Experiments towards the Synthesis of Corrins. Part XIV.[1] Oxidative Decarboxylation of 1-Hydroxypyrrolidine-2-carboxylic Acids and Oxidation of Some Δ^1-Pyrroline 1-Oxides by Hypobromite

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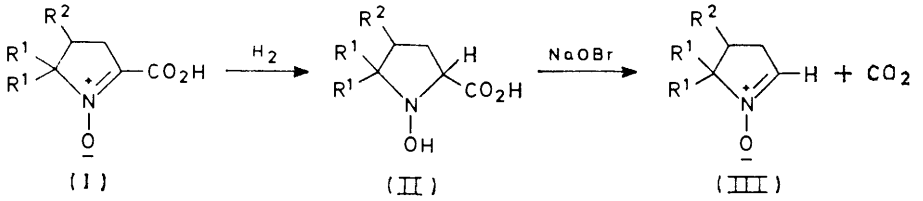
The action of sodium hypobromite on 1-hydroxypyrrolidine-2-carboxylic acids results in rapid evolution of carbon dioxide and formation of Δ^1-pyrroline 1-oxides. Oxidations of Δ^1-pyrrolinecarboxylic acid 1-oxides and a 2-methylpyrroline 1-oxide have also been studied.

A CONSIDERABLE amount of work has shown that oxidative decarboxylation of α-amino-acids gives products at the imine or equivalent level of oxidation. In view of the fact [2-4] that oxidative decarboxylation of proline yielded Δ^1-pyrroline, the effects of an oxidising agent on some 1-hydroxypyrrolidine-2-carboxylic acids were studied.

The pyrroline-2-carboxylic acid 1-oxides (Ia and b) were prepared by the methods of Bonnett *et al.*[5] and converted into the required hydroxyamino-acids (IIa and b) by hydrogenation. Because of its speed and the ease of isolation of the product, hydrogenation over platinum oxide at room temperature and atmospheric pressure was preferred to those methods of reduction previously described [5] for nitrones.

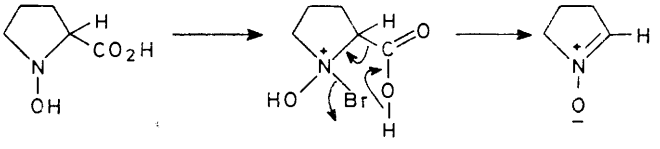
Sodium hypobromite was chosen as the oxidising agent for this study. When 1 equiv. of sodium hypobromite was added to an aqueous solution of either of the hydroxyamino-acids (II), immediate effervescence occurred and the hypobromite solution was decolourised. The reactions were worked up after a few minutes and the corresponding nitrones (III) were isolated and identified by comparison of their i.r. and u.v. spectra, and of their picrates, with those of authentic samples.[5] This oxidative decarboxylation was essentially quantitative and instantaneous. The reaction can be rationalised in terms of the sequence shown in Scheme 2, which is based on mechanistic arguments advanced [6-8] in the case of amino-acid oxidation.

There was never any indication of elimination of the 2-proton: such a process would re-form the initial nitrone acid (I). It was also found that the 2-methyl hydroxyamino-acid (V) [prepared by hydrogenation of the nitrone carboxylic acid (IV) [5]] underwent similar oxidative decarboxylation on treatment with sodium hypobromite to give the 2-methyl nitrone (VI) in 90% yield, identical with an authentic sample prepared by the route shown in Scheme 3. This oxidative decarboxylation procedure therefore provides a route to nitrones with either a hydrogen atom or an alkyl group in the



a; R^1 = Me, R^2 = H
b; R^1 = R^2 = Me

SCHEME 1



SCHEME 2

α-position. The nitrone 5-carboxylic acid (IV) affords a nitrone with the double bond in the position adjacent to that which it occupied prior to reduction. Conjugated bis-nitrones [*e.g.* (VIII)] can be prepared by sodamide-catalysed dimerisation followed by oxidation.[9-11] It was

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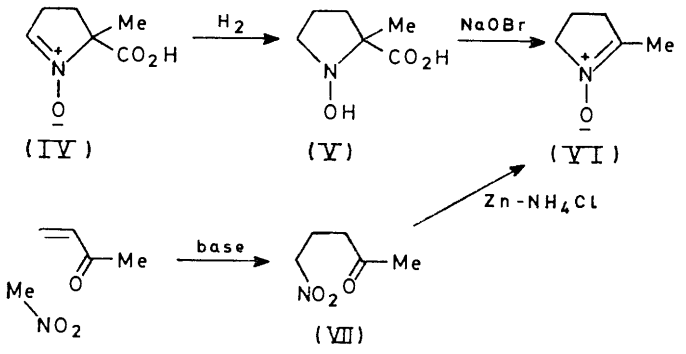
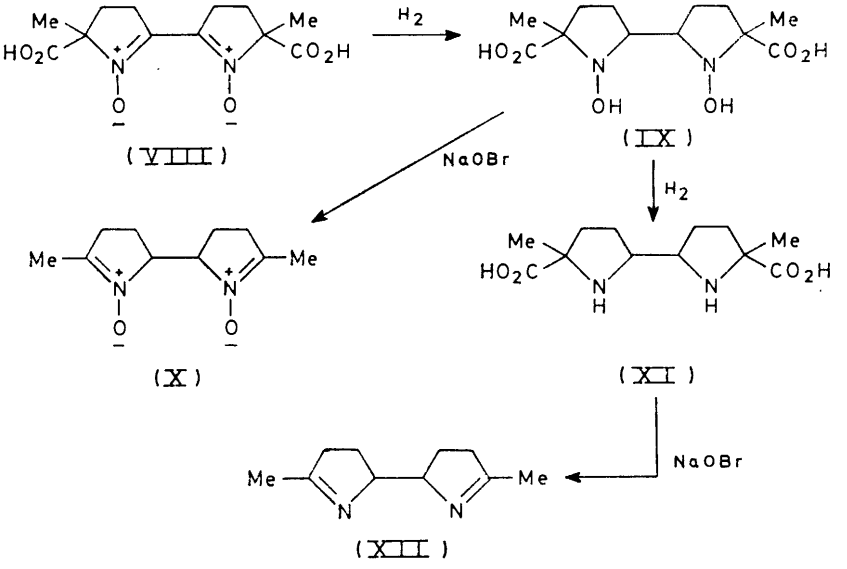
[1] Part XIII, D. St.C. Black, V. M. Clark, R. S. Thakur, and Lord Todd, preceding paper.
[2] K. Lang, *Z. physiol. Chem.*, 1936, **241**, 68.
[3] P. D. Bragg and L. Hough, *J. Chem. Soc.*, 1958, 4050.
[4] L. Skursky, *Z. Naturforsch.*, 1959, **14b**, 473.
[5] R. Bonnett, R. F. C. Brown, V. M. Clark, I. O. Sutherland, and Sir Alexander Todd, *J. Chem. Soc.*, 1959, 2094.
[6] E. E. van Tamelen, V. B. Haarstad, and R. L. Orvis, *Tetrahedron*, 1968, **24**, 687.
[7] R. M. Herbst and H. T. Clarke, *J. Biol. Chem.*, 1934, **104**, 769.
[8] C. C. Sweeley and E. C. Horning, *J. Amer. Chem. Soc.*, 1957, **79**, 2620.
[9] R. F. C. Brown, V. M. Clark, M. Lamchen, and Sir Alexander Todd, *J. Chem. Soc.*, 1959, 2116.
[10] B. Sklarz, Ph.D. Thesis, Cambridge, 1959.
[11] R. F. C. Brown, V. M. Clark, and Lord Todd, *J. Chem. Soc.*, 1965, 2337.

considered that the oxidation with hypobromite could allow their conversion into unconjugated bis-nitrones



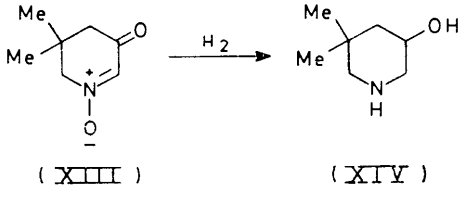
SCHEME 3

[*e.g.* (X)], which might then be used as reactive intermediates in the synthesis of extended pyrroline systems.



SCHEME 4

The bis-nitrone (VIII), prepared by a previously developed method,[10] was converted by hydrogenation



SCHEME 5

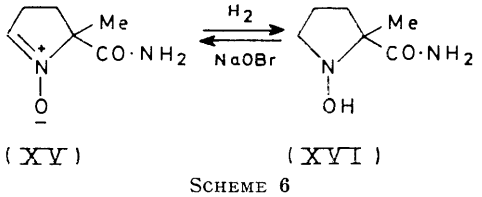
into a mixture of the corresponding bis-hydroxylamine (IX) and bipyrrolidinyl (XI). Compound (IX) could not be obtained by controlled hydrogenation as it rapidly absorbed more hydrogen to give (XI). A parallel for this hydrogenolysis of the N–O bond of a cyclic nitrone is provided by the report [12] that in the hydrogenation of the six-membered cyclic nitrone (XIII) over platinum oxide 3 mol. equiv. of hydrogen were taken up to yield the hydroxypiperidine (XIV). In this instance, uptake of the third mol. equiv. was slow, whereas in the case of the dimer (IX) overall hydrogen uptake was uniformly very rapid.

The presence of the bipyrrolidinyl (XI) was also confirmed by the oxidation results, which showed the formation of the bis-pyrroline (XII), characterised as its picrate. A second product was obtained only as an oil with an i.r. spectrum characteristic of 2-substituted nitrones ($\nu_{max.}$ 1 625 cm^{-1}) and u.v. absorption compatible with an unconjugated nitrone [$\lambda_{max.}$ 230 nm (ε 7 000)]. This evidence is consistent with the structure of the unconjugated bis-nitrone (X).

The decarboxylation of the bipyrrolidinyl (XI) to yield the bis-pyrroline (XII) parallels the conversion of proline into Δ^1-pyrroline, of which examples [2-4] have been mentioned above.

In all these examples decarboxylation is crucial to oxidation, and there is no evidence for proton elimination. However, such proton elimination can be effected by restricting decarboxylation, by the use of a carboxylic acid derivative.

Hydrogenation of the nitrone amide (XV) yielded the hydroxyamino-amide (XVI). Treatment of this with

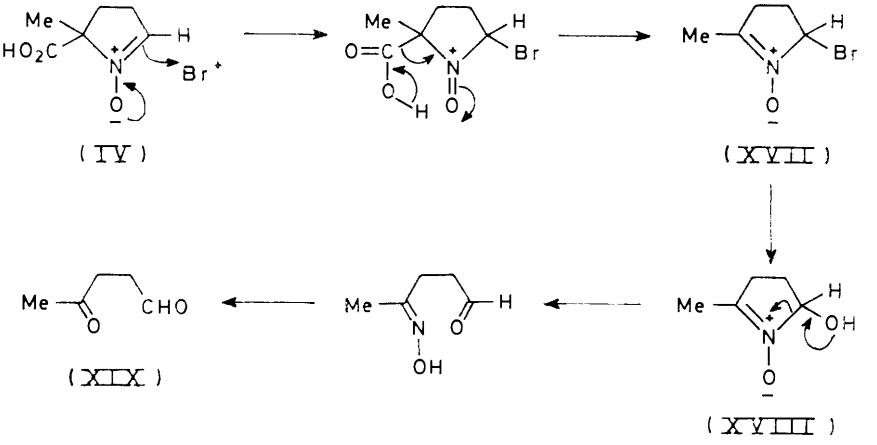


SCHEME 6

1 equiv. of sodium hypobromite at either pH 8 or 11, gave only the nitrone amide (XV).

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

Since sodium hypobromite readily oxidises 1-hydroxypyrrolidine-2-carboxylic acids to Δ^1-pyrroline 1-oxides, it was thought of interest to examine the behaviour of simple Δ^1-pyrroline 1-oxides and Δ^1-pyrroline-2- and -5-carboxylic acid 1-oxides under similar conditions. The results show that the nitrone group is capable of acting as an electron source towards sodium hypobromite, and ring opening is often involved.

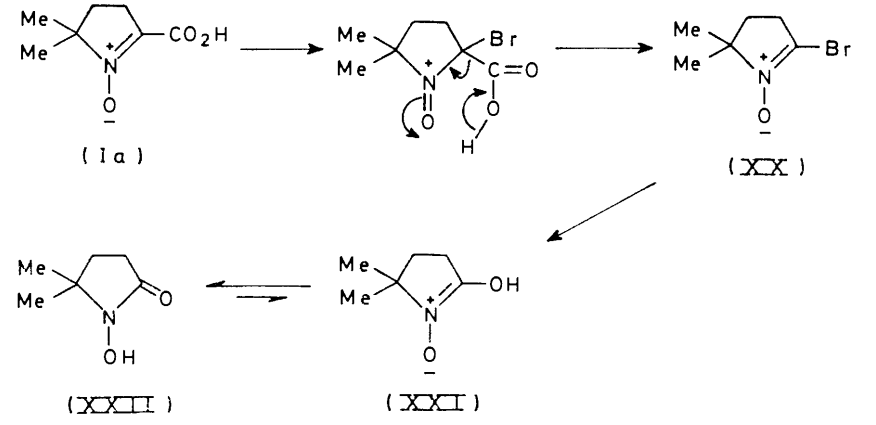


SCHEME 7

When the 5-carboxy-5-methyl nitrone[5] (IV) was treated with the oxidising agent, immediate effervescence occurred and the isolated product, $\nu_{max.}$ 2 720, 1 720, and 1 640 cm^{-1}, was laevulaldehyde (XIX), characterised as its 2,4-dinitrophenylhydrazone. A rational interpretation of the reaction sequence is shown in Scheme 7. Under more strongly alkaline conditions (pH 11) the related amide (XV) was also converted into laevulaldehyde (XIX).

as (XVIII)] are not known, and presumably under the conditions of this reaction prefer to undergo proton transfer and ring cleavage, whereas 2-hydroxy-nitrones are tautomeric with hydroxamic acids and are probably stabilised as a consequence. The stoicheiometry of this oxidation is important, as the hydroxamic acid (XXII) is rapidly oxidised by further hypobromite to the nitroso-acid dimer (XXV) [13] possibly by the pathway shown in Scheme 9. The postulated transformations through the bromo-compound (XXIII) and the hydroxy-compound (XXIV) are similar to those suggested in the oxidation of the nitrone carboxylic acid.

Since Δ^1-pyrroline 1-oxides behave [5] as extended carbonyl compounds, a 2-methyl derivative should behave in similar fashion to a methyl ketone, and undergo oxidation with hypobromite (the halogenoform reaction [14]) to yield a hydroxamic acid. Indeed the 2-methyl



SCHEME 8

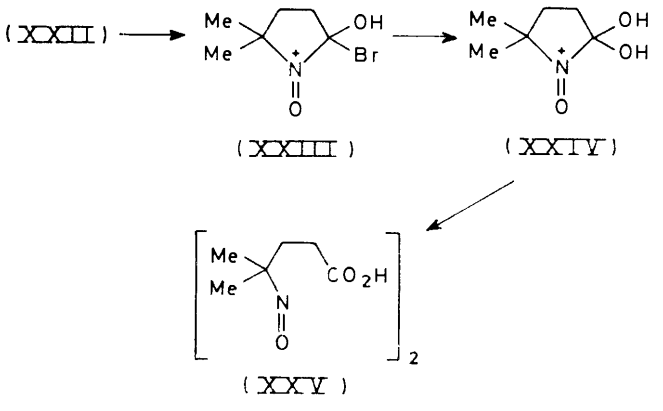
Oxidative decarboxylation of the conjugated nitrone acid [5] (Ia) did not open the pyrroline ring but yielded the cyclic hydroxamic acid (XXII).[5] A similar rationalisation of this process is suggested (Scheme 8).

In each of these Schemes, an initially formed bromonitrone [(XVII) or (XX)] is hydrolysed to a hydroxynitrone [(XVIII) or (XXI)]. 5-Hydroxy-nitrones [such

nitrone [5] (XXVI) gave a positive iodoform test, and on a preparative scale reacted vigorously with sodium hypobromite. When a deficiency of hypobromite was used, a crude sample of the presumed hydroxamic acid (XXVII)

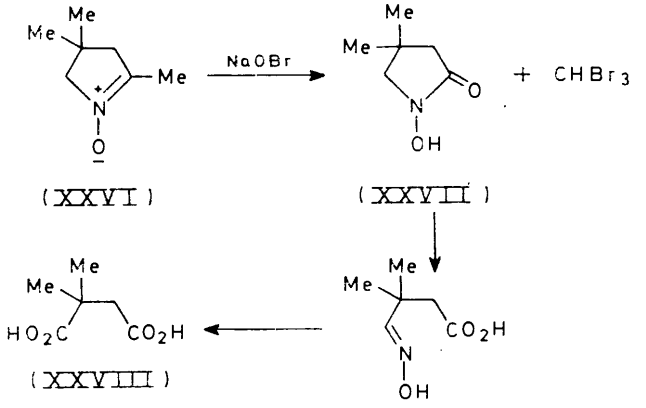
[13] V. M. Clark, B. Sklarz, and Sir Alexander Todd, *J. Chem. Soc.*, 1959, 2123.
[14] R. C. Fuson and B. A. Bull, *Chem. Rev.*, 1934, **15**, 275.

was isolated, but this was so susceptible to further oxidation that the transformation is of little practical value. In general, oxidation proceeded (possibly *via* the



SCHEME 9

sequence shown in Scheme 9) to 2,2-dimethylsuccinic acid (XXVIII), which was isolated in good yield.



SCHEME 10

The behaviour of a nitrone possessing an α-hydrogen atom under hypobromite oxidation conditions was also investigated. 5,5-Dimethyl-Δ^1-pyrroline 1-oxide [5] reacted slowly and after 2 days a low yield of the nitroso-acid dimer (XXV) was obtained. The remainder of the starting material was recovered

It is difficult to draw conclusions about the reaction process in this case. Direct attack on the nitrone linkage, in a manner similar to that already outlined, would lead to a nitro-acid. However, if the reaction proceeded by elimination of a proton, to form the cyclic hydroxamic acid (XXII), this would readily undergo further oxidation to the nitroso-acid dimer (XXV).

Oxidation of nitrones and cyclic hydroxamic acids has been reported by several other groups.[15] Our results for simple nitrones are complementary to these. It is evident, however, that, under controlled conditions, cyclic nitrones can be prepared in good yields by oxidative routes.

[15] N. J. A. Gutteridge and F. J. McGillan, *J. Chem. Soc.* (*C*), 1970, 641 and references cited therein.

EXPERIMENTAL

General information is the same as for Part XI.

1-Hydroxypyrrolidine-2-carboxylic Acids.—(i) *1-Hydroxy-5,5-dimethylpyrrolidine-2-carboxylic acid* (IIa). 5,5-Dimethyl-Δ^1-pyrroline-2-carboxylic acid 1-oxide [5] (0.4 g) in ethanol (15 ml) was hydrogenated at room temperature and atmospheric pressure over platinum oxide (0.1 g) for 15 mm. Filtration through a commercial filter-aid and evaporation at room temperature under reduced pressure left a glass which crystallised when triturated with ether. Recrystallisation from ethanol–cyclohexane yielded the *pyrrolidine* (IIa) (0.32 g, 80%), m.p. 116° (Found: C, 52.6; H, 8.8; N, 9.0%; equiv., 154. $C_7H_{13}NO_3$ requires C, 52.8; H, 8.2; N, 8.8%; equiv., 159). Titration in aqueous ethanol gave an apparent pK_a of 4.9.

(ii) *1-Hydroxy-4,5,5-trimethylpyrrolidine-2-carboxylic acid* (IIb). 4,5,5-Trimethyl-Δ^1-pyrroline-2-carboxylic acid 1-oxide [5] was hydrogenated as described in (i). Recrystallisation of the crude product from methylene chloride–ether yielded the *pyrrolidine* (IIb) (0.42 g, 84%), m.p. 158° (Found: C, 55.6; H, 8.6; N, 7.9%; equiv., 170. $C_8H_{13}NO_3$ requires C, 55.5; H, 8.7; N, 8.1%; equiv., 173). Titration in aqueous solution gave an apparent pK_a of 5.4.

(iii) *1-Hydroxy-2-methylpyrrolidine-2-carboxylic acid* (V). 5-Methyl-Δ^1-pyrroline-5-carboxylic acid 1-oxide [5] (0.4 g) was hydrogenated as described in (i). Recrystallisation of the crude product from ethanol yielded the *pyrrolidine* (V) (0.3 g, 75%), m.p. 177—178° (Found: C, 49.6; H, 7.3; N, 9.3%; equiv., 141. $C_6H_9O_3N$ requires C, 49.6; H, 7.6; N, 9.6%; equiv., 145). Titration in aqueous solution gave an apparent pK_a of 5.8.

Oxidative Decarboxylation of 1-Hydroxypyrrolidine-2-carboxylic Acids.—(i) *1-Hydroxy-5,5-dimethylpyrrolidine-2-carboxylic acid* (IIa). To a solution of the acid (0.25 g) in water (10 ml) was added 1 equiv. of sodium hypobromite (prepared with a 30% excess of sodium hydroxide) in water (3 ml). The addition was followed by immediate effervescence and discharge of the yellow colour of the hypobromite solution. After 5 min at room temperature, the solution was made alkaline (pH 9) with sodium hydroxide solution and extracted continuously with chloroform for 3 h. The solution yielded crude 5,5-dimethyl-Δ^1-pyrroline 1-oxide (IIIa) (0.17 g, 95%) as a hydroscopic oil. The i.r. spectrum $\nu_{max.}$ 1 573 cm^{-1}, was identical with that of an authentic sample.[5] The picrate was crystallised from ethanol–ether; m.p. and mixed m.p. 78—79°.

(ii) *1-Hydroxy-4,5,5-trimethylpyrrolidine-2-carboxylic acid* (IIb). To a solution of the acid (0.17 g) in water (5 ml) was added 1 equiv. of sodium hypobromite solution, as described in (i). The mixture, worked up in the same way, yielded crude 4,5,5-trimethyl-Δ^1-pyrroline 1-oxide (IIIb) (0.12 g, 95%) as a hygroscopic oil. The i.r. spectrum ($\nu_{max.}$ 1 572 cm^{-1}) was identical with that of an authentic sample.[5] The picrate was crystallised from ethanol–ether at −25 °C; m.p. and mixed m.p. 109°.

(iii) *1-Hydroxy-2-methylpyrrolidine-2-carboxylic acid* (V). To a solution of the acid (0.13 g) in water (10 ml) was added 1 equiv. of sodium hypobromite solution, as described in (i). The mixture, worked up in the same way, yielded crude 2-methyl-Δ^1-pyrroline 1-oxide (VI) (0.08 g, 90%) as a straw-coloured, hygroscopic oil. The i.r. spectrum ($\nu_{max.}$

1 615 cm^{-1}) was identical with that of an authentic sample. The picrate was crystallised from ethanol at −30 °C; m.p. and mixed m.p. 71—72°.

2-Methyl-Δ¹-pyrroline 1-Oxide.—(i) To sodium methoxide [from sodium (6 g) in methanol (250 ml); dried by distillation from magnesium methoxide)] was added freshly distilled nitromethane (160 g) in dry ether (100 ml). Freshly distilled methyl vinyl ketone (25 g) in ether (100 ml) was added dropwise over 1 h, and the solution, was heated for 17 h under reflux. The base was neutralised with glacial acetic acid, the methanol was removed under reduced pressure, and the residual oil was distributed between chloroform and water (300 ml of each). The water layer was extracted with chloroform (5 × 200 ml) and the combined chloroform solutions were washed in turn with 5% hydrochloric acid, 10% urea solution, and water (200 ml of each), and dried. Removal of the solvent left an oil which was distilled to give 5-nitropentan-2-one (VII) (30 g, 70%), b.p. 85—95° at 0.1 mmHg, $\nu_{max.}$ 1 713 and 1 555 cm^{-1}.

(ii) To a solution of ammonium chloride (10 g) in 50% aqueous ethanol (150 ml) was added 5-nitropentan-2-one (10 g). The solution was cooled to 5 °C and zinc powder (20 g) was added over 1 h, with vigorous stirring and continued cooling. The mixture was stirred for a further 3 h and filtered, the filter cake being washed with warm ethanol (100 ml). The filtrate and washings were evaporated to a sludge which was dissolved in chloroform. The dried solution yielded 2-methyl-Δ¹-pyrroline 1-oxide (VI) (5 g, 67%), b.p. 66° at 0.1 mmHg, $\nu_{max.}$ 1 615 cm^{-1}. The *picrate* had m.p. 75° (from ethanol) (Found: C, 40.3; H, 3.6; N, 16.8. $C_{11}H_{12}N_4O_8$ requires C, 40.2; H, 3.7; N, 17.1%).

5,5′-Dimethyl-2,2′-bi-Δ¹-pyrrolinyl-5,5′-dicarboxylic Acid 1,1-Dioxide [10] (VIII).—5-Methyl-Δ¹-pyrroline-5-carboxylic acid 1-oxide [5] (6.0 h) was dissolved in liquid ammonia (50 ml). To this was added a solution of sodamide [from sodium (13 g)] in liquid ammonia (500 ml). The mixture was stirred overnight and then allowed to evaporate at room temperature. When almost all the ammonia had evaporated, ammonium chloride (25 g) and water (40 ml) were added and the solution was allowed to come to room temperature. A solution prepared from copper(II) chloride (0.4 g) and aqueous ammonia (*d* 0.58; 5 ml) was added and air was bubbled through the mixture for 2 h. The excess of ammonia was removed and the solution was acidified with a slight excess of 5N-hydrochloric acid and left at 0 °C overnight. The precipitate was filtered off, washed in turn with dilute acid, water, ethanol, and ether and recrystallised from 75% aqueous methanol to yield the *bipyrrolinyl* (VIII) (3.0 g, 50%), m.p. 155° (decomp.), $\nu_{max.}$ 1 725 and 1 510 cm^{-1}, $\lambda_{max.}$ 338 nm (ε 19 500) (Found: C, 50.4; H, 5.6; N, 10.1%; equiv., 148. $C_{12}H_{16}N_2O_6$ requires C, 50.6; H, 5.6; N, 9.9%; equiv., 142). Titration in aqueous methanol gave an apparent pK_a value of 4.0.

Hydrogenation of the Bipyrrolinyldicarboxylic Acid (VIII); *Oxidation of the Product with Hypobromite*.—The dicarboxylic acid (VIII) (0.5 g) in 50% aqueous methanol (400 ml) was hydrogenated at room temperature and atmospheric pressure over platinum oxide (0.1 g). When hydrogenation was stopped after 5 min, uptake had exceeded the theoretical value by one third. The catalyst was filtered off (filter-aid) and the filtrate yielded a glass. This was dissolved in 50% aqueous methanol (20 ml) containing 1 equiv. of sodium hydroxide per carboxy-group. To this solution was added sodium hypobromite (1 equiv. per hydroxyamino-group) in water (10 ml). The mixture was left at room temperature for 2 h. Methanol was removed and the pH of the aqueous solution adjusted to 9 with sodium hydroxide. Extraction with chloroform (5 × 30 ml) yielded 2,2′-dimethyl-5,5′-bi-Δ¹-pyrrolinyl (XI) (0.1 g, 28%) as a straw-coloured oil, $\nu_{max.}$ 1 645 cm^{-1}. The *bis-picrate* crystallised from ethanol; m.p. 187—189° (Found: C, 42.5; H, 3.7; N, 17.8. $C_{22}H_{22}N_8O_{14}$ requires C, 42.5; H, 3.5; N, 18.0%). The aqueous layer remaining after extraction with chloroform by hand was continuously extracted with chloroform for 7 h. This extract yielded a hygroscopic gum (0.05 g), $\nu_{max.}$ 1 625 cm^{-1}, $\lambda_{max.}$ 230 nm (ε 7 000).

5-Methyl-Δ¹-pyrroline-5-carboxamide 1-Oxide (XV).—Ethyl 5-methyl-Δ¹-pyrroline-5-carboxylate 1-oxide [5] (5 g) was kept with aqueous ammonia (*d* 0.88; 50 ml) at room temperature with occasional shaking for 5 days, after which the mixture became homogeneous. The excess of ammonia was removed and the residual red oil was chromatographed on alumina. The crystalline product was eluted with 10% ethanol in chloroform and recrystallised from 2% ethanol–benzene to yield the *amide* (XV) (2.0 g, 48%), m.p. 137°, $\nu_{max.}$ 3 325, 3 160, 1 677, 1 633, 1 588, and 1 563 cm^{-1}, $\lambda_{max.}$ 236 (ε 4 700) (Found: C, 51.0; H, 7.3; N, 20.0. $C_6H_{10}N_2O_2$ requires C, 50.7; H, 7.1; N, 19.7%).

1-Hydroxy-2-methylpyrrolidine-2-carboxamide (XVI).—5-Methyl-Δ¹-pyrroline-5-carboxamide 1-oxide (0.21 g) in ethanol (20 ml) was hydrogenated at room temperature and atmospheric pressure over platinum oxide (0.05 g). Uptake stopped at the theoretical value after 5 min. The catalyst was filtered off (filter-aid) and the filtrate yielded the *amide* (XVI) (0.16 g; 76%), m.p. 98° (from benzene), $\nu_{max.}$ 3 400, 3 300, 1 655, and 1 555 cm^{-1} (Found: C, 49.9; H, 8.6; N, 19.2. $C_6H_{12}N_2O_2$ requires C, 50.0; H, 8.3; N, 19.4%).

Oxidation of 1-Hydroxy-2-methylpyrrolidine-2-carboxamide (XVI).—To a solution of the amide (XVI) (0.1 g) in water (5 ml) was added 1 equiv. of sodium hypobromite (prepared with a 30% excess of sodium hydroxide) in water (1 ml). Instant decolourisation of the hypobromite solution followed the addition but there was no effervescence. The solution was left overnight at room temperature and then extracted with chloroform continuously for 7 h. The semicrystalline residue was chromatographed on neutral alumina. The crystalline product was eluted with 2% ethanol in benzene and recrystallised from this solvent to yield 5-methyl-Δ¹-pyrroline-5-carboxamide 1-oxide (XV) (0.02 g, 20%), m.p. and mixed m.p. 130°. The i.r. spectrum was identical with that of an authentic sample.

Oxidation of 5-Methyl-Δ¹-pyrroline-5-carboxylic Acid 1-Oxide (IV).—To a solution of the acid [5] (1.0 g) in water (10 ml) was added 1 equiv. of sodium hypobromite (prepared with a 30% excess of sodium hydroxide) in water (10 ml). Immediate effervescence followed the addition. After 5 min the pH was adjusted to 9 with sodium hydroxide. The solution was extracted with chloroform (5 × 25 ml) to yield an oil (0.2 g), and a further quantity (0.2 g) was obtained after continuous extraction with chloroform for 7 h. The product showed $\nu_{max.}$ 2 720, 1 720, and 1 640 cm^{-1}.

When a solution of this oil (0.2 g) in ethanol (2 ml) was treated with 2,4-dinitrophenylhydrazine in ethanol containing 10% hydrochloric acid, laevulaldehyde bis-2,4-dinitrophenylhydrazone was obtained (0.5 g, 50%), m.p. and mixed m.p. 238° (Found: C, 44.3; H, 3.8; N, 24.6. Calc. for $C_{17}H_{16}N_8O_8$: C, 44.3; H, 3.5; N, 24.4%).

Oxidation of 5-Methyl-Δ¹-pyrroline-5-carboxamide 1-Oxide

(XV).—To a solution of the nitrone amide (0.22 g) in water (5 ml) containing sodium hydroxide (0.5 g) was added 1 equiv. of sodium hypobromite in water (2 ml). The yellow colour of the hypobromite solution faded in 15 min. Next day the mixture was continuously extracted with chloroform for 7 h. The residual oil ($\nu_{max.}$ 2 720, 1 720, and 1 620 cm^{-1}) was dissolved in ethanol (2 ml) and treated with an excess of 2,4-dinitrophenylhydrazine in ethanol containing 10% of dilute hydrochloric acid to yield laevulaldehyde bis-2,4-dinitrophenylhydrazone (0.2 g, 26%), m.p. and mixed m.p. 235° (Found: C, 44.4; H, 3.7; H, 24.3%).

Oxidation of 5,5-Dimethyl-Δ¹-pyrroline-2-carboxylic Acid 1-Oxide (Ia).—To a solution of the acid [5] (0.16 g) in water (10 ml) was added 1 equiv. of sodium hypobromite (prepared with a 30% excess of sodium hydroxide) in water (10 ml). Immediate effervescence followed the addition. After 5 min the pH was adjusted to 9 with sodium hydroxide and the solution was continuously extracted with chloroform for 8 h. A highly crystalline residue was obtained; one recrystallisation from n-hexane–cyclohexane provided 1-hydroxy-5,5-dimethylpyrrolidin-2-one (XXII) (0.1 g, 77%), m.p. 86°. The i.r. spectrum ($\nu_{max.}$ 3 320, 3 090, and 1 678 cm^{-1}) was identical with that of an authentic sample [5] (Found: C, 55.6; H, 8.5; N, 10.5. Calc. for $C_6H_{11}NO_2$: C, 55.8; H, 8.5; N, 10.9%).

Oxidation of 1-Hydroxy-5,5-dimethylpyrrolidin-2-one (XXII).—To an ice-cooled solution of the hydroxamic acid [5] (0.7 g) and sodium hydroxide (0.4 g) in water (10 ml) was slowly added bromine (0.25 ml) with stirring. A blue colour immediately appeared and after complete addition of bromine, the mixture was acidified (pH 5) and extracted with chloroform to yield the dimer of 4-methyl-4-nitrosopentanoic acid (XXV) (0.5 g, 60%), m.p. and mixed m.p. 106—108° (from chloroform–ether). The nitroso-acid dimer melted to a blue liquid. The i.r. spectrum was identical with that of an authentic sample.[13]

Oxidation of 2,4,4-Trimethyl-Δ¹-pyrroline 1-Oxide (XXVI) *with Less than 3 mol. equiv. of Sodium Hypobromite.*—To an ice-cooled solution of the nitrone [5] (10.7 g) and sodium hydroxide (3.5 g) in water (100 ml) was slowly added bromine (10 ml, 2.8 mol), with stirring. Addition was complete after 1 h, and after acidification the mixture was extracted with ether. After being washed with sodium hydrogen carbonate solution and water and dried, the extract was concentrated to give, as a yellow oil, the presumed 1-hydroxy-4,4-dimethylpyrrolidin-2-one (XXVII) (6.5 g, 60%) which could not be crystallised or further purified, $\nu_{max.}$ 3 300, 1 710, 1 380, and 1 360 cm^{-1}. A deep violet colour formed immediately on addition of iron(III) chloride solution.

Oxidation of 2,4,4-Trimethyl-Δ¹-pyrroline 1-Oxide (XXVI).—To a solution of the nitrone [5] (5.7 g) in water (30 ml) cooled in ice was added slowly with stirring a solution of sodium hypobromite [from bromine (8.4 ml) and sodium hydroxide (26.4 g)] in water (100 ml). Stirring was continued for 3 h, then the solution was acidified (pH 3) and extracted with ether to yield 2,2-dimethylsuccinic acid (XXVIII) (3.2 g, 55%), m.p. and mixed m.p. 138—140° (sublimation at 110° and 0.1 mmHg). The i.r. spectrum was identical with that of an authentic sample.[16]

Oxidation of 5,5-Dimethyl-Δ¹-pyrroline 1-Oxide (IIIa).—To a solution of the nitrone [5] (1.0 g) in 50% aqueous ethanol (30 ml) was added sodium hypobromite (2.5 equiv.) (prepared with a 30% excess of sodium hydroxide) in water (20 ml). A blue colour appeared after the addition. After 48 h the pH was adjusted to 9 with sodium hydroxide. The solution was extracted with chloroform (3 × 50 ml) to yield starting material. The aqueous layer was acidified with dilute hydrochloric acid and extracted with chloroform (3 × 50 ml) to yield a product which was recrystallised from aqueous ethanol to yield the dimer of 4-methyl-4-nitrosopentanoic acid (XXV) (0.2 g, 16%), m.p. and mixed m.p. 106—107°. The i.r. spectrum ($\nu_{max.}$ 1 720 and 1 535 cm^{-1}) was identical with that of an authentic sample.[13]

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[16] A. Higson and J. F. Thorpe, *J. Chem. Soc.*, 1906, **89**, 1455.