Latifine, a Biogenetic Isomer of Cherylline, from *Crinum latifolium* L.

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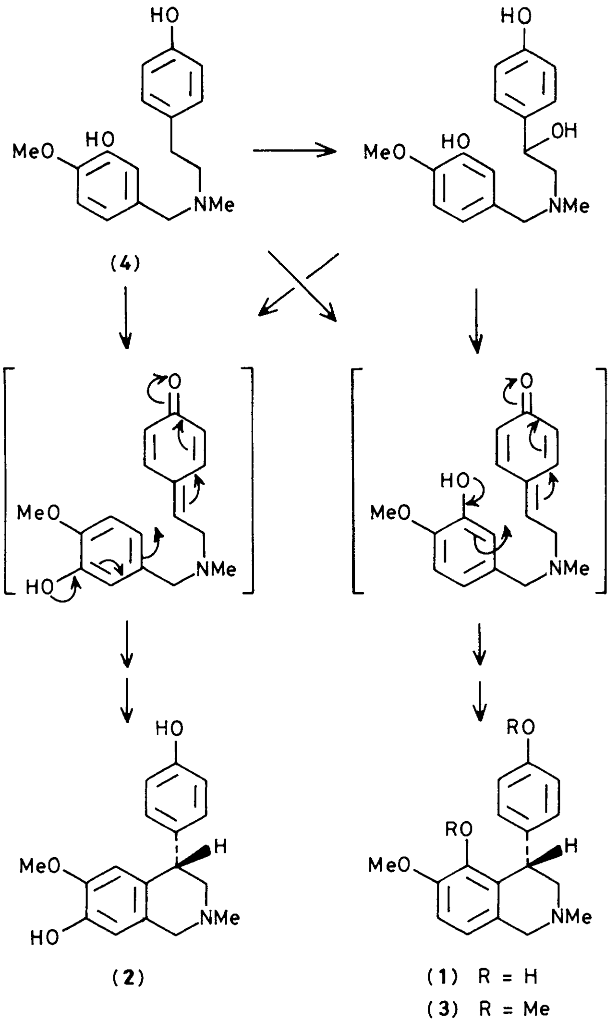
Latifine (**1**), a novel phenolic base and a possible anabolic or catabolic metabolite of *O,N*-dimethylnorbelladine (**4**), was isolated along with cherylline (**2**) from *Crinum latifolium* L. (Amaryllidaceae).

Crinum latifolium L. is used as a rubefacient and tonic.[1] We have isolated a new phenolic base, latifine (**1**) {m.p. 215—217 °C, $C_{17}H_{19}NO_3$, $[\alpha]_D$ −27.9° (MeOH, *c* 0.32)}, and cherylline (**2**)[2] from leaves of this plant. The base (**1**) gave a blue–violet colour with ferric chloride reagent. The i.r. spectrum showed an absorption for a hydroxy group at 3480 cm^{-1} but no absorption for a carbonyl group. The ^1H n.m.r. spectrum† showed signals characteristic of a 1,2,3,4-tetrasubstituted aromatic ring (δ 6.61 and 6.82) and of a second, *para*-disubstituted, aromatic ring (δ 6.62 and 6.88) in addition to OMe and NMe signals. These data, as well as the presence of AB-type doublets (δ 3.43 and 3.63) and ABX-type signals (δ 2.63, 2.89, and 4.24) indicated the partial formula, $PhCH_2NMeCH_2CH(Ph)$– for compound (**1**). The mass spectrum with its characteristic fragmentation pattern† was similar to that of cherylline (**2**).[2] These facts suggested that the base (**1**), like (**2**), has a 4-phenyltetrahydroisoquinoline skeleton.



Scheme 1

Methylation of the base (**1**) with diazomethane gave a methylated product (**3**), $C_{19}H_{23}NO_3$. In the ^1H n.m.r. spectrum of (**3**), one (δ 3.25) of the three singlets due to the OMe groups is shifted *ca.* 0.5 p.p.m. upfield from the other OMe signals, because of the anisotropic effect of the benzene ring, and therefore the OMe group in (**3**) must be located in a *peri*-position (C-5) to the second benzene ring. From these findings, the planar structure for latifine was concluded to be 5-hydroxy-4-(4′-hydroxyphenyl)-6-methoxy-2-methyl-1,2,3,4-tetrahydroisoquinoline (**1**). This assignment was supported by the ^{13}C n.m.r. spectrum† of (**1**) and the fact that latifine could be a metabolite of *N,O*-dimethylnorbelladine (**4**), like cherylline (**2**): (**2**) is formed by coupling of (**4**) *para* to the hydroxy group, while latifine (**1**) could be formed by coupling *ortho* to the group, as shown in Scheme 1.

C-4 of (**1**) was assigned the *S*-configuration as follows. The optical rotatory dispersion (ORD) curves of (**1**) and (**2**) were very similar and both showed negative Cotton effects (285 and 297 nm, respectively). From the findings of Toome *et al.*,[3] this fact suggested that C-4 of base (**1**), as well as (**2**), has the *S*-configuration. This suggestion was confirmed by a direct *X*-ray crystallographic study of (**1**).

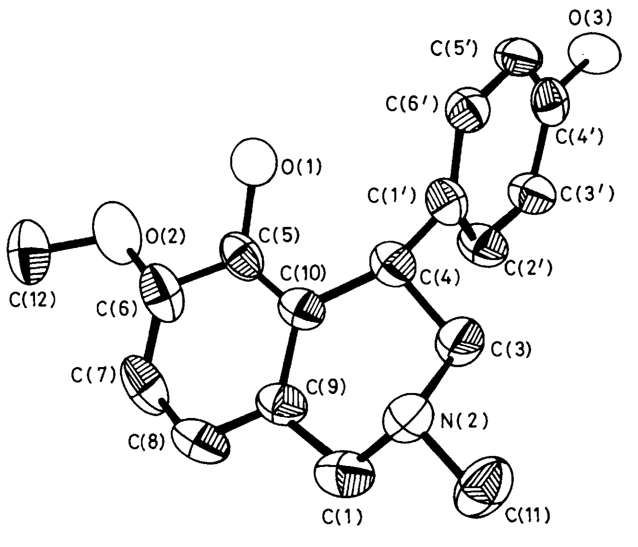


Figure 1. ORTEP drawing of the molecular structure of latifine (**1**).

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† Latifine (**1**), ^1H n.m.r. (CD_3OD): δ 2.31 (3H, s), 2.63 and 2.89 (each 1H, dd, *J* 10 and 5 Hz), 3.43 and 3.63 (each 1H, d, *J* 14 Hz), 3.80 (3H, s), 4.24 (1H, t, *J* 5 Hz), 6.61 and 6.82 (each 1H, d, *J* 9 Hz), 6.62 and 6.88 (each 2H, dd, *J* 8 and 2 Hz); *m/z* (%): 285(M^+) (80), 242 (92), 241 (61), 225 (71), 211 (83), 210 (100), 191 (74), 181 (71); ^{13}C n.m.r. (CD_3OD): δ 41.3 (d), 46.2 (q), 56.4 (q), 58.8 (t), 62.6 (t), 111.0 (d), 115.5 (d), 117.2 (d), 125.2 (s), 129.8 (s), 130.2 (s), 138.1 (d), 145.5 (s), 147.0 (s), and 156.4 (s).

Crystal data for (**1**): $C_{17}H_{19}NO_3$, orthorhombic, space group $P2_12_12_1$; $a = 9.096(1)$, $b = 25.594(3)$, $c = 6.149(1)$ Å; $U = 1431.6(3)$ Å^3; $Z = 4$ and $D_x = 1.32$ g cm^{-3}. A computer-controlled Rigaku four circle diffractometer with graphite monochromated Mo-K radiation was used for all measurements. With $2\theta \leqslant 50°$, 1394 independent reflections with $|F| \geqslant 6\sigma(F)$ were observed. The structure was determined by direct methods with MULTAN[4] and refined by the block-diagonal least-squares method to an R value of 0.042. All hydrogen atoms were located on a difference map and they were included only in calculations of structure factors with an isotropic temperature factor.‡

Figure 1 illustrates the absolute configuration of latifine (**1**) that was determined by analogy with that obtained by the anomalous-dispersion technique for the *N*-bromobenzoyl derivative of the related compound, cherylline (**2**).[3] These results confirm the *S*-configuration at C-4 in (**1**).

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‡ The atomic co-ordinates for in this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.