

BRUNONINE, A NEW C₂₀-DITERPENOID ALKALOID

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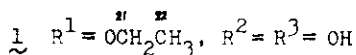
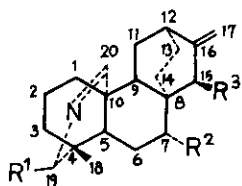
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Abstract - The structure of brunonine (1), a new C₂₀-diterpenoid alkaloid isolated from the whole plant of Delphinium brunonianum Royle, was established on the basis of spectroscopy and the result of X-ray crystallography. Brunonine (1) was shown to possess the atisine azomethine (4) skeleton, with an ethoxyl group at C(19) position.

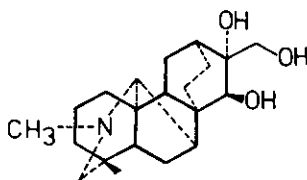
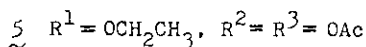
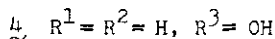
Delphinium brunonianum Royle, growing in the southwestern parts of China, is used in Tibet as folk medicine for influenza, itchy rash and snake-bite. Its alkaloidal constituents have now been investigated, a C₂₀-diterpenoid alkaloid designated as brunonine (1) along with two known bases dictysine (2) and ajaconine (3) was isolated.

Brunonine, C₂₂H₃₃NO₃ (M⁺ 359.2443, calc. 359.2461), mp 208-209°C, [α]_D²¹ +174° (c 0.067, EtOH), showed the presence of an exocyclic methylene group (115.7 ppm, s and 109.1 ppm, t) and a C-CH₃ group (40.97, 3H, s), demonstrating that it belongs to C₂₀-diterpenoid alkaloids. ¹H-NMR signal of one hydrogen at δ 8.03 and ¹³C-NMR signal of a doublet at 165.5 ppm as well as IR absorption (1654 cm⁻¹) suggested the presence of H-C=N moiety in the base. The existence of an ether-linkage in brunonine was deduced from the finding that no hydroxyl group absorption was found in the IR spectrum of its diacetate (5) (M⁺ 443, amorphous). That the ether takes the form in which OCH₂CH₃ is linked to one of the skeleton carbons as a side chain is justified by the following spectral data: ¹H-NMR δ 1.27 (3H, t, J = 7.2 Hz) and ¹³C-NMR 15.2 ppm (q) for OCH₂CH₃; ¹H-NMR δ 3.67 and 4.14 (1H each, dq, J = 7.2, 10.8 Hz) and ¹³C-NMR 64.6 ppm (t) for OCH₂CH₃. The ¹³C-NMR signal 94.7 ppm (d) pointed out that the ethoxyl group is bonded to C(19) or C(20) which in turn is linked to the nitrogen in the molecule. The location of OCH₂CH₃ group was then clarified by an

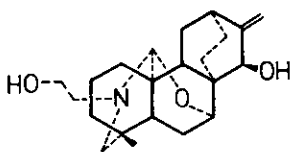
NOE demonstration. When the signal $\delta 0.97$ for C(4)-CH₃ was irradiated, the one-proton peak at $\delta 4.30$ (broadened by a long-range coupling with H-C=N), attributable to C(19), increased by 12% in intensity, while the other one-proton peak at $\delta 8.03$, which may then be assigned to C(20), remained unchanged. Brunonine yielded a pair of isomeric methylcyclohexanones (IR 1705 and 1710 cm⁻¹) upon acid-catalyzed allylic alcohol rearrangement, indicating that the compound bears C(15)-OH¹. This is in accordance with the assignment of the signal $\delta 5.45$ (1H, t, J = 1.5 Hz) appeared in ¹H-NMR spectrum of brunonine diacetate (5). The chemical shift of C(15) in ¹³C-NMR (70.6 ppm, d) was found, however, to be 4.6 ppm upper field than that of an analogous compound atisine azomethine (4)² (75.2 ppm) (see Table 1), implying that the second hydroxyl group could be situated at C(7), thereby a release of the non-bonding interaction between C(7)- α -H and C(15)- α -H was manifested³. The



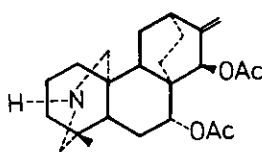
Brunonine



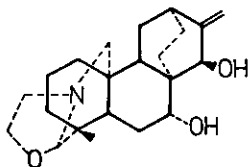
2 Dictysine



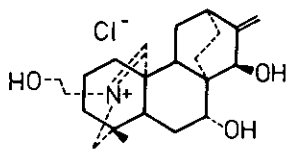
3 Ajaconine



6



7



8

presence of C(7)- α -OH, but not C(14)-OH, was justified by $^1\text{H-NMR}$ signal δ 4.75 (1H, dd, $J = 4.8, 11.0$ Hz) of diacetylbrunonine (5). Based upon the above reasoning, structure 1 was assigned to brunonine. Interestingly, the NaBH_4 -reduced product (6) ($M^+ 401$) of 5 showed the elimination of ethoxyl group (the disappearance of δ 4.14, 3.67 and 1.27 signals) simultaneously with the saturation of C=N double bond (the absorption at δ 8.01 vanished). The $^{13}\text{C-NMR}$ of structure 1 was in reasonable agreement with that of the known compounds atisine azomethine (4), 7- α -hydroxylisoatisine (7)⁴ and ajaconine hydrochloride (8)⁴ (Table 1). Brunonine has the structure 1⁵ was

Table 1. Carbon-13 NMR data^a of brunonine (1), atisine azomethine (4), 7- α -hydroxylisoatisine (7) and ajaconine hydrochloride (8)

Carbons	<u>1</u>	<u>4</u>	<u>7</u>	<u>8</u> ^b
1	35.1 (t)	42.4	40.3	42.6
2	19.5 (t)	20.0	22.0	21.1
3	34.0 (t)	34.1	39.6	37.3
4	36.2 (s)	32.8	38.1	35.2
5	48.5 (d)	46.9	46.4	44.8
6	19.5 (t)	19.6	20.7	20.6
7	69.5 (d)	31.0	70.6	70.7
8	42.9 (s)	37.4	42.6	44.3
9	38.2 (d)	38.1	39.6	41.3
10	42.6 (s)	42.5	35.7	48.1
11	28.2 (t)	28.1	28.4	29.6
12	35.9 (d)	36.0	36.2	36.4
13	28.0 (t)	26.1	28.3	29.6
14	25.5 (t)	25.5	25.5	26.8
15	70.6 (d)	75.2	71.9	72.2
16	155.7 (s)	156.2	155.8	156.5
17	109.1 (t)	108.9	110.1	112.9
18	24.9 (q)	25.8	24.3	26.2
19	94.7 (d)	60.0	98.3	66.2
20	165.5 (d)	166.4	49.5	184.7
21	64.6 (t)	-	54.9	61.5
22	15.2 (q)	-	58.8	59.8

a. Chemical shifts in ppm downfield from TMS in CDCl_3 . b. Solvent - D_2O .

confirmed later by X-ray crystallography⁶.

REFERENCES AND NOTES

- * Present address: Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences, Hai Dian District, Dong Bei Wang, Beijing, China.
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- 2. N.V. Mody and S.W. Pelletier, Tetrahedron, 1978, 24, 2421.
- 3. H. Beirbeck and J.K. Saunders, Can. J. Chem., 1976, 54, 2985.
- 4. S.W. Pelletier and N.V. Mody, J. Am. Chem. Soc., 1979, 101, 492.
- 5. Brunonine could be an artifact, possibly derived from the coexisting constituent ajaconine (3), but we failed to prove it so far by an attempted conversion starting with 3 under the condition of the ethanol-extraction of the whole plant at pH 6.4 and 60-70°C.
- 6. Qi Tai Zheng, "Brunonine Crystal Structure Determination", Personal communication.

Received, 28th October, 1985