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# PYRROLIZIDINE ALKALOIDS FROM *SENECIO CACALIASTER**

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**Key Word Index**—*Senecio cacaliaster*; Compositae; pyrrolizidine alkaloids; $O^7$-senecioylretronecine; $O^7$-senecioyl-9-sarracinyl-retronecine; sencalenine; bulgarsenine.

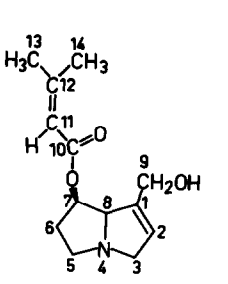
**Abstract**—Four pyrrolizidine alkaloids have been isolated from *Senecio cacaliaster* and their structures analysed by spectroscopic methods (IR, mass, $^1H$, $^{13}C$ NMR). One of them is new and the name sencalenine (**3**) is proposed. Alkaloids $O^7$-senecioylretronecine (**1**) and 7-senecioyl-9-sarracinylretronecine (**2**) have recently been identified elsewhere. The fourth is bulgarsenine (**4**) which was isolated from a *Senecio* species before.

## INTRODUCTION

*Senecio cacaliaster* is widely distributed in Europe. On account of the fact that this plant possesses no ligules, Linné adjoined it to the genus Cacalia and named it *S. cacaliaster*. However, in spite of the missing ligules this plant does resemble *S. nemorensis*, especially *S. nemorensis* subsp. *fuchsii* which may be implied from its outward shape. Both of them belong to the Betulo adenostyletea [1]. Ecologically *S. cacaliaster* is closely related to *S. nemorensis* subsp. *fuchsii*, from which the pyrrolizidine alkaloids (PA) fuchsisenecionine and senecionine could be isolated [2, 3]. *S. lamottei* is a hybrid of these two species. Therefore, a common precursor of *S. cacaliaster* and *S. nemorensis* has to be considered. We investigated *S. cacaliaster* with regard to its alkaloids in order to prove this relationship. We detected four major alkaloids by TLC, which we then separated by droplet counter current chromatography (DCCC).

## RESULTS AND DISCUSSION

Methanolic extraction of plant material was followed by purification of the residue as already described [3]. From the resulting residue four PAs have been isolated by DCCC. The mass spectra gave the formulae $C_{13}H_{19}NO_3$ for **1**, $C_{18}H_{25}NO_5$ for **2** and **3** and $C_{18}H_{27}NO_5$ for **4**. The fragmentation of the latter alkaloid is identical to that of bulgarsenine [4]. A typical fragmentation of **1**–**3** between *m/z* 136 and *m/z* 80 is characteristic for retronecine or its isomeric form. In addition, the fragmentations show that PAs **2** and **3** are isomeric diesters, whereas PA **1** must be a retronecine monoester. The mass spectrum also gives information about the esterification of PA **1** at C-7 with a 5-C-linked acid. The alkaloids **2** and **3**, having similar 5-C-linked acids, are esterified at both alcoholic positions. Likewise, the IR data show for alkaloid **1** one ester bond, whereas in **2**, **3** and **4** two such bonds were found. Further information about the structures is given by NMR analysis (Tables 1 and 2).



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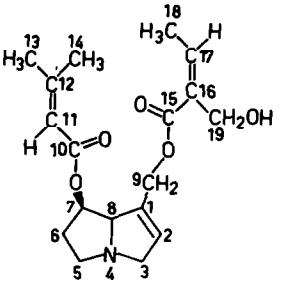

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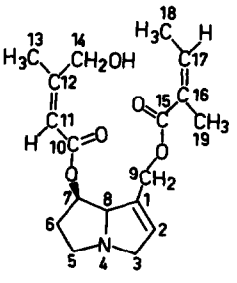

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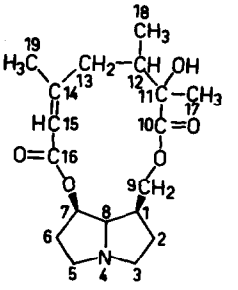

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The NMR data for **1** are reported for the first time; in the case of alkaloid **2** our data differ from those described recently [5] by interchange of the $^{13}C$-values for carbons 1/12/16 and 3/9 and 13/14. Likewise, there is some difference in the $^1H$ NMR data especially in the values for the C-5 $H_2$. All values were verified by decoupling experiments and by evaluation of coupled and noise-decoupled spectra. The value for C-6 $H_2$ is higher by 2 ppm for all three alkaloids. This also demonstrates that retronecine is the necic base [6, 7]. The NMR data indicate the structure of an $O^7$-senecioic-acid-retronecine-ester for PA **1**. This is clear from the $^1H$ peaks at $\delta$ 1.89 and 2.16 for two methyls and the corresponding

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

Table 1. $^1$H NMR data of 1, 2 and 3 ($CDCl_3$; TMS)

| | 1 | 2 | 3 |
|---|---|---|---|
| $C_{13}$-$H_3$ | 1.89, *d*, 3H *J* = 1 | 1.87, *d*, 3H *J* = 1 | 2.04, *d*, 3H |
| $C_{14}$-$H_3$ | 2.16, *d*, 3H *J* = 1 | 2.05, *d*, 3H *J* = 1 | — |
| $C_{14}$-$H_2$ | — | — | 3.62, *m*, 2H |
| $C_{14}$-OH | — | — | 4.73, *m*, OH |
| $C_6$-$H_2$ | 2.06, *m*, 2H | 2.67, *q*, 2H *J* = 9 | 2.33, *m*, 2H |
| $C_5$-$H_A$ | 2.71, *m*, 1H | 3.31, *m*, 1H | 2.29, *m*, 1H |
| $C_3$-$H_A$ | 3.28, *m*, 1H | 3.49, *m*, 1H | 3.1, *m*, 1H |
| $C_5$-$H_B$ | 3.38, *m*, 1H | 3.67, *m*, 1H | 3.6, *m*, 1H |
| $C_3$-$H_B$ | 3.89, *m*, 1H | 3.93, *m*, 1H | 3.75, *m*, 1H |
| $C_{18}$-$H_3$ | — | 2.02, *d*, 3H *J* = 7.5 | 1.97, 2*q*, 3H *J* = 7; 1.5 |
| $C_9$-$H_2$ | 4.1, *d*, 2H | 4.78, *m*, 2H | 4.71, *m*, 2H |
| $C_{19}$-$H_3$ | — | — | 1.87, *q*, 3H *J* = 1.5 |
| $C_{19}$-$H_2$ | — | 4.2, *s*, 2H | — |
| $C_{19}$-OH | — | 4.39, *m*, OH | — |
| $C_8$-H | 4.7, *m*, 1H | 4.51, *m*, 1H | 4.44, *m*, 1H |
| $C_9$-OH | 4.57, *m*, OH | — | — |
| $C_7$-H | 5.45, *m*, 1H | 5.4, *m*, 1H | 5.62, *m*, 1H |
| $C_{11}$-H | 5.6, *m*, 1H | 5.6, *m*, 1H | 5.97, *m*, 1H |
| $C_2$-H | 5.68, *m*, 1H | 5.78, *m*, 1H | 5.78, *m*, 1H |
| $C_{17}$-H | — | 6.38, *q*, 1H *J* = 7.5 | 6.16, 2*q*, 1H *J* = 7 |

$\delta$ values in ppm; *J* in Hz.

Table 2. $^{13}$NMR data of 1, 2 and 3 ($CDCl_3$; TMS)

| Carbon No. | 1 | 2 | 3 |
|---|---|---|---|
| 18 | — | 15.8 | 15.9 |
| 13 | 20.46 | 20.3 | 20.6 |
| 14 | 27.58 | 27.5 | 66.8 |
| 6 | 34.31 | 34.4 | 34.2 |
| 5 | 53.47 | 53.7 | 54.0 |
| 9 | 59.43 | 60.8 | 60.5 |
| 3 | 61.8 | 62.3 | 62.1 |
| 19 | — | 64.7 | 16.0 |
| 7 | 72.44 | 72.9 | 71.8 |
| 8 | 76.32 | 75.7 | 76.4 |
| 11 | 115.0 | 115.8 | 123.8 |
| 2 | 121.8 | 127.0 | 126.8 |
| 1 | 138.79 | 131.8 | 140.2 |
| 12 | 138.75 | 133.9 | 133.6 |
| 17 | — | 141.0 | 128.1 |
| 16 | — | 158.0 | 160.8 |
| 15 | — | 165.6 | 164.9 |
| 10 | 168.0 | 166.6 | 167.18 |

*$\delta$ values in ppm.

olefinic proton at 5.6. The structure of **1** is also verified from the corresponding $^{13}$C data. The NMR spectra of PA **2** show partially the same peaks as the NMR data of **1**; thus, **1** is found as a partial structure in **2**. Furthermore, in **2** the esterified acid at C-9 must be a hydroxyangelic acid. This is confirmed by a quartet at $\delta$ 2.02 with a coupling constant of 7.5 Hz for C-18 $H_3$ and the olefinic proton at 6.38 with the same coupling constant. The hydroxyl group must be located at position C-19 on account of the value $\delta$ 4.2 for the methylene group. This structure is also established by the following $^{13}$C data: $\delta$ 64.7 for C-19 and 15.8 for C-18. The data for compound **3** show that it is an isomer of **2**. Instead of peaks for the methyl group at C-14 those of a hydroxymethyl group at $\delta$ 4.73 ($^1$H) and 66.8 ($^{13}$C) are found. In comparison with **2**, peaks for an angelic acid are present in **3** for the acid at C-9: C-18 $H_3$: $\delta$ 1.97 (*J* = 7; 1.5 Hz) = $^1$H and 15.9 = $^{13}$C NMR; C-19 $H_3$: $\delta$ 1.87 (*J* = 1.5 Hz) = $^1$H and 16.0 = $^{13}$C NMR. The esterification of **2** and **3** as shown in the formulae is proved by mass spectrometry. The fragmentation pattern of **2** shows an intense ion at *m/z* 220. This ion is formed after ester cleavage at C-9 building a necine, esterified at C-7 with a 3-methyl-2-butenoic acid. Furthermore, ion *m/z* 219 shows a McLafferty rearrangement and a loss of 100 mu (*m/z* 119). The ion *m/z* 237 also proves the structure **2**. It is formed after rearrangement of the ester grouping at C-9 and the loss of $C_5H_6O_2$ indicating the hydroxymethyl group position at C-1. In the fragmentation pattern of **3** the ion *m/z* 219 is formed after McLafferty rearrangement and the loss of 116 mu. Only alkaloids which possess an open diester form show such rearrangements at C-7. Therefore, in **3** there must be an acid of MW 116 esterified at C-7. Furthermore, an ester cleavage is found at C-9 forming the ion *m/z* 236. This esterification at C-7 and C-9 in **3** is established by the fact that the ion *m/z* 220 is missing. For the fourth alkaloid (= bulgarsenine) we found similar data as reported earlier [4, 8]. For the new alkaloid **3** we propose the name sencalenine.

## EXPERIMENTAL

*S. cacaliaster* (Lam.) was collected in alpine Austria (Highlands of Grossglockner). The dried and pulverized drug was extracted and purified as mentioned earlier [3]. The resulting yellow residue was separated by DCCC using toluene–MeOH–$H_2O$–$CHCl_3$ in the ascending mode yielding the four PAs [9]. Content of PAs (GC; dry wt): **1**, 0.017%; **2**, 0.005%; **3**, 0.005%; **4**, 0.21%. GC conditions: glass column: 1.8 m, 2 mm; 4% SE 30 on Varaport 30; prog: 80–240° in four steps at 9°/min: 2 × 2°/min; 1 × 3°/min; 1 × 4°/min. Inj.: 200°. Det.: 260°; carrier gas ($N_2$): 40 ml/min. $R_{S_t}$ values (min): **1**, 1.53; **2**, 21.8; **3**, 17.6; **4**, 20.15.

*$O^7$-Senecioylretronecine* (**1**). Oily; $[\alpha]_D^{20} = -2$ (EtOH). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3385 (OH), 3010 (C=C), 1730 (satd ester), 1705 (unsatd ester), 1655 (C=C). CIMS ($CHCl_3$), 70 eV, *m/z* (% rel. int.): 237.137 $[M]^+$ (10.29), 219 $[M-H_2O]^+$ (1.47), 154 $[M-C_5H_7O]^+$ (11.05), 137 $[M-C_5H_8O_2]^+$ (38.64), 136 $[219-C_5H_7O]^+$ (30.76), 124 $[154-CH_2O]^+$ (34.31), 111 $[137-C_2H_2]^+$ (47.09), 106 $[137-CH_2-OH]^+$ (48.94), 94 $[111-OH]^+$ (24.77), 80 $[111-CH_2-OH]^+$ (100.0).

*7-Senecioyl-9-sarracinylretronecine* (**2**). Oily; $[\alpha]_D^{20} = +4$ (EtOH). IR $\nu_{max}^{KBr}$ cm$^{-1}$: 3390 (OH), 3010 (C=C), 1720 (satd ester) 1705 (unsatd ester), 1645 (C=C). CIMS ($CHCl_3$), 70 eV, *m/z* (rel. int.): 335.173 $[M]^+$ (9.06) 237 $[M-C_5H_6O_2]^+$ (42.32), 221 $[M-C_5H_6O_3]^+$ (7.08), 220 $[M-C_5H_7O_3]^+$ (40.85), 219 $[M-C_5H_8O_3]^+$ (8.79), 138 $[221-C_5H_7O]^+$ (12.81), 137 $[220-C_5H_7O]^+$ (11.96), 136 $[219-C_5H_7O]^+$ (100.0), 121 $[221-C_5H_8O_2]^+$ (17.59), 120 $[220-C_5H_8O_2]^+$ (37.08), 119 $[219-C_5H_8O_2]^+$ (28.93), 106 $[137-CH_3O]^+$ (8.67), 95 $[121-C_2H_2]^+$ (7.83), 94 $[120-C_2H_2]^+$ (46.57), 93 [119 − 26]$^+$ (67.31).

*Sencalenine* (3). Oily; $[\alpha]_D^{20} = -8$ (EtOH). IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3380 (OH), 3060 (C=C), 1730 (satd ester), 1710 (unsatd ester), 1660 (C=C). CIMS ($CHCl_3$) 70 eV, *m/z* (rel. int.): 335.172 $[M]^+$ (13.50), 252 $[M-C_5H_7O_2]^+$ (22.04), 236 $[M-C_5H_7O_2]^+$ (28.46), 235 $[M-C_5H_8O_2]^+$ (15.16), 219 $[M-C_5H_8O_3]^+$ (12.32), 154 $[252-C_5H_6O_2]^+$ (20.18), 137 $[219-C_5H_6O]^+$ (11.88), 136 $[235-C_5H_7O_2]^+$ (100.0), 122 $[237-C_5H_7O_3]^+$ (28.10), 120 $[219-C_5H_7O_2]^+$ (52.06), 119 $[235-C_5H_8O_3]^+$ (31.13), 106 $[137-CH_2-OH]^+$ (9.40), 94 $[120-C_2H_2]^+$ (60.88), 93 $[119-C_2H_2]^+$ (79.55), 80 $[122-C_3H_6]^+$ (18.27).

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