Phytochemistry, Vol. 28, No. 11, pp. 3093–3095, 1989.
Printed in Great Britain.

0031–9422/89 $3.00 + 0.00
Pergamon Press plc

FURANOEREMOPHILANES FROM *SENECIO LINIFOLIUS*

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(*Received* 13 *February* 1989)

Key Word Index—*Senecio linifolius*; Compositae; sesquiterpenes; furanoeremophilane derivatives.

Abstract—Investigation of *Senecio linifolius* gave, in addition to known compounds, four new furanoeremophilane sesquiterpenes whose structures were elucidated by spectroscopic methods.

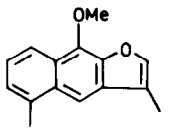
INTRODUCTION

Previously, we reported the presence of several new cacalohastin derivatives in the hexane fraction of the acetone extract of the aerial parts of *Senecio linifolius* [1]. A further study of the constituents of the same plant has resulted in the isolation of four new rearranged furanoeremophilanes.

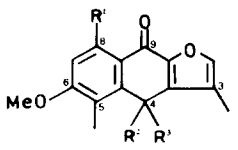
RESULTS AND DISCUSSION

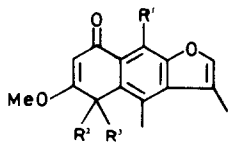
The chloroform fraction obtained from the acetone extract of *S. linifolius* afforded maturinone [2], angelic acid [3] and the new furanoeremophilanes **1**–**4**.

The ^{1}H NMR spectrum of **1** showed the typical signals of a dehydrocacalohastine [1, 4, 5]: three contiguous aromatic protons as well as coupled signals of one methyl and one proton in a furan ring. However, the absence of signals that could be assigned to any proton at C-14 and the presence of a singlet of an aromatic proton at δ7.70 (1H), let us propose for this compound the structure of 14-*nor*-dehydrocacalohastine (9-methoxy-3,5-dimethylnaphtho[2,3-*b*]furane). The structure proposed for **1** was also in agreement with the mass spectral fragmentation pattern.



1





	R¹	R²	R³
2	OH	Me	H
3	OH	Me	OH
3a	OAc	Me	OH
3b	OAc	Me	OAc
3c	OH	=CH$_2$	
3d	OAc	=CH$_2$	
3e	H	Me	OH
3f	OH	Me	OMe
4	OH	=O	

	R¹	R²	R³
5a	OH	Me	H
5b	OH	Me	OH
5c	OMe	Me	OH

The mass spectrum of compound **2** showed a $[M]^+$ at *m/z* 272 ($C_{16}H_{16}O_4$). The IR spectrum showed absorption bands of benzene and furan rings, hydroxyl groups and a conjugated carbonyl (1635 cm^{-1}). The ^{1}H NMR spectrum showed the signal of the hydroxyl group bonded intramolecularly with the carbonyl group [δ13.07 (1H, *s*)], signals of a methyl and a proton on a furane ring [2.18 (3H, *d*, J = 1 Hz) and δ7.52 (1H, *br s*)] and signals of a methoxyl, an aromatic methyl and an aliphatic methyl [δ1.37 (3H, *d*, J = 7 Hz)] coupled with a deshielded proton [δ4.15 (1H, *q*, J = 7 Hz)]. All the above spectral data are nearly the same than those described for compound **5a**, previously isolated from *S. inaequidens* [6] but the mp of **2** (129°) was slightly higher than that described for **5a** (124°).

An alternative structure also consistent with the observed spectral data was one in which the aromatic and aliphatic six-membered rings were inverted, that is, a tetrahydronaphtofuran-9-one instead of a tetrahydronaphthofuran-8-one skeleton assigned to **5a**. To discern between these two structures, differential NOE experiments were performed. The NOED traces showed that the irradiation on the furan methyl group produced a NOE on the aliphatic methyl doublet and on the proton quartet but not on the aromatic methyl. Similarly, irradiation on the aromatic methyl group caused NOE on the same methyl and aliphatic protons as before, but no effect was observed on the furane methyl group. We concluded that the correct structure is 8-hydroxy-6-methoxy-3,4,5-trimethylnaphtho[2,3-*b*]furan-9(4H)-one (**2**).

Compound **3** showed a $[M]^+$ at *m/z* 288 ($C_{16}H_{16}O_5$). The IR spectrum indicated the presence of a conjugated carbonyl group (1640 cm^{-1}). The ^{1}H NMR spectrum was similar to that of the compound **2** (Table 1). However, compound **3** showed a deshielded singlet at 1.83 ppm (3H) that could be assigned to a methyl group *geminal* to a

Table 1. ^{1}H NMR spectral data of compounds **2–4** [60 MHz (**2**, **3** and **3c** at 200 MHz), $CDCl_3$, TMS as internal standard]

	2	**3**	**3a**	**3b**	**3c**	**3d**	**4**
H-2	7.52 *br s*	7.46 *br s*	7.37 *m*	7.38 *m*	7.54 *br s*	7.38 *m*	7.48 *m*
H-7	6.89 *s*	6.80 *s*	6.95 *s*	6.92 *s*	6.94 *s*	7.00 *s*	6.77 *s*
Me-3	2.18 *d*	2.30 *d*	2.30 *br s*	2.13 *d*	2.34 *d*	2.27 *br s*	2.33 *d*
Me-5	2.41 *s*	2.70 *s*	2.80 *s*	2.60 *s*	2.65 *s*	2.76 *s*	2.70 *s*
OMe	3.90 *s*	3.84 *s*	3.80 *s*	3.83 *s*	3.95 *s*	3.83 *s*	3.95 *s*
R	13.07 *s*	13.08 *s*	2.42 *s*	2.43 *s*	13.07 *s*	2.43 *s*	13.17 *s*
R^1	1.37 *d*	1.83 *s*	1.83 *s*	1.88 *s*	6.26 *s* 6.14 *s*	6.13 *s* 6.00 *s*	
R^2	4.14 *q*	2.33 *br s*	2.10 *s*				

J (Hz): Compound **2**: 4, Me-4 = 7; 2, Me-3 = 1; compounds **3**, **3b**, **3c**, and **4**: 2, Me-3 = 1.

hydroxy group. This signal was not observed in the spectrum of **2** which in contrast showed a doublet at δ1.37 (3H). Furthermore, a broad singlet at δ2.33 (1H) in the ^{1}H NMR spectrum of **3** was removed by addition of D_2O. Treatment of **3** with acetic anhydride-pyridine afforded the monoacetate **3a**, the diacetate **3b** and the elimination products **3c** and **3d**. The spectral data shown by the natural product **3** and those of the products of acetylation, supported for the natural product either the structure of 4-hydroxy-3-methoxy-1-oxo-2,3-dehydrocacalol (**5b**) or the isomeric 6-hydroxy-3-methoxy-9-oxo derivative.

Comparison of the above data with those described for related substances such as **5c** isolated from *S. inaequidens* [7] or **3e** from *Cacalia delphiniifolia* [8], does not clarify the identification because both substances shown comparable spectral data.

The correct structure was deduced from the differential NOE that let us assign the constitution shown in **3** for our compound. In fact, when the furan methyl group of **3** was irradiated, we could observe a NOE on the furan proton, on the free hydroxyl proton and on the quaternary methyl group but not on the aromatic methyl group. Irradiation on this last methyl does not affect the furan methyl group but a NOE was observed on the hydroxyl and on the *geminal* methyl group.

The proposed structure was also confirmed in the elimination product **3c**. Irradiation on the vinyl proton at 6.26 ppm induced a NOE on the *geminal* proton and on the furan methyl doublet, and irradiation on the vinyl proton at 6.14 ppm induced a NOE on the *geminal* proton and on the aromatic methyl group.

Compound **4**, red needles with intense red fluorescence under UV light, showed in its IR spectrum a band at 1630 cm^{-1} of a highly conjugated ketone that suggested a quinone structure for this substance. The ^{1}H NMR spectrum was quite similar to those of compounds **2** and **3** (Table 1), but the signals assigned for the Me-4 protons were absent in compound **4**. All the above data and the $[M]^+$ displayed in the mass spectrum at *m/z* 272 ($C_{15}H_{12}O_5$), supports for **4** the structure of 8-hydroxy-6-methoxy-3,5-dimethylnaphtho [2,3-*b*] furan-4,9-dione.

Perhaps, the structures assigned to the compounds isolated from *S. inaequidens* [6, 7] should be changed to **2** and **3f**, respectively.

EXPERIMENTAL

General. Mp: uncorr. UV spectra were recorded in 96% EtOH or $CHCl_3$. ^{1}H NMR spectra were measured at 60 or 200 MHz with TMS as int. std, δ in ppm. MS was carried out at 70 eV.

Material, extraction and isolation. Plant material was collected from the Barranco de las Ovejas (Alicante, Spain) during November 1985 and identified at the Department of Botany of the University of Alicante. Dried and ground aerial parts of *S. linifolius* L. (3 188 g) were extracted in a Soxhlet with Me_2CO and the crude extract (212 g, 6.7% dry wt) was fractionated as previously described [1].

The $CHCl_3$ fr (49 g, 23.2%) was chromatographed on silica gel (Merck, 7734) with a hexane–EtOAc gradient (0→50% EtOAc) yielding angelic acid (716 mg) identified as its 4-phenylphenacyl ester, maturinone (45 mg), **1** (45 mg), **2** (66 mg), **3** (253 mg) and **4** (22 mg).

14-nor-*Dehydrocacalohastine* (**1**). Colourless oil. UV λ_{max}^{EtOH} nm (log ε): 264 (4.7), 329 (3.9), 344 (3.8). IR ν_{max}^{film} cm^{-1}: 1620, 1595, 1490, 1320, 1205, 1085, 830, 785, 740. ^{1}H NMR (60 MHz, $CDCl_3$): δ8.22 (1H, *m*, H-2), 7.70 (1H, *s*, H-6), 7.43 (1H, *m*, H-12) 7.28 (2H, *m*, H-1 and H-3), 4.33 (3H, *s*, OMe-9), 2.73 (3H, *s*, H-15), 2.27 (3H, *d*, *J* = 1.5 Hz, H-13). EIMS (GC) 70 eV, *m/z* (rel. int.): 226 $[M]^+$ (65), 211 $[M-Me]^+$ (100), 183 $[211-CO]^+$ (2), 154 (5), 153 (12), 139 (6).

8-*Hydroxy*-6-*methoxy*-3,4,5-*trimethylnaphtho* [2,3-*b*] *furan*-9(4H)-*one* (**2**). Orange crystals, mp 129° (hexane EtOAc). $[\alpha]_D$ +53° ($CHCl_3$; *c* 0.2). UV λ_{max}^{EtOH} nm (log ε): 232 (4.2), 256 (3.9), 270 (3.9), 279 (3.9), 320 (4.3), 384 (3.7). IR ν_{max}^{KBr} cm^{-1}: 3480, 1635, 1575, 1455, 1240, 1200, 985, 860, 800. EIMS (probe) 70 eV, *m/z* (rel. int.): 272 $[M]^+$ (65), 257 $[M-Me]^+$ (100), 241 $[M-OMe]^+$ (2), 229 $[257-CO]^+$ (55), 214 $[229-Me]^+$ (38), 213 $[241-CO]^+$ (5).

4,8-*Dihydroxy*-6-*methoxy*-3,4,5-*trimethylnaphtho* [2,3-*b*] *furan*-9(4H)-*one* (**3**). Yellow crystals, mp 208° (hexane–EtOAc). $[\alpha]_D$ +17° ($CHCl_3$; *c* 0.5). UV λ_{max}^{EtOH} nm (log ε): 232 (4.1), 261 (3.8), 284 (3.7), 335 (4.1), 395 (3.6). IR ν_{max}^{KBr} cm^{-1}: 3480, 1640, 1570, 1450, 1435, 1350, 1240, 1070, 1000, 960, 830, 800. EIMS (probe) 70 eV, *m/z* (rel. int.): 288 $[M]^+$ (35), 273 $[M-Me]^+$ (100), 257 $[M-OMe]^+$ (4), 245 $[273-CO]^+$ (10), 244 $[273-CHO]^+$ (4), 229 $[257-CO]^+$ (3).

Acetylation of **3**. A pyridine (3 ml) soln of **3** (220 mg) was added to Ac_2O (3 ml) and left to stand for 3 days (25°). Work-up as usual gave, after crystallization from Me_2CO, compound **3b** (83 mg). The residue was chromatographed on $AgNO_3$–silica gel

(1:9) with a hexane–EtOAc gradient (0→30% EtOAc) to afford **3a** (8 mg), **3c** (20 mg), and **3d** (27 mg).

Monoacetate (**3a**). Yellow crystals, mp 222° (EtOAc). $[\alpha]_D$: +12° ($CHCl_3$; *c* 0.6). UV λ_{max}^{EtOH} nm (log ε): 224 (4.7), 259 (4.2), 318 (4.4). IR ν_{max}^{KBr} cm^{-1}: 3420, 3100, 1750, 1640, 1585, 1355, 1190, 1070, 1005, 960, 905, 805, EIMS (probe) 70 eV, *m/z* (rel. int.): 287 $[M-COMe]^+$ (4), 272 $[287-Me]^+$ (69), 270 $[287-OH]^+$ (15), 257 $[272-Me]^+$ (100), 255 $[270-Me]^+$ (5), 229 $[257-CO]^+$ (16), 228 $[257-CHO]^+$ (5).

Diacetate (**3b**). Yellow crystals, mp 198° (Me_2CO). $[\alpha]_D$: +11° ($CHCl_3$; *c* 0.5). UV λ_{max}^{EtOH} nm (log ε): 225 (3.8), 316 (3.7) IR ν_{max}^{KBr} cm^{-1}: 3100, 1750, 1730, 1655, 1590, 1355, 1230, 1195, 1055, 970, 915, 865, 815. EIMS (probe) *m/z* 70 eV, (rel. int.): 312 $[M-AcOH]^+$ (9), 270 $[312-MeCHO]^+$ (100), 255 $[270-Me]^+$ (34), 241 $[270-CHO]^+$ (43), 227 $[255-CO]^+$ (16), 198 $[227-CHO]^+$ (6).

Dehydroalcohol (**3c**). Red crystals, mp 190° (EtOAc). UV λ_{max}^{EtOH} nm (log ε): 221 (4.1), 303 (3.9), 312 (3.9), 374 (3.6), 448 (3.3). IR ν_{max}^{KBr} cm^{-1}: 3400, 3110, 1620, 1590, 1450, 1435, 1300, 1230, 1110, 1085, 965, 845, 800. EIMS (probe) *m/z* 70 eV, (rel. int.): 270 $[M]^+$ (100), 255 $[M-Me]^+$ (32), 242 $[M-CO]^+$ (8), 241 $[M-CHO]^+$ (47), 227 $[255-CO]^+$ (24), 198 $[227-CHO]^+$ (8).

Dehydroacetate (**3d**). Orange crystals, mp 200° (hexane–EtOAc). UV λ_{max}^{EtOH} nm (log ε): 232 (4.1), 269 (4.1), 294 (4.0), 359 (4.0). IR ν_{max}^{KBr} cm^{-1}: 3120, 1745, 1635, 1585, 1470, 1355, 1205, 1180, 1100, 960, 915, 860, 795. EIMS (probe) *m/z* 70 eV, (rel. int.): 312 $[M]^+$ (4), 269 $[M-COMe]^+$ (100), 254 $[269-Me]^+$ (42), 241 $[269-CO]^+$ (18), 226 $[254-CO]^+$ (21), 225 $[254-CHO]^+$ (9), 211 $[226-Me]^+$ (10).

8-Hydroxy-6-methoxy-3,5-dimethylnaphtho [2,3-b] furan-4,9-dione (**4**). Red needles, mp 260° (Me_2CO). UV $\lambda_{max}^{CHCl_3}$ nm (log ε): 245 (4.2), 252 (4.2), 267 (4.1), 312 (3.8), 323 (3.8). IR ν_{max}^{KBr} cm^{-1}: 3400, 3110, 1630, 1580, 1455, 1405, 1310, 1245, 1220, 1105, 1070, 990, 785. EIMS (probe) *m/z* 70 eV, (rel. int.): 272 $[M]^+$ (100), 257 $[M-Me]^+$ (21), 244 $[M-CO]^+$ (9), 243 $[M-CHO]^+$ (48), 242 $[271-CHO]^+$ (5), 241 $[M-OMe]^+$ (5), 229 $[257-CO]^+$ (13), 215 $[244-CHO]^+$ (3), 201 $[229-CO]^+$ (13).

Acknowledgements—We thank Prof. I. Barba and Prof. M. C. Gómez (University of Alicante) for MS measurements. We also thank A. Cuenca for collecting the specimen and Prof. A. Escarré for plant material identification.

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