

A 16,17-EPOXY C₂₀-DITERPENOID ALKALOID FROM *ACONITUM DELPHINIFOLIUM*

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Key Word Index—*Aconitum delphinifolium*; Ranunculaceae; diterpenoid alkaloid; 16,17-epoxy.

Abstract—A minor base from *Aconitum delphinifolium* was identified as gomandonine 13-*O*-acetate, a 16,17-epoxy C₂₀-diterpenoid alkaloid.

INTRODUCTION

During a study of the alkaloids of *Aconitum delphinifolium* DC, which resulted in the identification of a number of C₁₉-diterpenoids [1] we isolated a small amount of a compound (X) which appeared to be of a novel structural type, albeit one which we could only incompletely characterize. Recent developments have supported our initial conclusions, and now allow us to arrive at a complete structure of the alkaloid.

RESULTS AND DISCUSSION

Alkaloid X was obtained as an amorphous solid, homogeneous when examined by TLC in several solvent systems, and whose spectroscopic properties were consistent with its being a pure substance. Its EIMS contained abundant ions at *m/z* 403 [M]⁺, 386 [M–17] and 344 [M–59] and as the ¹³C NMR spectrum of X (Table 1) showed resonances corresponding to 23 C-atoms we decided that the molecular formula of X was probably C₂₃H₃₃NO₅. The ¹H NMR spectrum (see Experimental) contained *inter alia* absorptions due to NMe and MeCOO groups (but no methoxyls) and we therefore recognised X as belonging to the C₂₀-diterpenoid alkaloids. Such compounds typically have atisinoid or veatchinoid skeletons; and almost invariably possess a Δ¹⁶⁽¹⁷⁾ exocyclic methylene functionality, the only exception known to us at that time being dictyzine (1) [2] in which this is replaced by a *vic*-diol system. However, the ¹³C NMR spectrum of X contained no signals attributable to a dictyzine-like 16,17-diol group, or an alkene functionality. We realised that features of both the ¹H and ¹³C NMR spectra of X were consistent with it being a 16,17-epoxide: with absorptions for a 2H AB system at δ 3.12 and 2.48 ppm, *J* = 4.5 Hz; and δ 64.2 (*s*) and 45.5 (*t*) ppm respectively. Hypothetically, such an epoxide might be an intermediate in the conversion of a Δ¹⁶⁽¹⁷⁾ system to the *vic*-diol one of dictyzine.

To account for the other oxygen atoms we noted that, besides a typical ester carbonyl absorption at 1735 cm^{–1}, the IR spectrum of X showed a strong absorption at 3430 cm^{–1}, and this, together with the appearance of

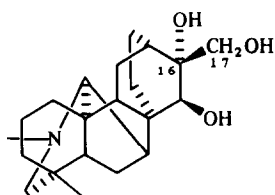
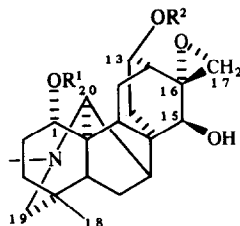
Table 1. ¹³C NMR chemical shift data* for gomandonine (2a) [3], yesoxine (2b) [4] and alkaloid X (2c)

C	2a	2b	2c
1	70.6	74.0	70.6 <i>d</i>
2	32.1	26.4	31.4 <i>t</i>
3	40.1	36.0	36.1 <i>t</i>
4	33.8	33.5	33.7 <i>s</i>
5	52.7	52.4	51.8 <i>d</i>
6	24.1	23.4	23.5 <i>t</i>
7	42.6	38.5	38.8 <i>d</i>
8	44.6	43.3	43.6 <i>s</i>
9	43.9	43.8	43.9 <i>d</i>
10	51.4	48.2	50.9 <i>s</i>
11	25.6	22.9	23.9 <i>t</i>
12	41.6	41.4	40.7 <i>d</i>
13	69.1	71.4	71.5 <i>d</i>
14	39.2	37.9	38.2 <i>t</i>
15	76.5	76.3	76.6 <i>d</i>
16	65.5	64.0	64.2 <i>s</i>
17	45.0	45.5	45.5 <i>t</i>
18	26.3	25.6	25.8 <i>q</i>
19	59.6	59.1	59.1 <i>t</i>
20	68.9	69.0	68.5 <i>d</i>
MeN	43.9	41.0	41.7 <i>q</i>
Me		21.3, 21.9	21.4 <i>q</i>
C=O		170.6, 170.7	170.7 <i>s</i>

* Shifts are relative to TMS; 2a was in pyridine-*d*₅, 2b and 2c in CDCl₃; assignments may be interchanged for C3 and 14, 6 and 11, and 7, 9 and 12.

resonances at δ 76.6 and 70.6 ppm in its ¹³C NMR spectrum, suggested that there were two hydroxyl groups in the molecule.

Thus we concluded that X was a heptacyclic C₂₀-diterpenoid alkaloid containing a 16,17-epoxide, N-Me,

**1**

- 2a** $R^1 = R^2 = H$
2b $R^1 = R^2 = Ac$
2c $R^1 = H, R^2 = Ac$

OAc, and two OH groups. However, we were unable to decide the nature of the carbon skeleton, or the site and orientation of attachment of the acetoxy and hydroxy functionalities. Attempts to prepare crystalline derivatives of **X** for X-ray crystallographic analysis were unsuccessful.

Recent reports describe the identification of two 16,17-epoxy alkaloids: gomandonine (**2a**) [3] and yesoxine (**2b**) [4], isolated from Japanese *Aconitum*. The ^{13}C NMR data for these alkaloids, whose structures were unequivocally established by X-ray crystallography, when compared with those for **X** (see Table 1) indicated that this alkaloid was gomandonine 13-*O*-acetate (**2c**).

The α -stereochemistry of these three epoxides corresponds to that seen at C-16 in dictyzine (and a recently discovered analogue, macrocentrine [5]), i.e. the hypothesis that the 16 α ,17 *vic*-diol system arises by S_N2 -type hydrolysis of a 16 α ,17-epoxide is likely to be correct.

EXPERIMENTAL

The processing of the plant material and fractionation of the alkaloid mixture which was obtained has been described previously [1]. Alkaloid **X** (35 mg) from 3.6 g of the alkaloid mixture was obtained as a colourless, amorphous solid homogeneous by TLC analysis. Apart from the ^{13}C NMR data given in Table 1, the salient features of its spectroscopic properties were as follows: IR ν_{max}^{KBr} 3430 (*br s*), 1735 (*s*), 1248 (*s*) and 754 (*s*) cm^{-1} ; EIMS (70 eV) m/z (rel. int.) for major ions above 200 mass units: 403 (65), 388 (75), 374 (55), 344 (100), 328 (70); 1H NMR (200 MHz, $CDCl_3$, $CHCl_3$ as internal ref; δ 7.24 ppm rel. TMS): δ 0.70 (3H, *s*, H-18); 2.06 (3H, *s*, $MeCOO$), 2.27 (3H, *s*, MeN), 2.48 (1H, *d*, $J = 4.5$ Hz H-17A), 3.12 (1H, *d*, $J = 4.5$ Hz H = 17B), 3.51 (1H, *br s*, H-20), 3.84 (1H, *dd*, $J = 9.5$ and 6.5 Hz, H-1) 4.18 (1H, *br s*, H-15); 4.91 (1H, *dd*, $J = 8.8$ and 4.0 Hz, H-13).

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