TRANSANNULAR CYCLIZATION OF THE E,E-GERMACRADIENOLIDE HANPHYLLIN

S. M. Adekenov, N. M. Gafurov, K. M. Turdybekov,
S. V. Lindeman, and Yu. T. Struchkov

The results are reported of the interaction of the trans,trans-germacradieno-
lide hanphyllin with m-chloroperbenzoic acid and with 50% sulfuric acid.
This leads to a cyclization reaction with the formation of eudesmanolides:
1β-hydroxy-3-oxo-1,4,5,7α(H),6β(H)-eudesm-11(13)-en-6,12-olide, ridentin B,
and 3β-hydroxy-5,7α(H),6β(H)-eudesma-4(15),11(13)-dien-6,12-olide; and also
products of the opening of the lactone ring as a consequence of transester-
ification. The structures of the compounds obtained are discussed on the
basis of spectral results (IR, PMR, and mass spectra) and of x-ray structural
analysis.

Germacranolides and their epoxy derivatives are considered to be biogenetic precursors
of sesquiterpene lactones of other skeletal types and, in particular, of the eudesmanolides
and guaianolides [1]. Starting from this hypothesis, a series of studies has been made
on the biomimetic transformation of germacranolides based on transannular cyclization [2-
4]. This cyclization is stereospecific, being controlled by the conformation of the ini-
tial molecule.

It must be mentioned that germacranolides are of particular interest among the vari-
ous skeletal types of sesquiterpene lactones from the point of view of the conformational
flexibility of the molecules of this group of compounds. The presence in the majority of
germacranolides of two intracyclic double bonds, of methyl groups at the C4 and C10 atoms,
and of hydroxy and ester groups largely determines the number of possible conformations
of the ten-membered ring. In the crystal structures of the nonlinear trans-linked E,E-
germacranolides only the chair-chair conformation is realized for the ten-membered ring.
Such a conformation is observed, in particular, for the molecule of hanphyllin (1) — a
characteristic component of the epigeal part of Handelia trichophylla, Heimerl, Artemisia
ashurbaevii Krasch, Tanacetum parthenium (L) Sch. Bip., and Achillea nobilis, L [5-8]. The
task of the present work was to study the cyclization of hanphyllin (1) using various re-
agents.

The interaction of hanphyllin (1) with m-chloroperbenzoic acid (MCPBA) in chloroform
at 0°C for 15 min gave a mixture of two substances, with R_f 0.45 and 0.25. By the chromato-
graphic separation of this mixture on a column of silica gel the two individual components
(2) and (3) were isolated with yields of 40 and 47.4%, respectively. The compounds (2)
and (3) obtained were crystalline substances with the same elementary composition, corre-
sponding to the formula $C_{15}H_{20}O_4$, but having different melting points and optical rotations.

The PMR spectrum of substance (2) with mp 187-189°C (Table 1) showed the signals of
the protons of a secondary methyl group as a doublet at 1.23 ppm (3 H, SSCC 8 Hz) and of
a tertiary methyl group as a singlet at 1.13 ppm (3 H), and also the signals of a gem-
hydroxylic proton as a doublet of doublets at 3.70 ppm (1 H, SSCCs 10, 6.5, and 4 Hz), of
a lactone proton at C6 in the form of a doublet of doublets at 4.04 ppm (1 H, SSCC 11.2
and 10.5 Hz), and of the protons of an exomethylene group at a lactone ring in the form
of two doublets at 5.43 and 6.08 ppm (each 1 H, SSCC 3 Hz). The presence of a hydroxy group
was confirmed by the appearance in the IR spectrum of an absorption band in the 3530 cm^{-1}
region, while an absorption band at 1740 cm^{-1} characterized a keto group.

TABLE 1. Chemical Shifts (ppm) and Spin-Spin Coupling Constants (in parentheses, Hz) for Hanphyllin and Its Derivatives (200.13 MHz; CDCl₃; C₅D₅N; δ scale)

Compound No.	Me-4	Me-10	H-1	H-2a	H-2b	H-3	H-4	H-5	H-6	H-13a	H-13b	H-15a	H-15b	Other protons
1	1,68 br.s	1,43 s	5,24 br.d (3)	—	—	4,90 br.dd (10; 5)	—	4,86 br.d (8,5)	4,12 q (10; 8,5)	5,52 d (3,5)	6,26 d (3,5)	—	—	—
2	1,23 d (8,0)	1,13 s	3,0 ddd (10; 6,5 4,0)	2,63 ddd (16;6,5;1)	2,64 dd (16; 10)	—	2,75 dd (3,0; 6,5; 1)	1,90 dd (11,2; 6,5)	4,04 dd (11,2;10,5)	5,43 d (3)	6,08 d (3,2)	—	—	—OH: 1,97 d (4,5)
3		1,05 s	3,79 br.dd (11,5;4)	2,32 m	2,63 m	4,40 br.dd (11,5)	—	2,23 br.d	4,23 tr (11)	5,35 d (3)	6,14 d (3)	5,26 d (1)	5,92 d (1)	—
4		0,63 s	—	—	—	4,0 br.dd (10; 6)	—	2,18 br.d (11)	3,98 tr (11)	5,39 d (3)	6,06 d (3)	4,95 br.s	5,24 br.s	—
5	1,31 s	0,99 s	—	—	—	3,80 dd (11,5; 5)	—	1,45 d (10,5)	4,16 br.tr (10)	5,66 br.s	6,21 br.s	—	—	2 CH₃O: 3,33 s and 3,73 s
6	1,26 s	0,94 s	—	—	—	3,5? dd (11,5; 4,5)	—	1,35 d (10,5)	4,10 br.tr (10)	5,71 br.s	6,27 br.s	—	—	CH₃O: 3,75 s

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The signal of the lactone proton in the PMR spectrum was split into a doublet of doublets through interaction with the two vicinal hydrogen atoms located at C5 and C7, the large coupling constants (11.2 and 10.5 Hz) showing that the dihedral angles $H-C_5-C_6-H$ and $H-C_6-C_7-H$ were greater than 120°C [9]. This gave grounds for considering that a trans-condensed eudesmanolide with the trans- linkage of the lactone ring in the C_6-C_7 position had been obtained. The formation of the trans-eudesmanolide (2) was confirmed by the presence in the PMR spectrum of the signal of an angular methyl group at C10 which was shifted downfield somewhat (s, 1.13 ppm) in comparison with its usual range of 0.6-0.9 ppm [9]. Such a shift may be caused by the descreening influence of the β-oriented hydroxy group at C1. This was confirmed by the presence of the signals of the gem-hydroxylic proton H1 in the PMR spectrum that was split into a broadened triplet through interaction with the equatorial protons in the C2 position.

A comparison of the spectral characteristics that we had obtained for (2) with literature information [10, 11] permitted the assumption that the molecule under study was structurally analogous to the eudesmanolide artecalin (7), isolated from Artemisia tripartita ssp. rupicola. However, differences in the physicochemical constants and in the C4—Me and H4 signals in the PMR spectra showed that these compounds were epimeric. Thus, in the PMR spectrum of (2) a doublet of doublets at 1.90 ppm was assigned to H-5, and its SSCCS of 11.2 and 6.5 Hz characterized its interaction with H-6 and H-4, respectively. The SSCC between H-5 and H-4 was less than 10 Hz, which showed their cis arrangement. Since the lactonic proton, H6, was β-oriented, H5 and H4 had the α-orientation, so that compound (2) was an epimer of artecalin with respect to the methyl group at C4.

The results of the investigations performed enabled us to conclude that lactone (2) had the structure of 1β-hydroxy-3-oxo-1,4,5,7α(H),6β(H)-eudesm-11(13)-en-6,12-olide.

The IR spectrum of substance (3), with mp 188-190°C, had absorption bands characteristic for hydroxy groups (strong band at 3400 cm^{-1}) and for a double bond (1680 and 1650 cm^{-1}). The PMR spectrum (see Table 1) contained the signals of an angular methyl group at C10: a singlet at 1.05 ppm (3H) that was shifted somewhat downfield, just as in the spectrum of lactone (2). In addition, the signals of two gem-hydroxylic protons were observed: the first in the form of a broadened doublet of doublets at 3.79 ppm (1 H, SSCCs 11.5 and 4 Hz), and the second at 4.40 ppm (1 H, doublet of doublets, SSCCs 11 and 5 Hz), and also the signals of a lactone proton, H6, as a sharp triplet at 4.23 ppm (1 H, SSCC 11 Hz), two doublet signals with their centers at 5.26 and 5.92 ppm (each 1 H, with SSCCs of 1 Hz), which are characteristic for the protons of an exomethylene group at C4, and the protons of an exomethylene group conjugated with the carbonyl of a γ-lactone in the form of doublets at 5.43 and 6.02 ppm (each 1 H, SSCC 3 H).

In its physicochemical constants and spectral characteristics, substance (3) proved to be identical with the eudesmanolide ridentin B, which has been isolated from Artemisia tripartita ssp. rupicola [12].

The formation of the 1β-oxygenated eudesmanolides (2) and (3) is shown in the scheme (see scheme on following page).

The formation of epi-artecalin (2) and of ridentin B (3) in this reaction showed that the process is stereospecific and is controlled by the conformation of the hanphyllin molecule (1). Furthermore, the results obtained permit the assumption that compounds of the type of hanphyllin (1) may be biogenetic precursors of the 3-hydroxyeudesmanolides.

The interaction of hanphyllin (1) with 50% sulfuric acid in methanol at 40°C for 10 min formed a mixture of three substances with R_f 0.67, 0.52, and 0.37. Separation of this mixture on a column of silica gel led to the isolation of three individual components, (4), (5), and (6), with yields of 25, 15, and 50%, respectively (see scheme). The derivatives obtained were colorless crystalline substances with different elementary compositions and physicochemical constants.

Substance (4) had the composition $C_{15}H_{20}O_3$, mp 175-177°C (chloroform). Its IR spectrum showed the presence of a hydroxy group (3500 cm^{-1}) and of double bonds (1640 cm^{-1}) in its molecule. Its PMR spectrum (Table 1) contained the signals of an angular methyl group in the form of a singlet at 0.63 ppm (3 H), and of a gem-hydroxylic proton at C3 in the form of a broadened doublet of doublets at 4.0 ppm (1 H, SSCCs 10 and 6 Hz). In addition, the signals were observed of an exomethylene group in the form of two broadened singlets in the 4.95 and 5.24 ppm regions, while the appearance of the signal of a lactone
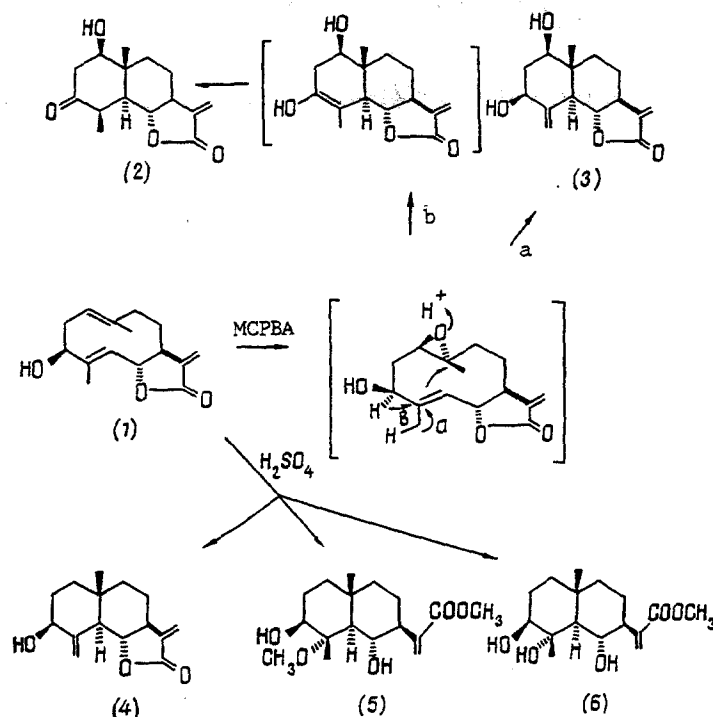
Formation of eudesmanolides from hanphyllin (1).

proton at C6 in the form of sharp triplet at 3.98 ppm (1 H SSCC 11 Hz) showed that this molecule was a eudesmanolide with the trans-linkage of the lactone ring in the C6-C7 position. The results obtained permitted us to propose for (4) the structure of 3β-hydroxy-5,7α(H),6β(H)-eudesma-4(15),11(13)-dien-6,12-olide.

Substance (5), $C_{17}H_{28}O_5$, mp 113-114°C. In its PMR spectrum (see Table 1) were observed the signal of the angular methyl group at C10 that is characteristic for the eudesmanolide type of skeleton, in the form of a singlet at 0.99 ppm (3 H), and that of a methyl geminal to a heteroatom, in the form of a singlet at 1.31 ppm (3 H), and also the signals of two methoxy groups, as singlets at 3.33 and 3.73 ppm (each 3 H). In addition, the following signals were detected: of a gem-hydroxylic proton at C-3 — a doublet of doublets at 3.80 ppm (1 H, SSCCs 11.5 and 5 Hz) split through interaction with the protons in the C2 position; of a proton at C-5 — doublet at 1.45 ppm (1 H, SSCC 10.5 Hz); and of gem-hydroxylic proton — broadened triplet at 4.16 ppm (1 H, SSCC 10 Hz); and also the signals of the protons of an exomethylene group in the form of broadened singlets at 5.66 and 6.21 ppm (1 H each).

Analysis of the signals of the exomethylene protons at C13 showed that these protons did not interact with the proton in the C7 position, while the SSCC of the protons of an exomethylene group at a γ-lactone ring usually amounts to 1-3 Hz. What has been stated above was confirmed by the double-resonance spectrum, where suppression of the H7 signals led to a change in the multiplicity only of the signals of the protons in the C6 and C8 positions, with no change in the multiplicity of the signals of the exomethylene protons at the γ-lactone ring, while the suppression of the signals of the exomethylene group did not change the multiplicity of the H7 signal. The absence of coupling constants between the exomethylene protons at C13 and the H7 proton indicated that the dihedral angle between these protons amounted to 90° [9]. A similar deviation of the spin-spin coupling constants of exomethylene protons may arise as a result of the opening of a γ-lactone ring on esterification with methanol, leading to the formation of a methyl ester at C-12 [13, 14].

Thus, the results obtained permitted the conclusion that compound (5) was based on a trans-condensed (5α,10β)-eudesmane carbocycle and was the methyl ester of 3β,6α-dihydroxy-4α-methoxyilicic acid.

The last component (6) had a comparatively low melting point (53-54°C). Its IR spectrum exhibited absorption bands characteristic for hydroxy groups (3550 cm^{-1}) and for a double bond, and also for an ether group [sic] (1080 cm^{-1}).

TABLE 2. Bond Lengths (Å) in the Molecule of
Compound (6)

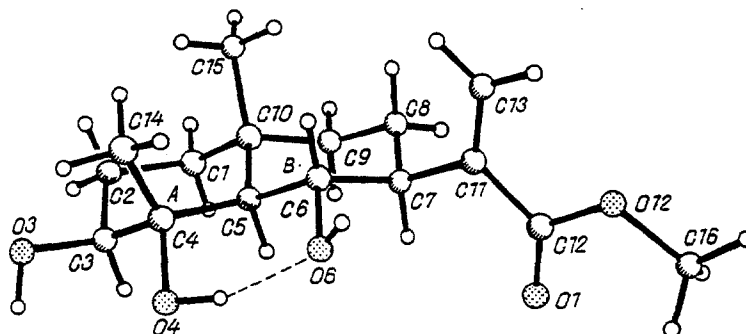| O1—C12	1,209 (9)	C4—C14	1,490 (10)
O3—C3	1,397 (8)	C5—C6	1,523 (7)
O4—C4	1,445 (8)	C5—C10	1,560 (7)
O6—C6	1,453 (6)	C6—C7	1,530 (10)
O12—C12	1,299 (9)	C7—C8	1,539 (8)
O12—C16	1,420 (10	C7—C11	1,504 (7)
C1—C2	1,520 (10)	C8—C9	1,515 (9)
C1—C10	1,519 (9)	C9—C10	1,520 (10)
C2—C3	1,515 (8)	C10—C15	1,520 (10)
C3—C4	1,525 (7)	C11—C12	1,460 (10)
C4—C5	1,548 (8)	C11—C13	1,320 (10)

Fig. 1. Structure of the molecule of compound (6).

To establish the structure and stereochemistry of the molecule of compound (6) we made
an x-ray structural investigation of it. The general shape of the (6) molecule is shown
in Fig. 1. The bond lengths (Table 2) and valence angles have the usual values [15]. We
may note only an appreciable decrease in the O4C4C3 valence angle [102.6(5)°].

The conformations of the six-membered rings, linked in the trans- manner [the torsional
angle H5C5C10C14 being −174(1)°] are somewhat distorted relative to an ideal chair. For
ring A the plane m passing through the C2 and C5 atoms is practically retained (ΔC_s^2 = 1.0°)
and the maximum ΔC_s^3 = 5.4°. In ring B a more uniform asymmetry is observed (ΔC_s^5 = 2.9°
(min.) and ΔC_s^6 = 5.3° (max.). The distortions of the conformations of the six-membered
rings of the eudesmane skeleton are obviously caused by nonvalent repulsion between the
C14 and C15 Me groups (the C14···C15 distance is 3.29 Å) and also by the O4–H···O6 intra-
molecular hydrogen bond, which may also be one of the reasons for the deviations of the
torsional angles in the rings (Table 3).

The O3, O4, and O6 hydroxy groups attached to the main skeleton have the β-, α-, and
α-equatorial orientations, respectively, and the C11 atom also has the β-equatorial orienta-
tion. The C11, C12, C13, O1, and O12 atoms lie in one plane (±0.02 Å) as a consequence
of π–π conjugation. The C16 atom of the methoxy group is also, in fact, present in this
plane (0.03 Å) thanks to p—π conjugation.

. In crystals of compound (6) each molecule forms an intramolecular H-bond O4–H···O6
(O–H 0.88 Å, O···O 2.615 Å, H···O 1.777 Å, angle O–H···O 159.0°), completing a six-membered
ring. Through the pairs of intermolecular H-bonds O3–H···O4 (1 − x, y, 3 − z) (O–H 0.92 Å,
O···O 2.755 Å, H···O 1.87 Å, angle O–H···O 161.5°) dimers are formed about an axis 2, which
are joined into layers perpendicular to the a axis by the H-bonds O6–H...OW (x, y,- 1, z)
(O–H 0.84 Å, O···O 2.82 Å, H···O 2.04 Å, angle O–H···O 152.5°) and OW–H···O1 (x, y, z) (O–H
1.03 Å, O···O 2.851 Å, H···O 1.84 Å, angle O–H···O 165°) (Fig. 2).

Thus, the results given above for the interaction of hanphyllin (1) with 50% sulfuric
acid in methanol show that the acid-catalyzed cyclization of an E,E-germacradienolide to
bicyclic derivatives takes place by the same mechanism as with m-chloroperbenzoic acid —
i.e., through the activation of the more nucleophilic $\Delta^{1(10)}$ double bond, leading to trans-
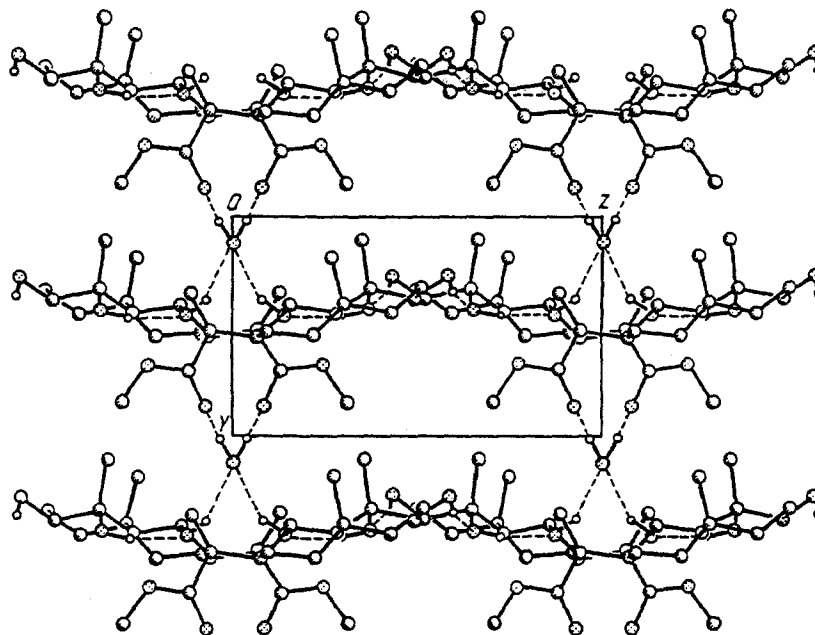condensed eudesmane structures.

Fig. 2. o,y,z projection of the structure of compound (6).

TABLE 3. Torsional Angles (degrees) in the
Rings of Compound (6)

C10C1C2C3	—60 (1)	C10C5C6C7	—62 (1)
C1C2C3C4	58 (1)	C5C6C7C8	56 (1)
C2C3C4C5	—54 (1)	C6C7C8C9	—54 (1)
C3C4C5C10	52 (1)	C7C8C9C10	57 (1)
C4C5C10C1	—53 (1)	C8C9C10C5	—59 (1)
C2C1C10C5	55 (1)	C6C5C10C9	61 (1)

EXPERIMENTAL

The hanphyllin for reaction was isolated from the epigeal part of <u>Achillea nobilis</u>
L. by a method described previously [8].

For column chromatography we used silica gel (100-160 mesh) of type LL (Chemapol) at
a ratio of total material to support of 1:30, and the eluent hexane with increasing (from
0 to 100%) concentrations of ethyl acetate. The individuality of the compounds was checked
by thin-layer chromatography (TLC) on Silufol plates, with revelation by saturated $KMnO_4$
solution. R_f values were measured with ethyl acetate (100%) as eluent.

PMR spectra were taken on a Bruker WP-200 SY instrument (200.13 MHz) for solutions
in $CHCl_3$; chemical shifts are given in ppm (δ scale) relative to TMS, and SSCCs in Hz.

IR spectra were taken on a UR-20 instrument for solutions of the compounds in $CHCl_3$
and in tablets with KBr.

Angles of optical rotation were determined on a CM-2 polarimeter for solutions in $CHCl_3$.

Melting points were determined in a Boëtius instrument.

The elementary compositions of the compounds obtained were determined with the use
of calculation on a Nairi-S computer from the accurate values of the mass numbers of the
molecular ions, which were determined by high-resolution mass spectrometry on a Finnigan
MAT-8200 instrument (direct introduction at 120°C, energy of the ionizing electrons 20 eV).
The mass spectra of the substances under investigation were taken on the same instrument.

1β-Hydroxy-3-oxoeudesm-11(13)-en-6,12-olide (2) and 1,3β-Dihydroxyeudesma-4(15),11(13)-
dien-6,12-olide (3). At 0°C, 200 ml of 66% m-chloroperbenzoic acid was added to a solution
of 200 mg (0.8 mmole) of hanphyllin in 10 ml of chloroform. The mixture was stirred at
the same temperature for 15 min. Then it was washed with a 1 M solution of $NaHCO_3$ (2 ×
10 ml) and with water, and was dried over anhydrous $MgSO_4$ and filtered, and the solvent
was distilled off. The residue (270 mg) was chromatographed on a column with elution

TABLE 4. Coordinates of the Atoms ($\times 10^4$; for H, $\times 10^3$) in the Structure of Compound (6)

Atom	x	y	z
O1	5946 (3)	8670 (0)	9237 (5)
O3	5782 (2)	2696 (12)	15749 (3)
C4	5298 (2)	4279 (13)	13504 (3)
O6	5461 (2)	4483 (12)	11327 (3)
O12	5916 (3)	6765 (12)	7655 (4)
C1	7117 (2)	4415 (17)	14181 (5)
C2	6743 (2)	3240 (17)	15153 (5)
C3	6090 (2)	3758 (15)	14884 (4)
C4	5872 (2)	3208 (14)	13640 (4)
C5	6273 (2)	4366 (13)	12736 (4)
C6	6092 (2)	4036 (13)	11456 (4)
C7	6419 (2)	5509 (14)	10556 (4)
C8	7096 (3)	5272 (17)	10844 (5)
C9	7269 (3)	5483 (18)	12129 (6)
C10	6952 (2)	3959 (15)	12910 (5)
C11	6251 (3)	5244 (13)	9382 (5)
C12	6019 (3)	7040 (13)	8769 (6)
C13	6289 (3)	3506 (15)	8312 (6)
C14	5783 (3)	1050 (15)	13446 (6)
C15	7158 (3)	1827 (16)	12610 (6)
C16	5715 (5)	8461 (19)	6981 (7)
OW	5000 (0)	11215 (15)	10000 (0)
HO3	544 (0)	345 (0)	1586 (0)
HO4	528 (0)	457 (0)	1284 (0)
HO6	534 (0)	379 (0)	1075 (0)
HW	529 (0)	1015 (0)	966 (0)

by hexane-ethyl acetate (1:4), and 84.5 mg (40%) of component (2), with R_f 0.45 (ethyl acetate) was isolated. Colorless crystalline substance with the composition $C_{15}H_{24}O_4$, mp 187-189°C (from ethyl acetate), $[\alpha]_D^{18}$ +46° (c 0.015). IR spectrum (ν_{max}^{KBr} cm^{-1}): 3530, 3000, 2950, 2920, 2890, 1780, 1740, 1620, 1460, 1430, 1400, 1350, 1300, 1280, 1150, 1070, 1000, 980, 880.

Elution of the column with ethyl acetate yielded 100 mg (47.4%) of component (3) with R_f 0.25 (ethyl acetate). Colorless crystalline substance with the composition $C_{15}H_{20}O_4$, mp 188-190°C (from ethyl acetate), $[\alpha]_D^{18}$ +30° (c 0.001). IR spectrum (ν_{max}^{KBr}, cm^{-1}): 3400, 2970, 2880, 1780, 1680, 1650, 1420, 1365, 1320, 1270, 1250, 1160, 1110, 1060, 1050, 1020, 980, 950.

Mass spectrum (m/z, %): 264 (M$^+$; 15.3), 246(9.4), 231(11.3), 217(11), 203(10.5), 189(10.8), 175(21.4), 165(45.4), 149(45), 133(22.7), 119(31.4), 107(32.7), 95(34), 91(35), 81(35), 67(26.6), 55(54), 43(100).

3β-Hydroxyeudesma-4(15),11(13)-dien-6,12-olide (4) and the Methyl Esters (5) and (6). At room temperature (18°C, a 50% solution of sulfuric acid* was added to a solution of 200 mg (0.8 mmole) of hanphyllin (1) in 10 ml of methanol. The mixture was stirred at 40°C for 10 min. Then, after cooling, the reaction product was extracted with chloroform (3 × 20 ml), the chloroform extract was washed with saturated NaHCO$_3$ solution (3 × 10 ml), dried over MgSO$_4$, and filtered, and the solvent was distilled off. The residue (250 mg) was chromatographed on a column containing 5 g of silica gel. Elution of the column with hexane-ethyl acetate (1:1) led to the isolation of 50 mg (25%) of substance (4) with R_f 0.67 (ethyl acetate). Colorless crystalline substance with the composition $C_{15}H_{20}O_3$, mp 175-177°C [from hexane-ethyl acetate (1:1)], $[\alpha]_D^{18}$ +106° (c 0.002). IR spectrum (ν_{max}, cm^{-1}): 3500, 3000, 2950, 2920, 2890, 1780, 1640, 1460, 1430, 1400, 1350, 1300, 1280, 1150, 1070, 1000, 980, 870.

By eluting the column with hexane-ethyl acetate (2:3) we isolated the colorless crystalline substance (5) with the composition $C_{17}H_{28}O_5$, mp 113-114°C [from hexane-ether (1:1)], $[\alpha]_D^{18}$ +40° (c 0.001), R_f 0.52 (ethyl acetate). Yield 34 mg (15%). IR spectrum (ν_{max}, cm^{-1}): 3000, 2950, 2920, 2890, 1760, 1630, 1470, 1400, 1300, 1280, 1150, 1080, 1050, 1010, 980, 870, 810.

Elution of the column with hexane-ethyl acetate (1:4) yielded the colorless crystalline substance (6) with the composition $C_{16}H_{26}O_5$, mp 53-54°C [from hexane-ether (1:1)], $[\alpha]_D^{18}$

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*Amount not given — Translator.

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−58° (c 0.01), R_f 0.37 (ethyl acetate). Yield 120 mg (50%). IR spectrum (ν_{max}, cm^{-1}):
3550, 3000, 2950, 2920, 2890, 1780, 1640, 1460, 1430, 1400, 1350, 1300, 1280, 1150, 1080,
1000, 980, 870, 810.

Mass spectrum (m/z, %): 298 M$^+$, 280 M$^+$ − H$_2$O (12.6), 262(24.4), 251(21.4), 230(20.5),
219(24.8), 205(13.1), 191(13), 173(9.6), 161(17.4), 153(22.7), 147(20), 135(18), 119(19),
109(26), 95(34.5), 87(15.3), 81(31), 69(23), 59(11), 55(29), 43(100).

X-Ray Structural Study of Compound (6). The cell parameters and the intensities of
2662 reflections were measured at 20°C on a Siemens P3/PS automatic four-circle diffractom-
eter (λ MoK$_\alpha$, graphite monochromator, θ/2θ scanning, 2θ < 60°). The crystals were rhom-
bic, a = 22.469(6), b = 6.574(2), c = 11.385(3) Å, β = 98.80(2)°, V = 1681 Å^3, M = 307.4,
d_{calc} = 1.214 g/cm^3, Z = 4, (C$_{16}$H$_{26}$O$_5$)·0.5 H$_2$O, space group C2.

In the calculations we used 1383 independent reflections with I > 3σ. The structure
was interpreted by the direct method and was refined by the full-matrix MLS in the aniso-
tropic approximation for the nonhydrogen atoms. The coordinates of all the H atoms, with
the exception of the hydrogens of the hydroxy groups, were revealed in a difference syn-
thesis and were calculated and fixed. The final residuals were R = 0.063 and R$_w$ = 0.059.
The coordinates of the atoms are given in Table 4. All the calculations were made on an
IBM PC/AT computer by means of the Siemens SHELXTL packet of programs (PC Version).

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