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CYCLIZATION AND REARRANGEMENT OF DITERPENOIDS.

IV. SYNTHESIS OF Δ^{12}- AND $\Delta^{13(14)}$-ISO-20-DEOXYLUTEONES

P. F. Vlad and N. D. Ungur

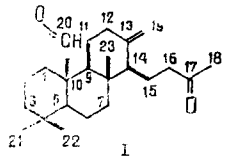
UDC: 547.596/599

Δ^{12}- and $\Delta^{13(14)}$-Iso-20-deoxyluteones have been synthesized from 13E- and 13Z-bicyclogeranylgeranylacetones. The latter were reduced to the corresponding alcohols, which were acetylated, and the acetates obtained were cyclized with fluorosulfonic acid in nitropropane. The reaction product was saponified to a mixture of tricyclic alcohols which were oxidized with the chromium trioxide-pyridine complex to a mixture of Δ^{12}- and $\Delta^{13(14)}$-iso-20-deoxyluteones and this was separated chromatographically.

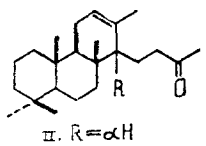
Recently, a binorsesterterpene ketone of the cheilanhane series, luteone (I), possessing a pleasant fruity aroma, has been isolated from the nudibranchiate mollusc Cadlina luteomarginata [1, 2].

In view of this, and also considering the fact that luteone and ketones related to it may serve as intermediates in the synthesis of certain sesterterpenes, we decided to perform the synthesis of its 20-deoxo analogs starting from readily available labdanoids.

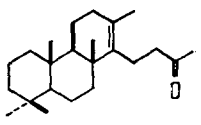
In the present communication we describe the synthesis of Δ^{12}- and $\Delta^{13(14)}$-iso-20-deoxoluteones (II-IV) from sclareol (V) and manool (VI).



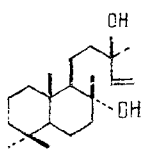
I



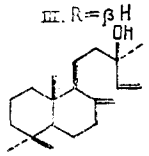
II. R=αH
III. R=βH



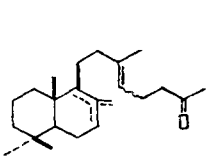
IV



V



VI



VII

Institute of Chemistry, Academy of Sciences of the Moldavian SSR, Kishinev. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 793-801, November-December, 1985. Original article submitted January 3, 1985.

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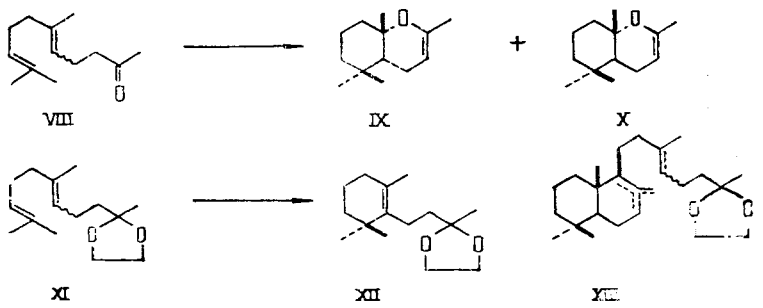


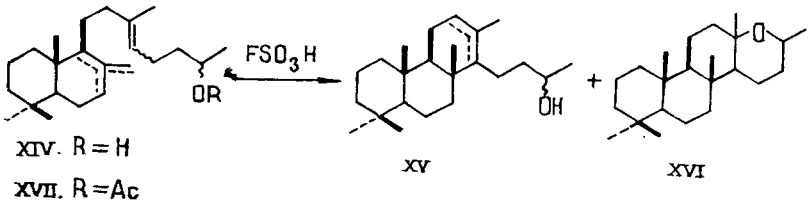
Scheme 1

Luteone (I) can be regarded as a 15-trishomo derivative of the isoagathane series. As is known [3], isoagathane compounds are formed on the electrophilic cyclization of bicyclic labdane diterpenoids. Consequently, 20-deoxo analogs of luteone could be obtained as the result of the cyclization of a mixture of dicyclogeranylgeranylacetones (VII), which are formed in good yield by the reaction of slareol (V) with acetoacetic ester [4].

Initially, the cyclization of the mixture of ketones (VII) was performed with 100% sulfuric acid in nitropropane, since it was known [5] that under these conditions cis- and trans-geranylacetones (VIII) are converted stereospecifically with good yield into cis- and trans-2,5,5,9-tetramethylhexahydrochromenes (IX) and (X), respectively. However, the action of 100% sulfuric acid in nitropropane on the mixture of ketones (VII) yielded no compounds of the isoagathane series. The reaction product consisted of a complex mixture of hydrocarbons.

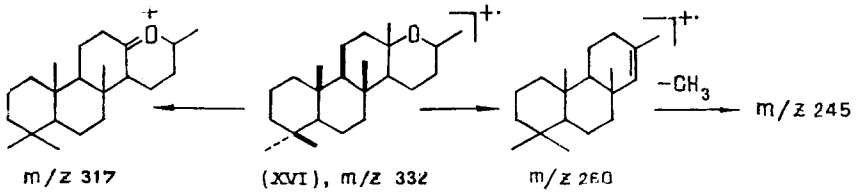
It has been shown previously [6] that the ethylene ketal of geranylacetone (XI) can be cyclized with ~65% yield into the ketal of dihydro-β-ionone (XII) with fluorosulfonic acid. Nevertheless, under the action of fluorosulfonic acid the mixture of ketals (XIII) gave only products of hydrocarbon nature, i.e., under the reaction conditions the ketal protection was eliminated with the subsequent cyclization of the free ketones initiated by the protonation of the carbonyl group, and the dehydration of tertiary alcohols formed. At the same time, the double bond in ring B of the ketones (VII) and their ketals (XIII) is fairly strongly screened and under the given cyclization conditions is protonated with difficulty.

We therefore subsequently decided to cyclize the mixture of alcohols (XIV) – the product of the reduction of mixture of ketones (VII) with lithium tetrahydroaluminate or potassium tetrahydroborate. The action on them of fluorosulfonic acid in nitropropane formed, together with a mixture of tricyclic alcohols (XV) (41%), tetrahydropyran derivatives of structure (XVI) (43%). When the reaction



Scheme 2

product was chromatographed on silica gel, a crystalline oxide was obtained. It was not oxidized by m-chloroperbenzoic acid. According to its PMR spectrum, its molecule contained a secondary and five tertiary methyls and one proton at a carbon atom linked to ethereal oxygen. The IR spectrum of compound (XVI) contained only the maxima characteristic for the tetrahydropyran ring. On the basis of these facts, the oxide product was assigned structure (XVI). This was confirmed by the mass spectrum which contained the peaks of ions with m/z 332, 317, 260, and 245, a possible pathway for the formation of which is shown in the following scheme:



Scheme 3

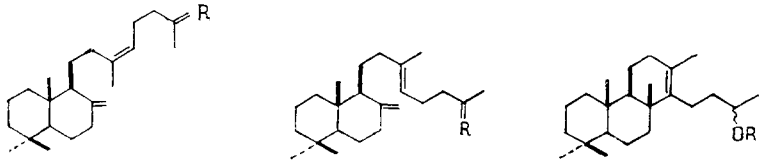
In view of the composition of the initial compound, the oxide product (XVI) must be a mixture of epimers at C_{14}. It is not excluded, however, that it consists of a more complex mixture of substances also epimeric at C_{13} and C_{17}.

The structure of the mixture of alcohols (XV) follows from its spectral characteristics: each of their molecules contains four tertiary methyls, a methyl at a double bond, and a hydroxy group.

In order to eliminate the formation of oxide compounds, the mixture of alcohols (XIV) was subsequently acetylated and the mixture of acetates (XVII) was subjected to cyclization under various conditions (see Table 1). It can be seen from Table 1 that it is possible to use fluorosulfonic and 72% perchloric acids and a mixture of 10% of concentrated sulfuric acid and 99% formic acid with equal success as cyclizing agents. At low temperatures, the reaction did not take place or took place with difficulty, but at higher temperatures the yields of cyclization products were good (~91-94%). However, in this case, as well, the cyclization products consisted of a mixture of epimers at C_{14} which could not be separated,

Therefore, to obtain the ketones (II-IV) in the individual state we subsequently started from the 13Z- and 13E-bicyclogeranylgeranylacetones (XVIII) and (XIX) separately, a mixture of them (3:7, GLC) having been obtained by the Carroll reaction from manool (VI) and having been separated into the individual stereoisomers by chromatography on silica gel impregnated with silver nitrate, which was prepared by the method described by Norin and Westfeld [7]. The structure and stereochemistry of the ketones (XVIII) and (XIX) followed from the results of PMR spectroscopy [8] (see the Experimental part) and agreed with those given in the literature [9]. They were reduced to the alcohols (XX) and (XXI), respectively, and these were esterified to form the acetates (XXII) and (XXIII).

Cyclization of the 13E-acetate (XXIII) with fluorosulfonic acid in 2-nitropropane at room temperature led to a mixture (1:1, GLC results) of the acetates (XXIV and XXV). All attempts to separate this mixture were unsuccessful. It was therefore saponified to form a mixture of the alcohols (XXVI) and (XXVII), which was oxidized with the chromium trioxide–pyridine complex in methylene chloride [10] to a mixture of the ketones (II) and (IV). This was separated by chromatography on silver-nitrate-impregnated silica gel. THe action of pyridine chlorochromate on the mixture of alcohols (XXVI) and (XXVII) led to their partial cyclization to the tetrahydropyran oxides (XVI).



XVIII. R=O
XX. R=H; OH
XXII. R=H, OAc

XIX. R=O
XXI. R=H, OH
XXIII. R=H, OAc

XXIV. R=Ac
XXVI. R=H

Scheme 4

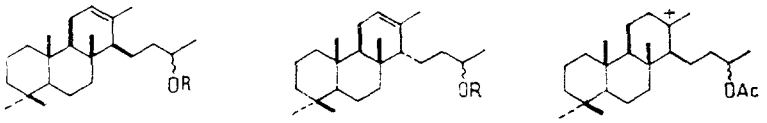
TABLE 1. Cyclization of the Mixture of Acetates (XVII) with Acid Agents*

Experiment No.	Cyclizing agent	Ratio of cyclizing agent to substrate, molar	Temperature, °C	Time, min	Composition of the reaction products, %† mixt. of (XXIV), (XXV) and (XXVIII)	mixt. of int. acetates (XVII)	Total yield
1	FSO_3H	2:1	−30 ÷ −33	10	—	100	—
2	FSO_3H	2:1	−3 ÷ −5	10	33	67	84.9
3	FSO_3H	2:1	+22 ÷ +23	10	100	—	92.3
4	FSO_3H	2:1	+22 ÷ +23	5	94	6	79.1
5	H_2SO_4 (100%)	2:1	−5 ÷ −7	10	35	65	84.4
6	$HClO_4$ (72%)	10:1	+22 ÷ +23	15	91	9	94.6
7	H_2SO_4/HCO_2H (1:9)	19:1 ‡	+22 ÷ +23	30	98	2	91.2

*Experiments 1-6 were performed in 2-nitropropane at a ratio of 1 mmole of the acetates (XVII) to 10 ml of solvent.

†The composition was determined by the GLC method at a column temperature of 230°C and an evaporator temperature of 250°C.

‡H_2SO_4:substrate ratio.



XXV. R = Ac
XXVII. R = H

XXVIII. R = Ac
XXIX. R = H

XXX

Scheme 4

In the IR spectrum of the less polar ketones there was the maximum of a methyl ketone group, and in its PMR spectrum there were the signals of four tertiary methyl groups, a methyl at a double bond, and a methyl ketone group but there were no signals of vinyl protons, i.e., it possesses structure (IV). In the IR spectrum of the more polar ketones there were the maxima of a methyl ketone group and of a trisubstituted double bond, and in its PMR spectra, in addition to the signals of the same three methyl groups as in the molecule of the less polar ketone, there was the signal of one vinyl proton. On the basis of the facts given, the more polar ketone was assigned structure (II). Its 14R configuration follows from the fact that its bicyclic precursor (XXIII) had the 13E configuration [11].

When the 13Z-acetate (XX) was cyclized under the same conditions, it gave a mixture of the acetates (XXIV and XVIII) in a ratio of 1:4 (GLC results). It was saponified to a mixture of the alcohols (XXVI) and (XXIX), which was oxidized with the chromium trioxide–pyridine complex to a mixture of the ketones (III) and (IV). They were separated chromatographically on silica gel impregnated with silver nitrate. The IR and PMR spectra on the ketone (III) were similar to those of the ketone (II) and showed that it had an identical structure. The difference amounted to the fact that ketone (III) had the 14S configuration, since it was obtained as the result of the cyclization of the bicyclic precursor (XXII) with a 13Z-double bond (II).

Thus, the cyclization of the acetates (XXII) and (XXIII) formed not only tricyclic compounds with a Δ^{12} double bond, which are the sole cyclization products of labdane compounds with similar structures, but also the $\Delta^{13(14)}$ isomers. The reason for this lies in the presence of voluminous side chains affecting the ratio of the stabilities of the tricyclic substances with Δ^{12} and $\Delta^{13(14)}$ double bonds. The configuration of the asymmetric center in C_{14} in the carbocation (XXX) arising on cyclization has a substantial influence on the ease of detachment of a proton from C_{14} on its stabilization: in the case of a quasi-equatorial configuration of the side chain in the carbocations (XXX), the detachment of protons from C_{12} and C_{14} takes place with equal ease, while in the case of the quasi-axial configuration of the side chain

the proton is detached from C_{12} more readily. However, in the cyclization of compounds (XXII) and (XXIII), as well, no isomers with a hemicyclic double bond are formed, which is characteristic for the process of converting bicyclic diterpenoids into tricyclic isoagathane compounds.

Analogs of luteone (I) cannot be obtained by the direct cyclization of bicyclic ketones of type (VII) and the ketals. Such analogs were synthesized by the cyclization of the acetates (XXII) and (XXIII), the subsequent saponification of the reaction products (XXIV), (XXV), and (XXVIII), and the oxidation of the resulting alcohols (XXVI), (XXVII), and (XXIX).

EXPERIMENTAL

Melting points were determined on a Boetius heated stage. Specific rotations were determined on a Polamat S instrument in chloroform. IR spectra were recorded on CCl_4 on a Specord 74 IR spectrophotometer, and PMR spectra in CCl_4 on a Specord 74 IR spectrophotometer, and PMR spectra in CCl_4 on a Tesla BS 467 (60 MHz) spectrometer with TMS as internal standard, the signals being given in the δ scale. The following abbreviations are used: s (singlet), d (doublet), br.s (broadened singlet), m (multiplet). Mass spectra were recorded on a MKh-1320 spectrometer with a glass system for the direct introduction of the sample into the ion source at an ionization voltage of 70 eV. GLC analysis was performed on a Chrom-5 chromatograph with a flame-ionization detector using a 1.5 m × 3 mm glass column containing 5% of SE-30 on Chromaton N-AW-DMCS as a stationary phase with helium as the carrier gas. Silica gel L 40/100 μ (Czechoslovakia) and silica gel impregnated with silver nitrate [7] were used for column chromatography. Solutions of the substances in organic solvents were dried with anhydrous sodium sulfate. The petroleum ether had bp 40-70°C. The analyses of all the compounds corresponded to the calculated figures.

Ketalization of the Mixture of Ketones (VII). A mixture of 729 mg of the mixture of ketones (VII) in 45 ml of dry benzene was boiled in a Dean-Stark instrument with 163 mg of p-toluenesulfonic acid and 1.2 ml of ethylene glycol for 3 h. The reaction mixture was washed with 2% KOH solution and with water to neutrality, and it was dried and the solvent was distilled off. This gave 820 mg (99%) of a mixture of the ketals (XIII) in the form of a colorless viscous liquid. IF spectrum (cm^{-1}): 1056, 1200 (ketal), 890, 1641 ($>C=CH_2$), 853, 1660 ($>C=C<_H$). . PMR spectrum (ppm): 0.64 (s, 3H, C_{10}—CH_3), 0.80 (s, 3H, C_4—CH_3), 0.85 (s, 3H, C_4—CH_3), 1.20 (s, 3H, —C(O,O)—CH_3), 1.58 (s, 3H, C_{13}—CH_3), 3.80 (s, 4H, CH_2—CH_2 of O,O-C), 4.37—5.17 (m, 3H, $>C=CH_2$ and C_{14}—H).

Reduction of the Mixture of Ketones (VII). a) Potassium Tetrahydroborate. Potassium tetrahydroborate (1.3 g) was carefully added to a solution of 5.4 g of the mixture of ketones (VII) in 250 ml of methanol, and the mixture was boiled under reflux for 3 h. The bulk of the methanol (180 ml) was distilled off, the residue was cooled, and a 10% solution of H_2SO_4 was carefully added to it. After the usual working up, 5.23 g of a mixture of the isomeric alcohols (XIV) was obtaned. IR spectrum (cm^{-1}): 3453, 3620 (OH group), 890, 1640 ($>C=CH_2$), 852, 1660 ($>C=C<_H$).

b) Lithium Tetrahydroaluminate. At room temperature, 285 mg of $LiAlH_4$ was added to a solution of 2.1 g of the mixture of ketones (VII) in 50 ml of absolute diethyl ether. The mixture was kept at the same temperature for 2.5 h, and the excess of $LiAlH_4$ was decomposed with ethyl acetate, after which the mixture was acidified with 10% H_2SO_4 solution and was worked up in the usual way. This gave 2.07 g of a mixture of the alcohols (XIV) identical with that which was obtained in paragraph a).

Cyclization of the mixture of Alcohols (XIV). At room temperature, with stirring, 210 mg of FSO_3H in 0.5 ml of 2-nitropropane was added to a solution of 330 mg of the mixture of alcohols (XIV) in 10 ml of 2-nitropropane. The reaction mixture was stirred for another 15 min, and then 0.8 ml of triethylamine was added to it and it was extracted three times with

hexane. The organic layer was washed with water to neutrality and was dried, and the solvent was distilled off. The residue (326 mg) was chromatographed on a column containing 6.5 g of SiO_2. Petroleum ether eluted 37.5 mg of hydrocarbons, which were not investigated further. Petroleum ether–ether acetate (19:1) eluted 141 mg of a crystalline fraction which was recrystallized from acetonitrile. This gave 78 mg of product (XVI) with mp 143-145°C. IR spectrum (cm^{-1}): 1078, 1098 (tetrahydropyran ring). PMR spectrum (ppm): 0.83 (s, 3 H, $C_{10}-CH_3$); 0.87 (s, 3 H) and 0.90 (s, 3 H) [$C_4-(CH_3)_2$]; 0.93 (s, 3 H, C_8-CH_3); 1.31 (s, 3 H, $C_{13}-CH_3$); 1.18 (d, J = 5 Hz, 3 H, $C_{17}-C_3$); 3.75 (m, 1 H, $C_{17}-H$). Mass spectrum (m/z, intensity, %): 332 (M^+, 14), 317 (100), 260 (16), 259 (11), 245 (9), 205 (16), 204 (13), 192 (11), 191 (23), 177 (6).

Then a mixture of the same solvents in a ratio of 9:1 eluted from the column 135.6 mg of a mixture of the unsaturated alcohols (XV) in the form of a colorless viscous liquid. IR spectrum (cm^{-1}): 1115, 3345 (band), 3610 (OH group).

Acetylation of the Mixture of Alcohols (XIV). The mixture of alcohols (XIV) (1.4 g) was acetylated with 15 ml of dry pyridine and 1.8 ml of acetic anhydride at room temperature for 16 h. The reaction mixture was diluted with water and was extracted three times with ether, and the ethereal extract was worked up in the usual way. The product consisted of a mixture of the acetates (XVII) in the form of a colorless viscous liquid. IR spectrum (cm^{-1}): 1240, 1730 (OAc), 840, 1662 ($>C=C<_H$), 890, 1640 ($C=CH_2$).

Cyclization of the Mixture of Unsaturated Acetates (XVII). a) At room temperature, with stirring, a solution of 85 mg of FSO_3H in 0.5 ml of 2-nitropropane was added to a solution of 150 mg of the mixture of acetates (XVII) in 3.5 ml of 2-nitropropane. The reaction mixture was stirred for another 10 min at the same temperature and was worked up as described above. This gave 138.4 mg of a mixture of the acetates (XXIV), (XXV) and (XXVIII) in a ratio of 8:7:5 (GLC results).

b) At room temperature, with stirring, 0.2 ml of 72% $HClO_4$ solution was added to a solution of 83 mg of a mixture of acetates (XVII) in 2.2 ml of 2-nitroproane. The mixture was stirred at the same temperature for 15 min and was worked up. This gave 78.5 mg of a mixture of the acetates (XXIV), (XXV), and (XXVIII) in approximately the same ratio as in paragraph a) according to GLC. In addition, 9% of a mixture of the uncyclized initial acetates (XXVII) was recovered.

c) At room temperature, 3 g of a solution of 10% H_2SO_4 in 99% formic acid was added to a solution of 60.2 mg of the mixture of the acetates (XVII). The reaction mixture was stirred at the same temperature for 30 min. Then it was diluted with water and was extracted three times with ether. The ethereal layer was washed with 1% KOH solution and with water to neutrality and was dried, and the solvent was distilled off. This gave 54.9 mg of a mixture of the acetates (XXIV), (XXV), and (XXVIII).

Interaction of Manool (VI) with Acetoacetic Ester. A solution of 1 g of manool (VI) in 1.4 ml of freshly distilled acetoacetic ester was heated in a Favorskii flask for 2 h (at 150-170°C for 1 h and at 210-220°C for 1 h). The mixture was cooled and was treated with 15 ml of ether, and then it was washed successively with water, saturated $NaHCO_3$ solution, and water again, and was dried, and the solvent was distilled off. The residue (1.1 g) consisted, according to GLC results, of a 3:7 mixture of the ketones (XVIII) and (XIX). It was chromatographed on a column containing 25 g of silica gel impregnated with $AgNO_3$ [7].

Petroleum ether eluted 0.03 g of a mixture of substances of low polarity which were not investigated. Petroleum ether–ethyl acetate (97:3) eluted 0.11 g of 13Z-bicyclogeranylgeranylacetone (XVIII) in the form of a colorless viscous liquid with $[\alpha]_D^{23}$ +25.4° (c 3.6). IR spectrum (cm^{-1}): 1353 and 1377 [$C(CH_3)_2$], 1710 ($>C=O$), 880, 1630 ($>C=CH_2$), 1653 ($>C=C<_H$).

PMR spectrum (ppm): 0.67 (s 3H, $C_{10}-CH_3$), 0.81 (s, 3H) and 0.87 (s 3H) [$C_4-(CH_3)_2$], 1.64 (s, 3H, $C_{13}-CH_3$), 2.03 (s 3H, $-\overset{\overset{O}{\|}}{C}-CH_3$), 4.57 (m) and 4.82 (m) (2H, $>C=CH_2$), 5.02 (m 1H, $C_{14}-H$).

Then a mixture of the same solvents eluted from the column 0.65 g of a mixture of the ketones (XVIII) and (XIX), followed by 0.25 g of 13E-bicyclogeranylgeranylacetone (XIX) in the form of a colorless viscous liquid with $[\alpha]_D^{23}$ +33.7° (c 2.7). IR spectrum (cm^{-1}): 1357 and

1380 [$C(CH_3)_2$], 1715 (>C=O), 890, 1635 (>C=CH_2), 851, 1660 (>C=C<$_H$). PMR spectrum (ppm): 0.69 (s, 3H, C_{10}—CH_3), 0.81 (s 3H) and 0.87 (s 3H) [C_4—$(CH_3)_2$], 1.59 (d, 3H, J=2 Hz, C_{13}—CH_3), 2.03 (s, 3H, —C(=O)—CH_3), 4.48 (m) and 4.80 (m) (2H, >C=CH_2), 5.03 (m, 1H, C_{14}—H).

Preparation of the 13E-Acetate (XXIII). A solution of 250 mg of the ketone (XIX) in 15 ml of absolute diethyl ether was treated with 35 mg of $LiAlH_4$, and the mixture was kept at room temperature for 2 h. It was worked up in the usual way, and 248.5 mg of the alcohol (XXI) was obtained in the form of a colorless viscous liquid with $[\alpha]_D^{22}$ + 31.7° (c 3.3). IR spectrum (cm^{-1}): 1372 and 1384 [$C(CH_3)_2$], 1116, 3463 (band), 3610 (OH group), 890, 1637 (>C=CH_2), 845, 1657 (>C=C<$_H$). A solution of 230 mg of the alcohol (XXI) in 8 ml of dry pyridine was treated with 0.5 ml of acetic anhydride, and the mixture was kept at the ordinary temperature for 18 h. After working up, 257.1 mg of reaction product was obtained, and this was purified by chromatography on a column containing 2.5 g of silica gel. Petroleum ether–ethyl acetate (19:1) eluted 243.6 mg (94%) of the 13E-acetate (XXIII) in the form of a colorless viscous liquid with $[\alpha]_D^{22}$ +34.4° (c 2.3). IR spectrum (cm^{-1}): 1233 and 1730 (OAc), 882, 1628 (>C=CH_2), 842, 1655 (>C=C<$_H$).

Preparation of the 13Z-Acetate (XXII). A solution of 95 mg of the ketone (XVIII) in 10 ml of absolute diethyl ether was treated with 15 mg of $LiAlH_4$, and the mixture was kept at room temperature for 2.5 h and it was then worked up. This gave 93.6 mg of the alcohol (XX) in the form of a colorless viscous liquid with $[\alpha]_D^{23}$ +21.6° (c 1.9). IR spectrum (cm^{-1}): 1357 and 1384 [$C(CH_3)_2$], 1112, 3453 (band), 3610 (OH group), 890, 1638 (>C=CH_2), 840, 1650 (>C=C<$_H$). A solution of 91.1 mg of the alcohol (XX) in 5 ml of dry pyridine was treated with 0.3 ml of acetic anhydride, and the mixture was kept at room temperature for 14.5 h. After working up, 100.7 mg of reaction product was obtained, and this was chromatographed on a column containing 2.1 g of silica gel. Petroleum ether–ethyl acetate (19:1) eluted 95.8 mg (93%) of the 13Z-acetate (XXII) with $[\alpha]_D^{22}$ +23.9° (c 2.9). IR spectrum (cm^{-1}): 1226, 1723 (OAc), 880, 1628 (>C=CH_2), 838 1653 (>C=C<$_H$).

Cyclization of the 13E-Acetate (XXIII). At room temperature, with stirring, a solution of 120 mg of FSO_3H in 0.5 ml of 2-nitropropane was added to a solution of 225 mg of the 13E-acetate (XXIII) in 5.5 ml of 2-nitropropane. The reaction mixture was stirred at the same temperature for 10 min and was worked up. This gave 207 mg of reaction product, which was chromatographed on a column containing 5 g of silica gel. Petroleum ether–ethyl acetate (97:3) eluted 167 mg of a mixture of the acetates (XXIV) and (XXV) in the form of a colorless viscous liquid. IR spectrum (cm^{-1}): 1240 and 1735 (OAc), 840, 1651 (>C=C<$_H$).

Preparation of the Ketones (II) and (IV). A solution of 150 g of a mixture of the acetates (XXIV) and (XXV) in 0.8 ml of ethanol was boiled with 8 ml of a 10% solution of KOH in ethanol under reflux for 1 h and was worked up in the usual way. This gave 129 mg of a mixture of the alcohols (XXVI) and (XXVII). IR spectrum (cm^{-1}): 1369 and 1384 [$C(CH_3)_2$], 1113, 3342 (band), 3612 (OH group), 842 (>C=C<$_H$). A solution of 125 mg of the mixture of the alcohols (XXVI) and (XXVII) in 5 ml of CH_2Cl_2 was treated with 250 mg of the $CrO_3 \cdot 2C_5H_5N$ complex prepared by the method of Collins et al. [10], and the mixture was stirred at room temperature for 54 h. The precipitate was filtered off, and the solvent was distilled off. THe residue (108.3 mg) was chromatographed on a column containing 4 g of $SiO_2 \cdot AgNO_3$. Petroleum ether–ethyl acetate (99:1) eluted 24.6 mg of the tricyclic ketone (IV) in the form of a colorless viscous liquid with $[\alpha]_D^{19}$ + 37.2° (c 2.4). IR spectrum (cm^{-1}): 1356 and 1376 [$C(CH_3)_2$], 1720 (>C=O). PMR spectrum (ppm): 0.83 (s, 6H, C_4—andC_{10}—CH_3), 0.87 (s, 3H, C_4—CH_3), 0.93 (s, 3H, C_8—CH_3), 1.27 (s, 3H, C_{13}—CH_3), 2.03 (s, 3H, —C(=O)—CH_3).

Then a mixture of the same solvents eluted from the column 58.1 mg of mixture of the ketones (II) and (IV), followed by 21.2 mg of the ketone (II) in the form of a colorless viscous liquid with $[\alpha]_D^{19}$ +11.4° (c 2.5). IR spectrum (cm^{-1}): 1357 and 1375 [$C(CH_3)_2$], 1718 (>C=O), 848, 1665 (>C=C<$_H$). PMR spectrum (ppm): 0.83 (s, 3H, C_{10}—CH_3), 0.87 (s, 3H) and 0.93 (s, 3H)

[C_4—$(CH_3)_2$], 0.96 (s, 3H, C_8—CH_3), 1.33 (s, 3H, C_{13}—CH_3), 2.03 (s, 3H, —C(=O)—CH_3), 5.45 (br., s, 1H, C_{12}—H).

Cyclization of the 13Z-Acetate (XXII). At room temperature, with stirring, 60 mg of FSO_3H in 0.3 ml of 2-nitropropane was added to a solution of 92 mg of the 13Z-acetate (XXII) in 2.2 ml of 2-nitropropane. The reaction mixture was stirred at the same temperature for another 10 min and was worked up. This gave 88.5 mg of reaction product, which was chromatographed on a column containing 2.5 g of silica gel. Petroleum ether–ethyl acetate (97:3) eluted 61.3 mg of a mixture of the acetates (XXIV) and (XXVIII) in the form of a colorless viscous liquid. IR spectrum (cm^{-1}): 1224 and 1737 (OAc), 1653 (>C=C<H).

Preparation of a Mixture of the Ketones (III) and (IV). A solution of 68 mg of a mixture of the acetates (XXIV) and (XXVIII) in 0.5 ml of ethanol was treated with 5 ml of a 10% solution of KOH in ethanol, and the solution was boiled under reflux for 1.5 h. Then it was worked up, giving 57.2 mg of a mixture of the alcohols (XXVI) and (XXIX) (1:4 according to GLC). IR spectrum (cm^{-1}): 845 (>C=C<H), 3460 (band), 3613 (OH group). A solution of 55 mg of the mixture of alcohols (XXVI) and (XXIX) in 3 ml of CH_2Cl_2 was treated with 105 mg of the complex $CrO_3 \cdot 2C_5H_5N$ [10], and the mixture was stirred at room temperature for 58 h and was worked up as described above. This gave 47.2 mg of reaction product which was chromatographed on a column containing 2.8 g of $SiO_2 \cdot AgNO_3$. Petroleum ether–ethyl acetate (99:1) eluted 5.3 mg of the ketone (IV), identical with the product obtained above. Then the same solvent eluted 11.8 mg of a mixture of the ketones (III) and (IV), followed 28.6 mg of the ketone (III) in the form of a colorless viscous liquid with $[\alpha]_D^{19}$ +8.6° (c 2.1). IR spectrum (cm^{-1}): 1353 and 1370 [$C(CH_3)_2$], 1717 (>C=O), 850, 1660 (>C=C<H). PMR spectrum (ppm): 0.88 (s, 6H, C_4—andC_{10}—CH_3), 0.96 (s, 6H, C_4—andC_8—CH_3), 1.35 (s, 3H, C_{13}—CH_3), 2.07 (s, 3H, —C(=O)—CH_3), 5.37 (br., s, 1H, C_{12}—H).

SUMMARY

The synthesis of Δ^{12}- and $\Delta^{13(14)}$-iso-2-deoxoluteones – analogs of natural luteone – has been performed starting from readily accessible bicyclogeranylgeranylacetones.

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