Reduction of Some *N*-Alkyl- and *N*-Aryl-pyrrolidin-2-ones and -piperidin-2-ones by Lithium Aluminium Hydride

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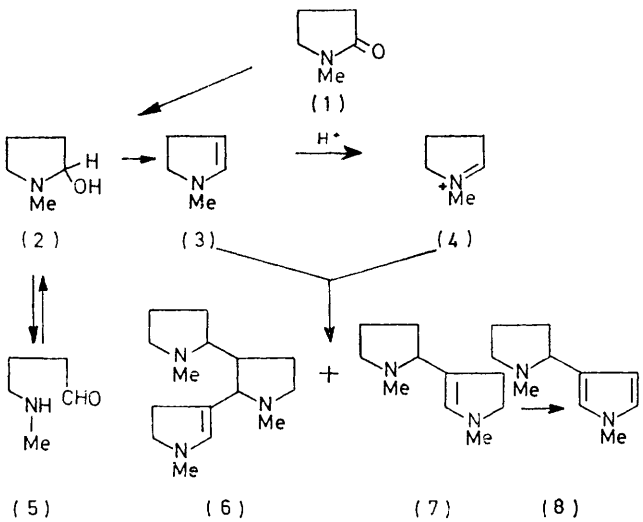
Reduction of 1-methyl-pyrrolidin-2-one (1) and -piperidin-2-one (9) by lithium aluminium hydride (0·25 mol. equiv.) yielded 1-methyl-3-(1-methylpyrrolidin-2-yl)-Δ^2-pyrroline (7) and 1,2,3,4-tetrahydro-1-methyl-5-(1-methylpiperidin-2-yl)pyridine (14), respectively. Similar reduction of 3,3-dimethyl-1-*p*-tolylpyrrolidin-2-one afforded 3,3-dimethyl-1-*p*-tolylpyrrolidin-2-ol (15); but 1-*p*-tolylpyrrolidin-2-one and 3-methyl-1-*p*-tolylpyrrolidin-2-one gave 2,3,3a,3b,4,5,6,11b-octahydro-10-methyl-1-*p*-tolyl-1*H*-dipyrrolo[1,2-*a*:3',2'-*c*]quinoline (19; R = Me) and 2,3,3a,3b,4,5,6,11b-octahydro-3a,4,10-trimethyl-1-*p*-tolyl-1*H*-dipyrrolo[1,2-*a*:3',2'-*c*]quinoline (25), respectively, each being obtained in two stereoisomeric forms. In the case of 1-*p*-tolylpiperidin-2-one it was possible to isolate 1,2,3,4-tetrahydro-1-*p*-tolylpyridine (30; R = Me).

REDUCTION of 1-methylpyrrolidin-2-one (1) by lithium aluminium hydride (0·25 mol. equiv.) was achieved by Galinovsky *et al.*,[1] who obtained the carbinolamine (2) existing in equilibrium with the amino-aldehyde (5), although neither of these products could be isolated. Loss of water from (2) should result in the formation of the enamine (3), which presumably dimerises rapidly. However, these workers were able to show the intermediate formation of a monomeric material by reaction with acetonedicarboxylic acid, yielding hygrine and cuscohygrine. Leonard and Cook [2] oxidised 1-methylpyrrolidine with mercury(II) acetate in acetic acid, and



again failed to isolate the resulting 1-methyl-Δ^2-pyrroline (3). They obtained a dimer, which they formulated as the pyrrolidinylpyrroline (7), and a trimer (6). They also showed that in solution the dimer existed in equilibrium with the monomer, so that it underwent slow reaction with ethyl acetoacetate to yield hygrine. Leete,[3] on the other hand, claimed that reduction of 1-methylpyrrolidin-2-one, followed by treatment of the product with acid, yielded the iminium salt (4), although his evidence that this was monomeric was not strong. Rueppel and Rapoport [4] isolated a corresponding iminium salt by acidification of the reduction product of 1,3-dimethylpyrrolidin-2-one.

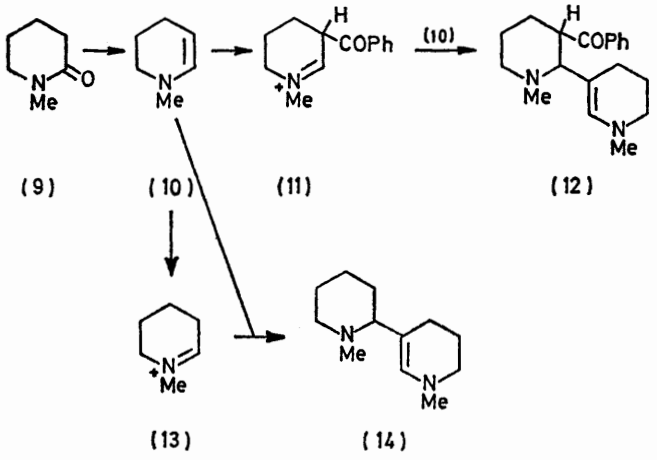
We obtained (6) and (7) by reduction of 1-methylpyrrolidin-2-one with either lithium aluminium hydride or sodium bis-(2-methoxyethoxy)aluminium hydride; and confirmed the identity of the i.r., n.m.r., and mass spectra of the dimeric products with those of that obtained by oxidation of 1-methylpyrrolidine with mercury(II) acetate. However, the reduction more readily yielded a pure product than did the oxidation method. Oxidation of (7) with alkaline ferricyanide afforded 1-methyl-3-(1-methylpyrrolidin-2-yl)pyrrole (8).

Likewise, by reduction of 1-methylpiperidin-2-one (9) with lithium aluminium hydride (at room temperature or at −70°), or with lithium diethoxyaluminium hydride or triethoxyaluminium hydride,[5] we obtained 1,2,3,4-tetrahydro-1-methyl-5-(1-methylpiperidin-2-yl)pyridine (14), which had previously been obtained by reduction of the same lactam with sodium and ethanol,[6,7] and also by oxidation of 1-methylpiperidine with mercury(II) acetate.[8] The crude product of reduction of 1-methylpiperidin-2-one with lithium aluminium hydride, when treated with hydrochloric acid, afforded a syrup, the n.m.r. spectra of which showed a broad singlet at τ 1·12, characteristic of an iminium ion ($=\overset{+}{N}=C-H$); *cf.* refs. 9 and 10. When this material was treated with benzoyl chloride in the presence of sodium hydroxide, it yielded a viscous syrup, which was evidently a benzoylated dimer, probably (12).

We have earlier described the reduction of strychnine to 10,11-didehydrostrychnidine;[11] we have now investigated the reduction of some 1-aryl-pyrrolidin-2-ones and -piperidin-2-ones.

[1] F. Galinovsky, A. Wagner, and R. Weiser, *Sitzungsber. Akad. Wiss. Wien*, 1951, Abt. 2B, **160**, 551.
[2] N. J. Leonard and A. G. Cook, *J. Amer. Chem. Soc.*, 1959, **81**, 5627.
[3] E. Leete, *J. Amer. Chem. Soc.*, 1967, **89**, 7081.
[4] M. L. Rueppel and H. Rapoport, *J. Amer. Chem. Soc.*, 1971, **93**, 7021.
[5] H. C. Brown and A. Tsukamoto, *J. Amer. Chem. Soc.*, 1964, **86**, 1089.
[6] R. Lukeš and J. Kovář, *Coll. Czech. Chem. Comm.*, 1954, **19**, 1215.
[7] C. Schöpf and H. L. de Waal, *Chem. Ber.*, 1956, **89**, 909.
[8] N. J. Leonard and F. P. Hauck, jun., *J. Amer. Chem. Soc.*, 1957, **79**, 5279.
[9] A. F. McDonagh and H. E. Smith, *J. Org. Chem.*, 1968, **33**, 8.
[10] H. Volz and H.-H. Kiltz, *Annalen*, 1971, **752**, 86.
[11] G. A. Swan and J. D. Wilcock, *J.C.S. Perkin I*, 1972, 1068.

The 1-arylpyrrolidin-2-ones were conveniently obtained by condensation of appropriate primary aromatic amines with γ-butyrolactones. 3-Methyl-1-*p*-tolylpyrrolidin-2-one was also obtained from 1-*p*-tolylpyrrolidin-2-one by treatment with diethyl carbonate in the



presence of sodium hydride, followed by methylation, hydrolysis, and decarboxylation.

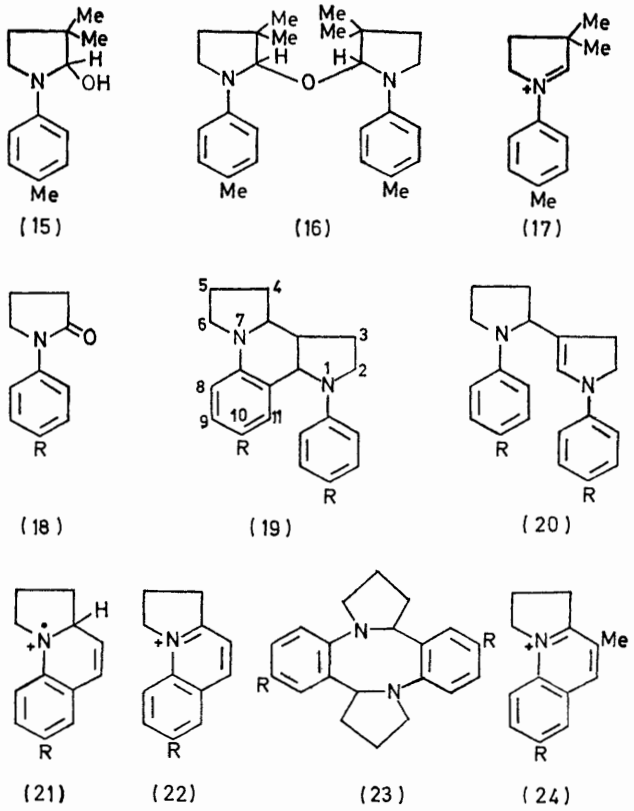
We encountered difficulty in using Krimm's [12] method for the preparation of 1-arylpiperidin-2-ones, as in our hands the reaction of cyclopentanone with aniline resulted predominantly in a 2 : 1, rather than a 1 : 1 condensation product. Therefore 1-aryl-2-pyridones, prepared essentially by Tschitschibabin and Jeletzky's method,[13] were hydrogenated catalytically to the corresponding 1-arylpiperidin-2-ones. Condensation of *p*-toluidine with δ-valerolactone also afforded 1-*p*-tolylpiperidin-2-one.

Reduction of 3,3-dimethyl-1-*p*-tolylpyrrolidin-2-one with lithium aluminium hydride afforded a crystalline product which appeared to consist mainly of the carbinolamine (15), containing a little of the corresponding ether (16). Attempts to separate these by chromatography on alumina or silica were only partly successful, interconversion evidently being easy. However, sublimation in vacuum yielded the ether, in the mass spectrum of which (at 120°) the molecular ion peak (*m/e* 392) was comparable in height to the *m/e* 205 peak. The n.m.r. spectrum of this showed singlets at τ 5·05 (N–CH–O), 7·78 (Ar*Me*), and 8·78 and 9·12 (CMe_2), but suggested that the compound was not pure, singlets (each representing only a fraction of one proton) being present at τ 4·9 and 9·2. It was therefore assumed that the bulk of this material consisted of the *meso*-ether, containing a small amount of the (±)-ether.

No mass spectrum of the carbinolamine was obtained which failed to give a peak at *m/e* 392 due to the presence of some of the ether (16), although in the best spectra this peak was very small compared with the molecular ion peak of the carbinolamine (*i.e.* *m/e* 205). The best spectra were obtained with rapid volatilisation (*e.g.* at 200°), although even at 120° the 392 peak was still small compared with the 205. The n.m.r. spectrum of the carbinolamine in carbon tetrachloride showed a doublet at τ 5·37 (*J* 6 Hz), attributed to the 2-proton of the pyrrolidine ring, coupled with the hydroxy-proton; exchange with deuterium oxide appeared to convert this into a singlet, although it was not possible to be certain, because of the proximity of the HOD peak. Singlets were present at τ 7·74 (ArMe) and at 8·9 and 9·11 (CMe_2).

Treatment of the above, crude material (mixture of carbinolamine and ether) with hydrochloric acid yielded a salt, the n.m.r. spectrum of which suggested it to be homogeneous (17).

Reduction of 1-*p*-tolylpyrrolidin-2-one (18; R = Me) yielded a mixture of two isomeric bases, $C_{22}H_{26}N_2$, which were separated by chromatography on silica. The faster-running isomer (A) had m.p. 144—145° and the slower-running (B) m.p. 115—116°. In most respects these two bases were alike. However, the u.v. spectrum of A showed maxima at 258 and 318 nm, unchanged (except for lowering in intensity) on acidification; whereas that of B showed maxima at 253 and 300, shifted to 262 and 335 nm on acidification. Initially it seemed possible that these isomers might have structures



(19; R = Me) and (20; R = Me), respectively. However, the latter was eliminated for the following reasons: (*a*) absence of an absorption maximum at 1650 cm^{-1} in the i.r. spectrum of either A or B [such an absorption is shown by (7)]; (*b*) failure to convert B into A by treatment with acid or by sublimation in vacuum; (*c*) the

[12] H. Krimm, *Chem. Ber.*, 1958, **91**, 1057.
[13] A. E. Tschitschibabin and N. P. Jeletzky, *Ber.*, 1924, **57**, 1158.

longest wavelength absorption band in the u.v. spectrum of (17) being at 282 nm; and (*d*) the great similarity between the mass spectra of A and B.

Bases A and B are therefore regarded as being stereoisomeric forms of the dipyrrolo[1,2-*a*:3′,2′-*c*]quinoline (19; R = Me). Peaks at *m/e* 185 and 184 in the mass spectra of both isomers were attributed to the ions (21; R = Me) and (22; R = Me), respectively. However the 185 peak is of much lower intensity than the 184 peak in the case of B, whereas in A these peaks are of comparable intensity.

The n.m.r. spectra of A and B showed doublets at τ 5·07 and 5·66, respectively, representing the 11b-proton coupled to the 3a-proton (*J* 7 and 8 Hz, respectively). The spectra of the two isomers obtained by reduction of 1-*p*-tolylpyrrolidin-2-one with lithium aluminium deuteride lacked these doublets, and were simpler in the τ 6·25—7·1 region (loss of signal due to 3b-proton).

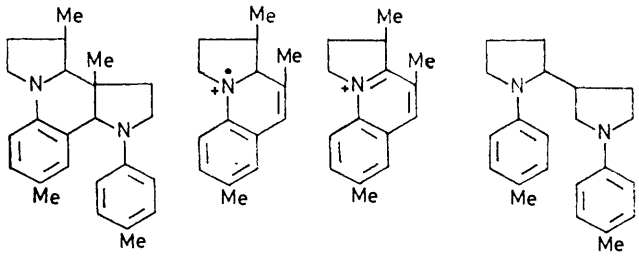
A phenhomazine structure (23) is also theoretically possible for either or both isomers; but is ruled out by reason of lack of symmetry: (*a*) A and B each show two separate methyl peaks in their n.m.r. spectra; and (*b*) the doublets at τ 5·07 and 5·66 each represent only one proton.

Reduction of 1-phenylpyrrolidin-2-one likewise yielded two isomers, formulated as (19; R = H), which corresponded in all the foregoing respects to compounds A and B. The m.p. and u.v. spectrum of the faster-running isomer corresponded to those given by Wittig and Sommer [14] for a compound which they obtained similarly, but which they incorrectly formulated as 1-phenyl-Δ^2-pyrroline. However, we confirmed that the compound described by these authors as 1-phenyl-Δ^3-pyrroline was correctly formulated, although its n.m.r. spectrum is deceptively simple (*cf.* ref. 15). We failed to isomerise this to 1-phenyl-Δ^2-pyrroline by heating with Raney nickel.

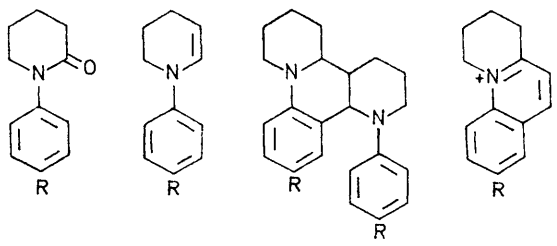
Very strong peaks at *m/e* 198 and 184 in the mass spectra of both isomers of (19; R = Me), and (19; R = H), respectively are attributed to the ions (24; R = Me) and (24; R = H), respectively. This formulation received support from the appearance in the spectrum of (19; R = H) of a metastable transition: $184^+ \longrightarrow 169^+ + 15$ (*i.e.* loss of Me). The metastable transitions $290^+ \longrightarrow 171^+ + 119$ and $171^+ \longrightarrow 170^+ +$ H also occur. The peaks at 171 and 170 represent (21; R = H) and (22; R = H), respectively.

Reduction of 3-methyl-1-*p*-tolylpyrrolidin-2-one likewise afforded two isomers, formulated as the dipyrrolo-[1,2-*a*:3′,2′-*c*]quinoline (25), the mass spectra of which showed intense peaks for fragment ions at *m/e* 213 and 212, corresponding to (26) and (27), respectively.

One possible explanation for the shift to longer wavelength in the u.v. spectra of the slower-running isomers (19; R = Me or H) and (25) on acidification might be that *C*- rather than *N*-protonation occurs. The n.m.r. spectra of the pairs of isomers (19; R = Me and H) were therefore compared by measurements (*a*) on the base in deuteriochloroform; (*b*) as (*a*) with the addition of methanesulphonic acid (1 equiv.); (*c*) as (*a*) with the addition of methanesulphonic acid (2—3 equiv.); (*d*) in $CF_3 \cdot CO_2H$; and (*e*) in $CF_3 \cdot CO_2D$. Acidification caused a downfield shift of most peaks, but a peak appeared in the τ 4 region. This was a somewhat broad singlet in the case of (19; R = Me), but a doublet (with further fine structure) in the case of (19; R = H); and appeared



(25) (26) (27) (28)



(29) (30) (31) (32)

equally with $CF_3 \cdot CO_2H$ or $CF_3 \cdot CO_2D$. This signal was therefore attributed to the aromatic 11-proton, which in the salts must presumably be shielded by the aryl residue attached to N-1. Moreover, in the case of both isomers, one of the methyl peaks moved upfield (to τ *ca.* 8·1) on the addition of 1 equiv. of acid, again presumably owing to the same shielding effect. The spectra of pairs of isomers under comparable conditions of acidity were very similar; no evidence for *C*-protonation was deduced from these spectra.

There was no evidence of rapid irreversible change occurring with dilute acid at room temperature, as the same isomers (A and B) could be obtained either by an isolation procedure avoiding contact with acid, or by one in which the bases were taken into acid, and then liberated by basification. However, long boiling of B with 2N-hydrochloric acid resulted in extensive decomposition, with the formation of a product which was not obtained pure, but which had the molecular formula $C_{22}H_{28}N_2$. Its spectra were consistent with the structure (28), which could have been formed through protonation at C-11a resulting in ring-opening to give (20; R = Me), followed by disproportionation.

Four configurations (A—D) for (19) are possible (represented schematically in the Figure), of which A and B appear to be consistent with the information

[14] G. Wittig and H. Sommer, *Annalen*, 1955, **594**, 1.
[15] L. F. Johnson, A. V. Robertson, W. J. R. Simpson, and B. Witkop, *Austral. J. Chem.*, 1966, **19**, 115.

known about the faster- and slower-running isomers, respectively. Of these configurations, Dreiding models (allowing reasonably full conjugation of each nitrogen atom with its appropriate aromatic ring) suggest that A is unstrained, and B only slightly strained; C is also

	A	B	C	D
3b-H	•	•	•	•
3a-H	•	○	•	○
11b-H	•	○	○	•

FIGURE

somewhat strained, and D is more strained than B. The torsion angle between the 3a- and 11b-protons for isomers A, B, C, and D is seen to be *ca.* 30, 35—40, 180, and 180°, respectively. In A H-11b can lie approximately in the plane of the aromatic ring attached to N-1; whereas in B this proton will be out of the plane. This could account for the lower field signal for H-11b in the n.m.r. spectrum of A than that of B. The shielding effects on H-11 and on the methyl group at position 10 are explicable on the assumption that protonation occurs first at N-1, the configuration of the latter nitrogen atom thus changing from planar to tetrahedral.

Under the acidic conditions used for the measurement of the n.m.r. spectra there seems little doubt that *N*-protonation occurs in both isomers. It is, however, possible that under the acidic conditions used for the measurement of u.v. spectra isomer B undergoes protonation at C-11a to a sufficient extent to show weak long wavelength absorption.

The formation of (19) could involve two steps, with the intermediary formation of (20); on the other hand a cycloaddition reaction might also be possible.

Roy and Swan[16] showed that the cation $(PhNMe{:}CH_2)^+$ condensed with ethyl vinyl ether to afford a quinoline derivative. We therefore carried out the reduction of 1-*p*-tolylpyrrolidin-2-one in the presence of ethyl vinyl ether, but failed to detect any product which might have been formed by the reaction of the latter with an iminium ion corresponding to (4).

From the products of reduction of 1-*p*-tolylpiperid-2-one (29; R = Me), an oil was isolated by chromatography, which although not pure, evidently consisted mainly of 1,2,3,4-tetrahydro-1-*p*-tolylpyridine (30; R = Me). The mass spectrum of this showed a molecular ion peak at *m/e* 173 ($C_{12}H_{15}N$); and its n.m.r. spectrum showed a multiplet at τ 5·05—5·4, attributed to the 3-proton of the pyridine ring, and only one Ar*Me* singlet at τ 7·75. This was unstable, and its isolation and purification were carried out so far as possible in the dark, as otherwise a red product was formed; a similar behaviour has been recorded for 1,4-dihydro-1-methylquinoline.[17]

Attempts to distil the aryltetrahydropyridine (30; R = Me) yielded a product, the mass spectrum of which showed a molecular ion peak at *m/e* 346 ($C_{24}H_{30}N_2$), together with an intense fragment ion peak at *m/e* 198 [probably (32; R = Me)], suggesting that dimerisation had occurred, giving the benzo[*h*]pyrido[2,1-*f*][1,6]naphthyridine (31; R = Me); the n.m.r. spectrum of the crude material was consistent with this. Similar reduction of 1-phenylpiperidin-2-one yielded 1,2,3,4-tetrahydro-1-phenylpyridine.

[16] R. B. Roy and G. A. Swan, *J. Chem. Soc.* (*C*), 1969, 1886.

[17] J. W. Bunting and W. G. Meathrel, *Tetrahedron Letters*, 1971, 133.

EXPERIMENTAL

N.m.r. spectra were measured in solutions in deuteriochloroform (except where otherwise stated), using tetramethylsilane as internal standard, with a Perkin-Elmer R10 spectrometer at 60 MHz. U.v. spectra were measured for solutions in ethanol. Mass spectra were obtained by use of an A.E.I. MS9 instrument, with direct insertion. I.r. spectra were measured for potassium bromide discs or liquid films. For column chromatography Hopkin and Williams M.F.C. silica gel and aluminium oxide were used. Merck Kieselgel G and aluminium oxide G (type E) were used for t.l.c., the spots being detected by exposure to iodine vapour. Light petroleum refers to the fraction of b.p. 40—60°, except where otherwise stated. Lithium aluminium hydride solution was prepared as described earlier.[11]

Reduction of 1-*Methylpyrrolidin*-2-*one* (1).—To a stirred solution of 1-methylpyrrolidin-2-one (9 ml) in benzene (50 ml) cooled in ice, one of sodium bis-(2-methoxyethoxy)-aluminium hydride (70% in benzene; 24 ml) diluted with benzene (30 ml) was added during 1 h. The mixture was allowed to come to room temperature, boiled under reflux for 1 h, then cooled in ice, decomposed with saturated aqueous potassium sodium tartrate, and extracted with benzene. The extract was then extracted with 2N-hydrochloric acid, and the latter extract was basified (40% sodium hydroxide), and extracted with ether. Distillation of the dried (K_2CO_3) ethereal extract afforded 1-methyl-3-(1-methylpyrrolidin-2-yl)-Δ²-pyrroline (7), b.p. *ca.* 100° at 16 mmHg (1·64 g), and 1-methyl-3-[1-methyl-3-(1-methylpyrrolidin-2-yl)pyrrolidin-2-yl]-Δ²-pyrroline (6), b.p. *ca.* 170° at 16 mmHg (2 g). The former fraction when redistilled had b.p. 100° at 16 mmHg (Found: M^+, 166. Calc. for $C_{10}H_{18}N_2$: *M*, 166), $\nu_{max.}$ 1650 cm^{-1} (C=C str.); τ (CCl_4) 4·3br (s, H-2), 7·52 (s, pyrroline NMe), and 7·9 (s, pyrrolidine NMe). This redistilled material (0·97 g) was added to a solution of potassium ferricyanide (4·6 g) and sodium hydroxide (1·1 g) in water (20 ml); the mixture was kept for 6·5 h in a refrigerator, and was then extracted with ether. Distillation of the dried (K_2CO_3) extract gave 1-*methyl*-3-(1-*methylpyrrolidin*-2-*yl*)*pyrrole* (8), b.p. 125° at 16 mmHg (0·46 g) (Found: M^+, 164. $C_{10}H_{16}N_2$ requires *M*, 164); τ (CCl_4) 3·6 (2H, resembling d, with fine splitting, pyrrole H-2 and -5), 4·03 (1H, resembling t, with fine splitting, pyrrole H-4, $J_{4,5}$ 2 Hz), 6·4 (3H, s, pyrrole NMe), and 7·9 (3H, s, pyrrolidine NMe).

1-*Methylpiperidin*-2-*one* (9).—1-Methyl-2-pyridone [18] was hydrogenated [19] to 1-methylpiperidin-2-one, τ 6·5—6·8 (2H, m, $N{\cdot}CH_2$), 7·03 (3H, s, NMe), 7·4—7·8 (2H, m, $CO{\cdot}CH_2$), and 8·0—8·3 (4H, m, $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2$).

Reduction of 1-*Methylpiperidin*-2-*one* (9).—An ethereal solution of lithium aluminium hydride (0·25 mol. equiv.)

[18] P. Beak, J. Bonham, and J. T. Lee, jun., *J. Amer. Chem. Soc.*, 1968, **90**, 1569.

[19] N. J. Leonard and E. Barthel, jun., *J. Amer. Chem. Soc.*, 1949, **71**, 3098.

was added with stirring during 1 h to one of 1-methylpiperidin-2-one (2·15 g); the mixture was boiled under reflux for 1 h, then cooled, and decomposed with saturated aqueous potassium sodium tartrate. The ether was removed from the dried (Na_2SO_4) organic layer; and the residue was chromatographed on silica. Elution with chloroform afforded 1-methylpiperidin-2-one (1·21 g), and elution with chloroform–ethanol (7 : 1) gave 1,2,3,4-tetrahydro-1-methyl-5-(1-methylpiperidin-2-yl)pyridine (14) as an oil (0·47 g) (Found: M^+, 194·1769. Calc. for $C_{12}H_{22}N_2$: M, 194·1783), $\nu_{max.}$ 1655 cm^{-1} (C=C str.); τ 4·12 (1H, s, H-2), 6·8—7·3 (5H, m, 2 × N·CH_2 and N·CH), 7·40 (3H, s, pyridine NMe), 7·75 (3H, s, piperidine NMe), and 7·8—8·6 (10H, m, 5 × CH_2); $\lambda_{max.}$ (neutral) 230 nm, $\lambda_{max.}$ (acidic) 262 nm. The dipicrolonate (from ethanol) had m.p. 149—150° (lit.,[1] 155—156°) (Found: C, 52·9; H, 5·0; N, 19·4. Calc. for $C_{12}H_{22}N_2$,$2C_{10}H_8N_4O_5$: C, 53·1; H, 5·25; N, 19·4%).

A similar reduction was carried out on 1-methylpiperidin-2-one (4·9 g), but the reaction mixture was decomposed with sodium hydroxide solution (25%; 20 ml), and the ethereal layer was extracted with 2N-hydrochloric acid. Evaporation of the aqueous layer under reduced pressure afforded the salt (13), as a syrup, which was dried (P_2O_5) in a vacuum. A portion of the residue was stirred for 3 h with a mixture of benzoyl chloride (4 ml) and 2N-sodium hydroxide (15 ml). Saturated aqueous sodium iodide was then added, and the resulting solid was collected, treated with 2N-hydrochloric acid, and then basified (NH_4OH). The mixture was extracted with chloroform, and the solvent was removed from the dried (Na_2SO_4) extract, yielding a syrup, *m/e* 298, 163, 136, 110, 105, and 77; τ 2·4—2·6 (6H, m, Ar and olefinic H), 7·48 and 7·86 (each 3H, s, 2 × NMe), and 6·3—9·0 (14H, m, remaining protons).

3,3-*Dimethyl*-1-p-*tolylpyrrolidin*-2-*one*.—A mixture of 2,2-dimethyl-γ-butyrolactone [20] (5·2 g) and *p*-toluidine (5·5 g) was heated in a sealed tube for 45 h at 290°. A solution of the residue in a little ethanol was diluted with light petroleum, and the resulting solid was recrystallised from light petroleum (b.p. 60—80°) (charcoal), yielding the *product* (7·35 g), m.p. 78° (Found: C, 77·4; H, 8·7; N, 6·85. $C_{13}H_{17}NO$ requires C, 76·8; H, 8·4; N, 6·9%); $\nu_{max.}$ 1685 cm^{-1} (C=O str.); τ (CCl_4) 2·42 and 2·8 (each 2H, *J* 8 Hz, Ar ABq), 6·3 and 8·08 (each 2H, t, *J* 8 Hz; N·CH_2·CH_2), 7·68 (3H, s, ArMe), 8·81 (6H, s, CMe_2).

Ethyl 2-*Oxo*-1-p-*tolylpyrrolidine*-3-*carboxylate*.—A solution of 1-*p*-tolylpyrrolidin-2-one [21,22] (20 g) in dry benzene (80 ml) was added during 2 h to a mixture of sodium hydride (10 g), diethyl carbonate (46 g), and dry benzene (100 ml), boiling under reflux. The mixture was boiled for a further 24 h and was then cooled, treated with water (60 ml), and acidified with acetic acid. The solvent was removed from the dried (Na_2SO_4) benzene layer, and the residue was recrystallised twice from benzene–light petroleum, yielding the *ester* (16·3 g, 58%), m.p. 80—81° (Found: C, 67·9; H, 6·85; N, 5·7. $C_{14}H_{17}NO_3$ requires C, 68·0; H, 6·9; N, 5·7%); $\nu_{max.}$ 1730 (ester C=O str.) and 1685 cm^{-1} (γ-lactam C=O str.); τ 2·49 and 2·79 (each 2H, *J* 9 Hz, Ar ABq), 5·72 (2H, q, *J* 8 Hz, CH_3·CH_2·O), 5·9—6·5 (3H, m, N·CH_2 and EtO·CO·CH·CO), 7·3—7·8 (2H, m, 4-H_2), 7·67 (3H, s, Ar*Me*), and 8·7 (3H, t, *J* 8 Hz, CH_3·CH_2·O).

Ethyl 3-*Methyl*-2-*oxo*-1-p-*tolylpyrrolidine*-3-*carboxylate*.—A solution of sodium (2 g) in ethanol (20 ml) was added to a solution of the above ester (16 g) in ethanol (200 ml), followed by methyl iodide (40 ml). The mixture was boiled under reflux for 24 h, and then cooled. The solvent was removed under reduced pressure, the residue was treated with water (30 ml), and the mixture was extracted with chloroform. The chloroform was removed from the dried (Na_2SO_4) extract, yielding a red oil, which crystallised when treated with hexane. Recrystallisation from hexane afforded the *product* (14·2 g), m.p. 41—42° (Found: C, 68·9; H, 7·2; N, 5·4. $C_{15}H_{19}NO_3$ requires C, 68·9; H, 7·25; N, 5·4%); $\nu_{max.}$ 1742 (ester C=O str.) and 1690 cm^{-1} (γ-lactam C=O str.); τ 2·52 and 2·87 (each 2H, *J* 9 Hz, Ar ABq), 5·85 (2H, q, *J* 8 Hz, CH_3·CH_2·O), 6·05—6·5 (2H, m, N·CH_2), 7·2—8·3 (2H, m, 4-H_2), 7·70 (3H, s, Ar*Me*), 8·60 (3H, s, 3-Me), and 8·78 (3H, t, *J* 8 Hz, CH_3·CH_2·O).

3-*Methyl*-2-*oxo*-1-p-*tolylpyrrolidine*-3-*carboxylic Acid*.—The above ester (14 g) was boiled under reflux for 20 h with 2N-hydrochloric acid (100 ml); the cooled mixture was then basified ($NaHCO_3$), and extracted with chloroform. The aqueous layer was acidified (HCl) and extracted with chloroform, affording the *acid* (12·1 g), m.p. 101—102° (Found: C, 67·0; H, 6·55; N, 6·15. $C_{13}H_{15}NO_3$ requires C, 67·0; H, 6·45; N, 6·0%); $\nu_{max.}$ 1716 (acid C=O str.) and 1684 cm^{-1} (γ-lactam C=O str.); τ −1·0 (1H, s, CO_2H), 2·54 and 2·86 (each 2H, *J* 9 Hz, Ar ABq), 6·0—6·45 (2H, m, N·CH_2), 7·2—8·2 (2H, m, 4-H_2), 7·71 (3H, s, Ar*Me*), and 8·52 (3H, s, 3-Me).

3-*Methyl*-1-p-*tolylpyrrolidin*-2-*one*.—(*a*) The above acid (12 g) was heated for 5 h at 160°. The residue, recrystallised from light petroleum, afforded the *product* (10·1 g), m.p. 60—60·5° (Found: C, 76·15; H, 7·95; N, 7·55. $C_{12}H_{15}NO$ requires C, 76·2; H, 7·95; N, 7·4%); $\nu_{max.}$ 1680 cm^{-1} (C=O str.); τ 2·53 and 2·97 (each 2H, *J* 9 Hz, Ar ABq), 6·3—6·6 (2H, m, N·CH_2), 7·4—8·6 (3H, m, 3-H and 4-H_2), 7·75 (3H, s, Ar*Me*), and 8·85 (3H, d, *J* 7 Hz 3-Me).

(*b*) The same product (6 g) was obtained by heating 2-methyl-γ-butyrolactone (4 g) with *p*-toluidine (4·85 g) for 90 h at 270°.

Reaction between Aniline and Cyclopentanone.—A mixture of aniline (31·5 g, 0·33 mol), cyclopentanone (25 g, 0·3 mol), and toluene (150 ml) was boiled for 15 h in an apparatus with a water-separator. Distillation of the remaining solution afforded an oil, b.p. 250° at 20 mmHg, which crystallised; the product had m.p. 53—54° (from ethanol) (Found: M^+, 225. Calc. for $C_{16}H_{19}N$: M, 225).

1-*Phenylpiperidin*-2-*one* (29; R = H).—1-Phenyl-2-pyridone was prepared by Tschitschibabin and Jeletzky's method,[13] except that the reaction mixture was heated for 12 instead of 6 h. The product isolated had m.p. 123—125° (yield 15·8%); further extraction of the reaction mixture with chloroform, followed by chromatography on alumina of the residue obtained by evaporation of the extract (elution with benzene), gave a further quantity (8·3%).

1-Phenyl-2-pyridone (17 g) was hydrogenated at 1 atm in acetic acid (60 ml) over Adams catalyst (0·1 g), yielding 1-phenylpiperidin-2-one (16·9 g), m.p. 101—103° (from benzene) (lit.,[12] 99—100°); $\nu_{max.}$ 1667 cm^{-1} (δ-lactam C=O str.).

1-p-*Tolylpiperidin*-2-*one* (29; R = Me).—(*a*) This aryl-piperidone, m.p. 86—87° (lit.,[23] 87—88°) (from hexane–

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benzene), was similarly obtained *via* 1-*p*-tolyl-2-pyridone; m.p. 125—128°, $\nu_{max.}$ 1670 cm^{-1} (C=O str.), prepared as above.

(*b*) The same compound was obtained by heating together equimolecular amounts of δ-valerolactone and *p*-toluidine for 30 h at 220°.

Reduction of 3,3-*Dimethyl*-1-p-*tolylpyrrolidin*-2-*one*.—Ethereal lithium aluminium hydride solution (0·37 mol. equiv.) was added dropwise to the lactam (2 g) in ether (25 ml) with stirring and cooling in ice; the mixture was then stirred for 2·5 h at room temperature, cooled in ice, and decomposed by dropwise addition of an excess of 2N-hydrochloric acid. The aqueous layer was separated, extracted with ether, then basified (NaOH), and again extracted with ether. The latter extract was dried (K_2CO_3) and evaporated. The residue, recrystallised from light petroleum, afforded a product consisting mainly of 3,3-dimethyl-1-*p*-tolylpyrrolidin-2-ol (15) (0·69 g). A solution of this in dilute hydrochloric acid was evaporated to dryness; the residue consisted of (17) as the chloride, τ 1·95 and 2·65 (each 2H, *J* 8 Hz, Ar ABq), 2·58 (1H, s, $=\overset{+}{N}=CH^-$), 5·05 (2H, t, *J* 7 Hz, $=\overset{+}{N}-CH_2$), 7·6 (2H, t, *J* 7 Hz, 4-H_2), 7·6 (3H, s, Ar*Me*), and 8·4 (6H, s, CMe_2); $\lambda_{max.}$ (neutral) 210, 248, and 303 nm; $\lambda_{max.}$ (acidic) 210, 227sh, and 282 nm.

Reduction of 1-p-*Tolylpyrrolidin*-2-*one* (18; R = Me).—Ethereal lithium aluminium hydride solution (0·25 mol. equiv.) was added dropwise to a stirred solution of the lactam (4 g) in ether (50 ml) at room temperature. After 3·5 h the mixture was decomposed by potassium sodium tartrate solution; and the ether was removed from the dried (Na_2SO_4) organic layer. The residue (3·8 g) showed 3 spots on t.l.c. (silica; benzene), R_F 0·95, 0·85, and 0·15; and was chromatographed on silica. Elution with benzene–light petroleum (1 : 1) yielded base A, 2,3,3a,3b,4,5,6,11b-*octahydro*-10-*methyl*-1-p-*tolyl*-1H-*dipyrrolo*[1,2-a:3′,2′-c]-*quinoline* (19; R = Me), R_F 0·95, m.p. 144—145° (from ethanol or benzene–light petroleum) (0·39 g) (Found: C, 82·85; H, 8·1. $C_{22}H_{26}N_2$ requires C, 83·0; H, 8·2%); τ 2·6—3·8 (7H, m, Ar), 5·07 (1H, d, *J* 7 Hz, H-11b), 6·25—7·1 (5H, m, 2 × N·CH_2 and N·CH), 7·50—8·5 (7H, m, other CH_2 and CH groups), 7·76 and 7·93 (each 3H, s, 2 × Ar*Me*); *m/e* 318 ($C_{22}H_{26}N_2$), 211, 210, 198, 185, 184, 170, 159, 157, 120, 93, 91, and 57; $\lambda_{max.}$ 258 and 318 nm (ε 24,800 and 6050). Elution with benzene gave the *stereoisomeric base* B, R_F 0·85, m.p. 115—116° (from ethanol or benzene–light petroleum) (0·38 g) (Found: C, 82·75; H, 8·0%); τ 2·7—3·7 (7H, m, Ar), 5·66 (1H, d, *J* 8 Hz, H-11b), 6·25—7·6 (5H, m, 2 × N·CH_2 and N·CH), 7·6—8·5 (7H, m, other CH_2 and CH groups), 7·76 and 7·84 (each 3H, s, 2 × Ar*Me*); *m/e* 318, 211, 210, 198, 185, 184, 170, 159, 156, 120, 93, 91, and 57; $\lambda_{max.}$ (neutral) 253 and 300 nm (ε 23,500 and 4140); $\lambda_{max.}$ (acidic) 262 and 335 nm. Elution with chloroform yielded 1-*p*-tolylpyrrolidin-2-one, R_F 0·15 (2·85 g).

Bases A and B were also isolated from a similar experiment in which the reaction products were taken into 2N-hydrochloric acid, and liberated by basification (NaOH).

Reduction of 1-*Phenylpyrrolidin*-2-*one* (18; R = H).—The lactam (3 g) was reduced as above. Elution with benzene–light petroleum (2 : 1) afforded 2,3,3a,3b,4,5,6,11b-*octahydro*-1-*phenyl*-1H-*dipyrrolo*[1,2-a:3′,2′-c]*quinoline* (19; R = H), R_F 0·74, m.p. 165—166° (from methanol) (0·38 g) (Found: C, 82·6; H, 7·45; N, 9·75. $C_{20}H_{22}N_2$ requires C, 82·8; H, 7·6; N, 9·6%); τ 2·5—3·6 (9H, m, Ar), 4·85 (1H, d, *J* 7 Hz, H-11b), 6·15—7·0 (5H, m, 2 × N·CH_2 and N·CH), and 7·35—8·5 (7H, m, other CH_2 and CH); *m/e* 290 ($C_{20}H_{22}N_2$), 196, 184, 171, 170, 156, 130, 115, 106, 91, and 77; $\lambda_{max.}$ 253 and 311 nm (ε 22,200 and 5800). Elution with benzene gave a *stereoisomer* of the preceding base, R_F 0·52, m.p. 153—154° (from methanol) (0·36 g) (Found: C, 82·55; H, 7·55; N, 9·8%); τ 2·6—3·5 (9H, m, Ar), 5·55 (1H, d, *J* 8 Hz, H-11b), 6·2—7·2 (5H, m, 2 × N·CH_2 and N·CH), and 7·2—8·5 (7H, m, other CH_2 and CH); *m/e* 290, 196, 184, 170, 156, 145, 130, 128, 115, 106, 91, and 77; $\lambda_{max.}$ (neutral) 251 and 294 nm (ε 19,700 and 3830); $\lambda_{max.}$ (acidic) 260 and 327 nm (ε 13,000 and 2900). Elution with chloroform yielded 1-phenylpyrrolidin-2-one, R_F 0·10 (2·1 g).

1-*Phenyl*-Δ³-*pyrroline*.—This was prepared by Wittig and Sommer's method,[14] and had m.p. 91—92° (lit.,[14] 99—100°), $\nu_{max.}$ 1630 cm^{-1} (C=C str.); τ 2·6—3·6 (5H, m, Ar), 4·12 (2H, s, 2 × olefinic H), and 5·95 (4H, s, 2 × N·CH_2). It was recovered unchanged after being boiled in xylene with Raney nickel for 15 h.

Reduction of 3-*Methyl*-1-p-*tolylpyrrolidin*-2-*one*.—The lactam (3 g) was reduced as above, and the crude product was chromatographed on silica. Elution with benzene–light petroleum (1 : 8) yielded 3-methyl-1-*p*-tolylpyrrolidine as an oil (0·11 g), R_F 0·96; τ 2·91 and 3·49 (each 2H, *J* 9 Hz, Ar ABq), 6·5—7·2 (4H, m, 2 × N·CH_2), 7·75 (3H, s, Ar*Me*), 8·88 (3H, d, *J* 8 Hz, 3-Me), and 7·8—8·6 (3H, m, CH_2·CH); (Found: M^+, 175. $C_{12}H_{17}N$ requires *M*, 175). Elution with benzene–light petroleum (1 : 6) afforded 2,3,3a,3b,-4,5,6,11b-*octahydro*-3a,4,10-*trimethyl*-1-p-*tolyl*-1H-*dipyrrolo*-[1,2-a:3′,2′-c]*quinoline* (25), R_F 0·88, m.p. 180—181° (from benzene) (0·26 g) (Found: C, 82·85; H, 8·45; N, 8·0%; M^+, 346·2418. $C_{24}H_{30}N_2$ requires C, 83·3; H, 8·65; N, 8·1%; *M*, 346·2409); τ 2·7—3·7 (7H, m, Ar), 5·41 (1H, s, H-11b), 6·45—7·2 (5H, m, 2 × N·CH_2 and N·CH), 7·3—8·7 (5H, m, other CH_2 and CH), 7·70 and 7·88 (each 3H, s, 2 × Ar*Me*), 8·82 (3H, d, *J* 6·5 Hz, 4-Me), and 9·02 (3H, s, 3a-Me); *m/e* 346, 342, 332, 331, 328, 226, 222, 213, 212, 198, 195, 184, 171, 144, 133, 120, 105, and 91; $\lambda_{max.}$ 258 and 316 nm (ε 26,400 and 5440). Elution with benzene–light petroleum (1 : 3) gave a *stereoisomer* of the preceding base, R_F 0·60, m.p. 118—120° (from benzene) (0·14 g) (Found: M^+, 346·2389); τ 2·75—3·45 (7H, m, Ar), 6·10 (1H, s, H-11b), 6·2—7·5 (5H, m, 2 × N·CH_2 and N·CH), 7·5—8·6 (5H, m, other CH_2 and CH), 7·70 and 7·80 (each 3H, s, 2 × Ar*Me*), 8·90 (6H, 1s and 1d, 3a- and 4-Me); *m/e* 346, 331, 267, 222, 213, 212, 196, 173, 120, 111, and 91; $\lambda_{max.}$ (neutral) 254 and 300 nm (ε 22,350 and 4230); $\lambda_{max.}$ (acidic) 260 and 333 nm (ε 19,900 and 4200). Elution with benzene–chloroform (1 : 3) gave 3-methyl-1-*p*-tolylpyrrolidin-2-one, R_F 0·15 (1·73 g).

Action of Acid on the Base B (19; R = Me).—Base B was recovered unchanged after being boiled under reflux in chloroform with benzoic acid for 7 days.

The base (0·26 g) was boiled under reflux for 10 h with 2N-hydrochloric acid (10 ml). The solution was then cooled, basified (NH_4OH), and extracted with chloroform. Removal of the solvent from the extract yielded a dark syrup (0·22 g), R_F 0·45, which was chromatographed on silica. Elution with chloroform gave a syrup (0·14 g) (Found: M^+, 320. $C_{22}H_{28}N_2$ requires *M*, 320); τ 2·8—3·7 (8H, m, Ar), 6·4—7·5 (7H, m, 3 × N·CH_2 and N·CH), 7·72 (6H, s, 2 × Ar*Me*), and 7·8—8·8 (7H, m, remaining CH_2 and CH).

Reduction of 1-p-*Tolylpiperidin*-2-*one* (29; R = Me).—

1-*p*-Tolylpiperidin-2-one (4 g) was reduced as above except that the reaction and work-up were carried out in the dark so far as possible. The crude product was a yellow, viscous oil (3·6 g), consisting of a mixture of at least three components, R_F 0·92, 0·57, and 0·10 (alumina; benzene); 0·90, 0·54, and 0·10 (silica; benzene). The mass spectrum of this showed 3 molecular ion peaks, M^+, 189, 175, and 173. Chromatography on alumina, and elution with benzene–light petroleum (1 : 2) gave 1-*p*-tolylpiperidine, R_F 0·92 (0·43 g). (Found: M^+, 175. Calc. for $C_{12}H_{17}N$: M, 175). Elution with benzene afforded 1,2,3,4-tetrahydro-1-*p*-tolylpyridine, R_F 0·57 (0·39 g) (Found: M^+, 173. Calc. for $C_{12}H_{15}N$: M, 173), which turned red on exposure to light. The alumina column became bright red; and more polar solvents failed to extract further material from it.

In a similar experiment, the crude product was chromatographed on silica. Elution with benzene–light petroleum (1 : 2) gave 1-*p*-tolylpiperidine, R_F 0·90 (0·37 g). Elution with benzene afforded 1,2,3,4-tetrahydro-1-*p*-tolylpyridine, R_F 0·54 (0·26 g). Elution with chloroform yielded 1-*p*-tolylpiperidin-2-one (1·8 g).

Reduction of 1-*Phenylpiperidin-2-one* (29; R = H). Similar reduction of 1-phenylpiperidin-2-one (4 g) and chromatography on silica afforded 1-phenylpiperidine, R_F 0·90 (0·38 g) [eluted by benzene–light petroleum (1 : 2)], 1,2,3,4-tetrahydro-1-phenylpyridine, R_F 0·60 (0·21 g) (Found: M^+, 159. $C_{11}H_{13}N$ requires M, 159) (eluted by benzene), and 1-phenylpiperidin-2-one, R_F 0·20 (1·7 g) (eluted by chloroform).

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