Synthesis of drim-8(9)-en-7-one, drima-5,8(9)-dien-7-one, and their 11,12-dibromo derivatives from norambreinolide

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A method was elaborated for the synthesis of polyfunctional compounds of the drimane series, *viz*., drim-8(9)-en-7-one, drima-5,8(9)-dien-7-one, and their 11,12-dibromo derivatives, potential intermediates for the synthesis of natural biologically active drimane sesquiterpenoids starting from norambreinolide. The key intermediate of the above drimane compounds is methyl 7-oxo-11-homodrim-8(9)-en-12-oate, prepared by electrochemical oxidation of a mixture of isomeric methyl bicyclohomofarnesenoates obtained from norambreinolide.

Key words: norambreinolide, sesquiterpenoids of drimane series, electrochemical oxidation, bromination; X-ray analysis.

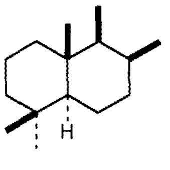
The ever-growing interest in drimane sesquiterpenoids, having the carbon skeleton of drimane (**1**) as a base, is principally explained by the existence of diverse biological activity in a great number of them.[1]

Several total syntheses of drimanes have been performed.[2] However, all of them have common drawbacks: they are multistep and afford racemic products, while as a rule, only one of the enantiomeric forms is biologically active.

Hence, a partial synthesis of drimanes in an optically active form from accessible higher terpenoids, primarily diterpenoids, seems more attractive. For this purpose, bicyclic, as well as tricyclic diterpenoids were used.[2] Apparently, the former are more appropriate, because in that case, the synthesis is reduced to shortening their side carbon chain. In recent years, drimanes were synthesized from accessible labdanoids, such as manool (**2**),[3] hispanolone (**3**),[4] sclareol (**4**),[5] zamoranic acid (**5**),[6] *etc.*[7,8]

In the present paper, a synthesis of drim-8(9)-en-7-one (**6**) and some related compounds from norambreinolide (**7**), a commercially available product of the cleavage of sclareol **4** (see Ref. 9), is reported.

It should be stressed that due to the position of the C=C and C=O bonds in ketone **6** which activate the C(6), C(11), and C(12) atoms this compound is a valuable chiron for important polyfunctional biologically active natural drimane derivatives. It can be also noted that ketone **6** is of interest as a fragrant substance.[10] Previously, drim-8(9)-en-7-one has been isolated from tobacco; simultaneously, its synthesis has been performed.[11]



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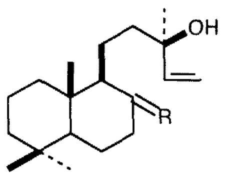
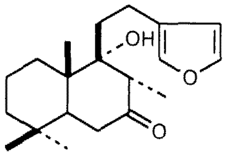


2, 4

R = CH$_2$ (**2**), Me, OH (**4**)



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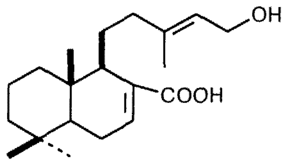

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We have realized[12] shorter and simpler synthesis of this compound starting from norambreinolide **7**. A mixture of isomeric esters **8**—**10** prepared from **7** as described previously[13] was oxidized with $K_2Cr_2O_7$ in AcOH giving oxo ester **11**. The product of saponification of the latter, oxo acid **12**, was decarboxylated to form ketone **6** (Scheme 1). However, the oxidation of a mixture of esters **8**—**10** to oxo ester **11** proceeds in low yield (*ca.* 40 %). Our attempts to improve it by varying oxidants and reaction conditions were unsuccessful.[12]

The yield of compound **11** could be increased by performing the electrochemical oxidation of a mixture of esters **8**—**10**. The reaction was carried out in an undivided cell equipped with graphite electrodes in methanol in the presence of $LiClO_4$ as an electrolyte.

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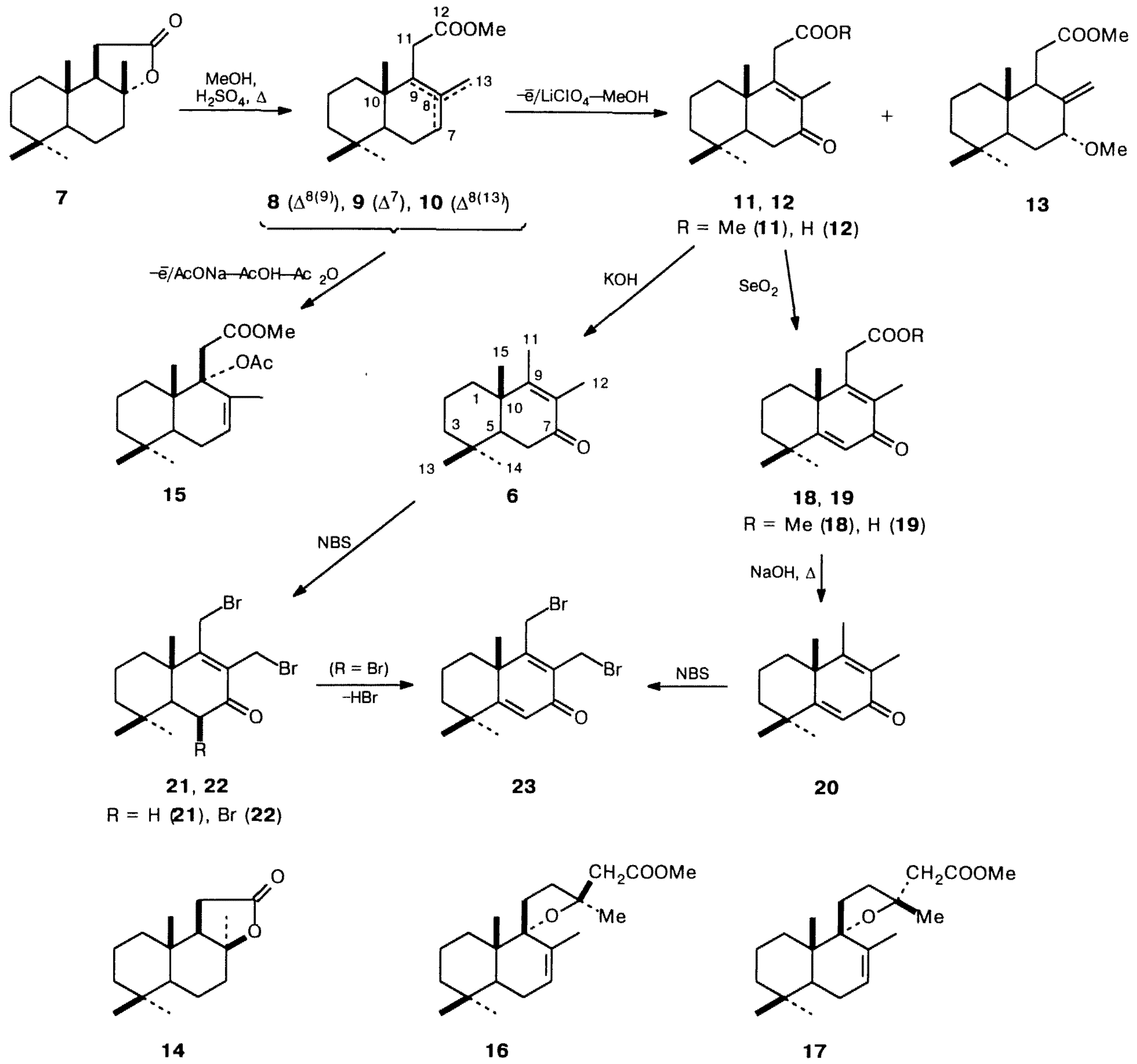
Scheme 1

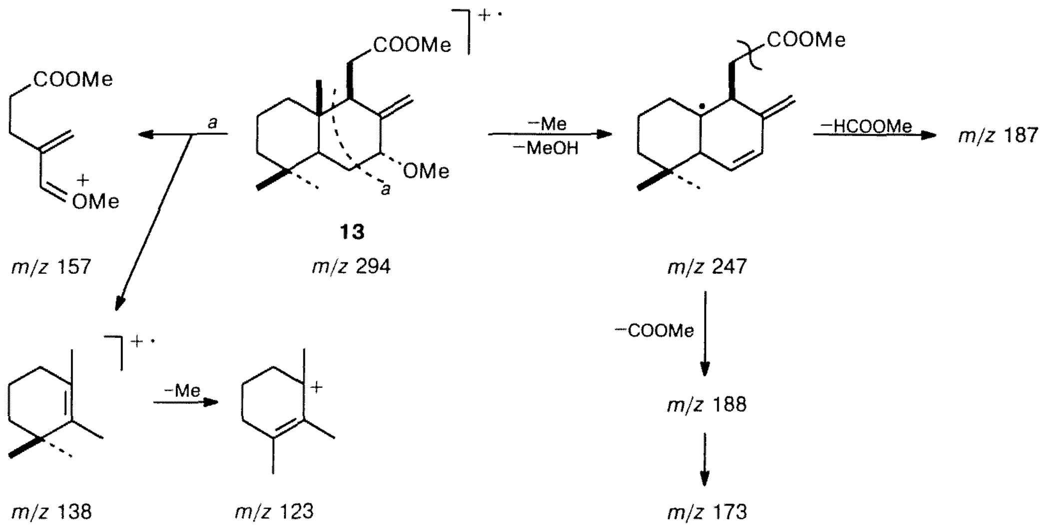


The method was found to be convenient, ecologically pure, and it provided an appropriate yield of oxo ester **11** (63 %). The reaction product was a mixture of at least five compounds, two of them (predominant products) were isolated by chromatography on a column with SiO_2. The major product, oxo ester **11**, was identified by comparison with an authentic sample.[12] Along with **11**, a small amount (*ca.* 10 %) of a less polar compound, methyl 7α-methoxy-11-homodrim-8(13)-en-12-oate (**13**) was isolated; its structure was established on the basis of spectral data. Its IR spectrum exhibited absorption bands of the ester and methoxyl groups and the exocyclic double bond. In the ^1H NMR spectrum of compound **13**, singlet three-proton signals of three tertiary methyl, methoxyl, and ester methyl groups; the doublet (2 H) of exomethylene double bond; the triplet signal of the proton at the C(7) atom; the doublet of doublets of the proton at C(9), and the signals (ddd) of the C(11)—CH_2 group were present. The shape of the signal of HC(7) and its broadening ($W_{1/2}$ = 7.2 Hz) indicate an equatorial position of this proton, and, hence, an axial configuration of the methoxyl group.

The structure of methoxy ester **13** was also confirmed by its mass spectrum. The most possible fragmentation pathways are presented in Experimental and in Scheme 2.

The yield of oxo ester **11** basically depends on the content of isomer **8** with the tetrasubstituted double bond in the mixture of esters **8**—**10**. The mixture obtained by refluxing norambreinolide **7** with conc. H_2SO_4

Scheme 2



in methanol for 96 h[13] contains 66 % of ester **8**, 33 % of isomer **9**, and trace amount of ester **10** (GLC data).

Compounds **8** and **9** were isolated in individual states and were oxidized separately. In oxidation of ester **8**, the yield of oxo ester **11** was 80 %. The oxidation of ester **9** under the same conditions afforded a complex mixture of products, in which four components were predominant; two of them, according to TLC, were identical to compounds **11** and **13**.

Attempts to increase the content of isomer **8** in a mixture of esters **8**—**10** by refluxing with I_2, *p*-TsOH, or KU-23 cation exchanger in benzene were unsuccessful. In the reaction of transesterification—dehydration of norambreinolide **7** in ethanol, the yield of the ester mixture decreased due to formation of 8-epinorambreinolide (**14**).

It should be stressed that in the preparative synthesis of ketone **6**, the process was significantly simplified, because the chromatographic isolation of oxo ester **11** could be omitted: the product of electrochemical oxidation was saponified (simultaneously, oxo acid **12** was decarboxylated), separated into acidic and neutral parts, and the latter (individual ketone **6**) was purified by crystallization.

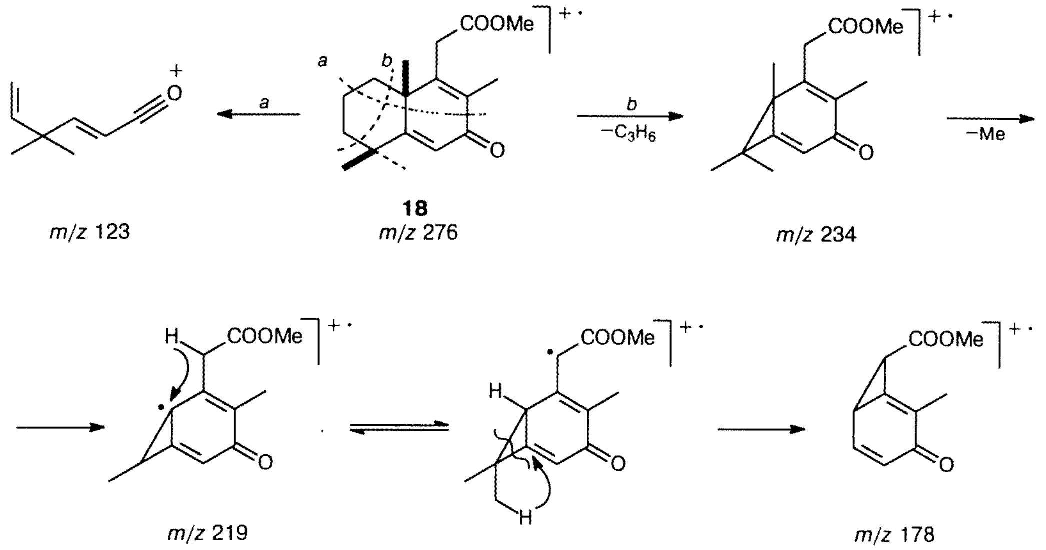
It should be also noted that the electrochemical oxidation of esters **8**—**10** depends significantly on the reaction conditions, in particular, on the supporting electrolyte and the solvent. In most cases studied by us, the reaction products were complex mixtures of compounds. The reaction proceeded more definitely in the presence of AcONa in an AcOH—Ac_2O (5 : 1) mixture. In this case, methyl 9α-acetoxy-11-homodrim-7-en-12-oate (**15**) (yield 51 %) was the major reaction product (see Scheme 1); the structure of **15** was assigned from the spectral data. In its IR spectrum, the absorption bands characteristic of a trisubstituted double bond and two ester groups are present, one of them being acetate. In the ^1H NMR spectrum of compound **15**, three-proton singlet signals of three tertiary methyl groups, the methyl group at the double bond, the ester and acetoxyl methyl groups, and the doublet (1 H) of the vinylic proton at C(7) are present. The acetoxyl group at the C(9) atom has an axial configuration that is unequivocally followed from the comparison of the chemical shifts of the tertiary methyl groups at C(4) and C(9) atoms of **15** and methyl esters of grindelic acid (**16**) and its 13-epimer (**17**).[14]

The reaction of oxo ester **11** with SeO_2 in dioxane results in its dehydrogenation affording diene ester **18** (yield 93 %). In the IR spectrum of the latter, along with the absorption bands of the ester group, the maxima characteristic of diene fragment (at 1605, 1625, and 1650 cm^{-1}) are observed, and in the ^1H NMR spectrum of **18**, the signals of protons of five methyl groups, the methylene $C(11)H_2$ group and the vinylic proton at C(6) are present. The structure of **18** was also confirmed by its mass spectrum, in which *m/z* 276 $[M]^+$, 236, 219, 178, and 123 are the most abundant ions (their possible formation is presented in Scheme 3).

Alkaline saponification of oxo ester **18** affords oxo acid **19**, which is more stable than oxo acid **12**; **19** is not decarboxylated spontaneously at ambient temperature. It decomposes on heating (200 °C) or alkaline saponification in ethylene glycol to form dienone **20** (yield 80 %). In its IR spectrum, the bands characteristic of the diene structure are observed, and in the ^1H NMR spectrum, the signals of five methyl groups, two of them are bonded with the trigonal C atoms, and of the vinylic proton at C(6) are present. The strong deshielding of methyl groups at the C(4) and C(10) atoms should be noted.

Ketone **6** easily reacts with *N*-bromosuccinimide when refluxed in CCl_4 for 2 h, giving 11,12-dibromodrim-8(9)-en-7-one (**21**) in 90 % yield; its structure was established on the basis of spectral data. The

Scheme 3



absorption bands in its IR spectrum are characteristic of C—Br bonds and enone groups. In the ^1H NMR spectrum, the signals of three methyl groups at the quaternary C atoms and of two AB spin systems belonging to the CH_2Br groups are observed.

The presence of the latter is also confirmed by the ^{13}C NMR data (see Experimental). The final proof of the structure of dibromoketone **21** was made by X-ray analysis (Fig. 1). According to the X-ray analysis data, the cyclohexane ring *A* in compound **21** has a chair conformation. Coplanarity of the planar fragment C(2)C(3)C(5)C(10) is within the 0.01 Å interval, the deviations of the C(1) and C(4) atoms from the plane are −0.79 and 0.64 Å, respectively. The conformation of cyclohexenone ring *B* can be considered as a half-chair.

In the planar fragment C(5)C(7)C(8)C(10), the coplanarity of which is in the 0.1 Å interval, the deviations of the C(6) and C(9) atoms are 0.63 and −0.10 Å, respectively; the C(8)—C(9) bond is a double bond, and its length is 1.31 Å. The Br atoms are located at different sides of the plane of the double bond at distances of −1.83 Å [Br(1)] and 1.79 Å [Br(2)]. A slight deviation of the lengths of the C—C bonds from their standard values, and also a deviation of the values of the endocyclic angles in the *A* and *B* rings (Table 1), can be explained by insufficient quality of the monocrystals, which prevented us from obtaining a large number of F_{exp}.

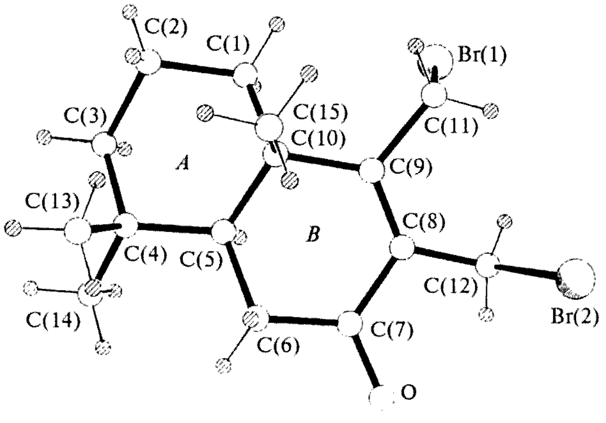


Fig. 1. Molecular structure of α,β-unsaturated dibromoketone **21**.

For a longer reaction time, the reaction of ketone **6** with *N*-bromosuccinimide, along with the major product **21**, affords two minor products: tribromoketone **22** and dibromodienone **23**, the structure of which follows from their spectral data. In the IR spectrum of compound **22**, the absorption bands characteristic of the C—Br bonds and the conjugated carbonyl group were observed. In its ^1H NMR spectrum, the signals of three tertiary methyl groups, two AB spin systems of two CH_2Br groups and the doublet signal of the proton at the saturated C atom, which is connected with the third Br atom [C(6)], are present. According to the elemental analysis data, the molecule of the compound studied contains three Br atoms. The Br at C(6) is axial, as can be judged from the *J* value for the protons at C(5) and C(6) (*J* = 3 Hz). The strong deshielding of the methyl group at C(10) and the axial methyl group at C(4) is in accord with this assumption. Tribromoketone **22** is labile and under the reaction conditions or on a short storage transforms to dibromoketone **23**, which was also obtained by interaction of dienone **20** with *N*-bromosuccinimide. In the IR spectrum of compound **20**, the absorption bands characteristic of the dienone fragment and Br atoms were observed, and in the ^1H NMR spectrum the signals of three tertiary methyl groups, two

Table 1. Bond lengths (*d*) and bond angles (ω) in molecules of **21** and **23**

Bond	*d*/Å	
	21	**23**
Br(1)—C(11)	1.97(2)	1.97(1)
Br(2)—C(12)	1.97(3)	1.98(1)
O—C(7)	1.26(4)	1.24(2)
C(1)—C(2)	1.54(4)	1.55(2)
C(1)—C(10)	1.52(4)	1.55(2)
C(2)—C(3)	1.63(5)	1.51(2)
C(3)—C(4)	1.53(5)	1.50(2)
C(4)—C(5)	1.53(4)	1.55(2)
C(4)—C(13)	1.53(4)	1.54(2)
C(4)—C(14)	1.47(4)	1.56(2)
C(5)—C(6)	1.56(4)	1.33(2)
C(5)—C(10)	1.51(4)	1.52(2)
C(6)—C(7)	1.52(4)	1.47(2)
C(7)—C(8)	1.46(4)	1.48(2)
C(8)—C(9)	1.31(4)	1.31(2)
C(8)—C(12)	1.47(3)	1.53(2)
C(9)—C(10)	1.53(4)	1.57(2)
C(9)—C(11)	1.53(3)	1.49(2)
C(10)—C(15)	1.68(3)	1.56(2)

Angle	ω/deg	
	21	**23**
C(2)—C(1)—C(10)	111.0(23)	110.8(11)
C(1)—C(2)—C(3)	106.7(26)	108.4(11)
C(2)—C(3)—C(4)	109.6(26)	113.7(11)
C(3)—C(4)—C(5)	109.9(23)	110.7(10)
C(3)—C(4)—C(13)	110.7(24)	108.5(10)
C(3)—C(4)—C(14)	108.4(24)	111.7(11)
C(5)—C(4)—C(13)	110.2(22)	109.8(10)
C(5)—C(4)—C(14)	112.1(22)	109.5(10)
C(13)—C(4)—C(14)	105.2(22)	106.3(10)
C(4)—C(5)—C(6)	113.5(22)	120.0(10)
C(4)—C(5)—C(10)	118.3(22)	118.1(9)
C(6)—C(5)—C(10)	111.4(22)	121.7(10)
C(5)—C(6)—C(7)	105.7(22)	121.4(11)
O—C(7)—C(6)	116.7(26)	120.7(11)
O—C(7)—C(8)	122.0(26)	121.7(11)
C(6)—C(7)—C(8)	120.1(24)	117.5(10)
C(7)—C(8)—C(9)	121.5(23)	120.3(11)
C(7)—C(8)—C(12)	113.5(22)	113.6(10)
C(9)—C(8)—C(12)	124.8(22)	125.7(11)
C(8)—C(9)—C(10)	122.4(22)	122.0(11)
C(8)—C(9)—C(11)	118.5(21)	120.8(11)
C(10)—C(9)—C(11)	118.9(20)	116.7(10)
C(1)—C(10)—C(5)	111.5(22)	111.7(10)
C(1)—C(10)—C(9)	113.3(21)	109.0(10)
C(1)—C(10)—C(15)	105.0(21)	111.6(10)
C(5)—C(10)—C(9)	110.3(21)	111.4(9)
C(5)—C(10)—C(13)	113.2(21)	109.2(9)
C(9)—C(10)—C(15)	102.9(20)	103.4(9)
Br(1)—C(11)—C(9)	109.7(16)	110.0(9)
Br(2)—C(12)—C(8)	111.4(17)	108.7(23)

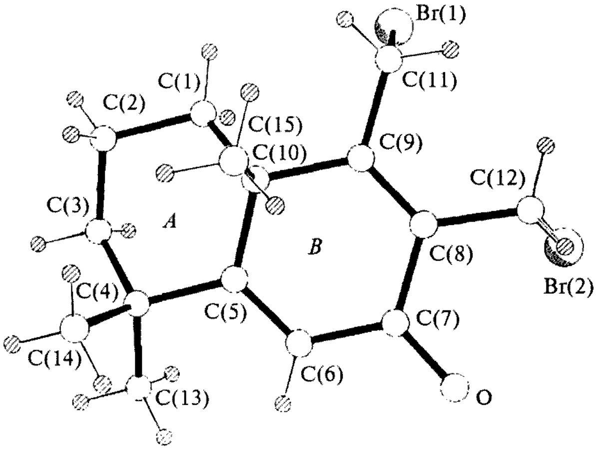


Fig. 2. Molecular structure of dienone **23**.

AB spin systems of CH_2Br groups, and one vinylic proton were present. The structure of dibromodienone **23** was confirmed by X-ray analysis (Fig. 2). The X-ray data indicate that cyclohexane ring *A* in compound **23** has a chair conformation with deviations of the C(1) and C(4) atoms from the plane C(2)C(3)C(5)C(10) (the coplanarity of which is within the 0.01 Å interval) equal to −0.68 Å and 0.56 Å, respectively. In the cyclohexadienone ring *B*, the C(6) and C(9) atoms are removed from the plane fragment C(5)C(7)C(8)C(9), coplanar within the 0.1 Å interval, by 0.08 and 0.14 Å, respectively. Unlike compound **21**, the Br atoms are located at the same side of the C(8)=C(9) double bond plane at the distances 1.86 Å [Br(1)] and 1.72 Å [Br(2)] in dibromoketone **23**.

Thus, starting from the available norambreinolide **7**, the syntheses of reactive, polyfunctional drimanes **6**, **20**, **21**, and **23** were performed; they can serve as starting materials in preparations of biologically active natural drimane sesquiterpenoids.

Experimental

Melting points were determined with a Boetius heating stage. Optical rotations were measured in $CHCl_3$ with SM and Polamat polarimeters. The IR spectra were recorded with a Specord-74 instrument in CCl_4, and the ^1H NMR spectra were measured with Tesla BS-467 (60 MHz) and Bruker WM-250 (250 MHz) spectrometers. The ^{13}C NMR spectra were registered with a Bruker AC-80 (80 MHz) spectrometer. The mass spectra were obtained with an MKh-1320 spectrometer at 70 eV using a direct inlet system. The GLC analyses were carried out with a Chrom-5 chromatograph (flame ionization detector, glass column 3000×3 mm, 5 % SE-30 stationary phase on Chromaton N-AW-DMCS). Column chromatography was performed on L 40/100 μm and L 100/250 μm silica gel. Separation of compounds was monitored by TLC on plates prepared using LS 5/40 μm silica gel containing 13 % of gypsum.

The solutions of compounds in organic solvents were dried with anhydrous Na_2SO_4.

A mixture of methyl $\Delta^{8(9)}$,Δ^7,$\Delta^{8(13)}$-bicyclohomofarnesenoates (8—10) was obtained by refluxing norambreinolide (7) with a solution of conc. H_2SO_4 in MeOH for 96 h[13] (yield 90 %). **Drim-8(9)-en-7-one (6)** was synthesized as described previously.[12]

Electrochemical oxidation of a mixture of esters (8—10)

Methyl 7-oxo-11-homodrim-8(9)-en-12-oate (11) and methyl 7α-methoxy-11-homodrim-8(13)-en-12-oate (13). A mixture of esters **8—10** (1 g, 3.8 mmol) and $LiClO_4$ (0.8 g, 7.4 mmol) in methanol (50 mL) was placed in an undivided cell having graphite electrodes and equipped with a magnetic stirrer and a thermometer. Electricity (7 F) was passed at 25—30 °C (current density 40 mA cm^{-2}, electrolysis time 3 h). After the reaction was completed, the major part of methanol was removed *in vacuo*, and the reaction mixture was diluted with water (50 mL) and extracted with ether (3×30 mL). The ethereal extract was dried and the solvent was removed. The residue (2 g) was chromatographed on a column with SiO_2, using a light petroleum—Et_2O mixture (0 → 2 % Et_2O). Ester **13** (0.1 g, 9 %) was isolated as a colorless oil. Found (%): C, 73.42; H, 9.92. $C_{18}H_{30}O_3$. Calculated (%): C, 73.68; H, 9.96. IR, ν/cm^{-1}: 1150, 1730 (COOMe); 900, 1640, 3075 ($C=CH_2$). ^{1}H NMR ($CDCl_3$), δ: 0.67 (s, 3 H, $C(10)CH_3$); 0.78 and 0.82 (both s, 3 H each, $C(4)(CH_3)_2$); ABX spin system: 2.34 (q, H_A, J_{AB} = 16 Hz, J_{AX} = 11 Hz), 2.50 (q, H_B, J_{BA} = 16 Hz, J_{BX} = 3.5 Hz), 2.66 (q, H_X, J_{XA} = 11 Hz, J_{XB} = 3.5 Hz); 3.16 (s, 3 H, OCH_3); 3.6 (s, 3 H, $COCH_3$); 3.72 (m, 1 H, $C(7)H_{eq}$, J = 3 Hz, $W_{1/2}$ = 7 Hz); 4.73 and 4.95 (both s, 2 H, $C=CH_2$). MS, m/z (I_{rel} (%)): 294 $[M]^+$, 279 $[M-CH_3]$ (3), 262 $[M-CH_3OH]$ (5.6), 247 $[M-CH_3OH-CH_3]$ (8.57), 221 $[M-CH_2COOCH_3]$ (9), 187 (9), 173 (12), 157 (98), 123 (34), and 41 (100). Further elution with the same solvent mixture gave crystalline ester **11** (0.66 g, 63 %), m.p. 101—102 °C (from light petroleum).[12]

Methyl 9α-acetoxy-11-homodrim-7-en-12-oate (15). Under the above conditions of electrolysis, 7.5 F of electricity was passed through a solution of a mixture of esters **8—10** (0.87 g, 3.3 mmol), AcONa (1.5 g, 18.3 mmol), AcOH (50 mL), and Ac_2O (10 mL) at 25—30 °C (reaction time 12 h). After completion of the reaction, the mixture was worked up as usual. The product (2.04 g) was obtained, it contained eight components (TLC data). Chromatography on a column with SiO_2 (eluent: light petroleum—EtOAc, 0 → 2 % EtOAc) afforded crystalline ester **15** (0.59 g, 51 %), m.p. 88.0—89.5 °C (from light petroleum). Found (%): C, 70.96; H, 9.21. $C_{19}H_{30}O_4$. Calculated (%): C, 70.78; H, 9.38. IR, ν/cm^{-1}: 840, 1660 (C=CH); 1160, 1240, 1730 ($COOCH_3$ + OAc). ^{1}H NMR ($CDCl_3$), δ: 0.83 (s, 3 H); 0.86 ($C(CH_3)_2$); 0.92 (s, 3 H, $C(10)CH_3$); 1.59 (s, 3 H, $C(8)CH_3$); 2.08 (s, 3 H, OAc); 3.04 and 3.14 (both d, AB spin system, 2 H, $C(11)H_2$, J = 11 Hz); 3.69 (s, 3 H, $COOCH_3$); 5.18 (d, 1 H, C(7)H, J = 3.5 Hz).

Methyl 7-oxo-11-homodrima-5,8(9)-dien-12-oate (18). SeO_2 (0.095 g, 1 mmol) was added to a solution of oxo ester **11** (0.14 g, 0.5 mmol) in dry dioxane (5 mL), and the mixture was refluxed for 30 min (TLC control). The solution was diluted with water (50 mL) and extracted with ether. The ethereal extract was washed with water, dried, and filtered, and the solvent was removed *in vacuo*. The product (0.12 g) was chromatographed on a column with SiO_2 (2.5 g) (eluent: ether—light petroleum, 2 % Et_2O). Crystalline dienone **18** (0.11 g, 93 %) was obtained, m.p. 114—115 °C (from light petroleum), $[\alpha]_D^{20}$ +50.8° (c 6.31). Found (%): C, 73.99; H, 8.96. $C_{17}H_{25}O_3$. Calculated (%): C, 73.88; H, 8.75. IR, ν/cm^{-1}: 1160, 1740 ($COOCH_3$); 1605, 1625 (C=C); 1360, 1380 ($C(CH_3)_2$). ^{1}H NMR (CCl_4), δ: 1.22 (s, 3 H, $C(4)CH_3$); 1.31 (s, 6 H, $C(4)CH_3$, $C(10)CH_3$); 1.85 (s, 3 H, $C(8)CH_3$); 3.41 (s, $C(11)H_2$); 3.70 (s, 3 H, $COOCH_3$); 6.32 (s, 1 H, C(6)H). MS, m/z (I_{rel} (%)): 276 $[M]^+$, 234 (26), 219 (65), 178 (60), 123 (53), and 43 (100) (see Scheme 3).

7-Oxo-11-homodrima-5,8(9)-dien-12-oic acid (19). Oxo ester **18** (0.12 g, 0.44 mmol) was added to a solution of NaOH (0.2 g) in EtOH (2 mL). The reaction mixture was refluxed for 15 min (TLC control), ethanol was removed *in vacuo*, and the residue was diluted with water and extracted with ether. The ethereal extract was washed with water, dried, filtered, and ether was removed. Crystalline acid **19** (0.12 g) was obtained, m.p. 135—137 °C (from light petroleum). IR, ν/cm^{-1}: 2400—2800, 1710 (COOH); 1600 (C=C); 1640 (C=O).

Drima-5,8(9)-dien-7-one (20). ***A.*** KOH (0.21 g), ethylene glycol (7 mL), and water (2 mL) were added to oxo ester **19** (0.21 g, 0.74 mmol). The mixture was refluxed for 30 min, and then it was cooled, diluted with 10 % H_2SO_4 (20 mL), and extracted with ether (3×30 mL). The ethereal extract was washed with water (3×30 mL) and dried, and ether was removed. The residue (0.16 g) was chromatographed on a column with SiO_2 (4 g) (eluent: ether—light petroleum, 5 % Et_2O). Dienone **20** (0.13 g, 80 %) was isolated as a colorless oil, $[\alpha]_D^{20}$ +75° (c 5.5). Found (%): C, 82.32; H, 10.11. $C_{15}H_{22}O$. Calculated (%): C, 82.51; H, 10.15. IR, ν/cm^{-1}: 1595, 1625, 1645, 1695 (C=CC(O)C=C); 1365, 1375 ($C(CH_3)_2$). ^{1}H NMR (CCl_4), δ: 1.08 (s, 3 H, $C(4)CH_3$); 1.16 (s, 6 H, $C(4)CH_3$, $C(10)CH_3$); 1.66 (s, 3 H, $C(12)H_3$); 1.75 (s, 3 H, $C(11)H_3$); 6.0 (s, 1 H, C(6)H).

B. Oxo acid **19** (0.1 g) was heated on a metal bath under Ar at 220 °C for 25 min. The product was dissolved in Et_2O, the ethereal extract was washed with water and filtered, and ether was removed. Ketone **20** (0.076 g, 80 %) was obtained.

11,12-Dibromodrim-8(9)-en-7-one (21). *N*-Bromosuccinimide (1.83 g, 10.4 mmol) was added to a solution of ketone **6** (0.65 g, 3 mmol) in dry CCl_4 (17.5 mL) and the mixture was refluxed for 2 h. After cooling, the mixture was filtered and CCl_4 was removed. The residue (1.51 g) was chromatographed on a column with SiO_2 (20 g). Crystalline enone **21** (1.02 g, 91 %) was eluted with a light petroleum—ether mixture (0.5 % of Et_2O), m.p. 107—108 °C (from light petroleum), $[\alpha]_D^{20}$ +30.5° (c 6.2). Found (%): C, 47.64; H, 5.50; Br, 42.22. $C_{15}H_{22}OBr_2$. Calculated (%): C, 47.64; H, 5.82; Br, 42.26. IR, ν/cm^{-1}: 600, 680 (CH_2Br); 1600 (C=C); 1670 (C=O). ^{1}H NMR (CCl_4), δ: 0.90 (s, 6 H, $C(4)(CH_3)_2$); 1.12 (s, 3 H, $C(10)CH_3$); 2.32 (d, 1 H, J = 5 Hz); 2.48 (s, 1 H, $C(6)H_2$); 4.10 and 4.31 (both d, AB spin system, 2 H, $C(8)CH_2Br$, J = 10 Hz); 4.10 and 4.42 (both d, AB spin system, 2 H, $C(9)CH_2Br$, J = 11 Hz). ^{13}C NMR ($CDCl_3$), δ: 196.8 (C=O); 165.4 and 134.7 (C=C); 35.1 and 35.04 (2 CH_2Br).

6,11,12-Tribromodrim-8(9)-en-7-one (22) and 11,12-dibromo-5,8(9)-dien-7-one (23). ***A.*** *N*-Bromosuccinimide (2.98 g, 16.9 mmol) was added to a solution of ketone **6** (1.46 g, 6.6 mmol) in CCl_4 (35 mL), and the mixture was refluxed for 2 h. After cooling, the mixture was filtered and the solvent was removed. The product (2.17 g) contained three components (TLC data). Chromatography on a column with SiO_2 (40 g) (eluent: light petroleum—Et_2O, 0 → 2 %) gave three fractions: *1* (0.14 g), *2* (1.03 g), and *3* (0.66 g) (the order corresponds to the increase in polarity). The first fraction was recrystallized from light petroleum, and tribromoketone **22** (0.07 g) was obtained (decomposed on heating). Found (%): C, 39.56; H, 4.63; Br, 52.64. $C_{15}H_{21}OBr_3$. Calculated (%): C, 39.42; H, 4.63; Br, 52.45. IR, ν/cm^{-1}: 560, 610, 660, 710 (CH_2Br); 1670 (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.09 (s, 3 H, $C(4)(CH_3)_{eq}$); 1.36 (s, 3 H, $C(4)(CH_3)_{ax}$); 1.60 (s, 3 H, $C(10)CH_3$); 1.93 (d, 1 H, C(5)H, J = 3 Hz); 4.05 and 4.33 (both d, AB spin system, 2 H, $C(8)CH_2Br$, J = 10.5 Hz); 4.08 and 4.58 (both d, AB spin system, 2 H, $C(9)CH_2Br$, J =

Table 2. Coordinates of basic atoms ($\times 10^4$) in molecules of **21** and **23** and equivalent isotropic temperature factors (B_{iso}^{eq})

Atoms	x	y	z	B_{iso}^{eq}/Å^2
Molecule **21**				
Br(1)	6533(2)	1132(4)	8782(5)	4.9(1)
Br(2)	7518(2)	4414(3)	12740(5)	5.1(1)
O	5077(12)	3810(19)	15290(21)	5.8(8)
C(1)	4909(12)	2650(18)	8760(28)	2.0(7)
C(2)	4130(19)	2920(21)	8380(30)	4.5(12)
C(3)	3690(18)	2500(22)	10110(35)	3.3(10)
C(4)	3913(14)	3330(16)	11660(29)	2.3(8)
C(5)	4713(14)	3270(19)	11880(18)	2.0(8)
C(6)	4989(13)	4080(21)	13450(29)	2.4(8)
C(7)	5733(15)	3620(18)	13780(27)	3.7(8)
C(8)	6177(12)	3220(15)	12340(29)	1.7(7)
C(9)	5942(12)	3200(14)	10730(27)	1.5(7)
C(10)	5172(14)	3450(16)	10280(29)	2.5(8)
C(11)	6465(13)	2970(17)	9260(26)	2.3(7)
C(12)	6900(13)	2910(17)	12860(30)	2.6(8)
C(13)	3672(14)	4700(18)	11410(30)	3.7(9)
C(14)	3538(15)	2880(16)	13220(28)	3.3(9)
C(15)	5180(19)	4970(19)	9520(29)	3.8(9)
Molecule **23**				
Br(1)	1927(7)	9072(2)	−1318(3)	4.40(4)
Br(2)	1700(8)	7088(2)	3870(2)	4.38(4)
O	3295(5)	5941(10)	4230(13)	4.2(3)
C(1)	3662(6)	9248(12)	−1580(20)	3.1(3)
C(2)	4368(7)	9884(14)	−1830(19)	3.4(4)
C(3)	4660(7)	10172(13)	0030(18)	3.0(4)
C(4)	4780(5)	8986(12)	1170(17)	2.2(3)
C(5)	4134(5)	8137(10)	1260(18)	1.8(2)
C(6)	3971(6)	7535(12)	2813(15)	2.0(3)
C(7)	3367(6)	6710(12)	2940(19)	2.4(3)
C(8)	2847(5)	6851(12)	1490(18)	2.2(3)
C(9)	2993(6)	7442(12)	−0060(19)	2.0(3)
C(10)	3721(6)	7963(12)	−0484(14)	1.9(3)
C(11)	2489(7)	7507(14)	−1580(20)	3.2(4)
C(12)	2184(6)	6136(14)	1920(17)	3.3(3)
C(13)	4983(7)	9417(14)	3110(18)	3.2(4)
C(14)	5380(6)	8160(18)	0430(19)	4.3(4)
C(15)	4040(6)	6861(14)	−01660(19)	3.2(3)

10 Hz); 4.65 (d, 1 H, C(6)H_{eq}, J = 3 Hz). Chromatographic fraction *2* was dibromoketone **21**. Chromatographic fraction *3* was recrystallized from light petroleum and 11,12-dibromo-5,8(9)-dien-7-one (**23**) was obtained, m.p. 136—137 °C, $[\alpha]_D^{20}$ +23.9° (*c* 3.4). Found (%): C, 48.05; H, 5.40; Br, 43.15. $C_{15}H_{20}OBr_2$. Calculated (%): C, 47.90; H, 5.36; Br, 42.48. IR, ν/cm^{-1}: 580, 600, 700 (C—Br); 1600, 1625 (C=C); 1650 (C=O). ^{1}H NMR ($CDCl_3$), δ: 1.26 and 1.33 (both s, 3 H each, $C(4)(CH_3)_2$); 1.45 (s, 3 H, $C(10)CH_3$); 4.16 and 4.45 (both d, AB spin system, 2 H, $C(8)CH_2Br$, J = 10 Hz); 4.16 and 4.56 (both d, AB spin system, 2 H, $C(9)CH_2Br$, J = 10.5 Hz).

B. *N*-Bromosuccinimide (0.39 g, 2.2 mmol) was added to a solution of ketone **20** (0.26 g, 1.2 mmol) in CCl_4 (15 mL). The mixture was refluxed for 5 h (TLC control), then cooled and filtered and CCl_4 was removed. The reaction product (0.55 g) was chromatographed on a column with SiO_2 (10 g). Dibromoketone **23** (0.34 g, 76 %) was eluted with a light petroleum—ether mixture (4 : 1), it was identical with the sample obtained by procedure ***A***.

X-Ray analysis of compounds 21 and 23. Crystals of **21** and **23** are colorless and irregularly shaped; their linear dimensions do not exceed 0.5 mm. The crystals are of rhombic syngony; the unit cell parameters of **21** and **23** are quite constant. For **21**: a = 19.070(6) Å, b = 10.547(3) Å, c = 7.701(2) Å, d_{calc} = 1.561 g cm^{-3}, Z = 4, space group $P2_12_12_1$, $C_{15}H_{22}OBr_2$. For **23**: a = 19.808(5) Å, b = 10.319(3) Å, c = 7.314(2) Å, d_{calc} = 1.558 g cm^{-3}, Z = 4, space group $P2_12_12_1$, $C_{15}H_{20}OBr_2$.

The X-ray diffraction determination for compound **21** was performed with an RED-4 diffractometer (Mo-Kα radiation). 728 independent reflections with $I > 3\sigma(I)$ were used for calculations. For compound **23**, the determination was performed with a DAP-UMB diffractometer (Cu-Kα radiation). 740 independent reflections with $I > 3\sigma(I)$ were used for calculations.

The structures of **21** and **23** were solved by the heavy atom method. The positions of the Br(1) and Br(2) atoms were obtained with the three-dimensional Patterson function. The refinement was carried out in the anisotropic approximation for non-hydrogen atoms using SHELXTL programs. The H atoms were not involved in the refinement of the structure.

The final R factor values were 0.059 (**21**) and 0.053 (**23**). The bond lengths and valent angles in molecules **21** and **23** are presented in Table 1; the coordinates of the basic atoms are given in Table 2. The spatial structures of compounds **21** and **23** are shown in Figs. 1 and 2, respectively.

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