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FURANOEREMOPHILANES FROM *SENECIO ANDREUXII*[1]

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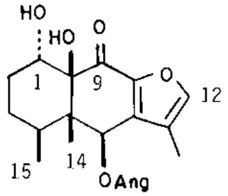
Abstract - From the leaves of *Senecio andreuxii* (Compositae) two new furanoeremophilanes, 1-deacetyl-6-angeloyl-2,3-deoxy-hilliardinol (1) and 3α-angeloyloxy-6β-senecioyloxy-10βH-furanoeremophil-9-one (2), and the known 3, were isolated and structurally elucidated.

Senecio is a large and complex genus of the Compositae (Tribe Senecioneae) which has been investigated in some detail.[2,3] A wide variety of sesquiterpenoids are biosynthesized by *Senecio* species and also diterpenes[4] and pyrrolizidine alkaloids have been characterized,[5] as well as other constituents.[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 $C_{20}H_{26}O_6$ by EIms. The ir ($\nu_{max}^{CHCl_3}$ 3477, 1714, 1673, 1531 cm^{-1}) and uv (λ_{max}^{MeOH} nm (log ε) 284 (3.7), 218 (3.6)) spectral 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 signals 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 nmr[10] and ^{13}C nmr (Table I) spectral data. The uv absorption at 284 nm indicated a keto group at C-9[11] and the ^{13}C nmr (Table I) showed the presence of three saturated carbons linked to oxygen (one tertiary 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 ($\Delta\delta_{C_5D_5N}^{CDCl_3} = -0.24$).[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 hydrogen 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).



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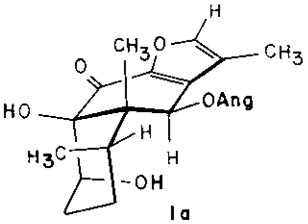

1a

^1H and ^{13}C nmr spectral data (ref. 13 and Table I) of compound 2 ($C_{25}H_{32}O_6$, 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, ^{13}C 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 ($\Delta\delta^{CDCl_3}_{C_5D_5N}$ = 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 $CDCl_3$) determined the equatorial orientation of this moiety at C-3. The singlet at δ 6.35 (in $CDCl_3$) 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-H_2O, 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-H_2O, 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-Diacyloxyfuranoeremophilanes 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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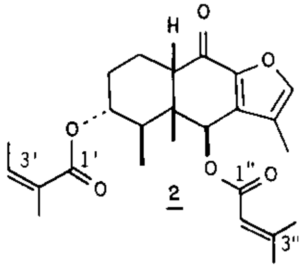

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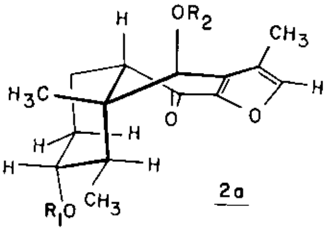
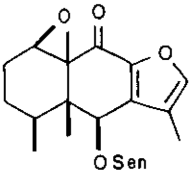


2a



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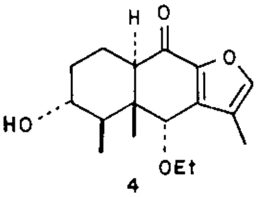

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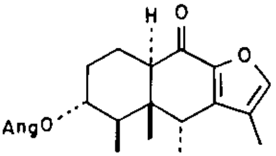

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Table I. ^{13}C Nmr (20 MHz, $CDCl_3$) data of 1, 2, and 3

C	1	2	3
1	68.19	30.71*	68.29
2	23.79*	30.74*	25.01
3	23.50*	73.95	19.54
4	32.26	46.60	32.26
5	50.32	50.25	45.30
6	62.28	74.25	62.61
7	146.28*	137.29*	137.51
8	147.26*	135.29*	146.65
9	186.23	185.26	181.07
10	80.26	54.52	65.55
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*

C	1	2	3
1'	167.07	166.20	
2'	126.99	128.26	
3'	147.12	146.36	
4'	24.90*	19.02*	
5'	23.83*	19.04*	
1"		167.61	166.01
2"		115.62	114.91
3"		159.67	160.68
4"		20.49*	20.62*
5"		27.56*	27.64*

(*): Interchangeable signals.

REFERENCES AND NOTES

1. Contribution 1004 from the Instituto de Química de la UNAM. Taken in part from the M. Sc. research work of B. R. submitted to the Universidad Autónoma del Estado de Morelos, México.
2. F. Bohlmann, K. H. Knoll, Ch. Zdero, P. K. Mahanta, M. Grenz, A. Suwita, D. Ehlers, N. Le Van, W. R. Abraham, and A. A. Natu, Phytochemistry, 1977, 16, 965.
3. F. Bohlmann, Ch. Zdero, J. Jakupovic, L. N. Misra, S. Banerjee, P. Singh, R. N. Baruah, M. A. Metwally, G. Schmeda-Hirshmann, L. P. D. Vincent, R. M. King, and H. Robinson, Phytochemistry, 1985, 24, 1249.
4. F. Bohlmann and Ch. Zdero, Phytochemistry, 1982, 21, 1697.
5. E. Roder, H. Weidenfeld, and M. Frisse, Phytochemistry, 1980, 19, 1275.
6. F. Bohlmann, J. Jakupovic, and D. Mohammadi, J. Nat. Prod., 1984, 47, 718.
7. W. H. Lewis and M. P. F. Elvin-Lewis, "Medical Botany", 1977, p. 322. John Wiley, New York.
8. L. B. Bull, C. C. J. Culvener, and A. T. Dick, "The Pyrrolizidine Alkaloids", 1968, North

Holland Publishing Company, Amsterdam.

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 needless, mp 127-129 °C, $[\alpha]_D^{25}$ + 12.7° ($CHCl_3$); 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, $CDCl_3$): 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, O*H*, exchangeable with D_2O), 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 C_5D_5N: 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); ^{13}C nmr: see Table I.
11. D. E. A. Rivet and G. R. Woolard, *Tetrahedron*, 1967, *23*, 2431.
12. F. Bohlmann and Ch. Zdero, *Phytochemistry*, 1978, *17*, 1333.
13. **2**: Colorless needless, mp 213-215 °C, $[\alpha]_D^{25}$ = -113.8° ($CHCl_3$); uv λ_{max}^{MeOH} nm (log ε): 218 (3.3), 276 (3.0); ir $\nu_{max}^{CHCl_3}$: 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, $CDCl_3$): 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 C_5D_5N: 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); ^{13}C nmr: see Table I.
14. Z. Samek, J. Harmatha, L. Novotny, and F. Sorm, *Coll. Czech. Chem. Commun.*, 1969, *34*, 2792.
15. M. Tada, T. Sato, T. Takahashi, K. Tori, I. Horibe, and K. Kuriyama, *J. Chem. Soc., Perkin Trans. I*, 1981, 2695.
16. **4**: Colorless oil, uv λ_{max}^{EtOH} nm (log ε): 215 (3.54), 227 (3.65), 276 (4.26), 292 (4.24); ir $\nu_{max}^{CHCl_3}$: 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, $CDCl_3$): δ 7.34 (q, J = 1 Hz, H-12), 4.13 (s, H-6), 3.52 (q, J = 7 Hz, $-C\underline{H}_2-CH_3$), 3.40 (ddd, J = 8, 8, and 4 Hz, H-3), 2.10 (s, H-13), 1.15 (t, J = 7 Hz, $-CH_2-C\underline{H}_3$), 1.12 (d, J = 7 Hz, H-15), 0.65 (s, H-14).
17. F. Bohlmann and K. H. Knoll, *Phytochemistry*, 1978, *17*, 461.
18. **5**: Colorless oil, ir $\nu_{max}^{CHCl_3}$: 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, $CDCl_3$): 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, $-OC\underline{H}_3$), 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).
19. A. Guerriero and F. Pietra, *Phytochemistry*, 1982, *21*, 2887.
20. K. Naya, M. Nagakawa, M. Hayashi, K. Tsuji, and M. Naito, *Tetrahedron Lett.*, 1971, 2961.
21. F. Bohlmann and Ch. Zdero, *Chem. Ber.*, 1974, *107*, 2912.
22. K. S. Khetwal and K. Manral, *Planta Medica*, 1988, 188.

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