559. *The Synthesis of* vic.-*Dioximes from Symmetrical Ketones.*

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Several *vic.*-dioximes have been synthesised by a simple method, which is probably of wide application. Direct bromination of ketones in aqueous acetic acid gave good yields of crude α-bromo-ketones, which on treatment with buffered hydroxylamine hydrochloride gave 25—50% yields of the dioximes of *cyclo*pentane-, *cyclo*hexane-, and 4-methyl*cyclo*hexane-1 : 2-dione, and pentane-2 : 3-dione.

vic.-DIOXIMES have received considerable attention as reagents for nickel,[1] and as precursors of the corresponding diamines, more particularly in the alicyclic series [2,3] where the monoketones are suitable starting materials. Several methods have been proposed for the preparation of *vic.*-dioximes,[3,6] most of which proceed through the hydroxyimino-ketone [3,4] or the diketone.[4-6] Oxidation of the mono- to the di-ketone by selenium dioxide, followed by oximation, has been recommended.[4]

Previous syntheses of *cyclo*pentane-1 : 2-dione dioxime have been unsatisfactory: Jaeger and Blumendal [2] used the glutaric–oxalic ester condensation, but it is tedious and expensive; Voter [7] obtained yields of <10% of diketone using selenium dioxide oxidation, and Acheson's [8] oxidation of 2-bromo*cyclo*pentanone to the diketone by ferric chloride has given us poor yields. The conversion of α-chloroacetone into methylglyoxime has been reported by Hantzsch and Wild [9] but later the reaction was neglected in preparative work. We found similarly that 2-bromo*cyclo*pentanone could be simultaneously oxidised and oximated to give *cyclo*pentane-1 : 2-dione dioxime, and this method was applied to the synthesis of higher homologues and pentane-2 : 3-dione dioxime.

Several workers [8-13] have prepared α-bromo-ketones by direct bromination, and we adapted Acheson's method [8] to the preparation of other α-bromo-ketones. Optimum conditions for the reactions were not investigated. When unsymmetrical ketones are brominated, two different α-bromo-ketones may be formed and purification then becomes essential. Although 2-methyl*cyclo*hexanone is not symmetrical, it is reported [12] to form 2-bromo-6-methyl*cyclo*hexanone by direct bromination, hence preparation of " 3-methyl nioxime " was attempted. Because of the tendency of α-bromo-ketones to decompose on storage or on being heated [11,12] no attempt was made to purify them: any by-product present at this stage did not interfere with the isolation of the dioximes.

Several techniques for converting the α-bromo-ketones into dioximes were investigated. Hantzsch and Wild's method [9] is only applicable to the water-soluble and the more reactive members. Buffered hydroxylamine solution was used, so that the reaction temperature could be increased. With the more water-soluble 2-bromo*cyclo*pentanone and 2-bromopentan-3-one, reaction was effected by slow addition of the bromo-ketone to refluxing aqueous hydroxylamine solution; for the other bromo-ketones aqueous–methanolic hydroxylamine was used. Addition of the bromo-ketone at a rate comparable with the rate of reaction minimised the formation of tar. The optimum conditions for the

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[1] Welcher, " Organic Analytical Reagents," D. Van Nostrand Co., New York, 1947, Vol. III.
[2] Jaeger and Blumendal, *Z. anorg. Chem.*, 1928, **175**, 164.
[3] Jaeger and van Dijk, *Proc. Acad. Sci. Amsterdam*, 1936, **39**, 384.
[4] Banks, Diehl, Rauh, and Smith, *J. Org. Chem.*, 1945, **10**, 199.
[5] Vander Haar, Voter, and Banks, *ibid.*, 1949, **14**, 836.
[6] Banks, Hooker, and Richard, *ibid.*, 1956, **21**, 547.
[7] Voter, Ph.D. Thesis, Iowa State Coll., Ames, Iowa, 1951.
[8] Acheson, *J.*, 1956, 4232.
[9] Hantzsch and Wild, *Annalen*, 1895, **289**, 285.
[10] Pauly, *Ber.*, 1901, **34**, 1771.
[11] Kötz, Blenderman, Kárpáti, and Rosenbusch, *Annalen*, 1913, **400**, 51.
[12] Kötz and Steinhorst, *ibid.*, 1911, **379**, 15.
[13] Schotte, *Acta Chem. Scand.*, 1951, **5**, 969.

oximations were not ascertained, but neither increase of reaction time nor a larger excess of hydroxylamine improved the yield of *cyclo*pentane-1 : 2-dione dioxime.

The reason for the formation of hydroxyimino-carboxylic acids in two of the oximation reactions is not known, but might be ascribed to preferential ring contraction, although this was not expected to occur with 2-bromo-6-methyl*cyclo*hexanone. These acids were not investigated further.

The proposed procedure eliminates the hazards and difficulties associated with the use of selenium dioxide, but precautions are necessary in the manipulation of the lachrymatory α-bromo-ketones. The preparations may be completed in one day and give yields comparable with those from other methods; with *cyclo*pentane-1 : 2-dione dioxime improved yields were obtained. The synthesis should be applicable to most symmetrical ketones and to ketones which form only one α-bromo-ketone.

EXPERIMENTAL

*2-Bromo*cyclo*pentanone.*—Bromination of *cyclo*pentanone in aqueous acetic acid by Acheson's method [8] gave the bromo-ketone in 80—90% yield.

cyclo*Pentane-*1 : 2*-dione Dioxime.*—Hydroxylamine hydrochloride (165 g.) and hydrated sodium acetate (330 g.) were refluxed in water (650 ml.), and freshly prepared 2-bromo*cyclo*pentanone (86 g.) was added dropwise during ¾ hr. After a further ½ hour's refluxing, charcoal was added and the hot solution was filtered. The light brown precipitate of dioxime was filtered off at 5°. Evaporation of the mother-liquor to 400 ml. gave a further crop from which sodium acetate was removed by cold water. The total yield of dioxime was 34 g. (50%). Two recrystallisations from water using charcoal gave colourless crystals which darkened before decomposing at 202—212° (Found: N, 21·8. Calc. for $C_5H_8O_2N_2$: N, 21·85%). M. p.s ranging from 208° to 234° have been given in the literature.[7, 14] The dioxime gave a characteristic, though pH-dependent, precipitate with nickel ions (cf. Voter [7]).

*2-Bromo*cyclo*hexanone.*—*cyclo*Hexanone (50 g.) was dissolved in water (120 ml.) and glacial acetic acid (80 ml.); two drops of bromine were added. The solution was heated at 45—50°. When reaction had started, more bromine (total 81·6 g.) was added with vigorous stirring during 15 min. Then the mixture was cooled and neutralised to Congo-red with solid sodium carbonate. The separated bromo-ketone was washed free from acid with dilute sodium carbonate solution and then with water. Addition of anhydrous sodium sulphate, followed by filtration, gave crude 2-bromo*cyclo*hexanone as a pale yellow liquid (64·2 g., 71%).

cyclo*Hexane-*1 : 2*-dione Dioxime* ("*Nioxime*").—Hydroxylamine hydrochloride (114 g.) and hydrated sodium acetate (228 g.) were dissolved in water (230 ml.) and methanol (200 ml.). Freshly prepared 2-bromo*cyclo*hexanone (64·2 g.) was added dropwise to the refluxing solution of hydroxylamine during 1¼ hr. Then the solution was refluxed for ¾ hr. and distilled; the distillate (200 ml.) was discarded. The residue was cooled to 0° and the precipitated sodium acetate was dissolved by addition of a small amount of water. After some hours at 0°, light pink crystals of "nioxime" (19 g., 37%) separated and were washed with benzene, then recrystallised from water; the colourless crystals (13·1 g.) had m. p. and mixed m. p. 186—188° and gave a characteristic red precipitate with nickel ions. The yield was improved by ether-extraction of the mother-liquor.

*2-Bromo-4-methyl*cyclo*hexanone.*—To 4-methyl*cyclo*hexanone (50 g.) were added two drops of bromine in water (120 ml.) and glacial acetic acid (92 ml.); the whole was heated to *ca.* 50° and the remainder of the bromine (total 74 g.) added to the stirred solution during 45 min., the temperature being kept at 35—40° by cooling. Working-up the product as for 2-bromo*cyclo*hexanone gave crude 2-bromo-4-methyl*cyclo*hexanone (66 g., 78%) as an almost water-white liquid.

*4-Methyl*cyclo*hexanone-*1 : 2*-dione Dioxime* ("*4-Methyl Nioxime*").—To hydroxylamine hydrochloride (119 g.) and hydrated sodium acetate (238 g.) in boiling water (240 ml.) and methanol (208 ml.), freshly prepared 2-bromo-4-methyl*cyclo*hexanone (54·4 g.) was added during 1 hr., then the solution was refluxed for a further hour and distilled until the residual liquid became turbid. It was then cooled and extracted with benzene (3 × 80 ml.). Light

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[14] Riley, Morley, and Friend, *J.*, 1932, 1875.

petroleum (320 ml.; b. p. 80—100°) was added to the combined benzene extracts, and the precipitated " methyl nioxime " (11 g., 25%) was removed. Recrystallisation from water gave " methyl nioxime," m. p. 181—182° (Banks *et al.*[6] gave 181—182°), which gave a characteristic precipitate with nickel ions. The yield may be improved to 29% by continuous benzene extraction.

*2-Bromo*cyclo*heptanone.*—*cyclo*Heptanone (25 g.) was brominated as above in water (57 ml.) and glacial acetic (30 ml.) at ~60° (35·6 g. of bromine added during 25 min.). Working-up as above gave 2-bromo*cyclo*heptanone (36 g., 85%) as a pale yellow liquid.

cyclo*Heptane-*1 : 2*-dione Dioxime* (" *Heptoxime* ").—To hydroxylamine hydrochloride (25·4 g.) and hydrated sodium acetate (50·8 g.) in boiling water (50 ml.) and methanol (45 ml.) was added freshly prepared 2-bromo*cyclo*heptanone (11·6 g.) during 2¾ hr., then the solution was refluxed for 1 hr. and then 40 ml. of distillate were taken off in a vacuum. The pink semisolid lumps which were formed were removed and washed with water. The filtrate deposited crystals which after recrystallisation from water and benzene gave an unidentified hydroxyiminocarboxylic acid (1·9 g.), m. p. 139—140°, which gave a pale yellow precipitate on being heated with nickel ions. The pink semisolid material gave impure " heptoxime " (0·68 g., 7·2%), m. p. 171—176° (from benzene and water) (Vander Haar *et al.*[5] gave 182°). Washing with sodium carbonate solution caused little improvement in the m. p. The dioxime gave the characteristic orange-yellow precipitate with nickel ions. A considerable amount of a glutinous pink material was recovered from the reaction mixture.

*Brominated 2-Methyl*cyclo*hexanone.*—2-Methyl*cyclo*hexanone (25 g.) was brominated in water (60 ml.) and acetic acid (45 ml.) as above at *ca.* 60° (37 g. of bromine added during 15 min.). When worked up as above, this gave the crude bromo-ketone (33 g., 78%).

*Oximation of Brominated 2-Methyl*cyclo*hexanone.*—To hydroxylamine hydrochloride (36 g.) and hydrated sodium acetate (72 g.) in boiling water (72 ml.) and methanol (60 ml.), the freshly prepared bromo-ketone (16·5 g.) was added during ½ hr. and the solution refluxed for a further hour, before distillation; 60 ml. of distillate were collected and discarded. A small amount of water was added to the residue to dissolve precipitated sodium acetate, and the solution was then cooled. A small amount of tar which separated was removed. The light pink solid (7·8 g.) deposited later was filtered off and washed with ice-cold water. Recrystallisation from water gave colourless crystals of a hydroxyimino-carboxylic acid, m. p. 143—145°, which gave no reaction with nickel ions. The mother-liquor gave an orange-red precipitate with nickel ions; this nickel-active material, presumed to be the required dioxime, was almost completely extracted with ether. Concentration of the extract gave only a small amount of glutinous product.

2-Bromopentan-3-one.—To diethyl ketone (50 g.) in water (120 ml.) and acetic acid (80 ml.), bromine (93 g.) was added as described for 2-bromo*cyclo*hexanone, at 65—70°. This gave crude 2-bromopentan-3-one (82·5 g., 86%).

Ethylmethylglyoxime.—To hydroxylamine hydrochloride (31·3 g.) and hydrated sodium acetate (63 g.) in boiling water (120 ml.) was added freshly prepared 2-bromopentan-2-one (16·5 g.) during 1¼ hr. The solution, which contained an oil, was refluxed for a further hour. The boiling solution was treated with charcoal and filtered immediately. Precipitation of the product was completed at 0°; this gave colourless ethylmethylglyoxime (6 g., 46%), m. p. 172—173° (from water) (Schotte [13] gave 172—173°). The dioxime gave a characteristic orange-red precipitate with nickel ions.

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