CARBON-13 NMR SPECTRA OF SOME FURANOID DITERPENES FROM TEUCRIUM SPECIES

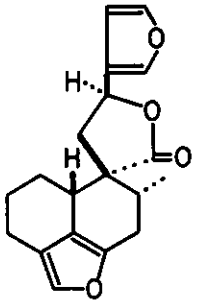
Eszter Gács-Baitz[+] *, Márton Kajtár[‡], Georgi Y. Papanov[o] and Peter Y. Malakov[o]

[+]NMR Laboratory, Central Research Institute of Chemistry, H-1525 Budapest, Hungary; [‡]Institute of Organic Chemistry, Eötvös University, H-1088 Budapest, Hungary; [o]University of Plovdiv, BG-4000 Plovdiv, Bulgaria

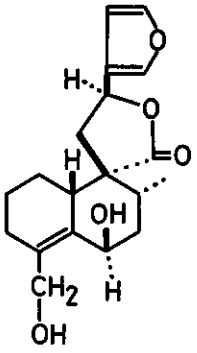
Abstract - By carbon-13 and ^{1}H NMR methods, the proposed constitution of eleven newly isolated furanoid diterpenes and some of their transformation products are confirmed and relative stereochemistries are established. CD spectra provide the absolute stereochemistry for teucrin A, 6-ketoteuscordin, teuscordinon and montanin D.

In previous communications, we reported on the constitution of furanoid diterpenes isolated from various Teucrium species: montanins A (1)[1], B (2)[1], C (3a)[2] and D (4a)[3] from Teucrium montanum; teucrins A (5)[4,5] and E (6)[4,5] from Teucrium chamaedrys; 6-ketoteuscordin (7)[6], 6-α-hydroxy-teuscordin (8)[6] and teuscordinon (9)[7] from Teucrium scordium; and teupolins I (10)[8] and II (11)[8] from Teucrium polium. As carbon-13 chemical shift data may prove useful in the identification of related natural products[9] we now describe the results of our ^{13}C NMR study on these diterpenoids and some of their transformation products (3b-d, 4b,c).[2,3]

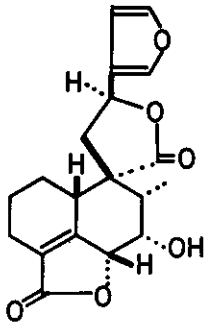
The interpretation of carbon-13 data in terms of constitution and stereochemistry required accurate knowledge of the relative configurations of substituted carbon atoms. Although some of the pertinent information was available from preliminary chemical and ^{1}H NMR spectral studies, or could be anticipated on biogenetic grounds, a systematic reinvestigation of the proton resonance parameters appeared warranted. Relevant ^{1}H chemical shift and coupling data are collected in the experimental section. Of general significance are the following



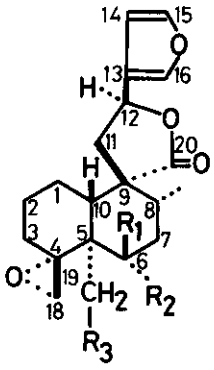
1



2



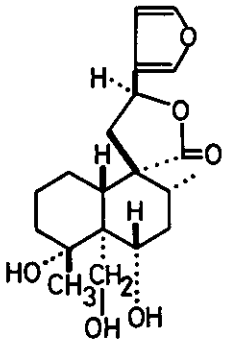
5



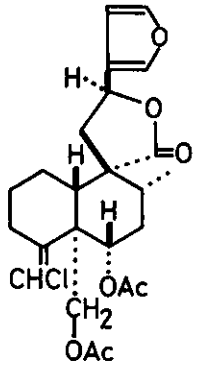
3a R_1=H, R_2=R_3=OAc

10 R_1=H, R_2=OH, R_3=OAc

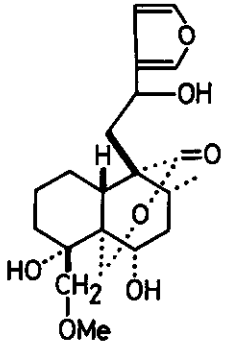
11 R_1=H, R_2=OAc, R_3=OH



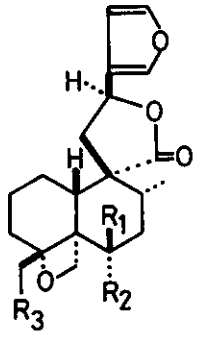
3b



3c



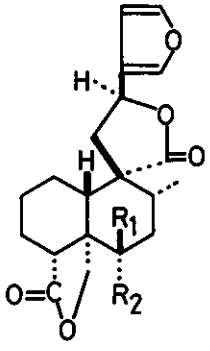
3d



4a R_1=R_3=OH, R_2=H

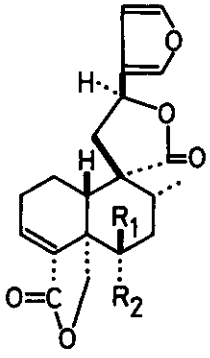
4b R_1=R_3=OAc, R_2=H

4c R_1,R_2=O, R_3=OAc



6 R_1=H, R_2=OH

7 R_1,R_2=O



8 R_1=H, R_2=OH

9 R_1,R_2=O

Table 1. ^{13}C NMR chemical shifts (ppm from internal TMS)

	1[a]	2[b]	5[b]	4a[a]	4b[a]	4c[a]	10[a]	11[a]	3a[a]	3b[b]	3c[a]	3d[b]	6[b]	7[a]	8[b]	9[b]
C-1	23.91†	21.57†	21.33	21.27	21.40	20.39	22.66	22.80	22.23	22.04	22.75	21.49	22.29	22.92	21.52	21.53
C-2	25.62†	25.83†	24.23	16.94	16.60	15.44	24.96	24.94	24.80	23.20	26.27	24.66	24.89	23.71	27.62	26.75
C-3	19.10	27.95	19.31	30.05	29.11	26.99	31.35	31.87	32.24	36.96†	25.65	30.58	22.45	23.87	134.74	136.45
C-4	117.02§	134.90§	127.19	88.57	86.44	87.52	66.56	65.22	64.78	78.70	143.63	76.57	46.63	41.51	136.39	132.04
C-5	119.71§	134.34§	158.65	47.50	46.54	54.62	45.31	46.33	45.49	47.13	49.50	42.32	46.97	55.36	49.40	58.18
C-6	147.92	63.52	80.27	69.59	73.03	208.74	73.45	73.74	71.85	75.41	74.59	72.34	76.53	208.20	75.30	206.13
C-7	30.03	36.31	71.68	33.09	29.94	43.49	33.88	32.37	32.97	35.87†	32.20	38.35	35.55	40.74	36.75	42.21
C-8	36.15	32.16	37.80	32.16	32.90	40.97	38.27	37.96	40.56	41.48	40.49	34.71	37.95	40.21	38.62	40.22
C-9	50.75	53.49	56.27	52.30	51.96	51.39	51.17	50.80	51.21	52.07	51.80	48.95	51.06	50.88	49.88	49.93
C-10	43.26	40.69	41.14	37.95	38.92	46.17	52.42	52.82	50.62	47.91	52.46	39.96	46.51	48.93	50.07	49.67
C-11	39.72	40.76	41.56	41.71	41.54	41.21	43.52	43.20	43.28	45.19	43.36	36.54	41.65	41.61	41.42	40.44
C-12	71.60	71.69	74.38	72.36	72.23	72.33	71.49	71.54	71.47	71.23	71.56	61.86	71.67	72.26	71.44	71.87
C-13	125.57	125.49	124.00	125.19	125.06	124.76	125.22	125.14	125.59	125.39	125.43	130.91	125.07	124.63	124.74	124.35
C-14	108.31	108.25	108.32	108.19	108.11	107.98	108.06	108.02	108.09	108.12	107.97	108.98	108.13	107.99	108.10	108.06
C-15	144.13	143.95	144.40	144.14	144.21	144.38	144.20	144.21	144.22	144.06	144.24	143.02	144.10	144.40	144.14	144.22
C-16	139.81	139.57	140.76	139.64	139.62	139.71	139.61	139.57	139.28	139.29	139.18	138.32	139.75	139.86	139.99	140.19
C-17	17.74	17.17	13.40	16.65	16.52	17.42	16.52	16.46	16.79	17.12	16.81	17.08	16.60	17.17	16.25	16.53
C-18	136.15	60.72	172.59	66.24	66.88	67.55	48.56	47.31	47.67	23.11	110.86	76.01	179.60	176.98	169.48	167.21
C-19	-	-	-	71.85	71.66	70.43	61.75	60.80	61.74	61.54	61.30	68.55	68.19	69.34	68.99	71.21
C-20	176.20	177.22	180.34	178.15	177.53	176.96	176.04	176.31	175.99	176.89	176.09	173.02	176.87	176.98	176.59	176.61
Ac-Me	-	-	-	-	20.87 21.35	20.91	21.23	21.25	21.09 21.20	-	21.17 21.17	-	-	-	-	-
Ac-CO	-	-	-	-	169.97 170.91	170.60	170.64	169.48	169.86 170.41	-	170.39 170.48	-	-	-	-	-
-OMe	-	-	-	-	-	-	-	-	-	-	-	59.46	-	-	-	-

a In $CDCl_3$.

b In $CDCl_3$-DMSO-d_6.

§, † Assignments may be interchanged.

stereochemical considerations. The relative configuration of C-9 (i.e. orientation of the C9-C20 bond) can usually be inferred from the magnitude of the chemical shift difference between C-7 methylene protons.[10] Thus, in molecules with axially oriented C9-C20 bond, the anisotropic shielding effect of the C-20 carbonyl group causes a substantial downfield shift of the resonance of $H\text{-}7_{ax}$ with respect to that of its $H\text{-}7_{eq}$ partner provided that ring B assumes chair conformation. Application of this stereochemical rule, however, may be impracticable in cases when the molecule contains a substituent at C-7 (see eg. 5). Another characteristic feature of the furanoid diterpenes studied was found to be the orientation of the methyl group at C-8. This stereochemical detail can be readily inferred from the magnitude of vicinal couplings of C-7 methylene protons. For most compounds investigated, the above data could be obtained from the analysis of 100 MHz spectra run in various solvents and solvent mixtures and the relative stereochemistries thus determined generally proved to be identical with those proposed in preliminary papers.[1-8] For 4b the proton NMR data were inferred from spectra run at high magnetic field, while in a few instances the relative stereochemistries at the substituted carbon atoms were established through comparison of carbon-13 chemical shift data with those of related compounds of known stereochemistry.

Carbon-13 chemical shift data are collected in Table 1. The assignment of resonances to individual carbon atoms in the molecules is based on standard carbon-13 FT NMR procedures.[11] In several instances, single frequency (low power) selective $^{13}C\text{-}\{^{1}H\}$ double resonance experiments were performed in order to eliminate ambiguities in the assignment of resonances due to carbon atoms of the same off-resonance multiplicity. Even in the most recent publications on furanoid diterpenes (see eg. ref. 12), resonances at 140 and 144 ppm are attributed alternatively to furan ring carbons C-15 and C-16. In order to eliminate this ambiguity, we recorded high resolution (proton-coupled) ^{13}C spectra of representative diterpenes, which showed that, in addition to carbon-proton couplings with furan ring protons, the resonance at higher field exhibited a splitting of 3.5 Hz due to three-bond interaction with H-12, hence this resonance must be attributed to C-16.

Analysis of the ^{1}H and ^{13}C data reported in this study leads to the following stereochemical conclusions. The ^{1}H and ^{13}C spectral properties of 1, 2 and 5 are in accord with published data on furanoid diterpenes featuring an α,β-(4,5)-unsaturated γ-lactone ring.[9] Thus for each of these compounds the chemical shift value of the allylic H-10 (2.82, 2.85, 2.95 ppm) suggests trans relative

orientation for this proton and the C-20 carbonyl group.[10] While, in 1 and 2, the coupling pattern of C-7 methylene protons clearly shows the C-8 methyl group to be equatorially oriented, the 2.5 Hz measured for J(7eq,8), the only H-7 vicinal coupling observable in the 7-hydroxyl molecule 5, is not specific for the stereochemistry at C-8. This stereochemical detail, however, can be readily inferred from carbon-13 results. Axially oriented C-8 methyl groups are expected to result- via γ-gauche interaction - in increased screening for the allylic C-10 carbon atom as eg. in teucvidin (38.8 ppm)[13] and teucrin H1 (36.3 ppm).[10] The 41.1 ppm (see Table 1) is practically identical with the value obtained for teucvin (42.0 ppm),[14] a related diterpene with an equatorially oriented C-8 methyl group but without hydroxyl substituent at C-7, which shows that, in 5, orientation of the C-8 methyl group is equatorial as had been anticipated on the basis of biogenetic considerations.[4,5] It may be noted that the 13.4 ppm observed for the C-8 methyl carbon atom in 5 is consistent with the stereochemical conclusion: the higher shielding (relative to the 17 ppm measured for equatorial C-8 methyls in 1, 2 and teucvin[14]) is the result of γ-gauche steric interaction with the axial hydroxyl group at C-7. Another noteworthy fact is the unusually high deshielding of the C-20 carbonyl carbon in 5 (180.3 ppm) which may be interpreted in terms of 1,3-syn-diaxial (or delta) steric interaction[15] between the carbonyl group and the hydroxyl substituent at C-7. It is known[16] that carbon atoms bearing the substituents participating in delta steric interaction also exhibit an increase in their chemical shift. This particular feature seems to be reflected in the 56.3 ppm measured for C-9 in 5, a value which is nearly 3 ppm higher than the chemical shift obtained for C-9 in teucvin (53.5 ppm)[14].

The CD curve of 5 shows a strong positive band at 230 nm associated with the π to π^* transition of the α,β-unsaturated lactone chromophore and a strong negative band at 201 nm. According to the Kuriyama rule[17] the sign of the 230 nm band corresponds to β-configuration of C-6H. This conclusion is confirmed by the fact that the signs of both CD bands are identical with those observed for teucvin[18] and opposite to those of respective bands in teuflin[19], teucvidin[18], teucrin H1[10] and teucrin H4[10]. Thus formula 5 represents the absolute stereochemistry of teucrin A which is in accord with conclusions based on CD spectra from the 6-oxo derivative of 5.[20]

Molecules 3a, 10 and 11 have an oxirane ring in position 4 and differ among themselves constitutionally in the number and position of the O-acetyl

groups. It will be recalled that the relative configuration of the spiro carbon atom C-4 can be inferred from the magnitude of the stereospecific long-range couplings between C-18 oxomethylene and C-3 methylene protons.[21] The four-bond couplings (1.5 to 2.3 Hz) observed between H-3_{ax}, and the lower field H-18 show that, orientation of the C4-C18 bond is pseudoaxial in each of these compounds. Another remarkable consequence of the given relative configuration is the unusually high shielding of H-3_{eq} protons (1 to 1.1 ppm), an effect attributable to the diamagnetic anisotropy of the oxirane ring. As observed in 3b, this effect was found to disappear due to cleavage of the oxirane ring. Molecules 3a and 10 were recently obtained *via* reduction and subsequent acetylation of 19-acetylgnaphalin,[22] respectively, and the spectral data of the synthetic products were compared with those reported in preliminary papers on montanin C (3a)[2] and teupolin I (10)[8]. While spectral comparison was considered satisfactory to show the identity of synthetic and natural teupolin I (10), the authors of ref. 22 questioned the correctness of structure 3a proposed by us[2] for montanin C. Inspection of the ^{1}H and ^{13}C parameters collected on 3a, 10 and 11 in the present study show, however, that the constitution and relative stereochemistry of montanin C are correctly represented by formula 3a as suggested in our preliminary report. This conclusion received further support by the ^{1}H and ^{13}C analysis of products 3b,c and d, obtained *via* chemical transformation of montanin C.

The proton and carbon-13 results for montanin D (4a) obtained in the present study gave full support for the proposed constitution of this molecule featuring a condensed four-membered ether ring and axially oriented hydroxyl function at C-6[3]. In addition, the detailed ^{1}H parameters inferred from the 400 MHz spectra of the diacetate (4b) (see experimental) showed the orientation of the methyl group at C-8 to be equatorial and that of the C9-C20 bond to be axial. Information regarding the preferred conformation of rings A and B was available from the carbon-13 chemical shift data. According to the data in Table 1, in 4a both C-10 and C-8 exhibit relatively low chemical shift values (37.95 and 32.16 ppm, respectively) which are readily interpreted in terms of γ-gauche interactions between the axially oriented C-6(OH) group and axially oriented protons at C-8 and C-10 available only in a chair-type conformation of ring B. The unusually high shielding observed for C-2 (16.9 ppm) suggests major conformational distortions for ring A which is not unexpected in view of the condensed four-membered ring. (According to molecular models, the preferred conformation of ring A

is presumably twist-boat.)

In our earlier paper 6-ketoteuscordin (7) isolated from Teucrium scordium[6] was assumed to be identical with the 6-oxo derivative of teuchamaedryn B(≡teucrin H2) isolated from Teucrium chamaedrys[5]. This conclusion was fully supported by proton and carbon-13 data obtained in the present study. Our recent ^{1}H NMR data also show that the orientation of the methyl group at C-8 is equatorial in both 6-oxo compounds (see ^{1}H NMR data), hence it must have the same orientation in the parent teucrin H2, as well, i.e. not axial as had been erroneously suggested earlier.[10]

CD curves of both 7 and 4c, the 6-oxo derivative of 4a, were recorded and the pertinent data are collected in the Experimental section. Similarly to some other 6-oxo furanoid diterpenes[23], the CD data provided no unequivocal information as to the absolute stereochemistry of chiral centres in the vicinity of the 6-oxo chromophore. However, it seems reasonable to assume that the weak bands at approx. 225 nm in both molecules arise from the spiro lactone chromophore and, since the observed negative sign is identical with that of the analogous band in the CD spectrum of teucrin H3, they reflect an identical absolute configuration at C-9. From the known absolute stereochemistry of teucrin H3[10,22] and the relative stereochemistries of 4c and 7 (see above) it then follows that formulas 4a-c and 7 represent with high probability the absolute stereochemistry of these diterpenes.

For the sake of completeness, Table 1 also includes carbon-13 data of some related furanoid diterpenes whose constitution and stereochemistry have been firmly established in earlier studies: teucrin E (6)[4,5], a long-time known congener of teucrin H2; 6α-hydroxy-teuscordin (8)[6] and teuscordinon (9)[7]. For compound 6 we note the downfield shift (absence of γ-gauche interactions with the OH function) experienced by resonances due to C-4, C-8 and C-10 compared to their values in teucrin H2[10] which shows that the configuration of C-6 is opposite in the two compounds. Both 8 and 9 are structurally related to bacchotricuneatin B, a related natural product (ex. Baccharis tricuneata) with no substituent group at C-6, the absolute stereochemistry of which is known from CD and X-ray studies[24]. Comparison of the data for 8 and 9 in Table 1 with those published on bacchotricuneatin B[24] shows the anticipated identity of the relative stereochemistry of these molecules.

According to the results of CD measurements performed on 9, the identity exists also in the absolute stereochemistry for these molecules. The negative sign of the Cotton effect attributable to the 6-oxo chromophore (299.5 nm) indicates 5α-configuration for the lactone methylene group. The band at 247 nm, on the other hand, is due to chromophore of the five-membered lactone conjugated with the exo-α,β-double bond. Theoretical considerations[25] and empirical rules[26] require that, with the assumed 5α-configured ring junction, the C=C-C=O chromophore should be of negative chirality and give rise to a negative Cotton effect which is in fact the case for the band at 247 nm. CD spectral comparison with related diterpenoids of known absolute stereochemistry (diterpenoids isolated from Baccharis trimera[27] and Baccharis tricuneata[24]) lends support for this conclusion and settles the absolute stereochemistry of 9 as shown in the formula.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a disk-augmented Varian XL-100/15 FT instrument operating at 100.1 and 25.16 Hz, respectively. High field ^{1}H NMR spectra were run on a Bruker WH-400E instrument operating at 400.13 MHz. CD measurements were performed at room temp on a Jobin-Yvon-Roussel-Jouan model III dichrograph using spectral grade acetonitrile.

(1) δH ppm ($CDCl_3$): 1.14 (3H,d,$J_{17,8}$=6.8Hz,H-17), 2.82 (1H,dd,$J_{10,1}$=6.0+1.5Hz, H-10). 2.44+2.68 (2H,m,J_{gem}=13.5Hz,$J_{11,12}$=9.0+8.5Hz,H-11), 5.45 (1H,dd,H-12), 6.42 (1H,m,H-14), 7.06 (1H,m,$J_{18,3}$=1.0+1.0Hz,H-18), 7.46 (2H,m,H-15+H-16), δH ppm (C_6D_6): 1.76 (1H,m,$J_{8,7}$=11.0+2.5Hz,H-8), 3.01 (1H,m,J_{gem}=16.5Hz, $J_{3ax,2}$=10.5+2.5Hz,H-3_{ax}), 2.35 (1H,m,H-3_{eq});

(2) δH ppm ($CDCl_3$+DMSO-d_6 5:1): 0.98 (3H,d,$J_{17,8}$=6.6Hz,H-17), 2.85 (1H,dd,$J_{10,1}$= 6.0+8.0Hz,H-10), 2.35+2.56 (2H,m,J_{gem}=14.0Hz,$J_{11,12}$=8.6+8.9Hz,H-11), 3.82+ 4.38 (2H,d,J_{gem}=12.0Hz,H-18), 4.92 (1H,t,$J_{6,7}$=2.4+2.8Hz,H-6), 5.36 (1H,t,H-12), 6.41 (1H,m,H-14), 7.44 (2H,m,H-15+H-16), 3.28+3.46 (2H,b,-OH), δ H ppm (C_6D_6): 1.94 (1H,m,J_{gem}=13.0Hz,$J_{7eq,8}$=1.0Hz,H-7_{eq}), 2.58 (1H,m,$J_{7ax,8}$=11.5Hz,H-7_{ax}), 2.35 (1H,m,H-8);

(3a) δH ppm ($CDCl_3$): 1.11 (3H,d,$J_{17,8}$=6.4Hz,H-17), 1.96+2.06 (6H,s,-$COCH_3$), 1.02 (1H,m,J_{gem}=13.0Hz,$J_{3eq,2}$=3.0+3.0Hz,H-3_{eq}), 2.05 (1H,m,H-3_{ax}), 1.52 (1H,m, $J_{7eq,6}$=4.0Hz,$J_{7eq,8}$=3.0Hz,J_{gem}=13.5Hz,H-7_{eq}), 2.16 (1H,m,$J_{7ax,6}$=11.0Hz,

$J_{7ax,8}$=11.5Hz,H-7_{ax}), 1.96 (1H,m,H-8), 2.18+2.93 (2H,dd,J_{gem}=4.2Hz,$J_{18,3ax}$= 2.3Hz,H-18), 2.30+2.53 (2H,m,J_{gem}=14.0Hz,$J_{11,12}$=8.0+9.0Hz,H-11), 5.35 (1H,dd, H-12), 4.79 (1H,m,H-6), 4.55+5.28 (2H,dd,J_{gem}=13.3Hz,$J_{19,6}$=1.2Hz,H-19), 6.40 (1H,m,H-14), 7.43 (2H,m,H-15+H-16);

(3b) δH ppm ($CDCl_3$): 1.14 (3H,d,$J_{17,8}$=6.5Hz,H-17), 1.42 (3H,s,H-18), 1.75 (1H,m, J_{gem}=13.5Hz,$J_{eq,6}$=3.5Hz,H-7_{eq}), 2.20 (1H,m,$J_{7ax,6}$=11.5Hz, $J_{7ax,8}$=12.0Hz,H-7_{ax}), 2.25+2.40 (2H,m,J_{gem}=14.0Hz,$J_{11,12}$=8.0+9.0Hz,H-11), 5.34 (1H,dd,H-12), 4.08 (1H,m,H-6), 4.40+5.28 (2H,dd,J_{gem}=13.0Hz,$J_{19,6}$= 1.2Hz,H-19), 6.35 (1H,m,H-14), 7.42 (2H,m,H-15+H-16);

(3c) δH ppm ($CDCl_3$): 1.12 (3H,d,$J_{17,8}$=6.5Hz,H-17), 1.97+2.00 (6H,s,-$COCH_3$), 3.02 (1H,m,J_{gem}=12.0Hz,$J_{3eq,2}$=4.0+1.0Hz,H-3_{eq}), 1.76 (1H,m,J_{gem}=11.5Hz,$J_{7eq,6}$= 3.5Hz,$J_{7eq,8}$=2.0Hz,H-7_{eq}), 2.04 (1H,m,$J_{7ax,6}$=10.5Hz,$J_{7ax,8}$=10.0Hz,H-7_{ax}), 2.30+2.46 (2H,m,J_{gem}=13.5Hz,$J_{11,12}$=8.0+9.0Hz,H-11), 5.36 (1H,dd,H-12), 5.08 (1H,m,H-6), 4.42+5.29 (2H,dd,J_{gem}=13.0Hz,$J_{19,6}$=1.0Hz,H-19), 5.72 (1H,d, $J_{18,3ax}$=0.8Hz,H-18), 6.38 (1H,m,H-14), 7.44 (2H,m,H-15+H-16);

(3d) δH ppm ($CDCl_3$): 1.04 (3H,d,$J_{17,8}$=6.5Hz,H-17), 1.48 (1H,m,J_{gem}=14.0Hz,$J_{7ax,6}$= 11.0Hz,$J_{7ax,8}$=12.7Hz,H-7_{ax}), 1.93 (1H,m,$J_{7eq,6}$=5.0Hz,$J_{7eq,8}$=4.5Hz,H-7_{eq}), 2.42 (1H,m,H-8), 1.88+2.62 (2H,m,J_{gem}=15.5Hz,$J_{11,12}$=9.3+2.5Hz,H-11), 4.63 (1H,dd,H-12), 3.96 (1H,m,H-6), 4.58+4.73 (2H,dd,J_{gem}=13.0Hz,$J_{19,6}$=1.2Hz,H-19), 3.68 (2H,s,H-18), 3.45 (3H,s,-OCH_3), 3.20 (1H,s,C4-OH), 3.6+4.7 (2H,b,-OH), 6.44 (1H,m,H-14), 7.41 (2H,m,H-15+H-16);

(4a) δH ppm ($CDCl_3$): 0.92 (3H,d,$J_{17,8}$=6.5Hz,H-17), 2.25+2.50 (2H,m,J_{gem}=14.0Hz, $J_{11,12}$=8.5+9.0Hz,H-11), 5.39 (1H,dd,H-12), 4.68 (1H,dd,H-6), 3.34+4.10 (2H, d,J_{gem}=11.5Hz,H-18), 4.02+4.73 (2H,d,J_{gem}=7.5Hz,H-19), 3.68 (2H,b,-OH), 6.39 (1H,m,H-14), 7.43 (2H,m,H-15+H-16);

Conversion of montanin D into its 18-O-acetyl derivative. Compound 4a (50 mg) was treated with the mixture of acetic anhydride (0.16 ml) and pyridine (1 ml) at room temp for 24 h. The 18-O-acetyl derivative was separated from unreacted 4a and diacetyl 4b through chromatography on silica gel ($PF_{254+366}$) using benzene-methanol (14:3) solvent mixture. Yield 30 mg.

Oxydation of 18-O-acetyl derivative of 4a into 4c. 18-O-acetyl derivative (10 mg) dissolved in dry dichloromethane (1 ml) was treated with pyridine-Cr_2O_3 complex (43 mg) at room temp for 24 h. The product 4c was purified on tlc plate.

(4b) δH ppm (400 MHz) ($CDCl_3$): 0.93 (3H,d,$J_{17,8}$=6.7Hz,H-17), 2.33+2.48 (2H,m,J_{gem}=13.8Hz,$J_{11,12}$=8.5+8.8Hz,H-11), 5.40 (1H,dd,H-12), 1.85 (1H,m,J_{gem}=15.0Hz, $J_{7eq,6}$=$J_{7eq,8}$=3.8Hz,H-7_{eq}), 2.12 (1H,m,$J_{7ax,6}$=2.1Hz,$J_{7ax,8}$=12.8Hz,H-7_{ax}), 5.68 (1H,dd,H-6), 4.07+4.11 (2H,d,J_{gem}=12.3Hz,H-18), 4.16+4.78 (2H,d,J_{gem}=7.9Hz,H-19), 6.39 (1H,dd,$J_{14,15}$=1.8Hz,$J_{14,16}$=0.9Hz,H-14), 7.44(2H,m,H-15+H-16), 2.06+2.09 (6H,s,-$COCH_3$);

(4c) δH ppm ($CDCl_3$): 1.08 (3H,d,$J_{17,8}$=6.5Hz,H-17), 2.30+2.50 (2H,m,J_{gem}=14.0Hz, $J_{11,12}$=8.5+8.5Hz,H-11), 5.47 (1H,t,H-12), 3.02 (1H,dd,J_{gem}=13.5Hz,$J_{7ax,8}$=11.0Hz,H-7_{ax}), 4.52 (2H,s,H-18), 4.58+4.90 (2H,d,J_{gem}=7.5Hz,H-19), 2.05 (3H,s,-$COCH_3$), 6.40 (1H,m,H-14), 7.47 (2H,m,H-15+H-16). CD (CH_3CN): λ,nm $\binom{(\Delta\varepsilon)}{([\theta])}$: 297 $\binom{(+0.32)}{(+1060)}$, 223.5 $\binom{(-0.74)}{(-2440)}$, 190 $\binom{(+7.0)}{(+23000)}$;

(5) δH ppm (DMSO-d_6+$CDCl_3$ 3:1): 1.20 (3H,d,$J_{17,8}$=6.3Hz,H-17), 2.18 (1H,m,$J_{8,7}$=2.5Hz,H-8), 2.95 (1H,m,$J_{10,1}$=6.0+9.0Hz,H-10) 2.68+2.70 (2H,m,J_{gem}=14.0Hz, $J_{11,12}$=8.0+9.0Hz,H-11), 5.70 (1H,dd,H-12), 4.10 (1H,dd,$J_{7,6}$=4.5Hz,H-7), 4.92 (1H,m,$J_{6,3}$=2.4+2.0Hz,$J_{6,10}$=1.5Hz,H-6), 6.49 (1H,m,H-14), 7.56 (1H,m, H-15), 7.64 (1H,m,H-16), 4.56 (1H,b,-OH). CD (CH_3CN): λ,nm $\binom{(\Delta\varepsilon)}{([\theta])}$: 299.5 $\binom{(-1.36)}{(-4490)}$, 247 $\binom{(-3.85)}{(-12700)}$, 220.5 $\binom{(+8.24)}{(+27200)}$, 196 $\binom{(-10.7)}{(-35300)}$;

(6) δH ppm (DMSO-d_6+$CDCl_3$ 3:1): 0.98 (3H,d,$J_{17,8}$=6.5Hz,H-17), 1.74 (1H,m,$J_{7eq,6}$=4.0Hz,$J_{7eq,8}$=3.8Hz,J_{gem}=13.5Hz,H-7_{eq}), 2.19 (1H,m,$J_{7ax,6}$=11.3Hz,$J_{7ax,8}$=11.5Hz,H-7_{ax}), 2.38+2.40 (2H,m,$J_{11,12}$=8.0+9.0Hz,H-11), 5.35 (1H,dd,H-12), 4.20+4.43 (2H,dd,J_{gem}=11.0Hz,$J_{19,6}$=0.7Hz,H-19), 3.49 (1H,m,H-6), 6.40 (1H,m, H-14), 7.44 (2H,m,H-15+H-16), 4.09 (1H,d,$J_{6,-OH}$=6.0Hz,-OH), δH ppm (C_6D_6): 2.48 (1H,dd,$J_{4,3}$=6.0+8.0Hz,H-4);

Oxydation of teucrin H2 into its 6-oxo derivative. Teucrin H_2 (20 mg) dissolved in dry dichloromethane (3 ml) was treated with pyridine-Cr_2O_3 complex (43 mg) at ambient temp for 7 h. Purification of the product was made on kieselgel plate (PF_{254}) with benzene-methanol (14:3) solvent mixture.

(7) δH ppm ($CDCl_3$): 1.12 (3H,d,$J_{17,8}$=6.5Hz), 2.44 (2H,d,$J_{11,12}$=8.5Hz,H-11), 5.42 (1H,t,H-12), 2.38(1H,dd,J_{gem}=14.3Hz,$J_{7eq,8}$=4.5Hz,H-7_{eq}), 3.41 (1H,dd,$J_{7ax,8}$=13.3Hz,H-7_{ax}), 2.89 (1H,dd,$J_{4,3}$=7.0+9.5Hz,H-4) 4.78+4.46 (1H,d,J_{gem}=11.3Hz, H-19), 6.41 (1H,m,H-14), 7.46 (2H,m,H-15+H-16). CD (CH_3CN):λ,nm $\binom{(\Delta\varepsilon)}{([\theta])}$: $\binom{(-0.97)}{(-3200)}$, 226 $\binom{(-1.40)}{(-4600)}$, 206 sh $\binom{(+0.37)}{(+1200)}$, 190 $\binom{(+6.7)}{(+22000)}$;

(8) δH ppm (DMSO-d_6+$CDCl_3$ 3:1): 1.01 (3H,d,$J_{17,8}$=6.3Hz,H-17), 2.45 (2H,d,$J_{11,12}$=

8.6Hz,H-11), 5.39 (1H,t,H-12), 3.63 (1H,m,$J_{6,7}$=11.1+4.0Hz,H-6), 3.88+4.80 (2H,dd,J_{gem}=10.0Hz,$J_{19,6}$=1.0Hz,H-19), 6.76 (1H,dd,$J_{3,2}$=6.4+2.9Hz,H-3), 6.40 (1H,m,H-14), 7.46 (2H,m,H-15+H-16), 4.36 (1H,d,$J_{6,-OH}$=6.5Hz,-OH), δ H ppm (pyridine-d_5): 1.79 (1H,m,H-8), 2.09 (1H,m,J_{gem}=13.5Hz,$J_{7eq,8}$=4.5Hz,H-7_{eq}), 2.51 (1H,m,$J_{7ax,8}$=11.5Hz,H-7_{ax};

(9) CD (CH_3CN): λ,nm $\frac{(\Delta\varepsilon)}{[\theta]}$: 299.5 $\frac{(-1.36)}{(-4490)}$, 247 $\frac{(-3.85)}{(-12700)}$, 220.5 $\frac{(+8.24)}{(+27200)}$, 196 $\frac{(-107)}{(-35300)}$;

(10) δH ppm ($CDCl_3$): 1.01 (3H,d,$J_{17,8}$=6.4Hz,H-17), 2.06 (3H,s,-$COCH_3$), 1.10 (1H,m, J_{gem}=12.5Hz,$J_{3eq,2}$=3.5+3.0Hz,H-3_{eq}), 2.35 (1H,m,H-3_{ax}), 1.62 (1H,m,$J_{7eq,6}$= 4.1 Hz, $J_{7eq,8}$=3.8Hz,J_{gem}=14.0Hz,H-7_{eq}), 2.44+3.22 (2H,dd,J_{gem}=3.9Hz,$J_{18,3ax}$= 2.2Hz,H-18), 2.35 (2H,d,$J_{11,12}$=8.7Hz,H-11), 5.33 (1H,t,H-12), 3.65 (1H,m,H-6), 4.69+5.03 (2H,dd,J_{gem}=13.0Hz,$J_{19,6}$=1.0Hz,H-19), 6.40 (1H,m,H-14), 7.42 (2H,m, H-15+H-16), 3.45 (1H,s,-OH), δH ppm (C_6D_6): 2.85 (1H,m,$J_{7ax,8}$=11.5Hz,H-7_{ax});

(11) δH ppm ($CDCl_3$): 0.99 (3H,d,$J_{17,8}$=6.6Hz,H-17), 2.04 (3H,s,-$COCH_3$), 1.09 (1H,m, J_{gem}=13.0Hz,$J_{3eq,2}$=3.0+3.5Hz,H-3_{eq}), 2.50 (1H,m,H-3_{ax}), 1.61 (1H,m,$J_{7eq,6}$= 4.6Hz,$J_{7eq,8}$=3.5Hz,J_{gem}=13.5Hz,H-7_{eq}), 2.40 (1H,m,$J_{7ax,6}$=11.8Hz,$J_{7ax,8}$=11.2Hz, H-7_{ax}), 2.0 (1H,m,H-8), 2.23+2.92 (2H,dd,J_{gem}=4.0Hz,$J_{18,3ax}$=2.3Hz,H-18), 2.38 (2H,d,$J_{11,12}$=8.7Hz,H-11), 5.35 (1H,t,H-12), 4.86 (1H,m,H-6), 4.0+4.71 (2H,dd, J_{gem}=13.1Hz,$J_{19,6}$=1.3Hz,H-19), 6.39 (1H,m,H-14), 7.44 (2H,m,H-15+H-16);

ACKNOWLEDGEMENTS

The authors are grateful to Prof. L. Szabó (Institute of Organic Chemistry, Technical University, Budapest) for the preparation of some of the derivatives. Thanks are due to Dr. H.P. Kellerhals (Spectrospin AG, Faellanden, Zürich, Switzerland) for his kind permission to use the company's high field NMR instrument.

REFERENCES

1. P.Y. Malakov, G.Y. Papanov and N.M. Mollov, Tetrahedron Letters, 1978, 2025.
2. P.Y. Malakov, G.Y. Papanov, N.M. Mollov and S.L. Spassov, Z. Naturforsch., 1978, 33b, 789.
3. P.Y. Malakov, G.Y. Papanov, N.M. Mollov and S.L. Spassov, Z. Naturforsch., 1978, 33b, 1142.
4. D.P. Popa and A.M. Reinbold, Khim. Prirodn. Soedin., 1972, 67; 1973, 31; D.P.

Popa, A.M. Reinbold and A.I. Rezvukhin, ibid., 1973, 169; A.M. Reinbold and D.P. Popa, ibid., 1974, 589.

5. G.Y. Papanov and P.Y. Malakov, Z. Naturforsch., 1980, 35b, 764.
6. G.Y. Papanov and P.Y. Malakov, Z. Naturforsch., 1981, 36b, 112.
7. G.Y. Papanov, P.Y. Malakov and F. Bohlmann, Phytochemistry, 1981, 20, 170.
8. P.Y. Malakov, G.Y. Papanov and N.M. Mollov, Z. Naturforsch., 1979, 34b, 1570.
9. F. Piozzi, Heterocycles, 1981, 15, 1489 and references cited therein.
10. E. Gács-Baitz, L. Radics, G.B. Oganessian and V.A. Mnatsakanian, Phytochemistry, 1978, 17, 1967.
11. F.W. Wehrli and T. Wirthlin, Interpretation of Carbon-13 NMR Spectra, Heyden and Sons Ltd, London, 1976.
12. T. Nakatsu, S. Ito and T. Kawashima, Heterocycles, 1981, 15, 241.
13. A. Chatterjee, A. Banerjee and F. Bohlmann, Tetrahedron, 1977, 33, 2407.
14. G. Savona, M.P. Paternostro, F. Piozzi, J.R. Hanson, P.B. Hitchcock and S.A. Thomas, J.C.S. Perkin I, 1978, 1080.
15. S.H. Grover and J.B. Stothers, Can. J. Chem., 1974, 52, 870.
16. J.B. Stothers, C.T. Tan and K.C. Teo, Can. J. Chem., 1976, 54, 1211.
17. I. Uchida and K. Kuriyama, Tetrahedron Letters, 1974, 3761.
18. I. Uchida, T. Fujita and E. Fujita, Tetrahedron, 1975, 31, 841.
19. G. Savona, M.P. Paternostro, F. Piozzi, J.R. Hanson, P.B. Hitchcock and S.A. Thomas, J.C.S. Perkin I, 1979, 1915.
20. D.P. Popa and A.M. Reinbold, Khim. Prirodn. Soedin., 1974, 321.
21. P. Joseph-Nathan and E. Diaz, Org. Magn. Reson., 1971, 3, 193.
22. M. Martinez-Ripoll, J. Fayos, B. Rodriguez, M.C. Garcia-Alvarez, G. Savona, F. Piozzi, M. Paternostro and J.R. Hanson, J.C.S. Perkin I, 1981, 1186.
23. D. Rogers, G.G. Ünal, D.J. Williams and S.V. Ley, J.C.S. Chem. Commun., 1979, 97.
24. H. Wagner, R. Seitz, H. Lotter and W. Herz, J. Org. Chem., 1978, 43, 3339.
25. H. Kreigh and F.S. Richardson, J.C.S. Perkin II, 1976, 1674.
26. A.F. Beecham, Tetrahedron, 1972, 28, 5543.
27. W. Herz, A.M. Pilotti, A.Ch. Söderholm, I.K. Shuhama and W. Vichnewski, J. Org. Chem., 1977, 42, 3913.

Received, 28th November, 1981