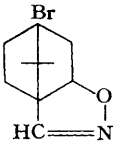
1108. *Dehydrohalogenation of the Anhydrobromonitrocamphanes.*

By H. O. Larson, (Mrs.) Joan S. Heald, and Oscar Levand.

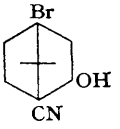
The reaction of anhydrobromonitrocamphane (I) or (II) with hydroxylamine gives a saturated oxime (V) which is rapidly dehydrohalogenated. The oxime (V), which retains all the carbon atoms of its progenitor, is an important link in the degradation of the bicyclic system present in compound (I) or (II). Cleavage products of the ketone (VII) are reported.

The stability of bridgehead halides was discovered by Bartlett and Knox[1] in a study of apocamphyl chloride. They showed that bridgehead halides are incapable of undergoing bimolecular nucleophilic displacement reactions and that normal elimination reactions of this class of halides fail. Eliel[2] has summarized the elimination reactions of bridgehead halides. The solvolysis[3] of 1-bromobicyclo[2,1,1]hexane yields methylcyclopentadiene by a rearrangement which requires the destruction of the bicyclic system.

Forster[4] described the rearrangement of 2-bromo-2-nitrocamphane by concentrated sulphuric acid, and structures for the products, anhydrobromonitrocamphane (I) and anhydrobromonitrocamphane (II) (2-hydroxy-4-bromoapocamphane-1-carbonitrile), were established decisively by van Tamelen and Brenner.[5] The β-hydroxy-nitrile (II) was degraded by aqueous alkali to 2,2-dimethyl-3-methylenecyclopentanecarbonitrile (III), for which the structure was carefully demonstrated.



(I)



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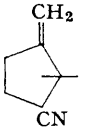

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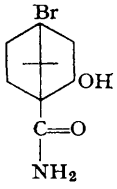
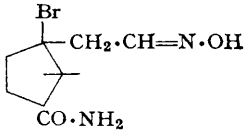
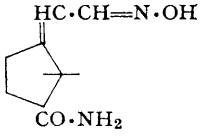


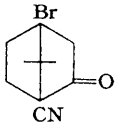
(IV)



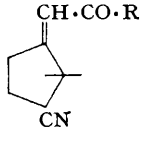
(V)



(VI)

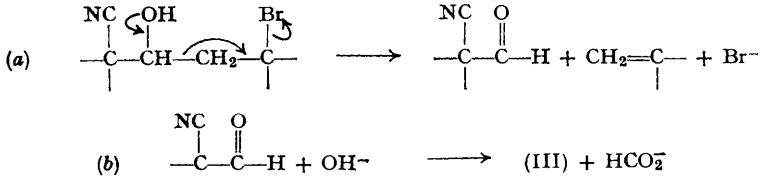


(VII)



(VIII)

The alkaline degradation of compound (II) was presented as a cleavage of the bond between C-2 and C-3, and the olefinic linkage was generated by elimination of the bromide ion (*a*).[5]

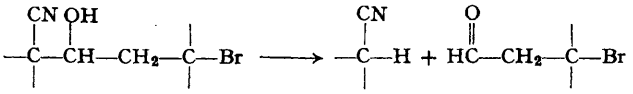


[1] P. D. Bartlett and L. H. Knox, *J. Amer. Chem. Soc.*, 1939, **61**, 3184.
[2] E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill, New York, 1962, p. 376.
[3] K. B. Wiberg and B. R. Lowry, *J. Amer. Chem. Soc.*, 1963, **85**, 3188.
[4] M. O. Forster, *J.*, 1899, **75**, 1141; M. O. Forster and W. Robertson, *J.*, 1901, **79**, 1003.
[5] E. E. van Tamelen and J. E. Brenner, *J. Amer. Chem. Soc.*, 1957, **79**, 3839.

Alkaline cleavage of an α-formyl-nitrile was suggested to yield the unsaturated nitrile (III) and the formate ion (*b*).

The cleavage between C-2 and C-3 (*a*) is unusual, although the second reaction (*b*) is general. Hydrolytic splitting of a carbon–carbon bond[6] would be expected between C-1 and

(*c*)



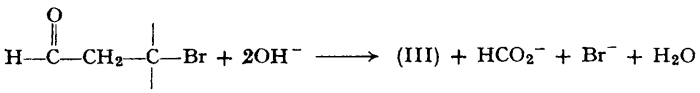
C-2 (*c*). Having an interest in the cleavage of carbon–carbon bonds,[7] we decided to study the dehydrohalogenation of the anhydrobromonitrocamphanes.

Forster[8] reported the formation of a product, $C_{10}H_{17}BrN_2O_2$, which retained all of the carbon atoms of the reactant as well as the halogen, by treatment of the anhydrobromonitrocamphanes with hydroxylamine. The new compound was dehydrohalogenated rapidly in aqueous alkali to form another derivative, $C_{10}H_{16}N_2O_2$. Forster did not attempt to assign structures to the two compounds, which might clarify the course of the dehydrohalogenation.

We have repeated and confirmed Forster's work. The conversion (I) → (II) by base has been established,[5] and analogies are available in closely related systems.[9] Thus, the products from the treatment of compound (I) or compound (II) with hydroxylamine under homogeneous conditions are the same. The mixture of products was separated conveniently by chromatography. The amide (IV), $C_{10}H_{16}BrNO_2$, which was not reported previously, was the major product. Apparently Forster assumed that the amide (IV) was compound (I). The physical properties of the two compounds are very similar, but the infrared spectra facilitate an obvious differentiation. Isolation of the amide (IV) suggested that Forster's compound $C_{10}H_{17}BrN_2O_2$, was the oxime (V), which was soluble in aqueous alkali. The infrared spectrum of compound (V) was not informative because of the similar absorption of the oximino- and the amido-groups in the carbonyl region.[10] However, the rapid dehydrohalogenation of the oxime with aqueous alkali requires the absence of a bicyclic system.[2] The ultraviolet absorption spectrum of the unsaturated oxime (VI) showed intense absorption at 226 mμ which is characteristic of an unsaturated oxime.[11] The presence of an oximino-group is indicated also by the amphoteric properties of compound (VI).

The hydroxy-amide (IV) gave the oxime (V), presumably by a reversed aldol reaction. The hydroxy-nitrile (II) might cleave similarly (*c*), although the nitrile group was not hydrolyzed under the heterogeneous conditions.[5] Attack of hydroxide ion on the carbonyl group (*d*) might result in β-elimination to give a modest yield (40%) of compound (III) as reported.[5] The oxime (V) was isolated in a very low yield (10%). Thus, the conversion of the oxime (V)

(*d*)



into the aldehyde and dehydrohalogenation of the aldehyde under experimental conditions comparable to the degradation[5] of compound (II) were impractical.

However, the cleavage of 4-bromo-2-oxoapocamphane-1-carbonitrile (VII) with bases might occur through the formation of intermediates in which C-2 became tetrahedral and geometrically similar to the alkoxide intermediate[5] in the degradation of compound (II) with aqueous alkali. Sodium ethoxide converted the ketone (VII) into the ester (VIII; R = OC_2H_5). Sodium hydroxide degraded the ketone (VII) to the nitrile (III) and the un-

[6] M. M. Shemyakin and L. A. Shchukina, *Quart. Rev.*, 1956, **10**, 261.
[7] H. O. Larson and E. K. W. Wat, *J. Amer. Chem. Soc.*, 1963, **85**, 827.
[8] M. O. Forster, *J.*, 1901, **79**, 653.
[9] W. S. Johnson and W. E. Shelberg, *J. Amer. Chem. Soc.*, 1945, **67**, 1745.
[10] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley & Sons, New York, 2nd edn., 1958.
[11] A. E. Gillam and E. S. Stern, "Electronic Absorption Spectroscopy," Arnold, London, 1954, p. 105.

saturated acid (VIII; R = OH). A salt of the β-bromocarboxylic acid that formed from the cleavage of the ketone (VII) would decarboxylate and undergo a β-elimination to give the unsaturated nitrile (III). The formation of the acid (VIII; R = OH) in appreciable, variable amounts is an anomalous reaction. Homoapocamphoric acid was obtained by prolonged alkaline treatment of the ketone (VII) followed by catalytic hydrogenation.

Experimental

Infrared spectra were measured for potassium bromide discs with a Beckman IR5 instrument. The ultraviolet spectrum was recorded with a Beckman DU spectrophotometer and ethanol as solvent. Melting points were taken in capillary tubes and are uncorrected. Merck's acid-washed alumina was used in chromatographic work. Analyses were by Dr. A. Bernhardt, Mulheim, Germany. Organic solutions were dried with anhydrous magnesium sulphate.

Reaction of Anhydrobromonitrocamphane (I) *with Hydroxylamine.*—Hydroxylamine hydrochloride (10 g.), sodium carbonate (8 g.), compound (I) (10 g.), ethanol (80 ml.), and water (30 ml.) were stirred under reflux for 5 hr. Sodium carbonate (3·2 g.) and hydroxylamine hydrochloride (4 g.) were added, and the solution was stirred under reflux for another 5 hr. The solvents were removed at reduced pressure, and the residue was dissolved in ether and washed with water. After removal of the ether, the residue (7 g.) was dissolved in tetrahydrofuran and chromatographed on alumina (70 g.). The solvent was removed, and the residue was crystallized from ethanol to give 4-*bromo*-2-*hydroxyapocamphane*-1-*carboxyamide* (3·6 g.), m. p. 226—228°; $\nu_{max.}$ 3402, 3333, 1660, and 1640 cm.$^{-1}$ (Found: C, 45·7; H, 6·3; Br, 30·55; N, 5·2. $C_{10}H_{16}BrNO_2$ requires C, 45·8; H, 6·1; Br, 30·5; N, 5·3%). The column was eluted with ethanol. Removal of the solvent left a residue which was crystallized from ethanol to give 1-*bromo*-2,2-*dimethyl*-3-*carbamoylcyclopentylacetaldehyde oxime* (1·1 g.), m. p. 202—203° (lit.,[8] 197°); $\nu_{max.}$ 3495, 3390, 3278, 1642, and 1587 cm.$^{-1}$ (Found: C, 43·3; H, 6·0; Br, 28·8; N, 10·1. $C_{10}H_{17}BrN_2O_2$ requires C, 43·3; H, 6·1; Br 28·9; N, 10·1%). The oxime was soluble in 10% aqueous sodium hydroxide.

Reaction of Anhydrobromonitrocamphane (II) *with Hydroxylamine.*—The hydroxy-nitrile (II) (11·5 g.), sodium carbonate (8 g.), hydroxylamine hydrochloride (10 g.), ethanol (80 ml.), and water (30 ml.) were stirred at the reflux temperature for 2 hr. Sodium carbonate (3·2 g.) and hydroxylamine hydrochloride (4·0 g.) were added, and the solution was heated again for 2 hr. The isolation was similar to the procedure described in the preceding section. Some hydroxy-nitrile (II) (3·5 g., m. p. 244—245°) was recovered. The hydroxy-amide (IV) (2 g., m. p. 225—227°) and the oxime (V) (1·1 g., m. p. 200—201°) were isolated. The infrared spectrum of each compound was identical with the spectrum of an authentic sample.

Dehydrohalogenation of the Oxime (V).—The oxime (V) (400 mg.) was suspended in 4 ml. of 15% aqueous sodium hydroxide. The suspension was heated for 2 min. The solution was cooled quickly and acidified with concentrated hydrochloric acid. The precipitate was extracted with ether, and the solvent was distilled. The residue was crystallized from ethanol to give 2,2-*dimethyl*-3-*carbamoylcyclopentylideneacetaldehyde oxime* (200 mg.) m. p. 215—216° (lit.,[8] 208°), $\lambda_{max.}$ 226 (ε 6520); $\nu_{max.}$ 3448, 3333, 3225, 1636, and 1600 cm.$^{-1}$ (Found: C, 61·5; H, 8·4; N, 14·5. $C_{10}H_{16}N_2O_2$ requires C, 61·2; H, 8·2; N, 14·3%). The oxime was soluble in both 10% aqueous sodium hydroxide and hydrochloric acid.

Ethyl 3-*Cyano*-2,2-*dimethylcyclopentylideneacetate.*—Sodium ethoxide was prepared from sodium (230 mg.) and ethanol (20 ml.). The ketone[5] (VII) (2·42 g.) was dissolved in ethanol (70 ml.) and was treated with sodium ethoxide for 3 hr. at room temperature. The solvent was removed at reduced pressure, and the product was dissolved in ether which was washed with water. The solvent was removed, and the residue was crystallized from cyclohexane to give *ethyl* 3-*cyano*-2,2-*dimethylcyclopentylideneacetate* (1·30 g.), m. p. 69—71°; $\nu_{max.}$ 2242 (saturated nitrile), 1698 αβ-unsaturated ester), 1645 cm.$^{-1}$ (conjugated C=C) (Found: C, 69·7; H, 8·2; N, 6·8. $C_{12}H_{17}NO_2$ requires C, 69·55; H, 8·25; N, 6·75%).

Cleavage of 4-*Bromo*-2-*oxoapocamphane*-1-*carbonitrile with Sodium Hydroxide.*—Sodium hydroxide (9·0 g.), ketone (VII) (9·0 g.), and water (30 ml.), were refluxed for 4 min. After the solution was cooled, acidification yielded a solid that was filtered off. Several crystallizations from a mixture of acetone and water gave 3-*cyano*-2,2-*dimethylcyclopentylideneacetic acid* (430 mg.), m. p. 186·5—187°; $\nu_{max.}$ 2242 (saturated nitrile), 1680 (αβ-unsaturated acid), 1634 cm.$^{-1}$ (conjugated C=C) (Found: C, 67·1; H, 7·3; N, 7·9. $C_{10}H_{13}NO_2$ requires C, 67·0; H, 7·3; N, 7·8%). Yields of the acid varied from 4 to 24%.

The filtrate was extracted with ether, and, after removal of the solvent, the nitrile (III) distilled at 82—85°/21 mm. (2·10 g.), n_D^{25} 1·4616 (lit.,[5] 1·4620).

Homoapocamphoric Acid.—A mixture of 4-bromo-2-oxoapocamphane-1-carbonitrile (2·0 g.), sodium hydroxide (3·0 g.), and water (10 ml.) was refluxed for 10 hr. Acidification gave a solid which was dissolved in dilute sodium hydrogen carbonate and filtered. The filtrate was placed in a Parr reduction unit with palladium oxide (50 mg.) and hydrogen at room temperature and 2 atm. When the reduction was complete, the catalyst was removed, and acidification gave the product which was crystallized from water. The homoapocamphoric acid (31 mg.) melted at 202—204° (lit.,[12] 202—203°) without decarboxylation (Found: C, 60·1; H, 8·0. Calc. for $C_{10}H_{16}O_4$: C, 60·0; H, 8·0%).

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[12] P. B. Talukdar and P. Bagchi, *J. Org. Chem.*, 1955, **20**, 21.