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CYCLIZATION AND REARRANGEMENTS OF DITERPENOIDS—I

SYNTHESIS OF TETRACYCLIC DITERPENOIDS WITH A NEW CARBON SKELETON FROM LABDANES

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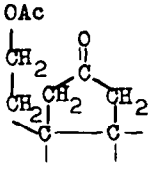
Abstract—Acid-catalyzed cyclization of Δ^{7}-, $\Delta^{8(9)}$- and $\Delta^{8(20)}$-labd-13-dien-15-ol acetates, sclareol, manool and epimanoyloxide gives a mixture of (14R)- and (14S)-isoagath-12-en-15-ols, hiban-14α-ol, two tetracyclic alcohols with a new carbon skeleton, and their esters. The new tetracyclic alcohols have been identified as 11- and 13-hydroxyderivatives of (1R,2S,7S,10S,12S) - 2,6,6,10,12 - pentamethyl-tetracyclo[10.2.1.0^{1,10}.0^{2,7}]eicosane proved by IR, NMR, MS, ORD and CD data and some chemical transformations.

According to the biogenetic isoprene rule[1,2] labdane diterpenoids ent-copalol **1** and manool **2** are biogenetic precursors of a range of polycyclic diterpenoids. With an aim of biomimetic syntheses elaboration of the latter the *in vitro* cyclization of alcohols **1** and **2** was undertaken.[3] It succeeded in realizing a biogenetic-like synthesis of tricyclic, but not tetracyclic diterpenoids.

It is to be noted that in the works[4-9] the labdanoids cyclization was carried out under more or less similar mild conditions by solvolysis of esters of bicyclogeranylgeraniol **1** and its isomers. In the same time it is well known[10-12] that 1,5-diene cyclization strongly depends on the method of reaction initiation, cyclizating agent, reaction medium, temperature, etc. The influence of these factors on labdane diterpenoids cyclization is not sufficiently studied.

We have investigated the cyclization of acetate mixture **3**[13] and its separate constituents using 10% sulphuric acid in 99% formic acid. In this paper are given the data on composition of oxygenated portion of cyclization products (yield 47–51%). It was shown this portion represents a mixture of five alcohols and their formates. Three of these alcohols appeared to be known: isoagathane compounds **4**, **5**[14] and hiban-14α-*ol* **6**.[5-7] These compounds were identified on the basis of spectral data and by direct comparison with authentic samples.

The remaining two alcohols (designated as A and B) appeared to be tetracyclic compounds with a new carbon skeleton. Their structure was elucidated as follows.



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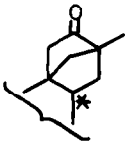

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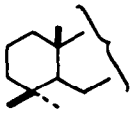

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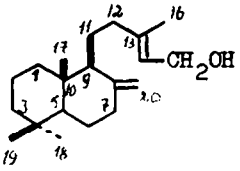
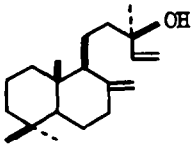
According to ^{1}H and ^{13}C NMR data, compounds A and B are secondary alcohols. The former alcohol does not possess hydrogen atoms at β-position to the hydroxyl group. Both alcohols contain five methyl groups at quaternary carbon atoms and hence they cannot belong to tetracyclic diterpenoids of known structural types.[3] Oxidation of alcohols A and B afforded ketones A and B respectively, their carbonyl groups being attached to five-membered ring (IR spectral data). Ketone B possesses a methylene group vicinal to carbonyl group and to a quaternary carbon atom, as it follows from its IR absorption at 1416 cm^{-1} and the presence of doublet of doublets of



(1)



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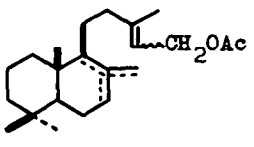

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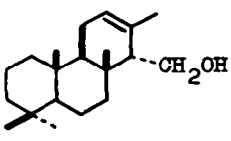

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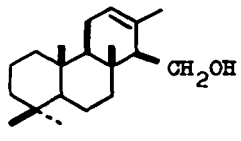

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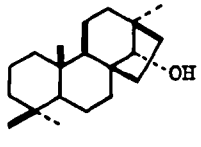
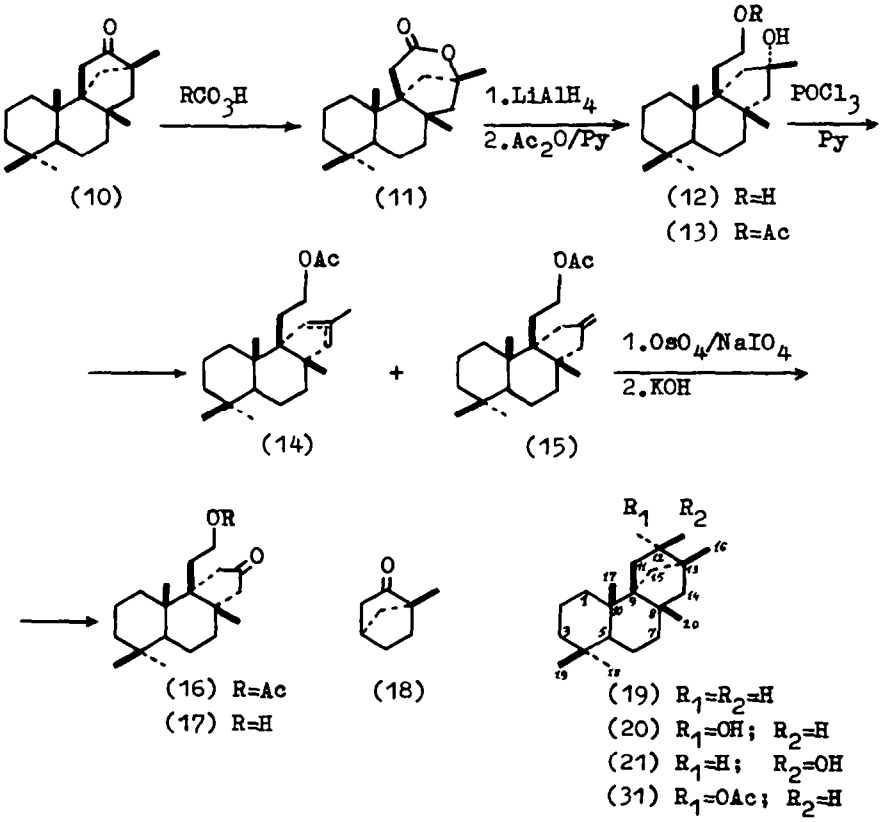


(6)

AB system in its PMR spectrum at 2.33 and 2.08 ppm, the former being additionally splitted with J = 4.7 Hz. Unlike ketone B, the carbonyl group of ketone A is sterically hindered. This ketone does not form carbonyl derivatives under the standard conditions and does not react with peracids. Huang–Minlon reduction of ketone B[15] or desulphurization of its thioketal with Raney Ni afforded a crystalline hydrocarbon, m.p. 72–73°. The latter was also obtained from ketone A under the same reduction conditions. Though these conditions[15] are sufficiently vigorous the hydrocarbon yield from ketone A is rather low. In this case, transformation of ketone A to alcohol A, apparently via diimide reduction, is predominated. Therefore both alcohols A and B possess the same carbon skeleton and differ only in their hydroxy group position. Being treated with acids, alcohols A and B or their acetates are mutually isomerized as a result of hydride shift which in terms of the above-mentioned data cannot be a 1,2-shift.

Owing to the inertness of ketone A further experiments directed to structure elucidation of alcohols A and B were carried out with ketone B. Baeyer–Villiger oxidation was found to proceed most efficiently with p-carbomethoxyperbenzoic acid[16] to afford a δ-lactone. Its saponification product (the corresponding hydroxy acid) is easily relactonized when heated in ether. The starting δ-lactone is also formed during silica gel chromatographic purification of the respective hydroxy acid methyl ester. The latter is not oxidized by chromium anhydride in pyridine. Therefore its hydroxy group is tertiary. Hence, ketone B carbonyl group is attached to the quaternary carbon atom bearing one of the methyl groups. This conclusion was confirmed by further chemical transformations of the δ-lactone. Thus, its hydride reduction leads to a primary–tertiary diol (IR and NMR data). Selective acetylation of its primary hydroxy group followed by dehydration of the resulted hydroxy acetate with phosphorus oxychloride in pyridine leads to the formation of the mixture of isomeric unsaturated acetates. Column chromatography of the mixture using silver nitrate impregnated silica gel allowed to isolate a mixture of two acetates with trisubstituted double bond and the isomer with exocyclic double bond (IR, NMR and GLC data). The latter was oxidized by osmium tetraoxide and sodium periodate to form a ketoacetate, which was saponified to hydroxy ketone with carbonyl group in cyclopentane ring (IR, 1747 cm^{-1}). In the ketoacetate PMR spectrum there are signals of $-CH_2CH_2OAc$ group and of two AB systems, indicating the presence of two methylene groups linked with quaternary carbon atoms and with the carbonyl group. Thus, the ketoacetate should contain the structural fragment **7**. Taking into consideration the above-mentioned sequence of ketone B transformation to ketoacetate it can be concluded that its molecule should contain the bicyclo [2,2,1] heptane moiety **8**. Ion peaks at *m/z* 137, 123, 121 and 107 in the ketone B mass spectrum indicate the presence of structural unit **9** in its molecule.[17] Both fragments **8** and **9** discount eighteen from twenty carbon atoms of alcohol under consid-

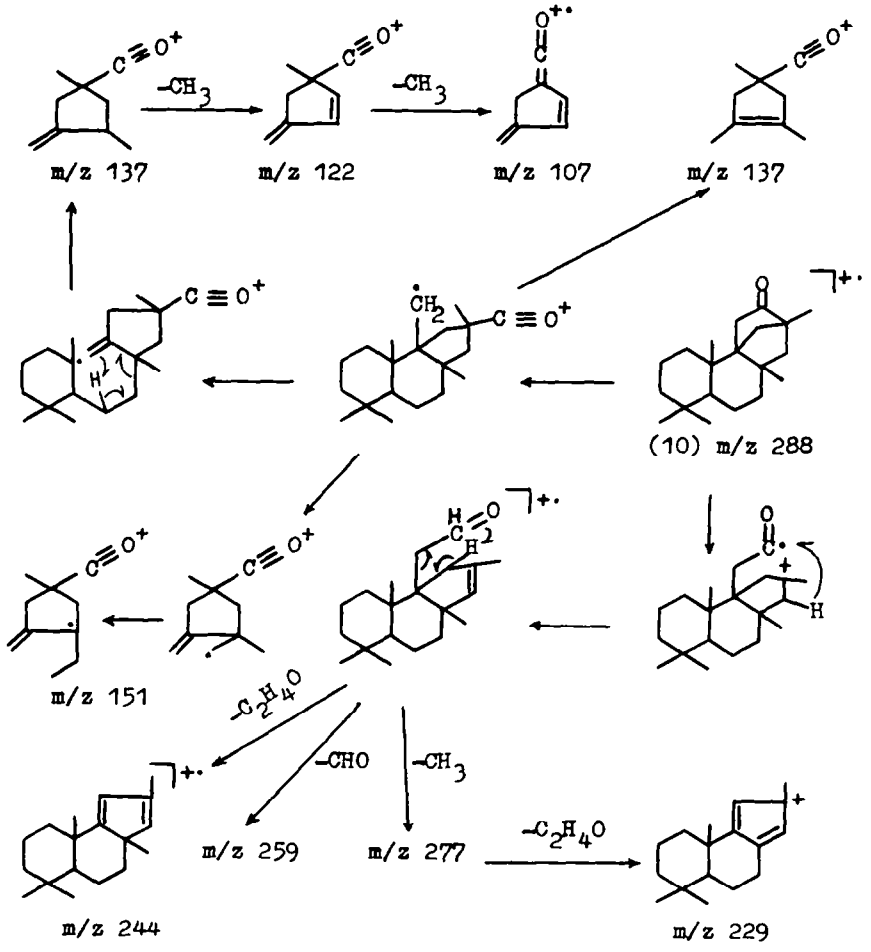


Scheme 1

Table 1. ^{13}C Chemical shifts and off-resonance data for compounds **10–13**, **19–21**, **27**, **28**, **31**

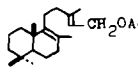
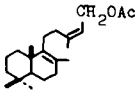
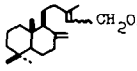
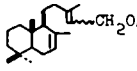
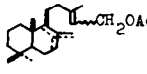
Carbon atom	(10)	(11)	(12)	(13)	(19)	(20)	(21)	(27)	(28)	(31)
C - 1	42.08t*	41.74t	39.39t	39.75t	42.42t	41.93t	42.36t	41.55t	42.33t	41.94t
C - 2	18.54t	18.37t	18.49t	18.57t	18.78t	18.65t	18.64t	18.42t	18.58t	18.65t
C - 3	42.22t	42.62t	41.61t	41.60t	42.80t	42.33t	42.36t	42.21t	42.47t	42.33t
C - 4	33.40s	33.35s	33.39s	33.52s	33.52s	33.48s	33.48s	33.46s	33.49s	33.49s
C - 5	49.96d	48.48d	48.24d	48.63d	41.59d	51.17d	50.56d	50.90d	51.41d	51.22d
C - 6	20.10t	19.58t	19.42t	19.29t	20.14t	20.14t	20.02t	18.42t	19.64t	20.11t
C - 7	35.86t	35.40t	35.40t	31.20t	35.80t	35.72t	35.60t	31.99t	26.94t	35.75t
C - 8	40.61s	43.37s	46.62s	46.95s	40.96s	40.22s	40.86s	50.20s	42.76s	40.23s
C - 9	57.30s	52.10s	54.24s	54.44s	60.09s	58.80s	59.40s	57.31s	59.13s	59.03s
C - 10	37.73s	38.97s	40.83s	40.76s	38.14s	37.71s	37.78s	57.36s	38.08s	37.74s
C - 11	43.30t	41.64t	44.92t	45.46t	37.35t	39.87t	43.76t	32.41t	35.11t	41.11t
C - 12	217.56s	173.14s	68.88t	64.11t	26.10t	177.62d	177.62d	24.74t	25.74t	79.83d
C - 13	54.47s	84.97s	75.77s	75.35s	43.04s	46.86s	46.77s	53.27s	47.60s	46.04s
C - 14	42.08t	35.65t	37.39t	37.45t	45.01t	38.24t	35.34t	34.19t	41.58t	36.37t
C - 15	52.19t	57.81t	58.97t	58.78t	58.07t	54.53t	47.43t	218.61s	87.66d	54.33t
C - 16	14.55q	24.73q	22.90q	23.21q	22.15q	16.91q	19.57q	14.99q	18.58q	17.10q
C - 17	18.00q	15.65q	17.03q	16.75q	17.53q	17.56q	17.43q	17.46q	17.69q	17.53q
C - 18	33.92q	34.22q	34.71q	34.72q	34.10q	34.02q	33.94q	33.95q	34.03q	34.02q
C - 19	21.99q	22.29q	22.30q	22.37q	22.15q	22.01q	21.96q	21.94q	22.13q	21.96q
C - 20	25.13q	25.19q	33.49q	33.58q	25.44q	24.92q	24.56q	20.00q	20.06q	24.95q
				21.15**						29.29**
				171.48**						170.45**

* s, d, t, q - singlet, doublet, triplet and quartet signals in the off-resonance spectra respectively;
** acetoxy-group signals.



Scheme 2

Table 2. The dependence of the saponified cyclization product composition on the structures of isomeric labdadien-15-ol acetates

Compound	Yield (%) of		The alcohol fraction composition, % *				
	hydrocarbon fraction	alcohol fraction	(14R)-isoagath-12-en-15-ol (4)	(14S)-isoagath-12-en-15-ol (5)	Hiban-14α-ol (6)	Tetracyclic alcohol A (28) m.p.133°C	Tetracyclic alcohol B (20) m.p. 160°C
1. 	38	47	4.7	7.5	-	54.5	33.3
2. 	42.2	51.1	8.3	5.7	-	59.3	26.7
3. 	49.4	49.3	13.5	23.5	15	31.8	16.2
4. 	45	47.4	18.1	15	-	29.3	37.6
5. 	50.6	46.9	12	14.6	16	36.3	21.1

* Determined by GLC on "Tsvet-106" chromatograph; column temperature = 170°C, injector port temperature = 220°C, glass column (l = 1 m, l.d.3.5 mm) with 5 % 5E-30 on Chromaton N-AW-DMCS, Helium flow rate = 50 ml/min, FID.

eration. One of the two remaining carbon atoms belongs to the methyl group because the starting compound contains five such groups; the second one is situated in the cycle B which therefore should be a six-membered one. Taking into account the structure of fragment **8** and the fact that the highest yield of alcohols A and B was achieved starting from *cis*- or *trans*-labd-8(9),13-dien-15-ol acetates **3** (see Table 2), we conclude that the remaining methyl group should be attached to the starred carbon atom of the fragment **8**. Hence, the structure of ketone B may be represented by formula **10** (stereochemistry yet not considered) and its transformation to ketoacetate by the Scheme 1.

The structure of ketone **10** was confirmed by ^{13}C NMR (see Table 1) and MS data. Its ^{13}C NMR spectrum showed signals of five quaternary and one tertiary carbon atoms as well as signals of five methyl groups. Its MS shows a certain analogy in the electron-impact induced fragmentation with camphor.[18] Probable pathways leading to formation of the most informative ions are shown in Scheme 2.

Evidence supporting the bicyclo[2,2,1]heptane backbone of ketone B **10** molecule has been obtained on its deuteration experiment. In spite of the fact that there is a methylene group adjacent to carbonyl group, only one of hydrogen atoms was substituted for deuterium (MS data). It is well known[19-23] that such behaviour is characteristic of the bicyclo [2,2,1]heptan-2-ones and is caused by the stereospecific attack of the base on the less sterically hindered α-exo-proton. The mass spectrum data for the deuterated ketone **10** followed the fragmentation pattern shown in Scheme 2 wherein the peaks of all ions except those at *m/z* 229 and 244 are shifted by one unit towards the higher mass region.

The stereochemistry of ketone **10** was established by CD and ORD methods. We cannot find model compounds with the structures similar to this ketone. However, the environment of its carbonyl group is similar to that of 1-methylbicyclo[2,2,1]heptan-2-one. The negative Cotton effect of the ketone **10** is of the same sign as that of (1S,4R)-1-methylbicyclo[2,2,1]heptan-2-one **18**[24] and this fact indicates that methylene bridge should occupy α-side of the molecule though the absolute value of $\Delta\epsilon$ for ketone **10** is twice that for ketone **18**. More convincing evidence (which is in agreement with that mentioned above) concerning the stereochemistry of the investigated compounds results from analysis of the CD of ketoester **16** (see Fig. 1). Absolute value of $\Delta\epsilon$ (2.95) strictly indicates that its B/C rings are *cis*-fused. Indeed, it is well known that for *cis*-fused 2-hydrindanones $\Delta\epsilon = 2.7–3.9$, but for *trans*-fused isomers $\Delta\epsilon$ is larger (5.0–6.0). Negative Cotton effect of the ketoacetate points out that stereochemistry of its B/C cycles junction can be represented by formula **16**. Unlike examples[25] wherein the equatorial substituent at β-carbon atom in the junction position of the 2-hydrindanone rings is a methyl group, in the case of ketoacetate **16** this substituent (acetoxyethyl group) is more bulky. However, it is known[25] that the influence of methyl group in such a position on the Cotton effect is negligible. Our data indicate that on replacement of methyl by acetoxyethyl group the situation is not altered. These facts lead to the conclusion that the ketone B stereochemistry may be represented by formula **10**. Hence, the corresponding hydrocarbon has the structure **19**.

Therefore, only hydroxy group configuration of the alcohol B remained unspecified. Since attack of small nucleophiles on the bornane type carbonium ions is known[21,22,26] to proceed from the exo-region, one might assume that this hydroxy group has exo-

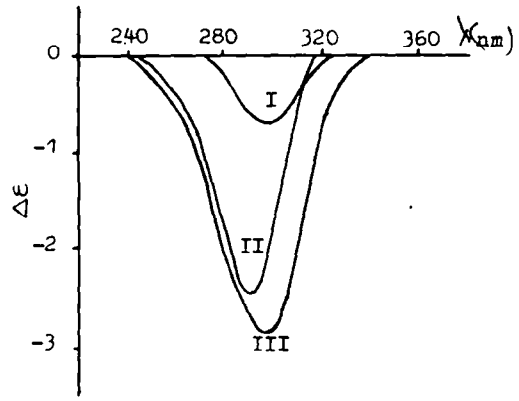
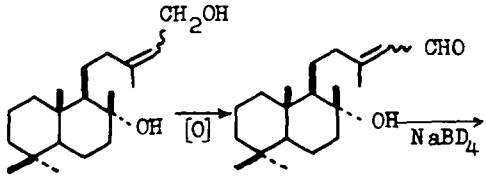


Fig. 1. CD curves of ketones 10(i), 27(ii) and of ketoacetate 16(iii).

configuration. To ascertain this question alcohol B epimer was prepared by the potassium borohydride reduction of ketone **10**. It should be noted that its sodium borohydride or lithium aluminium hydride reduction resulted in the formation of hardly separable epimeric alcohol mixtures. Carbinol proton of alcohol B resonates at higher field (3.46 ppm) than that of its epimer (3.71 ppm). This proves[22,27] exo-configuration of the hydroxy group in the first of them. It was also confirmed using Brewster method[28,29] [the difference between the molecular rotation of 3,5-dinitrobenzoate of alcohol B (157.3°) and that of alcohol B (40.4°) is positive (106.9°)]. This method revealed not only the alcohol B configuration but confirmed also the above discussed stereochemistry of bicyclo[2,2,1]heptane system. Thus, the structure and stereochemistry of alcohol B and its epimer are given by the formulae **20** and **21**, respectively.

Taking into account that (i) alcohols A and B possess the same carbon skeleton; (ii) their acetates are mutually isomerized; (iii) there is no hydrogen atom at an β-position to a hydroxy group in alcohol A (PMR data for alcohol A and corresponding ketone as well as the absence of deuterium exchange in ketone), we conclude that hydroxy group of alcohol A is situated either at C-14 or at C-15 position. The latter position was excluded for the reasons (i) the oxo group of ketone A is strongly hindered sterically; examination of molecular models shows that C-14 position is sterically more hindered than C-15; (ii) according to PMR spectra alcohol A oxidation to corresponding ketone results in the deshielding of two methyl groups; (iii) cyclization of the acetates mixture **25** with the deuterium label at C-15 gives deuterated alcohols A and B which are oxidized to ketones without the loss of deuterium. Moreover, in the MS of thus obtained deuteroketone **10** intensity ratio of ion peaks with m/z 244 and 245 (1.6) is lower in comparison with that (2.9) in the MS of nondeuterated ketone. The intensity ratio of peaks at m/z 229 and 230 (6.0 and 1.3 respectively) is also decreased. These data as well as other changes in its mass spectrum (see Experimental) as compared with those of the nondeuterated compound again confirm its fragmentation pattern and C-15 position for deuterium atom. Since the deuterium introduction method is not stereospecific but McLafferty fragmentation is, the shift of the ion with m/z 244 by 1 mass-unit towards the higher mass numbers should occur only partially, and this is the case.

The mixture of deuterated acetates **25** was synthesized according to the following scheme.



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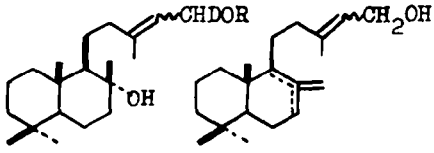
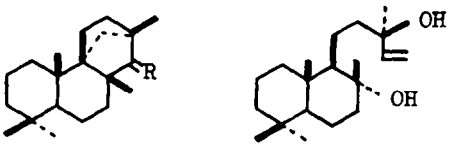


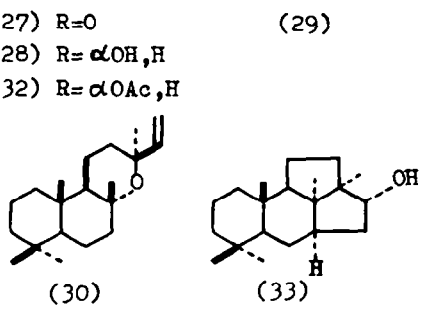
(24) R=H (26)
(25) R=Ac

Corey oxidation[30] of the alcohol mixture **22**[31] afforded the hydroxy aldehydes **23** which was reduced by $NaBD_4$ to the deuterated alcohols **24**. The latter were acetylated to acetates **25** and then cyclizated with sulphuric–formic acids. Alcohols A and B were isolated and oxidized to ketones as described earlier. Our attempt to perform the similar series of transformations with the unsaturated alcohols **26** failed owing to $NaBD_4$ reduction of the conjugated aldehydes prepared from this alcohol mixture gave mainly 1,4-addition products and led to the formation of hardly separable mixture of dienols and alcohols with a saturated side chain. It is known,[32] however, that acid catalyzed cyclization of Δ^{13}-labdanes with the double bonds at C-7 and C-8 positions or with hydroxy group at C-8 gives rise to the same products.[32]

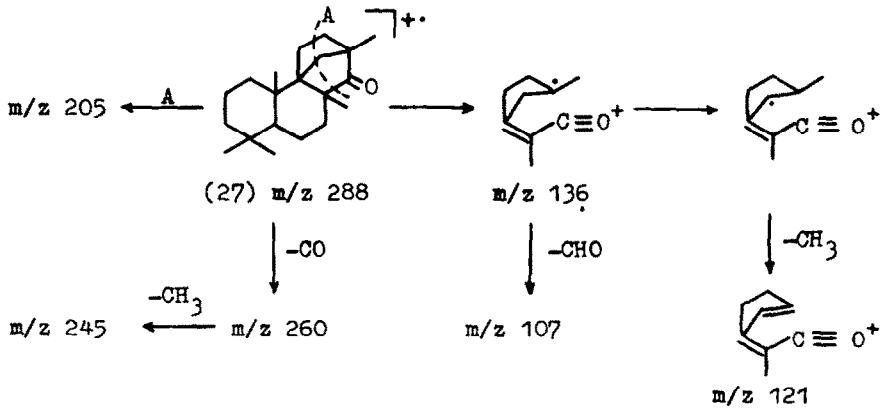
The evidence cited above leads to the conclusion that ketone A has structure **27** which is confirmed by its mass spectrum (Scheme 3). Fragmentation of the deuterated ketone **27** is represented by the same scheme where the peaks of all ions except of having m/z 205 are shifted by one unit to the higher mass region. Therefore, alcohol A has the structure **28**.



(27) R=O (29)
(28) R= αOH,H
(32) R= αOAc,H



(30) (33)



Scheme 3

Location of its carbinol proton signal in the ^{1}H NMR spectrum (3.21 ppm) indicates that its hydroxy group occupies an exo-position. More definite conclusion concerning its configuration could be made if we had its epimer. However, the ketone **27** hydride reduction proceeds stereospecifically giving in all cases the alcohol **28**.

On attempt to prepare 3,5-dinitrobenzoate of alcohols **28** large amounts of hydrocarbons and mixture of two compounds of comparable polarity were unexpectedly obtained. The less polar product was not saponified by 10% alkali hydroxide ethanolic solution but its lithium aluminium hydride reduction results in the formation of alcohol **28**. Difference between molecular rotations of 3,5-dinitrobenzoate and that of alcohol (+9°) indicates the S-configuration at C-14 (exo-hydroxy group) and is in agreement with NMR data. Saponification of more polar benzoylation product of alcohol **28** gave the compound with m.p. 85–87° spectral properties of which were close to and chromatographic behaviour was identical to those of alcohol **28**. Its oxidation affords ketone **27**. However, high resolution (270 MHz) ^{1}H NMR spectrum gives evidence that the product represents in fact mixture *ca* 1:1 of two compounds. The same mixture is formed also by lithium aluminium hydride reduction of more polar benzoate. Thus we have failed to obtain the individual epimer of alcohol **28**. The above given results suggest that on benzoylation of alcohol **28** a reversible alkyl–oxygen bond heterolysis takes place with formation of the epimeric alcohol benzoates mixture. In favour of such a possibility withneses a large amount of hydrocarbons which is formed at the alcohol **28** benzoylation under standard conditions.

The structure of alcohols **20** and **28** and their transformation products was confirmed by ^{13}C NMR spectra (see Table 1). The signals were assigned by comparison of their spectra between each other and with the published spectra of other diterpenoids. The influence of the functional groups on the signals of the atoms attached to them and the neighbouring carbons and the off-resonance data were taken into account as well. The assignment of the C-5 signal is simple because it is the only doublet signal in off-resonance spectra for all of the investigated compounds.

The hydrocarbon **19** off-resonance spectrum shows 4 quartet signals of primary carbon atoms at 17.53, 22.15, 25.44 and 34.10 ppm. The signal intensity at 22.15 ppm is approximately two times higher than that of the other signals. In the spectra of oxygen containing compounds it splits into two signals. Comparison of ^{13}C NMR spectrum of hydrocarbon **19** with that of labdane,[33,34] podocarpane,[35] kaurane[36] and hibane[37] diterpenoids unambiguously shows that C-18 carbon atom resonates in the lower field (34.10 ppm), C-17 carbon atom—in the highest field (17.53 ppm) and C-19 carbon atom resonates at 22.15 ppm. The remaining two quartet signals (22.15 and 25.44 ppm) belong to C-8 and C-13 methyl groups, respectively, because in the spectra of ketone **27** and alcohol **28** they were shifted upfield that is characteristic of carbon atoms at γ-position to a hydroxy group.[35,38] One of them (22.15 ppm) is shifted upfield also in the spectra of compounds **10**, **20** and **21** and therefore belong to C-16 atom. In agreement with Ref. 27, the exo-isomer **20** shows a larger shift. The remaining signal at 25.44 ppm is assigned to C-20 carbon atom.

In the off-resonance spectrum of hydrocarbon **19** there are five signals of quaternary carbon atoms at 33.52, 38.14, 40.96, 43.04 and 60.09 ppm. Comparison with the published data[33–37] reveals, that the signal at 33.52 ppm may be attributed to C-4 atom. This is in good agreement with its chemical shift value (33.20 ppm) calculated according to ref. 39. On passing from hydrocarbon **19** to alcohols **20** and **21** and to ketone **10**, the signal at 43.04 ppm shifts downfield by 3.83, 3.73 and 11.43 ppm, respectively. The values of these shifts are characteristic of carbon atoms at β-position to the mentioned functional groups.[38] The deshielding of C-4 carbon atom occurs also in acetate **31** and lactone **11**. Due to reasons cited above we assigned the signal at 43.04 ppm to C-13 carbon atom.

Passing from hydrocarbon **19** to compounds **10**, **11**, **20**, **21** and **27** the signal at 38.14 ppm is shifted upfield by 0.36–0.83 ppm, i.e. the corresponding carbon atom occupies δ-position to the carbon atom connected with the oxygen containing functional group.[38] According to these data and the fact that C-10 atom of diterpenoids of other structural types[23–37] resonates in the 37–39 ppm region the signal at 38.14 ppm in the spectrum of hydrocarbon **19** must be assigned to the same carbon atom.

The introduction of hydroxy or oxo groups in C-14 position of hydrocarbon **19** causes the downfield shift

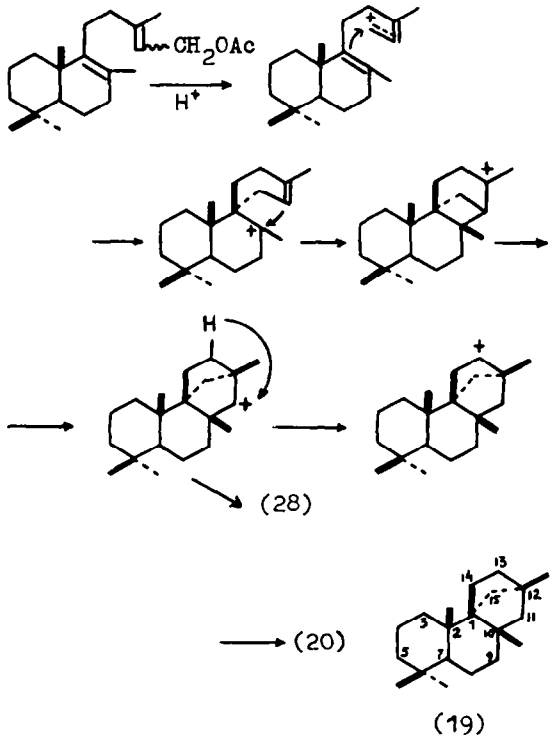
of signals at 40.96 and 43.04 ppm. Hence, these signals can be attributed to C-8 and to C-13 carbon atoms. Since the signal at 43.04 ppm has been assigned to C-13, the signal at 40.96 ppm corresponds to C-8 carbon atom, and the remaining singlet signal at 60.09 ppm to C-9 carbon atom. Indeed, the last signal in the compounds **10**, **20**, **21**, **27** and **28** spectra is shifted upfield by 0.69–2.38 ppm (γ-effect).[35] Thus, the carbon atom of hydrocarbon **19** having a chemical shift 60.09 ppm occupies γ-position to C-12 and C-14 atoms and is situated at C-9. Shift value of this atom in the ketone **27** spectrum (2.28 ppm) is larger as usual ($\sim$1.30 ppm) and is characteristic of bridged system carbon atoms situated at the bridgehead.[40-42] This explains probably the unusually strong δ- and γ-effects in the case of lactone **11**: the signals of C_8 and C_9 atoms in its spectrum are shifted, in comparison with their position in the spectrum of hydrocarbon **19** downfied and upfield by 2.42 and 7.99 ppm, respectively.

Off-resonance spectrum of hydrocarbon **19** shows 9 triplet signals of methylene groups. Comparison of their values with those published elsewhere[33-37] allowed to assign the signals at 18.78, 20.14, 42.21 and 42.80 ppm (the assignment of these latter two signals cannot be conclusive because the difference between them is less than 0.5 ppm), to C-2, C-6, C-1 and C-3 atoms respectively, the surrounding of them being the same for all the compared types of diterpenoids. Since the introduction of oxygen containing groups at C-12 and C-14 in hydrocarbon **19** leads to disappearance of triplet signals at 26.10 and 58.07 ppm they should be attributed to C-12 and C-14 carbon atoms. The signal at 35.80 ppm occupies rather constant position in the spectra of hydrocarbon **19** derivatives except of those for ketone **27** and alcohol **28** where it is shifted upfield. In the ^{13}C NMR spectra of diterpenoids of different structural types the signal of the C-7 atom appears at 35.90–43.20 ppm, and introduction of functional group in peri position to it (at C-14) results in upfield shift of its signal.[33-37]Therefore the signal at 35.80 ppm in the spectrum of hydrocarbon **19** is assigned to C-7. The introduction of oxygen-containing functional groups at C-12 in hydrocarbon **19** results in downfield shift of triplet signal at 37.35 ppm. Hence, it corresponds to C-11 carbon atom and the last triplet signal at 45.00 ppm must be attributed to C-15 atom.

To establish the influence of the structure of initial compound on composition of the cyclization product the esters **3** with Δ^7-, $\Delta^{8,9}$- and $\Delta^{8(20)}$-double bonds (as Δ^{13}-*cis*, *trans* mixtures) were prepared according to ref. 13 from manool **2** and its Δ^7- and $\Delta^{8(9)}$-isomers.[43] In the case of $\Delta^{8(9)}$-isomer the individual Δ^{13}-*cis* and Δ^{13}-*trans* compounds (3) were isolated. However, their cyclization lead to formation of both tricyclic alcohols **4** and **5**, this indicates on Δ^{13}-double bond isomerization before the cyclization. Therefore the cyclization of Δ^7- and $\Delta^{8(20)}$-acetates was carried out with the Δ^{13}-isomers mixtures (see Table 2). The highest total yield of tricyclic alcohols **4** and **5** (*ca* 37% of alcohol fraction) was obtained from the mixture of $\Delta^{8(20)}$-acetate **3** and of tetracyclic alcohols **20** and **23** (86–88% of alcohol fraction)—from acetates **3** with tetrasubstituted double bond in the cycle B.

We have shown that alcohols **4–6**, **20** and **28** are formed also on cyclization of the acetates mixture **3** by formic acid, of manool **2** by the mixture of aqueous acetic and sulphuric acids,[4,8] and of sclareol **29** and 13-epimanoyloxide **30** by the mixture of sulphuric and formic acids.

Thus, the cyclization of a series of labdane diterpenoids with several acids or their mixtures gives rise to 11- and 13-hydroxy derivatives of (1R,2S,7S,10S,12S) - 2,6,6,10,12 - pentamethyltetracyclo[10.2.1.$0^{1,10}$.$0^{2,7}$]eicosane **19**, i.e. hydrocarbon with a new bridged carbon skeleton. Their formation may be represented by the following scheme:



The validity of this scheme follows from the facts that the highest yield of alcohols **20** and **28** is obtained by cyclization of labd-8(9),13-dien-15-ol acetates, and the deuterium label in cyclization products of the deuterated acetate mixture **25** is situated at C-15.

After completion of this work (preliminary reports[44,45]) the communication of French chemists[46] had appeared describing a new tetracyclic alcohol which is formed with 82% yield from sclareol treated with perchloric acid in 1-nitropropane. The structure **33** has been assigned to this alcohol. Its physicochemical properties are very similar to those of alcohol **20** obtained by us and MS of its oxidation product coincided with that of ketone **10**. We have repeated the work[46] and established the identity of the compound described by these authors with alcohol **20**. However, the structure **33** proposed by French researchers does not explain why on the deuteration of the ketone formed by its oxidation only one of two hydrogen atoms is substituted for deuterium. Moreover, having accomplished the sequence of transformations with alcohol **33**, leading in our case to ketoacetate **16**, we should have obtained a ketoester,

the molecule of which would contain only one methylene group attached to the carbonyl group. In fact, there are two such groups. Finally, the structure **33** contains three tertiary and four quarternary carbon atoms, but ^{13}C NMR data show the investigated alcohol contains one tertiary and five quarternary carbon atoms.

No compound having the carbon skeleton described in the present paper have been found so far in the natural sources.

EXPERIMENTAL

M.ps were determined using Kofler apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$ on polarimeter Polamat S. IR spectra were taken in CCl_4 on UR-20 and "Specord 71 IR" spectrophotometers. ^1H NMR spectra were measured in $CDCl_3$ using RS-60 and Varian HA-100 spectrometers and ^{13}C NMR using a Varian CFT-20 spectrometer, with TMS as internal standard. The chemical shifts are presented in terms of δ values. Mass spectra were recorded on MX-1303 spectrometer at 70 eV, the sample being introduced directly into the inlet system. The ORD and CD curves were recorded on a Spectropol 1 spectrophotopolarimeter and on a Jouel dichrograph, respectively. Organic extracts were dried over anhydrous Na_2SO_4. Column chromatography was performed on 100/160 mkm L silica gel (Czechoslovakia) and neutral activity III alumina. For TLC silica gel LS 5/40 mkm (Czechoslovakia) was used.

Cyclization of the acetates mixture **3** *by concentrated sulphuric and formic acids*

The acetate mixture **3** (36.61 g) was added during 1 hr under continuous stirring to a soln of conc sulphuric acid (10 g) in 99% formic acid (74 ml) at $-2 \pm 2°$. Under stirring the reaction mixture was heated up to 20° for 30 min then stirred for 1 hr, then was diluted with ether and poured into ice water. Ether layer was separated and water layer extracted with ether. The combined ether extract was washed with water, then several times with sat $NaHCO_3$ and sodium sulphate solutions, again with water, and dried. After ether evaporation 30.8 g of crude product were obtained. It was purified by column chromatography on alumina. The following fractions of increasing polarity were obtained: (i) 15.2 g of hydrocarbons mixture; (ii) 1.5 g of esters mixture; (iii) 0.5 g of crystalline compound; (iv) 3.3 g mixture of 4 compounds; (v) 3.3 g, crystalline mixture of 3 substances; (vi) 0.22 g of crystalline compound; (vii) 0.25 g of crystalline product; (viii) 4.8 g of crystalline compound; (ix) 1.2 g of complex mixture of compounds (not investigated). Recrystallization of fraction (iii) from petroleum ether gave **6**, m.p. 111–111.5°; $[\alpha]_D^{22} - 6.3°$ (c 4.8). Its IR, NMR and mass spectra were identical with those of authentic hiban-14α-ol **6**. Recrystallization of fraction (vi) from petroleum ether gave alcohol **4**, m.p. 106–107°, $[\alpha]_D^{22} + 52.2°$ (c, 3.8) identical with an authentic sample. Recrystallization of fraction (vii) from petroleum ether gave alcohol **5**, m.p. 124.5–125°, $[\alpha]_D^{22} - 7.5°$ (c, 4.3) identical with an authentic sample.

Tetracyclic alcohol A **28**

Repeated recrystallization of fraction (v) from petroleum ether gave the alcohol **A 28** with m.p. 133–134.5°, $[\alpha]_D^{20}$ 4.4° (c, 6.8). Found, C, 82.60; H, 11.74. Calc for $C_{20}H_{34}O$: C, 82.69; H, 11.80%. IR (cm^{-1}): 1058, 3530, 3645 (OH), 1370, 1388 [$C(CH_3)_2$]. NMR (ppm) singlets (3H) at 0.83, 0.87, 0.85, 1.03, 1.06 (CH_3-groups at quaternary carbon atoms), singlet at 3.21 (>CHOH). This compound was not oxidized with p-nitroperbenzoic acid. Acetylation of alcohol **28** by Ac_2O–Py mixture gave the acetate **32**, m.p. 125–126° (CH_3CN), $[\alpha]_D^{22}$ 42.5° (c, 5.5). Found: C, 79.80; H, 10.92. Calc for $C_{22}H_{36}O_2$: C, 79.46; H, 10.91%. IR (cm^{-1}): 1242, 1742 (OAc).

Tetracyclic alcohol B **20**

Recrystallization of fraction (viii) from petroleum ether gave alcohol **B 20**, m.p. 160.5°–161.5°, $[\alpha]_D^{20} + 13.9°$ (c, 8.8). Found: C, 82.92; H, 11.70. Calc for $C_{20}H_{34}O$: C, 82.69; H, 11.80%. IR (cm^{-1}): 1050, 3500, 3636 (OH), 1367, 1384 [$C(CH_3)_2$]. NMR (ppm): singlets (3H) at 0.83, 0.88, 0.94, 1.00, 1.05 (CH_3-groups at quaternary carbon atoms), octet at 2.18 (1H, $J_1 = 14$ Hz, $J_2 = 7.2$ Hz, $J_3 = 3.6$ Hz), doublet with broadened signals at 3.46 (1H, $J = 6.8$ Hz, >CHOH). Product is not oxidized by p-nitroperbenzoic acid. Its acetylation by Ac_2O–Py mixture gave acetate **31** with m.p. 87–87.5° (CH_3CN). $[\alpha]_D^{22} + 72.5$ (c, 5.4). Found: C, 79.62; H, 10.92. Calc for $C_{22}H_{36}O_2$: C, 79.46; H, 10.91%. IR (cm^{-1}): 1245, 1740 (OAc). Tosylate of alcohol B, m.p. 116–117.5° (petroleum ether) was unstable even in a refrigerator. Its partial decomposition occurred during preparation. For this reason we did not succeed in obtaining satisfactory elemental analysis results.

Ketone **10**

The solution of alcohol **B 20** (350 mg) in 10 ml of dry pyridine was added with stirring to the complex obtained from CrO_3 (350 mg) in 3.6 ml of pyridine. The mixture was stirred for 7 hr and stored at room temp for 35 hr. Then it was poured into 200 ml of 5% hydrochloric acid, the precipitate was filtered off and the filtrate was extracted with ether. The extract was washed with 20% hydrochloric acid, water, sodium bicarbonate solution, water and then dried. The precipitate was dissolved in 5% sodium hydroxide and the solution was treated in the same manner. Both extracts were combined and ether was evaporated to give 341.1 mg of ketone **10**, m.p. 102–103° (ethanol–ether), $[\alpha]_D^{21}$ 15.3° (c, 5.3). Found: C, 83.10; H, 11.29%. Calc for $C_{20}H_{32}O$: C, 83.27; H, 11.18%. IR (cm^{-1}): 1742 (cyclopentanone), 1416 (CH_2CO). NMR (Bruker HX-270): singlets (3H) at 0.85; 0.90; 0.99; 1.07; 1.12 (C_4, C_8, C_{10} and C_{13}–CH_3), doublet of doublets of AB system at 2.33 (H_A, $J = 18$ Hz, the signals of this doublet are additionally splitted with $J = 4.7$ Hz, exo-H at C_{11}) and at 2.08 (H_B, $J = 18$ Hz, endo-H at C_{11}), multiplet at 2.21 (1H, C_{14}–H, deshielded by the carbonyl group). ^{13}C NMR data are tabulated. 2,4-Dinitrophenyl hydrazone, m.p. 212.5–213.5° (ethanol). Found: C, 66.67; H, 7.84; N, 11.82. Calc for $C_{26}H_{36}N_4O_4$: C, 66.64; H, 7.74; N, 11.96%. Tosylhydrazone, m.p. 187.5–188° (methanol). Mass spectrum (*m/z*, intensity in %): 288 (M, 60), 273 (6), 260 (3), 259 (9), 246 (8), 245 (15), 244 (44), 243 (3), 23 (3), 230 (5), 229 (23), 203 (3), 191 (11), 190 (3), 189 (5), 177 (4), 175 (7), 164 (3), 163 (9), 161 (6), 151 (7), 150 (20), 149 (16), 148 (3), 147 (5), 138 (13), 137 (100), 136 (52), 135 (13), 134 (4), 133 (5), 125 (3), 124 (4), 123 (18), 122 (12), 121 (28), 120 (9), 119 (13), 111 (4), 110 (6), 109 (32), 108 (33), 107 (46), 106 (7), 105 (12), 101 (3), 97 (4), 96 (5), 95 (40), 94 (16), 93 (20), 92 (3), 91 (16), 83 (52), 82 (8), 80 (3), 79 (15), 78 (3), 77 (9), 71 (4), 70 (3), 69 (39), 68 (5), 67 (9), 65 (4), 57 (9), 56 (7), 55 (40), 53 (9), 45 (7), 44 (8), 43 (27), 42 (5), 41 (53) (here and hereafter the peaks with the intensity less than 3% are not shown). The ORD curve (c, 0.2, methanol), 20°; $[\alpha]_{589} + 15°$, $[\alpha]_{360} + 15°$, $[\alpha]_{341}$ 0°, $[\alpha]_{330} - 22°$, $[\alpha]_{325} - 45°$, $[\alpha]_{320} - 83°$, $[\alpha]_{313} - 140°$, $[\alpha]_{305} - 70°$, $[\alpha]_{302}$ 0°, $[\alpha]_{295} + 260°$, $[\alpha]_{290} + 400°$, $[\alpha]_{284} + 487°$, $[\alpha]_{270} + 390°$, $[\alpha]_{255} + 305°$, $[\alpha]_{245} + 340°$. The CD curve in methanol at 20° (c, $6.93 \cdot 10^{-3}$ mol/l): $\Delta\epsilon_{max}^{298.5} - 0.70$ (Fig. 1, curve I).

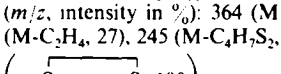
Deuterated ketone **10**

Ketone **10** (260 mg) was dissolved in 10 ml dry freshly distilled dioxane, 1.6 ml of deuterium oxide and 800 mg of sodium methylate were added to the solution, and the mixture was refluxed for 8 hr. The solvent was removed, then 10 ml of dioxane and 1.6 ml of deuterium oxide were added to the residue. The soln was refluxed for 6 hr, cooled and poured into 15 ml of 1 mol soln of KH_2PO_4 and then extracted with ether. The extract was washed with deuterium oxide and water, dried and the solvent was evapo-

rated to give 205 mg of deuterated ketone **10**, m.p. 93–95° (ethanol). Mass spectrum (*m/z*, intensivity in %): 289 (M^+, 43), 288 (6), 274 (6), 261 (3), 260 (9.5), 247 (3), 246 (10), 245 (16), 244 (50), 231 (3), 230 (7), 299 (35), 206 (3), 204 (3), 191 (3), 190 (5), 189 (3.5), 178 (3), 177 (3), 176 (4.5), 175 (6.5), 165 (3.5), 169 (9), 163 (6), 162 (5.5), 161 (6.5), 160 (3), 159 (3), 152 (5), 151 (20), 150 (15.5), 149 (8), 148 (5.5), 147 (5.5), 145 (3), 139 (14), 138 (81), 137 (54), 136 (19), 135 (12), 134 (9), 133 (8), 132 (3), 131 (3), 125 (4), 124 (9), 123 (23), 122 (23), 121 (24), 120 (18), 119 (14), 118 (3), 117 (4), 111 (6), 110 (20), 109 (35), 108 (67), 107 (34), 106 (19), 105 (15), 104 (3), 103 (3), 97 (4.5), 96 (12), 95 (47), 94 (35), 93 (26), 92 (19), 91 (25), 81 (11), 80 (13), 79 (35), 78 (16), 77 (24), 76 (11), 75 (18), 70 (8), 69 (53), 68 (14), 67 (32), 66 (6), 65 (8), 57 (10), 56 (19), 55 (67), 54 (7.5), 53 (20), 44 (4), 43 (31), 42 (18), 41 (100), 40 (7).

Ethylene thioketal of ketone **10**

BF_3 etherate (0.5 ml) and 200 mg of ethanedithiol were added to the solution of ketone (**10**; 200 mg) in 5 ml of glacial acetic acid. The solution was stored at 20° for 6 days. The precipitate was filtered and washed with methanol (yield 183.8 mg). The filtrate was diluted with ether and washed with 3% sodium hydroxide solution, water, dried and ether was evaporated to give additionally 66 mg of thioketal, m.p. 139–140° (methanol). Found: C, 72.49; H, 10.22. Calc for $C_{22}H_{36}S_2$: C, 72.46; H, 9.92%. Mass spectrum (*m/z*, intensity in %): 364 (M^+, 58), 349 ($M-CH_3$, 2), 336 ($M-C_2H_4$, 27), 245 ($M-C_4H_7S_2$, 20), 119 ($M-C_4H_7S_2$, 15), 105



Ketone 27

Alcohol A (**28**; 90 mg) was oxidized with the chromium anhydride–pyridine complex (100 mg) prepared as described above for ketone **10** to give 87.2 mg of ketone **27**, m.p. 105–106° (aqueous methanol), $[\alpha]_D^{20} - 109.2°$ (c, 1.8). Found: C, 83.10; H, 11.27. Calc for $C_{20}H_{32}O$: C, 83.27; H, 11.18%. IR (cm^{-1}): 1738 (cyclopentanone). NMR: singlets (3 H) at 0.86; 0.88; 1.01; 1.13; 1.23. ^{13}C NMR data are tabulated. Mass spectrum (*m/z*, intensity in %): 289 (18), 288 (M^-, 83), 273 (3), 261 (3), 260 (15), 259 (4), 246 (4), 245 (19), 209 (3), 208 (16), 207 (3), 205 (17), 191 (7), 190 (7.5), 189 (8), 179 (4), 177 (3), 175 (5), 164 (7.5), 163 (12), 161 (3.5), 152 (3), 151 (7), 150 (15), 149 (18), 147 (8), 138 (14), 137 (12), 136 (47), 135 (15), 134 (8), 133 (6), 124 (13), 123 (26), 122 (45), 121 (100), 120 (8), 119 (13), 115 (4), 111 (3.5), 110 (8), 109 (26), 108 (33), 107 (57), 106 (4), 105 (16), 101 (3.5), 97 (7), 36 (4), 95 (33), 94 (9), 93 (26), 92 (4), 91 (24), 84 (8), 83 (9), 82 (8), 81 (60), 80 (7), 79 (25), 78 (7), 77 (15), 69 (36), 68 (7), 67 (24), 65 (6), 63 (5), 57 (9), 56 (6), 55 (47), 53 (14), 46 (8), 45 (18), 44 (3), 43 (25), 42 (5.5), 41 (66), 40 (3), 39 (13). Ketone (27) does not give 2,4-dinitrophenyl hydrazone, tosylhydrazone and thioketal. It is not oxidized by peracids and is not deuterated. The ORD curve (c, 0.17, methanol), 20°, $[\alpha]_{589} - 63°$; $[\alpha]_{530} - 62°$; $[\alpha]_{450} - 103°$; $[\alpha]_{400} - 160°$; $[\alpha]_{350} - 310°$; $[\alpha]_{320} - 717°$; $[\alpha]_{305} - 1220°$; $[\alpha]_{288}$ 0°; $[\alpha]_{280} + 660°$; $[\alpha]_{270} + 947°$; $[\alpha]_{260} + 742°$; $[\alpha]_{250} + 1488°$. The CD curve in methanol at 20° (c, 7.39×10^{-3} mol/l); $\Delta\varepsilon_{max}^{290} - 2.65$ (Fig. 1, curve II).

Hydrocarbon **19**

(1) *Starting from ketone* **10**. (a) The soln of ketone **10** thioketal (107 mg) in 10 ml of dioxane was refluxed for 35 hr with Raney T-1 nickel prepared from 2 g of alloy.[47] The catalyst was filtered and washed with petroleum ether. The filtrate was evaporated and the residue was chromatographed on alumina (5 g, activity II). Petroleum ether eluted 51.7 mg of hydrocarbon **19**, m.p. 72–73° (alcohol), $[\alpha]_D^{20} + 16.8°$ (c, 26.7). Found: C, 87.68; H, 12.45. Calc for $C_{20}H_{34}$: C, 87.51; H, 12.49%. NMR: singlets (3H) at 0.79; 0.83; 0.90; 0.96 and 1.06.

(b) Metallic sodium (90 mg) was dissolved in 2 ml of freshly distilled diethyleneglycol, then 250 mg of anhydrous hydrazine and 200 mg of ketone **10** were added. The mixture was refluxed under argon atmosphere for 3 hr at 180° (temperature had risen to 210°), water and the excess of hydrazine was evaporated and the soln was refluxed at this temp for 4 hr. After cooling the mixture was poured into water and extracted with ether. The extract was washed with water, 10% sulphuric acid solution, dried and the ether was evaporated to give the crystalline residue (188 mg). Its recrystallization from methanol afforded a product with m.p. 76–77°, which did not show the melting point depression when mixed with the hydrocarbon obtained according to the above method. Both compounds have identical IR and NMR spectra.

Starting from ketone **27**. The reduction of ketone **27** (200 mg) under the conditions described above for ketone **10** gave 168 mg of three compounds mixture (TLC on silica gel). This mixture was chromatographed on alumina (5 g). Petroleum ether eluted 58 mg of a hydrocarbon, m.p. 76–77° (methanol), identical with hydrocarbon **19** obtained by reduction of the ketone **10**. Benzene–petroleum ether (4:6) mixture eluted 3.5 mg of the initial ketone and 13.7 mg of its mixture with a more polar compound. The elution with benzene gave 93 mg of the latter in the pure state. According to IR and NMR spectroacopy data it is identical to alcohol A, though its melting point (122-124°) is lower and did not change even after repeated recrystallization.

Lactone **11**

(a) p-Nitroperbenzoic acid (600 mg) and five drops of trifluoroacetic acid were added to the soln of ketone (**10**; 300 mg) in 10 ml of chloroform and the obtained mixture was stirred at room temp for 70 hr. The solution was diluted with ether, then water was added, the organic layer was washed with water, 3% sodium hydroxide solution, water, dried and ether was evaporated. The residue (340 mg) was chromatographed on silica gel (20 g). Petroleum ether–benzene (1:4) eluted a small amount of less polar impurity followed by lactone (**11**; 278 mg): m.p. 170.5–171° (petroleum ether); $[\alpha]_D^{23}$ 46.2° (c, 4.9). Found: C, 74.02; H, 10.81. Calc for $C_{20}H_{32}O_2$: C, 74.49; H, 10.62%. IR (cm^{-1}): 1736 (δ-lactone). NMR: singlets (3H) at 0.87; 0.92; 0.96 (C_4 and C_{10}–CH_3), 1.18 (C_8–CH_3), 1.44 (C_{13}–CH_3), doublet of doublets of AB system at 2.27 (H_B; J = 3 Hz) and 2.41 (H_A; J = 3 Hz).

(b) p-Carbmethoxyperbenzoic acid (300 mg) and 0.3 ml of trifluoroacetic acid were added to the solution of ketone **10** (350 mg) in 10 ml of dry chloroform. The mixture was stirred for 10 hr at room temp and then stored overnight. The mixture was treated as described above, the product was purified by column chromatography on silica gel then recrystallized from petroleum ether to give 313.4 mg of lactone (**11**; 88% yield, m.p. 170–171°).

Saponification of lactone **11**

(a) The soln of lactone (**11**; 47 mg) in 5 ml of 10% ethanolic NaOH was refluxed for 2 hr. After the usual work up 41.2 mg of crystalline product were obtained. After recrystallization from ether it had m.p. 167.5–169° and was identical to the initial lactone **11** (according to IR and TLC).

(b) 203 mg of lactone **11** were saponified as described above and the product was methylated with an excess of diazomethane ether solution to give a crystalline product containing trace amount of lactone **11** (TLC). It was chromatographed on silica gel (5 g). During chromatography it was completely transformed into lactone **11**.

(c) 164 mg of lactone **11** were saponified and methylated with diazomethane as described above. The product was dissolved in 3 ml of dry pyridine and chromium anhydride complex obtained from 170 mg of chromium anhydride was added to the solution. The mixture was stirred for 1 hr, stored at room temperature for 10 hr and then treated in a usual manner. The product was chromatographed on silica gel (5 g) to give the initial lactone **11**.

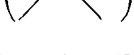
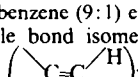
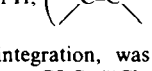
Diol (**12**)

Lithium aluminium hydride (500 mg) was added to the solution of lactone **11** (460 mg) in 50 ml of dry ether and the mixture was stored at room temperature for 5 hr. The excess of hydride was decomposed with ethyl acetate, the mixture was acidified with 10% sulphuric acid solution, water was added and the mixture was extracted with ether. The extract was washed with water, sodium bicarbonate solution, water, dried and ether was evaporated. The residue (470 mg) was recrystallized from ether to give diol **12**, m.p. 92–95°, $[\alpha]_D^{21}$ 35.2° (c, 5.7). Found: C, 78.08; H, 11.66%. Calc for $C_{20}H_{36}O_2$: C, 77.92; H, 11.70%. IR (cm^{-1}): 3280 (OH band). NMR: singlets at 0.88 (3H), 0.91 (3H) [$C_4(CH_3)_2$], 1.04 (6H, C_8 and C_{10}–CH_3), 1.44 (3H, C_{13}–CH_3), triplet at 3.79 (2H, J = 6.5 Hz; $-CH_2OH$), broadened signal at 3.50 (2H, OH-groups).

Hydroxyacetate (**13**)

Diol **12** (470 mg) was dissolved in 6 ml of dry pyridine and 1.7 ml of acetic anhydride was added. The mixture was stored for 1.5 hr at 22°, then 10% sulphuric acid was added and the mixture was extracted with ether. The extract was washed with water, sodium dicarbonate solution, water, dried, filtered and the solvent was evaporated. The obtained product (**13**; 515 mg) was recrystallized from petroleum ether, m.p. 110–110.5°, $[\alpha]_D^{21}$ 22.6° (c, 6.1). Found: C, 75.11; H, 10.76. Calc for $C_{22}H_{38}O_3$: C, 75.38; H, 10.92%. IR (cm^{-1}): 1030, 3520, 3605 (OH), 1244, 1733 (OAc). NMR: singlets (3H) at 0.88; 0.92; 1.04; 1.08 (C_4, C_8 and C_{10}–CH_3), 1.43 (>C(OH)CH_3), 2.04 (OAc), triplet at 4.28 (2H, J = 7.5 Hz; $-CH_2OAc$).

Unsaturated esters (**14**) *and* (**15**)

Freshly distilled cooled phosphorus oxychloride (0.67 ml) was gradually added to the cooled (0°) soln of hydroxyacetate **13** (490 mg) in 6.7 ml of dry pyridine. The mixture was stored at room temp for 15 hr. The crushed ice was added to the reaction mixture and it was diluted with water and extracted with ether. The extract was washed with 10% sulphuric acid, water, sodium bicarbonate soln, water, dried, filtered and evaporated to give 433 mg of viscous liquid product. It gives two spots on TLC on silver nitrate impregnated silica gel[48] (R_f 0.57 and 0.71, solvent benzene). Found: C, 79.50; H, 10.85. Calc for $C_{22}H_{36}O_2$: C, 79.47; H, 10.91%. IR (film, cm^{-1}): 828, 1700 (), 990, 1650 (), 1235, 1742 (OAc). The product (420 mg) was chromatographed on silver nitrate impregnated silica gel (15 g) obtained by the procedure[49] and activated at 130° for 15 hr. Petroleum ether–benzene (9:1) eluted the mixture of the trisubstituted double bond isomers **14** (319 mg). IR (film, cm^{-1}): 827, 1655 (); 1236, 1743 (OAc). NMR: singlets at 0.82 (6H), 0.95 (3H), 1.10 (3H) (C_8, C_{10} and C_4–CH_3), 1.65 (3H, ), 1.88 (3H, OAc), triplet at 3.79 (2H, $-CH_2OAc$, J = 7 Hz), multiplets at 4.87 and 5.29 (in the sum 1 H, ). Isomers content according to NMR integration, was 21 and 79%, respectively. According to GLC ("Chrom-4", 5% XE-60 on Chromaton N-AW-DMCS, glass column 2 m × 3.5 mm i.d., column temp programming from 160 to 230°, v = 3°/min, carrier gas helium, flow rate 45 ml/min) their content was 22% and 78%.

The same solvent mixture eluted 85 mg of ester **15** m.p. 49.5–50.5° (methanol). IR (film, cm^{-1}) 876, 1650, 3085, (), 1246, 1743 (OAc). NMR (CCl_4): singlets at 0.87 (6H), 1.04 (3H), 1.10 (3H), (C_4, C_8 and C_{10}–CH_3), 1.94 (3H, OAc), triplet at 4.15 (2H, J = 8 Hz, $-CH_2OAc$), broadened multiplet signal at 4.95 (2H, ).

Oxoacetate **16**

Osmium tetraoxide (12.2 mg) was added to the solution of ester **15** (83 mg) in the mixture of dioxane (5.7 ml), water (1.7 ml) and acetic acid (1.2 ml). The solution darkened in 15 min and then 930 mg of sodium periodate were added. The mixture was stored at room temp for the reaction completion (22 hr), then diluted with water and extracted with ether. The extract was thoroughly washed with water, sodium bicarbonate soln, water, dried and ether was evaporated. The residue (80 mg) was subjected to column chromatography over silica gel (2.5 g) to give 65 mg of ketoacetate **16**, m.p. 162–163° (petroleum ether–benzene). Found: C, 75.26; H, 10.11. Calc for $C_{21}H_{34}O_3$: C, 75.40; H, 10.24%. IR (cm^{-1}): 1238, 1748 (OAc and). NMR: singlets at 0.85 6H, [$C_4(CH_3)_2$], 1.16 (3H, C_{10}–CH_3), 1.26 (3H, C_8–CH_3), 2.04 (3H, OCO–CH_3), triplet at 4.41 (2H, J = 7 Hz, CH_2OAc), doublet of doublets of AB system at 2.04 and 2.22 (2H, J = 10 Hz, $-CH_2$–CO–), and doublet of doublets of another AB system at 2.34 and 2.78 (2H, J = 10 Hz, $-CH_2$–CO–). ORD curve (c, 0.49, CH_3OH), 20°, $[\alpha]_{550} - 38°$; $[\alpha]_{450} - 80°$; $[\alpha]_{350} - 325°$; $[\alpha]_{325} - 890°$; $[\alpha]_{323} - 933°$ (shoulder); $[\alpha]_{320} - 974°$; $[\alpha]_{313} - 1115°$; $[\alpha]_{305} - 669°$; $[\alpha]_{303} - 567°$ (shoulder); $[\alpha]_{300} - 325°$; $[\alpha]_{297}$ 0°; $[\alpha]_{290} + 649°$; $[\alpha]_{280} + 1217°$; $[\alpha]_{271} + 1298°$; $[\alpha]_{260} + 1135°$; $[\alpha]_{250} + 374°$. CD curve in methanol at 20° (c, 7.37×10^{-3} mol/l) (Fig. 1, curve III), $\Delta\epsilon_{max}^{298.5} - 2.95$.

Hydroxyketone (**17**)

Ketoacetate **16** (14.5 mg) was dissolved in an excess of 10% potassium hydroxide alcoholic soln and the mixture was stored at room temp for 1.5 hr. Water was added and the mixture was extracted with ether. The extract was washed with water, 10% sulphuric acid soln, water, dried and ether was evaporated to give 10 mg of hydroxyketone **17**, m.p. 124–125° (petroleum ether). IR spectrum (cm^{-1}): 1089, 3380, 3612 (OH), 1746 (cyclopentanone).

Alcohol (**21**)

KBH_4 (90 mg) was added to the solution of 90 mg of ketone **10** in 9 ml of methanol and the soln was stored at room temperature for 2 hr, then water and 10% sulphuric acid were added and the mixture was extracted with ether. The extract was worked up in usual manner, dried and the ether was evaporated to give 85 mg of compound **21**, m.p. 99–101° (acetonitrile), $[\alpha]_D^{20} - 10.3°$ (c, 3.6). Found: C, 82.76; H, 11.72%, Calc for $C_{20}H_{34}O$: C, 82.69; H, 11.80%. IR (cm^{-1}): 1065, 3500, 3638 (OH). NMR (Bruker HX-270): singlets (3H) at 0.81; 0.86; 0.89; 0.99; 1.18 (C_4, C_8, C_{10} and C_{13}–CH_3), octet at 3.71 (1H $J_1 = 10.5$ Hz; $J_2 = 3$ Hz; $J_3 = 1.5$ Hz, C_{12}–H).

Isomerization of alcohols (**20**) *and* (**28**)

The solns of alcohols A and B (50 mg) in 2 g of 10% sulphuric acid in formic acid solution were stirred at 70° for 30 min and worked up. In both cases the mixtures of alcohols A and B formates and hydrocarbons were obtained (TLC on SiO_2). Saponification of formates mixture afforded a mixture of alcohols A and B.

Hydroxyacetates mixture (**25**)

The soln of alcohols mixture **22** (1.45 g)[31] in 10 ml of methylene chloride was added on stirring at room temp to the mixture of potassium acetate (300 mg) and pyridine chlorochromate (4.5 g)[30] in 15 ml of methylene chloride. In 5 min 35 ml of ether was added to the mixture, the precipitate was filtered and washed with ether, the filtrate was washed with water, 10% sulphuric acid, water, sodium bicarbonate solution, water, dried and evaporated to dry-

ness. The residue (1.35 g) was subjected to column chromatography on SiO_2 (45 g). 25% Ethyl acetate in petroleum ether eluted under some pressure[50] 760 mg of the hydroxyaldehydes mixture **23**. IR (film, cm^{-1}): 1650 and 1680 (conjugated –CHO), 3500 (OH). This mixture was dissolved in 10 ml of methanol and 137 mg of sodium borodeuteride were added. The soln was stored at room temperature for 20 min and then was treated in a usual manner to give 650 mg of the diol mixture **24** identical according to IR spectra and TLC data with the mixture of nondeuterated alcohols **22**. The product was dissolved in 10 ml of dry pyridine, 2.2 ml of acetic anhydride was added and the mixture was stored at room temperature for 2.5 hr for the completion of reaction. After the usual work up of the reaction mixture, 680 mg of the acetates mixture **25** were obtained. The identification was carried out by the chromatographic comparison with the sample of the nondeuterated esters mixture.

Deuterated alcohols (**20**) *and* (**28**)

The mixture of acetates **25** (655 mg) was dissolved in the mixture of 0.3 g of concentrated sulphuric acid and 2.7 g of 99% formic acid, then heated to 65° and stirred for 20 min. The reaction mixture was treated in usual manner and the residue was saponified and chromatographed to give 270 mg of hydrocarbon and 240 mg of alcohol fractions. The alcohol fraction was chromatographed on silica gel column (20 g) under pressure. Elution with 7% ethylacetate in benzene give 18 mg of alcohol **28**, m.p. 131–132.5° (petroleum ether) and 30 mg of alcohol **20**, m.p. 159–160° (alcohol). Their IR spectra are identical with those of undeuterated products.

Deuterated ketone (**10**)

The deuterated at C-15 alcohol **20** (29 mg) was added with stirring to a mixture of 5 mg of potassium acetate and 66 mg of pyridinium chlorochromate in 2 ml of methylene chloride. The mixture was stirred at room temp for the reaction completion (2.5 hr) and treated as described above. The obtained product (17 mg) was crystallized from methanol, m.p. 99–100°. It shows no m.p. depression when mixed with the undeuterated ketone. Mass spectrum (*m/z*, intensity in %): 289 (M^+, 75), 288 (33), 274 (9), 273 (4), 260 (8), 259 (9), 247 (10), 246 (16), 245 (31), 244 (51), 232 (3), 231 (6), 230 (21), 229 (28), 205 (3), 203 (4), 199 (18), 191 (5), 189 (5), 177 (3), 176 (6), 175 (8), 164 (9), 161 (6), 152 (5), 151 (33), 150 (22), 149 (11), 148 (6), 147 (7), 146 (3), 139 (11), 138 (71), 137 (77), 135 (13), 134 (6), 133 (8), 125 (6), 123 (22), 122 (21), 121 (26), 120 (13), 119 (15), 110 (17), 109 (42), 108 (47), 107 (33), 106 (10), 105 (12), 97 (6), 96 (20), 95 (40), 94 (20), 93 (11), 92 (9), 91 (10), 83 (9), 82 (9), 81 (26), 80 (8), 79 (17), 78 (5), 77 (12), 70 (6), 69 (36), 68 (9), 67 (23), 65 (5), 57 (8), 56 (23), 55 (40), 45 (12), 44 (100), 43 (22), 42 (12), 41 (61), 40 (4).

Deuterated ketone (**27**)

The alcohol **28** with deuterium lable at C-15 (15 mg) was oxidized as described above to give 3.5 mg of ketone, m.p. 101–102° (methanol), which showed no melting point depression when mixed with undeuterated ketone sample. Mass spectrum (*m/z*, intensity in %): 291 (6), 290 (37), 289 (M^+, 100), 288 (38), 274 (8), 273 (3), 262 (6), 261 (22), 260 (11), 259 (4), 247 (7), 246 (30), 245 (9), 230 (4), 128 (3), 209 (12), 208 (17), 207 (3), 206 (5), 205 (12), 204 (6), 192 (5), 191 (8), 190 (14), 189 (8), 179 (6), 178 (6), 177 (6), 176 (8), 175 (4), 165 (9), 164 (10), 163 (10), 162 (5), 161 (5), 153 (3), 152 (8), 151 (15), 150 (15), 149 (18), 148 (9), 147 (8), 146 (4), 145 (4), 125 (10), 124 (12), 123 (49), 122 (53), 121 (54), 120 (9), 119 (11), 111 (8), 110 (9), 109 (42), 108 (52), 107 (26), 106 (9), 105 (14), 97 (7), 94 (9), 95 (27), 34 (14), 93 (23), 92 (11), 91 (16), 83 (10), 82 (25), 81 (31), 80 (13), 79 (17), 78 (6), 77 (9), 70 (7), 69 (37), 68 (11), 67 (21), 65 (4), 57 (14), 56 (30), 55 (36), 54 (5), 53 (10), 43 (30), 42 (8), 41 (42), 40 (4).

Reduction of ketone (**27**)

(a) Potassium borohydride (140 mg) was added to the soln of ketone **27** (134 mg) in 5 ml of methanol. The obtained mixture was heated to reflux and new portions of potassium borohydride were added (240 mg in 1 hr, 200 mg in 3.5 hr and 130 mg in 7 hr). The soln was stored overnight at room temp, acidified with 10% sulphuric acid, diluted with water, extracted with ether and the extract was treated in a usual manner to give 130 mg of the product. It was subjected to column chromatography over silica gel (5 g). Ethyl acetate–hexane (1:9) eluted 61 mg of initial ketone **27** and then 63 mg of alcohol **27**, m.p. 131–132.5° (petroleum ether).

(b) 200 mg of lithium aluminium hydride in 10 ml of absolute ether were added to the solution of ketone **27** (120 mg) in 5 ml of absolute ether. The solution was stored at room temp for 1 hr and then refluxed for 5 hr. The excess of hydride was decomposed by adding ethylacetate. After the usual work up 122 mg of **28**, m.p. 131.5–133° (petroleum ether), were obtained.

Benzoylation of alcohol (**28**)

Alcohol **28** (240 mg) in 2.5 ml of dry pyridine was added on ice cooling to 3,5-dinitrobenzoyl chloride obtained from 500 g of acid and thionilchloride. The soln was stored at room temp for 2 hr then water was added, the solution was acidified with 10% sulphuric acid and extracted with ether. The usual work up of extract afforded 345 mg of the product consisted of 3 components (TLC on SiO_2). The product was chromatographed on silica gel (15 g). Petroleum ether eluted 108.6 mg (31.5%) of hydrocarbons. Further elution with 2% of ethyl acetate in petroleum ether afforded 165.5 mg of a compound with m.p. 196–197.5° (petroleum ether), $[\alpha]_D^{19}$ 4.2° (c, 1.9) and 55 mg of a compound with m.p. 165–167° (petroleum ether), $[\alpha]_D^{19}$ 5° (c, 1.6). The former can not be saponified by refluxing with 10% potassium hydroxide ethanolic soln. This compound (17.5 mg) was refluxed for 1.5 hr with the soln of lithium aluminium hydride (10 mg) in 1 ml of absolute ether. The usual work up of the mixture gave 10.2 mg of product which was chromatographed on alumina (0.8 g). Petroleum ether eluted 4.3 mg of hydrocarbon fraction. Ethyl acetate–petroleum ether (5:95) mixture eluted 5.4 mg of alcohol **28**, m.p. 133–134° (acetonitrile/petroleum ether). Its oxidation afforded ketone **27**.

The benzoylation product with m.p. 165.5–167° (30 mg) was refluxed with an excess of 10% potassium hydroxide ethanolic soln for 1 hr. After the usual treatment the product (18 mg) was chromatographed on alumina (0.8 g) to give 3.5 mg of hydrocarbon fraction and 14.1 mg of crystalline compound, m.p. 121–122° (petroleum ether). Oxidation of this compound afforded ketone **27**.

In the other experiment the mixture of benzoylation products with m.p. 197° and 167° (210 mg) was saponified with 10% alkali hydroxide alcoholic solution. The product was subjected to column chromatography on silica gel (15 g). Ethyl acetate–petroleum ether (3:97) mixture eluted 88 mg of the product, m.p. 196–197°. Lithium aluminium hydride reduction furnished alcohol **28**. Further elution gave 56 mg of alcohol, m.p. 85–87° (acetonitrile). Its oxidation gave ketone **27**.

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REFERENCES

[1]L. Ruzicka, A. Eschenmoser and H. Heusser, *Experientia* **9**, 357 (1953).
[2]E. Wenkert, *Chem. Ind.* 282 (1955).
[3]P. F. Vlad, *Izv. Acad. Nauk Mold. SSR, Ser. Biol. Chim. Nauk* No. 2, 67 (1977). *C.A.* **88**, 121391 (1978).

[4]C. Asselineau and S. Bory, *Bull. Soc. Chim. Fr.* 1355 (1961).
[5]O. E. Edwards and R. S. Rosich, *Canad. J. Chem.* **46**, 1113 (1968).
[6]E. Wenkert and Z. Kumazawa, *Chem. Commun.* 140 (1968).
[7]S. F. Hall and A. C. Oehlschlager, *Tetrahedron* **28**, 3155 (1972).
[8]T. McCreadie and K. H. Overton, *J. Chem. Soc.* (C), 312 (1971).
[9]T. McCreadie, K. H. Overton and A. J. Allison, *J. Chem. Soc.* (C), 317 (1971).
[10]W. Johnson, *Acc. Chem. Res.* **1**, 1 (1968).
[11]E. E. van Tamelen, *Acc. Chem. Res.* **1**, 111 (1968).
[12]M. Kurbanov, A. V. Semenovsky, V. A. Smit and V. F. Kucherov, *Izv. Akad. Nauk SSSR, Ser. Khim.* 2541 (1971).
[13]P. F. Vlad and G. V. Lazur'evskii, *Izv. Akad. Nauk Mold. SSR* 12, 69 (1961).
[14]G. Cimino, D. De Rosa, S. De Stefano and I. Minale, *Tetrahedron* **30**, 645 (1974).
[15]D. H. R. Barton, D. A. J. Ires and B. R. Thomas, *J. Chem. Soc.* 2056 (1955); A. Yoshikoshi, M. Kitadani and Y. Kitahara, *Tetrahedron* **23**, 1175 (1967).
[16]T. S. Bylina, V. M. Jemilev, N. S. Vostrikov, G. A. Tolstikov, A. M. Moiseenkov, A. V. Semenovsky and S. S. Shavanov, *Izv. Acad. Nauk SSSR, Ser. Khim.* 447 (1978).
[17]C. R. Enzell and R. Ryhage, *Arkiv Kemi* **23**, 367 (1965).
[18] D. S. Weinberg and C. Djerassi, *J. Org. Chem.* **31**, 115 (1966).
[19]A. F. Thomas, R. A. Schneider and J. Meinwald, *J. Am. Chem. Soc.* **89**, 68 (1967).
[20]P. Barraclough and D. W. Young, *Tetrahedron Letters* 2293 (1970).
[21]H. C. Brown and J. H. Kawakami, *J. Am. Chem. Soc.* **92**, 201 (1970).
[22]C. A. Abad, S. P. Jindal and T. T. Tidwell, *J. Am. Chem. Soc.* **95**, 6326 (1973).
[23]S. Banerjec and N. H. Werstiuk, *Canad. J. Chem.* **53**, 1099 (1976).
[24]D. N. Kirk, *J. Chem. Soc.* Perkin Trans. I, 2122 (1977).
[25]D. N. Kirk and W. Klyne, *J. Chem. Soc.*, Perkin Trans. I, 762 (1976).
[26]E. Eliel, *Stereochemistry of Carbon Compounds*. McGraw-Hill, New York (1962).
[27]E. Lippmaa, T. Pehk, J. Paasivirta, N. Belicova and A. Plate, *Org. Magn. Res.* **2**, 581 (1970).
[28]J. H. Brewster, *Tetrahedron* **13**, 106 (1961).
[29]A. Lopez, C. van Carstenn-Lichterfelde, B. Rodriguez, J. Fayos and M. Martinez Ripoll, *J. Org. Chem.* **42**, 2517 (1977).
[30]E. J. Corey and J. W. Suggs, *Tetrahedron Letters* 2647 (1975).
[31]M. Fétizon and Trong Ahn Nguyen, *J. Chromatogr.* **35**, 192 (1968).
[32]S. Bory, M. Fétizon and P. Laszlo, *Bull. Soc. Chim. Fr.* 19 (1963).
[33]S. O. Almqvist, C. R. Enzell and F. W. Wehrli, *Acta Chem. Scand.* **B29**, 695 (1975).
[34]B. L. Buckwalter, I. R. Burfitt, A. A. Nagel, E. Wenkert and F. Näf, *Helv. Chim. Acta* **58**, 1567 (1975).
[35]I. Wahlberg, S. O. Almqvist, T. Nishida and C. R. Enzell, *Acta Chem. Scand.* **B29**, 1047 (1975).
[36]J. R. Hanson, M. Siverns, F. Piozzi and C. Savona, *J. Chem. Soc.* Perkin Trans. I, 114 (1976).
[37]C. von Carstenn-Lichterfelde, C. Pascual, J. Pons, R. M. Radanal, B. Rodriguez and S. Valverde, *Tetrahedron Letters* 3569 (1975); *Tetrahedron* **33**, 1989 (1977).
[38]G. Levi and G. Nelson, *Carbon-13 Nuclear Magnetic Resonance for Organic Chemists*. Wiley-Interscience, New York (1972).
[39]H. Beierbeck and J. F. Saunders, *Canad. J. Chem.* **53**, 1307 (1975).
[40]H. Eggert and C. Djerassi, *J. Org. Chem.* **38**, 3788 (1973).
[41]J. B. Grutzner, M. Jautelat, J. B. Dence, R. A. Smith and J. D. Roberts, *J. Am. Chem. Soc.* **92**, 7107 (1970).
[42]D. K. Dalling, D. M. Grant and E. C. Paul, *J. Am. Chem. Soc.* **95**, 3798 (1973).
[43]R. M. Carman, W. J. Craig and I. Shaw, *Austral. J. Chem.* **26**, 215 (1973).
[44]P. F. Vlad, M. N. Koltsa and N. D. Ungur, Abstracts of papers of *5th Soviet–Indian Symp. Chemistry of Natural Products*, Erevan, 18 (1978).
[45]P. F. Vlad, N. D. Ungur and M. N. Koltsa, *Khim. Prir. Soed.* 581 (1979).
[46]D. Joulain, F. Ruessac and J. Garnero, *Tetrahedron Letters* 3585 (1977).
[47]X. A. Dominguez, I. K. Lopez and R. Franco, *J. Org. Chem.* **26**, 1625 (1961).
[48]A. S. Gupta and Sukh Dev, *J. Chromatogr.* **12**, 189 (1963).
[49]T. Norin and L. Westfelt, *Acta Chem. Scand.* **17**, 1828 (1963).
[50]W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.* **43**, 2923 (1978).