Synthesis and Stability of 2-Methyl-2,4-diaza- and 2-Methyl-2,5-diazaindene † (2-Methyl-pyrrolo[3,4-*b*]pyridine and -pyrrolo[3,4-*c*]pyridine)

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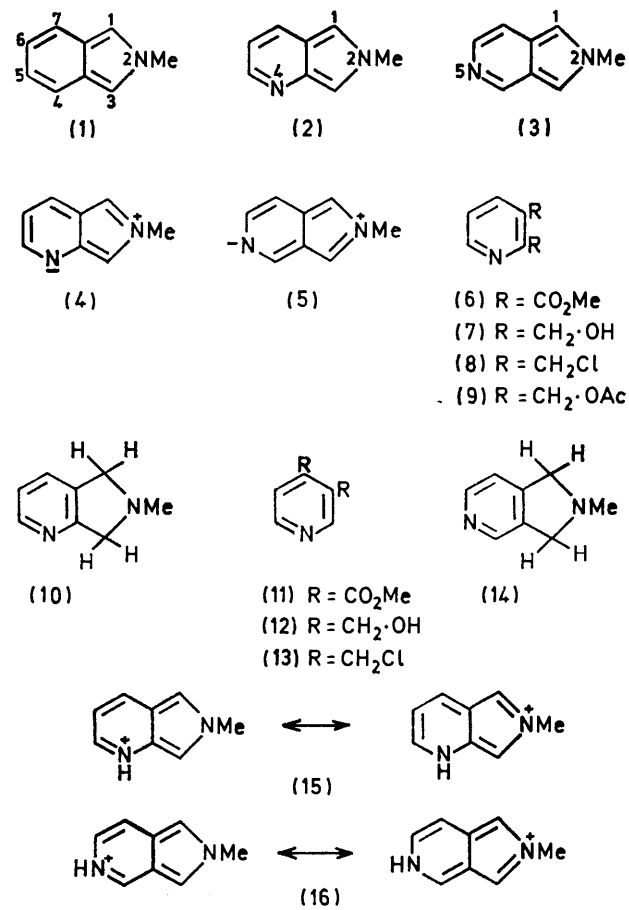
2-Methyl-2,4-diaza- (2) and 2-methyl-2,5-diaza- (3) indenes have been prepared by oxidation of 2,3-dihydro-2-methyl-1*H*-2,4-diaza- (10) and 2,3-dihydro-2-methyl-1*H*-2,5-diaza- (14) indene, respectively with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. They are more stable than 2-methyl-2-azaindene (1) in dilute acid, as neutral species in aqueous solution, and to aerial oxidation, and form stable picrates. The two diazaindenes (2) and (3) are relatively strong bases; and although protonation occurs predominantly on N-4 and N-5, respectively, to form resonance-stabilised cations, the ease of exchange of H-1 and H-3 (the former being greater) by deuterium in dilute acid, suggests that some protonation also takes place on C-1 and C-3, separately, as in 2-methyl-2-azaindene. The n.m.r. chemical shifts of H-1 and H-3 in the three azaindenes (1)—(3) indicate that they are aromatic systems.

ISOINDOLE (2-azaindene) has been shown to be unstable, but its existence as a transient intermediate has been confirmed by trapping as the Diels–Alder adducts with maleic acid and *N*-phenylmaleimide.[1] 2-Methylisoindole (2-methyl-2-azaindene) (1), on the other hand, has been isolated in crystalline form. Although it is more stable than isoindole, it deteriorates at room temperature and darkens rapidly in solution.[2] We have now studied the analogues, 2-methyl-2,4-diaza- (2) and 2-methyl-2,5-diaza- (3) indene; the insertion of the extra nitrogen atom was expected to make the system more stable [see resonance structures (4) and (5)]. Also, electron withdrawal by the inserted nitrogen atom presumably makes the pyrrole ring less reactive towards electrophilic attack, which is most probably the basis of its instability. Stable isoindoles with one and two nitrogen atoms in the benzene ring have been prepared but these examples had several substituents in one or both rings and were not compared directly with the benzene analogues.[3-5] Isoindoles with several substituents (*e.g.* methoxycarbonyl, alkyl, aryl, benzo) are known to be more stable than the parent compound.[6] We have synthesised the diazaindenes (2) and (3) and have found, by direct comparison, that they are more stable than 2-azaindene (2-methylisoindole).

Dimethyl pyridine-2,3-dicarboxylate (6) was reduced with lithium aluminium hydride to the corresponding diol (7). The crude diol was converted into the unstable hydrochloride of 2,3-bischloromethylpyridine (8), which when treated with an excess of ethanolic methylamine at room temperature formed 2,3-dihydro-2-methyl-1*H*-2,4-diazaindene (10). Dehydrogenation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone gave 2-methyl-2,4-diazaindene (2) in 21% yield. This reaction was carried out according to the method recently described for the dehydrogenation of dimethyl 2,3-dihydro-1*H*-2-azaindene-1,3-dicarboxylates with tetrachloro-1,4-benzoquinone.[7] Similarly dimethyl pyridine-3,4-dicarboxylate (11) was converted into 2-methyl-2,5-diazaindene (3) *via* the intermediates (12), (13), and (14). The higher yield (50%) in the last step of this synthesis compared with the previous one is attributed to the greater stability of the isomer (3) compared with (2) at the high pH values used in the isolation of the free bases.



† The azaindene terminology is used to facilitate comparisons between isoindoles and the analogous pyrrolopyridines.

[1] R. Kreher and J. Seubert, *Z. Naturforsch.*, 1965, **20***b*, 75.
[2] G. Wittig, H. Tenhaeff, W. Schoch, and G. Koenig, *Annalen*, 1951, **572**, 1.
[3] E. Benary, *Ber.*, 1918, **51**, 567.
[4] R. C. Anderson and R. H. Fleming, *Tetrahedron Letters*, 1969, 1581.
[5] R. Kreher and G. Vogt, *Angew. Chem. Internat. Edn.*, 1970, **9**, 955.
[6] J. D. White and M. E. Mann, *Adv. Heterocyclic Chem.*, 1969, **10**, 113.
[7] G. Cignarella and A. Saba, *Ann. Chim.* (*Italy*), 1970, **60**, 765.

The two diazaindenes (2) and (3) are stable crystalline solids which can be recrystallised and sublimed and form stable monopicrates. These can be stored at room temperature without appreciable deterioration and are unchanged when kept at 0° for a few months. They are unaltered when kept in deuteriochloroform solution for at least 2 days. In comparison, 2-methyl-2-azaindene darkens rapidly, and decomposes on treatment with picric acid in ethanol or benzene. In deuteriochloroform solution containing 2-methyl-2-azaindene a brown colour is formed at the air–solution interface after 15 min at 33° which is most probably caused by aerial oxidation. The diazaindenes did not give adducts similar to those of 2-methyl-2-azaindene with maleic anhydride.

The diazaindenes (2) and (3) are relatively strong bases, pK_a (water) 6·46 and 8·67, respectively. No difficulty was experienced in obtaining these values, each of which is the mean of at least seven measurements. They are stronger bases than pyridine (5·29) [8] and 1*H*-1-pyrindene (5·7; [9] note that the pK_a value of 8·7 for 1-methyl-1*H*-1-pyrindene is meaningless [10]). The increase in basic strength, which is contrary to what would be expected on making the system more π-deficient [11] by inserting a nitrogen atom into the benzene ring of 2-methyl-2-azaindene (estimated pK_a <0; *cf.* pK_a of 1-methylpyrrole,[8] −2·90), can be explained by the greater resonance stabilisation in the cations (15) and (16) compared with the neutral species (4) and (5), respectively. The u.v. spectra of the neutral species (pH 11) and cations (pH 4) of the diazaindenes (2) and (3) in aqueous buffers have three main bands (see Experimental section) and are in this respect similar to the spectrum of 2-methyl-2-azaindene (1) in water at pH 6·8. However, the spectra of the diazaindenes are barely altered after 2 days at 20°, whereas the spectrum of 2-methyl-2-azaindene changes immediately on mixing the solution and after 18 h the solution

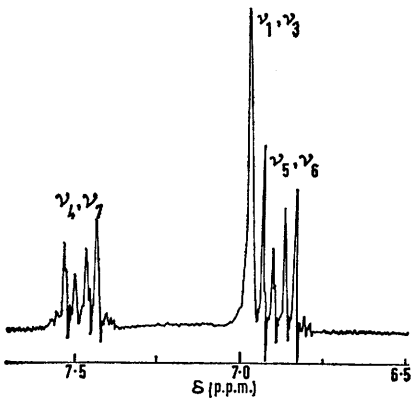


FIGURE 1 ^{1}H N.m.r. spectrum of 2-methyl-2-azaindene (1) ($CDCl_3$; 100 MHz); the methyl signal is not shown

darkens and strong absorption appears between 220 and 380 nm (see Experimental section).

[8] D. D. Perrin, 'Dissociation Constants of Organic Bases in Aqueous Solution,' Butterworths, London, 1965.

The ^{1}H n.m.r. spectra of 2-methyl-2-azaindene and the diazaindenes in deuteriochloroform are shown in Figures 1—3. The assignments of peaks and coupling

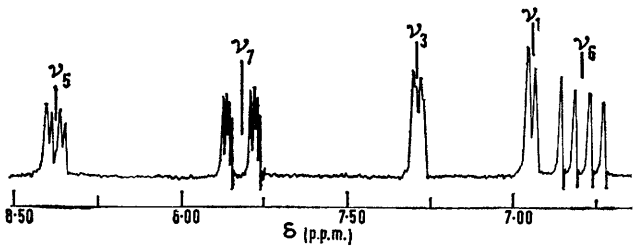


FIGURE 2 ^{1}H N.m.r. spectrum of 2-methyl-2,4-diazaindene (2) ($CDCl_3$; 100 MHz); the methyl signal is not shown

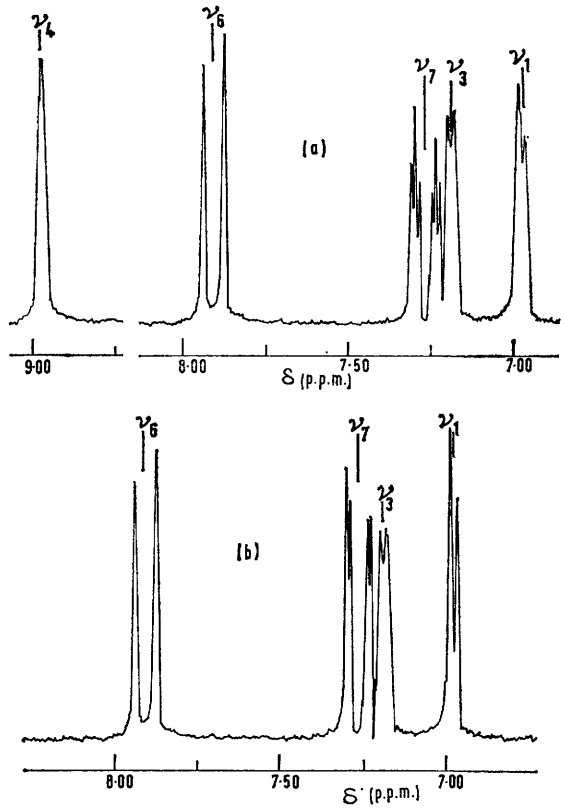


FIGURE 3 (a) ^{1}H N.m.r. spectrum of 2-methyl-2,5-diazaindene (3) ($CDCl_3$; 100 MHz); (b) decoupled spectrum obtained by irradiation at frequency of H-4 (the methyl signals are not shown)

constants are straightforward except for those of H-1 and H-3 in 2-methyl-2,5-diazaindene. In this case the upfield multiplet is from H-1; irradiation at the H-4 resonance frequency causes the multiplet from H-1 to collapse to a sharp doublet (still coupled with H-3). The coupling constants of 2-methyl-2-azaindene are too complex for first-order analysis. Like isobenzo-

[9] C. B. Reese, *J. Amer. Chem. Soc.*, 1962, **84**, 3979.
[10] A. G. Anderson, jun., and H. L. Ammon, *Tetrahedron*, 1967, **23**, 3601.
[11] A. Albert, 'Heterocyclic Chemistry,' Athlone Press, London, 1968, p. 67.

furan,[12] the chemical shifts of the signals from H-1 and H-3 of the three azaindenes are in the aromatic region and suggest that the five-membered rings are sustaining a ring current. The spectra of the diazaindenes in 0·5N-deuterium chloride in deuterium oxide (pH *ca.* 1) showed the characteristic downfield shifts and it was clear that exchange of H-1 and H-3 by deuterium was taking place. The exchange reactions took place as follows: 2-methyl-2,4-diazaindene, H-1 (90%), H-3 (0%) after 15 min; H-1 (100%), H-3 (80%) after 2 h; H-1 (100%), H-3 (100%) after 19 and 26 h; 2-methyl-2,5-diazaindene, H-1 (30%), H-3 (0%) after 5 min; H-1 (100%), H-3 (20%) after 2 h; H-1 (100%), H-3 (100%) after 19 and 26 h. The signals (and particularly the sharp signals from the methyl group) in the remainder of the spectra remained unchanged during this period, indicating that no appreciable chemical changes had occurred. Cations of the type (17) and (18) are probably formed in acid solution, with isomer (17) being more favoured than isomer (18), and account for the deuterium exchange. 2-Methyl-2-azaindene, on the other hand, became black and polymerised as soon as the dilute deuteriated acid was added to it. However, in concentrated deuteriosulphuric acid the spectrum can be assigned to the cation (19) with the signals from H-1 and NMe appearing at δ 4·68 and 3·50 p.p.m., respectively (*cf.* tetramethyl-2-azaindene cation in ref. 13); the colour of this solution darkened but the spectrum remained unchanged during 24 h.

The mass spectra of the azaindenes (1)—(3) are similar to one another and the molecular ion peaks are the base peaks. The second most intense peak corresponds to $M^+ - 1$ and is only 30% of the base peak indicating that the molecular ions are very stable. In the three compounds fragmentation takes place by loss of CH_3^+ and HCN^+. In comparison the dihydro-derivatives (10) and (14) give intense base peaks at *m/e* **133** attributable to cations such as (15) and (16) or (17) or (18), which lose CH_3^+ and HCN^+. 2,3-Dihydro-2,2-dimethyl-1*H*-2,5-diazaindene (20) also gives an intense base peak at *m/e* **133**.

Several unsuccessful attempts to synthesise 2,4- and 2,5-diazaindenes were made and will be described briefly. 2-Methylpyrrolo[3,4-*b*]quinoxaline was prepared in high yield by dissolving 2,3-bisbromomethylquinoxaline 1-oxide in anhydrous methylamine at −80°.[4] Similar treatment of 2,3-bisbromomethylpyridine 1-oxide hydrobromide (21), however, did not

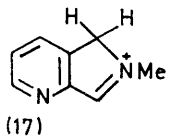
Proton magnetic resonance spectra of pyridines and azaindenes (60 MHz; 33°; δ in p.p.m.; *J* in Hz) [a]

Pyridine	H-1	H-2	H-2	H-4	H-5	H-6	H-7	Other H	Solvent
2,3-Dimethoxycarbonyl-				8·22(q, $J_{4,6}$ 1·5, $J_{4,5}$ 7·5)	7·52(q, $J_{5,4}$ 7·5, $J_{5,6}$ 5·3)	8·81(q, $J_{6,4}$ 1·5, $J_{6,5}$ 5·3)		3·94(s, CH_3), 4·00(s, CH_3)	$CDCl_3$
2,3-Bis-hydroxymethyl- [b]				8·07(q, $J_{4,6}$ 1·5, $J_{4,5}$ 8)	7·57(q, $J_{5,4}$ 8, $J_{5,6}$ 6)	8·65(q, $J_{6,4}$ 1·5, $J_{6,5}$ 6)		4·82(s, CH_2), 4·87(s, CH_2),	D_2O [c]
2,3-Bisacetoxymethyl-				8·01(q, $J_{4,5}$ 9, $J_{4,6}$ 2)	7·50(q, $J_{5,4}$ 9, $J_{5,6}$ 5)	7·99(q, $J_{6,4}$ 2, $J_{6,5}$ 5)		5·38(s, CH_2), 5·46(s, CH_2), 2·16(s, CH_3)	$CDCl_3$
3,4-Dimethoxycarbonyl-		9·18(s)			7·58(d, $J_{5,6}$ 5·3)	8·95(d, $J_{6,5}$ 5·3)		3·97(s, CH_3)	$CDCl_3$
3,4-Bis-hydroxymethyl- [b]		8·48(s)			7·52(d, $J_{5,6}$ 5·4)	8·50(d, $J_{6,5}$ 5·4)		4·70(s, CH_2), 4·79(s, CH_2)	D_2O [c]
3,4-Bisacetoxymethyl-		8·64(s)			7·34(d, $J_{5,6}$ 6)	8·65(d, $J_{6,5}$ 6)		5·21(s, 2 × CH_2), 2·10(s, CH_3), 2·14(s, CH_3)	$CDCl_3$
3,4-Bischloromethyl- [b]		8·53(s)			7·30(d, $J_{5,6}$ 5)	8·52(d, $J_{6,5}$ 5)		4·65(s, 2 × CH_2)	$CDCl_3$
3-Methoxycarbonyl-4-methyl-		9·08(s)			7·16(d, $J_{5,6}$ 5·5)	8·56(d, $J_{6,5}$ 5·5)		2·58(s, C-CH_3), 3·90(s, OCH_3)	$CDCl_3$
3-Hydroxymethyl-4-methyl-		8·45(s)			7·04(d, $J_{5,6}$ 5·5)	8·25(d, $J_{6,5}$ 5·5)		2·29(s, C-CH_3), 4·63(s, CH_2O), 5·45(s, OH) [c]	$CDCl_3$
4-Hydroxymethyl-3-methyl-		8·25(s)			7·48(d, $J_{5,6}$ 5·5)	8·34(d, $J_{6,5}$ 5·5)		2·20(s, C-CH_3), 4·69(s, CH_2O), 5·17(s, OH) [c]	$CDCl_3$
2,4-Diazaindene									
2-Methyl-	6·95(d, $J_{1,3}$ 2·5)		7·29(q, $J_{3,1}$ 2·5, $J_{3,7}$ 1·0)		8·38(q, $J_{5,6}$ 4·2, $J_{5,7}$ 1·6)	6·80(q, $J_{6,5}$ 4·2, $J_{6,7}$ 8·7)	7·84(octet, $J_{7,3}$ 1·0, $J_{7,5}$ 1·6, $J_{7,6}$ 8·7)	3·99(s, N-CH_3)	$CDCl_3$ [f]
2-Methyl- (cation)	7·46br(s)		7·65br(s)		8·65(q, $J_{5,6}$ 8·5, $J_{5,7}$ 2)	7·26(q, $J_{6,5}$ 8·5, $J_{6,7}$ 6)	8·49(q, $J_{7,5}$ 2, $J_{7,6}$ 6)	4·16(s, N-CH_3)	0·5N-DCl-D_2O [c, g]
2,3-Dihydro-2-methyl-1*H*-	3·95(s)		3·95(s)		8·40(q, $J_{5,6}$ 5, $J_{5,7}$ 1·5)	7·06(q, $J_{6,5}$ 5, $J_{6,7}$ 7·8)	7·50(q, $J_{7,6}$ 1·5, $J_{7,5}$ 7·8)	2·63(s, N-CH_3)	$CDCl_3$
2,3-Dihydro-3-hydroxy-3-methyl-1-oxo-1*H*-4-oxide					8·40(t, [d] *J* 4·0)	7·57(d, [d] *J* 4·0)	7·57(d, [d] *J* 4·0)	1·82(s, C-CH_3), 6·58br(s, OH), [e] 9·34br (s, NH) [e]	$(CD_3)_2SO$
2,5-Diazaindene									
2-Methyl-	6·98br(d, $J_{1,3}$ 2, $J_{1,4}$ <1)		7·19br(d, $J_{3,1}$ 2, $J_{3,7}$ 0·9) [h]	8·95br(s, $J_{4,1}$ <1, $J_{4,7}$ 0·9) [h]		7·88(d, $J_{6,7}$ 6·2)	7·26(sextet, $J_{7,3}$ 0·9, [h] $J_{7,5}$ 0·9, [h] $J_{7,6}$ 6·2)	3·98(s, N-CH_3)	$CDCl_3$ [f]
2-Methyl- (cation)	7·50br(s)		8·06br(s)	9·09br(s)		7·75(d, $J_{6,7}$ 6·5)	7·63(d, $J_{7,6}$ 6·5)	4·20(s, N-CH_3)	0·5N-DCl-D_2O [c, g]
2,3-Dihydro-2-methyl-1*H*-	3·85(s)		3·85(s)	8·40(s)		8·35(d, $J_{6,7}$ 5)	7·07(d, $J_{7,6}$ 5)	2·54(s, N-CH_3)	$CDCl_3$
2,3-Dihydro-2,2-dimethyl-1*H*- (iodide)	5·04(s)		5·04(s)	8·68(s)		8·64(d, $J_{6,7}$ 5)	7·59(d, $J_{7,6}$ 5)	3·45[s, $N(CH_3)_3^+$]	D_2O
2-Methyl-2-azaindene	6·97(s)		6·97(s)	7·48(m) [i, j]	6·88(q) [i]	6·88(q) [i]	7·48(m) [i, j]	3·90(s, N-CH_3)	$CDCl_3$
(cation)	4·68(s)		8·58(s)	←		6·8—8·0(m)	→	3·50(s, N-CH_3)	D_2SO_4

[a] First-order analysis of spectra; tetramethylsilane as internal standard; coupling constants are from an expanded scale (error ±0·2). [b] These spectra are of the crude substances but do not contain other signals from impurities. [c] Sodium 3-(trimethylsilyl)propanesulphonate as internal standard. [d] This is a deceptively simply ABX spectrum. [e] Exchanged by D_2O. [f] At 100 MHz, see Figures. [g] pH *ca.* 1·0. [h] Value obtained from decoupled spectrum, and from measurement of signals from H-7. [i] Multiplet not amenable to first-order analysis. [j] A quartet which is further coupled with H-1 and H-3.

[12] R. N. Warrener, *J. Amer. Chem. Soc.*, 1971, **93**, 2346.
[13] C. O. Bender and R. Bonnett, *Chem. Comm.*, 1966, 198.

give the desired product (2). All attempts to reduce 2,3-dihydro-3-hydroxy-3-methyl-1*H*-2,4-diazainden-1-one 4-oxide (22) or its 4-deoxy-derivative in several steps in order to obtain 3-methyl-2,4-diazaindene were unsatisfactory because reduction of the pyridine ring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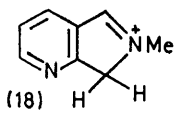
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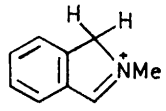
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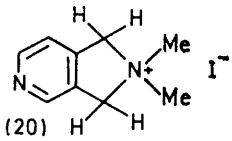
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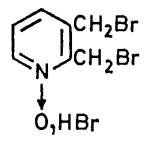
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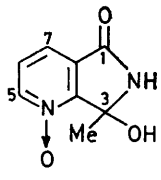
(22)

always occurred simultaneously with loss of oxygen. 2,3-Dihydro-2,2-dimethyl-1*H*-2,5-diazaindenium iodide (20) did not give the diazaindene (3) when treated with phenyl-lithium, a reagent which converts 2,3-dihydro-2,2-dimethyl-1*H*-2-azaindenium salts into 2-methyl-2-azaindenes in high yield.[2] This is probably because the reagent also adds across the C=N bond of the pyridine ring.[14] In earlier attempts at reducing dimethyl pyridine-3,4-dicarboxylate with sodium bis-(2-methoxyethoxy)aluminium hydride we isolated 4-hydroxymethyl-3-methylpyridine which was different from the known 3-hydroxymethyl-4-methylpyridine which we synthesised as described in the literature.[15]

EXPERIMENTAL

For general instrumentation see ref. 16. All extracts were dried over anhydrous sodium sulphate and evaporations were performed below 30° and at 20 mmHg. *J* Values are in Hz and tetramethylsilane was used as internal standard for ^{1}H n.m.r. spectra. I.r. spectra of solids (KBr discs) and liquids (films) were measured on a Perkin-Elmer 21 spectrometer.

2-Methyl-2-azaindene was prepared from 2,3-dihydro-2,2-dimethyl-1*H*-2-azaindenium iodide in ether and n-butyl-lithium in pentane in 58% yield (*cf.* lit. yields: 75% with phenyl-lithium;[2] 61 and 76% with methyl-lithium and benzyl-lithium [17]); *m/e* 132 (25%, $M^+ + 1$), 131 (100, M^+), 130 (30), 116 (24), 105 (9), 103 (10), 90 (12), 89 (20), 77 (10), and 63 (11). The u.v. spectrum in aqueous buffer at pH 6·8 after 4 s mixing had maxima at 216, 260 + 269, 320infl, and 386 nm; after 18 h the inflection at 320 nm had become a very broad band with a maximum at 327 nm, and the maxima at 260 and 269 nm had become an inflection. It could not be prepared by oxidation of 2,3-dihydro-2-methyl-1*H*-2-azaindene with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.

Dimethyl Pyridine-2,3-dicarboxylate.—To pyridine-2,3-dicarboxylic acid (50 g) in methanol (200 ml) at 0°, concentrated sulphuric acid (50 ml) was carefully added, and the mixture was heated on a steam-bath for 28 h. Excess of methanol was evaporated off and the cooled solution (ice-bath) was neutralised with saturated aqueous sodium carbonate. The solid that separated was collected and added to the chloroform extract of the filtrate. The dried extract gave the dimethyl ester (52 g, 89%), m.p. 55—56° (lit.,[18] 57—57·5° for material prepared from the acid and methanolic hydrogen chloride); $\nu_{max.}$ 1772 and 1302 (ester) cm^{-1}.

Similarly dimethyl pyridine-3,4-dicarboxylate, b.p. 104—105° at 0·8 mmHg, was obtained in 92% yield (lit.,[19] b.p. 95—100° at 15 mmHg); $\nu_{max.}$ 1730 and 1300 (ester) cm.$^{-1}$.

2,3-*Dihydro*-2-*methyl*-1H-2,4-*diazaindene* (10).—Dimethyl pyridine-2,3-dicarboxylate was reduced with lithium aluminium hydride in ether, as before.[20] 2,3-Bishydroxymethylpyridine was shown to be in the residue from the methanolic extract of the insoluble reduction product by conversion, with excess of acetic anhydride at 20° for 18 h, into 2,3-*bisacetoxymethylpyridine*, b.p. 128° at 1·1 mmHg (Found: C, 58·9; H, 6·0; N, 6·6. $C_{11}H_{13}NO_4$ requires C, 59·2; H, 5·9; N, 6·3%); $\nu_{max.}$ 1735 and 1235 (ester) cm.$^{-1}$. The crude diol (3·5 g), which could not be purified without decomposition, and thionyl chloride (20 ml) were heated under reflux for 30 min; the mixture was evaporated and the residue kept over potassium hydroxide *in vacuo* overnight. To the cooled (−20°) residue (containing 2,3-bischloromethylpyridine hydrochloride) suspended in methylene chloride (100 ml) was added cold 33% ethanolic methylamine (25 ml), and the mixture was shaken until all the black solid dissolved. The product was kept for 1 h at 0° and at 20° overnight, then 2N-sodium hydroxide saturated with sodium chloride was added and the mixture was extracted with methylene chloride. The dried extract was concentrated, passed through an alumina column (5 × 0·5 in; B.D.H.), and eluted with methylene chloride. Evaporation gave 2,3-*dihydro*-2-*methyl*-1H-2,4-*diazaindene*, b.p. 92° at 4 mmHg (1·9 g, 57%), as a hygroscopic oil which slowly darkened (Found: C, 71·5; H, 7·7; N, 20·8. $C_7H_{10}N_2$ requires C, 71·6; H, 7·5; N, 20·9%); $\nu_{max.}$ 2955, 2900, 2850 and 2784 (CH str.), 1607 (C=N str.), and 1590 (C=C str.) cm^{-1}; *m/e* 134 (40%, M^+), 133 (100, $M^+ - 1$), 118 (15), 106 (10), 92 (15), 79 (6), 78 (6), 77 (6), 65 (11), and 63 (11). The *dipicrate* had m.p. 206—207° (from methanol) (Found: C, 40·5; H, 2·8; N, 18·6. $C_{20}H_{16}N_8O_{14}$ requires C, 40·55; H, 2·7; N, 18·9%).

Similarly dimethyl (or diethyl) pyridine-3,4-dicarboxylate gave 3,4-*bisacetoxymethylpyridine*, m.p. 47—48° (from cyclohexane) (Found: C, 59·1; H, 6·2; N, 6·3%); $\nu_{max.}$

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1730 and 1245 cm^{-1}, except that it was purified *via* its *picrate*, m.p. 119—120° (from aqueous ethanol) (Found: C, 45·1; H, 3·8; N, 12·5. $C_{17}H_{16}N_4O_{11}$ requires C, 45·6 H, 3·5; N, 12·3%), which was passed through an alumina column and eluted with chloroform.

2,3-*Dihydro*-2-*methyl*-1H-2,5-*diazaindene* (14).—The crude 3,4-bishydroxymethylpyridine was similarly converted into 3,4-bischloromethylpyridine hydrochloride which, after passage through an alumina column in chloroform, gave crude 3,4-bischloromethylpyridine (strongly lachrimatory). This decomposed on attempted recrystallisation from benzene but gave a stable *picrate*, m.p. 141·5—142·5° (from ethanol) (Found: C, 38·4; H, 2·5; N, 13·6. $C_{13}H_{10}Cl_2N_4O_7$ requires C, 38·5; H, 2·5; N, 13·8%); δ[$(CD_3)_2SO$] 8·98 (s, H-2), 8·87 (d, H-6, *J* 7), 8·06 (d, H-5, *J* 7), 5·05 and 5·08 (2 × CH_2Cl), and 8·55 p.p.m. (s, picrate CH). Ethanolic methylamine and crude 3,4-bischloromethylpyridine hydrochloride as before gave 2,3-*dihydro*-*methyl*-1H-2,5-*diazaindene*, b.p. 60° at 1 mmHg (Found: C, 69·7; H, 7·6; N, 20·0. $C_8H_{10}N_2$,0·25H_2O requires C, 69·3; H, 7·6; N, 20·2%); $\nu_{max.}$ 2960, 2908, 2860, 2792 (CH str,), 1615, and 1580 (C=C str.), cm^{-1}; *m/e* 134 (37%, M^+), 133 (100), 118 (16), 106 (9), 92 (6·5), 77 (6), and 63 (11); its *dipicrate* had m.p. 214° (from water) (Found: C, 40·6; H, 2·7; N, 19·0%).

2,3-*Dihydro*-2,2-*dimethyl*-1H-2,5-*diazaindenium Iodide* (20).—The dihydro-derivative (14) (134 mg) in benzene (10 ml) was stirred with methyl iodide (144 mg, 1 mol. equiv.) for 16 h at 20° and the separated solid was collected and recrystallised from methanol–ether to give the *dimethyl iodide*, m.p. 206—207° (192 mg, 70%) (Found, C, 39·3; H, 4·9; N, 9·6. $C_9H_{13}IN_2$ requires C, 39·1; H, 4·7; N, 10·1%); *m/e* 150 (16%), 142 (49), 134 (28), 133 (100), 128 (53, HI^+), 127 (50, I^+), 118 (15), and 106 (18). The *dipicrate*, m.p. 190—191°, was prepared in water (Found: C, 41·1; H, 3·0; N, 18·3. $C_{21}H_{18}N_8O_{14}$ requires C, 41·6; H, 3·0; N, 18·45%).

2-*Methyl*-2,4-*diazaindene* (2).—The dihydro-derivative (10) (584 mg) in benzene (25 ml) under nitrogen was added to a solution of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (1·19 g, 1·1 mol. equiv.) in benzene (150 ml) and the mixture was stirred for 1·5 h at 20°. The black precipitate (1·5 g) was filtered off, washed with benzene, and dried *in vacuo*. The black solid was ground with aqueous 7N-ammonia (50 ml) and extracted with methylene chloride (6 × 50 ml). The extract was evaporated below 20° and at 18 mmHg, and the residue was extracted with cyclohexane at 40—50° (3 × 40 ml). The extract was evaporated until pale yellow needles crystallised out. These were washed with light petroleum (b.p. 40—60°) to give 2-*methyl*-2,4-*diazaindene*, m.p. 63° (121 mg, 21%) (Found: C, 72·4; H, 6·3; N, 21·4. $C_8H_8N_2$ requires C, 72·7; H, 6·1; N, 21·2%); $\nu_{max.}$ 3140, 1610, 1550, 1474, 1420, 1372, 1356, 1338, 1153, 1125, 996, 918, 794, 774, and 732 cm^{-1}; *m/e* 133 (10%, $M^+ - 1$), 132 (100, M^+), 131 (30), 117 (12), 104 (15), 91 (17), 79 (10), 78 (10), and 63 (18); pK_a (potentiometric [21]) 6·43 ± 0·05 (mean of seven points) and 6·49 ± 0·05 (mean of eight points in back-titration) at 10^{-3}M in water at 20°; u.v. (H_2O): neutral species at pH 11·0, $\lambda_{max.}$ (log ε) 227 (4·94), 286 (4·00) + 294 (3·99), and 356 (3·75), cation at pH 4·0, $\lambda_{max.}$ (log ε) 232 (4·52), 291 (4·05) + 297 (4·03), and 408 nm (3·42). The *picrate*, m.p. 216° (effervescence with darkening above 200°), was prepared in benzene, recrystallised from aqueous methanol, and dried at 80° for 2 h (Found: C, 46·7; H, 3·3; N, 19·2. $C_{14}H_{11}N_5O_7$ requires C, 46·5; H, 3·1; N, 19·4%).

2-*Methyl*-2,5-*diazaindene* (3).—This was similarly obtained as *needles*, m.p. 97—98° in higher yield (50%) by using aqueous 2N-sodium hydroxide to decompose the black quinol salt. It was purified by sublimation at 23° and 0·01 mmHg (Found: C, 72·6; H, 6·4; N, 21·3%); $\nu_{max.}$ 3120, 1616, 1598, 1367, 1342, 1243, 1181, 1142, 908, 812, and 763 cm^{-1}; *m/e* 133 (10%, M^+ + 1), 132 (100, M^+), 131 (30), 117 (23), 104 (10·5), 91 (10), 79 (7), and 63 (20); pK_a (spectrophotometric at 293 nm) [21] 8·67 ± 0·04 (mean of ten points), ionic strength 0·01 and at 0·49 × 10^{-4}M in water at 20°; u.v. (H_2O): neutral species at pH 11·0, $\lambda_{max.}$ (log ε) 223 (4·64), 260infl (3·37) + 273infl (3·22) + 282 (2·95), 342·5 (3·55); cation at pH 5·0, $\lambda_{max.}$ (log ε) 231 (4·62), 265 (3·55) + 283 (3·24), and 383 nm (3·50). The *picrate* had m.p. 194·5—195·5° (from ethanol) (Found, after drying at 80° for 2 h: C, 46·8; H, 3·4; N, 19·4%).

2,3-*Bisbromomethylpyridine* 1-*Oxide Hydrobromide* (21).—2·3-Bisacetoxymethylpyridine (3·7 g) in acetic acid (20 ml) and 30% hydrogen peroxide (4 ml) were heated at 80—90° for 3 h. More 30% hydrogen peroxide (4 ml) was added, heating was continued for 4 h, and the solution was then kept at 20° overnight and evaporated at 50° and 18 mmHg. The oily residue was dissolved in chloroform; the solution was shaken with saturated aqueous sodium carbonate, dried, and evaporated leaving a thick oil whose n.m.r. spectrum indicated that it was a 2 : 3 mixture of 2,3-bisacetoxymethylpyridine 1-oxide and 2,3-bis-hydroxymethylpyridine 1-oxide or 1,3-dihydrofuro[3,4-*b*]pyridine 4-oxide (2 g). This mixture (1·4 g) in 48% aqueous hydrobromic acid (10 ml) was heated under reflux for 3·5 h; the solution was then evaporated to dryness. The residue was kept over potassium hydroxide *in vacuo* overnight, then recrystallised from methanol–ether (1 : 15) to give 2,3-*bisbromomethylpyridine* 1-*oxide hydrobromide*, m.p. 156—157° (1·17 g, 26%) (Found, after drying at 90° for 1·5 h: C, 24·2; H, 2·7; Br, 62·2; N, 3·7. $C_7H_8Br_3NO$,0·75CH_3OH requires C, 24·1; H, 2·9; Br, 62·1; N, 3·6%); $\nu_{max.}$ 3040, 3009, 3005 (OH str.), 2035br, 1604 (C=N str.), and 1523 (C=C str.) cm^{-1}.

3-*Chloro*-3-*methylfuro*[3,4-b]*pyridine*-1(3H)-*one* N-*Oxide* (ψ-*Chloride of* 2-*Acetylnicotinic Acid* N-*Oxide*).—2-Acetylnicotonic acid *N*-oxide [22] (1·81 g) and thionyl chloride (6 ml) were heated under reflux for 30 min; the mixture was evaporated and the residue kept over potassium hydroxide *in vacuo* overnight. It was recrystallised from benzene to yield the ψ-*chloride* (1·65 g, 83%) as needles, m.p. 142—143° (effervescence) (Found: C, 48·0; H, 2·9; Cl, 18·1; N, 6·9. $C_8H_6ClNO_3$ requires C, 48·1; H, 3·0; Cl, 17·8; N, 7·0%); $\nu_{max.}$ 1800 cm^{-1} (C=O); δ[$(CD_3)_2SO$] 8·72 (q, H-5, *J* 1·5 and 6), 7·99 (q, H-7, *J* 1·5 and 8), 7·84 (q, H-6, *J* 6 and 8), and 2·38 p.p.m. (s, Me).

Similarly 3-*chloro*-3-*methylfuro*[3,4-b]*pyridin*-1(3H)-*one* (ψ-chloride of 2-acetylnicotinic acid) m.p. 81·5—82·5° was prepared (Found: C, 52·2; H, 3·4; N, 7·3. $C_8H_6ClNO_2$ requires C, 52·3; H, 3·3; N, 7·6%); $\nu_{max.}$ 1780 (C=O) cm^{-1}; δ($CDCl_3$) 8·98 (q, H-5, *J* 2 and 6), 8·26 (q, H-7, *J* 2 and 8), 7·60 (q, H-6, *J* 6 and 8), and 2·28 (s, CH_3).

2,3-*Dihydro*-3-*hydroxy*-3-*methyl*-1H-2,4-*diazainden*-1-*one* 4-*Oxide* (22).—The preceding ψ-chloride *N*-oxide (2·8 g) was shaken with saturated ethanolic ammonia (150 ml)

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for 2 h; the mixture was set aside at 20° for 2 days and evaporated to dryness. The residue was passed through an Amberlite column (100 ml; OH^- form) and eluted with aqueous 3N-ammonia to yield the *diazaindenone oxide* (2·2 g, 64%), m.p. 298—299° (decomp.) (from methanol) (Found: C, 53·3; H, 4·6; N, 15·5. $C_8H_8N_2O_3$ requires C, 53·3; H, 4·5; N, 15·55%); $\nu_{max.}$ 3425br (OH str.), 3270 (NH str.), 3110 (CH str.), 2690br (hydrogen-bonded OH or NH), and 1725 (C=O str.) cm^{-1}.

4-Hydroxymethyl-3-methylpyridine.—Sodium bis-(2-methoxyethoxy)aluminium hydride (70% in benzene; 35 ml) was added to dimethyl pyridine-3,4-dicarboxylate (10 g) in benzene (50 ml) under nitrogen. The mixture was boiled under reflux for 1 h and decomposed with saturated aqueous sodium chloride. The benzene layer was separated; the aqueous layer was extracted with chloroform and combined with the benzene layer, dried, and evaporated. The residue was purified by t.l.c. on alumina with chloroform–benzene (9 : 1) as solvent to give *4-hydroxymethyl-3-methylpyridine*, m.p. 81—82° (from cyclohexane) (385 mg, 6·1%), R_F 0·36 (Found: C, 66·0; H, 7·5; N, 10·7. $C_7H_9NO,0{\cdot}25H_2O$ requires C, 65·9; H, 7·5; N, 10·9%); $\nu_{max.}$ 3140br (OH str.) and 1607 (C=C and C=N str.) cm^{-1}; *m/e* 123 (53·5%, M^+), 105 (100, $M^+ - 18$), 94 (26), 68 (23), 65 (21), 51 (14), and 39 (38).

3-Hydroxymethyl-4-methylpyridine.— 4-Methylpyridine-3-carboxylic acid [15] was converted into a liquid methyl ester. *Methyl 4-methylpyridine-3-carboxylate picrate* had m.p. 149—150° (from aqueous ethanol) (Found: C, 43·9; H, 3·2; N, 14·5. $C_{14}H_{12}N_4O_9$ requires C, 44·2; H, 3·2; N, 14·7%). The methyl ester was reduced with lithium aluminium hydride in ether to give 3-hydroxymethyl-4-methylpyridine (78%), m.p. 47—48° after purification by t.l.c. like its isomer (R_F 0·35) and recrystallisation from cyclohexane [lit.,[15] m.p. 44—46° (from reduction of the ethyl ester)] (Found: C, 68·3; H, 7·5; N, 11·4. Calc. for C_7H_9NO: C, 68·3; H, 7·4; N, 11·4%); $\nu_{max.}$ 3300br (OH str.) and 1608 (C=C and C=N str.) cm^{-1}.

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