CHEMISTRY LETTERS, pp. 1313-1316, 1978. Published by the Chemical Society of Japan

NEW 14-OXOFURANOEREMOPHILANES AND RELATED SESQUITERPENES FROM SYNEILESIS PALMATA (THUNB.) MAXIM.

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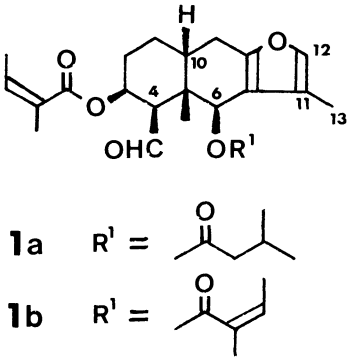
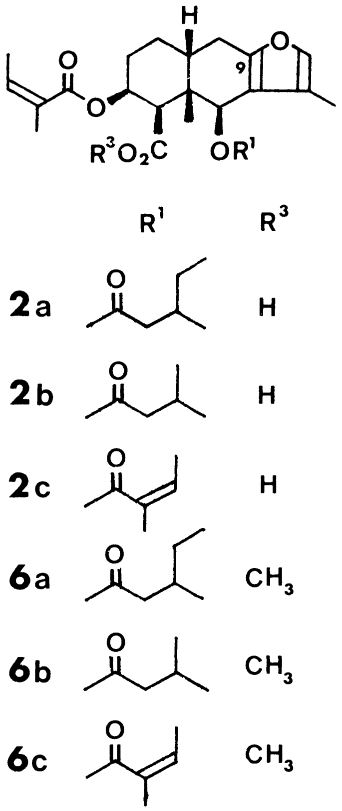
The presence of four new sesquiterpenes, 3β-angeloyloxy-6β-(3-methylbutanoyloxy)-14-oxofuranoeremophilane (1a), 3β,6β-bis(angeloyloxy)-14-oxofuranoeremophilane (1b), 3β-angeloyloxy-6β-(3-methylpentanoyloxy)furanoeremophilan-14-oic acid (2a), and 3β-angeloyloxy-6β-(3-methylbutanoyloxy)furanoeremophilan-14-oic acid (2b) in Syneilesis palmata (THUNB.) MAXIM. is described.

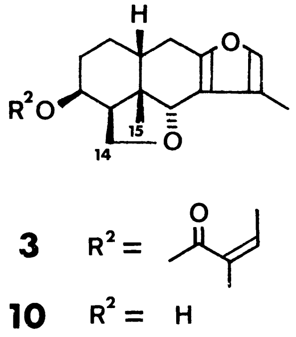
It has been reported that three alkaloids, syneilesine, acetylsyneilesine, and senecionine are isolated from Syneilesis palmata (THUNB.) MAXIM.$^{1)}$ We have examined sesquiterpene constituents of this plant$^{2)}$ and showed that the plant contains new aldehydes and acids. The present paper deals with the structure determination leading to 1a, 1b, 2a, and 2b for these substances. The compounds 1a and 1b constitute the first examples of furanoeremophilane-type sesquiterpene having an aldehyde group on C-4.

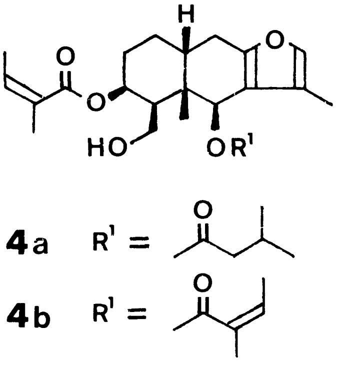
An ether extract of the roots of the plant was subjected to separation by silica gel column chromatography to give an aldehyde (1; yield 0.04 %), an acid (2; y. 0.17 %), and the known ether (3;$^{3)}$ y. 0.002 %). As described below, the aldehyde (1) and the acid (2) were shown to be a mixture of 1a and 1b, and a mixture of 2a, 2b, and 2c, respectively. Further separation of 1 by GLC and HPLC was unsuccessful because of a close proximity of retention times$^{4)}$ for its constituents and due to decomposition of 1 (1a and 1b) during these separation procedures. This was the same for the separation of 2 by GLC and HPLC (after methylation with diazomethane).

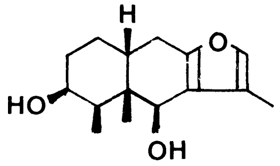
The mass spectrum of the aldehyde (1), mp 82-83 °C (one spot on TLC), showed











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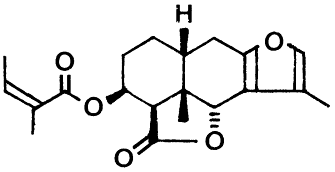

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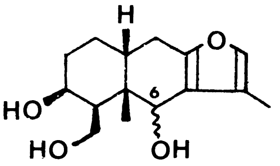

7 6β-OH

9 6α-OH

that 1 consisted of two constituents [M^+ at m/e 430.2334 (1a; $C_{25}H_{34}O_6$) and M^+ at m/e 428.2175 (1b; $C_{25}H_{32}O_6$)]. The IR (Nujol; 1725, 1715, 1640, 1565, and 1160 cm^{-1}) and PMR ($CDCl_3$) spectra suggested the presence of a tertiary methyl (δ 1.04, s, ca. 3H), a β-methyl substituted furan moiety (δ 1.83, d, J=1.5 Hz, ca. 3H) with an α-proton (δ 6.97, m, ca. 1H), and an aldehyde group (δ 9.97, d, J=1.5 Hz, ca. 1H; -CH-CHO), besides protons on carbon atoms bearing acyloxyl group [δ 5.47 (br. signal, ca. 1H; $C_{(3)}$-H), 6.28 (m, ca. 0.7H; $C_{(6)}$-H), and 6.36 (m, ca. 0.3H; $C_{(6)}$-H)]. Reduction of 1 with sodium borohydride gave a mixture of alcohols (4a and 4b), an oil, IR (neat) 3450 cm^{-1}, which was mesylated and then treated with lithium aluminium hydride to afford the known furanofukinol[5)] (5; 3β,6β-dihydroxyfuranoeremophilane). The observation shown above led to the location of the aldehyde group on C-4 and the acyloxyl groups on C-3β and C-6β for 1, because of the appearance of a doublet due to an aldehydic proton and of the signals due to a tertiary methyl and a methyl on the furan ring in the PMR spectrum of 1.

Alkaline hydrolysis of 1 gave a mixture of carboxylic acids. The acids were methylated with diazomethane to give a mixture of methyl angelate and methyl 3-methylbutanoate in a ratio of *ca.* 3:1 (examined by GC-MS, Hitachi 063; column: PEG-20M). It was shown that in the mass spectral measurement (by indirect inlet system) of 6-acyloxyfuranoeremophilane derivatives an acid moiety is easily eliminated to give the corresponding fragment ion.[6] The mass spectrum (indirect) of 4 showed a peak at m/e 330 $(M - R^1OH)^+$ [relative intensity 9; base peak m/e 55]; this suggests the presence of an angeloyloxyl group on C-3 for 4 (for both 4a and 4b). Therefore, the acyloxyl group on C-3 must be angeloyloxyl for 1 (for both 1a and 1b). Two constituents of 1 can be represented by 3β-angeloyloxy-6β-(3-methylbutanoyloxy)-14-oxofuranoeremophilane (1a) and 3β,6β-bis(angeloyloxy)-14-oxofuranoeremophilane (1b).

The acid (2), an oil (one spot on TLC), was methylated with diazomethane to give the corresponding methyl ester (6), an oil (one spot on TLC). The mass spectrum of the ester indicated that 6 contains three constituents [M^+ at m/e 474.2818 (6a, $C_{27}H_{38}O_7$), M^+ at m/e 460.2419 (6b, $C_{26}H_{36}O_7$), and M^+ at m/e 458.2296 (6c, $C_{26}H_{34}O_7$)]. The IR (neat; 3000, 1730, 1720, 1710, 1645, 1560, and 1160 cm^{-1}) and PMR (CCl_4) spectra of 2 suggested the presence of a tertiary methyl (δ 1.13, s, *ca.* 3H), a β-methyl substituted furan grouping (δ 1.81, d, J=1.5 Hz, *ca.* 3H) with an α-proton (δ 6.97, q, J=1.5 Hz, *ca.* 1H), a carboxyl group (δ 10.05, br. signal, *ca.* 1H; disappeared on addition of D_2O or on its conversion into 6), and protons on carbon atoms bearing acyloxyl group [δ 5.37 (br. signal, *ca.* 1H; $C_{(3)}$-H), 6.28 (m, *ca.* 0.2H; $C_{(6)}$-H), 6.37 (m, *ca.* 0.7H; $C_{(6)}$-H), and 6.48 (m, *ca.* 0.1H; $C_{(6)}$-H)]. Reduction of 6 with lithium aluminium hydride yielded a triol[7] (7; 3β,6β,14-trihydroxyfuranoeremophilane), mp 139-140 °C, M^+ at m/e 266 ($C_{15}H_{22}O_4$), UV λ_{max} (EtOH) 218 nm (ε 8600), IR (Nujol) 3250, 1635, and 1560 cm^{-1}, PMR (acetone-d_6) δ 0.97 (s, 3H), 2.03 (d, J=1.5 Hz, 3H), and 7.02 (m, 1H), which was found to be identical with a triol obtained from 1 by treatment with lithium aluminium hydride. Therefore, the carboxyl group must be located on C-4 and the acyloxyl groups on C-3β and C-6β for 2.

Alkaline hydrolysis of 2 gave a mixture of carboxylic acids derived from the acyloxyl moieties. Methylation of the acids with diazomethane gave a mixture of methyl angelate, methyl 3-methylbutanoate, and methyl 3-methylpentanoate in a ratio of *ca.* 6:4:1 (examined by GC-MS). The mass spectrum (indirect) of 6 showed a peak at m/e 358 $(M - R^1OH)^+$ [relative intensity 1.4; base peak m/e 55]. This suggests the presence of an angeloyloxyl group on C-3 for 6 (for 6a, 6b, and 6c) by the same arguments developed for 1. Three constituents of 2 should be 3β-angeloyloxy-6β-(3-methylpentanoyloxy)furanoeremophilan-14-oic acid (2a), 3β-angeloyloxy-6β-(3-methylbutanoyloxy)furanoeremophilan-14-oic acid (2b), and 3β,6β-bis(angeloyloxy)furanoeremophilan-14-oic acid[8] (2c).

The structure of the triol (7)[7] received support from the following transformations. The acid (2) in a mixture of benzene and acetic acid was heated under reflux to give a lactone (8), mp 112-116 °C, M^+ at m/e 344 ($C_{20}H_{24}O_5$), UV λ_{max} (EtOH) 216 nm (ε 16000), IR (Nujol) 1765, 1720, 1645, 1635, and 1565 cm^{-1}. The 6β-H configuration is suggested for 8 by the presence of intramolecular nuclear Overhauser effects (NOE: 25 %)[9] between $C_{(5)}$-CH_3 [δ (C_6D_6) 1.21; irradiated protons)] and $C_{(6)}$-H (δ 4.58; observed proton). Reduction of 8 with lithium aluminium hydride yielded a triol (9; 3β,6α,14-trihydroxyfuranoeremophilane), mp 170-172 °C, IR (Nujol) 3300 cm^{-1}, which was not identical with 7. On treatment with dilute hydrochloric acid, each of the triols (7 and 9) gave the same hydroxy ether (10), mp 136-138 °C, IR (Nujol) 3470 cm^{-1}, which was also obtained from 3[3] by reduction with lithium aluminium hydride.

REFERENCES

1) M. Hikichi and T. Furuya, Chem. Pharm. Bull., 24, 3178 (1976); M. Hikichi and T. Furuya, Tetrahedron Lett., 1974, 3657.
2) The authors wish to thank Mr. M. Sakata and Mr. N. Saito, University Forest at Chichibu, the University of Tokyo, for collecting *Syneilesis palmata* (THUNB.) MAXIM. Thanks are also due to Dr. T. Tsuyuki and Dr. Y. Moriyama for their valuable discussion and kind aid in the collection.
3) F. Bohlmann and N. Rao, Tetrahedron Lett., 1973, 613.
4) This would be due to the presence of an additional acyloxyl group at C-3, which may reduce the difference in GLC and HPLC properties between the acyloxyl groups at C-6 for 1a and 1b.
5) K. Naya, Y. Makiyama, T. Matsuura, N. Ii, H. Nagano, and T. Takahashi, Chem. Lett., 1978, 301.
6) *e.g*. The mass spectrum by indirect inlet system of 3β-angeloyloxy-6β-acetoxyfuranoeremophilane showed a peak at m/e 314 $(M - AcOH)^+$ [relative intensity (r.i.) 10; base peak m/e 159] and a peak at m/e 274 due to $(M - \text{angelic acid})^+$ was absent, while in the spectrum by direct inlet system both peaks at m/e 314 (r.i. 9; base peak m/e 124) and m/e 274 (r.i. 2) appeared in an intensity ratio of *ca*. 4.5:1. *cf*. H. Nagano, Doctoral Thesis, the University of Tokyo (1974), p. 138.
7) The triol (7) was registered in ref. 8. The PMR spectrum (270 MHz) of our sample (7) was kindly measured and compared with that of the specimen (7; ref. 8) by Professor F. Bohlmann, to whom the authors' sincere thanks are due. However, we were informed that the two compounds are not identical probably due to configurational isomerism.
8) F. Bohlmann, C. Zdero, and M. Granz, Chem. Ber., 107, 3928 (1974): isolation of 2c and related compounds from plants of the genus *Othonna* (Compositae) was reported.
9) The presence of NOE (28 %) between 5β-methyl [δ ($CDCl_3$) 1.26; irradiated protons] and 6β-H (δ 5.08; observed proton) was shown for furanoeremophilan-14β,6α-olide: Y. Ishizaki, Y. Tanahashi, T. Takahashi, and K. Tori, Chem. Commun., 1969, 551. The PMR spectrum of this lactone in C_6D_6 was recently measured to show the signal at δ 4.63 due to 6β-H.

(Received September 16, 1978)