The Structure of Ipalbine, a New Hexahydroindolizine Alkaloid, isolated from *Ipomoea alba* L.

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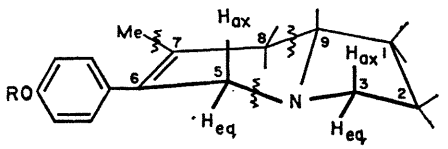
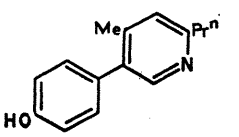
RECENT phytochemical studies have shown that the seeds of several members of the Convolvulaceae family, in particular certain *Rivea*, *Ipomoea*, and *Argyreia* species contain significant amounts of ergoline alkaloids.[1,2] We report the isolation and structural determination of a new hexahydroindolizine alkaloid from the seeds of *Ipomoea alba* L. (Moonflowers), the first time indolizines have been isolated from *Ipomoea* species.

The basic extract from the crushed seeds gave three compounds, ipalbine (I), ipalbidine (II), and a third minor unidentified alkaloid. Ipalbine (I), m.p. 118°, $[\alpha]_D^{23}$ + 32·5° (3% ethanol solution), ($C_{21}H_{29}NO_6$, *m/e* 391·1976), was readily hydrolysed in dilute acid solution to D-glucose and ipalbidine (II).



(I) R = β-D-glucosyl
(II) R = H
(V) R = COMe

Ipalbidine (II), m.p. 147–148°, ($C_{15}H_{19}NO$, *m/e* 229·1466), contained one C–CH_3 group (Kuhn–Roth), four double bonds (total reduction PtO_2, AcOH) including one ethylenic double bond (Pd/C, AcOH) and gave a positive test for a phenol ($FeCl_3$). ν_{max} (CS_2), 3588 cm.$^{-1}$ (OH), λ_{max} (EtOH), 236 (ε 10,040) and 278 nm. (ε 1730), shifted on adding alkali to 248 (ε 24,300) and 295 nm. (shoulder). It formed a picrate ($C_{21}H_{22}N_4O_8$) m.p. 178°, hydrochloride ($C_{15}H_{20}NOCl{\cdot}H_2O$) m.p. 104° and a methiodide ($C_{16}H_{22}NOI$) m.p. 206—207°.

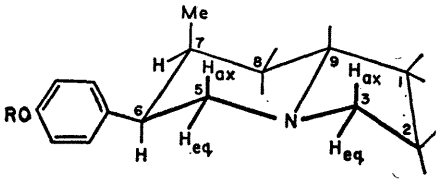


(III)

Ipalbidine was assigned the structure (II) on the basis of the following evidence. Dehydrogenation of (II) with selenium gave a crystalline solid, m.p. 108—109°, ($C_{15}H_{17}NO$, *m/e* 227·1310). The compound was identified as 5-*p*-hydroxy, phenyl-4-methyl-2-n-propylpyridine (III). ν_{max} (KBr)-3390 cm.$^{-1}$ (OH), $\lambda_{max.}$ (EtOH), 254 (ε 3160) and 278 nm. (shoulder), shifted on adding alkali to 240 (ε 2680) and 278 nm. (ε 2980). The ^{1}H n.m.r. spectral data ($CDCl_3$, 60 MHz) of (III) was assigned as follows; τ 2·0 (br s, 1H, ArO*H*, temperature dependent, exchanged with D_2O), 1·69 (s, 1H, H-6), 2·92 (s, 1H, H-3, long range coupled to $ArCH_3$), 2·97 (AA′BB′, 4H, J_{AB} 9·0 Hz, 1,4-subst. Ar), 7·18, 8·20, 9·03 (m, 7H, propyl), 7·70 (s, 3H, ArCH_3). The high resolution mass spectrum of ipalbidine supported the suggested structure showing the following major ions which were consistent with a fragmentation pattern shown in (II):

229[M]; 214[$M - CH_3$]; 160[$M - C_4H_7N$]; 145[$M - (C_4H_7N + CH_3)$]; 70[$M - C_{11}H_{11}O$].

The ^{1}H n.m.r. spectral data from (II) ($CDCl_3$, 100 MHz) was assigned as follows; τ 0·4 (s, 1H, ArO*H*, temperature dependent, exchanged with D_2O), 3·10 (AA'BB', 4H, J_{AB} 9·0 Hz, 1,4 subst. Ar), 6·75 (m, 1H, H-3 eq), 6·76 (AB, 2H, $\Delta\nu_{AB}$ 69·4 Hz, J_{AB} 15·8 Hz, homoallylic coupled to CH_3 [double resonance]), 8·40 (m, 3H, allylic C*H*$_3$). Signals for the remaining protons (8H) appeared as an envelope extending from τ 7·4—8·7. Hydrogenation of (II) (Pd/C, AcOH) gave dihydroipalbidine (IV), a pale yellow oil, b.p. 156—158°/3 mm., ($C_{15}H_{21}NO$, m/e 231·1623). ν_{max} (film), 3350 cm.$^{-1}$ (OH), λ_{max} (EtOH), 223 (ϵ 8400), 277 (ϵ 680) and 283 nm. (ϵ 570), shifted on adding alkali to 240 (ϵ 7500), 286 (ϵ 670) and 296 nm. (ϵ 630). The ^{1}H n.m.r. spectral data of (IV), ($CDCl_3$, 100 MHz) was assigned as follows; τ 2·94 (AA'BB', 4H, J_{AB} 8·5 Hz, 1,4 subst. Ar), 3·94 (s, 1H, ArO*H*, temperature dependent, exchanged with D_2O), 7·06 (m, 1H, H-3eq), 6·85, 7·28, 7·59 (AKM, m, 3H, H-5eq, H-5ax, H-6ax.) Double irradiation gave $J_{AK} = 1·9$, $J_{MK} = 4·0$ and $J_{AM} = 11·2$ Hz. Aromatic methine (H-6) was long range coupled to $H_AH_{A'}$), 9·32 (d, 3H, J 7·0 Hz, C*H*$_3$). Signals for the remaining protons (9H) appeared as an envelope extending from τ 7·8 to 9·0. (II) and (IV) formed *O*-acetyl derivatives (V), b.p. 135–137°/1 mm. and (VI) m.p. 76—77° respectively, with acetic anhydride in pyridine. These results gave the structure of ipalbidine as 1,2,3,5,8,9-hexahydro-6-*p*-hydroxyphenyl-7-methylindolizine (II). The ^{1}H n.m.r. spectra of ipalbine (I), $(CD_3)_2SO$, 100 MHz) showed among other signals, an ill defined doublet at τ 5·14 which was similar in appearance and chemical shift to that for the anomeric proton in phenyl-β-D-glucopyranoside.



(IV) R = H

(VI) R = COMe

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[1] A. Der Marderosian, *Lloydia*, 1967, **30**, 23.
[2] A. Der Marderosian, *Amer. J. Pharm.*, 1967, **139**, 19.