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TYPES OF SESQUITERPENE-COUMARIN ETHERS FROM *ACHILLEA OCHROLEUCA* AND *ARTEMISIA TRIPARTITA**

HARALD GREGER, OTMAR HOFER† and WOLFGANG ROBIEN†

Institute of Botany, University of Vienna, A-1030 Vienna, Austria; † Institute of Organic Chemistry, University of Vienna, A-1090 Vienna, Austria

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Key Word Index—*Achillea ochroleuca*; *Artemisia tripartita*; Compositae; sesquiterpene-coumarin ethers; ^{1}H and ^{13}C NMR; lanthanide induced shifts; chemosystematics.

Abstract—In addition to known derivatives, four new sesquiterpene-coumarin ethers were isolated from the roots of *Achillea ochroleuca* and *Artemisia tripartita* and identified by ^{1}H and ^{13}C NMR spectroscopy, including lanthanide induced shifts. The new compounds are isofraxidin derived ethers which differ from the previously described derivatives by ring cleavage and methyl migration within the terpenoid unit. The chemosystematic importance of sesquiterpene-coumarin ether accumulation within the two genera is briefly discussed.

INTRODUCTION

Although coumarins and sesquiterpenes are widely distributed within the Compositae, the formation of ethers with sesquiterpenes linked to a coumarin skeleton have been reported only for the Anthemideae genera *Artemisia* [1–3], *Achillea* [2, 4] and *Anthemis* [5]. In contrast to the umbelliferone derived sesquiterpene ethers isolated from the umbelliferous genus *Ferula* (see ref. [6]), the coumarin moiety in these genera has proved to be uniformly isofraxidin. Based on a representative survey within *Artemisia* and *Achillea*, it became apparent that the accumulation of these substances is confined to the section *Abrotanum* in the former [7] and to the *Achillea ochroleuca–A. pseudopectinata–A. depressa* complex in the latter. Thus, the distribution of sesquiterpene-coumarin ethers may serve as an additional chemical character within the two genera.

Up to now, 11 different derivatives have been isolated from the roots of various *Artemisia* and *Achillea* species. From these compounds the sesquiterpene moieties have proved to be either open-chain farnesyl or bicyclic drimenyl derivatives [1–4]. Comparative analyses of *Achillea ochroleuca* Ehrh. from different provenances have shown that the composition of the sesquiterpene moieties varies within the species by distinct accumulation tendencies towards different bicyclic drimenyl derivatives [2, 4].

In a continuation of these studies, we have now isolated four new derivatives from *A. ochroleuca* from another provenance (near Vácrátot, Hungary). The new derivatives differ from the previously described compounds by ring cleavage and migration of methyl groups in the terpenoid unit. One of these new derivatives has also been isolated from *Artemisia tripartita* Rydb. belonging to the North American *Tridentatae* group. With respect to the uncertain connections between the *Tridentatae* and other *Artemisia* groups [8], this chemical finding may be of some systematic relevance. The structures of all new compounds were confirmed by ^{1}H and ^{13}C NMR, and mass spectroscopy. Their relative stereochemistries were determined by ^{1}H NMR in connection with lanthanide induced shifts.

RESULTS AND DISCUSSION

The petrol–ether extracts of the roots of *A. ochroleuca* and *A. tripartita* afforded seven different isofraxidin sesquiterpene ethers. Compounds **3**–**6** proved to be new, whereas the structures and relative stereochemistry of farnochrol (**1**), epoxyfarnochrol (**2**) and drimartol B (**7**) had already been elucidated [2, 4].

A. tripartita afforded the new bicyclic sesquiterpene ether **4**, which we have named tripartol and, as minor constituents, the open-chain derivatives farnochrol (**1**) and epoxyfarnochrol (**2**). In addition, the rather widespread coumarins scopoletin (7-hydroxy-6-methoxycoumarin) and isofraxidin (7-hydroxy-6,8-dimethoxycoumarin) were also isolated.

From *A. ochroleuca*, we isolated **3** and **6** as major components, both of which have a monocyclic sesquiterpene moiety. Compound **3**, which we have named secodrial, proved to be the aldehyde of the corresponding alcohol **6** (secodriol). Apart from the different coumarinyl (isofraxidin) unit, the structure and stereochemistry of secodriol (**6**) has been found to be identical with the umbelliferone derived fekrinol [9]. The same relative configuration has also been reported for the corresponding galbanic acid [10]. Furthermore, farnochrol (**1**), tripartol (**4**) and drimartol B (**7**) were also found together with the new bicyclic derivative **5**, designated as drimachone.

It should be pointed out that all four new compounds belong to a new isofraxidin derived series characterized by methyl migration within the terpenoid derived unit. Starting from the drimenol skeleton (e.g. in **7**) in **3** and **6**, the axial C-8a methyl migrates to the C-1-ax position. In addition, the C-5–C-6 bond opens up resulting in a

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*Part 4 in the series "Naturally Occurring Sesquiterpene-Coumarin Ethers".

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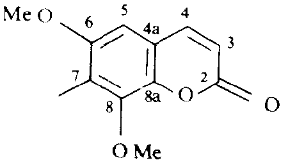

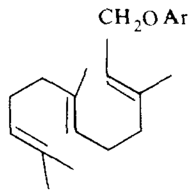

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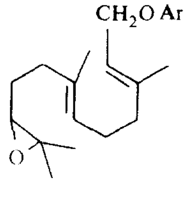

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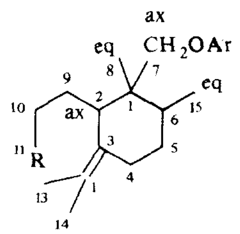
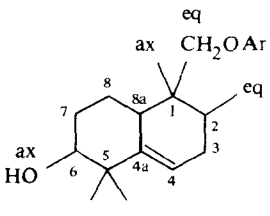


3 R = CHO
6 R = CH$_2$OH



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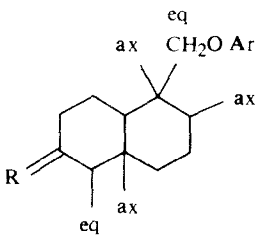
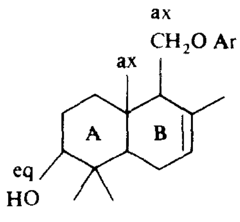


5 R = O
8 R = H, OH (ax)



7

$-CH_2-CH_2-CH_2OH$ side chain and an isopropylidene group attached to the former B-ring. This remaining cyclohexane ring adopts (by ring flipping and, thereby, changing all relative configurations of the substituents) a conformation with $-CH_2-CH_2-CH_2OH$ axial (necessarily equatorial in the original *trans* decalin system), C-1 methyl equatorial (originally C-1 methyl axial after the migration from C-8a methyl axial) C-1 CH_2OAr axial and C-6 methyl equatorial. In **4**, the axial methyl at C-8a has moved to C-1 ax and the double bond is found at the rather unusual C-4–C-4a position. In **5**, both axial methyl groups have moved to neighbouring axial positions: C-8a Me axial → C-1 Me axial and C-5 Me axial → C-4a Me axial.

In the following sections, the structure elucidation for **3**–**6** is outlined. The results prove the above discussed relative configurations and prove unambiguously the methyl *trans–trans* migration (cf. refs. [11–13] concerning methyl migration in the case of kamolone).

The ^{1}H NMR data for the isofraxidin part of the compounds under investigation are almost identical in all respects. The ^{13}C NMR spectral assignments have already been extensively discussed in a previous report [4]. The other ^{13}C NMR assignments of the sesquiterpene part listed in Tables 1 and 2 are based on the multiplicities in the off resonance spectra, on ^{13}C lanthanide induced shifts and selective ^{13}C $\{^1H\}$ double resonance. For assignment of ^{1}H resonances ^{1}H lanthanide induced shifts and proton decoupling were used (Tables 1 and 2).

Secodrial **3** *and secodriol* **6**

The ^{1}H and ^{13}C NMR spectra of **3** and **6** are very similar except for the characteristic signals for the different functional groups. Compound **3**: aldehyde hydrogen at δ 9.75, α-CH_2 at 2.31 (2H, *t*), aldehyde carbon at 202.8, α-carbon at 42.2. Compound **6**: $C\underline{H}_2OH$ at δ 3.65 (2H, *t*), the corresponding carbon at 63.6 (see Table 1). Chemical evidence shows clearly that **3** and **6** differ only in the functional groups at C-11. Thus, aldehyde **3** may be reduced to alcohol **6** giving a product identical with natural **6** (TLC, ^{1}H NMR, optical rotation). Consequently, the results proving the structure of secodriol **6** are also valid for secodrial **3**.

A new feature in the ^{1}H NMR spectra of the sesquiterpene ethers of the current series [2–4] is the simple AB system for $-CH_2OAr$ (δ 4.13 and 3.84, $J = 9.5$ Hz; in $CDCl_3$ the signal at 3.84 is covered by OMe; in C_6D_6 a clear AB may be observed: δ 4.27 and 3.97, $J = 9.5$ Hz). In the typical drimenol type sesquiterpene isofraxidin ethers (e.g. **7**) this is an ABX system [1–4]. In **6** there must obviously be a substituent geminal to $-CH_2OAr$ at C-1 (→ methyl migration). The triplet of 2H at δ 3.65 (3.43 in C_6D_6, see Table 1) indicates a $-CH_2-CH_2OH$ moiety which should belong to an open side chain. This is supported by ^{1}H lanthanide induced shift measurements giving decreasing values of δ 24.4, 10.4 ± 0.2 (Table 1) and 7.8 for three methylene units typical for $-CH_2-CH_2-CH_2OH$ [14]. In the ^{13}C NMR spectra an ad-

Table 1. NMR data for secodrial (3) and secodriol (6) (250 MHz, TMS as int. standard, lanthanide induced shifts extrapolated to L_0–S_0 = 1:1)

Carbon Nos.	Proton(s)	^{1}H NMR 3 (CDCl$_3$)	^{13}C NMR 3 (CDCl$_3$)	^{1}H NMR 6 (CDCl$_3$)	^{1}H NMR 6 (C$_6$D$_6$)	^{13}C NMR 6 (CDCl$_3$)	^{1}H LIS 6 (CDCl$_3$)	^{13}C LIS 6 (CDCl$_3$)
Isofraxidin								
2	—	—	160.4 *s*	—	—	160.6 *s*	—	0.95 §
3	H	6.33 *d*	114.7 *d*	6.31 *d*	5.95 *d*	114.7 *d*	0.61 §	0.75 §
4	H	7.61 *d*	143.3 *d*	7.60 *d*	6.59 *d*	143.5 *d*	0.36	0.65 §
4a	—	—	113.8 *s*	—	—	113.8 *s*	—	0.76
5	H	6.66 *s*	104.2 *d*	6.65 *s*	5.94 *s*	104.4 *d*	0.46	0.34
6	—	—	150.2 *s*	—	—	150.4 *s*	—	0.81
7	—	—	146.6 *s*	—	—	146.9 *s*	—	0.86
8	—	—	141.0 *s*	—	—	141.1 *s*	—	0.89
8a	—	—	143.0 *s*	—	—	143.7 *s*	—	0.89
(6)	OMe	3.86 *s*	56.2 *q*	3.85 *s*	3.27 *s*	56.3 *q*	0.51	0.50
(8)	OMe	3.98 *s*	61.7 *q*	3.97 *s*	3.75 *s*	61.8 *q*	0.64	0.76
Sesquiterpene								
1	—	—	41.5 *s*	—	—	41.6 *s*	—	2.06
2	Heq	2.96 *br t*	43.2 *d*	2.93 br t*	3.05 *dd*	43.7 *d*‡	3.81	3.87
3	—	—	130.1 *s*	—	—	131.1 *s*	—	2.71
4	Hax	1.85–1.95 *m*	24.8 *t*	1.88 *ddd*†	1.89 *ddd*	24.9 *t*‡	3.17	2.20
—	Heq	2.52 *ddd*	—	2.52 *ddd*†	2.51 *ddd*	—	1.61	—
5	Hax	1.16 *dddd*	31.7 *t*	1.15 *dddd*†	1.21 *dddd*	32.0 *t*	1.23	1.36
—	Heq	1.60 *m*	—	1.40–1.65 *dddd*†	1.20–1.50 *m*	—	1.12	—
6	Hax	1.85–1.95 *m*	35.1 *d*	1.84 *m*	1.57 *m*	35.3 *d*	2.20	1.60
7	H′	4.13 *d*	77.6 *t*	4.13 *d*	4.27 *d*	78.0 *t*	1.44	1.36
—	H″	3.83 *d*	—	3.84 *d*	3.97 *d*	—	1.17	—
8	H$_3$	1.26 *s*	22.3 *q*	1.21 *s*	1.35 *s*	22.3 *q*‡	1.96	2.05
9	H$_2$	1.85–1.95 *m*	19.9 *t*	1.40–1.65 *m*	1.20–1.50 *m*	23.5 *t*	7.80	7.04
10	H$_2$	2.31 *br t*	42.2 *t*	1.40–1.65 *m*	1.20–1.50 *m*	31.1 *t*	10.6/10.2‖	9.80
11	H/H$_2$	9.75 *br s*	202.8 *d*	3.65 *t*	3.43 *t*	63.6 *t*‡	24.40	38.80
12	—	—	126.1 *s*	—	—	124.7 *s*	—	2.54
13	H$_3$	1.65 *br s*	20.5 *q*	1.64 *br s*	1.76 *br s*	20.6 *q*‡	2.07	2.11
14	H$_3$	1.72 *br s*	20.3 *q*	1.69 *br s*	1.71 *br s*	20.4 *q*‡	1.20	1.43
15	H$_3$	0.91 *d*	16.0 *q*	0.90 *d*	0.94 *d*	16.2 *q*‡	0.77	0.87

J (Hz), compound **6**: isofraxidine 3,4 = 9.5; sesquiterpene 2,9 = 7 (in CDCl$_3$, 11 and 4.5 in C$_6$D$_6$); 4ax,4eq = 15; 4ax,5ax = 14; 4ax,5eq = 3; 4eq,5ax = 3; 4eq,5eq = 3; 5ax,5eq = 15; 5ax,6ax = 14; 5eq,6ax = 3; 6ax,15 = 7; 7H′,7H″ = 9.5; 10,11 = 7.

NOE-difference experiments: irradiation at 2.93 (H-2), effect at 3.84 (H″-7) and 1.64 (Me-13); irradiation at 2.52 (H-4eq), effect at 1.69 (Me-14); irradiation at 0.90 (Me-15), effect at 4.13 (H′-7).

*Changes from a *br t* (7 Hz) to a *dd* (11 and 4 Hz) in the Eu(dpm)$_3$ complex.

†Coupling constants are taken from Eu(dpm)$_3$ shifted spectra.

‡Assigned by selective ^{13}C {^{1}H} decoupling.

§Extrapolated from very low concentrations (L_0–S_0 = 0.0–0.1:1) since at higher concentrations some complex formation takes place at the carbonyl oxygen of isofraxidine C-2.

‖Diastereotopic protons separated.

Table 2. NMR data for tripartol (4) (250 MHz, TMS as int. standard, LIS values extrapolated to L_0–S_0 = 1:1)

Carbon Nos.	Proton(s)	^{1}H NMR (CDCl$_3$)	^{1}H NMR (C$_6$H$_6$)	^{13}C NMR (CDCl$_3$)	^{1}H LIS (CDCl$_3$)	^{13}C LIS (CDCl$_3$)
Isofraxidin						
2	—	—	—	160.5 *s*	—	0.73
3	H	6.34 *d*	5.95 *d*	115.1 *d*	0.25	0.59
4	H	7.60 *d*	6.59 *d*	143.4 *d*	0.24	0.45
4a	—	—	—	114.3 *s*	—	0.50
5	H	6.65 *s*	5.95 *s*	104.2 *d*	0.34	0.50
6	—	—	—	150.6 *s*	—	0.68
7	—	—	—	146.4 *s*	—	1.58
8	—	—	—	141.8 *s*	—	0.71
8a	—	—	—	143.3 *s*	—	0.53
(6)	OMe	3.85 *s*	3.26 *s*	56.3 *q*	0.43	0.54
(8)	OMe	3.99 *s*	3.73 *s*	61.9 *q*	0.46	0.60
Sesquiterpene						
1	—	—	—	38.7 *s*	—	1.96
2	Hax	1.83 *m**	††	32.1 *d*	1.45	1.57
3	Hax	1.71 *ddd*†,‡	††	31.5 *t*	1.07	1.85
—	Heq	2.15 *ddd* §	2.02 *ddd*	—	1.02	—
4	H	5.49 *br t*	5.41 *br t*	119.9 *d*	2.53	4.10
4a	—	—	—	142.6 *s*	—	3.96
5	—	—	—	42.2 *s*	—	4.55
6	H	3.47 *br s*‖	3.38 *br t*	76.7 *d*	8.20	19.00
7	Hax	1.96 *dddd*‡,¶	††	29.3 *t*	3.00	7.90
—	Heq	1.60–1.75 *m*	††	—	4.70	—
8	Hax	1.47 *dddd***	††	23.0 *t*	4.20	4.90
—	Heq	1.60–1.75 *m*	††	—	2.23	—
8a	Hax	2.51 *dd*	2.48 *dd*	38.0 *d*	2.35	4.00
(1)	Meax	1.19 *s*	‡‡	20.6 *q*	0.95	1.40
(1)	CH$_2$eq	4.01 *d*	4.07 *d*	78.4 *t*	0.92	1.25
		3.87 *d*	3.92 *d*	—	1.18	—
(2)	Meeq	0.97 *d*	0.98 *d*	15.2 *q*	0.58	0.85
(5)	Meax	1.11 *s*	‡‡	26.2 *q*	2.03	2.51
(5)	Meeq	1.11 *s*	‡‡	24.8 *q*	3.80	5.88

J (Hz): isofraxidine 3,4 = 9.5; sesquiterpene (C-1)CH$_2$(*gem*) = 9.5; 2,(2)Me = 7; 2,3ax = 10; 2,3eq = 3.5; 3ax,3eq = 17.5; 3ax,4 = 3; 3eq,4 = 4.5; 6,7ax = 5; 6,7eq = 4; 7ax,7eq = 15; 7ax,8ax = 14; 7ax,8eq = 4; 7eq,8ax = 4; 8ax,8a ax = 14; 8eq,8a ax = 2; 8ax,8eq = 15.

*Irradiation at Me-2: *dd* (14/4.5 Hz).

†Irradiation at H-4: sharpening.

‡Coupling constants are determined from Eu(dpm)$_3$ shifted spectra.

§Irradiation at H-4: *dd* (17.5/3.5).

‖Pseudo-s with $W_{1/2}$ = 7 Hz.

¶Irradiation at H-6: *ddd* (15/14/4).

**Irradiation at H-8a: *ddd* (15/14/4).

††Overlapping signals: 2.65–2.85 (4H), 1.45–1.55 (2H), *ca* 1.35 (1H).

‡‡Methyl signals (*s*) at δ 1.27, 1.11, 1.02.

ditional double bond is indicated in the carbon *sp*^{2} region with two singlets at δ 124.7 and 131.1. In the ^{1}H NMR spectra two olefinic methyl signals are found proving the presence of a $>C{=}C(Me)_2$ moiety. Therefore, **6** should be a monocyclic compound where the bridge-head methyl group has moved to C-1 and the bond between the oxidized carbon (C-6) and the quaternary (C-5) carbon positions is opened. This is in agreement with the molecular mass of 444 which is 2 mass units higher than that of all previously isolated bicyclic sesquiterpene isofraxidin ethers which have one double bond and a hydroxyl group as well. In the Eu(dpm)$_3$ shifted ^{1}H NMR spectra, all cyclohexane protons may be observed clearly and all coupling constants may be determined (see Table 1). The *dddd* of the axial hydrogen at C-5 with three large (1 *gem*, 2 *vic*) and one small coupling indicates that H-6 is axial and consequently, the C-6 methyl is equatorial. The H-6-ax proton is less suited to decide the relative stereochemistry at C-6 since it appears as a broad multiplet (*ddq*). The relative configurations at C-1 (–Me, –CH$_2$OAr) and C-6 (–H, –CH$_2$–CH$_2$–CH$_2$OH) cannot be determined by means of the coupling constants since no relevant vicinal ring proton couplings are available. However, a lanthanide induced shift calculation [16–18] was successful. The coordinating site is, at low reagent concentrations only, the primary side chain hydroxyl group. It is very interesting to note that the H-2 signal turns from a broad triplet (J = 7 Hz) in the free substrate to a clear double doublet with J = 11 and 4.5 Hz in the Eu(dpm)$_3$ complex. To allow an optimal co-ordination of the space consuming reagent a distinct favoured conformation is adopted in the complex, resulting in an H–H *transoid* and H–H *cisoid* vicinal coupling*. The side chain may, therefore, be attached at C-2 in four different geometries resulting from the combination of two different relative configurations (axial or equatorial) in two different possible conformations (possessing one H–H *transoid* (*anti*) and one H–H *cisoid* (*gauche*) arrangement in the staggered conformations obtainable by rotation about the C-2–C-9 bond). For the cyclohexane ring and the open side chain, standard bond lengths and standard bond angles were assumed in staggered conformations using the model building program COORD [15]. Only a calculation of lanthanide induced shifts using the geometry with $-CH_2-CH_2-CH_2OH$ axial, in the particular conformation shown in Fig. 1 (H^x–H^a *anti*, H^x–H^b *gauche*) agrees well with the experimental lanthanide induced shift data of all ring protons and methyl signals (average difference between calculated and observed LIS values < 5%). In the next step of the lanthanide induced shift evaluation the calculated optimal Eu(III) position may be used to compute expected values for C-1 methyl protons according to axial with respect to equatorial positions (in staggered conformations). The 'expected values' were: 1.56, 1.44 and 1.17 for the three axial methyl protons and 2.00, 1.40 and 2.39 for the equatorial methyl protons. The experimental value of 1.96 for the C-8 methyl group correlates perfectly with the value for the equatorial methyl (averaged value of all three proton positions 1.93). The experimental values of δ 1.46 and 1.20 for the C-1 $\underline{CH_2}OAr$ protons correlate very well with two of the remaining values for axial proton positions (1.44 for H′-7 and 1.17 for H″), the third one is occupied by –OAr [inspection of Dreiding models show that this conformation offers most space for the large –OAr group (see Fig. 1)]. The NOE difference measurements do not give either unambiguous results concerning the relative configurations at C-1, C-2 and C-6, or the necessary information on the possible conformations about the C-2–C-9 and C-1–C-7 bonds. They are, however, fully compatible with the lanthanide induced shifts outlined above (Table 1). Of particular interest is the response of one H-7 to irradiation at the C-15 methyl group and of the other one to irradiation at H-2 (H^x in **6**). The former corresponds to proton H″-7 the latter to H′-7 in Fig. 1 which agrees nicely with the lanthanide induced shift assignments with respect to configuration and conformation as well.

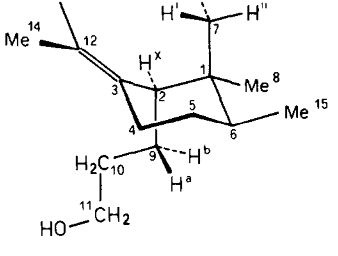


Fig. 1. Stereoformula of **6**.

Tripartol 4

The ^{1}H NMR spectrum of this compound shows a broad signal at δ 3.47 (CDCl$_3$), $W_{1/2}$ = 7 Hz, which is characteristic for drimenol derivatives with an axial hydroxyl group (the corresponding geminal equatorial proton does not exhibit a *trans*-ax–ax-coupling which would result in $W_{1/2} \simeq$ 17–19 Hz [2]). The $-CH_2OAr$ protons are represented by a geminal AB system (covered partially by a methoxyl group in deuterochloroform, clear in deuterobenzene) with no vicinal neighbour protons; again the C-8a methyl has migrated to the C-1 position. There is one double bond of the $-CH=C<$ type which may be seen clearly from the ^{1}H and off resonance ^{13}C NMR spectra (see Table 2). This agrees with a molecular mass of 442 which is consistent with a bicyclic terpenic unit with a hydroxyl group and one double bond. Addition of Eu(dpm)$_3$ allowed further decisions on the stereochemistry of **4**: (a) two geminal methyl groups next to the axial hydroxyl (Me-eq with a very large lanthanide induced shift, Me-ax still large, see Table 2); (b) the $-CH_2OAr$ moiety at C-1 is equatorial (no negative lanthanide induced shifts for isofraxidin resonances, see ref. [2]), the C-1 methyl is, therefore, axial; (c) the C-2 methyl is equatorial (H-2ax) since the H-3-ax (*ddd*) shows a coupling of 17.5 Hz (geminal), 10 Hz (ax–ax-*trans*-vicinal) and 3 Hz (to the vinylic H-4). These couplings are obscured by other resonances in the original spectrum, but are very clear in the Eu(dpm)$_3$ shifted ones. The position of the double bond is confirmed by ^{1}H–^{1}H decoupling as well. In principle a C-4=C-4a (B-ring) or C-8=C-8a (A-ring) double bond would be possible. In the latter case irradiation of the olefinic proton and H-6 should affect the same protons (at C-7). However, this is not the case (Table 2). Irradiation of the vinylic proton affects protons of the B-ring which is proved by the relatively small lanthanide induced shift values for these protons (H-3ax, eq, lanthanide induced shifts of 1.07 and 1.02, B-ring). Irradiation of H-6 affects a different proton (H-7ax, lanthanide induced shift of 3.00, A-ring; H-7eq is obscured by other resonances). The *trans*-decalin structure of the sesquiterpene unit is proved by the axial bridge-head proton (H-8a-ax shows an ax–ax vicinal coupling of 14 Hz). The chemical shift of this proton is at a very low field (δ 2.51 in deuterochloroform, 2.48 in deuterobenzene) because C-8a is a tertiary carbon next to a double bond.

Drimachone 5

The ^{13}C NMR spectrum indicates that **5** is a ketone (C=O at δ 212.3). In the ^{1}H NMR, a group of three protons is found at δ 2.4–2.35 (Hα to C=O). There is no double bond in the terpene unit. The molecular mass of 442 indicates a bicyclic sesquiterpene isofraxidin ether. The bridge-head proton at δ 2.06 (CDCl$_3$) is axial (*dd*, *J*

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*This conformational change is even sensitive to solvatation with aromatics. So in deuterobenzene the H-2 signal appears as a double doublet as well.

= 15, 3 Hz) proving the *trans*-decalin structure of the terpene unit. The $-CH_2OAr$ protons are represented by a very narrow AB system without any further coupling, allowing the conclusion that the C-8a methyl (of the usual drimenol derivatives) has moved to C-1. The ^1H NMR spectrum of **5** shows two methyl signals with doublet structure: one belongs to the usual C-2 methyl, the other to a C-5 methyl, the usual second (geminal) C-5 methyl has moved to C-4a. Decoupling by irradiation at the resonance of the C-2 methyl produces a double doublet for H-2 with coupling constants of 5 and 2 Hz. H-2 is obviously equatorial, the corresponding C-2 methyl is, therefore, axial. Irradiation at the C-5 methyl gives a sharp singlet for H-5 which is indicative for this proton between the carbonyl carbon and the quaternary bridge-head (C-4a) carbon. The lack of relevant ring coupling does not allow any information concerning the axial or equatorial position of the C-5 methyl. However, the relative configuration at C-5 and C-1 is established by the lanthanide induced shifts of the alcohol obtained by sodium borohydride reduction of **5**. The reduction product, **8**, has an axial hydroxyl (proved as usual [1–4] by the $W_{1/2}$ value of the H-6 resonance which is 8 Hz for **8**). The lanthanide induced shift for C-5 Me is δ 3.75, a rather large value which is only possible for an equatorial C-5 methyl (methyl group gauche to a hydroxyl; compare the lanthanide induced shifts for both C-5 methyl signals for **4**: 3.80 for the equatorial one; 2.03 for the axial). The lanthanide induced shifts for the isofraxidin moiety are characteristic for an equatorial C-1 CH_2OAr (no negative lanthanide induced shift see Experimental, compare refs. [2, 4]); C-1 methyl is, therefore, axial.

EXPERIMENTAL

Mps (uncorr.): Kofler micro-hotstage; MS: Varian MAT CH-7 mass spectrometer; NMR: Bruker WM-250 spectrometer equipped with an 80K Aspect 2000 computer (for typical NMR parameters see ref. [4]).

Plant material. Achillea ochroleuca, collected near Vácrátot, Hungary (A. Borhidi, 21/10/1981). *Artemisia tripartita* (AR-993), grown from achenes received from Wyoming, Albany County, U.S.A. (R. L. Hartman). Voucher specimens are deposited at the Herbarium of the Institute of Botany, University of Vienna (WU).

Fresh air-dried roots (*A. ochroleuca*, 55 g; *A. tripartita*, 40 g) were separately cut into small pieces and extracted with petrol (60–80°)–Et_2O for 2 days at room temp. The concd extract was roughly fractionated on a Si gel column with petrol–Et_2O (Et_2O increasing from 0 to 100 %) followed by Et_2O–MeOH (MeOH increasing from 3 to 10 %). The Et_2O and Et_2O–MeOH fractions containing the coumarin derivatives were further separated by TLC on 1 mm thick layers of Si gel GF 254 (Merck) using Et_2O–petrol (4:1) or CH_2Cl_2–EtOH (98.5.1.5) as solvents.

A. ochroleuca afforded 45 mg farnochrol (**1**), 70 mg secodrial (**3**), 23 mg tripartol (**4**), 10 mg drimachone (**5**), 55 mg secodriol (**6**) and 7 mg drimartol B (**7**). *A. tripartita* afforded traces (< 1 mg) of farnochrol (**1**), 1 mg epoxyfarnochrol (**2**), 5 mg tripartol (**4**), 2 mg scopoletin and 4 mg isofraxidin.

R_f values in Et_2O–petrol (9:1), Si gel 60 F 254 (Merck): **1** (0.60), **2** (0.47), **3** (0.50), **4** (0.39), **5** (0.36), **6** (0.34), **7** (0.20).

Secodrial (**3**) (1′*ax*, trans-2′, cis-6′)-6,8-*dimethoxy*-7-[(2′-*formylethyl-3′-isopropyliden*-1′,6′-*dimethylcyclohexyl*)*methoxy*]-2H-1-*benzopyran*-2-*one*. Colourless viscous oil: $[\alpha]_D^{20} = -11°$, $[\alpha]_{436}^{20} = -48°$ (Me_2CO; *c* 1); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2920, 1740 (*br*), 1565, 1490, 1460, 1425, 1410, 1290, 1270, 1230, 1195, 1150, 1125, 1085, 1045, 985, 840; UV λ_{max}^{EtOH} nm (ε): 340 (7800), 298 (9200), 227 (20 100), 207 (43 000); MS (70 eV, 140°) *m/z* (rel. int.): 442 $[M]^+$ (6.9), 223 (21), 222 (100, isofraxidin), 221 (15), 220 (16), 205 (35), 203 (26), 177 (13), 163 (14), 149 (21), 147 (18), 135 (18), 133 (24), 123 (19), 121 (32), 119 (28), 111 (14), 109 (34), 107 (30), 105 (25), 97 (23), 95 (48), 93 (26), 91 (23).

Tripartol (**4**) (1α,2β,6β,8aα)-6,8-*dimethoxy*-7-[(1,2,3,5,6,7,8,8*a*-*octahydro*-6-*hydroxy* -1, 2, 5, 5-*tetramethyl*-1-*napthalenyl*)*methoxy*]-1H-1-*benzopyran*-2-*one*. Colourless crystals from Et_2O, mp 167–169°; $[\alpha]_D^{20} = -36°$, $[\alpha]_{436}^{20} = -67°$ (Me_2CO; *c* 0.4); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3630, 3575, 2940, 1745, 1560, 1460, 1425, 1410, 1390, 1290, 1270, 1200, 1150, 1125, 1085, 1050, 990, 840; UV λ_{max}^{EtOH} nm (ε): 339 (7800), 295 (10 000), 227 (20 500), 207 (44 500); MS (70 eV, 100°) *m/z* (rel. int.): 442 $[M]^+$ (2.3), 223 (20), 222 (75), 221 (37), 220 (14), 204 (17), 203 (100), 177 (10), 173 (9), 161 (26), 159 (9), 149 (16), 147 (38), 145 (12), 135 (18), 134 (12), 133 (54), 131 (11), 123 (18), 121 (44), 120 (11), 119 (59), 111 (12), 109 (25), 107 (31), 105 (24), 97 (21), 95 (39), 93 (21), 91 (18).

Drimachone (**5**) (1α,2α,4aβ,5β,8aα)-6,8-*dimethoxy*-7-[(*decahydro*-1,2,4*a*,5-*tetramethyl*-6-*oxo*-1-*naphthalenyl*)*methoxy*]-2H-1-*benzopyran*-2-*one*. Colourless crystals from Et_2O, mp 164–165°; $[\alpha]_D^{20} = -38°$, $[\alpha]_{436}^{20} = -90°$ (Me_2CO; *c* 0.3); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2930, 1745, 1715, 1560, 1455, 1420, 1405, 1385, 1290, 1190, 1150, 1125, 1085, 1040, 990, 840; UV λ_{max}^{EtOH} nm (ε): 337 (7450), 295 (10 100), 227 (19 500), 208 (41 300); MS (70 eV, 120°) *m/z* (rel. int.): 442 $[M]^+$ (2.4), 223 (14), 222 (100), 109 (4), 95 (5); ^1H NMR ($CDCl_3$): δ 7.62 (*d*, *J* = 9.5 Hz, isofraxidine H-4), 6.68 (*s*, isofraxidine H-5), 6.36 (*d*, *J* = 9.5 Hz, isofraxidine H-3), 4.00 (3H, *s*, isofraxidine OMe-8), 3.90 (1H, *d*, *J* = 8 Hz, CH_2O-1), 3.87 (3H, *s*, isofraxidine OMe-6), 3.86 (1H, *d*, *J* = 8 Hz, CH_2O-1), 2.40–2.35 (2H, *m*, H-7ax and H-7eq), 2.33 (*q*, *J* = 7 Hz, H-5), 2.06 (*dd*, *J* = 15, 3 Hz, H-8a), 1.9–2.0 (2H, *m*), 1.79 (*dddd*, *J* = 14, 14, 14, 6 Hz, H-8ax), 1.60–1.65 (2H, *m*), 1.4–1.5 (2H, *m*), 1.25 (3H, *d*, *J* = 7 Hz, Me-2), 1.18 (3H, *s*, Me-1), 0.94 (3H, *d*, *J* = 7 Hz, Me-5), 0.83 (3H, *s*, Me-4a); ^1H NMR (C_6D_6): δ 6.63 (*d*, *J* = 9.5 Hz, isofraxidine H-4), 6.00 (*s*, isofraxidine H-5), 5.97 (*d*, *J* = 9.5 Hz, isofraxidine H-3), 3.81 (1H, *d*, *J* = 8 Hz, CH_2O-1), 3.75 (1H, *d*, *J* = 8 Hz, CH_2O-1), 3.73 (3H, *s*, isofraxidine OMe-8), 3.28 (3H, *s*, isofraxidine OMe-6), 2.33 (*ddd*, *J* = 14, 5, 2.5 Hz, H-7eq), 1.97 (*m*, *dd* upon irradiation at 1.29, *J* = 5, 2 Hz, H-2eq), 1.94 (*m*, H-7ax), 1.91 (*q*, *s* upon irradiation at 0.98, *J* = 7 Hz, H-5), 1.77 (*dd*, *J* = 15, 3 Hz, H-8a), 1.51 (1H, *m*), 1.2–1.4 (5H, *m*), 1.29 (3H, *d*, *J* = 7 Hz, Me-2), 1.10 (3H, *s*, Me-1), 0.98 (3H, *d*, *J* = 7 Hz, Me-5), 0.68 (3H, *s*, Me-4a); ^{13}C NMR ($CDCl_3$): δ 212.3 (*s*), 160.3 (*s*), 150.5 (*s*), 146.0 (*s*), 143.5 (*s*), 143.3 (*d*), 141.6 (*s*), 115.2 (*d*), 114.4 (*s*), 104.3 (*d*), 81.9 (*t*), 62.0 (*q*), 58.4 (*d*), 56.4 (*q*), 44.2 (*d*), 41.7 (*s*), 41.6 (*t*), 40.4 (*s*), 35.9 (*d*), 32.6 (*t*), 25.7 (*t*), 23.6 (*t*), 19.7 (*q*, Me-1), 14.7 (*q*, Me-4a), 14.5 (*q*, Me-2), 6.9 (*q*, Me-5), the Me groups are correlated with the corresponding ^1H-Me resonances by means of selective $^{13}C\{^1H\}$ double resonance.

Reduction of **5** *to* (1α,2α,4aβ,5β,6β,8aα)-6,8-*dimethoxy*-7-[(*decahydro*-6-*hydroxy*-1,2,4a,5-*tetramethyl*-1-*naphthalenyl*) *methoxy*]-2H-1-*benzopyran*-2-*one* (**8**). Compound **5** (5 mg) in 1 ml MeOH was treated with 5 mg $NaBH_4$ for 5 min at room temp. Then H_2O, dilute HCl, and Et_2O were added, the Et_2O layer was washed with H_2O, dried over Na_2SO_4 and evaporated. TLC of the crude product gave 3.5 mg **8**. Colourless viscous oil, $[\alpha]_D^{20} = +26°$, $[\alpha]_{436}^{20} = +68°$ (Me_2CO; *c* 0.3); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3640, (OH), 1745 (isofraxidine C=O); UV λ_{max}^{EtOH} nm (ε): 335 (7500), 293 (10 200), 225 (25 500), 206 (49 500); MS [70 eV, 100° *m/z* (rel. int.)]: 444 $[M]^+$ (1), 222 (100, isofraxidin); ^1H NMR ($CDCl_3$): δ (LIS in δ-values, extrapolated to L_0–S_0 = 1:1) 7.61 (*d*, *J* = 9.5 Hz, isofraxidin H-4, LIS = 0.12), 6.66 (*s*, isofr. H-5, LIS = 0.18), 6.34 (*d*, *J* = 9.5, Hz, isofr. H-3, LIS = 0.27), 3.99 (3H, *s*, isofraxidin OMe-8, LIS = 0.33), 3.86 (3H, *s*, isofraxidin OMe-6, LIS = 0.21), 3.86 (1H, *d*, $J = 8.5$ Hz, CH_2O-1, LIS = 1.00), 3.79 (1H, *d*, $J = 8.5$ Hz, CH_2O-1, LIS = 0.94), 3.77 (*m*, $W_{1/2} = 8$ Hz, H-6, LIS = 9.1), 1.85–2.02 (3H, *m*), 1.57–1.70 (4H, *m*), 1.25–1.45 (5H, *m*), 1.19 (3H, *s*, Me-1, LIS = 1.02), 1.18 (3H, *d*, $J = 7$ Hz, Me-2, LIS = 0.90), 1.08 (3H, *s*, Me-4a, LIS = 3.75), 0.97 (3H, *d*, $J = 7$ Hz, Me-5, LIS = 3.75).

Secodriol (**6**) (1′*ax*, trans-2′, cis-6′)-6,8-*dimethoxy*-7-[(3′-*hydroxypropyl*-3′-*isopropyliden*-1′, 6′-*dimethylcyclohexyl*)*methoxy*]-2H-1-*benzopyran*-2-*one*. Colourless viscous oil; $[\alpha]_D^{20} = -14°$, $[\alpha]_{436}^{20} = -58°$ (Me_2CO; *c* 0.6); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3640, 2920, 1745, 1560, 1460, 1425, 1410, 1290, 1270, 1195, 1150, 1125, 1085, 1045, 985, 835; UV λ_{max}^{EtOH} nm (ε): 340 (7600), 297 (8900), 226 (19 000, sh), 207 (42 600); MS [70 eV, 100°, *m/z* (rel. int.)]: 444 $[M]^+$ (4.2), 223 (25), 222 (100, isofraxidin), 205 (7), 179 (7), 163 (16), 149 (17), 137 (11), 135 (14), 123 (25), 121 (22), 111 (11), 109 (38), 107 (28), 105 (12), 97 (21), 95 (42), 93 (24), 91 (14).

By the same procedure, **6** was obtained from secodrial (**3**). The reduction product was shown to be identical with natural **6** by TLC, NMR and $[\alpha]_D$.

Lanthanide induced shifts and their calculation for **6**. For determination of the LIS values, increasing amounts of Eu(dpm)$_3$ [tris-(dipivalomethanato)-europium(III), Merck] were added to a soln of *ca* 5 mg of substrate in 0.5 ml $CDCl_3$. Spectra were recorded at five different reagent concns up to a concn ratio R_0–S_0 = 0.7:1. The LIS for the 1:1 complex were obtained by extrapolation. For **6**, the exptal data were simulated (McConnell–Robertson equation for the magnetic field of the coordinating lanthanide ion [16–19]) by a computer program (modified PDIGM [16, 17]) assuming different possible substrate geometries and Eu(III) positions within the complex. The best fit was obtained for the geometry shown in (Fig. 1) at $d = 2.3$ Å, $\rho = 40°$, $\zeta = 160°$ with an agreement factor of $R = 0.042$ (see refs. [16–18]).

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