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SESQUITERPENE-COUMARIN ETHERS AND POLYACETYLENES FROM *BROCCHIA CINEREA**

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Key Word Index—*Brocchia cinerea*; Compositae; sesquiterpene-coumarin ethers; 8-farnesylscopoletin; spiroketalenolether polyynes; chemotaxonomy.

Abstract—The roots of *Brocchia cinerea* afforded, in addition to known spiroketalenolether polyynes and sesquiterpene-coumarin ethers, two new isofraxidin-derived sesquiterpene ethers as well as the new 8-farnesylscopoletin. The structures of the new compounds were elucidated on the basis of spectroscopic evidence. The chemotaxonomic significance of sesquiterpene-coumarin ether and spiroketalenolether accumulation within the tribe Anthemideae is discussed.

INTRODUCTION

Brocchia cinerea (Del.) Vis. (tribe Anthemideae) is a small annual herb with discoid capitula and homogamous hermaphrodite florets. It is widely distributed in the Sahara desert and represents one of the monotypic Anthemideae genera which are characteristic of the North African flora. Originally it was recognized as a member of the genus *Cotula*. However, on the basis of fruit characters and general floral morphology, it clearly does not fit in with the current generic concept of *Cotula* [1].

In the course of current comparative chromatographic and spectroscopic analyses on characteristic chemical constituents within the tribe Anthemideae, it became apparent that the roots of *B. cinerea* contain large amounts of spiroketalenolether polyynes together with sesquiterpene-coumarin ethers. Since, to date, the accumulation of the latter compounds has been shown to be mainly confined to the genera *Achillea*, *Artemisia* [2–8] and *Anthemis* [9], this chemical trend deserves special systematic attention. On the other hand, the formation of spiroketalenolether polyynes represents a typical chemical feature of the Anthemideae which has not been detected so far in any of the other tribes. Their varying structures as well as their different distributions have also been shown to contribute to a more natural grouping within the tribe [10–12].

In the present paper, all the main sesquiterpene-coumarin ethers and polyacetylenes from the roots of *B. cinerea* have been isolated and identified in order to obtain more detailed information of their structural diversity, as well as their characteristic accumulation differences within the Anthemideae.

RESULTS AND DISCUSSION

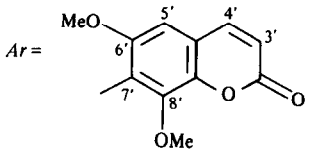
The petrol–ether extract of the roots of *B. cinerea* (collected in Egypt) afforded eight different sesquiterpene-coumarin ethers. Whereas the isofraxidin derivatives farnochrol (**1**), drimartol A (**2**), acetyldrimartol A (**3**), acetyldrimartol B (**4**) and pectachol (**7**), as well as the scopoletin derivative scopofarnol (**8**), have already been described in previous papers [3–5, 7], the stereoisomeric derivatives of pectachol (**5** and **6**) were detected for the first time. Moreover, a further new compound (**9**) was also isolated in which scopoletin was shown to be directly attached to farnesyl moiety by a carbon–carbon bond. The three new compounds were designated as pectachol B (**5**), acetylpectachol B (**6**) and 8-farnesylscopoletin (**9**).

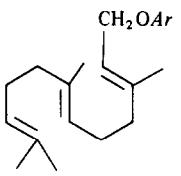
This set of coumarin ethers would suggest a closer affinity between *Brocchia* and species groups of *Achillea* and *Artemisia* [2–8] than with *Anthemis* ([9]; Hofer, O. and Greger, H., unpublished results). However, based on the data available so far, the accumulation of sesquiterpene-coumarin ethers proved most helpful in the determination of subgeneric species clusters rather than in determining intergeneric relationships.

The acetylene pattern is characterized by three *E*-spiroketalenolethers accompanied by small amounts of the corresponding *Z*-isomers which, however, may be formed at least partly as the result of UV irradiation [13]. With the five-membered dehydroringenolether (**11**) and the dominating acetate (**12**), the chemical complement resembles that found in the *Chrysanthemum–Leucanthemum–Santolina* group [11]. At the same time, the acetylene composition clearly deviates from the genus *Cotula*, which is characterized by the formation of C_{17}-dehydrofalcarinol derivatives [10, 11].

The structure of acetylpectachol B (**6**) followed immediately from comparison of the ^{1}H NMR spectrum with those of similar sesquiterpene derivatives [3]. The signals of isofraxidin and of *exo*-methylene together with the three singlets for the methyl resonances characterize these bicyclic sesquiterpene-isofraxidin ethers of the drimenol type. The double-doublet at δ4.51 (J = 9.5 and 7 Hz, axial H-6) and the acetyl methyl indicate an equatorial 6-acetyl derivative [3]. The AB part of an ABX system at δ4.33 and 4.08 is typical for an axial CH_2OAr substituent ($\Delta\delta_{A,B}$ = 0.25 ppm, cf [4]).

*Part 7 in the series "Naturally Occurring Sesquiterpene-Coumarin Ethers". For Part 6 see ref. [8].





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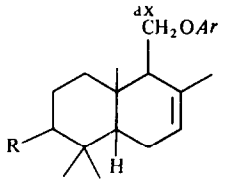
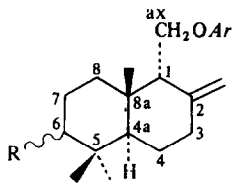


R

2 OH (ax)

3 OCOMe (ax)

4 OCOMe (eq)

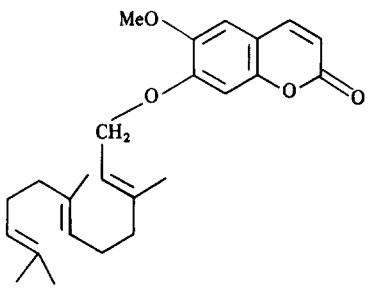


R

5 OH (eq)

6 OCOMe (eq)

7 OH (ax)



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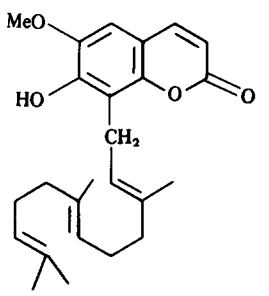

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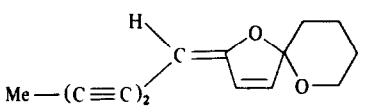

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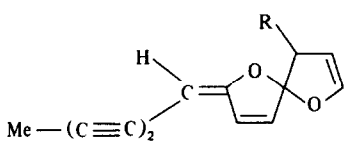

R

11 H

12 OCOMe

The absolute stereochemistry of **6** is rather interesting. The usual absolute configuration of the *trans*-decalin skeleton in drimenyl-derived sesquiterpene moieties of related compounds is 4a*S*,8a*R* (e.g. pectachol, drimartol A and acetyl derivatives [14]). However, one exception has already been reported. Thus drimartol B and its acetyl derivative have an opposite absolute stereochemistry [3] with 4a*R*,8a*S*. In the case of the *exo*-methylene series, the absolute configuration is indicated by a strong Cotton effect at *ca* 205 nm in the circular dichroism (CD) spectra [14]. A negative Cotton effect indicates 4a*S*,8a*R*, a positive 4a*R*,8a*S*. In the case of acetylpectachol B (**6**), a Cotton effect of +10.5 is observed at 205 nm. The absolute configuration is therefore 1*R*,4a*R*,6*S*,8a*S*, which is in agreement with the absolute stereochemistry of drimartol B (the *endo*-olefinic isomer of **6**), but in contrast to the usual trend in the sesquiterpene-isofraxidin series.

The parent alcohol of **6**, pectachol B (**5**), was isolated only as a minor constituent. However, the amount of material isolated (0.4 mg) was sufficient to record the ^{1}H NMR, UV and CD spectra. The structure is established from the NMR spectrum: H-6 gives a broad resonance signal at δ3.25 with $W_{1/2} = 20$ Hz which is typical for an equatorial hydroxyl group at C-6 [3]; the other resonances were very similar to the spectrum of **6**. The absolute configuration follows from the CD spectrum: a strongly positive Cotton effect with $\Delta\varepsilon = +9.5$ at 208 nm indicates 4a*R*,8a*S*-configuration of the *trans*-decalin moiety [14].

The ^{1}H NMR spectrum of the new compound **9** shows immediately that a methoxy-coumarin and a farnesyl moiety are present in the molecule: AB pattern for H-3' and H-4', methoxyl at δ3.95; 3 × =C<u>H</u>–C<u>H</u>$_2$– (*t*, *br*), 2 × =C–C<u>H</u>$_2$–C<u>H</u>$_2$–C= (m), 4 × =C–C<u>H</u>$_3$ (*s*, *br*).

The UV spectrum of **9** is nearly identical to that of the farnesylscopoletin ether, scopofarnol (**8**), which we have

recently isolated from *Artemisia persica* Boiss. [7]; differences to scopofarnol (or scopoletin itself) are only caused by small shifts of some absorption maxima (see Experimental and ref. [7]). The mass spectrum of **9** shows the same molecular ion ($m/z = 396$) as scopofarnol. However, the molecular ion of **9** is relatively intense (12%) compared with the farnesyl ethers we have isolated so far (< 1%) (supporting C–C linkage) and the fragmentation pattern is completely different as well.

In the ^{1}H NMR spectrum of **9** some of the resonances show significant deviations from the spectrum of scopofarnol. In the aromatic part, one proton (sharp *s*) is missing; on the other hand, an additional singlet (*br*, exchangeable with D_2O) is found; the CH_2-1 (*d*) of the farnesyl moiety is shifted from δ4.70 in scopofarnol (typical for $-CH_2OAr$) to δ3.59 (obviously $-CH_2Ar$). All these findings (NMR, UV, MS) suggest that in **9** scopoletin is directly attached to the farnesyl moiety by a carbon–carbon bond instead of the usual ether bond.

Comparison of the ^{1}H NMR spectra of 8-farnesylscopoletin (**9**) and scopoletin proves that **9** is an 8-alkyl substituted scopoletin derivative. H-3′, H-4′ and OMe-6′ are very similar for **9** and scopoletin. The aromatic solvent induced shifts in benzene make things even clearer. In scopoletin, H-5′ and H-8′ (both sharp *s* at δ6.86 and 6.93 in $CDCl_3$) are shifted to δ5.92 (H-5′) and 6.77 (H-8′). In **9** (C_6D_6), only a singlet for H-5′ at δ5.90 is found. Additional proof for the correct assignment of H-5′ and H-8′ is provided by the data for isofraxidine derivatives, where C-8′ is replaced by a methoxyl group and the remaining aromatic singlet at δ5.94–5.95 is necessarily H-5′. A related 8-substituted scopoletin derivative (8-dimethylallyl-7-hydroxy-6-methoxy-coumarin, cedrelopsin) has been isolated from *Cedrelopsis grevei* Baillon (Meliaceae) [15]. The ^{1}H NMR data for the scopoletin moiety of cedrelopsin (including the *d* for CH_2-1) are in very good agreement with the corresponding chemical shifts of **9** [16].

EXPERIMENTAL

B cinerea was collected near Qena, Sahra esh Sharqiya, Upper Egypt (H. Greger, 16 April 1982). Voucher specimens have been deposited at the Herbarium of the Institute of Botany, University of Vienna (WU).

Fresh air-dried roots were cut into small pieces and extracted in turn with petrol (60°–80°)–Et_2O (2:1) and Et_2O for several days at room temp. The combined, conc. extract was separated by TLC on silica gel (1 mm) using petrol–Et_2O and CH_2Cl_2–Et_2O mixtures as solvents. 8.5 g air dried roots of *B cinerea* afforded, according to increasing polarity, 5 mg **11** (*E*:*Z* = 3:1), 7 mg **10** (*E*:*Z* = 4:1), 25 mg **12** (*E*:*Z* = 93:7), 1 mg **8**, 2.4 mg **1**, 3 mg **9**, 1 mg **3**, 3 mg **6**, 1 mg **4**, 7 mg **2**, 4.5 mg **7** and 0.4 mg **5**.

Pectachol B (**5**) [(1R,4aR,6S,8aS)-6,8-*dimethoxy*-7[(6-*hydroxy*-*decahydro*-5,5,8a-*trimethyl*-2-*methylene*-1-*naphthalenyl*)*methoxy*]-2*H*-1-*benzopyran*-2-*one*]. UV λ_{max}^{EtOH} nm (ε): 340 (7800), 297 (10 500), 226 (21 500), 207 (48 000); CD (EtOH) nm: 294 (−0.65), 228 (+1.8), 208 (+9.5); ^{1}H NMR ($CDCl_3$): δ7.61 (*d*, 1H, *J* = 9.5 Hz, H-4′), 6.66 (*s*, 1H, H-5′), 6.35 (*d*, 1H, *J* = 9.5 Hz, H-3′), 4.86 (*s* (*br*), 1H, *exo*-methylene), 4.80 (*s* (*br*), 1H, *exo*-methylene), 4.30 (*dd*, 1H, *J* = 9 and 4 Hz, CH_2OAr), 4.09 (*dd*, 1H, *J* = 9 and 7.5 Hz, CH_2OAr), 3.99 (*s*, 3H, OMe), 3.87 (*s*, 3H, OMe), 3.25 (*m* (*br*), 1H, $W_{1/2}$ = 20 Hz, CH (OH)), 1.02 (*s*, 3H, Me), 1.01 (*s*, 3H, Me), 0.80 (*s*, 3H, Me).

Acetylpectachol B (**6**). [(1R,4aR,6S,8aS)-6,8-*dimethoxy*-7-[(6-*acetyloxy*-*decahydro*-5,5,8a-*trimethyl*-2-*methylene*-1-*naphthalenyl*)*methoxy*]-2*H*-1-*benzopyran*-2-*one*]. UV λ_{max}^{EtOH} nm (ε): 339 (7800), 296 (11 200), 227 (21 000), 206 (43 500); CD (EtOH) nm: 340 (−0.2, sh), 294 (−0.9), 205 (+10.5); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2930 (m), 1745 (s), 1555 (s), 1460 (m), 1420 (s), 1405 (m), 1285 (s), 1240 (w), 1150 (w), 1120 (m), 1040 (m), 840 (m); MS (70 eV, 100°) *m/z* (rel. int.): 484 [M]$^+$ (2.5%), 223 (20), 222 (100), 203 (45), 202 (17), 147 (23), 133 (20), 121 (11), 119 (25), 109 (20), 107 (20), 105 (22), 95 (35), 93 (17), 91 (22); ^{1}H NMR ($CDCl_3$): δ7.64 (*d*, 1H, *J* = 9.5 Hz, H-4′), 6.66 (*s*, 1H, H-5′), 6.36 (*d*, 1H, *J* = 9.5 Hz, H-3′), 4.86 (*s* (*br*), 1H, $W_{1/2}$ = 5 Hz, *exo*-methylene), 4.80 (*s br*), 1H, $W_{1/2}$ = 5 Hz, *exo*-methylene), 4.51 (*dd*, 1H, *J* = 9.5 and 7 Hz, H-6), 4.33 (*dd*, 1H, *J* = 9 and 5 Hz, CH_2OAr), 4.08 (*dd*, 1H, *J* = 9 and 8 Hz, CH_2OAr), 3.98 (*s*, 3H, OMe), 3.91 (*s*, 3H, OMe), 2.20–2.40 (*m*, 4H, H-1 + H-3ax and eq + H-8ax), 1.02 (*s*, 3H, Me), 0.90 (*s*, 3H, Me), 0.88 (*s*, 3H, Me).

8-*Farnesylscopoletin* (**9**) [7-*hydroxy*-6-*methoxy*-8-(3,7,11-*trimethyl*-2,6,10-*dodecatrienyl*)-2*H*-1-*benzopyran*-2-*one*]. Mp 120–121°; UV $\lambda_{max}^{Et_2O}$ nm (ε): 339 (12 500), 302 (8300), 258 (5600), 249 (6300), 217 (26 800); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3533 (m), 2925 (s), 2853 (m), 1736 (s), 1610 (w), 1578 (m), 1486 (m), 1462 (m), 1413 (m), 1374 (w), 1294 (s), 1273 (m), 1193 (w), 1146 (m), 1102 (w), 1061 (w), 901 (w), 844 (w); ^{1}H NMR ($CDCl_3$): δ7.59 (*d*, 1H, *J* = 9.5 Hz, H-4′), 6.73 (*s*, 1H, H-5′), 6.26 (*d*, 1H, *J* = 9.5 Hz, H-3′), 6.20 (*s* (*br*), 1H, exchangeable with D_2O, OH-7′), 5.29 (*t* (*br*), 1H, *J* = 7 Hz, H-2), 5.07 (*t* (*br*), 2*H*, *J* = 6.5 Hz, H-6 and H-10), 3.95 (*s*, 3H, OMe-6′), 3.59 (*d*, 2H, *J* = 7 Hz, CH_2-1), 1.9–2.1 (*m*, 8H, CH_2-4, CH_2-5, CH_2-8 and CH_2-9), 1.85 (*s* (*br*), 3H, Me), 1.66 (*s* (*br*), 3H, Me), 1.58 (*s*, 3H, Me), 1.55 (*s* (*br*), 3H, Me); ^{1}H NMR (C_6D_6): δ6.65 (*d*, 1H, *J* = 9 Hz, H-4′), 5.98 (*d*, 1H, *J* = 9 Hz, H-3′), 5.90 (*s*, 1H, H-5′), 5.81 (*s* (*br*), 1H, OH-7′), 5.64 (*t* (*br*), 1H, *J* = 7 Hz, H-2), 5.20 (*t* (*br*), 2H, *J* = 6.5 Hz, H-6 and H-10), 3.77 (*d*, 2H, *J* = 7 Hz, CH_2-1), 3.03 (*s*, 3H, OMe-6′), 1.95–2.15 (*m*, 8H, CH_2-4, CH_2-5, CH_2-8 and CH_2-9), 2.01 (*s* (*br*), 3H, Me), 1.68 (*s* (*br*), 3H, Me), 1.55 (*s* (*br*), 3H, Me), 1.52 (*s* (*br*), 3H, Me); MS (70 eV, 90°) *m/z* (rel. int.): 396 [M]$^+$ (12), 260 (27), 259 (20), 243 (16), 206 (37), 205 (100), 204 (50), 192 (5), 191 (31), 136 (11), 135 (14), 123 (10), 121 (17), 109 (16), 95 (11), 93 (12).

Scopoletin. ^{1}H NMR ($CDCl_3$): δ7.61 (*d*, 1H, *J* = 9.5 Hz, H-4), 6.93 (*s*, 1H, H-8), 6.86 (*s*, 1H, H-5), 6.29 (*d*, 1H, *J* = 9.5 Hz, H-3), 6.14 (*s* (*br*), 1H, OH-7), 3.96 (*s*, 3H, OMe-6); ^{1}H NMR (C_6D_6): δ6.77 (*s*, 1H, H-8), 6.57 (*d*, 1H, *J* = 9.5 Hz, H-4), 5.94 (*d*, 1H, *J* = 9.5 Hz, H-3), 5.92 (*s*, 1H, H-5), 5.56 (*s* (*br*), 1H, OH-7), 2.97 (*s*, 3H, OMe-6).

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REFERENCES

1. Visiani, R. de (1836) *Plantae quaedam Aegypti ac Nubiae*. Patavii (Padova), Typis Minervae Edit.
2. Bohlmann, F., Schumann, D. and Zdero, C. (1974) *Chem. Ber.* **107**, 644.
3. Greger, H., Hofer, O. and Nikiforov, A. (1982) *J. Nat. Prod.* **45**, 455.
4. Greger, H., Haslinger, E. and Hofer, O. (1982) *Monatsh. Chem.* **113**, 375.
5. Greger, H., Hofer, O. and Robien, W. (1983) *J. Nat. Prod.* **46**, 510.
6. Greger, H., Hofer, O. and Robien, W. (1983) *Phytochemistry* **22**, 1997.
7. Hofer, O. and Greger, H. (1984) *Phytochemistry* **23**, 181.
8. Hofer, O. and Greger, H. (1984) *Monatsh. Chem.* **115**, 477.
9. Bohlmann, F. and Zdero, C. (1975) *Chem. Ber.* **108**, 1902.
10. Bohlmann, F., Burkhardt, T. and Zdero, C. (1973) *Naturally*

Occurring Acetylenes. Academic Press, London.
11. Greger, H. (1977) in *The Biology and Chemistry of the Compositae* (Heywood, V. H., Harborne, J. B. and Turner, B. L., eds.), pp. 899–941. Academic Press, London.
12. Greger, H. (1982) in *Aromatic Plants Basic and Applied Aspects* (Margaris, N., Koedam, A. and Vokou, D., eds.), pp. 153–163. Martinus Nijhoff, The Hague.
13. Bohlmann, F., Herbst, P., Arndt, C., Schönowsky, H. and Gleinig, H. (1961) *Chem. Ber.* **94**, 3193.
14. Hofer, O., Weissensteiner, W. and Widhalm, M. (1983) *Monatsh. Chem.* **114**, 1399.
15. Eshiett, I. T. and Taylor, D. A. H. (1968) *J. Chem. Soc. C* 481.
16. Mondon, A., Callsen, H. and Hartmann, P. (1975) *Chem. Ber.* **108**, 1989.