4,9-Dimethyl-2,6-diazaspiro[4,5]dec-3-ene-1,7-dione: An Unusual Reaction Product from 2-Methylepichlorohydrin and Potassium Cyanide

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Summary. Reaction of 2-methylepichlorohydrin with unbuffered potassium cyanide solution (pH 11·5—12·5) leads to 4,9-dimethyl-2,6-diazaspiro[4,5]dec-3-ene-1,7-dione.

IN 1964 Johnson and Heeschen[1] reported the isolation of compound (I) from the reaction of unbuffered sodium cyanide solution (pH 11·5—12·5) with epichlorohydrin.

We now report that, in complete contrast, the reaction of 2-methylepichlorohydrin under the same conditions leads to an entirely different type of by-product (10·5%) to which we assign structure (II). The latter is a crystalline solid, m.p. 302—305° dec., with i.r. bands at 3200, 3080, 1700, 1680, 1650, and 1640 cm^{-1}. It separates spontaneously from the reaction mixture.†

Chemical and physical evidence reported below is compatible with its formulation as 4,9-dimethyl-2,6-diazaspiro[4,5]dec-3-ene-1,7-dione, (II).

The 100 MHz n.m.r. spectrum [$(CD_3)_2SO$, 70°] displays a doublet at δ 1·065, *J* 6·0 Hz, secondary methyl substituent of the piperidone ring, a doublet at δ 1·874, *J* 1·68 Hz, olefinic methyl, and a multiplet at δ 5·653, olefinic proton. The two low-field diffuse singlets we assign to the two *N*-H protons, the complex multiplet in the region δ 1·26—2·36 accounts for the five remaining protons. Although the line widths of both *N*-H resonances are dominated by quadrupole broadening[2] irradiation of the low-field *N*-H caused the olefinic multiplet to collapse, partially revealing a quartet

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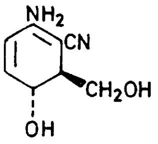
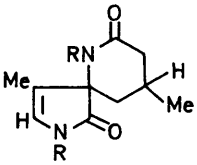
† The other products of the reaction are 3-hydroxy-3-methylglutaronitrile (43%) and 4-hydroxy-3-methylcrotononitrile (III, 14%). When the reaction is buffered by magnesium sulphate (pH *ca.* 9·5), 3-hydroxy-3-methylglutaronitrile (71%) becomes the major product of the reaction. F. Johnson, J. P. Panella and A. A. Carlson, *J. Org. Chem.*, 1962, **27**, 2241.

due to splitting by the adjacent methyl group. On the other hand, irradiation of the latter uncovered a 1·90 Hz coupling of the olefinic proton, to the low-field *N*-H.

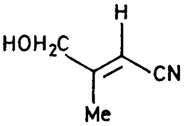
High-resolution mass spectrometry confirms the molecular formula of (II) to be $C_{10}H_{14}N_2O_2$, and permits further definition of the six-membered ring. All of the major peaks [*m/e* 179($M - CH_3$), 152($M - C_3H_6$, $179 - C_2H_3$), 124($M - C_4H_6O$, $152 - CO$), 111($C_5H_7N_2O$), 109($M - C_4H_7NO$), and 69(C_4H_5O)] are readily rationalized in terms of energetically favourable fragmentation processes. Support for this interpretation was provided by high-resolution mass spectral analysis of 4,6,6-trimethyl-2-piperidone which shows an analogous fragmentation pattern.‡



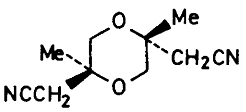
(I)



(II) R = H (IV) R = Ac
(V) R = Me (VI) R = CH₂·C₆H₄-*m*-Cl



(III)



(VII)

Hydrogenation of (II) in ethanol–dioxan over 10% Pd–C afforded a dioxan solvate of a dihydro-compound, $C_{10}H_{16}N_2O_2$, m.p. 286—288° dec. (from ethanol–dioxan).

Acetylation of (II) with refluxing acetic anhydride gave (IV) m.p 129—131° (from ethanol), the n.m.r. spectrum of which possesses two *N*-Ac absorptions at δ 2·44, and 2·53, respectively.§

Methylation of (II) by means of dimsyl sodium[3]/methyl iodide afforded the *NN'*-dimethyl derivative (V), m.p. 104—105° (from ethyl acetate–petroleum). The n.m.r. spectrum was similar to that observed for (II). The large chemical shift difference between the two *N*-methyl groups at δ 2·488 and 2·860 is presumably, due to the piperidone *N*-methyl being in the shielding region of the unsaturated functions.

The *NN'*-*m*-chlorobenzyl derivative (VI), m.p. 188° (from methanol) prepared in similar fashion, exhibited a singlet for one benzylic methylene group (δ 4·18) and an AB quartet for the other (J_{AB} 16·6 Hz, $\Delta\nu_{AB}$ 99·4 Hz, δ 4·035) in the n.m.r. spectrum. We associate the up-field AB absorption with the benzylic moiety attached to the piperidone ring; the magnetic non-equivalence arises from its greater proximity to a chiral centre.

Oxidation of (II) with nitric acid followed by diazomethane methylation of the acidic organic residue led to dimethyl methylsuccinate and dimethyl oxalate, derived no doubt from the further oxidation of 2-oxo-4-methyladipic acid, the expected initial product of oxidation.

The mechanism of transformation of 2-methylepichlorohydrin to (II) has not been established. It appears likely that (II) arises from two C_5 moieties and this we have demonstrated by the isolation of (II) after treatment of (III)¶ with either potassium cyanide or 8·0N-sodium hydroxide solution.

A second product of the reaction of *trans*-(III) with base is *trans*-2,5-biscyanomethyl-2,5-dimethyl-1,4-dioxan (VII), m.p. 176—178°. An astonishing reaction occurs when (VII) is heated at 155°. It is partially converted into (II).

We thank Mr. A. A. Carlson for the initial preparation of compound (II), Dr. L. Shadoff for mass spectral data, and Dr. E. Cavalieri, University of California, Berkeley, for a sample of 5,6-dihydro-4,6,6-trimethyl-2(1*H*)-pyridone.

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‡ Preparation from 5,6-dihydro-4,6,6-trimethyl-2(1H)-pyridone according to the procedure of H. K. Hall, *J. Amer. Chem. Soc.*, 1957, **79**, 5444. The molecular ion appears at 141 and there are major fragment ions at *m/e* 126 ($M - CH_3$), 99 ($M - C_3H_6$), and 69 (C_4H_5O).

§ Here, irradiation of the olefinic methyl doublet resulted in a sharp singlet for the olefinic proton.

¶ Steady-state and transient nuclear Overhauser experiments[4] were utilized to define the geometry of (III) as that in which the hydroxymethyl and cyano-groups are *trans* related. Irradiation of the methylene protons resulted in a positive polarization (10%) of the olefinic proton and, interestingly, irradiation of the hydroxylic proton also led to an enhancement (17%) of the olefinic intensity. No effect was observed upon irradiating the methyl group.

[1] F. Johnson and J. P. Heeschen, *J. Org. Chem.*, 1964, **29**, 3252.
[2] W. B. Moniz and H. S. Gutowsky, *J. Chem. Phys.*, 1963, **38**, 1155; J. A. Glasel, *Org. Magnetic Resonance*, 1969, **1**, 481.
[3] E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 1965, **87**, 1345.
[4] F. A. L. Anet and A. J. R. Bourn, *J. Amer. Chem. Soc.*, 1965, **87**, 5250; R. A. Hoffmann and S. Forsén, *J. Chem. Phys.*, 1966, **45**, 2049.