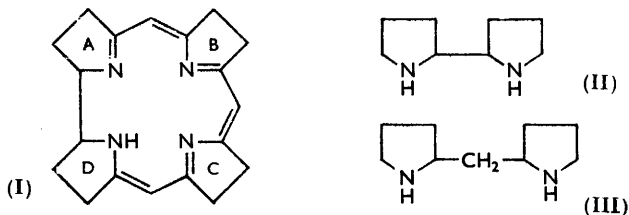


**427.** *Experiments towards the Synthesis of Corrins. Part VI.\* The Dimerisation of  $\Delta^1$ -Pyrroline 1-Oxides to 2-(1'-Hydroxypyrrolidin-2'-yl)- $\Delta^1$ -pyrroline 1-Oxides.*

By R. F. C. BROWN, V. M. CLARK, M. LAMCHEN, and SIR ALEXANDER TODD.

Under certain conditions, sodamide in liquid ammonia catalyses the dimerisation of  $\Delta^1$ -pyrroline 1-oxides to 2:2'-dipyrrolidinyl derivatives. In the case of 5:5-dimethyl- $\Delta^1$ -pyrroline 1-oxide a degradative proof of structure of the dimer is presented.

THE corrin nucleus (I), upon which the macrocyclic component of the vitamin B<sub>12</sub> chromophore<sup>1</sup> is based, is distinguished from the closely related porphyrins not only by the difference in oxidation level but also by the absence of a *meso*-carbon atom linking rings A and D. In exploring possible synthetic routes to the corrins we have therefore examined methods for the elaboration of intermediates related to 2:2'-bipyrrolidinyl (II), in addition to those based on dipyrrolidin-2-ylmethane (III). Derivatives of the latter formed the subject of the preceding paper in which the base-catalysed aldol-type reactions of various  $\Delta^1$ -pyrroline 1-oxides (IV) were recorded.



The nitron group (V), although capable of undergoing nucleophilic addition at the carbon atom,<sup>2</sup> might also be expected to exhibit electrophilic reactivity at that site as expressed by the canonical form (VI); indeed, the *N*-oxide linkage in pyridine 1-oxide is highly polarisable in both directions<sup>3</sup> and *electrophilic* substitution in the 4-position of pyridine oxide occurs readily.<sup>4</sup> Moreover, in the aliphatic series, the anion of nitromethane (V; R = H, R' = O<sup>-</sup>) dimerises by an addition equivalent to that of (V) to (VI) to yield, ultimately, nitroacetic acid;<sup>5</sup> and the adduct (V; R = H, R' = Ph) of formaldehyde and

\* Part V, preceding paper.

<sup>1</sup> Bonnett, Cannon, Clark, Johnson, Parker, Lester Smith, and Todd, *J.*, 1957, 1158, and references therein.

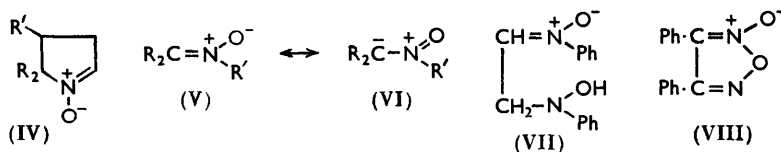
<sup>2</sup> Bonnett, Brown, Clark, Sutherland, and Todd, Part II, *J.*, 1959, 2094.

<sup>3</sup> Jaffé, *J. Amer. Chem. Soc.*, 1954, **76**, 3527; Katritzky, Randall, and Sutton, *J.*, 1957, 1769.

<sup>4</sup> Ochiai, *J. Org. Chem.*, 1953, **18**, 534; den Hertog, van Ammers, and Schukking, *Rec. Trav. chim.*, 1955, **74**, 1171.

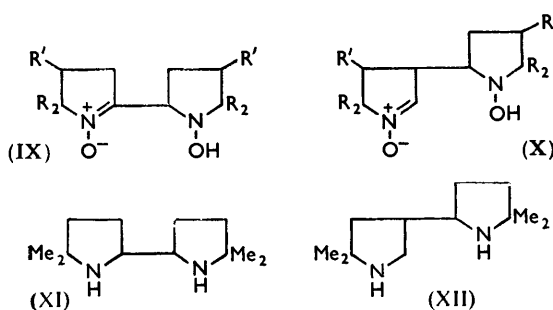
<sup>5</sup> Steinkopf, *Ber.*, 1909, **42**, 3925.

phenylhydroxylamine can only be isolated as an oxidation product of its dimer (VII).<sup>6</sup> The related nitrile oxide,  $\text{Ph}\cdot\text{C}\equiv\text{N}\cdot\text{O}^-$ , also dimerises in neutral or alkaline solution forming the furoxan derivative (VIII).<sup>7</sup>



Irradiation of a  $\Delta^1$ -pyrroline 1-oxide (IV; R = Me, R' = H) did not lead to any dimeric product but gave instead the oxaziran;<sup>8</sup> however, treatment with sodamide in liquid ammonia yielded a compound (IX; R = Me, R' = H) in which a 2 : 2'-linkage has been established: (IX) is then the direct analogue of (VII).

Earlier work on the action of bases on the  $\Delta^1$ -pyrroline 1-oxides had shown them to undergo aldol-type reactions (preceding paper) and with the oxide (IV; R = R' = Me) the action of triphenylmethylsodium gave rise to the bi-compound (X; R = R' = Me). When sodamide in liquid ammonia was used an isomeric product was obtained whose infrared spectrum exhibited bands at 3170 and 1603  $\text{cm}^{-1}$ , indicating the presence of a hydroxyamino- and a nitron group, though the position of the longer-wavelength band suggested a 2-substituted nitron (cf. IX) rather than the unsubstituted system (X).<sup>2</sup> Aerial oxidation of this isomeric product in the presence of cuprammonium ion gave a dinitron different from that obtained under similar conditions from the bi-compound (X; R = R' = Me). As the 4-methyl group (R' in IV) might have been the cause of isomerism attention was turned to 5:5-dimethyl- $\Delta^1$ -pyrroline 1-oxide (IV; R = Me, R' = H): treatment with triphenylmethylsodium or with sodamide in liquid ammonia again gave isomeric products, each product being shown to be a nitron-hydroxylamine on the basis of ultraviolet and infrared spectral evidence and its ability to reduce the triphenyltetrazolium chloride reagent.<sup>9</sup> The triphenylmethylsodium product exhibited an infrared band at 1575  $\text{cm}^{-1}$  indicative of an unsubstituted nitron, whilst the sodamide product absorbed at 1611  $\text{cm}^{-1}$  as expected of a 2-substituted nitron. Oxidation of each product either aerially in the presence of cuprammonium ion or by potassium ferricyanide<sup>10</sup> gave the corresponding dinitron: the triphenylmethylsodium product then



showed infrared bands at 1603 and 1570  $\text{cm}^{-1}$  to be expected of an unsubstituted and a 2-substituted nitron whilst the sodamide product exhibited a pronounced bathochromic shift to 1509 and 1503  $\text{cm}^{-1}$  suggestive of an  $\alpha$ -dinitron system  $^-\text{O}\cdot\text{N}^+=\text{C}\cdot\text{C}=\text{N}\cdot\text{O}^-$ . The ultraviolet spectra showed analogous changes: thus, the triphenylmethylsodium product

<sup>6</sup> Kalle and Co., D.R.-P. 87972 (Friedländer, 1894/97, **4**, 49); von Pechmann, *Ber.*, 1897, **30**, 2461; Bamberger, *Ber.*, 1900, **33**, 941; Hellmann and Teichmann, *Chem. Ber.*, 1956, **89**, 1134.

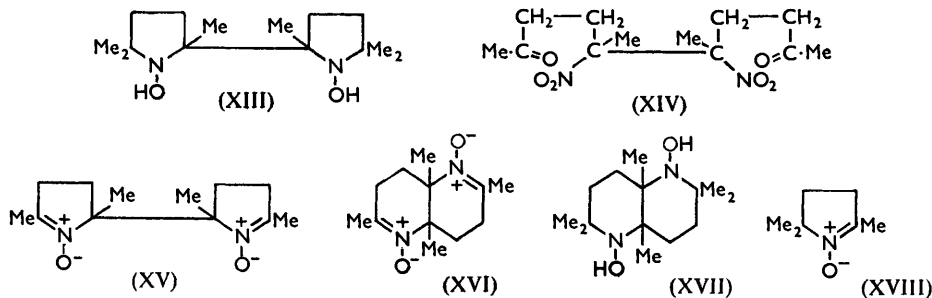
<sup>7</sup> Werner and Buss, *Ber.*, 1894, **27**, 2193; Wieland and Semper, *Ber.*, 1906, **39**, 2522.

<sup>8</sup> Bonnett, Clark, and Todd, Part III, *J.*, 1959, 2102.

<sup>9</sup> Rogers, *J.*, 1955, 769; Snow, *J.*, 1954, 2588.

<sup>10</sup> Thesing and Mayer, *Annalen*, 1957, **609**, 46.

had maximum absorption at  $237\text{ m}\mu$  ( $\epsilon$  16,500) as expected of two isolated nitron functions, whereas for the  $\alpha$ -dinitrone system of the sodamide product it was at  $331\text{ m}\mu$  ( $\epsilon$  18,500).



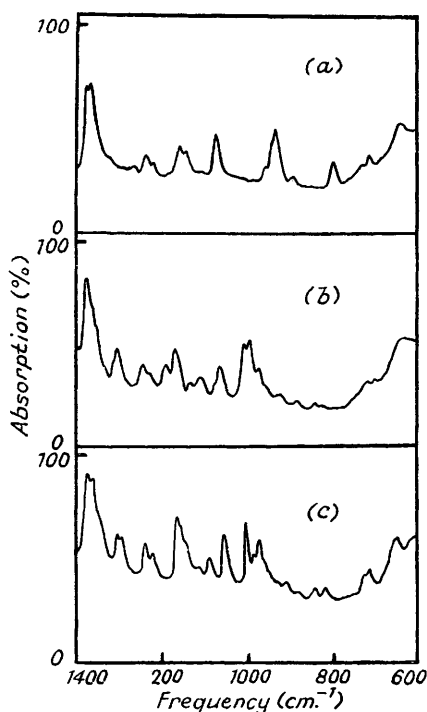
The nuclear magnetic resonance spectra were complex, but only the nitron-hydroxylamine dimer from the triphenylmethylsodium reaction showed any evidence of a uniquely situated hydrogen atom.

On the basis of this evidence we assign structure (IX; R = Me, R' = H) to the sodamide product, and (X; R = Me, R' = H) to the triphenylmethylsodium product.

The assignment (IX) is confirmed by the reactions described below.

Reduction of the products (IX and X; R = Me, R' = H) with aqueous sodium borohydride gave the bis-hydroxylamines, further reduction of which by zinc and hydrochloric acid gave the 2:2'-bipyrrolidinyl (XI) and the 2:3'-bipyrrolidinyl (XII). As expected, electrometric titration of the former disclosed two groups of different basicity ( $pK_{a1}$  6.95;  $pK_{a2}$  10.3), whereas the latter gave a single value ( $pK_a$  9.2).

Addition of methylmagnesium iodide to the  $\alpha$ -dinitrone derived from the 2:2'-bi-compound (IX; R = Me, R' = H) gave the bis-hydroxylamine (XIII), almost certainly as the racemic rather than the *meso*-product. Oxidation of 5-nitrohexan-2-one with ammonium persulphate<sup>11</sup> gave 5:6-dimethyl-5:6-dinitrodecane-2:9-dione (XIV) whose reduction with zinc dust and ammonium chloride<sup>2</sup> gave a mixture of two nitrones, A, m. p.  $150^\circ$ , and B, m. p.  $160$ – $170^\circ$ , one being (XV) and the other (XVI); addition of methylmagnesium iodide to each gave the corresponding bis-hydroxylamine A\* and B\* (presumably XIII and XVII). Neither was identical with the isomer obtained from the  $\alpha$ -nitron corresponding to (IX; R = Me, R' = H). The oxidative dimerisation to give the dinitro-diketone (XIV) would presumably give the *meso*-product and hence the bis-hydroxylamine (XIII) derived from it by way of the nitron (XV) would be *meso* whereas the isomer (XIII) derived from our dimerisation product (IX) would be the racemic isomer. The infrared spectra of A\* and of (XIII) derived from (IX) were closely similar,



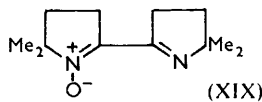
Infrared spectra of the bis-hydroxylamines (a) of B\*, structure (XVII), (b) of structure (XIII) derived from (IX), and (c) of structure A\*, (XIII) derived from (XV).

The infrared spectra of A\* and of (XIII) derived from (IX) were closely similar,

<sup>11</sup> Shechter and Kaplan, *J. Amer. Chem. Soc.*, 1953, **75**, 3980.

each differing somewhat in the fingerprint region from that of B\* (see Figure). On this basis we assign structure (XIII) to A\* and (XVII) to B\*. On aerial oxidation both isomers (XIII) underwent cleavage to yield the same nitron (XVIII),<sup>2</sup> this reaction being formally analogous to the cleavage of  $\alpha$ -glycols by sodium metaperiodate. Aerial oxidation of (XVII) also gave the mononitron (XVIII).

The function of the sodamide in the dimerisation of the pyrroline oxides (IV) to (IX) is uncertain. On occasion the use of sodamide gives aldol-type products<sup>12</sup> and in the present instance, with the compound (IV; R = Me, R' = H), a change of solvent from liquid ammonia to triethylamine led from the exclusive formation of the 2 : 2'-compound (IX; R = Me, R' = H) to the concurrent formation of some of the 2 : 3'-compound (X; R = Me, R' = H). In both solvents the nitron-hydroxylamine (IX; R = Me, R' = H) underwent, in part, the loss of the elements of water, the nitron-pyrroline (XIX) being also isolated. The direct linkage of aldehydic carbon atoms under basic conditions has been observed in the conversion of hydrobenzamide into amarin in the presence of potassamide,<sup>13</sup> and the removal of the aldehydic hydrogen atom under such conditions occurs in the formation of nitriles from *O*-esters of aromatic *anti*-aldoximes.<sup>14</sup> Whether or not the rôle of sodamide in the dimerisation of the nitron (IV) to (IX) is proton-abstraction has yet to be determined.



#### EXPERIMENTAL

*Dimerisation of 4 : 5 : 5-Trimethyl- $\Delta^1$ -pyrroline 1-Oxide with Sodamide in Liquid Ammonia.*—The pyrroline oxide (12.7 g.) in liquid ammonia (50 ml.) was added to a solution of sodamide (from 4.6 g. of sodium) in liquid ammonia (300 ml.). The solution was left overnight in a well-insulated flask, then excess of sodamide was decomposed by adding first ammonium chloride (10 g.), then water (125 ml.). After evaporation of ammonia, the aqueous solution was filtered and extracted with chloroform (4  $\times$  50 ml.). Evaporation of the dried (Na<sub>2</sub>SO<sub>4</sub>) chloroform extract and recrystallisation of the residue from chloroform–light petroleum gave the 2 : 2'-dimer, 2-(1'-hydroxy-4' : 5' : 5'-trimethylpyrrolidin-2'-yl)-4 : 5 : 5-trimethyl- $\Delta^1$ -pyrroline 1-oxide (IX; R = R' = Me) (3.6 g., 28%) as colourless rods, m. p. 176–177° (Found: C, 66.3; H, 10.1; N, 11.2. C<sub>14</sub>H<sub>26</sub>O<sub>2</sub>N<sub>2</sub> requires C, 66.1; H, 10.3; N, 11.0%),  $\lambda_{\max}$ . (in 95% ethanol) 233 m $\mu$  ( $\epsilon$  13,400),  $\nu_{\max}$ . (mull) 3170, 1603 cm.<sup>-1</sup>.

*Oxidation of 2 : 2'-Dimer.*—The above dimer (0.5 g.) was dissolved in water (100 ml.) and ammonia (5 ml.; *d* 0.880) containing copper sulphate (50 mg.) and oxidised by passing a stream of air through the solution for 3 hr. The product was extracted with chloroform (3  $\times$  25 ml.), and the crude solid obtained on evaporation of the chloroform extract was recrystallised from chloroform–low-boiling light petroleum to give a dinitron, 4 : 5 : 5 : 4' : 5' : 5'-hexamethyl-bi- $\Delta^1$ -pyrrolin-2-yl 1 : 1'-dioxide, as colourless rods, m. p. 160° (Found: C, 66.9; H, 10.0; N, 11.4. C<sub>14</sub>H<sub>24</sub>O<sub>2</sub>N<sub>2</sub> requires C, 66.7; H, 9.5; N, 11.1%),  $\lambda_{\max}$ . (in ethanol) 332 m $\mu$  ( $\epsilon$  9100),  $\nu_{\max}$ . (mull) 1504 cm.<sup>-1</sup>.

*Dimerisation of 5 : 5-Dimethyl- $\Delta^1$ -pyrroline 1-Oxide with Sodamide in Liquid Ammonia.*—The pyrroline oxide (10.0 g.) was treated with sodamide (from 2.0 g. of sodium) in liquid ammonia (300 ml.) as described for the 4 : 5 : 5-trimethyl compound. After addition of ammonium chloride and water to the reaction mixture and evaporation of ammonia, the aqueous solution was extracted with chloroform. Evaporation of the chloroform extract gave a thick oil which crystallised when stirred with light petroleum. Recrystallisation from chloroform–light petroleum gave colourless needles of the 2 : 2'-dimer, 2-(1'-hydroxy-5' : 5'-dimethylpyrrolidin-2'-yl)-5 : 5-dimethyl- $\Delta^1$ -pyrroline 1-oxide (IX; R = Me, R' = H) (4.9 g., 49%), m. p. 177° (Found: C, 63.5; H, 9.9; N, 12.6. C<sub>12</sub>H<sub>22</sub>O<sub>2</sub>N<sub>2</sub> requires C, 63.8; H, 9.7; N, 12.4%),  $\lambda_{\max}$ . (in 95% ethanol) 235 m $\mu$  ( $\epsilon$  10,500),  $\nu_{\max}$ . (mull) 3190, 1611 cm.<sup>-1</sup>.

<sup>12</sup> Brown, Clark, Sutherland, and Todd, preceding paper.

<sup>13</sup> Strain, *J. Amer. Chem. Soc.*, 1927, **49**, 1558.

<sup>14</sup> Vermillion and Hauser, *J. Org. Chem.*, 1941, **6**, 507; Hauser and Hoffenberg, *ibid.*, 1955, **20**, 1535.

In experiments using a larger proportion of sodamide (from 4.6 g. of sodium) the pyrroline oxide (10 g.) gave none of the above 2 : 2'-nitro-*nitro*-hydroxylamine dimer, but instead the nitro-pyrroline, 5 : 5 : 5' : 5'-*tetramethyl-2 : 2'-bi- $\Delta^1$ -pyrrolinyl 1-oxide* (XIX) was obtained in 10–20% yield. After sublimation at 90°/1 mm. and crystallisation from low-boiling light petroleum it formed colourless plates, m. p. 83° (Found: C, 69.4; H, 10.0; N, 13.5.  $C_{12}H_{20}ON_2$  requires C, 69.2; H, 9.6; N, 13.5%),  $\lambda_{max.}$  (in 95% ethanol) 224 and 285  $\mu$  ( $\epsilon$  2100 and 11,100),  $\nu_{max.}$  (mull) 1568 and 1542  $cm^{-1}$ .

*Oxidation of 2 : 2'-Dimer* (IX; R = Me, R' = H).—Aerial oxidation of the above dimer (1.0 g.) in water (50 ml.) and ammonia (5 ml.;  $d$  0.88) containing copper sulphate (0.2 g.) afforded 5 : 5 : 5' : 5'-*tetramethyl-2 : 2'-bi- $\Delta^1$ -pyrrolinyl 1 : 1'-dioxide* as colourless plates (from chloroform–light petroleum) (0.9 g.), m. p. 162° (Found: C, 64.0; H, 9.3; N, 12.3.  $C_{12}H_{20}O_2N_2$  requires C, 64.2; H, 8.9; N, 12.5%),  $\lambda_{max.}$  (in 95% ethanol), 250–254 ( $\epsilon$  3200) and 331  $\mu$  ( $\epsilon$  18,500),  $\nu_{max.}$  (in chloroform) 1509, 1503  $cm^{-1}$ .

Reduction of this dinitrone (0.1 g.) with sodium borohydride (0.1 g.) in water (2 ml.) gave the bishydroxylamine 1 : 1'-*dihydroxy-5 : 5 : 5' : 5'-tetramethyl-2 : 2'-bipyrrolidinyl* (0.07 g.) as colourless needles, m. p. 163° (Found: C, 62.9; H, 10.2; N, 12.6.  $C_{12}H_{24}O_2N_2$  requires C, 63.1; H, 10.5; N, 12.3%),  $\nu_{max.}$  (mull) 3260  $cm^{-1}$ .

*Borohydride Reduction of 2 : 2'-Dimer* (IX; R = Me, R' = H).—The dimer (1.0 g.) and sodium borohydride (0.7 g.) were dissolved in water (15 ml.) and the solution was left at room temperature for 48 hr. The solid which had crystallised was collected, the filtrate was extracted with ether, and the solid and the product of ether-extraction were combined. Recrystallisation from ethanol gave the bishydroxylamine, previously obtained by reduction of the dinitrone identified by its m. p., mixed m. p. 163°, and by comparison of infrared spectra.

5 : 5 : 5' : 5'-*Tetramethyl-2 : 2'-bipyrrolidinyl* (XI).—The above bishydroxylamine (1.75 g.) was treated in 20% w/v aqueous hydrochloric acid (10 ml.) with zinc dust (8 g.) in portions with shaking during 15 min., concentrated hydrochloric acid being added as necessary to dissolve the excess of zinc. The solution was filtered, made alkaline with ammonia, and extracted with chloroform. Evaporation of the dried ( $Na_2SO_4$ ) chloroform extract gave the crude *bipyrrolidinyl* as a viscous, extremely hygroscopic oil (1.35 g., 90%) (Found: equiv., 108, by electrometric titration.  $C_{12}H_{24}N_2$  requires equiv., 98). The oil had  $pK_{a1} = 6.95$  and  $pK_{a2} = 10.3$ . For analysis the product was converted into its *dipicrate* which crystallised from aqueous ethanol as yellow needles, m. p. 267° (Found: C, 44.0; H, 4.5; N, 16.5.  $C_{12}H_{24}N_2 \cdot 2C_6H_3O_7N_3$  requires C, 44.0; H, 4.6; N, 17.1%).

*Dimerisation of 5 : 5-Dimethyl- $\Delta^1$ -pyrroline 1-Oxide with Ethereal Triphenylmethylsodium*.—A solution of triphenylmethylsodium, prepared from triphenylmethyl chloride (90 g.) and 1.2% sodium amalgam (1250 g.) in ether (1500 ml.), was added to a solution of the pyrroline oxide (35 g.) in ether (100 ml.). The mixture was left at room temperature for 48 hr., evaporated to 700 ml., and extracted with 5*N*-hydrochloric acid ( $5 \times 50$  ml.). The acidic extract was washed with ether, made alkaline by addition of excess of ammonia, and extracted with chloroform ( $6 \times 40$  ml.). Evaporation of the chloroform yielded a crystalline mass (*ca.* 20 g.), which was washed with ether and recrystallised from the same solvent, to give the 2 : 3'-*dimer* (X; R = Me, R' = H) (13 g., 37%) (Found: C, 63.6; H, 10.0; N, 12.6.  $C_{12}H_{22}O_2N_2$  requires C, 63.8; H, 9.7; N, 12.4%),  $\nu_{max.}$  (mull) 1576  $cm^{-1}$ .

*Oxidation of 2 : 3'-Dimer*.—A solution of potassium ferricyanide (5 g.) in water (15 ml.) was added dropwise to a stirred solution of the above 2 : 3'-dimer (1.0 g.) and potassium hydroxide (1.4 g.) in water (10 ml.) at room temperature. The solution was left overnight and then continuously extracted with chloroform. The dried ( $Na_2SO_4$ ) chloroform extract was evaporated and the residue recrystallised from chloroform–ether to give 5 : 5 : 5' : 5'-*tetramethyl-2 : 3'-bi- $\Delta^1$ -pyrrolinyl 1 : 1'-dioxide* as colourless hygroscopic crystals, m. p. 140° (Found: C, 59.9; H, 8.7; N, 11.4.  $C_{12}H_{20}O_2N_2 \cdot H_2O$  requires C, 59.5; H, 9.1; N, 11.6%),  $\lambda_{max.}$  (in 95% ethanol) 237  $\mu$  ( $\epsilon$  16,500),  $\nu_{max.}$  (in chloroform) 1603, 1570  $cm^{-1}$ .

*Reduction of the 2 : 3'-Dimer* (X; R = Me, R' = H) with Sodium Borohydride.—Sodium borohydride (1 g.) was added to a solution of (X; R = Me, R' = H) (1 g.) in water (5 ml.) and set aside for 48 hr. The mixture was filtered, the filtrate extracted with chloroform, and the extract dried ( $Na_2SO_4$ ) and evaporated. The white crystalline residue of 1 : 1'-*dihydroxy-5 : 5 : 5' : 5'-tetramethyl-2 : 3'-bipyrrolidinyl* was recrystallised from ether–light petroleum and then had m. p. 132–133° (Found: C, 62.9; H, 11.0; N, 12.4.  $C_{12}H_{24}O_2N_2$  requires C, 63.1; H, 10.5; N, 12.3%).

5 : 5 : 5' : 5'-Tetramethyl-2 : 3'-bipyrrolidinyl (XII).—To the preceding bishydroxylamine (0.5 g.) in 20% w/v hydrochloric acid (10 ml.) zinc dust (3 g.) was added with shaking. After 40 hr. some zinc was still undissolved, so concentrated hydrochloric acid (5 ml.) was added, and the mixture heated on the steam-bath for 4 hr., cooled, and filtered. The filtrate was made strongly alkaline with sodium hydroxide and extracted with chloroform, and the extract dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated. The bipyrrolidinyl remained as a colourless viscous oil (0.36 g., 83%) which was purified by short-path distillation. It was extremely hygroscopic and in air gave a *dihydrate*, m. p. 38° (Found: C, 62.3; H, 12.5; N, 12.0%; equiv., 116.  $\text{C}_{12}\text{H}_{24}\text{N}_2 \cdot 2\text{H}_2\text{O}$  requires C, 62.0; H, 12.1; N, 12.1%; equiv., 116). The infrared spectrum of the dihydrate had bands corresponding both to OH and NH groupings; the base had a single  $\text{pK}_a$  9.2.

*Dimerisation of 5 : 5-Dimethyl- $\Delta^1$ -pyrroline 1-Oxide with Sodamide in Triethylamine.*—The pyrroline oxide (9.0 g.) was added to a suspension of sodamide (1.5 g.) in triethylamine (30 ml.). The mixture was stirred at room temperature for 18 hr., water (5 ml.) added, and the triethylamine evaporated. The residue was dissolved in water (15 ml.), and the solution extracted with chloroform (5  $\times$  30 ml.). The dried ( $\text{MgSO}_4$ ) chloroform extract was evaporated to an oil, which crystallised when stirred with pentane. Recrystallisation from light petroleum containing a little chloroform gave the 2 : 3'-dimer (X) (2.2 g., 24%), shown by comparison of infrared spectra and by the m. p. and mixed m. p. (152–153°) to be identical with that formed by the action of triphenylmethylsodium.

The pentane mother-liquors from the crystallisation of this compound were chromatographed on alumina (2  $\times$  20 cm.), and the column was eluted with benzene-chloroform (1 : 1). Evaporation of the eluate yielded a solid which on sublimation at 90°/1 mm. gave the 2 : 2'-nitronopyrroline (XIX) (1.5 g., 18%), identified by the m. p. and mixed m. p. (82–83°) and by comparison of its infrared spectrum with that of the product formed in the presence of excess of sodamide.

1 : 1'-Dihydroxy-2 : 5 : 5 : 2' : 5' : 5'-hexamethyl-2 : 2'-bipyrrolidinyl (XIII).—The dinitrone corresponding to (IX; R = Me, R' = H) (2.2 g.) in benzene (100 ml.) was added dropwise to methylmagnesium iodide (from 2.0 g. of magnesium) in ether (150 ml.) under reflux. The clear solution was heated for 2 hr., then cooled and excess of Grignard reagent decomposed by aqueous ammonium chloride (10 g. in 100 ml.). The organic layer was separated and evaporated under reduced pressure. The residue was distributed between water (50 ml.) and ether (50 ml.), and the ethereal layer evaporated. Recrystallisation of the residue from aqueous methanol gave the *bishydroxylamine* (XIII) (0.4 g.) as colourless leaflets, m. p. 122° (Found: C, 65.6; H, 11.3; N, 10.7.  $\text{C}_{14}\text{H}_{28}\text{O}_2\text{N}_2$  requires C, 65.6; H, 11.0; N, 10.9%),  $\nu_{\text{max}}$  (mull) 3400  $\text{cm}^{-1}$ .

*Oxidative Fission of Bishydroxylamine* (XIII).—The above bishydroxylamine (0.28 g.) was dissolved in 50% aqueous methanol (50 ml.), a solution of copper sulphate (20 mg.) in ammonia (2 ml.;  $d$  0.880) added, and air bubbled through the solution for 2 hr. Evaporation below 60° gave a syrup, and this was dissolved in methylene chloride (20 ml.). The dried ( $\text{K}_2\text{CO}_3$ ) solution was evaporated, and the residue treated with a slight excess of ethanolic picric acid. The precipitate recrystallised from ethanol as lemon-yellow needles (0.1 g.) of 2 : 5 : 5-trimethyl- $\Delta^1$ -pyrroline 1-oxide picrate, identified by comparison of infrared spectra and by its m. p. and mixed m. p. (98°<sup>2</sup>) (Found: C, 44.3; H, 4.7; N, 15.3. Calc. for  $\text{C}_{13}\text{H}_{16}\text{O}_8\text{N}_4$ : C, 43.8; H, 4.5; N, 15.7%).

*Oxidative Dimerisation of 5-Nitrohexan-2-one.*—A solution of the nitrohexanone<sup>15</sup> (120 g.) in ethanol (80 ml.) and 3*N*-aqueous sodium hydroxide (250 ml.) was stirred and cooled at 0–5° during dropwise addition of an ice-cold solution of ammonium persulphate (195 g.) and sodium acetate (88 g.) in water (400 ml.). Separation of the crystalline product was complete at 0° overnight. It was washed with water and recrystallised from aqueous methanol as prisms (31 g., 26%) of 5 : 6-dimethyl-5 : 6-dinitrodecane-2 : 9-dione, m. p. 88° (Found: C, 50.1; H, 7.3; N, 9.6.  $\text{C}_{12}\text{H}_{20}\text{O}_6\text{N}_2$  requires C, 50.0; H, 7.0; N, 9.7%),  $\nu_{\text{max}}$  (mull) 1720, 1547  $\text{cm}^{-1}$ .

*Reduction of 5 : 6-Dimethyl-5 : 6-dinitrodecane-2 : 9-dione.*—The dinitro-dione (7.0 g.), zinc dust (14 g.), and ammonium chloride (2 g.) were shaken together in 50% aqueous ethanol (120 ml.) at room temperature for 6 hr. The mixture was filtered and the filter cake washed with warm water (3  $\times$  25 ml.). The combined filtrate and washings were evaporated below 60° to a syrup. This was dissolved in methylene chloride (50 ml.), and the dried ( $\text{K}_2\text{CO}_3$ ) solution was passed through a short column of magnesium carbonate (5 g.), concentrated to 5 ml., and treated with ether (100 ml.). After 24 hr. the crystals which had separated were collected and

<sup>15</sup> Shechter, Ley, and Zeldin, *J. Amer. Chem. Soc.*, 1952, **74**, 3664.

recrystallised from methylene chloride-ether, to give pinkish prisms (1.9 g.) of crude dinitrone B, m. p. 160—170° (decomp.). This could not be purified further by crystallisation.

The *dipicrate* was prepared in ethanol and recrystallised therefrom as pale yellow needles, m. p. 190° (Found: C, 42.5; H, 4.0; N, 16.5.  $C_{24}H_{26}O_{16}N_8$  requires C, 42.2; H, 3.8; N, 16.4%). The pure *base B* (3 : 4 : 4a : 7 : 8 : 8a-hexahydro-2 : 4a : 6 : 8a-tetramethyl-1 : 5-diazanaphthalene 1 : 5-dioxide) (XVI) was regenerated from the picrate by decomposition with aqueous lithium hydroxide and continuous extraction with methylene chloride; it crystallised from benzene-ether as hygroscopic prisms, m. p. 194° (Found: C, 64.3; H, 8.7; N, 12.5.  $C_{12}H_{20}O_2N_2$  requires C, 64.3; H, 9.0; N, 12.5%),  $\lambda_{max}$  (in 95% ethanol) 234 m $\mu$  ( $\epsilon$  16,500),  $\nu_{max}$  1611  $cm^{-1}$ .

The combined methylene chloride-ether mother liquors from the crystallisation of crude dinitrone B were evaporated to a gum which was treated in ethanol (10 ml.) with an excess of ethanolic picric acid. The crystals which separated recrystallised from ethanol to give *dinitrone A monopicrate* (1.15 g.) as yellow needles, m. p. 188° (Found: C, 47.7; H, 4.9; N, 15.1.  $C_{18}H_{22}O_8N_5$  requires C, 47.7; H, 5.1; N, 15.5%). This picrate (1.0 g.) was passed in methylene chloride (50 ml.) through a column of alumina (25 g.). Pure *dinitrone A* (2 : 5 : 2' : 5'-tetramethyl-5 : 5'-bi- $\Delta^1$ -pyrrolinyl 1 : 1'-dioxide) (XV) was eluted with methylene chloride (300 ml.) and crystallised from methylene chloride-ether as colourless prisms (0.4 g.), m. p. 150° (Found: C, 64.0; H, 8.9; N, 12.5%),  $\lambda_{max}$  (in 95% ethanol) 231 m $\mu$  ( $\epsilon$  16,799),  $\nu_{max}$  (mull) 1603  $cm^{-1}$ .

*Addition of Methylmagnesium Iodide to Dinitrones A and B, and Oxidative Fission of Products.*—(a) Crude dinitrone B, m. p. 160—170° (decomp.) (0.67 g.), was treated with ethereal methylmagnesium iodide (from 0.6 g. of magnesium) as described in the analogous preparation of (XIII). The products were distributed between water (50 ml.) and ether (50 ml.), and the ethereal layer was evaporated. Recrystallisation of the residue from aqueous methanol gave the *bishydroxylamine B\** (1 : 5-dihydroxy-2 : 2 : 4a : 6 : 6 : 8a-hexamethyl-1 : 5-diazadecalin) (80 mg.) as colourless plates, m. p. 164° (Found: C, 65.5; H, 10.8; N, 10.7.  $C_{14}H_{28}O_2N_2$  requires C, 65.6; H, 11.0; N, 10.9%),  $\nu_{max}$  (mull) 3420  $cm^{-1}$ .

Aerial oxidation of this bishydroxylamine (80 mg.) in aqueous methanol containing ammonia and copper sulphate and isolation of the product as picrate yielded a crude picrate (52 mg.) having m. p. 92°. Repeated recrystallisation from ethanol finally gave lemon-yellow needles, m. p. 98°, identified by its m. p. and mixed m. p. and by comparison of infrared spectra as 2 : 5 : 5-trimethyl- $\Delta^1$ -pyrroline 1-oxide picrate.

(b) Dinitrone A (0.25 g.) was treated in the same way with methylmagnesium iodide (from 0.2 g. of magnesium). The bishydroxylamine, isolated as in (a), was recrystallised from the minimum volume of pentane. It underwent autoxidation very rapidly and two experiments failed because the product was autoxidised during working up. The most successful experiment gave the *bishydroxylamine A\** (1 : 1'-dihydroxy-2 : 5 : 5 : 2' : 5' : 5'-hexamethyl-2 : 2'-bipyrrolidinyl (20 mg.) as colourless needles, m. p. 102° (Found: C, 65.6; H, 10.8; N, 11.1%),  $\nu_{max}$  (mull) 3400  $cm^{-1}$ .

Aerial oxidation of bishydroxylamine A\* (15 mg.) in the usual way and isolation of the product as its picrate yielded a small quantity of lemon-yellow needles, m. p. 96°, which did not depress the m. p. of 2 : 5 : 5-trimethyl- $\Delta^1$ -pyrroline 1-oxide picrate (98°).

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