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THE STRUCTURE OF POLYSCHISTINE A, B AND C : THREE NEW DITERPENOID ALKALOIDS FROM *ACONITUM POLYSCHISTUM* HAND-MAZZ

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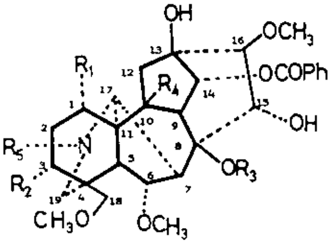
Abstract —— Tree new diterpnoid alkaloids named polyschistine A, B and C were isolated from the roots of *Aconitum polyschistum* Hand-Mazz collected Sichuan province in China. The structures of polyschistine A, B and C were determined on the basis of their ^{1}H- and ^{13}C-NMR spectra.

The roots of aconitum plants are frequently used for treatment of rheumatism, neuralgia and fracture in China. In continuation of our work on the constituents of Chinese aconitum plants, we now wish to report here the structural elucidation of three new C_{19}-diterpenoids alkaloids, polyschistine A, B and C, isolated from the alcohol extracts of *Aconitum polyschistum* Hand-Mazz. Polyschistine A (1) : mp 265-266℃. The high resolution MS{ M^+ 673.34265 (calc. 673.34585)] indicated the molecular formula $C_{36}H_{51}NO_{11}$. The ^{1}H-NMR spectrum[1] (for details see Table 1) exhibited the signals at 1.10(3H, t, J= 6.8 Hz, NCH_2CH_3, 7.44-8.04(5H, aromatic protons), 4.81(1H, d, J=5.1 Hz, C-14H) and for O-methyl proton signals at 3.21, 3.26, 3.29 and 3.73(3H each, s, CH_3O X 4) which could be assigned to C-18, C-1, C-6 and C-16 positions respectively because the ether protons on their carbons were observed at 3.13(1H, dd, J= 6.6, 10.7 Hz, C-1βH), 4.14(1H, d, J=7.1 Hz, C-6βH), 3.23(1H, d, J=5.6 Hz, C-16αH, 2.96 and 3.80(1H each, ABq, J=8.8 Hz, C-18H_2). The singlet signal at 2.18(3H, s) and the double doublet signal at

4.93(1H, dd, J=6.1, 12.9 Hz) suggested the presence of an acetoxyl group to be situated at C-3 position. When the signal at 3.49(1H, m) was irradiated, a prominent triplet signal at 0.57(3H, J=6.8 Hz) was changed to a doublet and the signal at 3.20(1H, m) also effected simultaneously. Hence these signals must consist of OCH_2CH_3 group. Since methyl signal of ethoxyl group was appeared in the unusually highfield(0.57 ppm), the methyl protons must be in the shielding range of the aromatic nucleus. Thus, the ethoxyl group of polyschistine A should be assigned at C-8 position. When the ^{13}C -NMR spectrum of 1 was compared with those of 3-acetylaconitine (4)[2] and some other aconite type alkaloids, the chemical shifts pattern of 1 is very close to that of 4 except for a few changes (see Table 2). All of the signals in the ^1H- and ^{13}C -NMR spectra of polyschistine A[3] are in agreement with the assigned structure (1).



(1) R_1=OCH_3, R_2=$OCOCH_3$, R_3=Et, R_4=H, R_5=Et

(2) R_1=OCH_3, R_2=H, R_3=$COCH_3$, R_4=OH, R_5=Et

(3) R_1=H, R_2=H, R_3=$COCH_3$, R_4=OH, R_5=H

(4) R_1=OCH_3, R_2=$OCOCH_3$, R_3=$COCH_3$, R_4=H, R_5=Et

Polyschistine B (2), mp 182-185℃ , FD-MS m/z 645 (M^+). The high resolution MS〔 m/z 614.30007 (M^+-OCH_3 , calc. 614.29627)〕 indicated the molecular formula $C_{34}H_{47}NO_{11}$. The ^1H-NMR spectrum of 2 revealed the presence of a benzene ring 〔 7.44-8.04, (5H)〕 , four methoxyl groups 〔 3.17, 3.29, 3.31, 3.74(3H each, s) 〕 , an acetyl group 〔 1.42(3H, s) 〕 and an ethyl group attached to a nitrogen atom 〔 1.17(3H, t, J=6.8 Hz)〕 . The proton signals due to C-1βH〔 3.70(dd, J=5.9, 9.2 HZ)〕 and C-14H 〔 5.40(d, J=5.1 Hz) 〕 were appeared at 0.57 and 0.59 ppm downfield respectively as compared with those of 1. In addition, the C-5βH 〔 2.45(d, J=6.1 Hz)〕 and C-12βH 〔 3.27(d, J=12.2 Hz)〕 signals were also observed at slightly downfield. These downfield shifts were attributable to the effect of a hydroxyl group at C-10 position as in the case of known aconitine type alkaloid, aconifine (nagarine) and beiwutine[4].

Table 1

The ^{1}H-NMR data(400 MHz, δ, $CDCl_3$) for polyschistine A, B and C

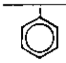
	Polyschistine A	Polyschistine B	Polyschistine C
C_1 αH			1.20 ∼ 2.35
C_1 βH	3.13, dd J=6.6, 10.7 Hz	3.70, dd J=5.9, 9.2 Hz	
C_2 αH	2.49, m	2.32, m	
C_2 βH	2.41, m	1.88, m	
C_3 αH		1.71, m	
C_3 βH	4.93, dd J=6.1, 12.9 Hz	1.71, m	
C_5-H	2.24, dd J=6.3 Hz	2.45, d J=6.1 Hz	2.51, d J=6.8 Hz
C_6-H	4.14, d J=7.1 Hz	4.00, d J=6.6 Hz	3.97, d J=6.8 Hz
C_7-H	2.69, s	2.88, s	2.84, s
C_9-H	2.68, dd J=5.1, 6.6 Hz	2.80, d J=5.1 Hz	2.72, d J=5.4 Hz
C_{10}-H	2.07, m		
C_{12} αH	2.12, m	2.12, d J=12.2 Hz	
C_{12} βH	2.96, m	3.27, d J=12.2 Hz	
C_{14}-H	4.81, d J=5.1 Hz	5.40, d J=5.1 Hz	5.36, d J=5.4 Hz
C_{15}-H	4.53, d J=5.6 Hz	4.50, d J=5.4 Hz	4.51, d J=5.6 Hz
C_{16}-H	3.23, d J=5.6 Hz	3.28, d J=5.4 Hz	3.34, d J=5.6 Hz
C_{17}-H	2.95, s	2.95, s	3.03, s
C_{18} H_a	2.96, d J=8.8 Hz	3.12, d J=8.3 Hz	3.14, d J=8.3 Hz
C_{18} H_b	3.80, d J=8.8 Hz	3.63, d J=8.3 Hz	3.57, d J=8.3 Hz
C_{19} H_a	2.31, d J=11.2 Hz	2.69, d J=10.5 Hz	2.60 ∼ 2.90
C_{19} H_b	2.85, d J=11.2 Hz	3.27, d J=10.5 Hz	
C_3-O_2CCH_3	2.18, s		
C_8-O_2CCH_3		1.42, s	1.42, s
OCH_3	3.21, 3.26 3.29, 3.73	3.17, 3.29 3.31, 3.74	3.17, 3.31 3.76
$NCH_2C\underline{H}_3$	1.10, t J=6.8 Hz	1.17, t J=6.8 Hz	
$NC\underline{H}_2CH_3$	2.56, m 2.67, m	2.64, m 2.81, m	
	7.44(2H) 7.56(1H) 8.04(2H)	7.47(2H) 7.57(1H) 8.03(2H)	7.47(2H) 7.59(1H) 8.04(2H)
C_8-$OCH_2C\underline{H}_3$	0.57, t J=6.84		
C_8-$OC\underline{H}_2CH_3$	3.20, m 3.49, m		

Table 2

The ^{13}C-NMR data(22.5 MHz, δ, $CDCl_3$) for polyschistine A, B, C and 3-acetylaconitine

carbon	polyschistine			3-acetyl-aconitine
	A	B	C	
1	83.6	81.6	30.4	83.8
2	32.1	30.9	30.2	32.1
3	71.8	38.0	30.8	71.9
4	42.4	39.7	38.0	42.5
5	45.7	46.9	48.9	46.2
6	82.2	79.3	83.1	82.3
7	45.5	44.6	43.8	45.6
8	82.4	89.3	89.3	92.1
9	43.7	52.4	52.7	44.9
10	41.1	78.1	79.6	40.8
11	50.3	55.9	57.5	49.9
12	37.1	44.6	40.3	36.6
13	74.9	77.9	74.7	74.3
14	79.6	78.3	78.8	79.1
15	78.5	78.3	79.6	79.1
16	93.7	88.5	89.2	90.4
17	62.2	61.2	63.1	61.1
18	71.8	74.8	69.2	71.1
19	49.1	55.3	47.2	49.1
N-CH_2	47.4	50.1		47.5
CH_3	13.4	11.2		13.5
C_1-$O\underline{C}H_3$	56.4	56.6		56.4
C_6-$O\underline{C}H_3$	57.2	58.8	58.2	58.4
C_{16}-$O\underline{C}H_3$	60.9	61.5	61.5	60.8
C_{18}-$O\underline{C}H_3$	58.8	59.2	59.1	58.9
C=O		172.7	172.3	172.5
CH_3		21.4	21.3	21.5
C=O	166.2	165.7	165.9	166.2
ph	128.3 129.7 130.6 132.8	127.8 129,5 129.5 133.4	128.7 129.7 129.7 133.3	128.8 129.8 130.1 133.4
CO	170.2			170.3
CH_3	21.2			21.3
O-CH_2	58.8			
CH_3	15.3			

The ^{13}C -NMR spectrum (Table 2) of 2 also indicated that polyschistine B contained a hydroxyl group at C-10 position, whose substitution produced the expected α shift(33.7 ppm), and furthermore the chemical shift of C-3(38.0 ppm) suggested that 2 was a 3-hydroxyaconitine type alkaloid. Thus, the structure of polyschistine B was confirmed as 10-hydroxy-3-deoxyaconitine (2).

Polyschistine C (3), amorphous solid. The high resolution MS spectrum of 3, m/z 587.27638 (M^+, calc. 587.27288) indicated the molecular formula $C_{13}H_{41}NO_{10}$. The ^1H-NMR spectrum of 3 showed the signals due to aromatic protons 〔 7.45-8.02 (5H)〕 and an acetyl protons 〔 1.42 (3H, s, C-8 $OCOCH_3$)〕 . The C-14 proton signal〔 5.36(1H, d, J=5.4 Hz)〕 was observed at 0.55 ppm downfield as in the case of 2 in comparison with that of 1, thereby suggesting the presence of a hyroxyl group at C-10. Three methoxyl proton signals 〔 3.17, 3.31 and 3.76(3H each, s, CH_3O X 3)〕 could be assigned to C-18, C-6 and C-16, because the ether protons attached on their carbon atoms were observed at 3.14 and 3.57(1H each, ABq, J=8.3 Hz, C-$18H_2$), 3.97(1H, d, J=6.8 Hz, C-6H), 3.34(1H, d, J=5.6 Hz, C-16H) respectively.

Four proton signals at 1.94, 4.01, 4.39 and 6.82(1H each) could be assigned to three hydroxyl and one amino protons since they were disappeared on addition of D_2O and the ^1H- and ^{13}C -NMR spectra of 3 did not show any signals attributable to the N-methyl or N-ethyl group. Furthermore, the absence of the C-1 oxygen function was supported by the chemical shift(30.4 ppm) of the C-1 signal and the ^1H-NMR data. These ^1H-and ^{13}C -NMR data are explained satisfactorily by the proposed structure 3, which is novel because it is only one C_{19} -diterpenoid alkaloid which has neither C-1 oxygen function nor N-alkyl in the molecule.

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REFERENCES AND NOTES

1) The ^1H-(400 MHz, δ) and ^{13}C -NMR(22.5 MHz, δ) data in the text were taken in $CDCl_3$ containing TMS as an internal standard.

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3) Recently, Prof. Sakai has reported the isolation of the aconitine type alkaloid, 8-O-ethylbenzoylmesaconine, having an ethoxyl group at C-8 position as an artifact 〔 S. Sakai et al., *Yakugaku Zasshi*, 104, 222(1984)〕 . Therefore,

polyschistine A may be an artifact resulting from 3-aetylaconitine during extraction procedures.

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