INCARTINE, A BIOSYNTHETIC INTERMEDIATE, FROM THE FLOWERS OF LYCORIS INCARNATA

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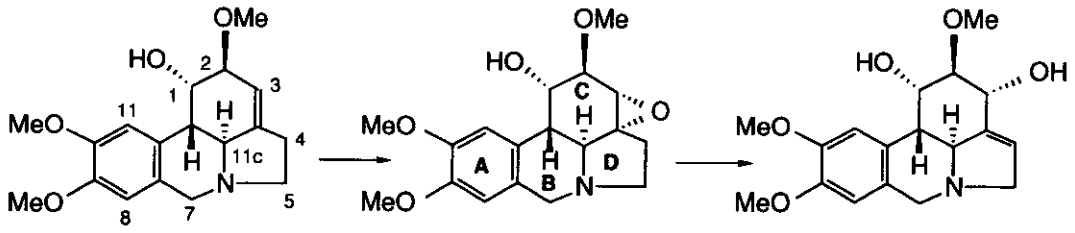
Abstract- Incartine(3), a biosynthetic intermediate from galanthine(1) to narcissidine(2), was isolated along with galanthine(1) from the flowers of Lycoris incarnata.

The Amaryllidaceae alkaloids constitute an important group of naturally occurring bases possessing a variety of functionalities and structures and there are many biosynthetic studies on this family.[1] Fuganti and co-workers[2] suggested that galanthine(1) may be biosynthesized to narcissidine(2) via galanthine α-3,3a-epoxide (3)(Scheme 1), since they found that galanthine(1) was converted to narcissidine(2) in Sempre avanti daffodil with loss of pro-S hydrogen from C-4. Toda and co-workers[3] provided a chemical support for the proposed biosynthetic pathway. However, the proposed intermediate α-epoxide(3) has never been isolated and synthesized. We now report the isolation of incartine(3) along with galanthine(1) from the flowers of Lycoris incarnata (Amaryllidaceae).

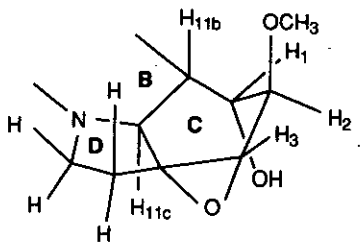
The fresh flowers(5.3 Kg) of Lycoris incarnata were extracted with $CHCl_3$-MeOH(2:1) and chromatographic separation of the extract of the $CHCl_3$ layer gave a new base incartine(14 mg, mp 183-185°C). The ir spectrum of incartine showed an absorption for a hydroxy group



1 3 2

Scheme 1

at 3433 cm^{-1} but no absorption for a carbonyl group. The ^1H nmr spectrum[4] showed signals for two aromatic OMe groups(δ 3.90 and 3.92), one aliphatic OMe group(δ 3.57) and two aromatic protons(δ 6.95 and 6.97) but no signal for a NMe group and an olefinic proton. In addition, the ^1H nmr spectrum also showed signals characteristic[1] of a skeleton of narcissidine(2) [δ 2.60(H-11b), 3.52(H-11c), 3.91(H-2), 4.55(H-1), 4.31 and 4.71(H_2-7)]. The correlation of these signals was supported by the H-H COSY spectrum. These findings and the molecular formula($C_{18}H_{23}NO_5$) suggest that incartine is an α- or β-3,3a-epoxy derivative of galanthine(1). The α-epoxy structure and the stereochemistry of incartine were established from the detailed analysis of its ^1H nmr spectrum as shown in Figure 1. The coupling constant(1.2 Hz) between H-2 and H-3 indicates the dihedral angle of them to be close to 90°. The long range coupling(0.8 Hz) between H-1 and H-3 was observed. These



Chemical Shift (ppm)

H_1	H_2	H_3	H_{11b}	H_{11c}
4.55(br s)	3.91(br s)	3.44(br s)	2.60(dd)	3.52(d)

Coupling Constant (Hz)

$J_{1,2}$	$J_{2,3}$	$J_{1,3}$	$J_{1,11b}$	$J_{11b,11c}$
2.9	1.2	0.8	3.0	13.4

Figure 1. Analysis of ^1H nmr spectrum(in $CDCl_3$, 400 MHz) of incartine.

facts show the C ring to be a distorted chair form conformation (Figure 1) due to the α-3,3a-epoxy ring formation. The β-orientation of the epoxy ring would not give the coupling constants shown in Figure 1. From these findings, the structure of incartine was concluded to be galanthine α-3,3a-epoxide(3).

Isolation and structural determination of incartine(3) with galanthine(1) in this study provide a certain proof of the biosynthetic pathway proposed by Fuganti and co-workers.[2]

REFERENCES AND NOTES

1 S.F.Martin, "The Alkaloids", Vol. 30, ed. by A.Brossi, Academic Press, New York, 1987, pp. 257-376.

2 C.Fuganti, D.Ghiringhelli, and P.Grasselli, J. Chem. Soc., Chem. Commun., 1974, 350.

3 J.Toda, T.Sano, and Y.Tsuda, Heterocycles, 1982, 17, 247; J.Toda, T.Sano, Y.Tsuda, and Y.Itatani, Chem. Pharm. Bull., 1982, 30, 1322.

4 Incartine(3), ^{1}H nmr($CDCl_3$, 400 MHz): 2.04(1H,dd,J=13.1 and 5.3 Hz,H-4α), 2.60(1H,dd, J=13.4 and 3.0 Hz,H-11b), 3.38(1H,ddd,J=13.1, 14.2 and 7.2 Hz,H-4β), 3.44(1H,br s,J=1.2 and 0.8 Hz, H-3), 3.52(1H,d,J=13.4 Hz,H-11c), 3.57(3H,s,OCH_3-2), 3.76(1H,ddd,J=10.8, 14.2 and 5.3 Hz,H-5α), 3.91(1H,br s,J=2.9 and 1.2 Hz,H-2), 3.90(3H,s,OCH_3-9), 3.92(3H, s, OCH_3-10), 4.08(1H,dd,J=10.8 and 7.2 Hz,H-5β), 4.31(1H,d,J=13.0 Hz,H-7α), 4.55(1H,br s, J=2.9, 3.0 and 0.8 Hz,H-1), 4.71(1H,d,J=13.0 Hz,H-7β), 6.95(1H,s,H-11), 6.97 (1H,s, H-8); m/z(%): 333(M^+)(50), 332(100), 296(25), 295(22), 294(20), 266(17), 259(74), 258 (65), 244(30), 242(23).

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