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Albartin—a New Sesquiterpene-Coumarin Ether from *Artemisia alba*[1]

Short Communication

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A new sesquiterpene isofraxidin ether (isofraxidin = 7-hydroxy-6,8-dimethoxy-coumarin) was isolated from the roots of *Artemisia alba* and characterized by means of ^{1}H-nmr, ^{13}C-nmr, ms, uv, and ir. Albartin is an exomethylene isomer of 3-acetyloxy-drimartol isofraxidin ether with —O*Ac* axial and —CH_2O*Ar* equatorial. The chemosystematic significance of this class of compounds within the genus *Artemisia* is briefly discussed.

[Keywords: Artemisia (Compositae-Anthemideae); Chemosystematics; ^{13}C-nmr; ^{1}H-nmr; Sesquiterpene-coumarin ethers]

Albartin — ein neuer Sesquiterpen-Cumarin-Ether aus Artemisia alba (Kurze Mitteilung)

Aus den Wurzeln von *Artemisia alba* wurde ein neuer Sesquiterpen-Isofraxidin Ether (Isofraxidin = 7-Hydroxy-6,8-dimethoxy-cumarin) isoliert und mittels ^{1}H-NMR, ^{13}C-NMR, MS, UV und IR charakterisiert. Albartin ist ein exo-Methylen-Isomer von 3-Acetyloxy-drimartol-isofraxidin-ether mit —O*Ac* axial und —CH_2O*Ar* equatorial. Die chemosystematische Bedeutung dieser Verbindungsklasse innerhalb der Gattung *Artemisia* wird kurz diskutiert.

Recently we reported the isolation and identification of five new sesquiterpene-isofraxidin ethers from the roots of several *Artemisia* and *Achillea* species[2]. During extensive chromatographic comparisons within the two genera it became apparent that the accumulation of these compounds represents a valuable systematic criterion which charac-

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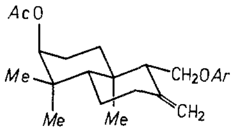
terizes species of the *Artemisia*-section *Abrotanum* Bess. as well as members of the *Achillea ochroleuca* Ehrh.—*A. pseudopectinata* Janka complex.

In continuation of these studies on sesquiterpene-coumarin ethers we have now isolated a new derivative as main component from the roots of *Artemisia alba* Turra (= *A. camphorata* Vill. = *A. lobelii* All.). The mainly Mediterranean species varies considerably in habit, pubescence, and in the presence of receptacular hairs. As a consequence, *A. alba* has an uncertain taxonomic position, either placed in the sect. *Absinthium* DC. or in the sect. *Abrotanum* Bess. Its affinity with the latter section is now supported by the present chemical findings.



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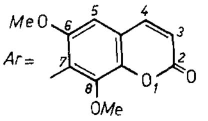

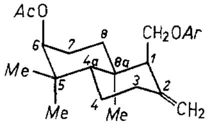

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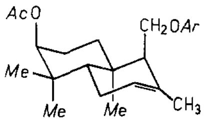

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The structure of the new derivative **1**, designated as albartin, was derived from the spectral data. Its ms is almost identical with those of other related acetyl derivatives [m/e 484 (M^+, 3%), 222 ($C_{11}H_{10}O_5$, isofraxidin, 100%), 203 ($C_{15}H_{23}$, terpenic fragment, 51%)] (see Refs.[2,3]).

The ^{1}H-nmr spectrum clearly shows that **1** belongs to the exomethylene series ($>C=CH_2$ at 5.01 and 5.00 ppm) and that —O*Ac* is in an axial position [the corresponding geminal proton $>CH(OAc)$ at 4.70 ppm is equatorial since it does not exhibit a large *trans-trans* vicinal coupling[2,4]]. The spectrum is similar to that of acetylpectachol (**2**), the main difference is within the AB part of the ABX system of the $>CH—CH_2—OAr$ protons: in **1** the AB part represents almost a pseudodoublet at 4.26 ppm (2 H), in **2** the A and B protons are resolved clearly into two separate dd (see Ref.[2]). The situation is similar for coladonin where the corresponding AB part of the system $>CH—CH_2—O$ (coumarinyl) is described as a doublet[5]. However, a series of decoupling experiments clearly characterizes the ABX system of **1** (δ_A 4.27, δ_B 4.25, δ_X 2.40 ppm, $J_{AB} = 10.5$, $J_{AX} = 6.5$, $J_{BX} = 5.3$ Hz).

Table 1. *^{13}C-nmr data for* **1** **3**; *ppm; in* $CDCl_3$; *TMS internal standard; Bruker WM 250 (250 MHz)*

ition ltipl.)	**1**	**2**	**3**	$\Delta_{1\text{-}2}^{h}$	Position (multipl.)	**1**	**2**	**3**	$\Delta_{1\text{-}2}^{h}$
raxidin moiety					Terpenic moiety				
(s)	160.3	160.4	160.4	—	C 1 (d)^{a}	56.1	58.5	56.2	—2.4
(d)^{b}	115.0	115.3	115.3	—	C 2 (s)	146.4	147.4	132.3	—1.0
(d)^{a}	143.4	143.3	143.4	—	C 3^{f}	37.3	32.3	122.9	+ 5.0
ι (s)	114.4	114.5	114.6	—	C 4 (t)^{e}	23.1	22.9	22.7	—
(d)^{b}	104.0	104.3	104.3	—	C 4a (d)^{a}	49.1	42.0	37.8	+ 7.1
	150.5	150.6	150.6	—	C 5 (s)	36.6	36.9	36.4	—
7, 8, 8a	145.6	146.0	145.4	—	C 6 (d)	77.9	78.4	78.9	—
(s)^{c}	143.0	143.3	143.4	—	C 7 (t)^{e}	23.2	23.2	23.5	—
	141.6	141.7	141.7	—	C 8 (t)	32.1	29.9	28.8	+ 2.2
O*Me* (q)^{d}	56.1	56.5	56.4	—	C 8a (s)	38.5	37.5	35.5	+ 1.0
O*Me* (q)^{d}	61.7	61.9	61.8	—	C 1-CH_2— (t)	71.7	73.5	74.5	—2.4
					C 2-*me*^{g}	107.7	110.9	21.8	—3.2
					C 5-*Me* eq (q)	28.0	28.0	27.6	—
					C 5-*Me* ax (q)	21.8	22.1	21.6	—
					C 6-O—C=O (s)	170.5	170.5	170.6	—
					Me (q)^{a}	21.1	21.2	21.1	—
					C 8a-*Me* (q)	15.0	22.2	22.7	—7.2

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[a] Assignment based on relative residual coupling in the off resonance spectra.

[b–e] Interchangeable.

[f] (t) for **1**, **2**; (d) for **3**.

[g] *me* $=CH_2$ in **1**, **2** (t); -*Me* in **3** (q).

[h] $\Delta(\delta_1 - \delta_2)$ values > 0.5 ppm are listed.

In addition, several further ring protons of the sesquiterpene unit could be identified by decoupling, thus proving the *trans*-decaline structure of the bicyclic terpenic moiety as well. The ^{1}H-nmr data imply that the only difference between albartin (**1**) and acetylpectachol (**2**) is the relative configuration of $—CH_2OAr$ which was proven to be in an axial position in **2**. Consequently, in **1** the position should be equatorial.

These relative configurations of $—CH_2OAr$ are fully confirmed by comparison of the ^{13}C-nmr data of **1** and **2** as shown in Table 1.

In addition, acetyldrimartol A (**3**) previously obtained by acetylation of the corresponding alcohol[3] could now be isolated as a natural product from *Achillea ochroleuca*. The structure of **3** is in agreement with all spectral data (^{13}C-nmr see Table 1) and was proven by acetylation of drimartol A as well.

The ^{13}C chemical shifts for the isofraxidin part of the ethers **1**—**3** are almost identical. The data for the sesquiterpenic part of **1** and **2** reflect clearly the the relative positions of the —CH_2OAr substituent at C 1. Differences $\Delta(\delta_1 — \delta_2)$ are observed for C 1 itself and its direct neighbours $\mathbf{C}H_2OAr$, C 2 and C 8a. The most interesting information about the stereochemistry of the C 1 substituent is gained from the observed γ-effects: C 3, C 4a, and C 8 exhibit less steric interactions if the bulky —CH_2OAr substituent is equatorial as in **1**, resulting in positive $\Delta(\delta_1 — \delta_2)$ values (+ 5.0, + 7.1, + 2.2 ppm, see Table 1). On the other hand, if —CH_2OAr is equatorial, the steric interactions with $C2{=}\mathbf{C}H_2$ and $C8a—\mathbf{C}H_3$ must be stronger than in case of compound **2**, resulting in negative $\Delta(\delta_1 — \delta_2)$ values (— 3.2 and — 7.2 ppm).

Comparing the data for **2** and **3**—which differ only in the position of the double bond in ring B—confirms these assignments. Gross changes are of course observed for C 2, C 3, and C 2—**C** (either methylene or methyl) while minor changes (2-4 ppm) may be detected for other carbons on ring B (C 4a, C 8a, and C 1) and very small changes (ca. 1 ppm) can still be observed for C 8 and $\mathbf{C}H_2OAr$ which are directly attached to ring B.

The ^{13}C-nmr assignments are additionally based on the multiplicities and in some cases on the residual coupling constants in the corresponding off resonance spectra (see Table 1). The formulas should express the relative configurations, determination of absolute configurations is in progress.

Acknowledgments

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Experimental

The compounds were isolated by a method described previously[2]. 155 g air dried roots of *Artemisia alba* (collected in Yugoslavia, Croatia, Velebit Mts. near Karlobag) afforded 45 mg **1**, 100 g roots of *Achillea pseudopectinata* (A-1074)[2] 3 mg of **3**. Voucher specimens are deposited at the herbarium of the Institute of Botany, University of Vienna (WU).

Albartin (**1**), *(1α,4aβ,6β,8aα)-7-[(6-acetyloxy-decadydro-5,5,8a-trimethyl-2-methylene-1-naphthalenyl)methoxy]-6,8-dimethoxy-2H-1-benzopyran-2-one*

Colourless viscous oil; $[\alpha]_D^{20} = +2°$, $[\alpha]_{436}^{20}$ — 3° (c = 1.5, acetone); ir (CCl_4, cm^{-1}): 2 930, 1 740, 1 560, 1 465, 1 420, 1 405, 1 285, 1 240, 1 150, 1 120, 1 040, 835; uv [*Et*OH, λ *max*/nm (ε)]: 339 (7 200), 297 (9 800), 228 (17 400), 208 (36 700); ms [70 eV, 120°, *m/e* (%)]: 484 (M^+, 3%), 223 (23), 222 (100), 221 (7), 204 (9), 203 (51), 202 (9), 161 (11), 147 (18), 133 (22), 121 (14), 119 (16), 111 (10), 109 (16), 107

(21), 105 (18), 95 (25), 93 (25), 91 (18); high resolution ms: calc. for $C_{28}H_{36}O_7$ 484.2461, found 484.246 ± 0.002; ^{1}H-nmr ($CDCl_3$, δ/ppm): 7.62 (d, 1 H, C 4isofr.-H, $J = 9.5$ Hz), 6.67 (s, 1 H, C 5isofr.-H), 6.35 (d, 1 H, C 3isofr.-H, $J = 9.5$ Hz), 5.01 (s, broad, 1 H, exomethylene), 5.00 (s, broad, 1 H, exomethylene), 4.70 (t, broad, $w_{1/2} = 9$ Hz, 1 H, C 6-H), 4.27 (dd, 1 H, C 1-CH_2—O, $J = 10.5$ and 6.5 Hz), 4.25 (dd, 1 H, C 1-CH_2—O, $J = 10.5$ and 5.3 Hz), 4.00 (s, 3 H, —O*Me*), 3.89 (s, 3 H, —O*Me*), 2.48 (ddd, 1 H, C 3-H eq, $J = 12$, 4, and 3 Hz), 2.40 (dd, resp. broad pseudo t, 1 H, C 1-H, $J = 6.5$ and 5.3 Hz), 2.18 (ddd, 1 H, C 3-H ax, $J = 12$, 12, and 3 Hz), 2.11 (s, 3 H, CO*Me*), 1.90 (ddd, 1 H, C 8-H ax, $J = 13$, 12, and 4 Hz), 1.75-1.60 (m, 5 H, C 4-H eq, C 4a-H, C 7-H ax and eq, C 8-H eq), 1.41 (dddd, 1 H, C 4-H ax, $J = 14$, 12, 12, and 4 Hz), 0.90 (s, 3 H, *Me*), 0.89 (s, 3 H, *Me*), 0.80 (s, 3 H, *Me*).

Acetyldrimartol A (**3**), *(1α,4aα,6α,8aβ)-7-[(6-acetyloxy-1,4,4a,5,6,7,8,8a-octahydro-2,5,5,8a-tetramethyl-1-naphthalenyl)methoxy]-6,8-dimethoxy-2H-1-benzopyran-2-one*

Colourless, viscous oil; $[\alpha]_D^{20} = +110°$, $[\alpha]_{436}^{20} = +235°$ ($c = 0.3$, acetone); ir (CCl_4, cm^{-1}): 2925, 1740, 1560, 1460, 1420, 1410, 1380, 1290, 1245, 1150, 1125, 1045, 980, 840; uv [*Et*OH, λ_{max}/nm (ε)]: 338 (7500), 297 (10500), 227 (18500), 206 (40000); ms [70 eV, 120°, *m/e* (%)]: 484 (M^+, 2%), 223 (24), 222 (83), 221 (9), 204 (17), 203 (100), 202 (7), 161 (28), 147 (19), 135 (13), 133 (24), 121 (17), 120 (6), 119 (31), 109 (23), 107 (26), 105 (21), 95 (31), 93 (18), 91 (13); ^{1}H-nmr ($CDCl_3$, δ/ppm): 7.62 (d, 1 H, C 4isofr.-H, $J = 9.5$ Hz), 6.67 (s, 1 H, C 5isofr.-H), 6.36 (d, 1 H, C 3isofr.-H, $J = 9.5$ Hz), 5.42 (t, broad, 1 H, C 3-H), 4.71 (t, broad, $w_{1/2} = 9$ Hz, 1 H, C 6-H), 4.21 (dd, 1 H, C 1-CH_2—O, $J = 11$ and 7 Hz), 3.91 (dd, 1 H, C 1-CH_2—O, $J = 11$ and 1 Hz, partially covered by O*Me*), 3.97 (s, 3 H, —O*Me*), 3.87 (s, 3 H, —O*Me*), 2.35 (ddd, 1 H, C 8-H ax, $J = 14$, 13, and 4 Hz), 2.05-1.75 (m, 6 H), 1.76 (s, broad, 3 H, C 2-*Me*), 1.32 (ddd, 1 H, C 8-H eq, $J = 14$, 4, and 3.5 Hz), 1.02 (s, 3 H, *Me*), 1.00 (s, 3 H, *Me*), 0.87 (s, 3 H, *Me*).

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[1] Part 2 in the series "Naturally Occurring Sesquiterpene-Coumarin Ethers".

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[4] $w_{1/2} = 9$ Hz is characteristic for H eq (O*R* ax, *R* = H or *Ac*), $w_{1/2} = 17$-19 Hz for H ax (O*R* eq) (see Ref.[2]).

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