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22,26-EPIMINOCHOLESTANE ALKALOIDS WITH UNUSUAL (20*R*)-CONFIGURATIONS FROM *SOLANUM* SPECIES*

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Key Word Index—*Solanum abutiloides*; *S. canense*; *S. fraxinifolium*; Solanaceae; steroid alkaloids; solafloridine; 20-isosolafloridine; 20,25-bisisoetioline.

Abstract—From the roots of *Solanum abutiloides*, solasodine, solafloridine and a new alkaloid have been isolated, the structure of which has been elucidated as 20-isosolafloridine [(20*R*,25*R*)-22,26-epiminocholest-22(*N*)-ene-3β,16α-diol]. The structure of an alkaloid from aerial parts of *S. canense* and *S. fraxinifolium* earlier supposed to be etioline has been recognized as 20,25-bisisoetioline [(20*R*,25*R*)-22,26-epiminocholesta-5,22(*N*)-diene-3β,16α-diol].

INTRODUCTION

From the roots of *Solanum abutiloides* (Griseb.) Bitt. et Lillo, solasodine, solafloridine (**1**) and a new alkaloid have been isolated, the structure of which has been elucidated as 20-isosolafloridine [(20*R*,25*R*)-22,26-epiminocholest-22(*N*)-ene-3β,16α-diol, **2**] as outlined below. The structure of a further alkaloid from leaves and stems of *S. canense* Rydb. and *S. fraxinifolium* Dun. earlier supposed to be etioline [2,3] has been recognized as 20,25-bisisoetioline [(20*R*,25*R*)-22,26-epiminocholesta-5,22(*N*)-diene-3β,16α-diol, **3**]. Both alkaloids **2** and **3** possess the unusual (20*R*)-configuration of 22,26-epiminocholestanes, which has recently been detected in (20*R*)-verazine [4].

RESULTS AND DISCUSSION

Compound **1** was identified by comparison with an authentic sample [5]. The elemental composition of alkaloid **2** was shown to be $C_{27}H_{45}NO_2$ by high resolution mass spectrometry. This indicated that **1** and **2** were isomers. Compound **3** had an elemental composition of $C_{27}H_{43}NO_2$. The diagnostic fragments at *m/z* 125 were in accordance with 22(*N*)-unsaturated 22,26-epiminocholestane structures [6]. Compounds **1**–**3** displayed positive circular dichroism [$\Delta\varepsilon_{249}$ + 1.90, $\Delta\varepsilon_{246}$ + 2.96, $\Delta\varepsilon_{246}$ + 2.48, in dioxane] in agreement with (25*R*)-configurations [7]. Etioline with a (25*S*)-configuration showed a negative Cotton effect [$\Delta\varepsilon_{243}$ − 2.54, in dioxane].

The ^{13}C NMR signals of **1**–**3** (Table 1) were assigned by comparison with literature data [8,9], and the ^{1}H signals by HMQC, ^{1}H–^{1}H DQF COSY and NOESY measurements. The assignments of the ^{13}C signals were supported by APT spectra. The NMR spectra of the alkaloids **1** and **2** differed mainly with regard to the chemical shifts of C-12, C-16, C-17, C-20–C-23, H-12α, H-12β, H-16, H-20, H_3-21, H-23a and H-23e (Table 1). Hence, it could be concluded that the structures of **1** and **2** disagreed in the configurations at C-16, C-17 and/or C-20. Nearly identical chemical shifts for C-18 and NOEs between H-16 and H_3-18 (Fig. 1) indicated 16α-hydroxyl groups in **1** and **2**. NOEs between H_3-18 and H-20 were in agreement with 17β-side chains of both alkaloids. NOEs in both compounds between H-20 on the one hand and H-16 and H_3-18 on the other indicated, at least approximately, antiperiplanar positions of H-17 and H-20. The coupling constants $^3J_{17,20}$ = 11.1 Hz measured in **1** as well as 7.9 Hz observed in **2** corresponded to this assumption. A NOE between H_3-18 and H_3-21 and the absence of a NOE between H-16 and H_3-21 measured in **1** agreed with the known (20*S*)-configuration of **1**, whereas a NOE between H-16 and H_3-21 observed in the alkaloid **2** indicated the (20*R*)-configuration for this compound. The ^{13}C NMR spectrum of alkaloid **3** showed that its structure differed from that of **2** by a 5-double bond (cf. e.g. the spectra of soladulcidine [10] and solasodine [8]) and, therefore, is 20,25-bisisoetioline.

Experiments showed **2** and **3** are not formed from **1** and 25-isoetioline, respectively, or vice versa, during the isolation procedure (hydrolysis with 1 M HCl in 90% ethanol, reflux for 3 hr).

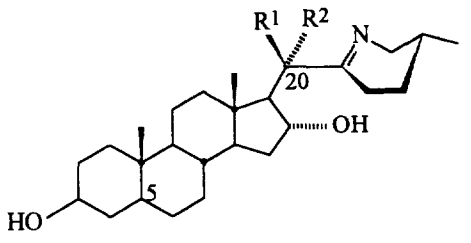
EXPERIMENTAL

Seeds of *S. abutiloides* were obtained from Hortus Botanicus, Nijmegen. Plants were grown in a field in Halle (Saale) and harvested in August 1992. A voucher specimen

*Part 136 in the series '*Solanum* Alkaloids'. For part 135 see ref. [1].

is retained in the Institute of Plant Biochemistry, Halle.

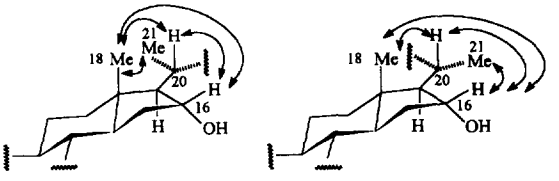
Isolation of alkaloids. Roots of *S. abutiloides* were dried at 60°, ground and extracted with MeOH at room temp. Evapn of MeOH *in vacuo* gave a residue which was partitioned between 0.5 M HCl and C_6H_6–Et_2O (1:1). After addition of $KHCO_3$ to the aq. layer, the latter was extracted with $CHCl_3$–EtOH (2:1). Evapn of solvents *in vacuo* gave a mixt. of alkaloids which was hydrolysed with a 50-fold amount of 1 M HCl in 90% EtOH for 3 hr under reflux. After evapn *in vacuo* and addition of aq. $KHCO_3$, the mixt. was extracted with $CHCl_3$. After drying over Na_2SO_4 and removal of the solvent *in vacuo*, the residue was chromatographed over silica gel. $CHCl_3$–MeOH (99:1) eluted solasodine (0.14%, crystallized from Me_2CO–H_2O), $CHCl_3$–MeOH (49:1) eluted



1 R^1 = H, R^2 = Me, 5αH

2 R^1 = Me, R^2 = H, 5αH

3 R^1 = Me, R^2 = H, Δ^5



1 **2**

Fig. 1. NOEs of **1** and **2** in pyridine-d_5.

Table 1. NMR data (δ values) for compounds **1–3** (pyridine-d_5, 126 MHz for ^{13}C, 500 MHz for ^1H)

	1		**2**		**3**
Position	δ_C	δ_H (α, β or a, e)	δ_C	δ_H (α, β or a, e)	δ_C
1	37.4	0.95, 1.68	37.5	0.98, 1.69	37.8
2	32.4	2.06, 1.71	32.4	2.05, 1.69	32.6
3	70.6	3.86, —	70.5	3.85, —	71.2
4	39.3	1.80, 1.58	39.3	1.80, 1.58	43.6
5	45.1	1.09, —	45.2	1.10, —	142.0
6	29.1	1.24, 1.24	29.1	1.26, 1.26	121.2
7	32.5	0.90, 1.63	32.5	0.91, 1.64	32.3
8	35.2	—, 1.34	35.2	—, 1.34	31.7
9	54.5	0.64, —	54.8	0.65, —	50.7
10	35.8	—	35.9	—	37.0
11	21.3	1.47, 1.25	21.1	1.50, 1.24	21.0
12	40.7	1.29, 1.88	38.6	1.12, 1.66	38.4
13	44.4	—	44.4	—	44.1
14	53.8	1.61, —	53.7	1.53, —	54.0
15	36.4	1.90, 1.60	37.2	1.94, 1.74	37.3
16	76.5	—, 4.14[a]	74.3	—, 4.39[b]	74.3
17	64.1	1.90, —	62.7	1.94, —	62.6
18	14.0	0.73	14.2	0.84	14.0
19	12.5	0.83	12.5	0.83	19.7
20	46.2	2.55[c]	44.3	2.69[d]	44.4
21	19.2	1.17[e]	18.2	1.40[f]	18.2
22	176.3	—	175.2	—	175.3
23	28.4	2.48,[g] 2.14	27.4	2.07, 2.33[h]	27.4
24	27.9	1.14, 1.65	28.3	1.13, 1.67	28.3
25	27.3	1.54, —	27.8	1.46, —	27.8
26	56.5	3.08,[i] 3.69[j]	57.0	3.01,[k] 3.81[l]	57.0
27	19.1	0.79[m]	19.4	0.81[n]	19.5

[a] *dd*, J = 5.8, 5.8 Hz; [b] *dd*, J = 7.0, 7.0 Hz; [c] *dq*, J = 11.1, 6.9 Hz; [d] *dq*, J = 7.9, 7.0 Hz; [e] *d*, J = 7.0 Hz; [f] *d*, J = 7.0 Hz; [g] *dd*, J = 18.2, 10.2 Hz; [h] *dd*, J = 18.3, 5.5 Hz; [i] *dd*, J = 16.8, 9.5 Hz; [j] *dd*, J = 16.6, 4.4 Hz; [k] *dd*, J = 16.8, 10.4 Hz; [l] *dd*, J = 16.8, 4.6 Hz; [m] *d*, J = 6.7 Hz; [n] *d*, J = 6.4 Hz.

a mixt. of solafloridine and 20-isosolafloridine, which was rechromatographed over silica gel with $CHCl_3$ shaken with an equal amount of conc. NH_3–toluene (1 : 1). 20,25-Bisisoetioline was isolated from aerial parts of *S. canense* Rydb. and *S. fraxinifolium* Dun. as described for the supposed etioline [2, 3].

Solafloridine (**1**). From Me_2CO: needles; yield 0.013%. Mp 169–172°, ref. [5]: 167–168°. $[\alpha]_D^{18}$ + 141.2° ($CHCl_3$; *c* 0.70), ref. [5]: + 127° ($CHCl_3$). R_f 0.36 (Merck TLC aluminium sheets, Silica gel 60 $WF_{254}S$, $CHCl_3$ shaken with an equal amount of conc. NH_3). EI-MS (70 eV) *m/z* (rel. int.): 415 $[M]^+$ (6), 397.3348 $[M - H_2O]^+$ ($C_{27}H_{43}NO$, calc. 397.3344) (57), 382 $[397 - Me]^+$ (42), 162.1275 ($C_{11}H_{16}N$, calc. 162.1283) (63), 148.1087 ($C_{10}H_{14}N$, calc. 148.1125) (23), 138.1264 ($C_9H_{16}N$, calc. 138.1283) (62), 125.1204 ($C_8H_{15}N$, calc.125.1204) (100), 98.0957 ($C_6H_{12}N$, calc. 98.0970) (33).

20-*Isosolafloridine* (**2**). From Me_2CO: needles; yield 0.014%. Mp 136–137°. $[\alpha]_D^{25}$ + 45.1° ($CHCl_3$; *c* 0.89). R_f 0.29 (see above). EI-MS (70 eV) *m/z* (rel. int.): 415.3430 $[M]^+$ ($C_{27}H_{45}NO_2$, calc. 415.3450) (7), 397 $[M - H_2O]^+$ (50), 382 $[397 - Me]^+$ (100), 162.1279 ($C_{11}H_{16}N$, calc. 162.1283) (38), 148.1102 ($C_{10}H_{14}N$, calc. 148.1125) (23), 138.1275 ($C_9H_{16}N$, calc. 138.1283) (17), 125.1207 ($C_8H_{15}N$, calc. 125.1204) (40), 98 (9).

20,25-*Bisisoetioline* (**3**). From Me_2CO; yield 0.064% from *S. canense*, 0.098% from *S. fraxinifolium*. Mp 158–161°. $[\alpha]_D^{20}$ − 11.8° ($CHCl_3$; *c* 0.69). R_f 0.29 (see above). EI-MS (70 eV) *m/z* (rel. int.): 413.3299 $[M]^+$ ($C_{27}H_{43}NO_2$, calc. 413.3294) (20), 395 $[M - H_2O]^+$ (55), 380 $[395 - Me]^+$ (89), 162 (21), 148 (29), 138 (61), 125 (100), 98 (26).

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