Journal of Natural Products
Vol. 52, No. 2, pp. 430-432, Mar-Apr 1989

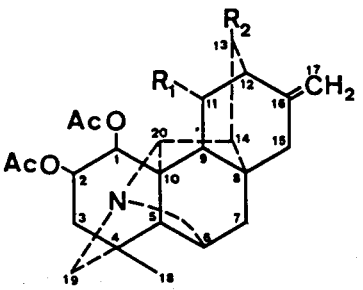
THE STRUCTURE OF PANICULATINE: A REVISION[1]

A. KATZ

Natural Products Research Laboratory, Oberwilerstrasse 9, 4054 Basel, Switzerland

ABSTRACT.—Comparison of the cd spectrum of dehydropaniculatine [**3**] with those of the parent 11- and 13-keto derivatives showed that the previously established structure **1** for paniculatine has to be revised to **2**.

On the basis of spectrometric data we had proposed structure **1** for the alkaloid paniculatine (2), a hetisine-type diterpenoid alkaloid that had been isolated from a local variety of *Aconitum paniculatum* Lam. (Ranunculaceae) (3,4). Nmr spectra revealed evidence that the benzoyloxy and the hydroxyl group are located at C-11 and C-13, but it was difficult to make the choice between the two possible structures **1** and **2** because of structural circumstances we had described (2). NOe experiments and considerations regarding the most likely conformation of the benzoyloxy group



1 R_1=OH, R_2=OBz
2 R_1=OBz, R_2=OH
3 R_1=OH, R_2=O

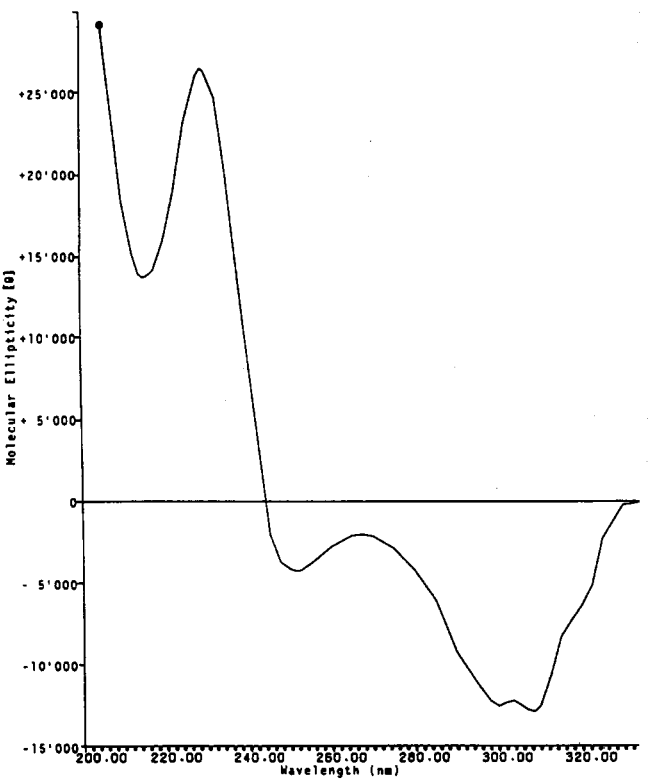


FIGURE 1. Circular dichroism of dehydropaniculatine [**3**].

[1]Communication No. 9 about *Aconitum*. For Communication No. 8, see Katz *et al.* (1).

led us to assign the latter to C-13 and consequently the hydroxyl to C-11. On the basis of the hypothetical character of the assumed conformation of the benzoyloxy group the author thought it desirable to verify the proposed structure by an alternative method. Recently in similar cases cd measurements proved to be useful to differentiate between C-11 and C-13 keto groups in hetisine-type alkaloids (5,6). The 11-keto derivatives showed a positive Cotton effect, whereas the 13-keto analogues displayed a negative Cotton effect. Application of cd to dehydropaniculatine [**3**] showed that this compound exhibited a negative Cotton effect. Hence, the keto function in dehydropanculatine [**3**], and consequently the hydroxyl in paniculatine [**2**], have to be assigned to C-13 and the benzoyloxy group to C-11. The arguments regarding the configuration of the oxygen functions at C-11 and C-13 are still valid.

The cd curve of **3** is represented in Figure 1, and Tables 1 and 2 present the spectrometric data of **2** and **3** which were only partially included in Katz and Staehelin (2).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Uv spectra were recorded on a Hitachi 101 spectrophotometer and ir spectra on a Perkin-Elmer instrument. Mass spectra were obtained on an AEI MS 30/C mass spectrometer using direct probe and electron impact. The cd spectrum was determined on a Jasco J-20 spectropolarimeter. ^{1}H- and ^{13}C-nmr spectra were measured on a Bruker instrument at 360 MHz and 90.5 MHz, respectively.

SPECTROMETRIC DATA.—*Paniculatine* [**2**].—Uv (EtOH) 2300 Å (log $\epsilon = 4.02$), 2700 Å (log $\epsilon = 2.98$); ir (KBr) 3150 br (OH), 1730 s and 1720 (shoulder) (C=O), 1650 w (=CH_2), 1600 w (bz); ms $[M]^+$ 533, 490, 474 (100%), 444,

TABLE 1. ^{1}H-nmr Spectra of Paniculatine [**2**] and 13-Dehydropaniculatine [**3**].[a]

Proton	Compound	
	2	**3**
H-1	5.84, d, $J = 3$ Hz	5.42, s
H-2	5.55, m, W½ = 9 Hz	5.49, m, W½ = 10 Hz
2H-3	1.97–1.88 + 1.84–1.78, 2m[b]	2.0–1.90 + 1.84–1.76, 2m[b,e]
H-5	2.05, s	2.14, s
H-6	3.29, m, W½ = 7 Hz	3.38, m, W½ = 7 Hz
2H-7	1.83–1.77 + 1.70–1.63, 2m[b]	2.0–1.90 + 1.84–1.76, 2m[b,e]
H-9	2.32; 2.29; 2.27; 2.26[c]	2.87, d, $J = 6$ Hz[d]
H-11	5.37, m	5.40
H-12	[c]	2.47, dd
H-13	4.19, m, W½ = 16 Hz	—
H-14	[c]	2.58[e]
2H-15	2.35 + 2.08, AB, $J_{AB} = 20$ Hz, $\Delta\delta_{AB} = 100$ Hz	2.58 + 2.28, AB, $J_{AB} = 18$ Hz, $\Delta\delta_{AB} = 100$ Hz
2H-17	4.90 + 4.77, 2s	5.06 + 4.95, 2s
3H-18	1.03, s	1.05, s
2H-19	2.88 + 2.51, AB, $J_{AB} = 15$ Hz, $\Delta\delta_{AB} = 145$ Hz	2.85 + 2.53, AB, $J_{AB} = 12$ Hz, $\Delta\delta_{AB} = 115$ Hz
H-20	4.30, s	3.94, s
HO-13	1.63, s (broad)	—
2 × H_3CCOO-	2.03	2.04 + 2.03, 2s
C_6H_5COO-	8.13, d; 7.58, t; 7.46, t	8.08, d; 7.62, t; 7.54, t

[a]Shifts are given in ppm to TMS. Solvent: $CDCl_3$.

[b]From ABX.

[c]The signals at 2.32, 2.29, 2.27, and 2.26 ppm are heavily crowded and overlapping. They are engendered by H-9, H-12 and H-14, but cannot be assigned exactly.

[d]Doublet discernible in the decoupled spectrum.

[e]Multiplicity and/or exact shift not readable.

TABLE 2. ^{13}C-nmr Spectra of Paniculatine [2] and Dehydropaniculatine [3].[a]

Carbon	Compound	
	2	3
C-1	71.6, d	72.1, d
C-2	70.9, d	71.6, d
C-3	34.1, t	33.5, t
C-4	36.9, s	36.7, s
C-5	51.7, d	51.5, d
C-6	65.6, d	66.8, d
C-7	33.1, t	32.8, t
C-8	44.0, s	43.6, s
C-9	64.2, d	64.4, d
C-10	54.6, s	54.4, s
C-11	68.7, d	68.3, d
C-12	51.8, d	60.6, d
C-13	75.3, d	206.7, s
C-14	50.0, d	59.9, d
C-15	36.3, t	34.6, t
C-16	144.3, s	138.3, s
C-17	109.0, t	113.1, t
C-18	29.4, q	29.3, q
C-19	64.0, t	63.4, t
C-20	58.1, d	57.7, d
$2CH_3$-COO-	21.3, q; 21.8, q; 170.1, s; 171.4, q	21.2, q; 21.4, q; 169.6, s; 170.9, s
C_6H_5-COO-	128.6, d; 129.9, d; 130.3, s; 133.0, d; 165.5, s	128.8, d; 129.9, d; 129.9, s; 133.3, d; 165.4, s

[a]Shifts are given in ppm to TMS. Solvent: $CDCl_3$.

430, 414, 368, 352, 310, 292, 282, 264, 252, 207, 181, 141, 122, 105, metastable peaks 421 (*m/e* 533↦474), 361 (*m/e* 474↦414); ^{1}H nmr see Table 1; ^{13}C nmr see Table 2.

Dehydropaniculatine [3].—Uv (EtOH) 2300 Å (log ε = 4.02), 2800 Å (log ε = 3.05), 3000 Å (log ε = 2.47); ms [M]$^+$ 531, 488, 472 (100%), 459, 444, 430, 412, 384, 366, 350, 308, 290, 280, 264, 250, 207, 181, 149, 105, metastable peak 419 (*m/e* 531↦472); cd see Figure 1 (EtOH abs. *c* = 0.095) [θ]/nm min. −12904/308.5, max. −12231/303.5, min. −12568/300.0, max. −2020/267.5, min. −4264/251.5, max. +26482/229.0, min. +13690/215.0; ^{1}H nmr see Table 1; ^{13}C nmr see Table 2.

ACKNOWLEDGMENTS

The author is grateful to Dr. P. Moser, Ciba-Geigy A.G., Basel, for the cd measurements. Thanks are also due to Mrs. Th. Zardin and Dr. H.R. Loosli, Sandoz A.G., Basel, for nmr spectra, as well as to Prof. Dr. H.H.A. Linde, Pharmaceutical Institute of the University of Basel, for the permission to use the Institute's ir and uv spectrophotometers.

LITERATURE CITED

1. A. Katz, H. Rudin, and E. Staehelin, *Pharm. Acta Helv.* **62**, 216 (1987).
2. A. Katz and E. Staehelin, *Tetrahedron Lett.*, **23**, 1155 (1982).
3. G.E. Brunner, "Über den Alkaloidgehalt von *Aconitum nopellus* L. und *Aconitum paniculatum* Lam. unter spezieller Berücksichtigung der offizinellen Droge." Diss. ETH Zürich, 1921, p. 60.
4. E. Staehelin and A. Katz, *Pharm. Acta Helv.* **55**, 221 (1981).
5. S.W. Pelletier, B.S. Joshi, H.K. Desai, A. Panu, and A. Katz, *Heterocycles*, **24**, 1275 (1986).
6. J.A. Glinski, B.S. Joshi, Q.P. Jiang, and S.W. Pelletier, *Heterocycles*, **27**, 185 (1988).

Received 14 October 1988