Acozerine as a New Diterpenoid Alkaloid from *Aconitum zeravshanicum*

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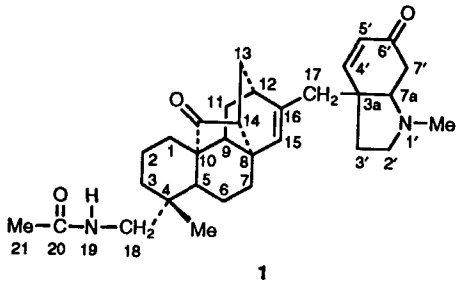
The structure of a new diterpenoid alkaloid acozerine isolated from *Aconitum zeravshanicum* has been elucidated by mass, NMR and IR spectral data.



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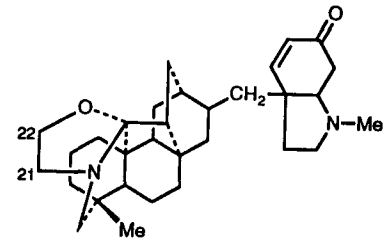

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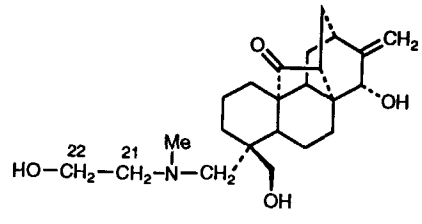

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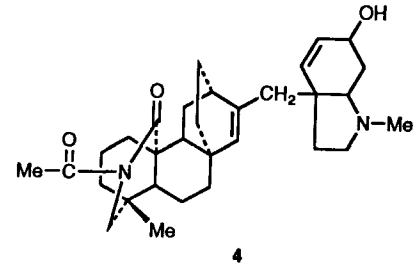

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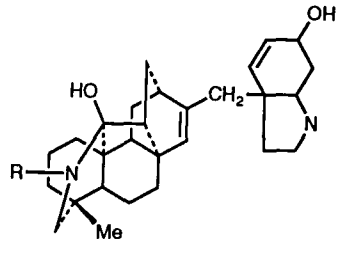

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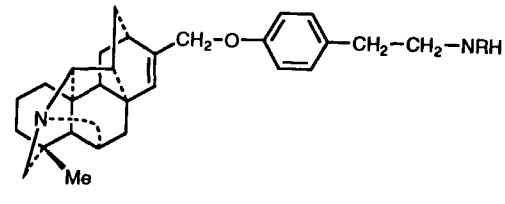

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In our earlier publications we reported on the isolation of an alkaloid with the molecular formula $C_{31}H_{42}N_2O_3$ from *Aconitum zeravshanicum*.[1,2] In this paper we present a set of data that allow us to ascribe structure **1** to the alkaloid named acozerine. The base contains an α,β-unsaturated carbonyl group in its six-membered ring, based on ^{1}H NMR, ^{13}C NMR and IR spectral data.† Absorption bands at 1725 cm^{-1} (IR) and at δ 228.5s (^{13}C NMR) are due to the presence of another carbonyl group in the five-membered ring. Acozerine also contains a trisubstituted double bond, an *N*-acetyl, an *N*-methyl and C–CH_3 groups that are responsible for the resonance of the olefin proton at 5.59 ppm as a broad singlet and three singlets from the methyl groups at 1.98, 2.29 and 0.96 ppm in the ^{1}H NMR spectrum. As for the ^{13}C NMR spectrum, the groups reveal themselves at 145.7 and 131.2 ppm, 170.2 and 23.6 ppm, and 40.1 and 27.3 ppm, respectively. In addition to the α,β-unsaturated carbonyl group, a group NH–Ac also contributes to a broad band at 1685 cm^{-1} in the IR spectrum, which is 3–4 times more intense than the above-mentioned band at 1725 cm^{-1}. Due to the presence of the NH–Ac group, there arises a narrow band at 3390 cm^{-1}, and two bands at 1555 and 1295 cm^{-1}, the latter corresponding to II and III amide bands of the secondary amide group. The mass spectrum of the alkaloid shows a molecular ion peak with *m/z* 490 (6%), and also ion peaks with *m/z* 462(17), 448(14), 447(41), 341(6), 150(22), 149(100) and 148(11). In our recent report we described the isolation of a new alkaloid corifine **2** from *A. coreanum*.[3] In addition to the C_{20}-diterpenoid moiety, the alkaloid contains a 2,3,3a,7a,6,7-hexahydro-*N*-methylindol-6-one system.[2] Acozerine also has this system, which is confirmed by the total similarity of the ^{1}H, ^{13}C NMR and mass spectral data obtained for **1** and **2**. High resolution mass spectrometry provided a molecular formula for the alkaloid, as well as elemental compositions for the fragments of the ions with *m/z* 462($C_{30}H_{42}N_2O_2$), 341($C_{22}H_{31}NO_2$), 150($C_9H_{12}NO$) and 149($C_9H_{11}NO$). The fragments with *m/z* 341 and 149 are formed upon cleavage of the C_{17}–C_{3a} bond, accompanied by migration of a hydrogen probably from C_{7a} to C_{17}. The charge is localized mainly on the hexahydroindole fragment, as opposed to that in corifine[2] where the major peak in its mass spectrum is due to the formation of an ion of the diterpenoid moiety. The difference evidently results from different basicities of the nitrogen in the diterpenoid fragments of the two alkaloids.

The structural formula of acozerine differs from that of

† ^{1}H NMR δ 5.90, 1H, d, *J* 9 Hz; 6.57, 1H, d, *J* 9 Hz; ^{13}C NMR δ 197.1s; 155.6d; 126.7d; IR ν 1685 cm^{-1}.

Table 1 Chemical shifts in the ^{13}C NMR spectra of acozerine **1**, corifine **2** and albovionitine **3**.

C	1	2	3
1	37.2	44.4	29.6
2	21.7	23.1	18.3
3	39.9	41.5	30.2
4	36.8	35.0	41.2
5	54.5	53.3	50.6
6	19.4	19.9	21.6
7	35.6	34.4	31.6
8	42.6	43.8	43.4
9	51.8	48.3	47.2
10	53.9	47.1	53.4
11	28.2	27.9	28.2
12	35.7	35.6	34.6
13	30.9	31.4	32.6
14	54.3	54.5	51.4
15	131.2	136.3	71.3
16	145.7	146.5	156.0
17	34.1	34.7	106.9
18	27.3	28.5	73.9
19	43.7	57.8	57.4
20	228.5	105.7	227.4
21	170.2	51.7	62.6
22	23.6	61.4	59.9
1′	40.1	40.0	45.2 (N–Me)
2′	54.6	54.6	
3′	36.2	36.0	
4′	155.6	156.1	
5′	126.3	125.9	
6′	197.1	197.6	
7′	38.0	37.3	
3a	47.1	47.4	
7a	70.0	70.1	

corifine by an additional oxygen atom. Accounting for the whole set of data stated here, the structure **1** may be assigned to acozerine. The ^{13}C NMR data agree perfectly with the structure suggested (Table 1). An unusually low-field shift of the resonance observed for the carbonyl in the five-membered ring may be rationalized by the presence of five carbons in the β-position to the carbonyl group. A similar resonance (δ 227.4) was found in the spectrum of alkaloid albovionitine **3** recently isolated from *A. alboviolaceum* by our Chinese colleagues.[4] To compare **1** and **2**: these compounds differ mostly by the chemical shifts of C_8, C_9, C_{10} and C_{19}, with no account of those at C_{20}, C_{21} and C_{22} that are due to the presence of NH–Ac and $C_{20}=O$ groups in **1**. It should be noted that a series of resonances (C_1, C_7–C_{14}, C_{16}–C_{18}, C_{20}, $C_{3'}$, $C_{6'}$, $C_{7'}$, C_{3a}) in the ^{13}C NMR spectrum of **1** are doubled, their chemical shifts being only slightly different within 0.01–0.03 ppm.This is probably due to the temporary existence of a structure having an $NH\cdots O=C_{20}$ hydrogen bond. This hydrogen bond may be responsible for a somewhat lower value (1725 cm^{-1}) of the band for the carbonyl group in the five-membered ring.

Acozerine is the third compound in the series of diterpenoid alkaloids with hexahydroindole fragments. In addition to corifine, another alkaloid corifidine **4** was isolated from *A coreanum*.[3] According to our earlier assumption,[2] an alkaloid formulated as zeraconine **6**, isolated from *A. zeravshanicum*[5] *via* an intermediate product of the Claisen rearrangement followed by cyclization,[2] may be a precursor for some alkaloids such as corifine. Alkaloids like **1** and **3** can be prepared *via* an oxidation intermediate product such as **5** with a carbinolamine function, that can disproportionate further to result in compounds such as **1** and **3**.

Mass spectra were recorded on an MX–1320 instrument in which a sample was inserted directly into an ionic tube. IR spectra were recorded as KBr discs on a UR 20 instrument. ^1H and ^{13}C NMR spectra were registered on a Bruker AM300 instrument for dilute solutions of the samples in $CDCl_3$. The multiplicity of the resonances in the ^{13}C NMR spectra was found according to the standard procedure JMODXH.

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