# CCLV.—*The Isomerism of the Oximes. Part XXXI. The Furfuraldoximes and 2-Methoxy- and 4-Methoxy-1-naphthaldoximes.*

By Oscar Lisle Brady and Richard Frank Goldstein.

The greater part of the study of the aldoximes from the point of view of stereoisomerism has been devoted to those in which the aldoximino-group is attached to the benzene ring. The stability of the α-isomeride in the benzaldoximes, in contrast with the aliphatic aldoximes where the β-form is the normal product, makes it of some interest to consider the effect of other ring systems on the relative stability of the two isomerides. The case of furfuraldoxime is of historic importance, since this was the first aldoxime to be obtained in two forms (Odernheimer, *Ber.*, 1883, **16**, 2988). Goldschmidt and Zanoli (*Ber.*, 1892, **25**, 2573) also prepared the two isomerides and determined their configuration, but thought they found indications of abnormal behaviour, since in the acetylation of the α-oxime and subsequent hydrolysis some furfuronitrile and a mixture of the two oximes were obtained. Similarly, Minunni

(*Gazzetta*, 1896, **26**, i, 463) obtained a mixture of oximes on hydrolysis of benzoyl-α-furfuraldoxime.

This work has now been repeated and the origin of the difficulties of previous workers traced to the fact that the α-oxime in the presence of hot solvents is partly converted into the β-isomeride, a phenomenon never observed in the benzaldoximes. With care, a crystalline acetyl-α-furfuraldoxime can be prepared; this on hydrolysis gives nearly pure α-furfuraldoxime, which can also be obtained by hydrolysis of the benzoyl compound and isolation of the oxime by special means. β-Furfuraldoxime is obtainable under conditions which will not give β-benzaldoxime, being much more stable than that compound. The furfuraldoximes accordingly occupy an intermediate position between the benzaldoximes and the aliphatic aldoximes.

No oximes of the naphthalene series have been investigated from the point of view of the stereochemical hypothesis, so 2-methoxy-1-naphthaldoxime and 4-methoxy-1-naphthaldoxime have now been studied. The products of oximation have the α-aldoxime structure and we have been unable to convert either into the β-isomeride. As they may both be regarded as *o*-substituted benzaldoximes, this was not unexpected. On methylation of 2-methoxy-1-naphthaldoxime, a mixture of *N*- and *O*-ethers was obtained, the former predominating; 4-methoxy-1-naphthaldoxime gave a mixture of about equal amounts of *N*- and *O*-ethers. Both oximes therefore differ markedly from the α-benzaldoximes in the relative amounts of *N*- and *O*-ethers produced on methylation.

## EXPERIMENTAL.

*α-Furfuraldoxime.*—Furfuraldehyde (13·5 g.) was added slowly to a cold mixture of sodium hydroxide (14 g. in 15 c.c of water) and hydroxylamine hydrochloride (12 g. in 30 c.c. of water). After 1 hour, the solution was filtered and cooled in a freezing mixture and a slight excess of an ice-cold, saturated aqueous solution of ammonium chloride was slowly added with stirring. The crystalline precipitate was washed with a little ice-cold water and air-dried. The yield of crude oxime (m. p. 51—64°) was 11·5 g. After crystallising three times from benzene and light petroleum, 4 g. of pure α-oxime were obtained, m. p. 75—76° (Goldschmidt and Zanoli, *loc. cit.*, give 73°). The details must be carefully followed, otherwise an inseparable mixture of the two isomerides may be obtained. In one experiment, a crude oxime, m. p. 42—45°, was obtained and repeated crystallisations failed to raise the melting point above 48—52°. It is probable that the material (m. p. 49—56°) obtained by Odernheimer (*loc. cit.*) was a similar mixture. When the pure α-oxime (0·5 g.) was boiled with benzene (20 c.c.) under reflux for 4 hours and the solvent evaporated, a product, m. p. 47—48°, was obtained which was apparently a mixture of the α- and β-isomerides, since the addition of either raised its melting point.

*Acetyl-α-furfuraldoxime.*—α-Furfuraldoxime (2·5 g.) was slowly added to acetic anhydride (12 c.c.), and warmed to 30°; it then dissolved. On decomposing the excess of anhydride with 2*N*-sodium carbonate, crystals separated which were collected, air-dried, and dissolved in warm light petroleum; on cooling the solution to − 20° or − 40°, *acetyl-α-furfuraldoxime* separated in colourless prisms, m. p. 34—35° (Found: N, 9·4. $C_7H_7O_3N$ requires N, 9·2%). The acetyl derivative was warmed with 2*N*-sodium hydroxide until it dissolved; there was no odour of furfuronitrile. On cooling the solution, adding saturated ammonium chloride solution, extracting the mixture twice with ether, and evaporating the solvent with a current of air, an oxime was obtained which, after being pressed on a porous tile, melted at 69—72° and was nearly pure α-oxime. Goldschmidt and Zanoli (*loc. cit.*) obtained on acetylation an oil which on hydrolysis gave some furfuronitrile and an oxime, m. p. 49—60°.

*Benzoyl-α-furfuraldoxime.*—Crude α-furfuraldoxime, m. p. 51—57° (7 g.) was slowly added with cooling to benzoyl chloride (30 g.) and the product was poured into 2*N*-sodium hydroxide (250 c.c.), vigorously shaken for 30 minutes, and kept for 12 hours. The benzoyl derivative which separated was crystallised three times from alcohol; it then melted at 138—139° (compare Minunni, *loc. cit.*). The benzoyl derivative (5 g.) was heated with 2*N*-sodium hydroxide (50 c.c.), and the solution was cooled, saturated with carbon dioxide, and extracted with ether; removal of the solvent by a current of air gave a nearly pure α-oxime, m. p. 68—73°. It is essential that the solutions of the α-oxime should not be warmed, otherwise partial conversion into the β-oxime occurs.

β-*Furfuraldoxime.*—Hydroxylamine hydrochloride (10 g.) in methyl alcohol (40 c.c.) was treated with crystallised sodium acetate (19·5 g.) in dilute alcohol (40 c.c.), and furfuraldehyde (12 g.) added. The mixture was kept for 24 hours, the precipitated sodium chloride removed, and the solution evaporated in a vacuum at room temperature to about 30 c.c. and then poured into water (70 c.c.). The precipitated β-oxime (m. p. 89—91°) was crystallised three times from 10% alcohol with the addition of a little animal charcoal; a nearly quantitative yield was then obtained of the pure β-oxime, m. p. 91—92° (Goldschmidt and Zanoli give 89°). The β-oxime (2·5 g.) was dissolved in acetic anhydride (10 c.c.) at 30° and poured into 2*N*-sodium carbonate. When all the anhydride was decomposed, the oil was extracted with ether and hydrolysed, after removal of the solvent, by boiling it with 40% potassium hydroxide solution. Ammonia was evolved and extraction of the acidified solution with ether yielded pyromucic acid, identified by its reactions and by comparison with an authentic specimen.

α-2-*Methoxy*-1-*naphthaldoxime*.—To a mixture of hydroxylamine hydrochloride (7·5 g.) and sodium hydroxide (10 g.) in water (110 c.c.) was added a solution of 2-methoxy-1-naphthaldehyde (14 g.) in hot alcohol (20 c.c). The sodium salt of the oxime (which is very sparingly soluble in water) separated as a mass of crystals; after 1 hour, the oxime was liberated by addition of excess of a saturated solution of ammonium chloride, filtered off, washed, and dried (yield, almost quantitative). After three crystallisations from hot benzene, α-2-*methoxy*-1-*naphthaldoxime* formed white plates, m. p. 154—155° (Found : N, 7·3. $C_{12}H_{11}O_2N$ requires N, 7·0%).

α-*Acetyl*-2-*methoxy*-1-*naphthaldoxime*, prepared in the usual way, and crystallised from alcohol, formed white needles, m. p. 79—80° (Found : N, 5·9. $C_{14}H_{13}O_3N$ requires N, 5·8%). On hydrolysis with hot 2*N*-sodium hydroxide, the needles of the acetyl derivative are gradually replaced by the plates of the sodium salt of the oxime. On addition of ammonium chloride, the α-oxime was recovered unchanged.

α-2-*Methoxy*-1-*naphthaldoxime Hydrochloride*.—The oxime (2 g.) was dissolved in boiling chloroform (75 c.c.), and dry hydrogen chloride passed in for 20 minutes. The precipitated *hydrochloride* was collected, washed with chloroform, and pressed on a porous tile. It formed a bright yellow powder, m. p. 145—147° (decomp.) (Found : Cl, 16·4. $C_{12}H_{11}O_2N,HCl$ requires Cl, 14·9%). With sodium hydroxide and ammonium chloride, the hydrochloride regenerated the α-oxime; no inversion had taken place.

*Methylation of* α-2-*Methoxy*-1-*naphthaldoxime*.—The oxime (7·0 g.), dissolved in hot alcohol (85 c.c.), was treated with sodium ethoxide (1·05 g. of sodium in 25 c.c. of alcohol), and methyl iodide (5 g.) added. The solution was boiled under reflux for 30 minutes and kept for 12 hours, the alcohol allowed to evaporate somewhat, and excess of water added. An emulsion was formed, which was extracted first with ether, then with chloroform. The ethereal extract on evaporation gave a thick oil (2·4 g.) which solidified when cooled, yielding a hard, brown solid, m. p. 51—54°, consisting mainly of *O*-ether, but also containing a little *N*-ether, unchanged oxime, and other impurities. The *O*-ether is best separated by prolonged distillation in steam, in which it is difficultly volatile; it was identified in the distillate by comparison with an authentic specimen obtained by synthesis.

The chloroform extract gave a solid (4·6 g.), m. p. 106—107°. After some weeks, the m. p. had fallen to 83—87°. This compound on crystallisation from benzene gave pure N-*methyl*-2-*methoxy*-1-*naphthaldoxime hydrate*, fine needles, m. p. 88—89° (Found : N, 6·0; $H_2O$, 7·6. $C_{13}H_{13}O_2N,H_2O$ requires N, 6·0; $H_2O$, 7·7%). The anhydrous N-*methyl*-2-*methoxy*-1-*naphthaldoxime*, obtained by desiccation of the hydrate in a vacuum over calcium chloride, formed stout prisms, m. p. 118—119°, which hydrate readily (Found : N, 6·5. $C_{13}H_{13}O_2N$ requires N, 6·5%). Both the hydrated and the anhydrous ether yield *N*-methylhydroxylamine and 2-methoxy-1-naphthaldehyde on gentle boiling with acids.

α-O-*Methyl*-2-*methoxy*-1-*naphthaldoxime*.—2-Methoxy-1-naphthaldehyde (3·5 g.) and *O*-methylhydroxylamine (0·95 g.) were dissolved in alcohol (30 c.c.) and kept for 12 hours. The alcohol was allowed to evaporate spontaneously, and the dark solid residue purified by steam distillation and crystallisation from alcohol. α-O-*Methyl*-2-*methoxy*-1-*naphthaldoxime* formed colourless, short prisms, m. p. 65° (Found : N, 6·8. $C_{13}H_{13}O_2N$ requires N, 6·5%).

4-*Methoxy*-1-*naphthaldehyde*.—4-Hydroxy-1-naphthaldehyde (24 g.) was heated with potassium hydroxide (8 g. in 35 c.c. of water), and methyl sulphate (13 c.c.) added slowly with shaking. The mixture was heated on the water-bath for 30 minutes, potassium hydroxide (5·5 g. in 20 c.c. of water) and methyl sulphate (8 c.c.) were then added alternately in small quantities with shaking. Heating was continued for 30 minutes, and the solution was cooled and extracted with ether. The aqueous portion on acidification gave 4·8 g. of impure 4-hydroxy-1-naphthaldehyde. The ethereal portion was well washed with dilute sodium hydroxide solution, then with water, dried, and evaporated. The yield of crude methoxyaldehyde, which was sufficiently pure for the next operation, was 10·8 g. A considerable quantity of tar was formed. 4-Methoxy-1-naphthaldehyde has previously been prepared by boiling 4-hydroxy-1-naphthaldehyde with methyl iodide and potassium hydroxide in alcoholic solution (Gattermann, *Annalen*, 1907, **357**, 365).

α-4-*Methoxy*-1-*naphthaldoxime*, prepared from the crude aldehyde in a similar way to the 2-methoxy-compound, crystallised from benzene in white needles, m. p. 107—108° (Found : N, 7·3. $C_{12}H_{11}O_2N$ requires N, 7·0%).

α-*Acetyl*-4-*methoxy*-1-*naphthaldoxime*, prepared in the usual way, crystallised from alcohol in colourless needles, m. p. 102° (Found : N, 5·8. $C_{14}H_{13}O_3N$ requires N, 5·8%). On warming it with 2*N*-sodium hydroxide and saturating the solution with carbon dioxide, the original α-oxime was obtained.

α-4-*Methoxy*-1-*naphthaldoxime hydrochloride*, prepared in the same way as the corresponding 2-methoxy-compound, formed a yellowish-green powder, m. p. 144—145° (decomp.) (Found : Cl, 15·1. $C_{12}H_{11}O_2N,HCl$ requires Cl, 14·9%). On decomposing it with 2*N*-sodium carbonate, the original oxime was regenerated.

*Methylation of* α-4-*Methoxy*-1-*naphthaldoxime*.—The oxime (6·55 g. in 59 c.c. of alcohol), sodium (0·8 g. in 20 c.c. of alcohol), and methyl iodide (5·1 g. in 20 c.c. of alcohol) were boiled under reflux for 20 minutes and kept for 12 hours. The methylated product was worked up in the same way as the 2-methoxy-oxime, there being obtained 3·1 g. of *O*-methyl ether and 3·0 g. of *N*-methyl ether. α-O-*Methyl*-4-*methoxy*-1-*naphthaldoxime* formed colourless needles, m. p. 38—39°, from alcohol and water (Found : N, 6·5. $C_{13}H_{13}O_2N$ requires N, 6·5%). α-N-*Methyl*-4-*methoxy*-1-*naphthaldoxime* is dimorphic and separated from hot benzene in yellow prisms, m. p. 158—159° (Found : N, 6·4%), which changed to dark grey plates on keeping in contact with the mother-liquor for 2 hours. The grey modification passed back into the yellow on crystallisation or on heating at 100° for some time.

THE RALPH FORSTER LABORATORIES OF ORGANIC CHEMISTRY,
UNIVERSITY COLLEGE, LONDON. [*Received, June* 15*th*, 1927.]