424. *Experiments towards the Synthesis of Corrins. Part III.* Formation of a Bicyclic Oxaziran from a Δ^1-Pyrroline and from the Corresponding Nitrone.*

By R. Bonnett, V. M. Clark, and Sir Alexander Todd.

Irradiation of 5 : 5-dimethyl-Δ^1-pyrroline 1-oxide yields the bicyclic oxaziran (IV), also obtained by oxidation of 5 : 5-dimethylpyrroline with aqueous hydrogen peroxide. Thermal rearrangement of the oxaziran (IV) leads to 5 : 5-dimethylpyrrolid-2-one, whereas acidic hydrolysis yields lævulic aldehyde.

Investigation of a reported 3-hydroxyoxaziran shows it to be the isomeric hydroxamic acid.

Recent investigations[1,2] have revived interest in compounds containing the three-membered carbon–nitrogen–oxygen (oxaziran) ring (I), a formulation at one time suggested for the nitrones (azomethine *N*-oxides) (II) only to be subsequently discarded. The oxazirans and the azomethine *N*-oxides might be regarded as *electronic* tautomers and, indeed, irradiation of nitrones can yield oxazirans,[3] thermal decomposition of which regenerates the original nitrones.[4]

In the course of our work on Δ^1-pyrroline 1-oxides we irradiated 5 : 5-dimethyl-Δ^1-pyrroline 1-oxide[5] (III), whereupon the nitrone was converted into an isomer to which we assign the oxaziran structure (IV). The same material was obtained on oxidation of 5 : 5-dimethyl-Δ^1-pyrroline[6] with aqueous hydrogen peroxide.

The product is assigned structure (IV) on the basis of its analysis and active-oxygen content (cf. ref. 1), and the absence of ultraviolet absorption (in ethanol), of infrared maxima (liquid film) in the N–H and double-bond regions, and of basic properties. The

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* Part II, preceding paper.

[1] Emmons, *J. Amer. Chem. Soc.*, 1956, **78**, 6208; 1957, **79**, 5739.

[2] Farbenfabriken Bayer, B.P. 743,940; Krimm, *Chem. Ber.*, 1958, **91**, 1057.

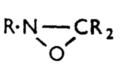
[3] Kamlet and Kaplan, *J. Org. Chem.*, 1957, **22**, 576; Splitter and Calvin, *ibid.*, 1958, **23**, 651.

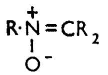
[4] Hawthorne and Strahm, *ibid.*, 1957, **22**, 1263.

[5] Bonnett, Brown, Clark, Sutherland, and Todd, preceding paper.

[6] Bonnett, Clark, Giddey, and Todd, *J.*, 1959, 2087.

nuclear magnetic resonance spectrum of the liquid measured at 40 Mc./sec. exhibited chemical shifts σ of $+1{\cdot}0$, $+3{\cdot}2$, $+3{\cdot}9$, $+4{\cdot}12$, $+4{\cdot}34$ (in parts per million relative to water) in accordance with the proposed structure.


(I)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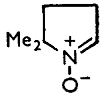
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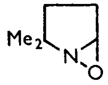
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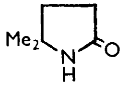
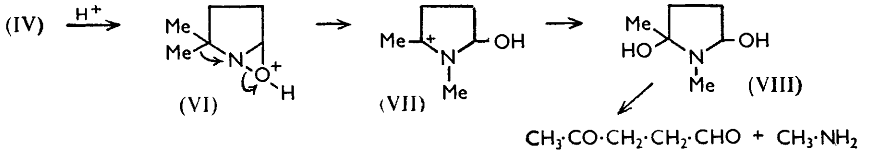

(V)

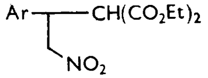
The compound (IV) behaved in a fashion analogous to the similarly substituted monocyclic oxazirans.[1] When it was heated, the nitrone (III) was not re-formed but, instead, there was a slow isomerisation to the corresponding amide, 5 : 5-dimethylpyrrolid-2-one

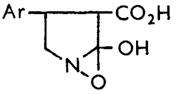


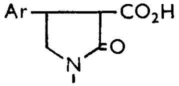
(V). Treatment with acid resulted in rearrangement to lævulaldehyde, isolable as its bisdinitrophenylhydrazone, the reaction possibly following the course (VI ⟶ VIII). No methylamine was detected, but the acidic solution gave a strong Ehrlich reaction as would be expected from pyrrole derivatives which might be formed from (VIII) or its equivalent.

Irradiation of 2-substituted Δ^1-pyrroline 1-oxides failed to yield oxazirans, as did oxidation of the corresponding pyrrolines, owing presumably to a combination of steric and electronic factors.

Reichert and Wegner[7] have reported that controlled catalytic reduction of the nitro-ester (IX; Ar = *o*-methoxyphenyl) followed by hydrolysis gave a compound $C_{12}H_{13}O_5N,H_2O$ for which they proposed structure (X). On the basis of present knowledge it is to be


(IX)


(X)


(XI)

expected that the product will be the related α-hydroxy-nitrone, existing as the tautomeric hydroxamic acid (XI). Repetition of Reichert and Wegner's work gave a product which, in accordance with structure (XI), exhibited carbonyl bands in the infrared spectrum at 1738 and 1667 cm.$^{-1}$ and on electrometric titration in aqueous solution had pK_a values of 2·5 and 7·2, corresponding to the carboxylic and hydroxamic acid respectively. It also gave a purple colour with ferric chloride.

EXPERIMENTAL

2 : 2-*Dimethyl*-6-*oxa*-1-*aza*bicyclo[3 : 1 : 0]*hexane*.—(a) *By oxidation of* 5 : 5-*dimethyl*-Δ^1-*pyrroline*. Hydrogen peroxide (20 ml. of " 30 vol.") was added to the pyrroline (11 g.) in water (15 ml.) and kept at 0° for 2 days, during which two layers were formed. A trace of platinum powder was added and after effervescence had subsided the suspension was extracted with ether (2 × 50 ml.): the extract was dried (Na_2SO_4) and evaporated, leaving the neutral liquid 2 : 2-*dimethyl*-6-*oxa*-1-*aza*bicyclo[3 : 1 : 0]*hexane* (8·2 g., 64%), b. p. 60°/32 mm. (Found: C, 63·9; H, 10·1; N, 11·8; active O, 13·6. $C_6H_{11}ON$ requires C, 63·7; H, 9·8; N, 12·4; active O, 14·2%). Under atmospheric pressure the b. p. was *ca.* 150° but on occasion explosion occurred at this temperature. The proton magnetic resonance spectrum of the liquid

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[7] Reichert and Wegner, *Ber.*, 1938, **71**, 1254.

(*cyclo*hexane as internal standard) exhibited peaks with chemical shifts σ, −1·90 (very weak, possibly from impurity), +1·0 (H at $C_{(5)}$), +3·2, +3·9 (ring CH_2), +4·12, +4·34 (*gem*-dimethyl). The active-oxygen titre of an aqueous solution of the oxaziran decreased to half its initial value in 30 days.

(b) *By irradiation of* 5 : 5-*dimethyl*-Δ^1-*pyrroline* 1-*oxide*. The nitrone [5] (1·6 g.) in *cyclo*hexane–ethanol (10 ml. of each) was placed 10 mm. from an Hanovia UVS 250 lamp and irradiated for 5 days. Fractionation of the product gave the crude oxaziran (0·18 g., 11%; b. p. 55—60°/25 mm.) whose infrared spectrum (liquid film) contained the same strong peaks in the fingerprint region as that of the oxidation product of the pyrroline; the active-oxygen titre was 12·6%. The infrared spectrum (film) of the distillation residue showed maxima corresponding to unchanged nitrone and the pyrrolidone (V) derived by thermal rearrangement of the oxaziran.

Action of Heat upon the Oxaziran (IV).—Infrared spectroscopy indicated little change in a solution of the oxaziran (0·4 g.) in *cyclo*hexane (1 ml.) kept under reflux for 36 hr. Removal of the solvent and elevation of the temperature to 130° for 14 hr. brought about development of a strong band at 1690 $cm.^{-1}$. After removal of unchanged oxaziran under reduced pressure, sublimation of the residue yielded a small quantity of a deliquescent solid, m. p. 36—38° (lit.,[8] 37—41°) whose infrared spectrum was consistent with the product's being 5 : 5-dimethylpyrrolid-2-one.

Action of Acid upon the Oxaziran (IV).—Dissolution of the oxaziran (0·66 g.) in 50% sulphuric acid (2 ml.) was accompanied by a rise in temperature and the development of a red colour; an Ehrlich test on this solution was strongly positive. The solution was heated for 10 min. on a steam-bath, diluted with 1 : 1 aqueous ethanol (20 ml.), and treated with 2 : 4-dinitrophenylhydrazine in methanolic hydrogen chloride, whereupon the bis-2 : 4-dinitrophenylhydrazone of lævulic aldehyde separated (0·33 g., 13%), having m. p. 237°: undepressed on admixture with a sample prepared from sylvan [9] (Found: C, 44·3; H, 3·75; N, 24·1. Calc. for $C_{17}H_{16}O_8N_8$: C, 44·3; H, 3·5; N, 24·2%). The infrared spectra of the two samples were identical.

Repetition of Reichert and Wegner's Experiment.—The nitro-diester (3 g.) obtained by addition of malonic ester to the condensation product of nitromethane and *o*-methoxybenzaldehyde [7] was hydrogenated in methanol at room temperature over platinum oxide. After 2 mols. of hydrogen had been absorbed the catalyst and solvent were removed, the residue was dissolved in ether, and the product extracted with aqueous alkali. Acidification gave a crystalline precipitate (0·55 g., 23%), recrystallisation of which from water gave 1-*hydroxy*-4-o-*methoxyphenyl*-2-*oxopyrrolidine*-3-*carboxylic acid monohydrate*, m. p. 130° (Found: C, 53·6; H, 5·8; N, 5·25. $C_{12}H_{13}O_5N,H_2O$ requires C, 53·5; H, 5·6; N, 5·2%). The infrared spectrum showed principal maxima at 3435, 3140, 2550, 1738, and 1667 $cm.^{-1}$; electrometric titration in water gave pK_{a_1} 2·5, pK_{a_2} 7·2, equiv. 132 (required, 135). The product gave a purple colour with ferric chloride solution, as did the residue arising from thermal decarboxylation at 160°.

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[8] Moffett and White, *J. Org. Chem.*, 1952, **17**, 407.
[9] Wilson, *J. Amer. Chem. Soc.*, 1948, **70**, 1313.