Communications to the Editor

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STRUCTURES OF SECOJESACONITINE AND SUBDESCULINE, TWO NEW DITERPENOID ALKALOIDS FROM ACONITUM JAPONICUM THUNB.

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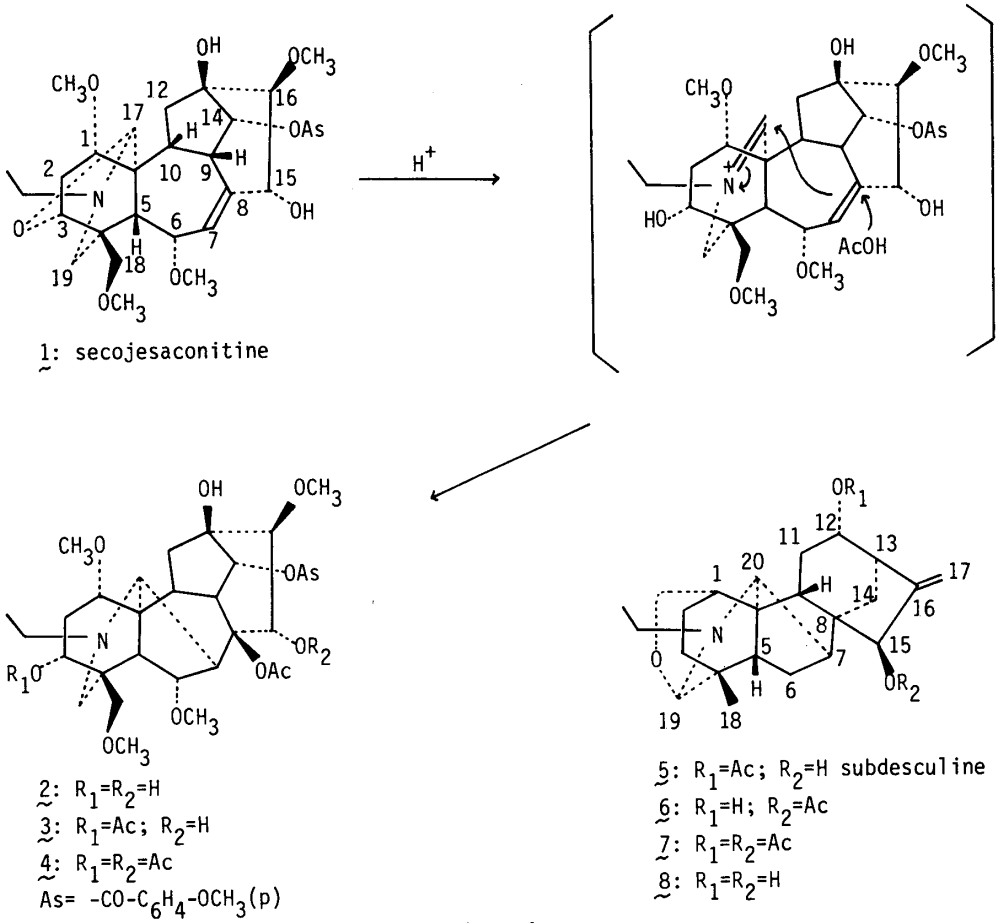
The structures of two new diterpenoid alkaloids, secojesaconitine (1) and subdesculine (5), from Aconitum japonicum Thunb. were determined on the basis of spectral and chemical evidence. The structure of an unusual epoxide (1) was confirmed by X-ray analysis and was the first example of an epoxy ring between C_3 and C_{17}. Treatment of the epoxide (1) with acetic acid and acetylation were found to afford the normal C_{19}-aconitine type alkaloid.

KEYWORDS ——— Aconitum japonicum; diterpenoid alkaloid; secojesaconitine; subdesculine; jesaconitine; X-ray analysis

We have determined the structure of two new diterpenoid alkaloids, named secojesaconitine (1) and subdesculine (5), isolated from the roots of Aconitum japonicum Thunb.[1] Secojesaconitine (1) was the first known example of a C-19 diterpenoid alkaloid having an epoxy ring between C_3 and C_{17}.

Secojesaconitine (1) was obtained as colorless prisms, mp 175-180°C (from $CHCl_3$-acetone), $[\alpha]_D^{20}$ +12.5° (c= 1.0, CH_3OH), $C_{33}H_{45}NO_{10}\cdot CHCl_3$ (Anal. Calcd: C; 55.55, H; 6.30, N; 1.90. Found: C; 55.57, H; 6.37, N; 1.70), UV_{max}^{EtOH} nm(log ε): 208 (4.15), 258.5 (4.11), IR_{max}^{KBr} cm^{-1}: 3460, 1710, 1600, 1250, 1130, 1090, 830, ^{1}H-NMR (270 MHz, $CDCl_3$) δ: 1.07(3H, t, J= 7.2 Hz, N-CH_2CH_3), 3.27, 3.28, 3.30, and 3.65 (each 3H, s, OCH_3), 3.86 (3H, s, aromatic OCH_3), 4.02(1H, d, J= 5.0 Hz, C_3-βH), 4.22(1H, s, C_{17}-H), 4.54(1H, ddd, J= 8.5, 6.2, 2.3 Hz, C_6-βH), 4.75(1H, m, C_{15}-βH), 5.06(1H, d, J= 3.7 Hz, C_{14}-βH), 5.97(1H, d, J= 5.6 Hz, C_7-H), 6.93, 8.02(each 2H, d, J= 8.9 Hz, A_2B_2 pattern of anisoyl group). NMR signal assignments were determined by 2D experiments. The crystal of 1 was used for X-ray analysis and the observed crystal data were as follows: orthorhombic, $P2_12_12_1$, a= 15.368(3) Å, b= 15.783(2), c= 14.861(4), U= 3605(1) $Å^3$, Z= 4. The number of reflections were 3315 and the final R value was 5.91%. X-ray analysis showed that 1 was a new type of C-19 diterpenoid alkaloid in which the C_7-C_{17} bond was cleaved and an epoxy ring was formed between C_3 and C_{17} (Fig. 1). Acetylation of 1 with acetic anhydride in pyridine gave 3-acetyljesaconitine (3)[2] and 3,15-diacetyljesaconitine (4).[3] The latter was not usually yielded by the acetylation of jesaconitine (2) having the hindered hydroxy group at C_{15} by shielding effect of aromatic ring. Treatment of 1 with acetic acid gave 2.



1: secojesaconitine

2: R_1=R_2=H
3: R_1=Ac; R_2=H
4: R_1=R_2=Ac
As= -CO-C_6H_4-OCH_3(p)

5: R_1=Ac; R_2=H subdesculine
6: R_1=H; R_2=Ac
7: R_1=R_2=Ac
8: R_1=R_2=H

Chart 1

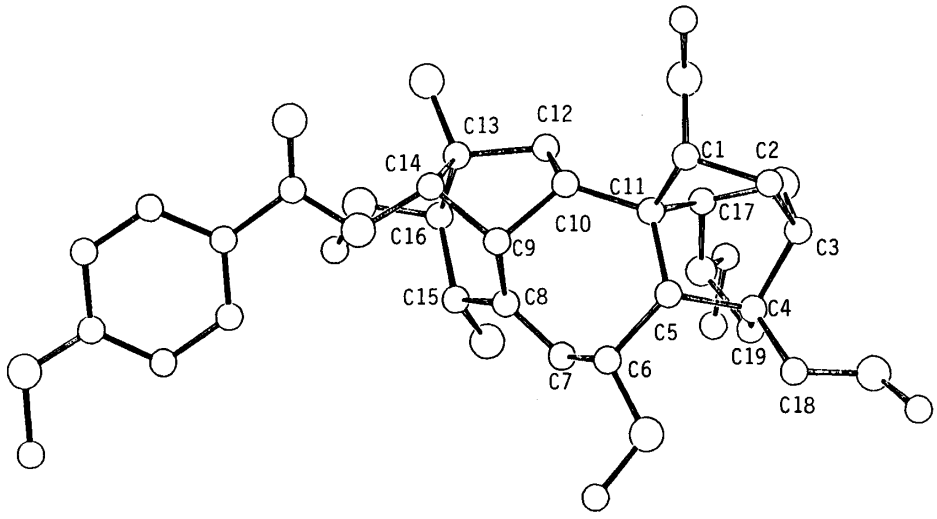


Fig. 1. Perspective View of 1

These chemical data indicate that the mechanism of transformation into the normal aconitine type skelton is involved in the lone-pair electrons on the nitrogen atom, in view of the reactivity at C_8 in aconitine type alkaloids (Chart 1).[4,5]

Subdesculine (5) showed the following properties: mp 135-145°C (dec., perchlorate), $[\alpha]_D^{19}$+7.3° (c= 0.3, $CHCl_3$), $C_{24}H_{33}NO_4$ (m/z; M^+ 399), IR_{max}^{KBr} cm^{-1}: 3340, 1730, 1640, 1230, 1080, 890, ^{1}H-NMR ($CDCl_3$): 0.81(3H, s, C_4-CH_3), 1.02(3H, t, J= 7.1 Hz, N-CH_2CH_3), 2.04(3H, s, $OCOCH_3$), 3.69(1H, s, C_{19}-H), 4.04(1H, d, J= 4.9 Hz, C_1-βH), 4.24(1H, br s, C_{15}-αH), 4.59(1H, dd, J= 8.0, 6.0 Hz, C_{12}-βH), 5.23 and 5.34 (each 1H, s, exomethylene). The molecular formula and ^{1}H-NMR spectrum suggested that compound 5 was a C_{20}-diterpenoid derivative. Compared with the ^{1}H-NMR spectra of dehydrolucidusculine (6)[6], 12-acetyldehydrolucidusculine (7)[7], and dehydrolucliculine (8)[7], the broad singlet signal at δ 4.24 ppm showed a hydroxyl methine assignable to C_{15}-αH and the double doublet signal at δ 4.59 showed a methine geminal to the ester group at C_{12}. These spectra showed that the structure of 5 was 12-acetyldehydroluciculine, and the structure was confirmed by the ^{13}C-NMR spectrum[8] of 5. We have already reported the precise assignments of ^{13}C-chemical shifts[7] in dehydroluciculine (8) and its related derivatives.

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REFERENCES AND NOTES

1) Compound 1 (650 mg) and compound 2 (7 mg) were purified by repeated silica gel chromatography on the fraction B[4] which was obtained from the crude extract.

2) Amorphous, MS(m/z): 717(M^+), 686(M^+-OCH_3), 657(M^+-AcOH), 626[M^+-(OCH_3+AcOH), base peak], IR_{max}^{KBr} cm^{-1}: 3460, 1710, 1600, 1250, ^{1}H-NMR(δ): 1.10(3H, t, J= 7.3 Hz, N-CH_2CH_3), 1.43, 2.06(each 3H, s, $OCOCH_3$), 3.20(6H, s), 3.25(3H, s), 3.73 (3H, s), 3.86(3H, s), 4.08(1H, d, J= 7.3 Hz, C_6-βH), 4.37(1H, d, J= 3.0 Hz, C_{15}-OH), 4.45(1H, dd, J= 5.3, 3.0 Hz, C_{15}-βH), 4.83(1H, d, J= 5.0 Hz, C_{14}-βH), 4.91 (1H, dd, J= 12.5, 5.6 Hz, C_3-βH), 6.93(2H, d, J= 8.9 Hz), 7.97(2H, d, J= 8.9 Hz).

3) mp 201-203°C, MS(m/z): 759(M^+), 728(M^+-OCH_3), 700(M^+-OAc), IR_{max}^{KBr} cm^{-1}: 3450, 1730, 1600, 1250, ^{1}H-NMR(δ): 1.15(3H, t, J= 7.2 Hz, N-CH_2CH_3), 1.31, 2.07, 2.15 (each 3H, s, $OCOCH_3$), 3.19(6H, s), 3.26(3H, s), 3.57(3H, s), 3.85(3H, s), 4.06 (1H, d, J= 7.2 Hz, C_6-βH), 4.87(1H, d, J= 5.0 Hz, C_{14}-βH), 4.92(1H, dd, J= 12.2, 6.6 Hz, C_3-βH), 6.03(1H, d, J= 5.9 Hz, C_{15}-βH), 6.96(2H, d, J= 8.9 Hz), 8.08(2H, d, J= 8.9 Hz).

4) H. Bando, K. Wada, M. Watanabe, T. Mori, and T. Amiya, Chem. Pharm. Bull., 33. 4717 (1985).

5) S. Sakai, I. Yamamoto, K. Hotoda, K. Yamaguchi, N. Aimi, E. Yamanaka, J. Haginiwa, and T. Okamoto, Yakugaku Zasshi, 104, 222 (1984).

6) K. Wada, H. Bando, and T. Amiya, Heterocycles, 23, 2473 (1985).

7) H. Bando, K. Wada, T. Amiya, K. Kobayashi, Y. Fujimoto, and T. Sakurai, Heterocycles, 26, 2623 (1987).

8) ^{13}C-NMR(ppm, $CDCl_3$): 67.7(C_1), 29.7(C_2), 24.4(C_3), 37.7(C_4), 45.9(C_5), 23.9(C_6), 48.7(C_7), 50.2(C_8), 32.2(C_9), 51.8(C_{10}), 26.3(C_{11}), 76.8(C_{12}), 43.0(C_{13}), 28.1 (C_{14}), 77.2(C_{15}), 156.5(C_{16}), 110.5(C_{17}), 18.9(C_{18}), 92.9(C_{19}), 65.9(C_{20}), 48.3 (N-CH_2CH_3), 14.2(N-CH_2CH_3), 170.4, 21.3($COCH_3$).

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