ISOMERIZATION OF KETOLACTONE OF OXABICYCLO[2.2.2]OCTANE PATTERN IN THE E RING OF URSANE DERIVATIVES*

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Alkaline hydrolysis of ketolactones *I* and *II* is accompanied by quantitative acyloin rearrangement of the 20-hydroxy-21-oxo derivative *III* formed, under simultaneous migration of the methyl group from the position 20α to the position 21α.

In the preceding paper[1] we described the oxidation of 3β-acetoxy-21-oxo-18α,19β--H-ursan-28→20β-olide (*II*) with oxygen in alkaline medium. This oxidation, followed by acetylation of the 3β-hydroxy group, led to hydroxy acid *XVII* with a contracted E ring. The lactone ring remained intact in the reaction. In addition to hydroxy acid *XVII* another substance was formed in the reaction as a by-product which has not been identified in that study[1]. In this paper we should like to demonstrate that the by-product is formed under the effect of alkaline medium on lactone *II* and that it is isomeric with it. We derive structure *XII* for it. Since the fragmentation of ketolactone *XII* in the mass spectrum does not quite correspond to our expectations[2], we considered it purposeful to check the proposed structure by preparing some further derivatives, also suitable for mass spectral measurements.

Under the effect of alkaline medium and conditions appropriate for the hydrolysis of the 3β-acetoxy group (and subsequent acidification) ketolactone *II* afforded 3β-hydroxyketolactone *XI* as the sole product. On acetylation 3β-acetoxyketolactone *XII*, identical with the side product of the oxidation of ketolactone *II* in alkaline medium[1] was prepared. The structure of the isomeric ketolactone *XII* follows from its IR spectrum, according to which the substance contains a keto group in a six-membered cycle and a five-membered lactone ring. The formation of ketolactone *XII* from ketolactone *II* can be explained by an acyloin rearrangement[3] taking place during alkaline hydrolysis and subsequent acidification of the reaction mixture: Hydrolysis of the δ-lactone ring of ketolactone *II* gives rise to a transient formation of hydroxyketo acid *III* in which the 20α-methyl group migrates into the position

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21α under formation of hydroxyketo acid *IV*. On acidification the γ-lactone ring of ketolactone *XII* is closed. In our endeavour to get the mentioned intermediates *III* and *IV* we hydrolysed both ketolactones, *II* and *XII*, under various conditions. Heating of ketolactone *II* with 2·5% potassium hydroxide solution in benzene–methanol did not practically change the lactone ring (the reaction course was monitored by thin-layer chromatography), and the 3β-acetoxy group was hydrolysed only under formation of 3β-hydroxy derivative *I*. In the reaction with 5% potassium hydroxide in a mixture of benzene and methanol the δ-lactone ring was hydrolysed and when the reaction mixture was neutralized the rearranged hydroxyketo acid *IV* was obtained as the sole product. This acid *IV* was the only product also in the hydrolysis of the γ-lactone *XII*. In these isomerizations the equilibrium is always shifted unambiguously in favour of 20-oxo derivatives, *i.e.* the acid *IV* or lactone *XI*; in no case were we able to isolate the unrearranged acid *III* or the γ-lactone *I* regenerated from it by acidification. Hydroxy acid *IV* was characterized as methyl ester *V* and methyl ester acetate *VI* in which one hydroxyl group still remained unacetylated. Acidification easily brought about lactonization of acid *IV* to ketolactone *XI*, while methyl ester *V* was easily converted to the same lactone on heating to the melting temperature. Hydrolysis of ketolactone *XII* in D_2O followed by conversion of the acid formed to methyl ester, and subsequent pyrolysis of the latter gave monodeuteriolactone *XIII*. On reaction of ketolactone *XII* with bromine under catalysis with hydrobromic acid a corresponding monobromo derivative *XVI* was formed from which ketolactone *XII* could be regenerated under the effect of zinc in acetic acid. Reduction of the 20-oxo group of ketolactone *XII* with sodium borohydride leads to the formation of a mixture of isomeric 20-hydroxy derivatives *VII* and *IX*. β-Configuration of the hydroxyl group has been assigned to the prevailing isomer *VII* on the basis of the formation of an intramolecular hydrogen bond ($\nu_{(OH)}$ 3 510 cm^{-1}). The isomeric 20α-hydroxylactone *IX* was present in the mixture in a negligible amount. Both isomeric 20-hydroxy lactones *VII* and *IX* were converted to corresponding diacetates *VIII* and *X*; from 20β-hydroxy lactone *VII* the starting ketolactone *XII* was obtained by oxidation with chromium trioxide in acetic acid. Oxidation of acid *IV* at the stage of its sodium salt with lead tetraacetate in acetic acid led to the cleavage of the bond between $C_{(20)}$ and $C_{(21)}$, under formation of a diacid. This diacid was isolated in the form of an anhydride *XIV* (1 815, 1 765, 1 730, 1 425 cm^{-1}) which was further converted to the 3-acetate *XV*. From the ^{1}H-NMR spectrum of anhydride *XV* the presence of a three-carbon chain $—CH_2—CO—CH_3$ on the quaternary carbon atom could be inferred (singlet of the methyl group at 2·12 ppm and AB system of the isolated CH_2-group at ~2·53 ppm, overlapped with the signal of a further hydrogen atom). The secondary methyl group on $C_{(19)}$ remained preserved in anhydride *XV* (doublet at 1·33 ppm, J = 7 Hz, $C_{(19)}$ at 39·8 ppm).

The structure of lactone *XII* and its derivatives follows from the above-mentioned reaction sequence and it is further confirmed by ^{1}H-NMR and ^{13}C-NMR spectra.

I, R¹ = H
II, R¹ = Ac
III
IV, R¹ = R² = H
V, R¹ = H, R² = CH₃
VI, R¹ = Ac, R² = CH₃
VII, R¹ = Ac, R² = H
VIII, R¹ = R² = Ac
IX, R¹ = Ac, R² = H
X, R¹ = R² = Ac
XI, R¹ = R² = H
XII, R¹ = Ac, R² = H
XIII, R¹ = H, R² = D
XIV, R¹ = H
XV, R¹ = Ac
XVI
XVII
XVIII

TABLE I

Characteristic Parameters of the ^{1}H-NMR Spectra of Lactones (Chemical shifts are given in ppm, δ-scale)

Compound	19-CH_3	20-CH_3 or 21-CH_3	22-H_2		20-H
II	0·90[a]	1·38	2·20 d	2·47 d[b]	—
VIII	1·11[a]	1·28	1·71 d	1·95 d[c]	4·48 d[e]
X	1·01[a]	1·26	[d]	[d]	5·06 d[f]
XI	1·27[a]	1·43	1·83 d	2·20 d[c]	—
XII	1·28[a]	1·44	1·85 d	2·21 d[c]	—
XIII	1·25 s	1·48	1·82 d	2·20 d[c]	—
XVI	1·94 s	1·52	1·7—1·9 d	2·25 d[c]	—

[a] Doublet, J = 6·5—7·5 Hz; [b] J_{gem} = 20 Hz; [c] J_{gem} = 12—13 Hz; [d] overlapped by other bands; [e] $J_{19,20}$ = 7·7 Hz; [f] $J_{19,20} \sim 5$ Hz.

TABLE II

Characteristic Parameters of the ^{13}C-NMR Spectra of Lactones (Chemical shifts are given in ppm, δ-scale)

Carbon number[a]	*II*	*VIII*	*XII*	*XIII*	*XV*	*XVI*
17	44·1	47·3	47·3	47·6	46·1	45·4
18	47·4	47·3	49·0	49·0	—	52·5
19	42·8	36·9	42·6[b]	[c]	39·8[b]	62·6
20	88·0	81·2	206·4	206·4	168·7[d]	197·0
21	204·9	81·0	83·4	83·4	203·8	83·3
22	45·5[b]	47·6	47·6[b]	47·6[b]	50·9[b]	48·9
28	174·3	177·6	177·4	177·4	171·3[d]	176·2
29	—	—	18·2	—	—	30·4
30	—	—	—	—	27·9	—

[a] The signals $C_{(18)}$, $C_{(29)}$ and $C_{(30)}$, which could not be assigned unambiguously, are not given in the table. The total number and the multiplicity of the signals agrees with the number of methyl, methylene and methine groups and quaternary carbon atoms in the proposed structures; [b] the signal was assigned on the basis of selective decoupling; [c] the signal disappears in the noise; [d] the signals can be mutually interchanged.

In the ^{1}H-NMR spectra of the starting (*II*) and the rearranged (*XII*) ketolactones and their derivatives the singlet of the methyl group near the lactone oxygen is shifted downfield. The doublet of the methyl group on $C_{(19)}$ in the rearranged ketolactone *XII* is shifted by about 0·4 ppm downfield in comparison with the starting ketolactone *II*. In view of the chemical shift value it seems probable that the methyl group in the position 19 remains in α-configuration even in the rearranged ketolactone *XII* and its derivatives, since for the β-configuration (which seems improbable for sterical reasons) an upfield shift can be more likely expected in consequence of the shielding effect of the close-by lactone carbonyl. In deuterioketolactone *XIII* and bromoketolactone *XVI* a singlet corresponds to the $C_{(19)}$-methyl group (distinctly shifted downfield in bromo derivative *XVI*), which is an evidence for the substitution with deuterium or bromine in the position 19. In the ^{1}H-NMR spectrum of the starting ketolactone *II* an AB system of $C_{(22)}H_2$ with $J = 20$ Hz is distinctly evident. Such a high coupling constant is typical[4] of mutual orientation of the methylene group and the keto group in which the keto group is located symmetrically with respect to both hydrogen atoms, that is in the same way as in the fixed boat form of ketolactone *II*. In the rearranged ketolactone *XII* the AB system of the $C_{(22)}H_2$ group is mildly shifted upfield and coupling constant is 13 Hz. In the ^{1}H-NMR spectra of diacetates *VIII* and *X* doublets of the protons at $C_{(20)}$ are present. In the ^{1}H-NMR spectrum of the 20α-H isomer *VIII* it is a sharp doublet at 4·48 ppm; in the spectrum of the 20β-H isomer *X* the doublet is mildly broadened in consequence of a long-range interaction, probably with the equatorial β-hydrogen in the position 22 which forms a planar *W*-system with the 20β-H. From the vicinal coupling constants $J_{19,20}$ of both isomeric lactone diacetates *VIII* and *X* it may be concluded that the E ring is flattened. The $J_{19,20}$ value found in 20β-acetoxy lactone *VIII* (diaxial arrangement of 19β-H and 20α-H) is lower and in the 20α-acetoxy lactone *X* (axial-equatorial arrangement of 19β-H and 20β-H) higher by about 2·5 Hz in comparison with the values given[5] for analogous diaxial (~10 Hz) and axial-equatorial (~2·5 Hz) coupling constants.

From the ^{13}C-NMR spectrum of the starting ketolactone *II* the chemical shift of the lactone carbonyl carbon atom is 174·3 ppm; it is higher than the usual value[6] for a simple six-membered lactone ring and this is evidently due to the strain of this bicyclic system. The shift of the signal of the lactone carbonyl carbon atom to a lower field (177·4 ppm) in the rearranged ketolactone *XII* is in agreement with its five-membered lactone ring. Using selective decoupling the signal at 42·6 ppm in the spectrum of ketolactone *XII* was assigned to the carbon in the position 19; this signal disappeared in the spectrum of deuterioketolactone *XIII*, which is in agreement with the deuteration in the position 19. From the ^{13}C-NMR spectrum of bromoketolactone *XVI* the confirmation followed that the substitution with bromine took place in the position 19. In the spectrum of bromoketolactone *XVI* the signal $C_{(19)}$ is shifted to 62·6 ppm and simultaneously the multiplicity of the signal in the off-

-resonance spectrum is changed from a doublet to a singlet; the signal of the methyl group on $C_{(19)}$ is shifted from 18·2 to 30·4 ppm in relation to ketolactone *XII*, and the signal of $C_{(20)}$ from 206·4 to 197 ppm. In all the ^{13}C-NMR spectra the number and the multiplicity of the signals determined by off-resonance agreed with the total number of methyl, methylene and methine groups and the quaternary carbon atoms in the structures mentioned.

For the measurement of the mass spectra[2] the series of lactones described in this and in the preceding paper[1] was completed by 3-oxoketolactone *XVIII*; this derivative was prepared by oxidation of 3β,21α-dihydroxy-18α,19β-H-ursan-28→20β-olide[7] with chromium trioxide in acetic acid.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. Specific rotation was measured in chloroform on an automatic polarimeter ETL-NPL (Bendix–Ericsson) with a 2° accuracy. The infrared spectra were measured in chloroform on a UR-20 (Zeiss, Jena) instrument. The NMR spectra were measured in deuteriochloroform using tetramethylsilane as internal reference, chemical shifts are given in ppm δ-scale. ^{1}H-NMR spectra were measured on Varian HA-100 and Tesla BS-487 (80 HMz) instruments, while ^{13}C-NMR spectra were recorded on an FX-60 (JEOL, 15 MHz for ^{13}C) apparatus. The mass spectra were measured on a Varian MAT-311 spectrometer, the energy of the ionizing electrons was 70 eV, the ionizing electron current was 1 mA, the temperature of the ion source was 200°C and the temperature of the direct inlet system was 130—200°C. The purity of the samples was checked by thin-layer chromatography on silica gel according to Stahl (type 60). The samples for analysis were dried over phosphorus pentoxide at 100°C and 13—130 Pa for 8 h. The preparation of acetate was carried out with a mixture of pyridine and acetic anhydride (1 : 1) at room temperature, for about 12 h. The methyl esters were prepared with ethereal diazomethane solution.

Hydrolysis of Ketolactone *II*

a) Ketolactone *II* (0·12 g) was refluxed in a 2·5% KOH solution in benzene–methanol 1 : 1 (20 ml) for 1 h. The hydrolysis course was monitored by thin-layer chromatography on a silica gel plate and the reaction was terminated as soon as acid material began to increase (in concentration). The mixture was poured into water, acidified with dilute hydrochloric acid and extracted with ether. The ethereal solution was washed with water and dried over sodium sulfate. 3-Hydroxyketolactone *I* (0·11 g) of m.p. 302—306°C (chloroform–heptane) was formed, $[\alpha]_D$ +33° (*c* 0·50). IR spectrum: 3630, 1750, 1770 (inflexion) cm^{-1}. Acetylation gave acetate *II*, m.p. 358—360° (chloroform–heptane), $[\alpha]_D$ +44° (*c* 0·59), which according to IR spectrum was identical with an authentic sample; according to TLC it contained traces of ketolactone *XII*.

b) Ketolactone *II* (3·0 g) was refluxed in a 5% solution of KOH in benzene–ethanol 1 : 1 (200 ml) for 2·5 h. Half the solvent was distilled off and the residue acidified with dilute hydrochloric acid. The separated ketolactone *XI* (2·9 g) was filtered off under suction and crystallized from chloroform. M.p. 303—306°C, $[\alpha]_D$ +58° (*c* 0·25). IR spectrum: 3630, 1790, 1738, 1370 cm^{-1}. ^{1}H-NMR spectrum: 0·76, 0·85, 0·93, 0·95, 1·11 (5 . CH_3); 1·27 d, $J \sim 7{\cdot}5$ Hz (19α-CH_3); 1·43 (21-CH_3); 1·83 d and 2·20 d, J = 13 Hz ($C_{(22)}H_2$). Mass spectrum: see ref.[2]. For $C_{30}H_{46}O_4$ (470·7) calculated: 76·55% C, 9·85% H; found: 76·67% C, 10·02% H.

Acetate XII: m.p. 335–340°C (chloroform–heptane), $[\alpha]_D$ +73° (*c* 0·76). IR spectrum: 1790, 1738, 1390, 1260 cm^{-1}. ^{1}H-NMR spectrum: 0·85 (2 . CH_3); 0·88, 0·95, 1·10 (3 . CH_3); 1·28 d, J = 6·6 Hz (19α-CH_3); 1·44 (21-CH_3); 1·85 d and 2·21 d, J = 13 Hz ($C_{(22)}H_2$); 2·03 (CH_3COO); 4·45 m (3α-H). Mass spectrum: see ref.[2]. For $C_{32}H_{48}O_5$ (512·7) calculated: 74·96% C, 9·44% H; found: 74·76% C, 9·34% H.

c) Ketolactone *II* (0·05 g) was refluxed with a 5% solution of KOH in benzene–ethanol 1 : 1 (20 ml) for 2·5 h. The mixture was poured into water, neutralized with dilute hydrochloric acid and the product was extracted with ether. The ethereal solution was washed with water, dried over sodium sulfate and evaporated. The residue (0·04 g) was treated with ethereal diazomethane solution, allowed to stand at room temperature for 2 h, and the excess of the reagent was distilled off. Double crystallization from chloroform–heptane gave methyl ester *V*, m.p. 252–260°C, and, after resolidification, 302–305°C; $[\alpha]_D$ +5° (*c* 0·45), which according to TLC and IR spectrum was identical with the preparation obtained on hydrolysis of ketolactone *XII*.

Hydrolysis of Ketolactone *XII*

Under the conditions mentioned for ketolactone *II* (under *c*)) ketolactone *XII* (0·1 g) afforded methyl ester *V* (0·09 g), m.p. 256–262°C and – after crystallizing – 302–305°C; $[\alpha]_D$ +3·5° (*c* 0·52). IR spectrum: 3630, 3550, 1730, 1715, 1398, 1355 cm^{-1}. Mass spectrum, *m/e* (%): 486 (2), 474 (4), 468 (5), 456 (14), 452 (44), 444 (42), 437 (19), 425 (5), 416 (16), 409 (18), 401 (7), 370 (10), 207 (55), 189 (100). For $C_{31}H_{50}O_5$ (502·7) calculated: 74·06% C, 10·03% H; found: 73·90% C, 9·86% H.

Acetate VI: m.p. (chloroform–heptane) 250–260°C and after crystallization 318–328°C, $[\alpha]_D$ +15·5° (*c* 0·64). IR spectrum: 3550, 1730, 1715 (inflexion), 1445, 1400, 1375, 1260 cm^{-1}. ^{1}H-NMR spectrum: 0·83 (3 . CH_3); 0·86, 0·96 (2 . CH_3); 1·16 d, $J \sim 7$ Hz (19-CH_3); 1·26 (21-CH_3); 1·71 d and 2·23 d, J = 14 Hz ($C_{(22)}H_2$); 2·01 (CH_3COO); 3·43 ($COOCH_3$); 4·47 m (3α-H). Mass spectrum: *m/e* (%): 544 (M^+, 0·1), 498 ($C_{32}H_{50}O_4$, 5%), 486 ($C_{30}H_{46}O_5$, 10%), 458 ($C_{29}H_{46}O_4$, 7%), 452 ($C_{30}H_{44}O_3$, 28%), 437 ($C_{29}H_{41}O_3$, 22%), 409 ($C_{27}H_{37}O_3$, 25%), 370 ($C_{24}H_{34}O_3$, 7%), 189 ($C_{14}H_{21}$, 68%), 43 (100). For $C_{33}H_{52}O_6$ (544·7) calculated: 72·75% C, 9·69% H; found: 73·04% C, 9·92% H.

Pyrolysis of Methyl Ester *V*

Methyl ester *V* was heated at 290°C under argon for 1 min. After cooling the sample was dissolved in chloroform and filtered through a layer of alumina. The chromatographically pure product had m.p. 304–308°C (heptane), $[\alpha]_D$ +63° (*c* 0·17) and according to TLC and IR spectrum it was identical with lactone *XI*.

Reduction of Ketolactone *XII* with Sodium Borohydride

Sodium borohydride (0·07 g) was added to a solution of ketolactone *XII* (0·13 g) in a mixture of benzene (20 ml) and methanol (10 ml) and the mixture was allowed to stand at room temperature for 2 h. After dilution with water and acidification with hydrochloric acid the product was extracted with a mixture of ether and ethyl acetate, the organic layer was washed with water and evaporated to dryness. The residue (0·13 g) was extracted with boiling chloroform and ether. M.p. of the insoluble material, *i.e.* 20β-hydroxylactone *VII*: it does not melt up to 360°C. IR spectrum: ν(OH) (saturated solution in CCl_4): 3510 cm^{-1}. Mass spectrum: see ref.[2].

Acetate VIII: m.p. 317—320°C (chloroform–heptane), $[\alpha]_D$ +26° (*c* 0·42). IR spectrum: 1770, 1738—1748 (broad), 1260 cm^{-1}. ^{1}H-NMR spectrum: 0·85 (2 . CH_3); 0·88, 0·93, 1·08 (3 . CH_3); 1·11d, $J \sim 6{\cdot}5$ Hz (19-CH_3); 1·23 (21-CH_3); 1·71 d and 1·95 d, $J \sim 12$ Hz ($C_{(22)}H_2$); 2·05 and 2·13 (2 . CH_3COO); 4·48 d, $J = 7{\cdot}7$ Hz (20α-H); 4·46 m (3α-H). For $C_{34}H_{52}O_6$ (556·8) calculated: 74·34% C, 9·41% H; found: 74·32% C, 9·26% H.

The chloroform and ethereal extracts after the isolation of hydroxy derivative *VII* were combined (0·06 g) and separated on a thin layer of silica gel (developed with light petroleum); in addition to a further amount of 20β-hydroxylactone *VII* (0·04 g) 20α-hydroxylactone *IX* (0·02 g) was obtained which melted at 317—321°C (chloroform–heptane), $[\alpha]_D$ +16° (*c* 0·45). IR spectrum: 3640, 1775, 1730, 1260 cm^{-1}. ν(O—H) (CCl_4): 3640 cm^{-1}. Mass spectrum: see ref.[2].

Acetate X: m.p. 298—304°C (chloroform–heptane), $[\alpha]_D$ +28° (*c* 0·36). IR spectrum: 1783, 1750, 1738, 1260 cm^{-1}. ^{1}H-NMR spectrum: 0·84 (2 . CH_3); 0·85, 0·92, 1·03 (3 . CH_3); 1·01 d, $J \sim 7{\cdot}5$ Hz (19-CH_3); 1·26 (21-CH_3); 2·00 and 2·07 (2 . CH_3COO); 4·47 m (3α-H); 5·06 d, $J_{19,20} \sim 5$ Hz, $J_{1,9} \sim 1$ Hz (20β-H). Mass spectrum: see ref.[2]. For $C_{34}H_{52}O_6$ (556·8) calculated: 74·34% C, 9·41% H; found: 74·30% C, 9·52% H.

Deuterioketolactone *XIII*

A solution of ketolactone *XII* (0·1 g) in dioxane (30 ml) was added to lithium aluminum hydride (0·3 g) and 5 ml of D_2O were poured into the solution, followed by 5 mg triethylbenzylammonium chloride. The suspension was refluxed for 5 h and then allowed to stand at room temperature for 56 h. The mixture was decomposed with solid carbon dioxide, filtered and the filtrate extracted with ether and ethyl acetate. After evaporation of the solvents under reduced pressure the residue (0·1 g) was treated with ethereal diazomethane solution. After 2 h standing at room temperature the excess of reagent was evaporated. The crude methyl ester was heated under argon at 280°C for 3 min. Crystallization from chloroform–heptane gave deuterioketolactone *XIII*, m.p. 296—303°C, $[\alpha]_D$ +58° (*c* 0·29). IR spectrum: 3630, 1787, 1735 cm^{-1}. ^{1}H-NMR spectrum: 0·76, 0·85, 1·08 (3 . CH_3); 0·95 (2 . CH_3); 1·25 s (19-CH_3); 1·48 (21-CH_3); 1·82 d and 2·20 d, $J \sim 13$ Hz ($C_{(22)}H_2$); 4·46 m (3α-H). Mass spectrum: see ref.[2].

Bromoketolactone *XVI*

A solution of bromine (0·02 g) in acetic acid (0·2 ml) and 2 drops of acetic acid saturated with gaseous HBr were added to a solution of ketolactone *XII* (0·05 g) in a mixture of chloroform (2·5 ml) and acetic acid. After 4 days standing at room temperature the mixture was poured into water and the product extracted with ether. The extract was washed with a sodium carbonate solution and water, and dried over sodium sulfate. From the crude residue (0·07 g) bromoketolactone *XVI* (0·04 g) was obtained by crystallization from chloroform–heptane. M.p. 254—260°C (decomp.), $[\alpha]_D$ +74° (*c* 0·63). IR spectrum: 1795, 1745, 1725 (inflexion), 1390, 1260 cm^{-1}. ^{1}H-NMR spectrum: 0·83 (2 . CH_3); 0·89, 0·99, 1·13 (3 . CH_3); 1·94 (19-CH_3); 1·52 (21-CH_3); 1·7—1·9 d and 2·25 d, $J \sim 13$ Hz ($C_{(22)}H_2$); 2·03 (CH_3COO); 4·45 m (3α-H). Mass spectrum: *m/e* (%): 590 (M^+; 0·5%), 530 (2), 515 (2), 510 (5), 466 (10), 450 (15), 435 (10); 407 (22), 189 (65), 43 (100). For $C_{32}H_{47}BrO_5$ (591·6) calculated: 64·15% C, 8·01% H; found: 64·41% C, 8·09% H.

Reduction of Bromoketolactone *XVI*

Bromoketolactone *XVI* (0·02 g) was refluxed with 0·1 g of zinc dust in 8 ml of acetic acid for 2 h. The mixture was poured into a saturated solution of sodium carbonate and extracted with chloroform. The extract was dried by filtration through a layer of alumina. The product (0·015)

had m.p. 331—336°C (chloroform–heptane), $[\alpha]_D$ +72° (*c* 0·64), and according to TLC and IR spectrum it was identical with ketolactone *XII*.

Oxidation of Hydroxyketo Acid *IV* with Lead Tetraacetate

Ketolactone *XII* (0·05 g) was refluxed with 5% potassium hydroxide solution in benzene–ethanol 1 : 1 (6 ml) for 1 h. The solvents were distilled off under reduced pressure and benzene (5 ml), acetic acid (10 ml) and lead tetraacetate (0·2 g) were added to the residue. After 22 h standing at room temperature glycerol and water were added to the reaction mixture and the product was extracted with ether after previous acidification of the mixture with hydrochloric acid. The ethereal solution was washed with water and dried over sodium sulfate. The crude product (0·05 g) was extracted with boiling ether and the insoluble part was crystallized from chloroform–heptane. The m.p. of the anhydride thus obtained (*XIV*) was 205—215°C and — after solidification — 255—285°C (decomp.), $[\alpha]_D$ −10·5° (*c* 0·47). IR spectrum: 3630, 1815, 1765, 1730, 1425 cm^{-1}. For $C_{30}H_{46}O_5$ (486·7) calculated: 74·03% C, 9·53% H; found: 73·93% C, 9·72% H.

Acetate XV: m.p. 232—239°C and after resolidification 270—280°C (decomp.; from chloroform–heptane), $[\alpha]_D$ −3° (*c* 0·52). IR spectrum: 1817, 1768, 1730, 1425, 1260 cm^{-1}. ^{1}H-NMR spectrum: 0·85 (3 . CH_3); 0·92, 0·96 (2 . CH_3); 1·33 d, $J \sim 7{\cdot}0$ Hz (19-CH_3); 2·04 (CH_3COO); 2·12 (CH_3CO); 2·55 d, $J \sim 5$ Hz (3 . H; $C_{(22)}H_2$ and 19-H); 4·46 m (3α-H). Mass spectrum: *m/e* (%): 528 (M^+; 1%), 484 (43), 468 (25), 453 (12), 425 (23), 189 (61), 43 (100). For $C_{32}H_{48}O_6$ (528·7) calculated: 72·69% C, 9·15% H; found: 72·72% C, 9·37% H.

3,21-Dioxo-18α,19β-H-ursan-28→20β-olide (*XVIII*)

A solution of 3β,21α-dihydroxy-18α,19β-H-ursan-28→20β-olide (see ref.[7]; 0·02 g) and chromium trioxide (0·02 g) in acetic acid (5 ml) was left to stand at room temperature for 16 h. The excess of chromium trioxide was reduced by addition of methanol and the mixture was diluted with water. The separated product (0·02 g) was filtered off under suction and crystallized from chloroform–methanol. Dioxolactone *XVIII* was thus obtained with m.p. 282—285°C, $[\alpha]_D$ +65° (*c* 0·36). IR spectrum: 1715, 1760 cm^{-1}. Mass spectrum: see ref.[2]. For $C_{30}H_{44}O_4$ (468·7) calculated: 76·88% C, 9·46% H; found: 77·01% C, 9·53% H.

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