Diazaindenes (Azaindoles). Part VI.[1] Preparation and Some Properties of 1,7-Diazaindene 7-Oxide and 6,7,8,9-Tetrahydro-γ-carboline 2-Oxide

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Treatment of the *N*-acetyl derivatives of 1,7-diazaindene and 6,7,8,9-tetrahydro-γ-carboline with *m*-chloroperoxybenzoic acid gave the 7-oxide (6) and the 2-oxide (13), respectively. The reaction of the *N*-oxide (13) with acetic anhydride yielded 6,7,8,9-tetrahydro-γ-carbolin-1(2*H*)-one (24), and the 7-oxide (6) gave 1,7-diazainden-6(7*H*)-one (26). 1-Chloro-6,7,8,9-tetrahydro-γ-carboline (14) was obtained directly from the *N*-oxide (13), but the 7-oxide (6) gave 4-chloro-1,7-diazaindene (8); the chlorine atom in (8) was not easily replaced by nucleophiles. The tetrahydro-γ-carboline *N*-oxide (13) was converted into 1-cyano- (16) and 1-anilino-tetrahydro-γ-carboline (18).

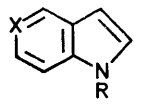
DIAZAINDENE *N*-OXIDES are of interest as intermediates in the preparation of other functionally substituted diazaindenes. Some diazaindene *N*-oxide derivatives have been obtained by Tacconi *et al.*[2] by indolisation of appropriate pyridylhydrazone *N*-oxides in the presence of zinc chloride, but this method cannot readily be applied to the preparation of the parent heterocycle *N*-oxides. Direct oxidation of 1,5- (1) and 1,7-diazaindene (4) and some simple derivatives with hydrogen peroxide–acetic acid has caused opening of the pyrrole ring to yield pyridine derivatives.[3,4] Robison [5] oxidised 2,3-dihydro-1,7-diazaindene to its 7-oxide but this route introduces additional hydrogenation and dehydrogenation steps if the 7-oxide (6) is required from (4). We report studies on the oxidation of 1,7-diazaindene and the 1,5-diazaindene derivative, 6,7,8,9-tetrahydro-γ-carboline (10).

We have recently shown that 1-acetyl-1,5-diazaindene (2) may be converted into 1,5-diazaindene 5-oxide (3) by treatment with *m*-chloroperoxybenzoic acid.[1] Similarly, 1-acetyl-1,7-diazaindene (5) gave 1,7-diazaindene 7-oxide (6), but in this case yields were variable (30—80%). Also, 5-acetyl-6,7,8,9-tetrahydro-γ-carboline (11) yielded the corresponding 2-oxide (12) which, on hydrolysis, gave 6,7,8,9-tetrahydro-γ-carboline 2-oxide (13). This compound was probably obtained previously by Tacconi and Pietra,[2] who subjected cyclohexanone 4-(1-oxopyridyl)-hydrazone hydrochloride to Fischer indolisation in the presence of zinc chloride, and obtained an intermediate [probably the *N*-oxide (13), but it was not purified and characterised] which was reduced to (10). Our attempts to repeat this work gave a small yield of (10) directly, but none of the *N*-oxide was isolated. When the same indolisation conditions were applied to cyclohexanone 4-(1-oxopyridyl)hydrazone the tetrahydrocarboline *N*-oxide (13) was obtained in very low yield. It seems likely that the high temperature required for the cyclisation causes deoxygenation. Attempts to obtain a diazaindene *N*-oxide by thermal indolisation (*i.e.* in the absence of catalyst) of cyclohexanone 4-(1-oxopyridyl)hydrazone yielded only 6,7,8,9-tetrahydro-γ-carboline, but in approximately half the yield obtained from cyclohexanone 4-pyridylhydrazone.[6]

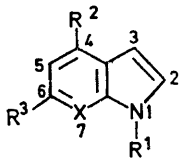
Each of the *N*-oxides (3), (6), and (13) had a mass spectrum which showed a strong peak due to the molecular ion and a characteristic fragment ion at $M - 16$, probably formed by thermal deoxygenation.[7] N.m.r.

[1] Part V, B. A. J. Clark and J. Parrick, *J.C.S. Perkin I*, 1974, 1531.
[2] G. Tacconi and S. Pietra, *Ann. Chim. (Italy)*, 1965, **55**, 810.
[3] B. A. J. Clark and J. Parrick, *Tetrahedron*, 1974, **30**, 475.
[4] P. A. Crooks, M.Sc. Thesis, University of Manchester, 1967, p. 65.
[5] M. M. Robison, B. L. Robison, and F. P. Butler, *J. Amer. Chem. Soc.*, 1959, **81**, 743.
[6] A. H. Kelly and J. Parrick, *J. Chem. Soc. (C)*, 1970, 303.
[7] A. M. Duffield and O. Buchardt, *Acta Chem. Scand.*, 1972, **26**, 2423.

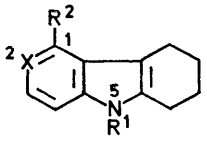
data for 1,5- and 1,7-diazaindene and their *N*-oxides and *N*-oxide hydrochlorides are listed in the Table. Noteworthy features are the large deshielding of the NH



(1) R = H, X = N
(2) R = Ac, X = N^+
(3) R = H, X = $N{-}O^-$



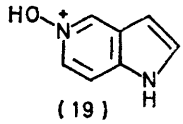
(4) $R^1 = R^2 = R^3 = H, X = N$
(5) R^1 = Ac $R^2 = R^3 = H, X = N$
(6) $R^1 = R^2 = R^3 = H, X = N{-}O$
(7) R^1 = Ac, $R^2 = H, R^3 = OAc, X = N$
(8) $R^1 = R^3 = H, R^2 = Cl, X = N$
(9) $R^1 = R^2 = H, R^3 = Cl, X = N$



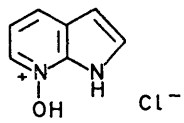
(10) $R^1 = R^2 = H, X = N$
(11) R^1 = Ac, $R^2 = H, X = N$
(12) R^1 = Ac, $R^2 = H, X = N{-}O^-$
(13) $R^1 = R^2 = H, X = N{-}O^-$
(14) $R^1 = H, R^2 = Cl, X = N$
(15) $R^1 = H, R^2 = NH{\cdot}N{:}CMe_2, X = N$
(16) $R^1 = H, R^2 = CN, X = N$
(17) R^1 = Ac, $R^2 = CH_2{\cdot}NAc_2, X = N$
(18) $R^1 = H, R^2 = NHPh, X = N$

proton in 1,5-diazaindene 5-oxide hydrochloride (19) and the considerable difference in the deshielding of the protons β to the $N^+{-}OH$ group, *i.e.* 0·6 and 0·1 p.p.m. for 1,5- (19) and 1,7-diazaindene *N*-oxide hydrochloride (20), respectively, as compared with the corresponding diazaindenes. These differences are presumably caused by the increased positive charge developed at the 1-position in the hydrochloride (19) due to a significant contribution from the canonical form (21), and the effect of this charge on the *peri*-hydrogen atom. This explanation is supported by the large deshielding relative to the parent diazaindene of the 2-proton in the 1,5-diazaindene

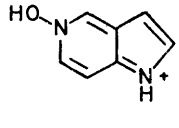
The reaction of 1,5-diazaindene 4-oxide hydrochloride (19) with acetic anhydride to give 1-acetyl-1,5-diazaindene-4(5*H*)-one (22) has been discussed.[1] 6,7,8,9-Tetrahydro-γ-carboline 2-oxide (13) on treatment with acetic anhydride and sodium acetate yielded one product whose i.r. and n.m.r. spectra showed similarities to those of (22), *e.g.* $\nu_{max.}$ (KBr) 3180 (NH), 1770 (CO), and 1660 cm^{-1} (CO), and overlap of the pyridone ring proton signals to give a singlet at δ 2·63. Hydrolysis of the compound yielded a deacetylated product whose n.m.r. spectrum showed a pair of doublets at δ 7·50 and 6·83 (*J* 8·0 Hz), clearly indicating the compounds to be (23) and (24), respectively. No evidence for the lactim tautomer was found.



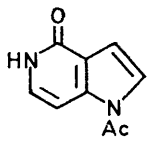
(19) Cl^-



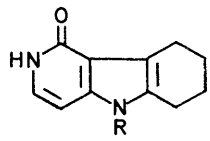
(20) Cl^-



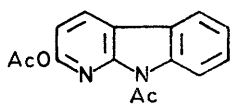
(21) Cl^-



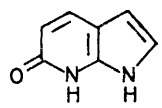
(22)



(23) R = Ac
(24) R = H



(25)



(26)

The action of acetic anhydride and acetate on 1,7-diazaindene 7-oxide (5) yielded a solid whose i.r. spectrum

	δ [solvent $(CD_3)_2SO$]							*J*/Hz		
	1-H	2-H	3-H	4-H	6-H	7-H	OH	$J_{2,3}$	$J_{6,7}$	$J_{4,6}$
(1)	11·46	7·45	6·60	8·86	8·18	7·40		3·6	5·6	
(3)	12·70	7·50	6·52	8·57	7·89	7·40		3·4	7·0	2·0
(19)	14·67	7·93	6·93	9·43	8·52	7·97	11·90	3·0	7·0	2·0
	1-H	2-H	3-H	4-H	5-H	6-H	OH	$J_{2,3}$	$J_{4,5}$	$J_{5,6}$
(4)	11·67	7·48	6·46	7·97	7·33	8·27		3·2	8·0	5·0
(6)	12·50	7·51	6·58	7·70	7·12	8·18		3·6	8·0	6·0
(20)	13·43	7·83	6·90	8·43	7·43	8·68	10·93	3·4	8·0	6·0

5-oxide hydrochloride as compared with that in the 1,7-isomer. 4,6-Coupling is not observed in the spectrum of the parent diazaindene or in that of 1-methyl-1,5-diazaindene.[8] There is evidence of 1,3-coupling in the spectrum of (19), since the 3-H signal appears as a broad singlet at 6·93, but changes to a doublet (*J* 3·0 Hz) on addition of D_2O. These effects are not observed in the spectrum of the corresponding 1,7-isomers.

showed the presence of two CO groups ($\nu_{max.}$ 1705 and 1760 cm^{-1}) and the absence of NH and OH groups; the n.m.r. spectrum showed the presence of two CH_3 groups. The compound was thought to be 6-acetoxy-1-acetyl-1,7-diazaindene (7). T.l.c. and g.l.c. analysis of the reaction product indicated the presence of probably less than

[8] P. G. Riley and B. Robinson, *Canad. J. Chem.*, 1969, **47**, 3257.

5% of a second, possibly isomeric, product. The stability of the acetoxy-group in (7) to mild hydrolysis conditions is similar to that noted for (25).[9] More vigorous hydrolysis conditions gave 1,7-diazainden-6 (7*H*)-one (26), which exists as the lactam tautomer and had been obtained before by Robison.[5]

In our hands, the preparation [10] of (1) proved troublesome, though the reported yields of (4) were readily obtained by a similar procedure. As a consequence, the available tetrahydrocarboline *N*-oxides (12) and (13) were used as model compounds in further investigations of reactions of the 1,5-diazaindene 5-oxide system. Treatment of the 1-acetyl *N*-oxide (12) with phosphoric trichloride followed by alkaline hydrolysis yielded a chlorinated tetrahydro-γ-carboline. The same compound was also obtained directly from the *N*-oxide (13) and the lactam (24) by treatment with phosphoric trichloride, the latter reaction establishing the structure of the chloro-compound as (14). 1,7-Diazaindene 7-oxide similarly gave a chloro-1,7-diazaindene in good yield. The n.m.r. spectrum of this chloro-compound showed no signal at about δ 7·9 (4-H), and the pyridine ring proton signals at δ 7·22 and 8·23 (a pair of doublets, *J* 5·1 Hz) were as expected for the 5- and 6-protons of a 1,7-diazaindene ($J_{5,6}$ 4·5; *cf.* ref. 11, $J_{4,5}$ 7·5 Hz); the compound was therefore thought to be 4-chloro-1,7-diazaindene (8). Support for this assignment was obtained when the 6-chloro-isomer (9) was obtained from (26) and was different from (8), showing $J_{4,5}$ 8·3 Hz.

A few reactions of the chloro-compounds (8) and (14) were studied. Treatment of (14) with hydrazine hydrate gave, after treatment of the reaction mixture with acetone, a derivative for which the analytical figures and the n.m.r. spectrum data agreed with expected structure (15). Attempts to bring about nucleophilic replacement of the chlorine in (8) by treatment with refluxing aqueous sodium hydroxide or sodium methoxide in methanol were unsuccessful.

The tetrahydrocarboline-1-carbonitrile (16) was obtained by treatment of the *N*-oxide (12) or (13) with benzoyl chloride and silver cyanide, but not by the action of the chloride and potassium cyanide on (13). Only one nitrile compound was obtained in these reactions, and the same product was isolated after treatment of (13) with potassium cyanide and acetic anhydride. In contrast, 1,7-diazaindene 7-oxide gave no product on treatment with benzoyl chloride and silver cyanide. Reduction of the cyanide (16) with Raney nickel and hydrogen gave a triacetyl derivative whose n.m.r. and i.r. spectra showed no NH peaks. The n.m.r. spectrum showed peaks due to aromatic (pair of doublets), 8 alicyclic, 2 methylene (singlet), and 6 methyl protons (2 singlets) in agreement with the structure (17).

The tetrahydrocarboline *N*-oxide (13) undergoes 1,3-dipolar cycloaddition with refluxing phenyl isocyanate in dimethylformamide to give 1-anilino-6,7,8,9-tetrahydro-γ-carboline (18). No reaction was observed when chloroform was used as solvent and no product was obtained when the reaction (in dimethylformamide) was attempted with 1,7-diazaindene 7-oxide. In this and other examples cited, the 4-position of 1,5-diazaindene 5-oxide is more susceptible to nucleophilic attack then the 6-position of 1,7-diazaindene 7-oxide.

[9] L. Stephenson and W. K. Warburton, *J. Chem. Soc.* (*C*), 1970, 1355.

EXPERIMENTAL

I.r., n.m.r., and mass spectra were recorded as described in Part V.[1]

1,7-*Diazaindene* 7-*Oxide Hydrochloride* (1H-*Pyrrolo*[2,3-b]-*pyridine* 7-*Oxide Hydrochloride*) (20).—1-Acetyl-1,7-diazaindene [3] (1·45 g) in dichloromethane (7 ml) was added to a solution of *m*-chloroperoxybenzoic acid (4·4 g) in dichloromethane (55 ml). After 5 days the solid was removed, the filtrate (A) extracted with 3M-hydrochloric acid (3 × 25 ml), and the aqueous solution evaporated to dryness. The residue was dissolved in hot ethanol (charcoal) and was crystallised from ethanol–ethyl acetate and then ethanol–benzene to give 1,7-*diazaindene* 7-*oxide hydrochloride* (1·1 g, 74%), m.p. 162—164° (Found: C, 49·5; H, 4·4. $C_7H_7ClN_2O$ requires C, 49·3; H, 4·1%), $\nu_{max.}$ 3099 (NH) and 2480 (OH) cm^{-1}, δ [$(CD_3)_2SO$] 13·43 (1H, s, exchanged with D_2O, NH), 10·93 (1H, s, exchanged with D_2O, OH), 8·68 (1H, d, *J* 6·0 Hz, 6-H), 8·43 (1H, d, *J* 8·0 Hz, 4-H), 7·83 (1H, d, *J* 3·4 Hz, 2-H), 7·43 (1H, q, *J* 6·0 and 8·0 Hz, 5-H), and 6·9 (1H, d, *J* 3·4 Hz, 3-H).

1,7-*Diazaindene* 7-*Oxide* (1H-*Pyrrolo*[2,3-b]*pyridine* 7-*Oxide*) (6).—*Method* 1. The filtrate (A) obtained as described in the foregoing reaction was evaporated to dryness and the residue dissolved in saturated aqueous sodium carbonate. Continuous extraction with chloroform afforded 1,7-*diazaindene* 7-*oxide* (30—80%), m.p. 134—135° (from benzene) (Found: C, 62·5; H, 4·7. $C_7H_6N_2O$ requires C, 62·8; H, 4·5%), $\nu_{max.}$ 3275 (NH) cm^{-1}, δ [$(CD_3)_2SO$] 12·50 (1H, s, exchanged with D_2O, NH), 8·18 (1H, d, *J* 6·0 Hz, 6-H), 7·70 (1H, d, *J* 8·0 Hz, 4-H), 7·51 (1H, d, *J* 3·6 Hz, 2-H), 7·12 (1H, q, *J* 7·0 and 8·0 Hz, 5-H), and 6·58 (1H, d, *J* 3·6 Hz, 3-H).

Method 2. The hydrochloride (1·1 g) was dissolved in the minimum volume of water and the solution basified to pH 9 with saturated potassium carbonate solution. The oxide (0·55 g, 64%) formed as an oil which quickly solidified.

6-*Acetoxy*-1-*acetyl*-1,7-*diazaindene* (6-*Acetoxy*-1-*acetyl*-1H-*pyrrolo*[2,3-b]*pyridine*) (7).—1,7-Diazaindene 7-oxide (1·0 g), anhydrous sodium acetate (0·5 g), and acetic anhydride (25 ml) were refluxed for 7 h. The solution was cooled, the sodium acetate filtered off, acetic anhydride distilled off, water added to the cooled residue, and the mixture heated on a water-bath. The precipitated solid was filtered off, washed with ethanol, and crystallised from ethanol to give 6-*acetoxy*-1-*acetyl*-1,7-*diazaindene* (0·46 g, 62%) m.p. 125—126° (subl.) (Found: C, 60·5; H, 4·74; N, 13·2. $C_{11}H_{10}N_2O_3$ requires C, 60·6; H, 4·59; N, 12·8%), $\nu_{max.}$ 1760 (CO) and 1711 cm^{-1} (CO), δ ($CDCl_3$) 7·97 (1H, d, *J* 4·5 Hz, 2-H), 7·93 (1H, d, *J* 8·3 Hz, 4-H), 6·95 (1H, d, *J* 8·3 Hz, 5-H), 6·60 (1H, d, *J* 4·5 Hz, 3-H), 3·00 (3H, s, OAc), and 2·37 (3H, s, Ac).

1,7-*Dihydro*-1,7-*diazainden*-6-*one* (1,7-*Dihydropyrrolo*[2,3-b]*pyridin*-6-*one*) (26).—6-Acetoxy-1-acetyl-1,7-diazaindene (2·2 g) was warmed with dilute hydrochloric acid (15 ml; 5%) on a boiling water-bath for 1·5 h under nitrogen. Solid was filtered from the hot mixture and the filtrate evaporated

[10] R. R. Lorenz, B. F. Tullar, C. F. Koelsch, and S. Archer, *J. Org. Chem.*, 1965, **30**, 2531.

[11] R. E. Willette, *Adv. Heterocyclic Chem.*, 1968, **9**, 27.

to dryness under reduced pressure. The residue (0·13 g, 96%) was sublimed at 150° and 0·04 mmHg to give 1,7-dihydro-1,7-diazainden-6-one, m.p. 228—230° (lit.,[5] 226—226·5°), $\nu_{max.}$ 3325 (NH) and 1655 (CO) cm^{-1}.

6-*Chloro*-1,7-*diazaindene* (6-*Chloropyrrolo*[2,3-b]*pyridine*) (9).—The ketone (26) (0·66 g) and phosphoric trichloride (5 ml) were heated at 170—180° for 5 h. Water was added and the dark solid filtered off. The filtrate was basified to pH 10 with saturated potassium carbonate solution to give 6-*chloro*-1,7-*diazaindene* (0·3 g, 40%); a sample prepared by sublimation at 110° and 0·1 mmHg had m.p. 170—171° (subl.) (Found: N, 18·1. $C_7H_5ClN_2$ requires N, 18·4%), $\nu_{max.}$ 3200 cm^{-1} (NH), δ [$(CD_3)_2SO$] 11·88 (1H, s, exchanged with D_2O, NH), 8·03 (1H, d, *J* 8·3 Hz, 4-H), 7·52 (1H, m, 2-H), 7·12 (1H, d, *J* 8·3 Hz, 5-H), and 6·50 (1H, m, 3-H) (each multiplet became a doublet (*J* 3·8 Hz) after the addition of D_2O).

4-*Chloro*-1,7-*diazaindene* (4-*Chloropyrrolo*[2,3-*b*]*pyridine*) (8).—1,7-Diazaindene 7-oxide (1·0 g) was added in portions to cooled phosphoric trichloride (10 ml) and the mixture then gently refluxed for 5 h. Phosphoric trichloride was then distilled off under reduced pressure and water (10 ml) was added to the cooled residue. The solution was basified with sodium carbonate, and after 1 h the precipitate was filtered off. The dry solid was sublimed at 110° and 0·25 mmHg to give 4-*chloro*-1,7-*diazaindene* (0·7 g, 62%), m.p. 175—176·5° (Found: C, 55·1; H, 3·8; N, 17·9. $C_7H_5ClN_2$ requires C, 55·1; H, 3·3; N, 18·4%), $\nu_{max.}$ 3145 cm^{-1} (NH), δ [$(CD_3)_2SO$] 12·10 (1H, s, exchanged with D_2O, NH), 8·23 (1H, d, *J* 5·1 Hz, 6-H), 7·63 (1H, d, *J* 3·4 Hz, 2-H), 7·22 (1H, d, *J* 5·1 Hz, 5-H), and 6·55 (1H, d, *J* 3·4 Hz, 3-H).

5-*Acetyl*-6,7,8,9-*tetrahydro*-γ-*carboline* (11).—6,7,8,9-Tetrahydro-γ-carboline[6] (25 g) and acetic anhydride (125 ml) were heated on a water-bath for 2 h. The *acetyl derivative* was filtered off from the cold mixture and crystallised from ethanol; yield 25 g (81%), m.p. 152·5—154° (Found: C, 72·7; H, 6·5; N, 12·7. $C_{13}H_{14}N_2O$ requires C, 72·8; H, 6·55; N, 13·1%), $\nu_{max.}$ 1709 cm^{-1} (CO), δ ($CDCl_3$) 8·58 (1H, s, 5-H), 8·32 (1H, d, *J* 6·0 Hz, 3-H), 7·73 (1H, d, *J* 6·0 Hz, 2-H), 2·87 (2H, m, CH_2), and 1·81 (4H, m, 2 × CH_2).

5-*Acetyl*-6,7,8,9-*tetrahydro*-γ-*carboline* 2-*Oxide* (12).—5-Acetyl-6,7,8,9-tetrahydro-γ-carboline (1·6 g) in dichloromethane (20 ml) and *m*-chloroperoxybenzoic acid (3·7 g) in dichloromethane (40 ml) were mixed. After 16 days at room temperature the solvent was removed under reduced pressure and the residue dissolved in a solution of sodium carbonate (1·4 g) in water (10 ml). Continuous extraction of the aqueous solution with chloroform and evaporation of the dried ($MgSO_4$,H_2O) extract gave the 2-*oxide* (12) (1·5 g, 93%), m.p. 193—194° (from benzene) (Found: C, 67·5; H, 5·9; N, 11·8. $C_{13}H_{14}N_2O_2$ requires C, 67·8; H, 6·1; N, 12·2%), $\nu_{max.}$ 1692 cm^{-1} (CO), δ ($CDCl_3$) 8·37 (1H, s, 1-H), 8·13 (1H, s, 1p, 3-H), 7·33 (1H, s, 4-H), 3·00 (2H, m, CH_2), 2·67 (3H, s, CH_3), 2·63 (2H, m, CH_2), and 1·93 (2H, m, 2 × CH_2).

6,7,8,9-*Tetrahydro*-γ-*carboline* 2-*Oxide* (13).—Compound (12) (1·5 g) and 3M-sodium hydroxide (15 ml) were heated on a water-bath for 0·5 h. The cold solution was extracted with chloroform and the extract dried ($MgSO_4$,H_2O) and evaporated; the residue crystallised from ethanol to yield the 2-*oxide* (13) (0·12 g, 80%), m.p. 262—264° (Found: N, 14·6%; M^+, 188·0952. $C_{11}H_{12}N_2O$ requires N, 14·9%; *M*, 188·0950), $\nu_{max.}$ 3085 (NH) cm^{-1}.

5-*Acetyl*-2,5,6,7,8,9-*hexahydro*-γ-*carboline*-1-*one* (23).—6,7,8,9-Tetrahydro-γ-carboline 2-oxide (2·3 g), anhydrous sodium acetate (1·1 g), and acetic anhydride (50 ml) were refluxed for 3 h. The solution was cooled, the solid removed and the liquid evaporated to dryness under reduced pressure. Addition of water to the residue gave a solid which crystallised from ethanol as the *lactam* (23) (2·2 g, 78%), m.p. 242—244° (Found: C, 67·5; H, 6·2; N, 12·0. $C_{13}H_{14}N_2O_2$ requires C, 67·8; H, 6·1; N, 12·2%), $\nu_{max.}$ 3149 (NH), 1707 (CO), and 1651 (CO) cm^{-1}, δ [$(CD_3)_2SO$] 11·20 (1H, s, exchanged with D_2O, NH), 7·03 (2H, s, 3- and 4-H), 2·85 (4H, m, 2 × CH_2), 2·63 (3H, s, CH_3), and 1·73 (4H, m, 2 × CH_2).

2,5,6,7,8,9-*Hexahydro*-γ-*carbolin*-1-*one* (24).—The ketone (23) (0·16 g), methanol (20 ml), and 3N-sodium hydroxide (5 ml) were refluxed for 2 h. The methanol was distilled off and water added to the residue. The solid was filtered off and crystallised from ethanol to give the *amide* (24), m.p. 340—342° (Found: C, 70·5; H, 6·2; N, 15·2. $C_{11}H_{12}N_2O$ requires C, 70·2; H, 6·4; N, 14·9%), $\nu_{max.}$ 3260 (NH), 3208 (NH), and 1629 (CO) cm^{-1}, δ [$(CD_3)_2SO$] 12·05 (1H, s, exchanged with D_2O, NH), 11·53 (1H, s, exchanged with D_2O, NH), 7·50 (1H, d, *J* 8·0 Hz, 3-H), 6·83 (1H, d, *J* 8·0 Hz, 4-H), 2·97 (4H, m, 2 × CH_2), and 1·88 (4H, m, 2 × CH_2).

1-*Chloro*-6,7,8,9-*tetrahydro*-γ-*carboline* (14).—*Method* 1. 1-Acetyl-2,5,6,7,8,9-hexahydro-γ-carboline-1-one (0·48 g) and phosphoric trichloride (10·0 ml) were refluxed for 2 h. Phosphoric trichloride was distilled off and water (6 ml) added to the residue. The precipitate (0·3 g) was filtered off and washed, and the combined filtrate and washings were basified with saturated potassium carbonate solution. The mixture was heated on a water-bath for 10 min. The cold solution deposited a solid (0·1 g). The combined solids (95%) were crystallised from ethanol to afford 1-*chloro*-6,7,8,9-*tetrahydro*-γ-*carboline*, m.p. 259—260° (subl.) (Found: C, 64·2; H, 5·5; Cl, 16·9; N, 13·4. $C_{11}H_{11}ClN_2$ requires C, 63·9; H, 5·3; Cl, 17·2; N, 13·5%), $\nu_{max.}$ 3150 (NH) cm^{-1}, δ [$(CD_3)_2SO$] 12·90 (1H, s, exchanged with D_2O, NH), 8·75 (1H, d, *J* 6·0 Hz, 3-H), 8·08 (1H, d, *J* 6·0 Hz, 4-H), 3·10 (4H, m, 2 × CH_2), and 2·00 (4H, m, 2 × CH_2).

Method 2. A similar procedure with the *N*-oxide (24) (0·5 g) and phosphoric trichloride (5 ml) gave the crude chloro-compound in 55% yield.

Method 3. 5-Acetyl-6,7,8,9-tetrahydro-γ-carboline 2-oxide (0·5 g) and phosphoric trichloride (5 ml) similarly yielded the crude chloro-compound (75%).

1-(2-*Isopropylidenehydrazino*)-6,7,8,9-*tetrahydro*-γ-*carboline* (15).—1-Chloro-6,7,8,9-tetrahydro-γ-carboline (1·3 g), hydrazine hydrate (1·5 ml; 98%), and methylcellosolve (20 ml) were refluxed for 24 h. Solid impurities were filtered from the cold mixture and the filtrate was evaporated to dryness. The residue was extracted with hot water to remove hydrazine hydrochloride and the remaining solid was crystallised from ethanol to yield 1-chloro-6,7,8,9-tetrahydro-γ-carboline (30 mg). The ethanolic filtrate was evaporated to dryness, acetone was added, and the mixture was warmed. Evaporation, and crystallisation of the residue from ethanol afforded the *hydrazino-derivative* (15) (0·25 g, 17%), m.p. 154—155° (Found: C, 69·7; H, 7·6. $C_{14}H_{18}N_4$ requires C, 69·4; H, 7·5%), $\nu_{max.}$ 3300 (NH) and 3148 (NH) cm^{-1}, δ [$(CD_3)_2SO$] 12·73 (1H, s, exchanged with D_2O, NH), 7·63 (1H, d, *J* 7·0 Hz, 3-H), 7·13 (1H, d, *J* 7·0 Hz, 4-H), 4·30br (1H, s, exchanged with D_2O, NH·N:), 3·00 (2H, m, CH_2), 2·73 (2H, m, CH_2), 2·17 [6H, s, splits into 2 singlets (each 3H) on addition of D_2O, Me_2C], and 1·80 (4H, m, 2 × CH_2).

6,7,8,9-*Tetrahydro*-γ-*carboline*-1-*carbonitrile* (16).—*Method* 1. 5-Acetyl-6,7,8,9-tetrahydro-γ-carboline 2-oxide (1·1 g) was dissolved in chloroform (15 ml) and benzoyl chloride (1·4 ml) was added dropwise with stirring. Silver cyanide

(1·5 g) was added and the mixture stirred and refluxed for 48 h. Silver cyanide was filtered from the cold mixture and the filtrate evaporated to dryness. The residue was basified with 3M-sodium hydroxide and warmed on a water-bath for 1 h. The cooled solution deposited the ***nitrile*** (16) (0·32 g, 34%), m.p. 236—237° (from ethanol) (subl.) (Found: C, 73·2; H, 6·0; N, 20·7. $C_{12}H_{11}N_3$ requires C, 73·1; H, 5·6; N, 21·3%), $\nu_{max.}$ 3190 (NH) and 2275 (CN) cm^{-1}, δ [$(CD_3)_2SO$] 11·80 (1H, s, exchanged with D_2O, NH), 8·24 (1H, d, *J* 5·7 Hz, 3-H), 7·53 (1H, d, *J* 5·7 Hz, 4-H), 2·80 (4H, m, 2 × CH_2), and 1·85 (4H, m, 2 × CH_2).

Method 2. 6,7,8,9-Tetrahydro-γ-carboline 2-oxide also yielded the nitrile (38%) by a similar procedure.

Method 3. 6,7,8,9-Tetrahydro-γ-carboline 2-oxide (0·18 g), potassium cyanide (0·33 g), and acetic anhydride (5 ml) were refluxed for 5 h. The solvent was distilled off and dilute aqueous ammonia was added to the residue. The solid was collected and dried, and then extracted with chloroform (Soxhlet). The extract was passed through a column of basic alumina with chloroform as solvent to give the nitrile (47%).

5-*Acetyl*-1-*diacetylaminomethyl*-6,7,8,9-*tetrahydro*-γ-*carboline* (17).—The nitrile (16) (0·3 g), anhydrous sodium acetate (1 g), and acetic anhydride (20 ml) were shaken at 70° in the presence of Raney nickel (0·1 g) and hydrogen (initial pressure 3 atm) for 2 h. The solid was removed from the cold mixture and the solution evaporated to dryness under reduced pressure. Water was added to the residue and the solid was filtered off and washed with water and ethanol. Crystallisation from dimethyl sulphoxide gave the ***imide*** (17) (0·11, 25%), m.p. 200—200·5° (Found: C, 65·7; H, 6·5; N, 12·8. $C_{18}H_{21}N_3O_3$ requires C, 66·0; H, 6·4; N, 12·8%), $\nu_{max.}$ 1700 (CO) cm^{-1}, δ [$(CD_3)_2SO$] 8·28 (1H, d, *J* 5·6 Hz, 3-H), 7·95 (1H, d, *J* 5·6 Hz, 4-H), 5·42 (2H, s, ·CH_2·NH·), 3·02 (4H, m, 2 × CH_2), 2·72 (3H, s, 1-Ac), 2·37 (6H, s, 2 × CH_3), and 1·83 (4H, m, 2 × CH_2).

1-*Anilino*-6,7,8,9-*tetrahydro*-γ-*carboline* (18).—A suspension of 6,7,8,9-tetrahydro-γ-carboline 2-oxide (0·28 g) in dry dimethylformamide (8 ml) was mixed with phenyl isocyanate (0·18 g) in dimethylformamide (2 ml) and refluxed under nitrogen for 3 h. The cold solution deposited the oxide (13) (0·1 g), which was filtered off. The filtrate was concentrated to small volume under reduced pressure and water was added. The precipitated 5-*anilino*-6,7,8,9-*tetrahydro*-γ-*carboline* (0·18 g, 46%) was crystallised from ethanol; m.p. 223—224° (Found: C, 77·5; H, 6·5; N, 15·9. $C_{17}H_{17}N_3$ requires C, 77·6; H, 6·5; N, 16·0%), $\nu_{max.}$ 3249 (NH) and 3100 (NH) cm^{-1}, δ [$(CD_3)_2SO$] 11·00 (1H, s, exchanged with D_2O, NH), 7·6—6·8 (5H, m, Ph), 7·68 (1H, d, 3-H), 6·82 (1H, d, *J* 5·6 Hz, 4-H), 1·97 (2H, m, CH_2), 1·67 (2H, m, CH_2), and 1·81 (4H, m, 2 × CH_2).

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