

FURANOEREMOPHILANES FROM SENECIO ANDREUXII¹

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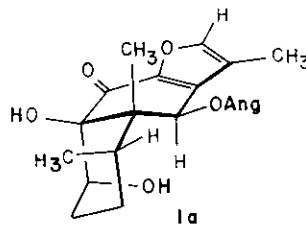
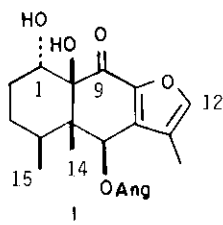
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Abstract - From the leaves of Senecio andreuxii (Compositae) two new furano-
eremophilanes, 1-deacetyl-6-angeloyl-2,3-deoxy-hilliardinol (1) and 3 α -
angeloyloxy-6 β -seneciolyloxy-10 β H-furanoeremophil-9-one (2), and the known 3,
were isolated and structurally elucidated.

Senecio is a large and complex genus of the Compositae (Tribe Senecioneae) which has been investi-
gated in some detail.^{2,3} A wide variety of sesquiterpenoids are biosynthesized by Senecio species
and also diterpenes⁴ and pyrrolizidine alkaloids have been characterized,⁵ as well as other con-
stituents.⁶ This group of plants is of interest since several species belonging to it are used in
traditional medicine while others are highly toxic.^{7,8} Here we report the isolation and structural
elucidation of two new furanoeremophilanes from the leaves of S. andreuxii.⁹

Compound 1 (0.006% from dried plant)¹⁰ was found to have a molecular formula of C₂₀H₂₆O₆ by EIMS.
The ir ($\nu_{\text{max}}^{\text{CHCl}_3}$ 3477, 1714, 1673, 1531 cm⁻¹) and uv ($\lambda_{\text{max}}^{\text{MeOH}}$ nm (log ϵ) 284 (3.7), 218 (3.6)) spec-
tral data indicated that this substance is an alcohol with an oxo group conjugated with a furan
ring. The presence of an angeloyl residue in the molecule was supported by the characteristic sig-
nals in the ¹H nmr spectrum.¹⁰ Therefore, the main skeleton belongs to the furanoeremophilane
series, since the three remaining sesquiterpenoid methyl groups were evident from the ¹H nmr¹⁰ and
¹³C nmr (Table I) spectral data. The uv absorption at 284 nm indicated a keto group at C-9¹¹ and
the ¹³C nmr (Table I) showed the presence of three saturated carbons linked to oxygen (one terti-
ary and two secondary). A tertiary hydroxyl group must be at C-10 and cis- to the methyl at C-5
since it was observed a large negative pyridine induced solvent shift ($\Delta\delta_{\text{C}_5\text{D}_5\text{N}}^{\text{CDCl}_3} = -0.24$).¹⁰ The
multiplicity (dd) of the signal at δ 3.98 located the secondary hydroxyl group at C-1, and the
coupling constants (2.5, 2.5 Hz) indicated the absence of trans diaxial interaction of the hydro-
gen geminal to the hydroxyl group. The chemical shift of the hydrogen geminal to the ester (δ
7.15) revealed that this group is β attached at C-6 and that the oxygen at C-1 is α oriented,
deshielding H-6. Therefore, 1 exists in a non-steroidal conformation (1a). The ¹H nmr spectral

data of 1 were very close to that of 2,3-deoxyhilliardinol derivatives isolated from *S. mauricei*¹² when allowance was made for the different groups attached at C-1 and C-6. This comparison confirmed that the substance from *S. andreuxii* was 1-deacetyl-2,3-deoxyhilliardinol (1).



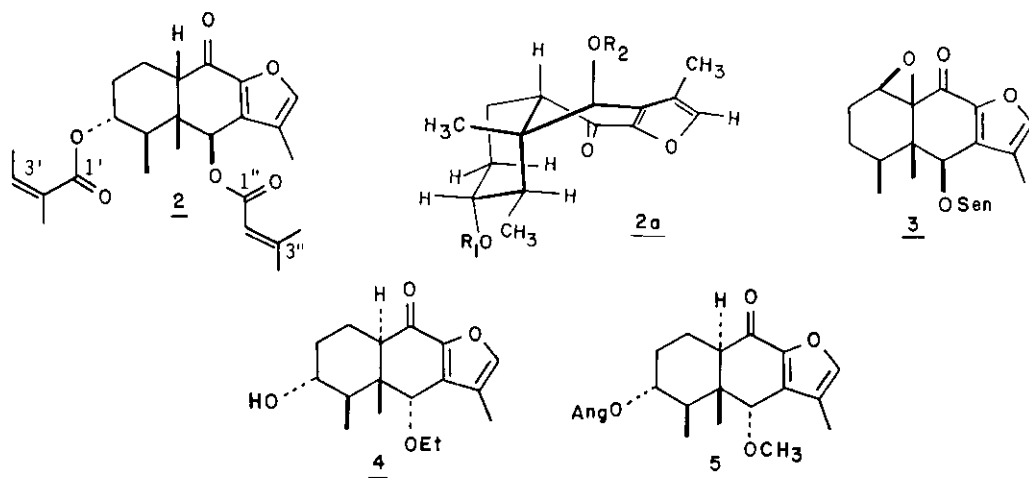
¹H and ¹³C nmr spectral data (ref. 13 and Table I) of compound 2 (C₂₅H₃₂O₆, 0.01% from the dried plant)¹³ were in agreement with a diester of a furanoeremophilane structure. The acyl residues were clearly established as senecioyl and angeloyl moieties by their typical signals in the ¹H, ¹³C nmr, and ms, in full agreement with the molecular formula. Likewise the uv spectrum of 1, the absorption at λ_{max} 274 nm of 2 indicated that it was a 9-oxofuranoeremophilane.¹¹ The A/B *cis* fusion was determined by the chemical shift of the methyl at C-5, which resonates at δ 1.03 (in the A/B *trans* series this signal is at δ 0.94-0.65).¹⁴ The pyridine induced solvent shift (Δδ_{C₅D₅N}³ = 0.14)¹³ of the C-15 protons indicated that an ester is attached at C-3. The coupling constants (ddd, 8, 8 and 4 Hz) of the signal at δ 4.72 (in CDCl₃) determined the equatorial orientation of this moiety at C-3. The singlet at δ 6.35 (in CDCl₃) in the ¹H nmr spectrum revealed that the second ester is attached at C-6 with a β-orientation,¹⁴ establishing that this molecule adopts a steroidal conformation (2a).¹⁵ The problem of assigning the senecioate and angelate groups to C-3 and C-6 was solved in the following manner: alkaline hydrolysis (KOH, EtOH-H₂O, room temperature, 2 h) of 2 afforded the ethyl ether 4,¹⁶ which displayed ¹H nmr spectral characteristics of a *trans*-furanoeremophilane, with an α-C(6) ether group, according with previous results.¹⁷ A short treatment of 2 with base (KOH, MeOH-H₂O, room temperature, 1 min) allowed the isolation of the monoester 5,^{14,18} due to the high solvolytic reactivity at C-6,¹⁹ confirming that the natural compound was 3α-angeloyloxy-6β-senecioyloxy-10βH-furanoeremophil-9-one (2). *cis*-3α,6β-Diacyloxy-furanoeremophilanes have been previously characterized.²⁰

6β-Senecioyloxy-1(10)β-epoxyfuranoeremophil-9-one (3), previously isolated from *S. glastifolius*²¹ was also a natural constituent of *S. andreuxii* (0.005% from the dried plant). Structural analogs of 3 have been recently characterized from *S. arnicoides*.²²

The composition of *S. andreuxii* is very representative of this group of plants, since it contains typical oxygenated furanoeremophilanes.^{2,3}

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Table I. ^{13}C Nmr (20 MHz, CDCl_3) data of 1, 2, and 3

C	<u>1</u>	<u>2</u>	<u>3</u>	C	<u>1</u>	<u>2</u>	<u>3</u>
1	68.19	30.71*	68.29	1'	167.07	166.20	
2	23.79*	30.74*	25.01	2'	126.99	128.26	
3	23.50*	73.95	19.54	3'	147.12	146.36	
4	32.26	46.60	32.26	4'	24.90*	19.02*	
5	50.32	50.25	45.30	5'	23.83*	19.04*	
6	62.28	74.25	62.61	1''		167.61	166.01
7	146.28*	137.29*	137.51	2''		115.62	114.91
8	147.26*	135.29*	146.65	3''		159.67	160.68
9	186.23	185.26	181.07	4''		20.49*	20.62*
10	80.26	54.52	65.55	5''		27.56*	27.64*
11	121.29	121.25	121.87				
12	140.73	137.30	146.65				
13	8.16	8.04	8.24				
14	15.96*	12.19	15.62*				
15	15.92*	15.63	15.85*				

(*): Interchangeable signals.

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9. Air dried leaves (4 kg) of *S. andreuxii* DC (collected in the State of Guerrero, voucher deposited at the National Herbarium, UNAM, M-9535), were extracted twice with acetone at room temperature. The oily residue (220 g) was chromatographed on a silica gel column (2 kg) packed with *n*-hexane and eluting with increasing amounts of EtOAc.
10. 1: Colorless needles, mp 127-129 °C, $[\alpha]_D^{25} + 12.7^\circ$ (CHCl₃); EIMS (70 eV) *m/z* (rel. int.): 344 (1), 189 (17), 137 (4), 91 (16), 83 (100), 55 (90); uv and ir: see the text; ¹H nmr (80 MHz, CDCl₃): δ 7.46 (q, *J* = 1 Hz, H-12), 7.15 (s, H-6), 6.24 (qq, *J* = 7 and 1 Hz, H-3'), 4.00 (2H, br s, OH, exchangeable with D₂O), 3.98 (dd, *J* = 2.5 and 2.5 Hz, H-1), 2.07 (dq, *J* = 7 and 1 Hz, H-4'), 2.00 (dq, *J* = 1 and 1 Hz, H-5'), 1.93 (d, *J* = 1 Hz, H-13), 1.15 (d, *J* = 7 Hz, H-15), 1.10 (s, H-14); in C₅D₅N: δ 7.73 (s, H-6), 7.16 (q, *J* = 1 Hz, H-12), 6.15 (qq, *J* = 7 and 1 Hz, H-3'), 4.43 (dd, *J* = 2.5 and 2.5 Hz, H-1), 2.15 (dq, *J* = 7 and 1 Hz, H-4'), 2.00 (dq, *J* = 7 and 1 Hz, H-5'), 1.34 (s, H-14), 1.30 (d, *J* = 7 Hz, H-15); ¹³C nmr: see Table I.
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13. 2: Colorless needles, mp 213-215 °C, $[\alpha]_D^{25} = -113.8^\circ$ (CHCl₃); uv $\lambda_{\max}^{\text{MeOH}}$ nm (log ϵ): 218 (3.3), 276 (3.0); ir $\nu_{\max}^{\text{CHCl}_3}$: 1708, 1678, 1640, 1525 cm⁻¹; EIMS (70 eV) *m/z* (rel. int.): 428 (1), 345 (1), 328 (17), 246 (13), 83 (100), 55 (61); ¹H nmr (80 MHz, CDCl₃): δ 7.29 (q, *J* = 1 Hz, H-12), 6.35 (s, H-6), 6.05 (qq, *J* = 7 and 1 Hz, H-3'), 5.48 (m, H-2'), 4.72 (ddd, *J* = 8, 8, and 4 Hz, H-3), 2.10 (d, *J* = 1 Hz, H-13), 1.98 (dq, *J* = 7 and 1 Hz, H-4'), 1.94 (d, *J* = 1 Hz, H-4''), 1.87 (d, *J* = 1 Hz, H-5''), 1.85 (dd, *J* = 1 and 1 Hz, H-5'), 1.03 (s, H-14), 0.89 (d, *J* = 7 Hz, H-15); in C₅D₅N: δ 7.15 (q, *J* = 1 Hz, H-12), 6.60 (s, H-6), 5.95 (qq, *J* = 7 and 1 Hz, H-3'), 5.90 (m, H-2'), 4.85 (ddd, *J* = 8, 8, and 4 Hz, H-3), 2.05 (dq, *J* = 7 and 1 Hz, H-4'), 1.95 (d, *J* = 1 Hz, H-4''), 1.90 (d, *J* = 1 Hz, H-5''), 1.85 (dd, *J* = 1 and 1 Hz, H-5'), 1.05 (d, *J* = 7 Hz, H-15), 1.00 (s, H-14); ¹³C nmr: see Table I.
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16. 4: Colorless oil, uv $\lambda_{\max}^{\text{EtOH}}$ nm (log ϵ): 215 (3.54), 227 (3.65), 276 (4.26), 292 (4.24); ir $\nu_{\max}^{\text{CHCl}_3}$: 3600, 1673, 1528 cm⁻¹; EIMS (70 eV) *m/z* (rel. int.): 292 (1), 274 (8), 263 (15), 225 (10), 121 (100), 93 (60), 43 (12); ¹H nmr (80 MHz, CDCl₃): δ 7.34 (q, *J* = 1 Hz, H-12), 4.13 (s, H-6), 3.52 (q, *J* = 7 Hz, -CH₂-CH₃), 3.40 (ddd, *J* = 8, 8, and 4 Hz, H-3), 2.10 (s, H-13), 1.15 (t, *J* = 7 Hz, -CH₂-CH₃), 1.12 (d, *J* = 7 Hz, H-15), 0.65 (s, H-14).
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18. 5: Colorless oil, ir $\nu_{\max}^{\text{CHCl}_3}$: 1712, 1678, 1535, 890 cm⁻¹; EIMS (70 eV) *m/z* (rel. int.): 360 (1), 345 (10), 300 (12), 285 (10), 121 (40), 100 (60), 91 (16), 83 (100), 55 (61); ¹H nmr (80 MHz, CDCl₃): δ 7.36 (q, *J* = 1 Hz, H-12), 6.02 (dq, *J* = 7 and 1 Hz, H-3'), 4.73 (ddd, *J* = 8, 8, and 4 Hz, H-3), 4.08 (s, H-6), 3.37 (s, -OCH₃), 2.13 (dq, *J* = 7 and 1 Hz, H-4'), 1.92 (dd, *J* = 1 and 1 Hz, H-5'), 1.90 (d, *J* = 1 Hz, H-13), 1.09 (d, *J* = 7 Hz, H-15), 0.68 (s, H-14).
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