

Experiments towards the Synthesis of Corrins. Part XI.¹ Attempted Synthesis of β -Dinitrones by Oxidative Routes

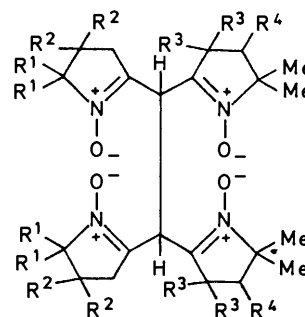
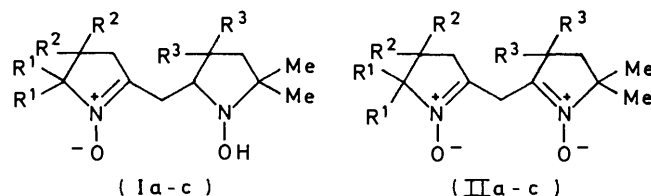
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Methylenebis-nitrone of the Δ^1 -pyrroline 1-oxide series, when generated under a variety of oxidising conditions, undergo self-condensation yielding tetrasubstituted ethanes or ethylenes.

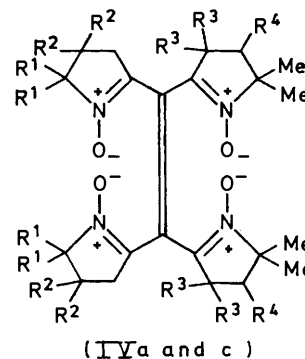
THE AB component of the corrin² ring system is formally related to the diaza-analogue of a β -diketone. Earlier work³ established that aldol-type condensation of 1-pyrroline 1-oxides yields the nitrone-hydroxylamines (I), which can be readily oxidised to the corresponding β -dinitrones (II). These β -dinitrones are themselves unstable under oxidising conditions, and the formation of a tetrasubstituted ethylene derivative from (IIa) has already been described.³

Further attempts to isolate monomeric β -dinitrones from controlled oxidation of the corresponding nitrone-hydroxylamines are now reported. Oxidation of the hexamethyl compound (Ib)³ yielded two colourless, crystalline compounds (A), m.p. 196°, and (B), m.p. 180°, which were separated by fractional crystallisation and shown to be isomers of structure (IIIb). Reactions of (Ib) with various oxidising agents led to (A) and (B) in various proportions, some reagents producing (A) exclusively. Copper-catalysed aerial oxidation⁴ produced (A) in 50% yield together with a trace of a bright yellow compound (m.p. 225°) presumed to be a tetrasubstituted ethylene [*cf.* (IV)]; no (B) was formed. Compound (A) was formed exclusively by using chloranil,⁵ whereas use of manganese dioxide⁶ led predominantly to (A) but some (B) was also produced. Use of 4 mol. equiv. of alkaline potassium hexacyanoferrate(III) gave the two isomers in approximately equal proportions; the action of 2 mol. equiv. yielded a hygroscopic oil which was not clearly characterised but appeared to be a mixture containing much starting material. Compounds (A) and (B) had the same empirical formula; molecular weight determinations indicated that they were each derived from two molecules of (Ib). However, a comparison of their properties with those of the ethylene derivative (IVa) ruled out structures of this olefinic type. The i.r. spectrum of (A) contained a nitrone peak at 1580 cm^{-1} , the corresponding absorption of (B) being at 1590 cm^{-1} . The two compounds absorbed in the same region of the u.v., with maxima at 262 nm (ϵ 11 140) for (A) and 259 nm (ϵ 11 220) for (B): these values are consistent with those expected for β -dinitrones or their prototropic tautomers. The ¹H n.m.r. spectra of (A) and (B) were essentially identical, but too complex to allow clear analysis. For

this, among other reasons, attention was turned to the nitrone-hydroxylamine (Ic) where there would be no problems due to chirality in the resulting product.



(III b and c: various enolic forms are also possible)



a; R¹ = R³ = H, R² = R⁴ = Me
 b; R¹ = R⁴ = H, R² = R³ = Me
 c; R¹ = Me, R² = R³ = R⁴ = H

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¹ Part X, R. F. C. Brown, V. M. Clark, and Lord Todd, *Tetrahedron*, Suppl. 8, Part 1, 1966, 15.

² R. F. C. Brown, V. M. Clark, M. Lamchen, and Sir Alexander Todd, *J. Chem. Soc.*, 1959, 2116.

³ R. F. C. Brown, V. M. Clark, I. O. Sutherland, and Sir Alexander Todd, *J. Chem. Soc.*, 1959, 2109.

Oxidation of (Ic) with air in the presence of cuprammonium acetate until the first appearance of a blue colour

⁴ D. H. Johnson, M. A. T. Rogers, and G. Trappe, *J. Chem. Soc.*, 1956, 1093.

⁵ L. M. Jackman, 'Advances in Organic Chemistry—Methods and Results,' Interscience, New York, 1960, p. 329.

⁶ N. L. Wendler, H. L. Slates, and M. Tishler, *J. Amer. Chem. Soc.*, 1949, **71**, 3267; R. M. Evans, *Quart. Rev.*, 1959, **13**, 61.

(15 min) led to a colourless crystalline product (IIIc). Extension of the time of oxidation gave the yellow olefin (IVc), which was readily recognised by its spectroscopic properties, in particular its ^1H n.m.r. spectrum, which showed only resonances of the geminal dimethyl groups at τ 8.64 and the A_2B_2 spin-spin coupling pattern (two triplets) of the nitron methylene groups at τ 7.95(t) and 7.31(t).

The properties of the colourless oxidation product were incompatible with those of a β -dinitrone such as (IIc); in particular the u.v. absorption maximum at 246 nm was unchanged on addition of alkali. The molecular weight and ^1H n.m.r. spectrum were consistent with the dimeric ethane type structure (IIIc). In addition to the methyl and methylene resonances a singlet attributable to the methine protons was observed at τ 5.13. The same two products were isolated when the hydroxylamine (Ic) was oxidised in carbon tetrachloride with ≥ 2 mol. equiv. of mercury(II) oxide.⁷ When only 1 mol. equiv. was used, starting material (Ic) and (IIIc) were isolated. The crude product had a u.v. absorption maximum at 330 nm, changing to 357 nm in alkali (both bands were weak in comparison with that at 240 nm). Since these long-wave bands disappeared on further oxidation, they may have arisen from a trace of the β -dinitrone (IIc); however, no product with this structure was isolated.

Monomeric β -dinitrones (II) have not been isolated from any oxidation reaction of a nitron-hydroxylamine (I). It appears that their rate of formation is equalled or exceeded by that of their oxidative self-condensation. This is perhaps not surprising since the free radical which undergoes dimerisation is stabilised by delocalisation of the odd electron involving both nitrogen atoms: it is a particular type of vinylogous nitroxide radical.⁸ In consequence, β -dinitrones (II) of the 1-pyrroline 1-oxide series are probably inaccessible by oxidative routes.

EXPERIMENTAL

Unless otherwise stated, u.v. spectra were determined with a Cary 14 spectrophotometer, i.r. spectra with a Perkin-Elmer 137 or Unicam SP 200 instrument, and n.m.r. spectra with a Perkin-Elmer R 10 instrument at 60 MHz. Light petroleum refers to the fraction of b.p. 60–80°.

Oxidation of 2-(1-hydroxy-3,3,5,5-tetramethylpyrrolidin-2-ylmethyl)-4,4-dimethyl- Δ^1 -pyrroline 1-Oxide (Ib).—(a) *Copper-catalysed oxidation.* The hydroxylamine (Ib) (0.5 g) and copper acetate (0.01 g) were dissolved in water (250 ml) containing aqueous ammonia (35%; 0.5 ml). Air was passed through the solution for 30 min, after which the initial blue colour had reappeared. Extraction with chloroform yielded a solid which was separated by chromatography on alumina into a yellow solid, m.p. 225° (0.01 g), and colourless needles of 1,2-bis-(4,4-dimethyl- Δ^1 -pyrrolin-2-yl)-1,2-bis-(3,3,5,5-tetramethyl- Δ^1 -pyrrolin-2-yl)ethane tetra-N-oxide (IIIb; A) (0.25 g, 50%), m.p. 196° (from methylene chloride–light petroleum).

(b) *Oxidation with potassium hexacyanoferrate(III).* The hydroxylamine (Ib) (0.5 g), potassium hexacyanoferrate (2.46 g, 4 mol. equiv.) and sodium carbonate (2.0 g) were dissolved in water (100 ml) and the solution was kept for 1 h at room temperature. Chloroform extracted a pale yellow solid, which was separated by fractional crystallisation (from

methylene chloride–light petroleum) into two isomers (IIIb), (A) (0.135 g, 27%), m.p. 196°, and (B) (0.115 g, 23%), m.p. 180°.

(c) *Oxidation with chloranil.* Chloranil (0.73 g) in benzene (25 ml) was added to the hydroxylamine (Ib) (0.265 g) in benzene (5 ml). After 15 min, the benzene was removed and the bases were extracted into dilute hydrochloric acid in the presence of ether. The acidic extract was made alkaline and extracted with chloroform to yield (IIIb, A), (0.13 g, 50%), m.p. 196°.

(d) *Oxidation with manganese dioxide.* The hydroxylamine (Ib) (0.23 g) in chloroform (25 ml) was shaken gently overnight with manganese dioxide (James Woolley & Co.) to yield, after filtration and recrystallisation, two isomers (IIIb), (A) (0.09 g, 39%), m.p. 196°, and (B) (0.03 g, 13%), m.p. 180°; (A), ν_{max} (CHCl_3) 3 320 and 1 580 cm^{-1} , λ_{max} (EtOH) 262 nm (ϵ 11 140), τ 8.93, 8.68, 8.13, 6.53, and 4.30 [Found: C, 67.6; H, 9.7; N, 10.5%; M (cryoscopic), 559. $\text{C}_{30}\text{H}_{50}\text{N}_4\text{O}_4$ requires C, 67.9; H, 9.5; N, 10.6%; M , 531]; (B), ν_{max} (CHCl_3) 3 320 and 1 590 cm^{-1} , λ_{max} (EtOH) 259 nm (ϵ 11 220); τ 8.85, 8.65, 8.10, 7.50, 6.88, 6.48, and 4.25 [Found: C, 68.0; H, 9.1; N, 10.5%; M (cryoscopic), 544. $\text{C}_{30}\text{H}_{50}\text{N}_4\text{O}_4$ requires C, 67.9; H, 9.5; N, 10.6%; M , 531].

2-(1-Hydroxy-5,5-dimethylpyrrolidin-2-ylmethyl)-5,5-dimethyl- Δ^1 -pyrroline 1-Oxide (Ic).—Sodamide-catalysed condensation of 2,5,5-trimethyl- Δ^1 -pyrroline 1-oxide (5 g) with 5,5-dimethyl- Δ^1 -pyrroline 1-oxide (5 g) in the manner previously described,³ gave the product (Ic), which was recrystallised from ether–light petroleum (yield 5.6 g, 59%); m.p. 107° (Found: C, 64.8; H, 10.1; N, 11.8. $\text{C}_{13}\text{H}_{24}\text{N}_2\text{O}_2$ requires C, 65.0; H, 10.1; N, 11.7%).

Oxidation of the Nitron-hydroxylamine (Ic).—(a) *Copper-catalysed oxidation.* The hydroxylamine (Ic) (0.5 g) in water (30 ml) containing copper acetate (20 mg) and aqueous ammonia (35%; 1 ml) was aerated until an intense blue colour was restored (15 min.). Extraction with chloroform yielded colourless rosettes (0.4 g) of 1,1,2,2-tetrakis-(5,5-dimethyl- Δ^1 -pyrrolin-2-yl)ethane tetra-N-oxide (IIIc), m.p. 173° (decomp.) (from benzene–light petroleum), ν_{max} (Nujol) 1 580 cm^{-1} , λ_{max} (EtOH) 245 nm (ϵ 10 270), τ (CDCl_3) 8.66 (12 H, s), 8.0 (t) and 7.12 (t) (8 H), and 5.13 (1 H, s) [Found: C, 65.7; H, 9.2; N, 11.7%; M (cryoscopic), 475. $\text{C}_{28}\text{H}_{42}\text{N}_4\text{O}_4$ requires C, 65.8; H, 8.9; N, 11.8%; M , 475]. Under more vigorous conditions (passage of air through a solution at 70 °C for 2 h), further oxidation occurred yielding 1,1,2,2-tetrakis-(5,5-dimethyl- Δ^1 -pyrrolin-2-yl)ethylene tetra-N-oxide (IVc) (60%), m.p. 226° (decomp.), ν_{max} 1 540 cm^{-1} , λ_{max} (EtOH) 383 (ϵ 11 330) and 252 nm (ϵ 13 640), τ (CHCl_3) 8.64 (3 H, s), 7.96 (1 H, t), and 7.31 (1 H, t) (Found: C, 65.7; H, 8.8; N, 11.6. $\text{C}_{26}\text{H}_{40}\text{N}_4\text{O}_4$ requires C, 66.0; H, 8.5; N, 11.8%).

(b) *Oxidation with mercury(II) oxide.* The hydroxylamine (0.5 g) in dry carbon tetrachloride (20 ml) was treated with mercury(II) oxide (1.0 g, 2.2 mol. equiv. After the appearance of metallic mercury, the solution was filtered and worked up in the usual manner to yield (IIIc), (0.42 g, 84%), identical with the product of oxidation (a).

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⁷ J. Thesing and W. Sirrenberg, *Chem. Ber.*, 1959, **92**, 1748.

⁸ A. R. Forrester, J. M. Hay, and R. H. Thomson, 'Organic Chemistry of Stable Free Radicals,' Academic Press, London, 1968, p. 180.