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

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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
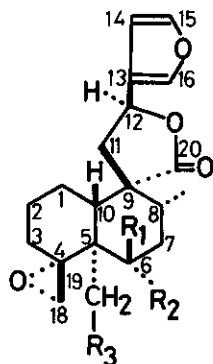
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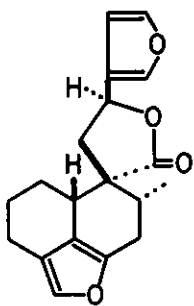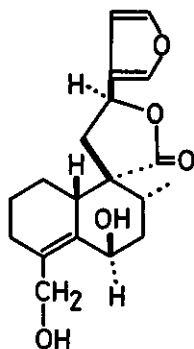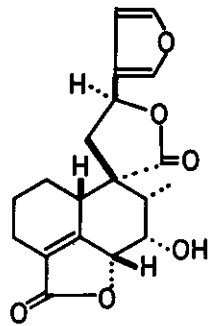
3a R₁=H, R₂=R₃=OAc

$\underline{3a}$ R$_1$=H, R$_2$=R$_3$=OAc

$\underline{10}$ R$_1$=H, R$_2$=OH, R$_3$=OAc

$\underline{11}$ R$_1$=H, R$_2$=OAc, R$_3$=OH
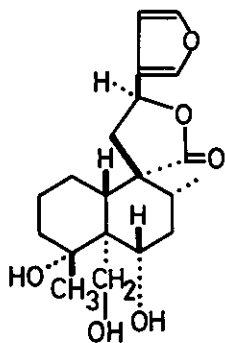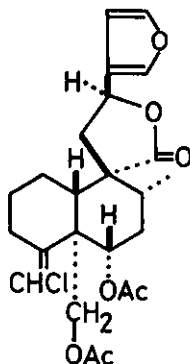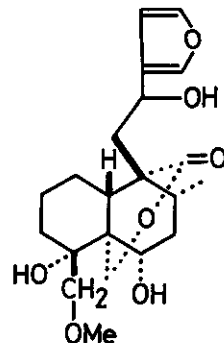
$\underline{3b}$ $\underline{3c}$ $\underline{3d}$
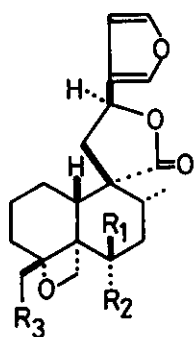
$\underline{4a}$ R$_1$=R$_3$=OH, R$_2$=H

$\underline{4b}$ R$_1$=R$_3$=OAc, R$_2$=H

$\underline{4c}$ R$_1$,R$_2$=O, R$_3$=OAc
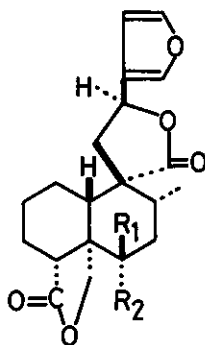
$\underline{6}$ R$_1$=H, R$_2$=OH

$\underline{7}$ R$_1$,R$_2$=O
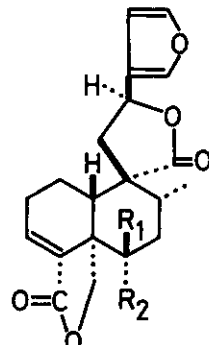
$\underline{8}$ R$_1$=H, R$_2$=OH

$\underline{9}$ 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._ orienta-
tion 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 $H-7_{ax}$ with respect to
that of its $H-7_{eq}$ partner provided that ring B assumes chair conformation. Applica-
tion 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 magni-
tude of vicinal couplings of C-7 methylene protons. For most compounds investi-
gated, 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 $^{13}C-\{^{1}H\}$ double resonance experiments were performed in order to elim-
inate ambiguities in the assignment of resonances due to carbon atoms of the same
off-resonance multiplicity. Even in the most recent publications on furanoid di-
terpenes (see _eg_. ref. 12), resonances at 140 and 144 ppm are attributed alterna-
tively to furan ring carbons C-15 and C-16. In order to eliminate this ambigu-
ity, 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 fol-
lowing 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 vic-
inal coupling observable in the 7-hydroxyl molecule 5, is not specific for the
stereochemistry at C-8. This stereochemical detail, however, can be readily in-
ferred 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 bio-
genetic 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 substit-
uents 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 neg-
ative 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 stereo-
chemistry 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 $\underline{9}$, 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 $\underline{exo}$-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 $\underline{Baccharis}$ $\underline{trimera}$[27] and $\underline{Baccharis}$ $\underline{tricuneata}$[24]) lends support for this conclusion and settles the absolute stereochemistry of $\underline{9}$ 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.

($\underline{1}$) 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$_6$D$_6$): 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$_{eq}$);

($\underline{2}$) 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$_6$D$_6$): 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);

($\underline{3a}$) 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);

(<u>3b</u>) 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,$J_{7eq,8}$=4.0Hz,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);

(<u>3c</u>) 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);

(<u>3d</u>) 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);

(<u>4a</u>) 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 <u>4a</u> (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 un-reacted <u>4a</u> and diacetyl <u>4b</u> 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 <u>4a</u> into <u>4c</u>. 18-O-acetyl derivative (10 mg) dissolved in dry dichloromethane (1 ml) was treated with pyridine-Cr$_2$O$_3$ complex (43 mg) at room temp for 24 h. The product <u>4c</u> 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$_3$CN): 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$_3$CN): 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), δ H ppm (C$_6$D$_6$): 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$_2$O$_3$ 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$_3$CN):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};

(<u>9</u>) CD (CH$_3$CN): λ,nm $\genfrac{}{}{0pt}{}{(\Delta\varepsilon)}{([\theta])}$: 299.5 $\genfrac{}{}{0pt}{}{(-1.36)}{(-4490)}$, 247 $\genfrac{}{}{0pt}{}{(-3.85)}{(-12700)}$, 220.5 $\genfrac{}{}{0pt}{}{(+8.24)}{(+27200)}$, 196

(-107)
(-35300);

(<u>10</u>) δ H 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), δ H ppm (C$_6$D$_6$): 2.85 (1H,m,$J_{7ax,8}$=11.5Hz,H-7_{ax});

(<u>11</u>) δ H 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);

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REFERENCES

1. P.Y. Malakov, G.Y. Papanov and N.M. Mollov, <u>Tetrahedron Letters</u>, 1978, 2025.

2. P.Y. Malakov, G.Y. Papanov, N.M. Mollov and S.L. Spassov, <u>Z. Naturforsch.</u>,
   1978, 33b, 789.

3. P.Y. Malakov, G.Y. Papanov, N.M. Mollov and S.L. Spassov, <u>Z. Naturforsch.</u>,
   1978, 33b, 1142.

4. D.P. Popa and A.M. Reinbold, <u>Khim. Prirodn. Soedin.</u>, 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.