NEW SESQUITERPENE COUMARIN ETHERS FROM *ACHILLEA OCHROLEUCA*.[1] ^{13}C-NMR OF ISOFRAXIDIN-DERIVED OPEN-CHAIN, AND BICYCLIC SESQUITERPENE ETHERS

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ABSTRACT.—The roots of *Achillea ochroleuca* afforded, in addition to known sesquiterpene isofraxidin ethers, four new derivatives: epoxyfarnochrol (**2**), oxofarnochrol (**3**), isodrimartol A (**5**), and acetylisodrimartol A (**5a**). The ^{13}C-nmr data of all derivatives isolated to date from various *Achillea* and *Artemisia* species are discussed in detail.

During the search for additional chemical characters in the tribe *Anthemideae* (Compositae), it appeared that the accumulation of isofraxidin-derived sesquiterpene ethers may contribute to a more natural arrangement of species within the large genera *Artemisia* and *Achillea* (1,2). At the same time, this biogenetic trend resembles the umbelliferone-derived sesquiterpene ethers that, to date have been found only in the *Umbelliferae* (3-5). In addition to the other chemical similarities between the *Compositae* and the *Umbelliferae* (*e.g.*, sesquiterpene lactones, polyacetylenes etc.), this chemical capacity also suggests close affinities between the two families.

Within the genus *Achillea*, the accumulation of sesquiterpene coumarin ethers is apparently confined to the morphologically distinct *A. ochroleuca-A. pseudopectinata* complex. Preliminary chromatographic analyses of different provenances of *A. ochroleuca* Ehrh. (=*A. pectinata* Willd.=*A. kitaibeliana* Soó) have shown that the composition of these compounds varies within the species by different sesquiterpene moieties. Whereas the formation of the open-chain derivatives **1-3** represents a common chemical trend in that species, the different provenances may be distinguished by distinct accumulation tendencies towards different bicyclic drimenyl derivatives. These differences mainly result from the position of the double bond in the terpenic unit and from different configurations at C-13 and C-21 (see formulas).

Recently, we reported the isolation and identification of drimartol B (**6**) with -CH_2OAr axial (C-13) and -OH equatorial (C-21) as the main component from *A. ochroleuca* collected 50 km southeast of Budapest (Hungary) (1). The present investigation of another provenance (A-1223), originating from the Botanical Garden at Budapest, reveals a further isomer with -CH_2OAr equatorial and -OH axial in large quantities (340 mg **5** from 185 g of roots). The new compound was designated as isodrimartol A (**5**).

The corresponding acetyl derivative (**5a**), as well as the known drimartol A (**4**) and drimartol B (**6**) (1), could also be isolated as minor constituents. Additionally, in the less polar fractions, the previously isolated farnochrol (**1**) (1), together with the corresponding oxidation products **2** and **3**, could be isolated. The latter compounds have been proven new and were named epoxyfarnochrol (**2**) and oxofarnochrol (**3**). Their structures were determined by ^{1}H-nmr and ^{13}C-nmr.

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

To date, 11 different isofraxidin sesquiterpene ethers have been isolated from the roots of various *Artemisia* and *Achillea* species. We have carried out a detailed ^{13}C-nmr analysis[2] of these derivatives to facilitate the stereochemical assignment of further derivatives. The ^{13}C-nmr data are summarized in table 1.

^{13}C-NMR

Isofraxidin Moiety. In all spectra recorded, the 11 lines of the isofraxidin moiety remain almost unchanged (signals 1-11, table 1). Compound **5** was used to assign lines 1-11 by the ^{13}C-^{1}H coupled spectrum and selective ^{13}C[^{1}H] decoupling experiments. The results for **5** are valid for all other compounds as well, because corresponding isofraxidin carbons do not differ by more than 0.4 ppm in the complete series; the only exception is C-7 (0.9 ppm), because this carbon is directly attached to the different sesquiterpene units. (The observed limits in the chemical shifts are given in brackets in the following discussion).

The ^{13}C signals of carbons C-2, C-3, and C-5 (doublets in the off-resonance spectra) could be identified by selective ^{13}C[^{1}H] double resonance (compare experimental data,

TABLE 1. ^{13}C data for compound **1-8a** ($CDCl_3$, TMS, δ/ppm)

No.	1	2	3	4	4a	5	5a	6	7	7a	8a
1	160.4	160.5	160.5	160.4	160.4	160.4	160.3	160.4	160.5	160.4	160.3
2	115.1	115.3	115.2	115.2	115.3	114.9	115.3	115.2	115.3	115.3	115.0
3	143.3	143.5	143.5	143.5	143.4	143.4	143.4	143.3	143.4	143.3	143.4
4	114.4	114.5	114.5	114.6	114.6	114.3	114.5	114.5	114.5	114.5	114.4
5	103.8	103.8	103.9	104.1	104.2	104.1	104.2	104.1	104.1	104.2	104.0
6	150.7	150.7	150.7	150.6	150.6	150.5	150.6	150.5	150.7	150.6	150.5
7	145.8	145.1	145.3	145.3	145.4	145.5	145.6	145.4	145.6	146.0	145.6
8	141.9	141.9	141.9	141.8	141.7	141.6	141.7	141.7	141.7	141.6	141.5
9	143.1	143.2	143.1	143.2	143.4	143.2	143.4	143.2	143.4	143.3	143.0
10	56.4	56.4	56.4	56.4	56.4	56.2	56.3	56.3	56.5	56.5	56.1
11	61.6	61.7	61.7	62.0	61.8	61.7	61.9	61.8	62.0	61.9	61.7
12	70.3	70.3	70.3	73.3	74.5	72.8	72.9	73.4	73.7	73.5	71.1
13	119.7	119.9	119.8	55.8	56.2	54.9	55.3	55.7	58.4	58.5	56.1
14	142.4	142.3	142.3	131.8	132.3	133.5	133.6	131.6	147.8	147.4	146.4
15	39.6	39.6	39.5	123.5	122.9	122.8	123.0	123.1	32.5	32.3	37.3
16	26.4	26.3	26.4	23.7	23.5	23.2	23.2	23.7	23.1	22.9	23.1[a]
17	124.3	124.4	124.3	37.0	37.8	43.4	44.6	42.5	40.8	42.0	49.1
18	135.4	134.6	134.3	35.6	35.5	35.6	35.7	35.8	37.7[a]	37.5	38.4
19	39.7	36.4	39.1	28.0	28.8	31.3	32.3	34.0	29.2	29.9	32.1
20	26.8	27.6	33.6	25.4	22.7	25.2	22.8	27.6	25.7	23.2	23.2[a]
21	123.8	64.2	211.5	76.8	78.9	75.7	78.2	79.4	76.2	78.5	77.5
22	131.2	58.2	40.9	37.4	36.4	37.1	36.5	38.7	37.8[a]	36.9	36.8
23	16.4	16.4	16.4	22.8	22.8	21.4	21.6[a]	22.6	110.7	110.9	107.7
24	15.9	16.0	16.1	21.8	21.8[a]	14.2	14.4	21.7	22.1	22.1[a]	15.0
25	25.6	24.9	18.3	22.4	21.6[a]	22.3	22.0[a]	15.2	22.5	22.2[a]	21.8
26	17.6	18.8	18.3	28.2	27.6	27.9	27.7	27.9	28.4	28.0	28.0
27					170.6		170.6			170.5	170.5
28					21.1		21.2			21.2	21.1

[a]Values may be reversed in any vertical column.

[2]With regard to related compounds ^{13}C-nmr data for coladonin and its acetate coladin (umbelliferone-derived sesquiterpene-coumarin ethers): H. Duddeck and M. Kaiser, *Org. Magn. Reson.* **20**, 55 (1982); E. Wenkert, B.L. Buckwalter, I.R. Burfitt, M.J. Gasic, H.E. Gottlieb, E.W. Hagaman, F.M. Schell, and P.M. Wovkulich, Topics in Carbon-13 NMR Spectroscopy (G.C. Levy, ed.), Wiley, New York, Vol. 2, 81 (1976).

compound **5**): C-2 (114.9-115.3), C-3 (143.3-143.5), C-5 (103.8-104.2). C-1, C-4, and C-6 - C-9 appear as singlets in the off-resonance spectra. The carbonyl C-1 (160.3-160.5) may be assigned in a straightforward manner, in all other cases (C-4 and C-6 - C-9) long-range ^{13}C-^{1}H couplings could be used for proper assignments (6,7); C-4 (114.3-114.6) exhibits one *trans*-$^{3}J(^{13}C$-$^{1}H)$ coupling of 7.5 Hz, C-7 (145.1-146.0) appears also as a doublet in the ^{13}C-^{1}H-coupled spectrum with a *trans*-^{3}J of 8.3 Hz; C-7 carries on -OR group and is, therefore, found at lower field compared with C-4. For C-9 (143.0-143.4) two *trans*-^{3}J couplings are possible: the signal appears as a sharp dd with ^{13}C-^{1}H couplings of 5.6 and 9.2 Hz.

The signals for C-6 and C-8 remain to be assigned. In the ^{13}C-^{1}H-coupled spectrum of **5**, the signal at 150.5 ppm appears as a narrow pseudo-triplet (dd, 2 × 3.7 Hz) the signal at 141.5 as an unresolved multiplet. The broad m is due to $^{3}J_{C\text{-}H}$ coupling to the protons of the methoxyl group in addition to long-range couplings to the coumarin protons at C-3 and C-5. Irradiation at 3.99 ppm (OMe 11) sharpens the m at 141.5 ppm significantly; this signal belongs, therefore, to C-8. The pseudo-*t* at 150.5 remains virtually unchanged upon irradiation at 3.99 and 3.87 ppm (OMe 11 and OMe 10), because the long-range couplings to the coumarin protons are the only dominant ones. Based on these selective ^{13}C [^{1}H] decoupling experiments, C-6 is assigned to the signals between 150.5-150.7 and C-8 to 141.5-141.9 ppm for compounds **1-8a** (see table 1).

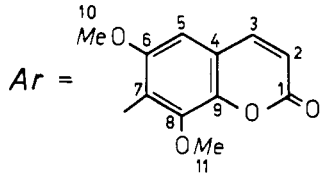
Concerning the two methoxy groups, C-10 and C-11, it was proved by selective ^{13}C [^{1}H] decoupling that the signal at 56.2 ppm corresponds to the ^{1}H-Me signal at 3.87 ppm, and this, in turn, could be assigned to the C-10 Me by a NOE-difference experiment from H C-5; therefore, C-10 (56.1-56.5) and C-11 (61.2-62.0). An additional argument based on the ^{1}H spectra of all compounds investigated is that the C-10 Me signal is always clearly broadened (compared with C-11 Me) by a long-range coupling to C-5 H.

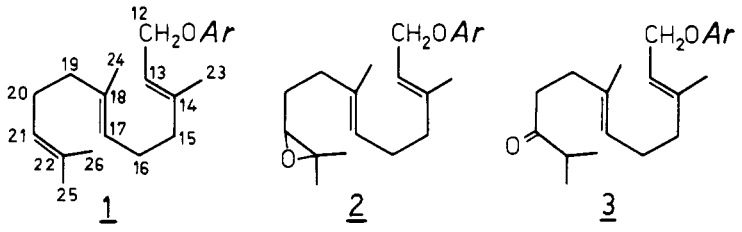
SESQUITERPENE MOIETY

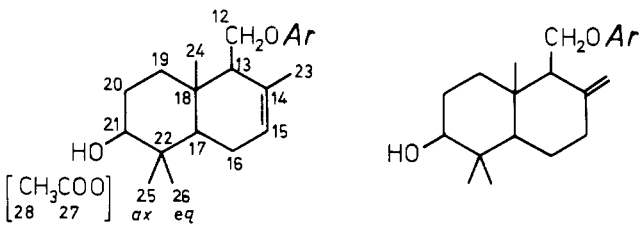
Open Chain Sesquiterpene Derivatives **1-3**. The assignment of ^{13}C signals for the terpene moiety of the open-chain-type compounds **1-3** are based on corresponding data for farnesol (8): in farnochrol (**1**) only C-12, C-13, and C-14 differ significantly from farnesol due to the formation of the isofraxidin ether bond (8,9). The ^{13}C data of the oxidation products of **1**, epoxyfarnochrol (**2**) and oxofarnochrol (**3**), may be correlated with the data of **1**. In **2** the olefinic signals for C-21 and C-22 are shifted towards the C-O-region (64.2 and 58.2 ppm), further slight shift changes are observed for C-19, -20, -25, and -26, as well (see table 1). In **3**, C-21 becomes a carbonyl C (211.5 ppm); further differences in the chemical shifts (compared with **1**) may be observed for C-20, -22, -25, and -26 (see table 1).

Bicyclic Sesquiterpene Derivatives (Drimenol Type) **4-8a**. For assignment of the terpenic ^{13}C signals in the bicyclic derivatives extensive shift comparisons (10) of the compounds under investigation were used. Especially acetyl shifts (11) and shifts upon change of relative configurations at C-21 and C-13 were utilized in addition to multiplicities (and residual splittings) known from the off-resonance spectra.

Several lines may be assigned in a straightforward manner. For all compounds, a doublet for C-21 (C-OH or C-OAc, 75.7-78.9 ppm) is observed, the acetyl shifts are between 2.1 and 2.5 ppm. The triplet for C-12 (-CH_2OAr) is found at 73.3-74.5 ppm for compounds **4, 4a, 6, 7,** and **7a** (-CH_2OAr axial) or 71.1-72.9 for **5, 5a,** and **8a** (-CH_2OAr equatorial). Assignment of the olefinic C of compounds **4-6** (C-14 and C-15) and of compounds of the exo-methylene series (**7, 8,** C-14 and C-23) can be made without any problems, based on multiplicities and chemical shifts.





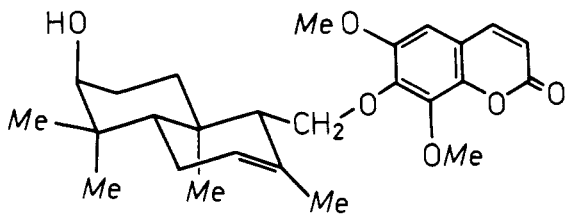


	OH	CH_2OAr
4	*ax*	*ax*
5	*ax*	*eq*
6	*eq*	*ax*

	OH	CH_2OAr
7	*ax*	*ax*

	OAc	CH_2OAr
4a	*ax*	*ax*
5a	*ax*	*eq*

	OAc	CH_2OAr
7a	*ax*	*ax*
8a	*ax*	*eq*



5

From the ^{13}C signals left for the drimenol unit, we have two singlets (C-18, C-22), two doublets (C-13, C-17), three or four triplets (C-16, C-19, C-20, plus C-15 in the exo-methylene series), and four or three quartets (C-23, C-24, C-25, C-26, minus C-23 in the exo-methylene series). These groups of signals will be treated step by step in the following discussion.

The singlet for C-22 should exhibit a negative acetyl shift (11): observed −1.0 ppm for **4**/**4a**, −0.6 for **5**/**5a**, −0.9 for **7**/**7a**. The s for C-18 should remain unchanged upon acetylation (±0.1 ppm, see table 1). An additional argument for the assignment of the s C-18 and C-22 is the change observed when comparing **4** (C-21-OH ax) with **6**

(C-21-OH eq): C-18 remains uneffected, C-22 (close to OH) is different in **4** and **6** (see table 1).

The doublets for C-17 shoud exhibit a positive acetyl shift (11): observed +0.8 for **4**, +1.2 for **5**, +1.2 ppm for **7**. Shift arguments, based on comparison of **6** (OH eq, CH_2OAr ax) with **4** (OH ax, Ch_2OAr ax), **5** (OH ax, Ch_2OAr eq) with **4**, and **8a** (OAc ax, CH_2OAr eq) with **7a** (OAc ax, CH_2OAr ax), may be used in addition for assignment of C-17. C-17 suffers severe γ-effects from substituents either at C-13 (CH_2OAr) or C-21 (OH or OAc): C-17 $\Delta\delta$(**6-4**)= 5.5 ppm, $\Delta\delta$(**5-4**)= 6.4 ppm, $\Delta\delta$(**8a-7a**)= 7.1 ppm.

The triplets C-20 and C-19 are identified by acetyl shifts (11) (−2.7/+0.8 for **4**/**4a**, −2.4/+1.0 for **5**/**5a**, −2.5/+0.7 ppm for **7**/**7a**; t C-16 and C-15 in the exo-methylene series ±0.1 ppm). In **4-6**, the remaining t belongs necessarily to C-16 (23.2-23.7 ppm), in **7-8a** (exo-methylene series) an additional t (C-15) occurs at significantly different field relative to all other triplets: 37.3 ppm in **8a** and 32.5/32.3 in **7**/**7a** (all other t are below 30 ppm). For C-15 $\Delta\delta$(**8a-7a**)= 5.0 ppm is again explained by a γ-effect caused by the axial CH_2OAr substituent in compounds **7** and **7a**. For t C-19 (analoguous to d C-17) γ-effects caused by axial OH or CH_2OAr can be observed: $\Delta\delta$(**6-4**)= 6.0, $\Delta\delta$(**5-4**)= 3.2, and $\Delta\delta$(**8a-7a**)= 2.2 ppm. For C-16 no significant γ-effects are expected and the corresponding ^{13}C signals are found within a very narrow range for all compounds (23.2-23.7 for **4-6** and 22.9-23.1 ppm for the exo-methylene type **7-8a**).

One of the quartets that is always distinctly separated from all others (27.6-28.4, all others below 23 ppm) does not show any significant changes in the chemical shift upon alteration of the stereochemistry in this series (only a very weak acetyl shift may be detected, see table 1). This carbon is attributed to C-26 (equatorial Me). C-25 (axial Me) is sensitive to the configuration of the close OH: β-eq effect (10) $\Delta\delta$(**4-6**)= 7.2 ppm for C-25. In **6** (OH eq) C-25 is found at 15.2 ppm, in all other compounds (all OH ax) at 21.6-22.5 ppm. C-24 (axial Me at the bridge-head) is sensitive to the configuration of CH_2OAr (again a β-eq effect): compare **4**/**5**, **4a**/**5a**, and **7a**/**8a** with corresponding C-24 $\Delta\delta$ of 7.6, 7.4, and 7.1 ppm (see table 1). In **5**, **5a**, **8a** the C-24 resonance is found at 14.2-15.0 ppm, in all other cases at 21.7-22.1 ppm. Further quartets are the olefinic Me in **4-6** (C-23; 22.6-22.8 in **4**, **4a**, and **6**, with CH_2OAr ax; 21.4-21.6 in **5** and **5a** with CH_2OAr eq) and the acetyl Me in acetates **4a**, **5a**, **7a**, and **8a** (21.1-21.2 ppm); both can be identified by relative residual splittings in the off-resonance spectra or by selective ^{13}C [^1H] decoupling.

^1H-NMR

The discussion of the ^1H-nmr spectra will be confined to the newly isolated compounds **2**, **3**, **5**, and **5a** (for all others, see refs. 1, 2).

The spectrum of epoxyfarnochrol (**2**) may be compared with the spectrum of farnochrol (**1**) (1). The epoxidation of the terminal double bond is indicated by characteristic upfield shifts for the protons at C-20, C-21, C-25, and C-26: C-20-H_2 (*ca.* 2.05 ppm in **1**↦*ca.* 1.60 in **2**; C-21-H (5.09↦2.69); C-25-Me/C-26-Me (1.67/1.59 in **1**↦1.29/1.25 ppm in **2**). All other signals are not significantly different for **1** and **2**.

The spectrum of oxofarnochrol (**3**) shows three protons α to CO (CH-CO-CH_2-, 2.53-2.60 ppm). The structure was proved by extensive use of homonuclear decoupling experiments, for instance the characteristic terminal structural element -CH_2^d-CH_2-CO-CH(CH_3^f)$_2$ by irradiation at ^{d} and ^{f} (compare Experimental).

The ^1H-nmr spectra of **5** and **5a** are typical for the drimenol type (1,2). The axial position of the C-21-OH function is indicated by relatively narrow signals of the corresponding equatorial C-21-H [3.48 ppm for **5**, 4.71 ppm for acetyl derivative **5a**, w½=

7 Hz for both, therefore, no *trans-trans* vicinal coupling to C-20-H ax, which would broaden the signal to w½ *ca.* 17-19 Hz, (1)]. The equatorial position of -CH_2OAr is usually indicated by very close AB proton signals of the ABX system >CH-CH_2-OAr (1,2). However, this is not so clear for **5** and **5a**. δ_A and δ_B are well separated [$\Delta\delta_{AB}$=0.07 ppm for **5** and 0.06 ppm for **5a**; compared with 0.02 ppm for **8a** (2) and *ca.* 0.00 ppm for coladonin (12)]. The equatorial configuration of -CH_2OAr could be derived clearly either from ^{13}C data (strong shift of C-24 comparing **5** with **4** or **5a** with **4a**) or by comparison of the lanthanide-induced shifts of **5** with **4**. These data reflect clearly the almost identical geometry of the drimenol unit in both compounds and the different relative configurations of -CH_2OAr (LIS **5**/**4**: C-26-Me eq 3.88/3.61 ppm; C-25-Me ax 1.96/1.85; C-24-Me 1.49/1.54; C-23-Me 0.46/0.62; C-15-H 0.84/0.81; C-10-Me 0.09/−0.25; C-5-H 0.13/−0.43.[3]

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Melting points (uncorrected); Kofler micro-hotstage; optical rotations: Perkin-Elmer 141 polarimeter; ir ($\bar{\nu}$/cm^{-1}): Perkin-Elmer 273 spectrometer; uv [λ max/nm (ε max/1 mol^{-1} cm^{-1})]: Cary-15 spectrometer; ms [*m/z* (relat. Int. %)]: Varian MAT CH-7 ms; nmr (δ/ppm (TMS)]: Brüker WM-250 spectrometer equipped with an 80K Aspect 2000 computer.

Typical nmr parameters used: ^1H: solvent $CDCl_3$, AQ=3.27 s, PW= 1 μs (15°), SW= 2500 Hz. ^{13}C: solvent $CDCl_3$, concentration 4-80 mg/0.5 ml, temp. 303 K, SW= 15 kHz, PW= 6 μs (30°), AQ 1.08 s, NS= 2000- 20 000. Multiplicity assignment was achieved either by SFORD-spectra or *J*-modulated spin-echoes. Pulse sequence: RD − π/2 − τ(DO) − π − τ(BB) − FID. RD= 2.5 s, PW(90°)= 18 μs, τ= 1/*J*= 0.0078 *s* for *J* = 128 Hz. TMS was used as internal standard, and the deuterium resonance of the solvent provided the field frequency lock signal.

PLANT MATERIAL.—Plant material was grown from seeds (received from the Botanical Garden Budapest) under field conditions in the Botanical Garden of the University of Vienna. Voucher specimens (A-1223) are deposited at the herbarium of the Institute of Botany, University of Vienna (WU).

Fresh, air-dried roots (185 g) from *A. ochroleuca* (1) afforded 30 mg of **2**, 11 mg of **3**, 45 mg of **4**, 340 mg of **5**, 20 mg of **5a**, and 25 mg of **6**.

Rf values in Et_2O-petroleum ether (9:1), silica gel 60 F 254 (Merck) were: (**2**) 0.47, (**3**) 0.50, (**4**) 0.32, (**5**) 0.26, (**5a**) 0.41, and (**6**) 0.20.

Epoxyfarnochrol (**2**). 6,8-Dimethoxy-7-(10,11-epoxy-3,7,11-trimethyl-dodeca-2,6,10-trienoxy)-2H-1-benzopyran-2-one; colorless, viscous oil; $[\alpha]^{20}D=-9°$, $[\alpha]^{20}_{436}=-19°$ (c=0.7, acetone); ir (CCl_4): 2960, 2940, 1745, 1560, 1485, 1460, 1420, 1410, 1375, 1345, 1290, 1195, 1150, 1125, 1080, 1040, 980, 840; uv (EtOH): 339 (7 200), 297 (10 200), 226 (23 000, sh), 207 (52 100); ms (70 eV, 100°): 442 (M^+, 0.22%), 223 (52), 222 (100),221 (10), 220 (19), 215 (34), 207 (13), 205 (43), 173 (14), 149 (9), 128 (10), 119 (10), 115 (12), 112 (11), 109 (9), 107 (11), 105 (10), 97 (10), 95 (15), 93 (20), 91 (16); ^1H-nmr ($CDCl_3$): 7.62 (*d*, 1H, C-3-H, *J*=9.5 Hz), 6.66 (s, 1H, C-5-H), 6.33 (d, 1H, C-2-H, *J*=9.5 Hz), 5.54 (t, broad, 1H, C-13-H, *J*=7 Hz), 5.13 (t, very broad, 1H, C-17-H), 4.66 (d, 2H, C-12-H_2-OAr, *J*=7 Hz), 4.02 (s, 3H, OMe11), 3.88 (s, 3H, OMe10), 2.69 (t, 1H, C-21-H, *J*=7 Hz), 2.00-2.12 (m, 6H, 3×>C=Ć-CH_2-), 1.69 (s, broad, 3H, >C=Ć-Me), 1.59 (s, broad, 3H, >C=Ć-Me), 1.55-1.65 (m, 2H, C-20-H_2), 1.29 (s, 3H, Me), 1.25 (s, 3H, Me).

Oxofarnochrol (**3**). 6,8-Dimethoxy-7-(3,7,11-trimethyl-10-oxo-dodeca-2,6,10-trienoxy)-2H-1-benzopyran-2-one; colorless, viscous oil; ir (CCl_4); 2940, 1745, 1720 sh, 1560, 1485, 1460, 1420, 1410, 1385, 1290, 1195, 1150, 1130, 1085, 1045, 1000, 840; uv (EtOH): 338 (7 200), 296 (10 000), 227 (24 200, sh), 206 (52 500); ms (70 eV, 120°): 442 (M^+, 0.2%), 318 (2), 223 (24), 222 (100), 221 (7), 153 (16), 135 (10), 128 (8), 119 (6), 93 (9), 91 (21); ^1H-nmr ($CDCl_3$); 7.62 (d, 1H, C-3-H, *J*=9.5 Hz), 6.66 (s, 1H, C-5-H), 6.35 (d, 1H, C-2-H, *J*=9.5 Hz), 5.56[a] (t, broad, 1H, C-13-H, *J*=7 Hz), 5.09[b] (t, very broad, 1H, C-17-H), 4.68[c] (d, 2H, C-12-H_2-OAr, *J*=7 Hz), 4.04 (s, 3H, OMe11), 3.89 (s, 3H, OMe10), 2.60 (hept, 1H, C-22-H, *J*=7 Hz), 2.53 (t, 2H, C-20-H_2, *J*=7 Hz), 2.22[d] (t, broad, 2H, C-19-H_2), 2.06[e] (pseudo s, very broad, 4H, C-15-H_2+C-16-H_2), 1.69 (s, broad, 3H, Me23), 1.59 (s, broad, 3H, Me24), 1.09[f] (d, 6H, Me25+26, *J*=7 Hz); decoupling: irradiation at[a]: 4.68 (d↦s), 1.69 (broad s↦sharp s);[b]: 1.59 (broad s↦sharp s); [c]: 5.56 (broad t↦broad s); [d]: 2.53 (t↦s); [e]: 5.09 (very broad t↦broad s); [f]: 2.60 (hept↦s).

[3]See Experimental section for **5** and, for a detailed discussion of LIS and the data for **4**, see reference (1).

Isodrimartol A (**5**). (1α,4aβ,6β,8aα)-6,8-Dimethoxy-7[(1,4,4a,5,6,7,8,8a-octahydro-6-hydroxy-2,5,5,8a-tetramethyl-1-naphthalenyl)methoxy]-2H-1-benzopyran-2-one; white crystals (ether), mp: 144-145°. $[\alpha]^{20}D = -32°$, $[\alpha]^{20}436 = -63°$ (c=0.5, acetone); ir (CCl_4): 3640, 2940, 1745, 1560, 1460, 1420, 1410, 1390, 1290, 1190, 1150, 1125, 1085, 1040,, 985, 840; uv (EtOH): 338 (7 900), 296 (10 700), 227 (23 500), 207 (49 200); ms (70 eV, 130°): 442 (M^+, 3%), 223 (27), 222 (100), 221 (26), 220 (8), 204 (14), 203 (75), 187 (9), 161 (17), 149 (27), 147 (25), 135 (14), 133 (31), 123 (10), 121 (17), 119 (23), 109 (26), 107 (19), 105 (18), 95 (26), 93 (16), 91 (13); ^{1}H-nmr ($CDCl_3$): 7.61 (d, 1H, C-3-H, J=9.5 Hz), 6.66 (s, 1H, C-5-H), 6.33 (d, 1H, C-2-H, J=9.5 Hz), 5.54 (pseudo s, broad, C-15-H, w½=9 Hz), 4.22 (dd, 1H, C-12-H, J=10 and 3 Hz), 4.15 (dd, 1H, C-12-H, J=10 and 6 Hz), 3.99 (s, 3H, OMe11), 3.87 (s, 3H, OMe10), 3.48 (pseudo s, broad, C-21-H, w½=7 Hz), 2.31 (pseudo s, broad, C-13-H, w½=14 Hz), 1.95 (s, broad, 3H, Me23), 1.90-2.00 (m, 3H), 1.55-1.75 (m, 5H), 0.98 (s, 3H, Me), 0.94 (s, 3H, Me), 0.90 (s, 3H, Me); ^{1}H-LIS ($CDCl_3$, $Eu(dpm)_3$, extrapolated for $L_o:S_o$=1:1, ppm): C-2-H 0.32, C-3-H 0.09, C-5-H 0.13, C-10-Me 0.09, C-11-Me 0.23, C-12-H_2 0.87 resp. 0.83, C-15-H 0.84, C-23-Me 0.46, C-24-Me 1.49, C-25-Me 1.96, C-26-Me 3.88; ^{13}C-^{1}H couplings: C-1 (dd, 4.6 and 11.1 Hz), C-2 (d, 172.9 Hz), C-3 (dd, 163.7 and 5.6 Hz), C-4 (d, 7.5 Hz), C-5 (dd, 161.8 and 3.7 Hz), C-6 (pseudo t, 2×3.7 Hz), C-7 (d, 8.3 Hz), C-8 (m, unresolved), C-9 (dd, 9.2 and 5.6 Hz); selective ^{13}C [^{1}H] decouplings: irradiated at 7.61 (C-3 d↦s), 6.66 (C-5 d↦s), 6.33 (C-2 d↦s), 3.99 (C-8 m↦sharpened), 3.87 (C-10 q↦s), 1.95 (C-23↦s).

Acetylisodrimartol A (**5a**). (1α,4aβ,6β,8aα)-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; colorless, viscous oil; $[\alpha]^{20}D = -28°$, $[\alpha]^{20}436 = -65°$ (=0.5, acetone); ir (CCl_4): 2940, 1745, 1560, 1460, 1420, 1410, 1390, 1370, 1290, 1245, 1150, 1130, 1085, 1040, 985, 840; uv (EtOH): 339 (7 600), 297 (10 300), 227 (20 100), 207 (45 300); Ms (70 eV, 130°): 484 (M^+, 3%), 263 (4), 223 (25), 222 (99), 204 (17), 203 (100), 187 (9), 161 (15), 153 (10), 147 (24), 135 (17), 133 (32), 128 (38), 123 (8), 121 (15), 119 (24), 109 (21), 107 (20), 105 (17), 95 (25), 93 (18), 91 (64); ^{1}H-NMR ($CDCl_3$): 7.62 (d, 1H, C-3-H, J=9.5 Hz), 6.67 (s, 1H, C-5-H), 6.35 (d, 1H, C-2-H, J=9.5 Hz), 5.55 (pseudo s, broad, 1H, w½=9 Hz, C-15-H), 4.71 (pseudo s, broad, 1H, C-21-H, w½=7 Hz), 4.21 (dd, 1H, C-12-H, J=10 and 3 Hz), 4.15 (dd, 1H, C-12-H, J=10 and 6 Hz), 4.00 (s, 3H, OMe11), 3.87 (s, 3H, OMe10), 2.34[a] (pseudo s, broad, 1H, C-13-H, w½=15 Hz), 2.06 (s, 3H, OCO-Me), 1.95 (s, broad, 3H, Me23), 1.90-2.00 (m, 2H), 1.60-1.80 (m, 5H), 1.00 (s, 3H, Me), 0.93 (s, 3H, Me), 0.90 (s, 3H, Me); [a] irradiated at 2.34: 4.21 (dd↦d), 4.15 (dd↦d).

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