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THE DITERPENOID ALKALOIDS FROM ACONITUM NAPELLUS

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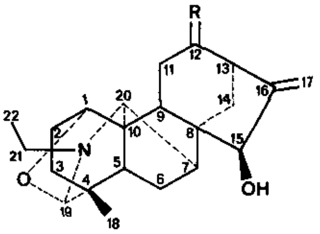
Abstract —— From Aconitum napellus L. subsp. castellanum J. Molero et C. Blanché, were isolated three new diterpenoid alkaloids, 12-epi-dehydronapelline (1), 12-epi-acetyldehydronapelline (2), and 1,14-diacetylneoline (6), together with neoline (7), aconitine, and songoramine (5). The structures of the new bases were determined by spectroscopic data and chemical correlation.

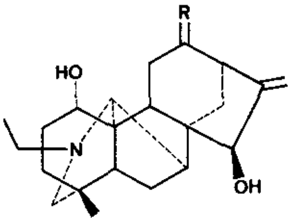
From the cool ethanolic extract of the above ground parts of plants of Aconitum napellus L. Subsp. castellanum J. Molero et C. Blanché, collected growing in wet soils. in loco dicto Laguna del Marquesado, Cuenca Province, Spain,[1] we have isolated three new diterpenoid alkaloids, 12-epi-dehydronapelline (1) and 12-epi-acetyldehydronapelline (2), of the veatchin type, and 1,14-diacetylneoline (6), of the aconitine type.

12-Epi-dehydronapelline (1), isolated as a resin, $C_{22}H_{31}NO_3$ (M^+ 357.2291, calc. 357.2303), had $|\alpha|_D$+45° (c=0.17, EtOH). Ir ($CHCl_3$), 3580, 3500, and 3450 (br) (OH), and 1650 and 875 cm^{-1} (exomethylene). The ms provided ions at m/z, 357 (26%) M^+, 342 (6%) M^+-CH_3, 340 (15%) M^+-OH, 329 (18%) M^+-CO, 312 (4%) $|M^+-OH|-CO$, 301 (38%) $M^+-C_3H_4O$, 286 (16%) $|M^+-C_3H_4O|-CH_3$, and 122 (100%). The ^1H-nmr spectrum of 12-epi-dehydronapelline (1) (200 MHz, $CDCl_3$) displayed characteristic signals of napelline-type alkaloids[2] at δ 0.81 (3H, s, CH_3), 1.00 (3H, t, J = 7 Hz, $N-CH_2-C\underline{H}_3$), 2.66 and 2.67 (1H each, dq, J = 7.1 Hz, $N-C\underline{H}_2-CH_3$), 2.73 (1H, d, J = 1.7 Hz, H-20), 2.80 (1H, dd, J_1 = 8.7 Hz, J_2 = 4.5 Hz, H-13), 4.12 (1H, dd, J_1 = 8.5 Hz, J_2 = 4.0 Hz, H-12α), 4.27 (1H, br s, H-15α), and 5.20 and 5.39 (1H, each, br s, $C = CH_2$).

The ir absorptions at 1010 and 950 cm^{-1}, the loss of a molecule of acrolein in



1 R=αH,βOH
2 R=αH,βOAc
5 R=O



3 R=O
4 R=αH,βOH

the ms,[3,4] together with the nmr signals at δ 4.01 (1H, d, J = 5 Hz, H-1β), 3.67 (1H, br s, H-19), 69.9 (d, C-1), and 93.1 (d, C-19), indicated the presence of a C-1-C-19 carbinolamine inner ether in the new alkaloid.

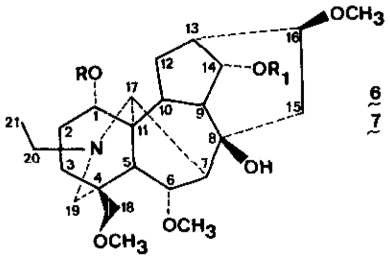
The structure of 12-epi-dehydronapelline (1) was confirmed by its correlation with songoramine (5),[4] also isolated from this plant and identified by mp, ms, and ^{1}H- and ^{13}C-nmr. Reduction of songoramine (5) with $LiAlH_4$ in boiling ether afforded 12-epi-napelline (4),[2] identified by mp, and ^{1}H- and ^{13}C-nmr, and 12-epi-dehydronapelline (1), in 78% and 6% yields, respectively. Oxidation of 12-epi-napelline (4) with $KMnO_4$ in aqueous acetone,[5] at room temperature, gave 12-epi-dehydronapelline (1) in 65% yield. 12-Fpi-dehydronapelline obtained in both cases was identical with the natural alkaloid.

12-Epi-acetyldehydronapelline (2), also isolated as a resin, $C_{24}H_{33}NO_4$ (M^+ 399.2402, calc. 399.2409), had $|\alpha|_D$ +25° (c=0.22, EtOH). Ir ($CHCl_3$), 3560, 1720, 1650, 1240, 1020, 970, and 870 cm^{-1}. Ms, m/z, 399 (8%) M^+, 384 (4%) M^+-CH_3, 382 (4%) M^+-OH, 371 (3%) M^+-CO, 356 (3%) M^+-Ac, 343 (19%) $M^+-C_3H_4O$, 340 (99%) M^+-OAc, 122 (60%) and 43 (100%). Its ^{1}H-nmr ($CDCl_3$) spectrum gave signals at δ 0.82 (3H, s, CH_3), 1.01 (3H, t, J = 7 Hz, $N\text{-}CH_2\text{-}\underline{CH_3}$), 1.99 (3H, s, Ac), 2.67 and 2.68 (1H each, dq, J = 7.2 Hz, $N\text{-}\underline{CH_2}\text{-}CH_3$), 2.73 (1H, br s, H-20), 3.02 (1H, dd, J_1 = 8.6 Hz, J_2 = 5.5 Hz, H-13), 3.68 (1H, s, H-19), 4.01 (1H, d, J = 4.9 Hz, H-1β), 4.24 (1H, br s, H-15α), 4.95 and 5.22 (1H each, br s, C = CH_2), and 5.11 (1H, dd, J_1 = 8.5 Hz, J_2 = 6.1 Hz, H-12α).

The ^{13}C-nmr spectra of 12-epi-dehydronapelline (1) and 12-epi-acetyldehydronapelline (2) were in agreement with the proposed structures. The assignments given in

Table 1, including those for songoramine (5), were made by comparison with the spectra of 12-epi-napelline (4)[2] and songorine (3),[6] and other published ^{13}C-nmr data for related alkaloids.[7]

1,14-Diacetylneoline (6), isolated from this plant as a resin, $|\alpha|_D$+15° (c=0.68, EtOH), $C_{28}H_{43}NO_8$ (M^+ 521.2926, calc. 521.2988), has not been reported as a natural alkaloid.



6 $R=R_1=Ac$
7 $R=R_1=H$

Its spectral data were in accordance with an aconitine-type alkaloid.[8-10] Ir ($CHCl_3$), 3570 (OH), 1730, 1720 and 1240 (Acetate), and 1085 cm^{-1} (C-O). Ms, m/z, 521 (1%) M^+, 506 (1%) M^+-CH_3, 490 (2%) M^+-OCH_3, 462 (99%) M^+-OAc, 446 (4%)$|M^+-CH_3|$-AcOH, 430 (4%)$|M^+-OCH_3|$-AcOH, 402 (15%)$|M^+$-OAc$|$AcOH, 149 (30%), and 43 (100%). ^{1}H-nmr ($CDCl_3$), δ 1.07 (3H, t, J = 7 Hz), 2.00 and 2.02 (3H each, s, two Ac), 2.13 (1H, d, J = 6.8 Hz, H-5), 2.68 (1H, d, J = 12 Hz, H-19β), 2.94 (1H, s, H-17), 3.13 (1H, dd, J_1 = 10 Hz, J_2 = 4.6 Hz, H-16α), 3.21, 3.27, and 3.31 (3H each, s, three OCH_3), 3.63 (1H, d, J = 8.5 Hz, H-18β), 4.11 (1H, d, J = 6.8 Hz, H-6β), 4.74 (1H, t, J = 5 Hz, H-14β), and 4.81 (1H, dd, J_1 = 10.2 Hz, J_2 = 7.5 Hz, H-1β). ^{13}C-nmr ($CDCl_3$), δ 13.7 (q, C-21), 21.3 and 22.1 (two q, two $CO\underline{C}H_3$), 27.8 (t, C-2), 29.2 (t, C-12), 34.7 (t, C-3), 35.7 (d, C-13), 39.2 (s, C-4), 41.3 (t, C-15), 44.1 (d, C-10), 47.0 (d, C-9), 48.7 (t, C-20), 49.2 (s, C-11), 50.1 (d, C-5), 53.6 (d, C-7), 54.4 (t, C-19), 56.2 (q, C-16'), 57.7 (q, C-6'), 59.2 (q, C-18'), 61.1 (d, C-17), 73.5 (s, C-8), 76.7 (d, C-1), 78.0 (d, C-14), 80.5 (t, C-18), 82.0 (d, C-16), 82.5 (d, C-6), and 170.4 and 170.5 (two s, two $\underline{C}OCH_3$). Those assignments are given by comparison with the spectrum of neoline (7)[11] and other reported spectra for related compounds.[8] The acetylation of neoline (7) with Ac_2O-Py led to 1,14-diacetylneoline, identical with the natural compound.

From this plant we have also isolated aconitine, as the major alkaloid, and neoline, 3-acetylaconitine, chasmanine, delsoline, delcosine,[8] and songoramine,[4] as minor constituents. Those alkaloids were identified by comparison, either with authentic samples, or their spectral data with those reported in the literature.[8]

Table 1. ^{13}*C-nmr chemical shifts and assignments for 12-epi-dehydronapelline (1),* 12-epi-acetyldehydronapelline (2), 12-epi-napelline (4), songoramine (5), and songorine (3).

C	1	2	4	5	3	C	1	2	4	5	3
1	67.9	67.9	67.2	67.9	70.1	13	42.6	40.2	44.0	53.3	53.6
2	30.0	29.8	29.7	29.9	31.5	14	31.9	31.6	36.3	37.5	38.0
3	24.8	24.5	31.7	24.4	31.9	15	77.3	77.2	77.0	77.1	76.9
4	37.9	38.0	33.8	37.9	34.0	16	154.0	153.9	155.0	149.9	150.3
5	48.9	49.0	48.8	48.7	49.0	17	112.6	111.8	111.4	111.9	111.1
6	24.2	24.2	23.6	24.1	23.0	18	19.1	19.1	26.3	19.0	26.0
7	46.0	46.1	44.0	46.1	43.4	19	93.1	93.2	58.3	93.1	57.2
8	50.9	50.9	51.1	50.4	49.7	20	66.1	66.0	66.2	66.4	65.8
9	33.3	33.8	37.2	31.6	35.1	21	48.5	48.5	50.9	48.5	50.8
10	52.1	52.1	52.6	51.9	52.1	22	14.4	14.4	13.3	14.4	13.5
11	30.9	27.1	32.7	31.4	37.3	CO	—	170.8			
12	67.5	72.3	70.0	209.0	209.6	CH_3	—	21.5			

Chemical shifts in ppm downfield from TMS. Solvent deuterochloroform.

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