposition of bisnitrosylbenzyl and of bisnitrosyl-*p*-nitrobenzyl, obtained approximately equal amounts of α- and β-benzaldoximes and α- and β-*p*-nitrobenzaldoximes, respectively, but it is difficult to say whether the α-oxime was a product of isomeric change of the β-oxime during the somewhat lengthy manipulations. If the structure of the bisnitrosyl compound adopted by Behrend be accepted (V) and the reaction be

$$(V.)\quad \begin{matrix} R\cdot CH_2\cdot N\!-\!O \\ \qquad\quad | \\ \qquad O\!-\!N\cdot CH_2R \end{matrix}$$

regarded as a depolymerisation followed by tautomeric change of the nitrosobenzyl, the formation of a mixture of the two isomerides might be expected. Unfortunately, although there is considerable evidence that the decomposition of bisnitrosyl-*o*-methoxybenzyl

leads to the formation of some β-methoxybenzaldoxime, it has not been possible to isolate enough of the β-oxime to identify it as thoroughly as could be desired.

EXPERIMENTAL.

N-o-*Methoxybenzyl*-p-*methoxybenzaldoxime* (I).—*o*-Methoxybenzyl chloride was prepared (1) by methylating saligenin with methyl iodide, methyl alcohol, and sodium methoxide, hydrolysing the product to *o*-methoxybenzyl alcohol, and converting this into the chloride with dry hydrogen chloride (Pschorr, Wolfes, and Buckow, *Ber.*, 1900, **33**, 165), (2) from *o*-methoxybenzaldehyde (from salicylaldehyde) by the Cannizzaro reaction.

A cold solution of β-*p*-methoxybenzaldoxime (10 g.) in the minimum quantity of absolute alcohol was treated with a cold solution of sodium (1·52 g.) in absolute alcohol and with an alcoholic solution of freshly distilled *o*-methoxybenzyl chloride (10 g.); a cloudiness appeared almost at once and heat was developed. After 12 hours, some of the *N*-ether had crystallised. Ice-cold water was added, and the crude *N*-ether separating was collected and dried over solid sodium hydroxide (yield, 95%). *o*-Methoxybenzyl chloride is readily hydrolysed by water, which must be excluded as completely as possible in the above preparation, otherwise the yield is much reduced. Crystallised from chloroform and light petroleum, N-o-*methoxybenzyl*-p-*methoxybenzaldoxime* formed colourless, monoclinic prisms, m. p. 123° (Found: N, 5·2. $C_{16}H_{17}O_3N$ requires N, 5·2%).

N-o-*Methoxybenzylhydroxylamine Hydrochloride* (II).—The crude *N*-ether obtained above was hydrolysed by boiling it under reflux for an hour with 20% hydrochloric acid; the *p*-methoxybenzaldehyde produced and any *O*-*o*-methoxybenzyl-*p*-methoxybenzaldoxime formed during methylation were then distilled in steam (*O*-ethers are not appreciably hydrolysed under these conditions). When the distillate no longer contained aldehyde, the hydrochloric acid solution remaining in the flask was evaporated on the water-bath until crystals appeared on the surface; on cooling, the greater part of the *N*-*o*-methoxybenzylhydroxylamine hydrochloride separated in crystals, usually tinged pink. Crystallised from absolute alcohol and dry ether, N-o-*methoxybenzylhydroxylamine hydrochloride* formed small, white needles, m. p. 136° (Found: N, 7·5; Cl, 18·6. $C_8H_{11}O_2N$,HCl requires N, 7·4; Cl, 18·7%). It is a powerful reducing agent, acting upon ferric chloride and Fehling's solution immediately at room temperature.

Nitroso-N-o-*methoxybenzylhydroxylamine* (III).—A 3% aqueous solution of the above hydrochloride was cooled in ice, and an

equivalent amount of sodium nitrite in the minimum amount of water added with stirring. After an hour the solution was thick with crystals, which were collected, washed with water, and air-dried (yield, 70%). Crystallised from chloroform and light petroleum, *nitroso*-N-o-*methoxybenzylhydroxylamine* was obtained in pale yellow, microscopic crystals, m. p. 73—74° (Found: N, 15·7. $C_8H_{10}O_3N_2$ requires N, 15·4%).

Bisnitrosyl-o-methoxybenzyl (IV).—*N-o*-Methoxybenzylhydroxylamine hydrochloride (5 g.) was dissolved in water (200 c.c.) and cooled in ice; a solution of hydrated sodium carbonate (4·2 g.) was added followed by glacial acetic acid (7·5 g.). Ether was poured on the mixture to form a layer, and an aqueous solution of potassium dichromate (2·66 g.) run in with vigorous stirring. After some time, the brown, flocculent, crystalline substance which had collected at the water–ether interface was removed, washed with a little ether, and dried (yield, 40—60%).

A much purer product was obtained by the following method. Nitroso-*N-o*-methoxybenzylhydroxylamine (5 g.) was dissolved in ether (60—70 c.c.), and glacial acetic acid (15 c.c.) was added together with one drop of fuming nitric acid. A steady stream of gas was evolved and after some time the sparingly soluble bisnitrosyl compound separated in 30—40% yield. After crystallising from chloroform and light petroleum, *bisnitrosyl-o-methoxybenzyl* was obtained in colourless needles, m. p. 125° (Found: N, 9·2. $C_{16}H_{18}O_4N_2$ requires N, 9·3%).

Action of Alkalis on Bisnitrosyl-o-methoxybenzyl.—Bisnitrosyl-*o*-methoxybenzyl was ground for some hours with 10% aqueous sodium hydroxide, cooling in ice. The undecomposed compound was filtered off, and a slight excess of an ice-cold, saturated solution of ammonium chloride added to the filtrate. The oxime, which was precipitated as an oil, was extracted with ether; on removal of the solvent, white crystals were obtained. These melted at 80—82°, and in admixture with α-*o*-methoxybenzaldoxime (m. p. 92°) at 59°. Under the microscope, they were seen to be a mixture of the characteristic long needles of the α-oxime and thin plates. Solution in alcohol and evaporation gave an oil which soon crystallised to the almost pure α-oxime, indicating that some unstable compound was present which changed rapidly to the α-oxime.

With 25% methyl-alcoholic potassium hydroxide, a more rapid decomposition of the bisnitrosyl compound occurred and the addition of ammonium chloride precipitated a compound, which melted alone at 80—85° and at 65° when mixed with the α-oxime. On crystallising it twice from acetone and water, a very small quantity

of a product, m. p. 101—102°, was obtained as compact, white prisms distinct from the slender crystals of the α-oxime. This appeared to be the β-oxime. It was very unstable and when after a few days an attempt was made to determine its configuration it was found that the m. p. had fallen to 92° and that the compound then consisted of the pure α-oxime. In subsequent preparations, using various methods of alkaline decomposition, we were never successful in obtaining this high-melting product again, but the low-melting, crude oxime always gave an orange-red coloration with alcoholic ferric chloride—a reaction characteristic of the β-aldoximes (Beck and Hase, *Annalen*, 1907, **355**, 29) and not given by α-*o*-methoxybenzaldoxime. Moreover, treatment of the crude product with acetic anhydride and then with sodium carbonate solution, extraction with ether, and hydrolysis of the oily product with sodium hydroxide resulted in the evolution of some ammonia. This indicated the presence of nitrile, probably formed from β-oxime in the crude product. The hydrolysis product was saturated with carbon dioxide and extracted with ether; the ether on evaporation gave α-*o*-methoxybenzaldoxime. The aqueous solution was acidified with dilute sulphuric acid and again extracted with ether; *o*-methoxybenzoic acid was then obtained. The ratio of oxime to acid was approximately 4 to 1. The difficulty encountered in obtaining the β-oxime by this method seems to be due to the slowness of the decomposition of the bisnitrosyl compound; owing to the instability of the β-oxime, most of it probably changes to the α-isomeride during manipulation; and fractional crystallisation of the product provides still further opportunity for the isomerisation to occur.

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