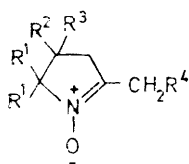


Experiments towards the Synthesis of Corrins. Part XIII.¹ A New Synthesis of 2-Cyano- Δ^1 -pyrroline 1-Oxides and their Behaviour towards a Grignard Reagent

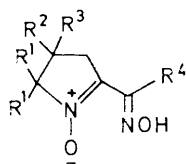
By David St.C. Black,*† V. Malcolm Clark, R. S. Thakur, and Lord Todd, University Chemical Laboratory, Cambridge CB2 1EW

2-Alkyl- Δ^1 -pyrroline 1-oxides are readily nitrosated by isopentyl nitrite, giving the oximes of the corresponding pyrroline-2-carbonyl compounds. The pyrroline-2-carbaldehyde oximes can be dehydrated to 2-cyano-derivatives by treatment with thionyl chloride in pyridine. Attack of methylmagnesium iodide on the sterically hindered 2-cyano-3,3,5,5-tetramethyl- Δ^1 -pyrroline 1-oxide occurred at the cyano-group, to yield the corresponding 2-acetyl compound. In less hindered analogues preferential attack on the nitron carbon atom was observed; the cyano-hydroxylamine derivatives so formed can undergo elimination of MgICN, yielding the parent Δ^1 -pyrroline 1-oxide.

2-CYANO- Δ^1 -PYRROLINE 1-OXIDES can readily be prepared² by a two-step process from Δ^1 -pyrroline 1-oxides.

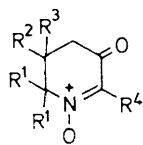


(I a-f)

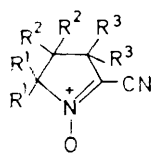


(II a-f)

- a ; R¹ = R⁴ = H, R² = R³ = Me
 b ; R¹ = Me, R² = R³ = R⁴ = H
 c ; R¹ = R² = Me, R³ = R⁴ = H
 d ; R¹ = H, R² = R³ = R⁴ = Me
 e ; R¹ = R⁴ = Me, R² = R³ = H
 f ; R¹ = R² = R⁴ = Me, R³ = H



(III a and e)



(IV a-c)

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

Addition of aqueous hydrogen cyanide to pyrroline 1-oxides with a hydrogen atom at position 2 results in 2-cyano-1-hydroxypyrrolidines, analogous to cyanohydrins. These cyano-hydroxylamines undergo copper-catalysed aerial oxidation to form the 2-cyano-nitrones. We now describe a synthetic pathway from 2-methyl- Δ^1 -pyrroline 1-oxides to the corresponding 2-cyano- Δ^1 -pyrroline 1-oxides *via* the 2-hydroxyiminomethyl derivatives.

Oxidation of 2-alkyl- Δ^1 -pyrroline 1-oxides with selenium dioxide yields 2-acyl compounds,³ which are highly

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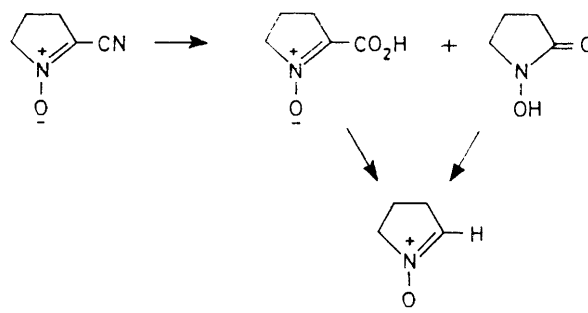
¹ Part XII, D. St.C. Black, V. M. Clark, B. G. Odell, and Lord Todd, preceding paper.

² R. Bonnett, R. F. C. Brown, V. M. Clark, I. O. Sutherland, and Sir Alexander Todd, *J. Chem. Soc.*, 1959, 2094.

sensitive to acids and undergo hydrolytic transformations into the related tetrahydropyridones. The formation of oximes by the reaction of these acyl-nitrones with hydroxylamine has been affected,⁴ although C-nitrosation can be more readily carried out in high yield by the reaction of alkyl- Δ^1 -pyrroline 1-oxides (Ia-f) with isopentyl nitrite in the presence of sodium methoxide. The resulting oximes (IIa-f) are highly crystalline, colourless compounds which absorb in the region 279–293 nm in the u.v. and at *ca.* 1555 cm⁻¹ in the i.r., consistent with the conjugated hydroxyimino-structure (II). On mild acidic hydrolysis, the oximes (IIa and e) afforded the corresponding tetrahydropyridone 1-oxides (IIIa and e), respectively, presumably *via* the exocyclic carbonyl compounds.

The oximes (IIa and b) were dehydrated to the nitriles (IVa and b) respectively, with thionyl chloride in pyridine. The nitrile (IVb) has already been described,² and the spectroscopic properties of (IVa) are similar (ν_{\max} . 2225 and 1553 cm⁻¹, τ_{\max} . 271 nm).

Earlier work² has dealt with the alkaline hydrolysis of 2-cyano- Δ^1 -pyrroline 1-oxides to yield mixtures of the corresponding carboxylic and hydroxamic acids. Each of these products can be converted into the related nitron, by decarboxylation² and reduction,⁵ respectively.



SCHEME 1

Thus, an overall demethylation of a 2-methyl- Δ^1 -pyrroline 1-oxide can be effected as indicated in Scheme 1.

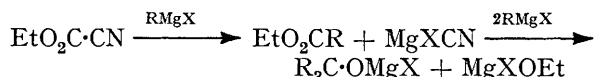
Grignard Reactions of 2-Cyano- Δ^1 -pyrroline 1-Oxides.—In view of the fact that Grignard reagents add² to nitrones

³ R. F. C. Brown, V. M. Clark, and Sir Alexander Todd, *J. Chem. Soc.*, 1959, 2105.

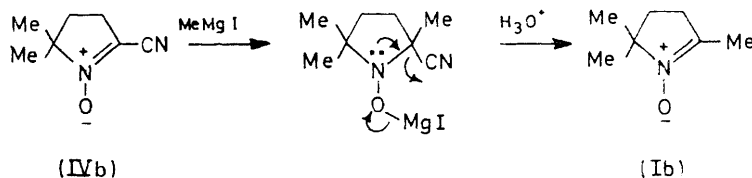
⁴ W. D. S. Bowering, V. M. Clark, R. S. Thakur, and Lord Todd, *Annalen*, 1963, 669, 106.

⁵ H. O. House and R. W. Magin, *J. Org. Chem.*, 1963, 28, 647.

in a manner analogous to that observed with carbonyl compounds, the 2-cyano-nitrone present an interesting comparative study. Grignard reagents react⁶ readily with nitriles to produce substituted imines, which are usually hydrolysed to the ketones. Thus, reaction with 2-cyano-nitrone could lead to mixed products, as there are two positions susceptible to nucleophilic attack. Reaction with the cyano-group would produce an acyl-nitrone, whereas reaction at the nitrone carbon atom would lead to reduction or cyanide displacement. In general, nitriles are less reactive towards Grignard reagents than the corresponding aldehydes or ketones. (A noteworthy exception is 2-cyanocyclopentanone; in this case phenyl-⁸ and ethyl-magnesium bromide⁹ preferentially attack the cyano-group.) The analogous carbonyl system, *i.e.* that found in acyl cyanides, has received little attention, but Grignard reagents displace¹⁰ the cyano-group of benzoyl cyanide to yield a ketone which can react further to give the tertiary alcohol. Again ethyl cyanofornate undergoes¹¹ a similar cyanide displacement process:

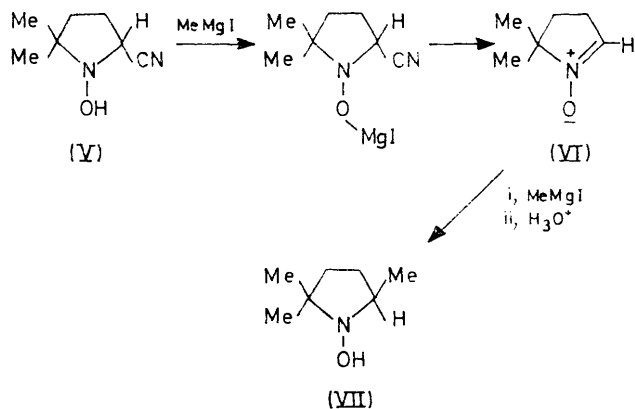


Related to this behaviour is the displacement of cyanide from benzoyl cyanide by a nitroalkane anion¹² and by hydride ion.¹³



SCHEME 2

It is known² that the carbon atom of a nitrone is less electrophilic than that of a carbonyl compound, so that



SCHEME 3

any selection between attack at the nitrone or the nitrile

⁶ M. S. Kharasch and O. Reinmuth, 'Grignard Reactions of Non-metallic Substances,' New York, 1954, p. 767.

⁷ C. E. Entemann and J. R. Johnson, *J. Amer. Chem. Soc.*, 1933, **55**, 2900.

centre would almost certainly be finely balanced. In the present study, this is indeed shown to be the case. In the first example, 2-cyano-5,5-dimethyl- Δ^1 -pyrroline 1-oxide (IVb), nucleophilic attack occurred on the nitrone rather than the nitrile group. By use of 2 mol. equiv. of methylmagnesium iodide, 2,5,5-trimethyl- Δ^1 -pyrroline 1-oxide (Ib) was formed in high yield. This result is most readily explained on the assumption that the cyanohydroxylamine derivative formed by addition of the Grignard reagent readily eliminates MgICN. In view of the potential value of such an elimination, the reaction of methylmagnesium iodide with the cyanohydroxylamine (V) was investigated. One mol. equiv. of reagent was sufficient to effect elimination of MgICN to give the nitrone (VI); an excess of reagent led to the trimethyl hydroxylamine (VII).

The cyano-hydroxylamine (V) is analogous to an α -amino-nitrile or an extended cyanohydrin. The nitrile group of cyanohydrins is usually displaced¹⁴ by a Grignard reagent, and similar behaviour can occur¹⁵ with α -amino-nitriles. However, Grignard reagents sometimes¹⁶ attack the nitrile group of α -amino-nitriles to form ketones.

The formation of (VI) by this route offers an alternative to the hypobromite oxidation¹⁷ of hydroxyamino-acids, but its usefulness is limited to the immediate formation of nitrones bearing an α -hydrogen atom. Cyanide ion could not be added¹⁸ to an $\alpha\alpha$ -disubstituted nitrone, and the

addition of a Grignard reagent to a cyano-nitrone is precluded by the above elimination.

It seems from the Grignard reactions discussed above that the nitrone group is more susceptible to nucleophilic attack than the cyano-group, although attack on the nitrone is probably not exclusive. It seemed probable that this situation might be reversed by suitable

⁸ R. D. Campbell and W. L. Harmer, *J. Org. Chem.*, 1963, **28**, 379.

⁹ O. Riobé, M. Lamant, and F. Bussière, *Bull. Soc. chim. France*, 1963, 2892; M. Lamant, O. Riobé, and F. Bussière, *ibid.*, p. 2895.

¹⁰ R. Adams, H. B. Bramlet, and F. H. Tendick, *J. Amer. Chem. Soc.*, 1920, **42**, 2369.

¹¹ A. McKenzie and G. K. Duff, *Ber.*, 1927, **60**, 1335.

¹² G. B. Bachman and T. Hokama, *J. Amer. Chem. Soc.*, 1959, **81**, 4882.

¹³ A. Dornow and H. Theidel, *Chem. Ber.*, 1955, **88**, 1267.

¹⁴ T. S. Stevens, J. M. Cowan, and J. MacKinnon, *J. Chem. Soc.*, 1931, 2568; T. Thomson and T. S. Stevens, *ibid.*, 1932, 2607.

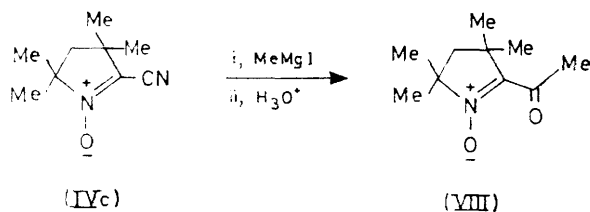
¹⁵ H. M. Taylor and C. R. Hauser, *J. Amer. Chem. Soc.*, 1960, **82**, 1960.

¹⁶ L. H. Goodson and H. Christopher, *J. Amer. Chem. Soc.*, 1950, **72**, 358; Z. Welvert, *Compt. rend.*, 1960, **250**, 1870.

¹⁷ Part XIV, G. W. Alderson, D. St.C. Black, V. M. Clark, and Lord Todd, following paper.

¹⁸ G. V. Baddeley, personal communication.

substitution of the cyano-compound used. This proved to be so; the hindered cyano-nitrone (IVc), prepared by adding cyanide ion to 3,3,5,5-tetramethyl- Δ^1 -pyrroline 1-oxide, reacted with 2 mol. equiv. of methylmagnesium iodide to give a 90% yield of the 2-acyl-nitrone (VIII), ν_{\max} . 1 665 and 1 520 cm^{-1} , λ_{\max} . 289 nm (ϵ 10 000),



SCHEME 4

characterised as its oxime. In this instance, the action of a Grignard reagent on the cyano-nitrone provides a good route to the 2-acyl-nitrone.

EXPERIMENTAL

General information is the same as for Part XI.

The 2-alkyl- Δ^1 -pyrroline 1-oxides (Ia, b, and e) were prepared as previously described.²

2-Ethyl-4,4-dimethyl- Δ^1 -pyrroline 1-Oxide (Id).—A mixture of 5-methylhex-4-en-3-one¹⁹ (35.0 g, 1 mol), nitromethane (200 g, 10 mol), diethylamine (24.0 g, 1 mol), and hydroquinone (1 g) was heated under reflux in the dark for 48 h. Fractional distillation afforded 5,5-dimethyl-6-nitrohexan-3-one (15 g, 30%), b.p. 118—122° at 14 mmHg, ν_{\max} (liquid) 1 715 and 1 550 cm^{-1} . The 2,4-dinitrophenylhydrazones formed needles, m.p. 100° (from ethanol), λ_{\max} . 359 (ϵ 22 060) and 226 nm (16 420) (Found: C, 47.9; H, 5.6. $\text{C}_{14}\text{H}_{19}\text{N}_5\text{O}_6$ requires C, 47.6; H, 5.4%).

The nitroketone (14.8 g) and ammonium chloride (3.7 g) in water (100 ml) cooled in ice were stirred vigorously while zinc dust (18.5 g) was added during 1 h. Stirring was continued for a further 2 h. An oil, isolated in the usual way,² was distilled to yield the product (Id) (7.2 g, 60%), b.p. 72—74° at 0.1 mmHg, λ_{\max} . 231 nm (ϵ 7 940), ν_{\max} (film) 1 603 and 1 525 cm^{-1} . The *picrate* formed needles, m.p. 100° (from ethanol) (Found: C, 45.8; H, 5.2. $\text{C}_{14}\text{H}_{18}\text{N}_4\text{O}_8$ requires C, 45.5; H, 4.9%).

2,4,5,5-Tetramethyl- Δ^1 -pyrroline 1-Oxide (Ic).—Addition of methylmagnesium iodide to 4,5,5-trimethyl- Δ^1 -pyrroline 1-oxide yielded 1-hydroxy-2,2,3,5-tetramethylpyrrolidine (79%), b.p. 56° at 4 mmHg (Found: C, 67.0; H, 12.0; N, 10.1. $\text{C}_8\text{H}_{17}\text{NO}$ requires C, 67.1; H, 12.0; N, 9.8%).

Oxidation of the hydroxylamine with alkaline potassium hexacyanoferrate(III) yielded the Δ^1 -pyrroline 1-oxide (Ic)²⁰ (66%), b.p. 82° at 1 mmHg, ν_{\max} (film) 1 605 cm^{-1} . The *picrate* formed needles, m.p. 131—132° (from methanol) (Found: C, 45.5; H, 4.9; N, 15.4. $\text{C}_{14}\text{H}_{18}\text{N}_4\text{O}_8$ requires C, 45.4; H, 4.9; N, 15.1%).

2-Ethyl-4,5,5-trimethyl- Δ^1 -pyrroline 1-Oxide (If).—Addition of ethylmagnesium bromide to 4,5,5-trimethyl- Δ^1 -pyrroline 1-oxide yielded 5-ethyl-1-hydroxy-2,3,3-trimethylpyrrolidine (80%), b.p. 74° at 3 mmHg, oxidation of which with alkaline potassium hexacyanoferrate(III) yielded the

Δ^1 -pyrroline 1-oxide (If), b.p. 86° at 1 mmHg, ν_{\max} (liquid) 1 590 cm^{-1} . The *picrate* had m.p. 86.5—87.5° (from ethanol) (Found: C, 47.1; H, 5.3; N, 14.5. $\text{C}_{15}\text{H}_{20}\text{N}_4\text{O}_8$ requires C, 46.9; H, 5.3; N, 14.6%).

Nitrosation of 2-Alkyl- Δ^1 -pyrroline 1-Oxides.—2-Hydroxyiminomethyl-4,4-dimethyl- Δ^1 -pyrroline 1-oxide (IIa). 2,4,4-Trimethyl- Δ^1 -pyrroline 1-oxide (1.3 g) and isopentyl nitrate (2.0 g) were separately and concomitantly added to a stirred, cooled (0—5 °C) suspension of dry sodium methoxide (0.6 g) in anhydrous ether (50 ml). The mixture was stirred for a further 2 h. Unchanged isopentyl nitrite and solvent were removed under reduced pressure, leaving a solid residue which was dissolved in water (25 ml) and neutralised with hydrochloric acid. A colourless solid separated and further product was obtained by extraction with ether. Recrystallisation of the combined material from methanol afforded the *oxime* (IIa) (1.45 g, 90%), m.p. 209—210°, λ_{\max} (MeOH) 292 nm (ϵ 11 620), ν_{\max} (Nujol) 3 100 and 1 588 cm^{-1} (Found: C, 53.7; H, 7.5; N, 17.8. $\text{C}_7\text{H}_{12}\text{N}_2\text{O}_2$ requires C, 53.8; H, 7.7; N, 17.9%). The remaining oximes were prepared in the same manner.

2-Hydroxyiminomethyl-5,5-dimethyl- Δ^1 -pyrroline 1-oxide (IIb) (90%) had m.p. 198—199° (from methanol-benzene-cyclohexane), λ_{\max} . 292 nm (ϵ 12 170), ν_{\max} (Nujol) 3 100 and 1 560 cm^{-1} (Found: C, 53.7; H, 7.9; N, 17.7. $\text{C}_7\text{H}_{12}\text{N}_2\text{O}_2$ requires C, 53.8; H, 7.7; N, 17.9%). 2-Hydroxyiminomethyl-4,5,5-trimethyl- Δ^1 -pyrroline 1-oxide (IIc) (65%) had m.p. 192—193° (from methanol-benzene-cyclohexane), λ_{\max} (MeOH) 293 nm (ϵ 12 880), ν_{\max} (Nujol) 3 100 and 1 555 cm^{-1} (Found: C, 56.9; H, 8.3; N, 16.8. $\text{C}_8\text{H}_{14}\text{N}_2\text{O}_2$ requires C, 56.6; H, 8.2; N, 16.5%). 2-(1-Hydroxyiminoethyl)-4,4-dimethyl- Δ^1 -pyrroline 1-oxide (IIId) (75%) had m.p. 180—181° (from methanol-benzene-cyclohexane), λ_{\max} (MeOH) 279 nm (ϵ 12 760), ν_{\max} (Nujol) 3 100 and 1 588 cm^{-1} (Found: C, 56.4; H, 8.0. $\text{C}_8\text{H}_{14}\text{N}_2\text{O}_2$ requires C, 56.5; H, 8.2%). 2-(1-Hydroxyiminoethyl)-5,5-dimethyl- Δ^1 -pyrroline 1-oxide (IIe)⁴ (80%) had m.p. 190—191° (from methanol-benzene-cyclohexane), λ_{\max} (MeOH) 279 nm (ν 13 600), ν_{\max} (Nujol) 3 140 and 1 557 cm^{-1} (Found: C, 56.2; H, 8.5; N, 16.8. Calc. for $\text{C}_8\text{H}_{14}\text{N}_2\text{O}_2$: C, 56.6; H, 8.3; N, 16.5%). 2-(1-Hydroxyiminoethyl)-4,5,5-trimethyl- Δ^1 -pyrroline 1-oxide (IIIf) (90%) had m.p. 170° (from methanol), λ_{\max} (MeOH) 279 nm (ϵ 14 000), ν_{\max} . 3 100 and 1 556 cm^{-1} (Found: C, 58.8; H, 9.0; N, 15.3. $\text{C}_9\text{H}_{16}\text{N}_2\text{O}_2$ requires C, 58.7; H, 8.7; N, 15.2%).

Hydrolyses of Hydroxyimino- Δ^1 -pyrroline 1-Oxides.—2-Hydroxyiminomethyl-4,4-dimethyl- Δ^1 -pyrroline 1-oxide (IIa). Compound (IIa) was refluxed for 2 h with 10% sulphuric acid. Extraction with ether yielded 5,6-dihydro-5,5-dimethylpyridin-3(4H)-one 1-oxide (IIIa), m.p. 75°, identical with an authentic sample.³

2-(1-Hydroxyiminoethyl)-5,5-dimethyl- Δ^1 -pyrroline 1-oxide (IIe). Similar treatment of (IIe) yielded 5,6-dihydro-2,6,6-trimethylpyridin-3(4H)-one 1-oxide (IIIe), m.p. 102—103° (from methanol-cyclohexane-benzene), λ_{\max} (cyclohexane) 288 nm (ϵ 17 850); ν_{\max} (Nujol) 1 662, 1 517, 1 351, 1 321, and 1 225 cm^{-1} (Found: C, 61.8; H, 8.7; N, 9.2. $\text{C}_8\text{H}_{13}\text{NO}_2$ requires C, 61.9; H, 8.5; N, 9.0%), identical with that obtained by treating 2-acetyl-5,5-dimethyl- Δ^1 -pyrroline 1-oxide⁴ with cold dilute hydrochloric acid.

Dehydration of Hydroxyimino- Δ^1 -pyrroline 1-Oxides.—2-Hydroxyiminomethyl-4,4-dimethyl- Δ^1 -pyrroline 1-oxide

¹⁹ J. Colonge and M. Reymermier, *Bull. Soc. chim. France*, 1956, 188.

²⁰ E. Lunt, 'International Symposium on Nitro Compounds,' Warsaw, 1963, *Tetrahedron*, 1964, 20 (Suppl. 1), 291; J. B. Bapat and D. St. C. Black, *Austral. J. Chem.*, 1968, 21, 2483.

(IIa) (1.4 g, 0.09 mol) was stirred in dry pyridine (40 ml) below 0 °C, and freshly distilled thionyl chloride (3.5 g, 0.25 mol) was added slowly. The solution became yellow, then orange, and finally dark green. After complete addition of thionyl chloride (1 h), stirring was continued for a further 2 h, and the mixture was then kept at room temperature for 8 h. The mixture was evaporated under reduced pressure and the residue dissolved in water (20 ml) and extracted continuously (48 h) with ether. The extract yielded a solid which, on recrystallisation from benzene, gave 2-cyano-4,4-dimethyl- Δ^1 -pyrroline 1-oxide (IVa) (0.7 g, 50%), m.p. 79–80°, λ_{\max} (MeOH) 271 nm (ϵ 10 485), ν_{\max} 2 225 and 1 553 cm^{-1} (Found: C, 60.9; H, 7.3; N, 20.0. $\text{C}_7\text{H}_{10}\text{N}_2\text{O}$ requires C, 60.9; H, 7.3; N, 20.3%).

2-Cyano-5,5-dimethyl- Δ^1 -pyrroline 1-oxide (IVb) was prepared in a similar manner from 2-hydroxyiminomethyl-5,5-dimethyl- Δ^1 -pyrroline 1-oxide (IIb). The product (45%) had b.p. 110° at 0.5 mmHg. The i.r. spectrum was identical with that of an authentic sample.²

Reaction of 2-Cyano-5,5-dimethyl- Δ^1 -pyrroline 1-Oxide (IVb) with Methylmagnesium Iodide.—A solution of the cyano-nitrone ² (2.6 g) in ether was added to ethereal methylmagnesium iodide [from magnesium (0.9 g) and methyl iodide (5.5 g, 2 mol. equiv.)]. A yellow precipitate formed. The mixture was heated under reflux for 2 h and the magnesium complex was then decomposed by adding aqueous ammonium chloride. The dried ethereal extract contained a trace of an *N*-hydroxypyrrolidine. Extraction of the aqueous solution with chloroform produced an oil which, after chromatography on alumina, yielded 2,5,5-trimethyl- Δ^1 -pyrroline 1-oxide (Ib) (2.0 g, 83%). The i.r. spectrum was identical with that of an authentic sample.² The picrate had m.p. and mixed m.p. 101° (from ethanol).

Reaction of 5-Cyano-1-hydroxy-2,2-dimethylpyrrolidine (V) with Methylmagnesium Iodide. (a) A solution of the cyano-hydroxylamine ² (1.4 g) in ether (50 ml) was added to methylmagnesium iodide [from magnesium (0.25 g) and methyl iodide (1.5 g, 1 mol. equiv.)]. The solution became turbid and was stirred and heated under reflux for 2 h. Dilute ammonium chloride solution was added and the ethereal extract dried and concentrated to give 5,5-dimethyl- Δ^1 -pyrroline 1-oxide (VI) (1.0 g, 90%) as an oil. The i.r. spectrum was identical with that of an authentic sample.² The picrate had m.p. and mixed m.p. 81° (from ethanol).

(b) In a similar reaction with 2 mol. equiv. of methylmagnesium iodide, 1-hydroxy-2,2,5-trimethylpyrrolidine

(VII) was formed. This was oxidised to the nitrone (Ib), characterised as its picrate, m.p. and mixed m.p. 101°.²

*2-Cyano-3,3,5,5-tetramethyl- Δ^1 -pyrroline 1-Oxide (IVc).*²¹—2*N*-Hydrochloric acid (32 ml) was added during 2 h to a stirred solution of 3,3,5,5-tetramethyl- Δ^1 -pyrroline 1-oxide (8.8 g) and potassium cyanide (5.0 g) in water (40 ml) at 0 °C. A white solid was precipitated. After a further 2 h, the mixture was brought to pH 11 with 10% sodium hydroxide and continuously extracted with ether for 2 days. The extract was dried and concentrated to yield 5-cyano-1-hydroxy-2,2,4,4-tetramethylpyrrolidine as an oil (9.0 g). This was dissolved in 60:40 water-ethanol (100 ml) and treated with copper acetate (1.5 h) and ammonia (5 ml). Air was passed through the decolourised solution until a permanent blue colour was restored (3 h). The aqueous solution was extracted with chloroform (3 \times 100 ml), dried, and concentrated to yield the nitrone (IVc) (2.6 g, 25%), m.p. 106° (from ethyl acetate-light petroleum), λ_{\max} 271 nm (ϵ 10 200), ν_{\max} (Nujol) 2 220 and 1 549 cm^{-1} (Found: C, 64.8; H, 8.3; N, 16.5. $\text{C}_9\text{H}_{14}\text{N}_2\text{O}$ requires C, 65.0; H, 8.5; N, 16.9%).

Reaction of 2-Cyano-3,3,5,5-tetramethyl- Δ^1 -pyrroline 1-Oxide (IVc) with Methylmagnesium Iodide.—A solution of the cyano-nitrone (0.2 g) in ether was added to methylmagnesium iodide [from magnesium (0.05 g) and methyl iodide (0.35 g, 2 mol. equiv.)] in ether. A yellow precipitate was formed immediately. After heating under reflux for 1 h, dilute aqueous ammonium chloride was added and the ethereal extract was dried and concentrated to yield 2-acetyl-3,3,5,5-tetramethyl- Δ^1 -pyrroline 1-oxide (VIII) (0.15 g, 68%) as a pale yellow oil, λ_{\max} 289 nm (ϵ 10 000), ν_{\max} (liquid) 1 665 and 1 520 cm^{-1} . More product (0.05 g, 22%) was extracted with chloroform. The ketone gave a positive nitroprusside test. The oxime crystallised from ethanol; m.p. 148°, λ_{\max} 275 nm, ν_{\max} 3 100 and 1 560 cm^{-1} (Found: C, 61.0; H, 9.0. $\text{C}_{10}\text{H}_{18}\text{N}_2\text{O}_2$ requires C, 60.6; H, 9.1%).

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[6/379 Received, 23rd February, 1976]

²¹ Independently prepared by R. F. C. Brown (personal communication).