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FURTHER PYRROLIZIDINE ALKALOIDS AND FUROEREMOPHILANES FROM *SENECIO* SPECIES

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Key Word Index—*Senecio*; Compositae; pyrrolizidine alkaloids; sesquiterpenes; eremophilanes; furoeremophilanes; shikimic acid derivative; acetylenic compound.

Abstract—The investigation of 17 *Senecio* species afforded in addition to 14 known pyrrolizidine alkaloids 20 new ones, including some compounds of a novel type with an additional lactone moiety. Furthermore seven known and 11 new furoeremophilanes, two known and a new eremophilone, a further shikimic acid derivative and an acetylenic compound, most likely formed by intramolecular Diels–Alder reaction were isolated. The structures were elucidated by spectroscopic methods, especially high field ^{1}H and ^{13}C NMR and NOE difference spectroscopy. The configuration of the seneremophilondiol esters has been corrected.

INTRODUCTION

The large, very diverse genus *Senecio* has already been studied extensively for its secondary chemicals. Pyrrolizidine alkaloids and furoeremophilanes are particularly characteristic for large parts of the genus, though there are many species which lack these compounds. In some cases the furoeremophilanes are replaced by their precursors, but there are other groups, especially the succulents, where other types of sesquiterpenes predominate [1]. We now have re-studied 16 species. The results are discussed in this paper.

RESULTS AND DISCUSSION

The aerial parts of *Senecio multivenius* Benth. in Oerst. afforded seneciphylline [2], senecionine [3] and α-curcumene, but no eremophilane derivatives. *Senecio megaphyllus* Green. like the latter from Costa Rica, gave to pyrrolizidine alkaloids, the isomeric epoxides **19** and **20**, which have not been reported previously. The structures followed from the molecular formula and from comparison of the ^{1}H NMR spectra with that of seneciphylline and related compounds. The presence of an expoxide of seneciphylline followed from the pair of doublets at δ2.76 and 2.73 (J = 4 Hz) and the upfield shift of the H-13 signals while most of the other signals agreed with those of seneciphylline (Table 1). The ^{1}H NMR spectral data of **20** differed only slightly from those of **19** (Table 1). The signals of H-16 and H-17 were shifted in the expected manner and small shifts of some others could be observed. Again no eremophilanes were detected. From the aerial parts of *S. usgorensis* Cuatr. also **19** was isolated, while the other constituents were reported previously [4].

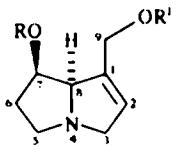
The aerial parts of *Senecio discolor* (Sw.) DC. [= *Pentacalia discolor* (Sw.) H. Robinson] gave retrorsin [5], 6β-isovaleryloxy-, 6β-senecioyloxy- and 6β-acetoxyfuroeremophil-9-one [6, 7] and 6β-isovaleryloxy-, 6β-isobutyryloxy-, 6β-angeloyloxy-, 6β-senecioyloxy-4α-hydroxyfuroeremophil-9-one [8]. The structure of retrorsin followed from the ^{1}H NMR spectrum.

The aerial parts of *Senecio richii* A. Gray gave in addition ot α-curcumene, germacrene D and α-humulene, senaetnin [1] and isosenaetnin [9]. No eremophilanes were observed. The roots of *Senecio coahuilensis* Greenm. gave cacalol methyl ether [10] and dehydrocacalohastin [10]. Senkirkin, where the structure is established by X-ray analysis [11] and florisenin [12] were isolated from the aerial parts of *S. quebradensis* Greenm. The ^{1}H NMR spectral data of senkirkin and florisenin are presented in Table 2.

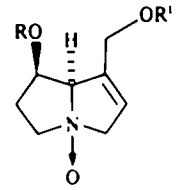
The aerial parts of *Senecio salignus* DC. [= *Barkleyanthus salicifolius* (HBK) H. Rob. et Brett.] gave in addition to the furoeremophilanes reported previously [13] 7-angeloyl heliotridin [14] (for ^{1}H NMR spectra data, see Table 4).

The aerial parts of the succulent species *Senecio mandralicae* Jacobs. afforded 1β-angeloyloxy-4β-hydroxyeudesm-7-ene [1] and the acyl pyrroles senaetnin, 14*E*-senaetnin [15] and isopterophorin [16] and no eremophilane derivatives, while the aerial parts of *S. grandifolius* Less. [= *Telanthophora grandifolia* (Less.) Rob.] afforded the furoeremophilanes **34** and **35–41** as well as senkirkin, neosenkirkin [17], spathulenol, γ- and δ-cadinene.

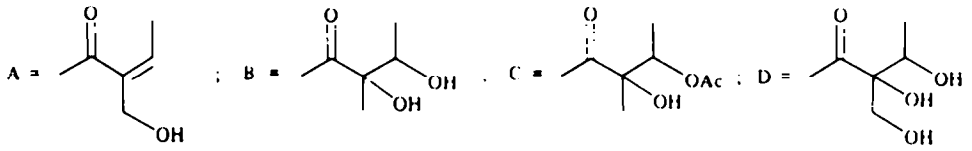
The structure of **34** clearly followed from the ^{1}H NMR spectrum (Table 3). While most signals were close to those of similar 6β-angelates of a 9-oxo-furoeremophilane [13] the presence of a 3-keto group followed from the downfield shift of H-4. Spin decoupling allowed the assignment of all signals. The ^{1}H NMR spectra of **35**, **36** and **39–41** (Table 3) differed fom that of **34** by the presence of additional signals which indicated a changed oxygen function. The chemical shift of the H-3 signal in the spectra of **39–41** required a free, axial orientated hydroxyl

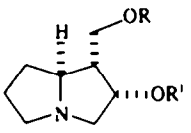


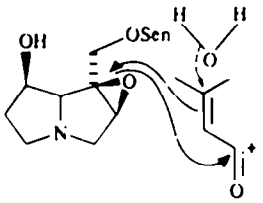
	1	2	3	4	5	6	7
R	H	Sen	Sen	Sen	Sen	Sen	Ang (α)
R'	Sen	H	A	B	C	D	H

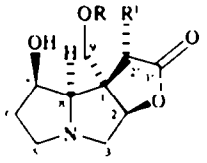


	8	9	10	11	12
R	H	H	Sen	Sen	Sen
R'	H	Sen	A	B	C

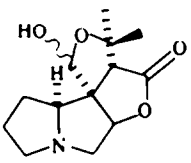




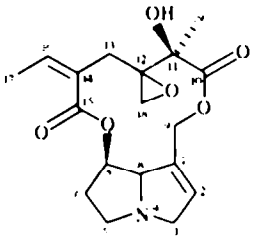




	13	14	15	16	17
R	H	Sen	R	Sen	iVal	Sen
R'	Sen	H	R'	C(OH)Me$_2$	C(OH)Me$_2$	H



18a 9α OH
18b 9β OH



19
20 14*E*

group, while that of **35** and **36** showed that a 3β-acetoxy group had to be assumed. Since the signals of H-6 were nearly unchanged the relative position of the ester groups were settled. As has been shown in similar cases the presence of an unsaturated ester group always caused a downfield shift of the corresponding proton under the ester group. The ^{13}C NMR of **35** agreed well with the expected one (Table 8). The ^{1}H NMR spectra of **37** and **38** (Table 3) differed from those of the other furoeremophilanes by the splitting of a low field signal at δ4.19 and 5.14 respectively. The results of spin decoupling only agreed with a 2α position for the oxygen function. Again the unchanged chemical shift of H-6 determined the relative positions of the ester groups.

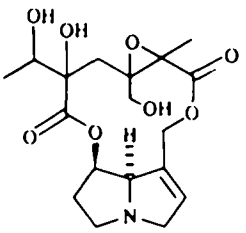
The roots of the South African *Senecio stapeliaeformis* Phill. only gave the acyl pyrrole **24** and again no eremophilanes. The structure of **24** followed from the ^{1}H NMR spectrum (Table 4) and the mass spectrum which showed elimination of angelic acid. This showed that the latter was at C-7. The nature of the second ester group easily could be deduced from the typical ^{1}H NMR signals while the remaining signals were close to those of the protons H-2, H-3, H-6 and H-9 of senaetnine [1]. Mild reaction with diazabicycloundecene gave angelic acid. This supported the presence of a 7-angeloyloxy derivative since elimination to the fully conjugated system is favoured [1]. The corresponding 5-desoxo-5-acetoxy derivative has been isolated previously [1].

The aerial parts of a *Senecio dolichodoryius* Cuatr. from Peru gave α-humulene, caryophyllene 1,10-epoxide, spathulenol, the 6β-angeloyloxy- and 6β-propionyloxy-1(10)-dehydrofuroeremophil-9-one [16, 17] and a new pyrrolizidine alkaloid, the epoxide **21**. The structures followed from the ^{1}H NMR and ^{13}C NMR spectra

(Tables 1 and 8) and from the high resolution mass spectrum which, however, showed no molecular ion. As in similar cases, the highest ion was due to $[M - H_2O]$. The ^{13}C NMR spectrum showed only two singlets for epoxide carbons. Thus a second epoxide could be excluded which would have been in agreement with the highest peak in the mass spectrum. Furthermore the observed chemical shift of H-16 and the coupling $J_{16,17}$ required a hydroxyl group at C-16. Most of the ^1H NMR signals were close to those reported for erucifoline [19] which is the corresponding precursor of **21** with 14*Z*-double bond. The stereochemistry at C-11, C-12, C-14 and C-16 could not be assigned while that at C-7 and C-8 obviously is the same as in senecionine as followed from the ^1H NMR signals of H-7 and H-8 (Table 1).

The aerial parts of a further species from Peru, *Senecio laricifolius* H.B.K. afforded seneciphylline, senecionine, senkirkine, 18-hydroxy and 18-acetoxy senkirkine (**22** and **23**) as well as the acetylenic aldehyde **32**. The structures of **22** and **23** could be deduced from the ^1H NMR spectra (Table 2) which were close to that of senkirkine. The position of the additional oxygen function followed by the presence of pairs of signals at δ4.21 and 4.10 as well as δ4.04 and 3.61, which replaced the methyl doublet at δ0.88 in the spectrum of senkirkine (Table 2). An alkaloid was isolated from *Gynura scandens* [20] that surely is the precursor of **22**.

The structure and the stereochemistry of **32** was elucidated by its ^1H and ^{13}C NMR spectrum (Table 6) and the data of the corresponding alcohol **33** obtained by



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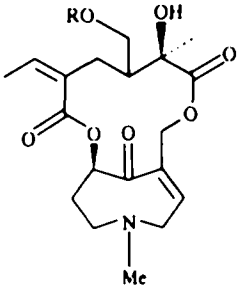
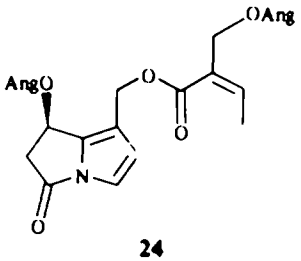


22 R = H
23 R = Ac



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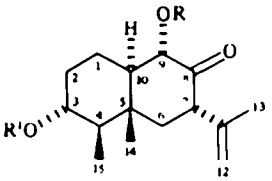
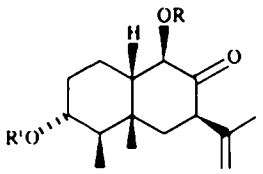


25 **26** **27**
R Tigl Sen Mesen
R¹ Sen Tigl Ang



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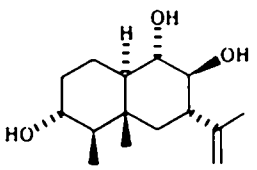

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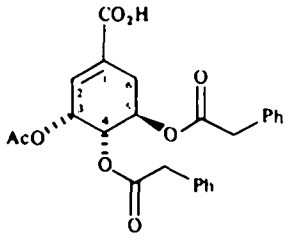
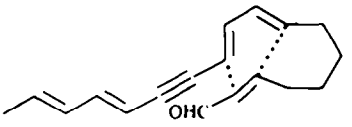


30

sodium boranate reduction. Spin decoupling allowed the assignment of nearly all signals. Only a few of the saturated ring protons were overlapped multiplets. The *cis*-orientation of H-2 and H-11 followed from the small coupling $J_{2,11}$ (*ca* 5 Hz), while a large coupling $J_{2,3}$ indicated *trans*-diaxial protons at C-2 and C-3. A NOE between H-2 and H-8 further established the stereochemistry. The ^{13}C NMR data also agreed with the structure. Comparison with similar acetylenic compounds [21] allowed the assignment of the signals of the unsaturated carbons. In the mass spectrum splitting of the 11,12-bond led to the base peak *m/z* 91 $[C_7H_7]^+$, while loss of the side chain followed by elimination of hydrogen gave the fragments *m/z* 133, 131, 129 and 128. Most likely **32** was formed via intramolecular Diels–Alder reaction of **31**, which, however, was not isolated from this plant.

The alkaloid fraction of the aerial parts of *Senecio pimpinellifolius* H.B.K. afforded senecionine and the corresponding *N*-oxide, while the neutral fraction only gave widespread sesquiterpenes.

Two South African species, *Senecio umgeniensis* Thell. and *S. variabilis* Sch. Bip. gave eremophilanes and pyrrolizidine alkaloids. The aerial parts and the roots of both species gave the isomeric ketones **25** and **26** as well as the corresponding 4-methyl senecioate **27**. The nature of the ester groups clearly followed from the typical ^1H NMR signals (Table 9) and the relative position were deduced from the mass spectrum which showed a strong fragment for the elimination of $C_5H_9CO_2H$ and a very weak one for $[M - C_4H_7CO_2H]^+$. This only can be explained with the C_6-ester at C-9 where elimination leads to a conjugated ketone. Furthermore the chemical shift of the olefinic proton of the ester side chain is influenced by the neighbouring keto group. Accordingly, the signal of the



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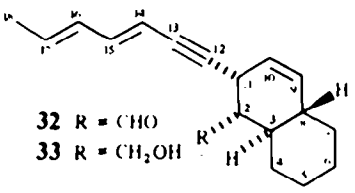
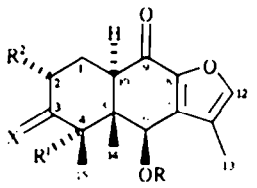
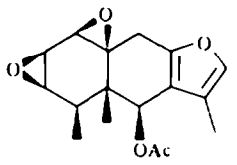


32 R = CHO
33 R = CH_2OH



	34	**35**	**36**	**37**	**38**	**39**	**40**	**41**
R	Ang	Ang	Mesen	Mesen	Mesen	Ang	Sen	Mesen
R^1	H	H	H	H	H	H	H	H
R^2	H	H	H	OAc	OH	H	H	H
X	O	βOAc,H	βOAc,H	H_2	H_2	βOH,H	βOH,H	βOH,H



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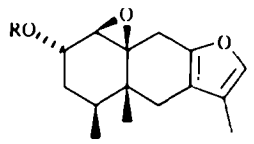
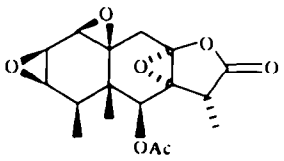


43 R = MeacI
44 R = iBu



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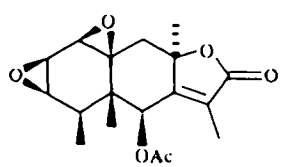

46

olefinic proton of the senecioate **25** is also shifted downfield if compared with that of **26**. As the stereochemistry of the isopropenyl side chain of petasin [22] and similar eremophilanes has been changed, that of **25–27** also was in doubt. We therefore have reduced all three compounds with lithium alanate which gave the triol **29**. The relative stereochemistry at C-7–C-10 followed from the couplings and the assignment of the signals could be achieved by spin decoupling. NOE difference spectroscopy led to the stereochemistry presented in **29**. Irradiation of H-15 gave clear NOEs with H-3, H-7 and H-9, while saturation of the H-14 signal gave NOEs with H-3 and H-6α. Further NOEs were observed between H-13 and H-7 and H-8, and between H-12, H-6β, H-7 and H-8. In all cases the corresponding couplings are exactly the same as in **25**–**27** and thus the stereochemistries of all seneremophilonediols [1, 8, 23–29] have to be corrected from **28** to the configuration with 7β-, 9β- and 10α-H.

The extract of *Senecio variabilis* further afforded some widespread compounds, 5α-hydroxyeudesm-4(15)-ene [24], 6α-tigloyloxyeudesm-5(15)-ene [25] as well as large amounts of the shikimic acid derivatives **30** and the triphenyl acetate [30]. The acid **30** was transformed with diazomethane to the methyl ester. The ^{1}H NMR spectral data (Table 9) were close to those of the corresponding triphenyl acetate [30]. The relative positions were deduced from the differences of the chemical shift of H-3 in the esters of **30** and the corresponding triphenylacetate as well as from the behaviour on fragmentation of the two compounds. The methyl ester of **30** showed a relatively strong fragment formed by loss of acetic acid and a very weak fragment by loss of phenylacetic acid. This feature is more likely for a 3-acetoxy than for a 3-phenylacetoxy derivative. The pyrrolizidine alkaloids **1**, **2** and **3** were isolated from *S. variabilis*, while the aerial parts of *S. umgeniensis* gave **10**, the *N*-oxide of **3**. The structures of **1** and **2** clearly followed from the ^{1}H NMR spectra (Table 4). Spin decoupling allowed the assignment of all signals. The relative position of the oxygen function followed from the chemical shifts of H-7 and H-9 respectively. The configuration at C-7 could be deduced from the couplings observed and by comparison with the data of the known isomers of the corresponding diol [14] and with the ^{1}H NMR spectrum of **7** with a 7α-angeloyloxy group.

The ^{1}H NMR spectrum of **3** (Table 4) was in part similar to that of **2**. However, the presence of a second ester group, its nature following from the typical signals, caused a downfield shift of the H-9 signals if compared with the spectrum of **2**. Accordingly, most likely the 5-hydroxyangelate of **2** was present. The relative position of the ester groups was deduced from the mass spectrum, which showed elimination of the ketene derived from the hydroxy acid and of the corresponding acyloxy radical (*m/z* 237 and 220 respectively). This clearly favoured the presence of a 7-senecioyloxy derivative with the 5-hydroxyangeloyl group at C-9. The data of **2** and **3** agreed with those reported for two compounds just obtained from *Senecio cacaliaster* [31]. The structure of **10** also could be deduced from the ^{1}H NMR spectrum (Table 4). As expected the deshielding effect of the *N*-oxide caused a downfield shift of all ring protons. The nature of the ester groups clearly followed from the typical ^{1}H NMR signals, while the relative position of the ester groups again could be deduced from the mass spectrum which gave no molecular ion. The largest fragments were due to [M − O] and [M − H_2O] which were followed by loss of the ketene derived from 5-hydroxyangelic acid and by loss of $C_5H_7O_3$, obviously the acyloxy radical of 5-hydroxyangelic acid. Furthermore *m/z* 233 was visible which agreed with loss of senecio acid. These results favoured the proposed positions of the ester groups.

The aerial parts of *Senecio caudatus* DC. gave a very complex alkaloid fraction. After repeated TLC and HPLC finally the pyrrazoline alkaloids **2–6** and **8–18** were obtained. The spectral data of **2**, **3** and **10** agreed with those of the esters described above. The nature of the ester groups of **4** followed from the ^{1}H NMR spectrum (Table 4) and the molecular formula ($C_{18}H_{27}NO_6$). The relative position again could be deduced from the fragments in the mass spectrum. The ester group at C-7 was eliminated as the acid and at C-9 loss of the acyloxy radical was observed which led to the base peak (*m/z* 220). The same behaviour showed the corresponding acetate **5**. The position of the acetate group could be deduced from the downfield shift of the quartet of H-3′ (Table 4). Again the MS fragments [M − $C_4H_7CO_2H$] and [M − RCO_2] were characteristic. The molecular formula of **6** indicated the presence of an additional oxygen function, while the ^{1}H NMR spectrum (Table 4) showed that the ester side chain in **5** was changed. The methyl doublet in the spectrum of **5** was replaced by a pair of doublets at δ3.81 and 3.63 indicating a hydroxymethyl group. Also in this case the mass spectrum showed the same fragmentation pattern, elimination of senecio acid and of the acyloxy radical leading to *m/z* 269 and 220. While the stereochemistry of **4–6** at C-7 and C-8 obviously was the same as in **1–3** the configuration of the chiral centres of the ester groups could not be determined.

The ^{1}H NMR spectra of **8–12** (Table 4) clearly showed that these compounds were the *N*-oxides of the corresponding pyrrolizidines. As discussed for **10** (see above) the deshielding effect of the *N*-oxide caused a considerable downfield shift of the signals of the ring protons. Again no molecular ions could be observed. In all cases [M − O] and [M − H_2O] fragments were the most intense ions. The ^{13}C NMR of **9** (Table 8) also agreed with the proposed structure.

The spectral data of **13** and **14** indicated that a 2-*O*- and a 9-*O*-senecioate respectively of macronecine [32] were present. From the ^{1}H NMR spectra (Table 5) the relative positions of the ester groups easily could be deduced. In both cases all signals could be assigned by spin decoupling. The couplings observed allowed the assignment of the stereochemistry at C-1, C-2 and C-8, which differed from that of the corresponding 2-*O*-tiglate from a *Petasites* species [33]. The isomeric diols were reported previously [32]. Only one of them showed similar couplings. NOE difference spectroscopy with **14** supported the proposed stereochemistry as NOEs were observed between H-8 and H-9 as well as between H-2 and H-3α. The latter showed no coupling with the former since the angle between these protons is 90°.

The structure of **15**, molecular formula $C_{18}H_{27}NO_6$, also could be deduced from the ^{1}H NMR spectrum (Table 5). Characteristic signals showed that a senecioate was present. Furthermore a triplet at δ5.49, a pair of doublets at δ4.56 and 4.50 and a broadened triplet at δ4.32 indicated, together with the results of spin decoupling, that oxygen functions were at C-2, C-7 and C-9. Although **15** was isomeric with **4**, a signal of the olefinic H-2 proton was missing. The band at 1775 cm^{-1} in the IR spectrum

Table 8*. Infrared and mass spectral data of compounds 1–6, 8–24, 27, 29, 30 and 33–46

	IR†	MS
1	3600, 1720	237.136 [M]$^+$ (8) ($C_{13}H_{19}NO_3$), 80 [C_5H_6N]$^+$ (100)
2	3620, 1715	237.136 [M]$^+$ (15) ($C_{13}H_{19}NO_3$), 80 [C_5H_6N]$^+$ (100)
3	3600, 1710	335.173 [M]$^+$ (5) ($C_{18}H_{25}NO_5$), 136 [M − OCR, RCO_2H]$^+$ (100)
4	3610, 1740, 1720	353.184 [M]$^+$ (2) ($C_{18}H_{27}NO_6$), 220 [M − OCOR]$^+$ (100)
5	3610, 1745, 1720	395.194 [M]$^+$ (3) ($C_{20}H_{29}NO_7$), 83 [C_4H_7CO]$^+$ (100)
6	3600, 1740, 1720	369.179 [M]$^+$ (6) ($C_{18}H_{27}NO_7$), 220 [M − OCOR]$^+$ (100)
8	3600	153.079 [M − H_2O]$^+$ (100) ($C_8H_{11}NO_2$)
9	3610, 1720	235.121 [M − H_2O]$^+$ (21) ($C_{13}H_{17}NO_3$), 83 [C_4H_7CO]$^+$ (100)
10	3600, 1720	335 173 [M − O]$^+$ (4), ($C_{18}H_{25}NO_5$), 83 [C_4H_7CO]$^+$ (100)
11	3600, 1735, 1720	353 [M − O]$^+$ (0.5), 100 [O=C=(Me)CH(OH)Me]$^+$ (100)
12	3640, 1735, 1720	393.179 [M − H_2O]$^+$ (0.6) ($C_{20}H_{27}NO_7$), 104 (100)
13	3620, 1720	239.152 [M]$^+$ (6) ($C_{13}H_{21}NO_3$), 83 [C_4H_7CO]$^+$ (100)
14	3400, 1710	239.152 [M]$^+$ (12) ($C_{13}H_{21}NO_3$), 83 [C_4H_7CO]$^+$ (100)
15	3610, 1720	353.184 [M]$^+$ (1) ($C_{18}H_{27}NO_6$), 83 [C_4H_7CO]$^+$ (100)
16	3620, 1770, 1730	340.176 [M − Me]$^+$ (22) ($C_{17}H_{26}NO_6$) CIMS 356 [M + 1]$^+$ (100)
17	3620, 1770, 1730	295.142 [M]$^+$ (0.5) ($C_{15}H_{21}NO_5$), 83 [C_4H_7CO]$^+$ (100)
18a/b	3580, 1770	253.131 [M]$^+$ (22) ($C_{13}H_{19}NO_4$), 83 [C_4H_7CO]$^+$ (100)
19	3520, 1730, 1710	349.153 [M]$^+$ (18) ($C_{18}H_{23}NO_6$), 120 (100)
20	3520, 1730, 1710	349.153 [M]$^+$ (15) ($C_{18}H_{23}NO_6$), 120 (100)
21	3590, 1745	365.147 [M]$^+$ (8) ($C_{18}H_{23}NO_7$), 119 (100)
22	3540, 1725	381.179 [M]$^+$ (1.5) ($C_{19}H_{27}NO_7$), 107 (100)
23	3580, 1745, 1730	423.189 [M]$^+$ (4) ($C_{21}H_{29}NO_8$), 151 (100)
24	1770, 1720	329.126 [M − RCO_2H]$^+$ (0.5) ($C_{18}H_{19}NO_5$), 83 [C_4H_7CO]$^+$ (100)
27	1720	430.272 [M]$^+$ (1.5) ($C_{26}H_{38}O_5$), 83 [C_4H_7CO]$^+$ (100)
29	3580	236.178 [M − H_2O]$^+$ (9) ($C_{15}H_{24}O_2$), 55 (100)
30	Me ester 1750, 1720	392.126 [M − HOAc]$^+$ (3) ($C_{23}H_{20}O_6$), 91 (100)
33	3540, 2200	256.135 [M]$^+$ (29) ($C_{16}H_{24}O$), 91 (100)
34	1720, 1690	344.162 [M]$^+$ (8) ($C_{20}H_{24}O_5$), 83 [C_4H_7CO]$^+$ (100)
35	1740, 1710, 1690	388.189 [M]$^+$ (2) ($C_{22}H_{28}O_6$), 83 [C_4H_7CO]$^+$ (100)
36	1745, 1725, 1695	402.204 [M]$^+$ (2) ($C_{23}H_{30}O_6$), 97 [C_5H_9CO]$^+$ (100)
37	1745, 1730, 1695	402.204 [M]$^+$ (6.5) ($C_{23}H_{30}O_6$), 97 [C_5H_9CO]$^+$ (100)
38	3620, 1720, 1690	360.194 [M]$^+$ (4.5) ($C_{21}H_{28}O_5$), 97 [C_5H_9CO]$^+$ (100)
39	3620, 1720, 1690	346.178 [M]$^+$ (20) ($C_{20}H_{26}O_5$), 83 [C_4H_7CO]$^+$ (100)
40	3600, 1720, 1695	346.178 [M]$^+$ (2) ($C_{20}H_{26}O_5$), 83 [C_4H_7CO]$^+$ (100)
41	3620, 1725, 1695	360.194 [M]$^+$ (6) ($C_{21}H_{28}O_5$), 97 [C_5H_9CO]$^+$ (100)
42	1755	304.131 [M]$^+$ (12) ($C_{17}H_{20}O_5$), 229 [M − HOAc, Me]$^+$ (100)
43	1720	316.167 [M]$^+$ (73) ($C_{19}H_{24}O_4$), 69 [C_5H_5CO]$^+$ (100)
44	1735	318.183 [M]$^+$ (78) ($C_{19}H_{26}O_4$), 71 [C_5H_7CO]$^+$ (100)
45	1810, 1760	293.103 [M − COMe]$^+$ (2) ($C_{15}H_{17}O_6$), 151 (100)
46	3600, 1780, 1740	336.121 [M]$^+$ (3) ($C_{17}H_{20}O_7$), 55 (100)

*NMR data (Tables 1–7) are deposited in the National Data Bank and copies may be obtained on application to the Editorial office of the journal at Reading.

†Compounds 1–23 in $CHCl_3$, others in CCl_4.

indicated the presence of a γ-lactone, and the chemical shift of the H-7 signal showed that a free hydroxyl was at C-7. The corresponding proton was coupled with a broadened doublet at δ4.08 which must be due to H-8. As the double doublets at δ3.16 and 3.05 were coupled with the triplet at δ5.49 the γ-lactone oxygen was at C-2. The pair of doublets around δ4.5 obviously were those of H-9 while the chemical shifts of two methyl singlets at δ1.50 and a 1.40 required a neighbouring oxygen function. The presence of a dimethyl carbinol residue was further supported by the MS fragment *m/z* 294 [M − C(OH)Me_2]. Thus all data agreed with the proposed structure **15**. The stereochemistry was established by NOE difference spectroscopy. Clear NOEs were observed between H-2 and H-9_1, between H-7 and H-9_2, between H-4′ and H-8 and H-9_2, between the senecioyl methyl and H-8, and between H-2′ and H-8. Thus the α-orientation of H-2, H-7, H-8, CH_2OSen and C(OH)Me_2 was settled, completing the resolution of the stereochemistry.

The ^{1}H NMR spectral data of **16** (Table 5) were close to those of **15**. However, the senecioate signals were replaced by those of an isovalerate. As all shifts and couplings were nearly the same as in the spectrum of **15** the stereochemistry also was the same.

The ^{1}H NMR spectrum of **17** (Table 5) also was close to that of **15**. However the molecular formula was $C_{15}H_{21}NO_5$. Inspection of the ^{1}H NMR spectrum showed, when compared with that of **15**, that in the spectrum of **17** the methyl singlets were missing and the singlet at δ2.99 was replaced by a pair of doublets at δ3.06 and 2.42. All the other signals could be assigned by spin decoupling. The relatively large shift difference for H-8 may be due to the missing deshielding effect of the dimethyl carbinol residue which indirectly supported the proposed stereochemistry at C-2′. **17** obviously is formed by a Retro-Aldol reaction of **15**.

Table 9. Constituents of the *Senecio* species analysed

Senecio species (voucher, origin)	Quantity	Constituents
S. multiniveus (voucher 83/1567, Costa Rica)	1 kg	10 mg α-curcumene, 10 mg senecipylline, 2 mg senecionine
S. megaphyllus (voucher 83/1568, Costa Rica)	700 g	10 mg **19**, 1 mg **20**
S. usgorensis (voucher RMK 9130, Peru)	180 g	2 mg **19** and compounds as previously [4]
S. discolor (voucher Jam. 16, Jamacia)	80 g	5 mg germacrene D, 8 mg 6β-isovaleryloxyfuroeremophil-9-one, 2 mg of the 6β-senecioyloxy and 40 mg of the 6β-acetoxy derivative, 2 mg 6β-senecioyloxy-4α-hydroxyfuroeremophil-9-one, 1 mg of the 6β-angeloyloxy and 6 mg of the isobutyryloxy derivative
S. richii (voucher RMK 9000 Peru)	240 g	2 mg germacrene D, 4 mg α-humulene, 3 mg α-curcumene, 6 mg senaetnin, 4 mg isosenaetnin
S. quabradensis (voucher 84/1650, Mexico)	295 g	1 mg senkirkine, 5 mg florisenin
S. coahuilensis (voucher 84/1644)	35 g	10 mg cacalol methyl ether, 2 mg dehydrocacalohastin
S. salignus (voucher 84/1653, Mexico)	150 g	3 mg **7**
S. madralicae (Bot. Garden Berlin-Dahlem)	100 g	10 mg lupenone, 15 mg 1β-angeloyloxy-4β-hydroxyeudesm-7-ene, 6 mg senaetnin, 2 mg 14*E*-senaetnin, 5 mg isopterophorin
S. grandifolius (voucher Turner 15149 (TEX), Mexico)	400 g	2 mg senkirkine, 5 mg neosenkirkine, 15 mg δ-cadinene, 10 mg γ-cadinene, 2 mg spathulenol, 8 mg **34**, 3 mg **35**, 7 mg **36**, 4 mg **37**, 5 mg **38**, 30 mg **39**, 2 mg **40**, 20 mg **41**
S. stapeliaeformis (voucher 81/128, Transvaal)	100 g	1 mg **24** (50 g roots: 6 mg **24**)
S. dolichodoryius (voucher RMK 9261, Peru)	250 g	5 mg **21**, 10 mg α-humulene, 10 mg α-humulene-1,10-epoxide, 50 mg spathulenol, 40 mg 6β-angeloyloxy-1 (10)-dehydrofuroeremophil-9-one, 20 mg of the 6β-propionyloxy derivative
S. laricifolius (voucher RMK 9188, Peru)	380 g	2 mg senecionine, 2 mg seneciphylline, 2 mg **22**, 2 mg senkirkine, 3 mg **23**, 3 mg **32**
S. umgeniensis (voucher Vincent 1990, Natal)	20 g	2 mg **10**, 15 mg **25**, 25 mg **26**, 15 mg **27**
S. variabilis (voucher Vincent 213, Natal)	45 g	3 mg **1**, 2 mg **2**, 3 mg **3**, 5 mg β-farnesene, 10 mg germacrene D, 2 mg caryophyllene-1,10-epoxide, 2 mg α-humulene-1,10-epoxide, 2 mg spathulenol, 4 mg manoyloxide, 8 mg manool, 10 mg *ent*-kauren-19-oic acid, 10 mg of 9,11-dehydro derivative, 3 mg 5α-hydroxyeudesm-4(15)-ene, 5 mg 6α-tigloyloxyeudesm-4(15)-ene, 170 mg **25**, 120 mg **26**, 700 mg **30** and 700 mg of the triphenyl acetate.
S. caudatus (voucher Vincent 191, Natal)	100 g	7 mg **14**, 2 mg **18a/b**, 4 mg **4**, 1 mg **5**, 6 mg **2**, 1.5 mg **3**, 2 mg **16**, 2 mg **13**, 5.5 mg **15**, 1 mg **14**, 1 mg **17**, 1 mg **12**, 1 mg **8**, 4 mg **9**, 2 mg **10**, 1 mg **6**, 0.5 mg **9**, 0.5 mg **6**, 1 mg **11**, 10 mg caryopyhellene-1,10-epoxide, 5 mg 6β-methacryloyloxy-, 1 mg senecioyloxy- and 1 mg isobutyryloxy-1, 10β-epoxyfuroeremophil-9-one, 50 mg **42**, 1.5 mg **43**, 1.5 mg **44**, 5 mg **45** and 1.5 mg **46**.

The ^{1}H NMR spectrum of **18a/b** (Table 5) clearly showed that we were dealing with a pair of epimers, but again several signals were close to those of **15–17**. However, a downfield signal which could be assigned to H-7 and the signals of the senecionate residue were missing. Furthermore the typical H-9 doublets were replaced by a pair of singlets at δ5.41 and 5.47. The presence of a γ-lactone was indicated by the IR band and a pair of doublets at δ5.27 and 4.61. Spin decoupling showed that the latter were the signals of H-2. Inspection of models indicated that the proposed stereochemistry would nicely explain the shift difference of H-2 which most likely was due to the strong deshielding effect of a 9α-hydroxyl group. Also the shift differences of the methyl singlets can be explained from the models.

The desacyl derivative of **15** and **16** we have named senecicaudatin, **17** norsenecicaudatin-9-*O*-senecioate and **18a/b** senecicaudatinal semiacetal. The biogenesis of **15–18** is not very clear, but most likely the epoxide of **1** is the precursor of **15** which may be formed by addition of a senecioyl cation.

The neutral fraction afforded caryophyllene-1,10-epoxide, the known furoeremophilanes 6β-isobutyryloxy-1(10)-dehydrofuroeremophil-9-one [18], 6β-methacryloyloxy-, 6β-isobutyryloxy- and 6β-senecioyloxy-1β,10β-epoxyfuroeremophil-9-one [13, 23] as well as **42–44** and the lactones **45** and **46**.

The structure of **42**, which was the main constituent, followed from the molecular formula ($C_{17}H_{20}O_5$), the ^{1}H NMR (Table 7) and the ^{13}C NMR spectra (Table 7). The ^{1}H NMR signals clearly could be assigned by spin decoupling and by comparison with those of other furoeremophilanes [1]. The presence of a 6β-acetoxy derivative was indicated by the typical signals for H-6 and

H-9. The chemical shift of H-9β showed that a 10β-oxygen function was present, which most likely was an epoxide. This was deduced from the chemical shifts and the coupling of a doublet at δ3.23. Irradiation collapsed a double doublet at δ3.42 to a doublet. The latter was further transformed to a doublet on irradiation of a double doublet at δ3.13. The proton, represented by the latter, was further coupled with a double quartet at δ1.95, and thus the protons H-1–H-4 were assigned. The presence of a 1β,10β,2β,3β-bisepoxide was deduced from the couplings $J_{2,3}$ and $J_{3,4}$. The proposal was confirmed by NOE difference spectroscopy. Clear NOEs were observed between H-6, H-4, H-3 and H-2, between H-14 and H-9β, between H-4 and H-6, between H-2 and H-6 as well as between H-3 and H-6. Furthermore the shifts in the ^{13}C NMR of C-1–C-3 and C-10 clearly showed that there were epoxide bearing carbons, though they were unusually shielded (δ61.3, 55.5, 49.5, 48.8).

The ^{1}H NMR spectral data (Table 7) of **43** and **44** were in part similar to those of **42**. However, the characteristic signals of a methacrylate and an isobutyrate replaced the signals of the 2,3-epoxide. Spin decoupling clearly showed that the ester group was at C-2. Inspection of models indicated that the couplings and the different deshielding of H-1 by the ester groups require an α-orientation of the acyloxy groups.

The ^{1}H and the ^{13}C NMR spectra of **45** (Table 7) showed that this compound differed from **42** only by an alteration in the furan moiety. An unusual long range coupling through five bonds between H-4 and H-9α (*ca* 0.5 Hz) was present, which also was observed with **42**. As can be deduced from the *IR*, lactone was present. A quartet at δ3.01, which collapsed to a singlet by irradiation of the doublet at δ1.28, obviously was due to H-11. This required that no hydrogen was at C-7. In agreement with the molecular formula a 7,8-epoxide therefore was assumed, which was supported by the ^{13}C NMR signals at δ85.7 (C-8) and 58.5 (C-7). Careful NOE difference spectroscopy established the proposed structure and configuration. NOEs were present between H-14 and H-11, H-9 and H-4, between H-15 and H-4, between H-4 and H-6, H-3 and H-14, between acetate methyl and H-13 as well as between H-6 and H-3, H-4 and weakly H-2. Inspection of a model shows that these results required the proposed stereochemistry with a 7α,8α-epoxide.

The ^{1}H NMR spectrum of **46** (Table 7) was again similar to that of **42** and **45**. Accordingly, most signals were nearly identical. However, the changed situation in the furan moiety was obvious. A coupling between H-6 and an olefinic methyl doublet at δ1.90 indicated a 7,11-double bond while the absence of a proton at C-8 was indicated by the doublets of H-9. The chemical shifts of these protons in agreement with the IR and MS favoured the presence of a hydroxyl group at C-8, which most likely was α-oriented since an 8β-hydroxyl group should deshield H-9β. Furthermore H-1α was deshielded by the 8α-hydroxyl group. Surely **45** and **46** are derived from **42** by oxidative transformations. The roots also gave 6β-methacryloyloxy- and 6β-senecioyloxy-1β,10β-epoxy-furoeremophil-9-one.

The investigation of 16 further *Senecio* species has thus shown considerable chemical diversity which is typical of this very diverse genus. Many species of both the senecioid and cacaloic types contain mainly alkaloids and furoeremophilanes as characteristic compounds [1]. In two South African species these were replaced by eremophilones which are the probable precursors of the furans. Two Costa Rican species and the distinctive Peruvian *Senecio laricifolinus* lack eremophilanes but the latter has a distinctive acetylenic aldehyde. The more simple alkaloids like **1**–**18** without a macrocyclic lactone moiety may be of chemotaxonomic importance. However, more results are necessary to get a clear picture.

EXPERIMENTAL

The air dried plant material was extracted with Et_2O–petrol–MeOH, 1:1:1, and the extracts obtained were worked-up and separated in the usual fashion [34]. For the isolation of alkaloids the extract of the aerial parts were treated with 2 N HCl and $CHCl_3$. To the aq. phase conc. NH_3 was added and the alkaloids were extracted with $CHCl_3$, again separated from the organic phase by shaking with 2 N HCl and isolated after addition of conc. NH_3 by extraction with $CHCl_3$. Separation was achieved by TLC (SiO_2) using mixtures of CH_2Cl_2–MeOH–conc. NH_3, 85:14:1 (solvent I), 92:7:1 (solvent II) or 94:5:1 (solvent III) and by HPLC (RP 8, flow rate, 3 ml/min, *ca* 200 bar). Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material and by co-TLC or by rigorous structure elucidation by NMR, mass and IR spectroscopy and comparing the data with those in the literature. In several cases, probably due to the small quantities, no crystals could be obtained, these compounds were colourless oils. The purity of all compounds was determined by TLC in different solvent mixtures and by ^{1}H NMR.

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