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SECO-EREMOPHILANES AND OTHER CONSTITUENTS FROM SOUTH AFRICAN *SENECIO* SPECIES

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Key Word Index—*Senecio glutinosus*, *S. asperulus*, *S. othonnaeflorus*; Compositae; sesquiterpenes; furoeremophilanes; *seco*-furoeremophilane; eremophilane; *nor-seco*-eremophilane, pyrrolizidine alkaloids.

Abstract—The investigation of the South African *Senecio glutinosus* afforded, in addition to known compounds, a new *seco*-furoeremophilane, an eremophilane and a derived *seco-nor*-eremophilane while alkaloids could not be detected. *Senecio othonnaeflorus* contained high concentrations of pyrrolizidine alkaloids but gave no sesquiterpenes. *Senecio asperulus* contains also pyrrolizidine alkaloids and in addition several known furoeremophilones as well as some diterpenes. The structures were elucidated by high field ^{1}H NMR spectroscopy.

INTRODUCTION

The South African *Senecio* species are rich in furoeremophilanes but also many other constituents have been reported from representatives of this and related genera. In continuation of our chemotaxonomic studies of this complicated group, we now have investigated three further South African species, *S. glutinosus* Thunb., *S. asperulus* DC and *S. othonnaeflorus* DC. The results are discussed in this paper.

RESULTS AND DISCUSSION

The extract of the aerial parts of *S. glutinosus* afforded, in addition to widespread compounds (Experimental), the *seco*-furoeremophilanes **1** [1, 2] and **2** as well as the eremophilane **3** and the derived *seco*-derivative **4**.

The structure of **2** followed from the molecular formula ($C_{20}H_{24}O_3$) and from the ^{1}H NMR spectrum (Table 1) which was similar to that of **1** [1]. However, the additional low field signals and the altered molecular formula indicated the presence of an aromatic compound. In agreement with this, the methyl singlets and the H-9 signal were shifted downfield. Spin decoupling showed that the substitution pattern was identical with that of **1**. Most likely both the angelates **1** and **2** were formed by fragmentation of a corresponding 6-angeloyloxy-4-hydroxyfuroeremophilane as pointed out previously [1]. We have named compound **2** senglutinosin.

The structure of **3** could be deduced from its ^{1}H NMR spectrum (Table 1) especially in deuteriobenzene where all signals could be assigned by spin decoupling. The spectrum was in part similar to that of the corresponding 3-desoxy compound [3] where the configurations were established by the observed NOE's. The presence of an additional hydroxy group followed from the three-fold doublet at δ3.20 and its position from the splitting of H-4 which was a doublet of quartets. The observed couplings indicated that the 3-hydroxy, the isopropenyl and the 4-methyl group all were equatorial, leading to a conformation which obviously is the most stable one.

Table 1. ^{1}H NMR spectral data of compounds **2**–**4** (400 MHz, δ-values)

H	**2** ($CDCl_3$)	**3** (C_6D_6)	**4** ($CDCl_3$)
1 } 1′ }	7.09 *br d*	2.28 *br d* } 1.71 *m* }	4.91 *ddd*
2 } 2′ }	7.00 *dd*	1.68 *m* 1.28 *m*	2.04 *ddt* 1.85 *dt*
3 } 3′ }	6.91 *br dd* }	3.20 *ddd*	2.72 *dt* 2.62 *dt*
4		1.10 *dq*	—
6 } 6′ }	4.98 *s*	1.79 *ddd* } 1.01 *t* }	7.46 *br s*
7	—	2.23 *dddd*	—
8	—	2.45 *ddd*	—
8′	—	1.89 *dd*	—
9	4.02 *s*	—	7.13 *s*
10	—	1.55 *br d*	—
12	7.02 *br s*	1.54 *br s*	—
13	2.01 *d*	{ 4.76 *br s* { 4.66 *br s*	2.61 *s*
14	2.28 *s*	0.71 *s*	2.29 *br s*
15	2.21 *s*	0.86 *d*	2.18 *s*

J [Hz]: Compound **2**: 1,3 = 1.5; 2,3 = 7; 12,13 = 1 (OAng: 6.04 *qq*, 1.96 *dq* (*J* = 7, 1.5 Hz), 1.85 *qq* (*J* = 1.5, 1.5); compound **3**: 1,1′ = 15; 1,10 ~ 4; 2,3 = 3,4 ~ 9.5; 2′,3 = 4,15 = 7; 6,6′ = 13.5; 6,7 = 6,8 = 2.5; 6′,7 = 13.5; 7,8 = 3; 7,8′ = 8,8′ = 13; compound **4**: 1,2 = 3.5; 1,2′ = 7; 1,OH = 3.5; 2,2′ = 14; 2,3 = 2,3′ = 2′,3 = 2′,3′ ~ 7; 3,3′ = 18 (1-OH: 2.49 *d*, 8-OH: 12.07 *s*).

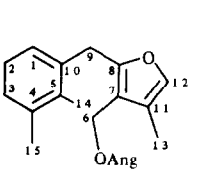
The structure of **4** also followed from its molecular formula ($C_{14}H_{18}O_4$) and its ^{1}H NMR spectrum (Table 1). A sharp singlet at δ12.07 indicated the presence of an *o*-hydroxy ketone and singlets at δ7.46 and 7.13 required a tetrasubstituted benzene derivative. A small allylic coup-

ling of H-6 with H-14 supported the proposed substitution pattern while the remaining signals only agreed with the presence of the hydroxy ketone side chain and of a methyl ketone (δ2.61 *s*). The structure was further supported by the fragmentation pattern. Thus the ion with *m/z* 192 is formed by McLafferty process while that with *m/z* 179 is probably formed by loss of $MeCOCH_2CH_2$. The base peak (*m/z* 177) is the result of loss of methyl from *m/z* 192. Compound **4** we have named *nor-seco*-glutinosone. Most likely this ketone is formed by fragmentation of the triol **5** (Scheme 1) followed by oxidative degradation. The methanol extract of the aerial parts gave no definite alkaloids.

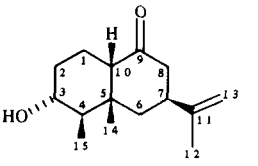
The aerial parts of *S. othonnaeflorus* gave squalene and no furoeremophilanes. However, the methanol extract afforded the pyrrolizidine alkaloids retrorsine [4, 5] and isatidine [4, 5]. Reduction of the neutral parts gave again retrorsine. Accordingly, the corresponding *N*-oxide also was present [5].

The extract of the aerial parts of *S. asperulus* already has been shown to contain *N*-oxides of pyrrolizidine alkaloids [6]. A reinvestigation gave the furoeremophilanes **6** [2], **7** [2], **8** [3], **9** [7], **10** [8], **11** [2], **12** [2], **13** [2], **14** [8] and **15** [8] and α-humulene, *ent*-kaurenic acid, *ent*-kaurenol as well as the corresponding beyerene derivatives **16** [9] and **17** [10].

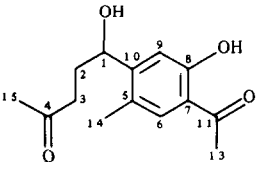
The chemistry of these three *Senecio* species shows again that this large genus is not uniform. The constituents of *S. glutinosus* resembles those of *S. elegans* and related species [2] while those of *S. asperulus* show similarities to those of *S. hypochoerideus* [8]. Further studies may show whether these results are of taxonomic value. The investigation of the generic and sectional limits in *Senecio* are still in progress [11].



1
2 Δ^2



3



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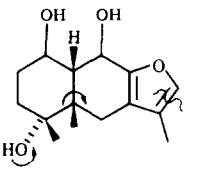

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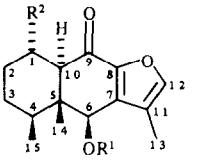
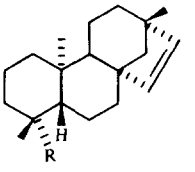


	6	7	8	9	10	11	12	13	14	15
R^1	*i*Bu	Ang	Tigl	Sen	H	H	H	Ac	Ac	H
R^2	H	H	H	H	OH	O*i*Bu	OTigl	O*i*Bu	OSen	OH 10βH



16 R = CO_2H
17 R = CH_2OH

EXPERIMENTAL

The air-dried aerial parts were collected near Grahamstown (RSA) and extracted with MeOH–Et_2O–petrol (1:1:1) and for alkaloids with MeOH. Vouchers are deposited in the Albany Museum at Grahamstown. The extract of the aerial parts (150 g) of *S. glutinosus* (collected in September 1985, voucher JRL 10) gave by CC (silica gel), TLC (silica gel) and HPLC (always RP 8, flow rate, 3 ml/min) 2 mg α-humulene, 20 mg sitosterol, 20 mg stigmasterol, 5 mg **1**, 2 mg **2** (TLC: Et_2O–petrol, 1:1, R_f 0.45), 2 mg **3** (HPLC: MeOH–H_2O, 7:3, R_t 4.8 min) and 10 mg **4** (HPLC: MeOH–H_2O, 13:7, R_t 3.2 min). The MeOH extract of 200 g aerial parts was worked-up as below. No alkaloids could be identified.

The aerial parts (270 g) of *S. othonnaeflorus* (collected in December 1984, voucher JRL 2) gave 20 mg squalene and no furoeremophilanes. The MeOH extract of 390 g aerial parts was acidified with dil. H_2SO_4 and filtered. The soluble part was made alkaline with NH_3. The $CHCl_3$ extract gave by CC ($CHCl_3$–MeOH–NH_3, 85:14:1) 1.55 g retrorsine and 0.62 g isatidine. The water phase was acidified again and treated with Zn dust. After addition of NH_3 and $CHCl_3$ extract gave by CC (s.a.) 2.95 g retrorsine (the alkaloids were identified by comparing the mp, optical rotations and spectroscopic data with those in the lit.).

The extract of 240 g aerial parts of *S. asperulus* (collected in January 1985, voucher JRL 5) gave by CC and TLC (s.a.) 10 mg α-humulene, 50 mg *ent*-kaurenic acid, 140 mg **16**, 50 mg *ent*-kaurenol, 100 mg **4**, 60 mg **6**, 20 mg **7**, 20 mg **8**, 10 mg **9**, 500 mg **13**, 20 mg **14**, 500 mg **11**, 20 mg **12**, 100 mg **10** and 50 mg **15**.

Known compounds were identified by comparison of the high field ^1H NMR spectra with those of authentic material.

Senglutinosin (**2**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1730, 1650 (C=CCO_2R); MS *m/z* (rel. int.): 312.172 $[M]^+$ (0.5) (calc. for $C_{20}H_{24}O_3$: 312.172), 212 $[M-RCO_2H]^+$ (70), 197 $[212-Me]^+$ (100), 83 $[RCO]^+$ (34), 55 $[83-CO]^+$ (52).

3α-Hydroxy-10β-H-eremophil-11(13)-en-9-one (**3**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 1720 (C=O); MS *m/z* (rel. int.): 236.178 $[M]^+$ (2.3) (calc. for $C_{15}H_{24}O_2$: 236.178), 218 $[M-H_2O]^+$ (46), 203 $[218-Me]^+$ (11), 185 (9), 109 (61), 107 (55), 99 (100); CD (MeCN): $\Delta\varepsilon_{294}$ −0.66.

nor-seco- *Glutinosone* (**4**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610 (OH), 3500–2600, 1650 (hydrogen bonded aromatic ketone), 1720 (C=O); MS *m/z* (rel. int.): 250.121 $[M]^+$ (54) (calc. for $C_{14}H_{18}O_4$: 250.121), 232 $[M-H_2O]^+$ (42), 217 $[232-Me]^+$ (11), 192 $[M-Me_2C{=}O]^+$ (80), 179 $[M-CH_2CH_2COMe]^+$ (71), 177 $[192-Me]^+$ (100); $[\alpha]_D^{24}$ +43 ($CHCl_3$; *c* 0.2).

REFERENCES

1. Bohlmann, F., Zdero, C. and Grenz, M. (1974) *Chem. Ber.* **107**, 2730.
2. Bohlmann, F. and Zdero, C. (1974) *Chem. Ber.* **107**, 2912.
3. Bohlmann, F., Jakupovic, J., Warning, U., Grenz, M., Chau-Thi, T. V., King, R. M. and Robinson, H. (1986) *Bull. Soc. Chim. Belg.* **95**, 707.
4. Leisegang, E. C. and Warren, F. L. (1950) *J. Chem. Soc.* 702.
5. Adams, R. (1953) *Angew. Chem.* **65**, 433.
6. Mattocks, A. and Jukes, R. J. (1987) *J. Nat. Prod.* **50**, 161.
7. Bohlmann, F., Knoll, K. H., Zdero, C., Mahanta, K. P., Grenz, M., Suwita, A., Ehlers, D., Le Van, N., Abraham, W. R. and Natu, A. A. (1978) *Phytochemistry* **17**, 965.
8. Bohlmann, F., Ehlers, D. and Zdero, C. (1978) *Phytochemistry* **17**, 467.
9. Bohlmann, F. and Le Van, N. (1976) *Chem. Ber.* **109**, 1446.
10. McCrindle, R., Martin, A. and Murray, R. D. H. (1968) *J. Chem. Soc. C* 2349.
11. Jeffrey, C. (1979) *Kew Bull.* **34**, 49.

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DITERPENOIDS FROM *RABDOSIA FLEXICAULIS*

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Key Word Index—*Rabdosia flexicaulis*; Labiatae; *ent*-kaurene diterpenoids; flexicaulin A; ^{1}H, ^{13}C NMR.

Abstract—A new diterpenoid, named flexicaulin A, and two known diterpenoids were isolated from the leaves of *Rabdosia flexicaulis*. Their structures were determined by spectroscopic and chemical means.

INTRODUCTION

Rabdosia flexicaulis C. Y. Wu et. H. W. Li., a perennial herb of the Labiatae family, grows abundantly in south-western Sichuan. Its chemical constituents have not been investigated before. We now describe the isolation and structure elucidation of a new diterpenoid, named flexicaulin A (**1**) from this species, which also contained two known diterpenoids (**5** and **6**).

RESULTS AND DISCUSSION

The ethereal extract of dried leaves of *R. flexicaulis* afforded, in addition to henryin A (**5**) [1] and rabdoloxin B (**6**) [2], flexicaulin A (**1**), a new diterpenoid. Their structures were established mainly by spectroscopic methods (^{1}H and ^{13}C NMR, UV, IR and MS) and some chemical transformations.

Flexicaulin A (**1**), $C_{22}H_{32}O_6$(M^+ at m/z 392), was shown by ^{1}H and ^{13}C NMR spectroscopy to contain two tertiary methyl, five methylenes, seven methines, three quaternary carbons, two methine carbons, and an acetoxy group. The UV[λ_{max} 238 nm (log ε 3.82)], IR[ν_{max} 1723, 1644 cm^{-1}], ^{1}H NMR [δ5.46, 6.34 (each 1H, *s*, C$=$CH$_2$)] and ^{13}C NMR [δ113.7 (*t*), 150.8 (*s*), 206.7 (*s*)] spectra indicated the presence of a five-membered ketone conjugated with an *exo*-methylene group. Considering these facts, together with the minus Cotton effect of dihydroflexicaulin A (**3**), we presumed that flexicaulin A (**1**) has the *ent*-15-oxo-16-kaurene nucleus as a basic skeleton.

The spectral data of **1** showed, besides the signals of two tertiary methyl groups [δ0.80, 0.89 (each 3H, *s*)], one acetoxyl and three secondary hydroxyl groups [ν_{max} 3280, 1748, 1240, 1225 cm^{-1}; δ2.10 (3H, *s*, OAc), 5.91, 7.17, 8.57 (each 1H, *br s*, disappeared after D_2O, 3 × OH)] which could be confirmed by forming its acetate. Acetylation of **1** with pyridine–acetic anhydride afforded tetra-acetate **2** [$C_{28}H_{38}O_9$(M^+ at m/z 518), ν_{max} 1740, 1725, 1240, 1225 cm^{-1}; δ1.88, 1.96, 2.14 (each 3H, *s*, 3 × OAc); δ21.1, 21.2, 22.4 (each *q*, 3 × OAc)]. The locations of the three hydroxy groups on **1** were deduced from the following spectral data and chemical findings. In the ^{1}H NMR spectrum of **1**, the signal at δ5.26 due to the 14α-proton appeared as a broad singlet. Treatment of **1** with 2,2-dimethoxypropane in the presence of toluenesulphonic acid gave the acetonide (**4**) [$C_{25}H_{36}O_6$(M^+ at m/z 432), δ1.42, 1.64 (each 3H, *s*, 2 × Me on dimethoxypropyl group); δ25.6 (*q*, C-2′), 31.2 (*q*, C-3′)], confirming the presence of the 7α-hydroxyl [δ5.01 (1H, *dd*, $J=6$, 10 Hz, 7β-H)] which has a *cis*-relationship to the 14β-hydroxyl. The third secondary hydroxyl group was assumed to be present at the 11β-position, based on the chemical shift value at δ4.59 (1H) with the coupling constant of 5 Hz in the ^{1}H NMR spectrum. The AB type signals at δ4.55 (1H) and 5.05 (1H) with the coupling constant of 12 Hz in the ^{1}H NMR spectrum was very similar to those of henryin A (**5**), showing the presence of one acetoxyl at C-20. Flexicaulin A (**1**) was therefore elucidated as structure **1**. This was confirmed by comparing the ^{13}C NMR chemical shifts with those of henryin A (see Table 1).