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PYRROLIZIDINE ALKALOIDS FROM *ALKANNA TINCTORIA**

ERHARD ROEDER, HELMUT WIEDENFELD and RAINER SCHRAUT

Pharmazeutisches Institut der Universität Bonn, An der Immenburg 4, D-5300 Bonn 1, West Germany

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Key Word Index—*Alkanna tinctoria*; Boraginaceae; pyrrolizidine alkaloids; O^7-angelylretronecine; triangularine; dihydroxytriangularine.

Abstract—Three pyrrolizidine alkaloids were isolated from *Alkanna tinctoria* and their structures analysed by spectroscopic methods. One of them is new and the name dihydroxytriangularine is proposed for it.

INTRODUCTION

The medicinal plant *Alkanna tinctoria* Tausch contains alkannan, anchusic acid, alkanna acid, choline, consolidine (a neurotoxin), consolicine (a toxic alkaloid) and cerotic acid carnauboic ester. Other unidentified alkaloids have been reported [1], and since *A. tinctoria* belongs to the Boraginaceae, it may be presumed that pyrrolizidines should be present. We have now detected four such alkaloids by TLC and three of them have been isolated and identified.

RESULTS AND DISCUSSION

The methanolic extract was purified by fractionation as described previously [2]. Three pyrrolizidine alkaloids, **1**–**3**, were then separated by DCCC. The IR spectral data indicate that alkaloid **1** is a monoester, whereas alkaloids **2** and **3** are diesters. Furthermore, **3** shows an intense hydroxy absorption, which indicates that several alcoholic groups are present. The molecular formulae $C_{13}H_{19}NO_3$ (**1**), $C_{18}H_{25}NO_5$ (**2**) and $C_{18}H_{27}NO_7$ (**3**) were determined by the mass spectra. The fragmentation pattern of **1** indicates that it must be an isomer of O^7-angelylheliotridine, namely O^7-angelylretronecine (3). The typical fragmentation between m/z 140 and 80 of the three alkaloids indicates that all three are retronecine derivatives. The appearance of the ion m/z 237 in the fragmentation patterns of **2** and **3** shows that the partial structure of O^7-angelylretronecine is present too (as in **1**). Other important structural information is provided by the ^{1}H NMR spectral data (Table 1) and ^{13}C NMR spectral data (Table 2). Thus, the structure of **1** as O^7-angelylretronecine is confirmed; the ^{1}H value of 6.11 ppm for C-12 H and the ^{13}C value of 15.8 ppm for C-13 confirm the presence of angelic acid. Similar values can be found for **2** and **3**. In the ^{1}H NMR spectra of **2** and **3**, a broad singlet for two protons at *ca* δ4.7–4.8 for C-9 H_2 can be recognized. From this it is evident that both alkaloids are open diesters, which is typical for Boraginaceae alkaloids. Thus, the structures of the acids in **2** and **3**, which are esterified at C-9, have to be hydroxyangelic acid and 2-hydroxymethyl-2,3-dihydroxybutanoic acid. This is clear from the ^{13}C values for C-18 (15 and 17 ppm) and for C-19 (64 and 65 ppm) and from the coupling constants of the ^{1}H NMR signals for C-17 (J = 7 and 1 Hz for **2** and 7 Hz for **3**). The positions of the hydroxyl groups in alkaloid **3** are settled by ^{13}C NMR spectral analysis; the signals for C-18 and C-19 indicate a *trans*-relationship and thereby define the struc-

Table 1. ^{1}H NMR spectral data for alkaloids **1**–**3** ($CDCl_3$; TMS as internal standard)

	1	**2**	**3**
C-14 H_3	1.82, *dq*, 3H J = 1.5, J = 1.5	1.80, *dq*, 3H J = 1.5, J = 1.5	1.74, *dq*, 3H J = 1.5, J = 1.5
C-13 H_3	1.97, *dq*, 3H J = 7, J = 1.5	1.94, *dq*, 3H J = 7.5, J = 1.5	2.86, *dq*, 3H J = 7, J = 1.5
C-18 H_3	—	2.04, *d*, 3H J = 7	1.14, *d*, 3H J = 7
C-6 H_2	2.16, *m*, 2H	2.17, *m*, 2H	2.10, *m*, 2H
C-5 H_A	2.75, *m*, 1H	2.71, *q*, 1H J = 8	2.75, *q*, 1H J = 8
C-9 OH	3.35, *s*, 1H	—	—
C-5 H_B	3.36, *m*, 1H	3.48, *m*, 1H	3.30, *q*, 1H J = 3.5
C-3 H_A	3.48, *m*, 1H	3.36, *m*, 1H	3.42, *m*, 1H
C-3 H_B	4.02, *m*, 1H	4.04, *m*, 1H	4.01, *m*, 1H
C-9 H_2	4.21, *s*, 2H	4.88, *s*, 2H	4.68, *s*, 2H
C-19 H_2	—	4.22, *s*, 2H	3.67, *d*, 2H J = 7.5
C-8 H	4.46, *m*, 1H	4.50, *m*, 1H	4.35, m, 1H
C-16 OH	—	—	4.53, *s*, 1H
C-17 OH	—	—	4.53, *s*, 1H
C-19 OH	—	4.75, *s*, 1H	4.53, *s*, 1H
C-7 H	5.46, *dd*, 1H J = 3.5, J = 2	5.44, *m*, 1H	5.67, *m*, 1H
C-2 H	5.66, *m*, 1H	5.81, *m*, 1H	5.81, *m*, 1H
C-12 H	6.11, *dq*, 1H J = 7.5, J = 1.5	6.11, *dq*, 1H J = 7, J = 1.5	6.09, *dq*, 1H J = 7, J = 1.5
C-17 H	—	6.38, *q*, 1H J = 7	3.95, *q*, 1H J = 6.5

δ Values in ppm; J in Hz.

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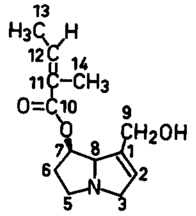
*Dedicated to Professor Maximilian Steiner on the occasion of his 80th birthday.



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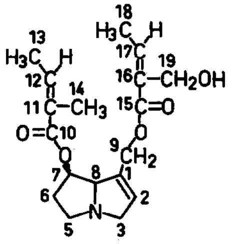

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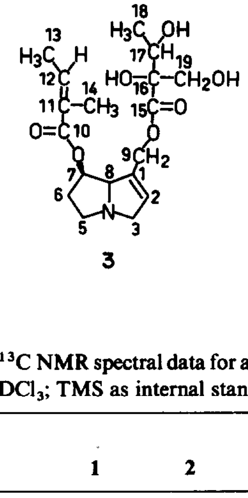

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Table 2. ^{13}C NMR spectral data for alkaloids 1–3 ($CDCl_3$; TMS as internal standard)

Carbon No.	1	2	3
13	15.76	15.76	15.79
18	—	15.76	17.54
14	20.59	20.52	20.55
6	34.67	34.54	34.44
5	53.60	53.67	53.86
9	60.04	60.72	62.08
3	63.21	62.47	62.63
19	—	64.70	65.19
17	—	141.03	69.33
7	74.06	73.60	73.73
8	75.78	75.68	75.55
16	—	131.80	82.47
1	127.69	127.50	127.53
12	124.01	127.24	128.05
11	139.47	133.84	133.51
2	138.96	139.50	139.34
10	167.31	166.83	166.92
15	—	166.63	174.07

δ values in ppm.

ture as shown. The data indicate that **2** is triangularine, an alkaloid recently isolated from *Senecio triangularis* [3]. Our ^{13}C NMR spectra data differ, however, from those reported in the above-mentioned paper in the values for C-1/C-2 and C-11/C-12, respectively. On account of the ^3J coupling constants, we set a value of 127.5 ppm for C-1 and of 139.5 ppm for C-2. The other report [3] gives the value for C-11 at 133.8 and for C-12 at 127.2 ppm. Other authors have interchanged the signals for these two pairs of carbons [3].

All NMR data were established both by decoupling experiments and by evaluation of coupled and noise-decoupled spectra. Of the three alkaloids, **1–3**, present in *Alkanna tinctoria*, compound **3** is new and we propose to call it dihydroxy-triangularine.

EXPERIMENTAL

Extraction of the plant material was carried out as described earlier [2]. The resulting residue was separated in ascending mode by DCCC using the solvent system C_6H_5Me–$CHCl_3$–MeOH–H_2O (5:5:7:2) [4]. Three alkaloids were isolated and purified by preparative DC (silica gel). Substance **1** was recrystallized from Me_2CO–petrol (2:1). Alkaloids **2** and **3** were oils.

O^7-*Angelylretronecine* (**1**). Mp 79° (lit. 76–77° [5]); $[\alpha]_D^{20}$ +67° ($CHCl_3$) (lit. $[\alpha]_D^{24}$ +49° (EtOH) [5]). IR ν_{max}^{KBr} cm^{-1}: 3140 (OH), 1720 (unsatd ester), 1660 (C=C); CIMS (MeOH) 70 eV, *m/z* (rel. int.): 237 $[M]^+$ (4.9), 219 $[M-H_2O]^+$ (8.7), 154 $[M-C_5H_7O]^+$ (4.6), 137 $[M-C_4H_7COOH]^+$ (30), 124 $[154-CH_2O]^+$ (28.8), 111 $[137-C_2H_2]^+$ (39.8), 106 $[137-CH_2OH]^+$ (46), 94 $[111-OH]^+$ (30.5), 80 $[111-CH_2OH]^+$ (100).

Triangularine (**2**). $[\alpha]_D^{20}$ +6.7° ($CHCl_3$) (lit. $[\alpha]_D^{25}$ +2.2° ($CHCl_3$) [3]); IR ν_{max}^{KBr} cm^{-1}: 3400 (OH), 1730 (satd ester), 1710 (unsatd ester), 1660 (C=C); CIMS (MeOH) 70 eV, *m/z* (rel. int.): 335 $[M]^+$ (6.6), 237 $[M-C_5H_6O_2]^+$ (33.3), 221 $[M-C_5H_6O_3]^+$ (8.6), 220 $[M-C_5H_7O_3]^+$ (49.4), 219 $[M-C_5H_8O_3]^+$ (29.5), 138 $[221-C_5H_7O]^+$ (5.5), 137 $[237-C_5H_8O_2]^+$ (13.1), 136 $[219-C_5H_7O]^+$ (100), 121 $[221-C_5H_8O_2]^+$ (22.1), 120 $[220-C_5H_8O_2]^+$ (54.8), 119 $[219-C_5H_8O_2]^+$ (28.8), 95 $[121-C_2H_2]^+$ (10), 94 $[120-C_2H_2]^+$ (47.4), 93 $[119-C_2H_2]^+$ (81.6), 80 $[95-Me]^+$ (14.1).

Dihydroxytriangularine (**3**). $[\alpha]_D^{20}$ +14.7° ($CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 3400 (3 × OH), 1745 (satd ester), 1720 (unsatd ester), 1650 (C=C); CIMS (MeOH) 70 eV, *m/z* (rel. int.): 369 $[M]^+$ (2.2), 338 $[M-CH_2OH]^+$ (0.5), 324 $[M-MeCHOH]^+$ (0.6), 269 $[M-C_4H_7COOH]^+$ (5.3), 237 $[M-C_5H_8O_4]^+$ (4.4), 220 $[338-C_4H_6O_4]^+$ (100), 219 $[M-C_5H_{10}O_5]^+$ (12.4), 138 $[220-C_5H_6O]^+$ (5.8), 137 (9.2), 136 (66.5), 121 (13.2), 120 (55.5), 119 (19.4), 95 (6.4), 94 (34.9), 93 (55.4), 80 (18.4).

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