STRUCTURE AND THE PROPERTIES OF 18α,19βH-URSANE DERIVATIVES WITH A LACTONE BRIDGE TO RING E*

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Oxidation of ketolactone *II* in alkaline medium led predominantly to hydroxy acid *VI* with an oxabicycloheptane arrangement of the E ring. Further oxidation of hydroxy acid *VI* with lead tetraacetate or the pyrolysis of its diacetate, *VII*, gave ketone *XV* which on further oxidation gave either lactone *XVIII* or *XXIV*, depending on conditions. The structure of both lactones was confirmed by reduction to tetrol *XIX* or pentol *XXV*, from lactone *XXIV* diketone *XXXI* was also obtained.

In the preceding paper[1] we investigated the oxidation of 21-oxo-20β,28-epoxy-18α,19β*H*-ursane (*I*) with oxygen in alkaline medium. In this reaction the cleavage of the $C_{(21)}$—$C_{(22)}$ bond under formation of *E*-secodiacid and the benzilic rearrangement of the intermediary α-diketone, leading to hydroxy acid *III* with a contracted E ring, took place to an equal extent. A series of unusual reactions of hydroxy acid *III* and derived compounds with oxabicycloheptane arrangement in ring E was observed[1], which are probably due to considerable steric strain of this system. Therefore, in this study, the oxidation and the reactivity of an analogous system with a lactone ring, *i.e.* 3β-acetoxy-21-oxo-18α,19β*H*-ursan-28→20β-olide (*II*), was investigated.

The starting ketolactone *II* (ref.[2]) was oxidized with oxygen in tert-butyl alcohol in the presence of potassium tert-butylate at 50–60°C, *i.e.* under the conditions used[1] in the case of keto ether *I*. In the mixture of products obtained α-hydroxy acid *VI* highly predominated (above 80%). A great part of it was isolated directly, while the rest was obtained in the form of its diacetate *VII* after acetylation and chromatographic separation of the mixture of the products. The second component of the mixture (less than 20%) was a non-polar product, isomeric with ketolactone *II*, the structure of which will be published elsewhere[3]. Hydroxy acid *VI* can be considered, similarly as in the case of the oxidation of keto ether *I*, as a product of benzilic rearrangement[4,5] of α-diketone *V*, which, however, could not be isolated. The structure of hydroxy acid *VI* was confirmed on the basis of the following reaction sequence,

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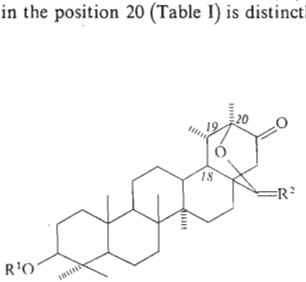
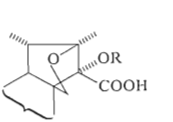
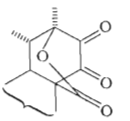
characteristic[1] of α-hydroxy acids with tertiary hydroxyl groups. On reaction with diazomethane hydroxy acid *VI* gives methyl ester *VIII* the acetylation of which gave monoacetate *X*, while in the case of the free acid the tertiary hydroxyl is acetylated (under formation of diacetate *VII*), probably *via* a mixed anhydride. The mentioned diacetate gives methyl ester *IX* with diazomethane. In all derivatives of hydroxy acid *VI* mentioned the presence of the five-membered lactone ring is evident from the IR spectra (1790 to 1795 cm^{-1}). In the ^{1}H-NMR spectrum of methyl ester *IX* the doublet of the methyl group at $C_{(19)}$ is present and the singlet of the methyl group in the position 20 (Table I) is distinctly shifted downfield. Of both possible hydroxy



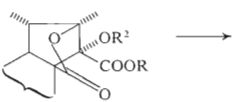
I, R^1 = Ac, R^2 = H_2
II, R^1 = Ac, R^2 = O



III, R = H
IV, R = Ac

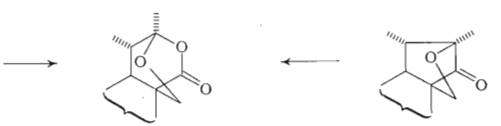


V



VI, R^1 = R^2 = R^3 = H
VII, R^1 = R^2 = Ac, R^3 = H
VIII, R^1 = R^2 = H, R^3 = CH_3
IX, R^1 = R^2 = Ac, R^3 = CH_3
X, R^1 = Ac, R^2 = H, R^3 = CH_3

XI, R^1 = R^2 = H
XII, R^1 = R^2 = Ac



XIII, R^1 = Ac

XIV

acids, epimeric at $C_{(22)}$, only one was obtained. The configuration at $C_{(22)}$ cannot be unambiguously predicted on the basis of stereochemical course of the benzilic rearrangement[4,5], but according to the analogy[1] with the hydroxy acid *II* we consider the α-configuration of the hydroxyl group more probable. Similarly as in methyl ester of hydroxy acid *III* (see[1]) the absorption of the intramolecular hydrogen bond in the IR spectrum of methyl ester *X* has a pattern characteristic of α-hydroxy acid esters[6]. No other absorption in the OH stretching region was observed which could correspond to the bond of the hydroxyl group on the lactone ring.

On reduction of diacetate *VII* with lithium aluminum hydride pentol *XI* was prepared and characterized as triacetate *XII*. On oxidation of pentol *XI* with sodium periodate the known[1] lactone *XIII* was obtained, which can be considered as a product of intramolecular cyclization of the expected keto acid *XXVII*. This lactone was prepared earlier by oxidation of norketone *XIV*. Structure *XIII* was proposed[1] on the basis of its ^{1}H-NMR spectrum and the assumed course of the oxidative reactions used. The formation of lactone *XIII* from hydroxy acid *VI* by the procedure used in this paper represents an independent confirmation of its structure.

When heated at the melting temperature (270°C) the acetoxy acid *VII* is decomposed and converted quantitatively to norketone *XV*, which represents the same type of pyrolysis as observed[1] in the acetoxy acid *IV* with a 20β,28-epoxy bridge. Norketone *XV* gives oxime *XVI* on reaction with hydroxylamine and on reduction with sodium borohydride it gives noralcohol *XXI*. This alcohol *XXI* is formulated as 22α-isomer, since only the band of the free hydroxyl group was found in the OH stretching region of IR spectrum (3630 cm^{-1}). Acetylation of noralcohol *XXI* gave acetate *XXII*. In the ^{1}H-NMR spectrum of acetate *XXII* a sharp singlet of 22β-H at 4·75 ppm is present in addition to the signals characteristic of this type of substituted E ring (doublet of 19α-CH_3 and the downfield shifted singlet of the 20-CH_3 group) and two acetoxyl groups.

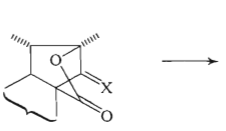
Norketone *XV* is also formed on oxidation of α-hydroxy acid *VI* with lead tetraacetate and subsequent acetylation of the product. At room temperature this oxidation does not take place, probably owing to the small solubility of the starting acid.

TABLE I

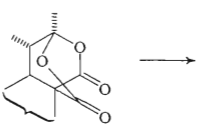
Chemical Shifts (δ-scale, ppm) of the $C_{(20)}$—CH_3 Group in the ^{1}H-NMR Spectra

Compound	*I*	*II*	*XV*	*IX*	*XXII*	*XVIII*	*XXIV*	*XXXII*/*XXXIII*
$C_{(20)}$—CH_3	1·13	1·38	1·37	1·38	1·33	1·69	1·56	1·41

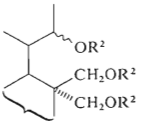
At a higher temperature (80–90°C, 2 h) the norketone was obtained as the main component after acetylation and separation of the mixture of products. Prolongation of the reaction time (9 h) results in further oxidation of norketone *XV* to dilactone *XVIII*. The isolation of norketone *XV* from the reaction with lead tetraacetate indicates its lower reactivity in comparison with analogous epoxy norketone *XIV* which was oxidized[1] with this reagent to latone *XIII* even at room temperature. When pyridine was used as solvent the oxidation of hydroxy acid *VI* with lead tetraacetate took place at room temperature and dilactone *XVII* was formed as the only product. Dilactone *XVII* was further converted to acetate *XVIII*.



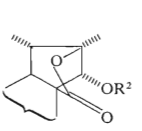
XV, R^1 = Ac, X = O
XVI, R^1 = Ac, X = NOH



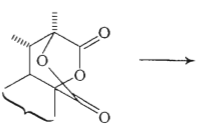
XVII, R^1 = H
XVIII, R^1 = Ac



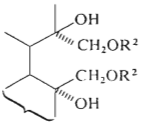
XIX, $R^1 = R^2$ = H
XX, $R^1 = R^2$ = Ac



XXI, R^1 = Ac, R^2 = H
XXII, $R^1 = R^2$ = Ac



XXIII, R^1 = H
XXIV, R^1 = Ac



XXV, $R^1 = R^2$ = H
XXVI, $R^1 = R^2$ = Ac

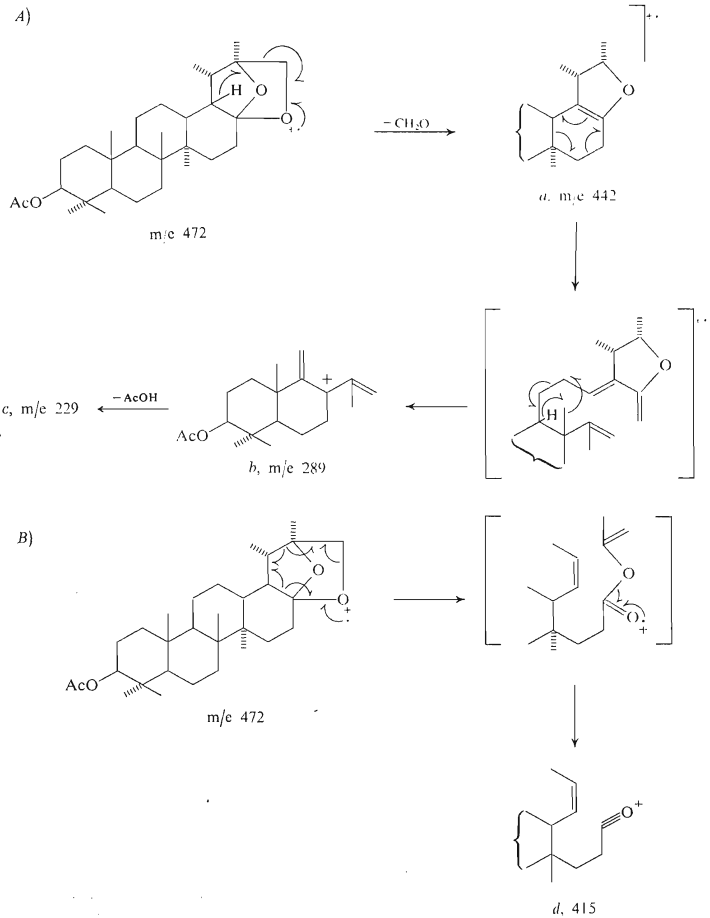
Oxidation of norketone *XV* with 3-chloroperoxybenzoic acid led mainly to dilactone *XXIV*, isomeric with dilactone *XVIII*. Dilactone *XVIII* was also formed in this reaction in small amount. The differentiation between the structures of *XVIII* and *XXIV* follows from their IR spectra (dilactones *XVII* and *XVIII* show two absorption bands of the lactone carbonyl groups −1770 and 1805 cm^{-1}, while dilactones *XXIII* and *XXIV* show only a single band −1780 cm^{-1}), and from the shift of the methyl group at $C_{(20)}$ in the ^{1}H-NMR spectra (1·568 ppm in dilactone *XXIV* and 1·694 ppm in dilactone *XVIII*, see Table I). The proposed structures of dilactones *XVIII* and *XXIV* were confirmed by reduction with lithium aluminum hydride: from dilactone *XVIII* a mixture of tetrols *XIX* was formed which are evidently isomeric at $C_{(20)}$ and could not be separated even after conversion to tetraacetates *XX*. According to IR spectra tetraacetates *XX* do not contain a hydroxyl group; in mass spectrum the molecular ion gradually looses four molecules of acetic

acid. A mixture of the same tetrols *XIX* and their acetates *XX* (identity according to TLC, IR and mass spectra) was also obtained from lactone *XIII* on reduction with lithium aluminum hydride. On reduction with lithium aluminum hydride the isomeric dilactone *XXIV* afforded pentol *XXV* the acetylation of which gave triacetate *XXVI*. The presence of two non-acetylated hydroxyl groups is evident from the IR spectrum and it was also confirmed by the ^{1}H-NMR spectrum, using the trichloroacetyl isocyanate method (signals of N—H at 8·80 and 8·45 ppm, a distinct downfield shift of the $C_{(20)}$-methyl group by 0·32 ppm, and a change in the chemical shifts of the overlapping doublets of both CH_2OCOCH_3 groups). A further confirmation of the structure of dilactone *XXIV* follows from alkaline hydrolysis in which diacid *XXVIII* is formed. On acidification of the reaction mixture this diacid is easily cyclized to dilactone *XXIII*; careful working up and addition of diazomethane to the crude diacid gave dimethyl ester *XXIX* which on heating at melting temperature is also converted to dilactone *XXIII*. Dimethyl ester *XXIX* was further characterized as acetate *XXX*. In this acetate unacetylated hydroxyl groups are still present. In ^{1}H-NMR spectrum of acetate *XXX* the doublet of the 19α-methyl group is present in addition to the signals of two methyl ester groups and the downfield shifted singlet of the methyl group at $C_{(20)}$.

Under the effect of lead tetraacetate in pyridine the salt of diacid *XXVIII* gave diketone *XXXI* the structure of which was confirmed by mass spectrometry: the molecular ion looses the methyl ethyl ketone radical under formation of the distinct ion *m/e* 315.

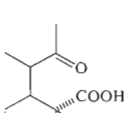
Another attempt at the confirmation of the structure of dilactone *XXIV* consisted in the oxidation of the vicinal diol systems in pentol *XXV* with sodium periodate. However, the reaction gave a complex mixture of products from which the main component was isolated in about 40% yield. According to IR spectrometry this compound does not contain a carbonyl group and in its composition it corresponds to the oxidation of one diol grouping and subsequent intramolecular cyclization to an acetal. From the present data it is difficult to decide between the two probable structures, *XXXII* and *XXXIII*. Both considered structures are in agreement with the doublet of the $C_{(19)}$-methyl group in the ^{1}H-NMR spectrum, as well as the two doublets of the hydrogen atoms in the CH_2—O— group, one of which has a distinct long-range interaction due to the planar W-system. This W-system can be found in either of these structures: it is formed by 19α- and 22β-hydrogen atoms in structure *XXXII* and by 18α-H and the exocyclic $C_{(28)}$-H in structure *XXXIII*. According to the values given in Table I for other compounds of this series the chemical shift of the $C_{(20)}$ methyl group corresponds rather to structure *XXXIII*.

From the mass spectra of both the 3-hydroxy derivative and its acetate it follows that the fragmentation takes place in two ways (Scheme 1): *A*) The molecular ions loose formaldehyde under formation of ion *a* (*m/e* 400 in hydroxy and 442 in acetoxy derivatives) which is converted to ion *b* by the proposed mechanism combined with the loss of the methyl radical and the shift of hydrogen (*m/e* 247 or 289, respectively). The ions of type *b* then loose a molecule of water or acetic acid under formation of ions of type *c* (*m/e* 229). This type of fragmentation does not exclude any of the alternative structures, *XXXII* and *XXXIII*. *B*) By the mechanism proposed the molecular ions loose the radical C_3H_5O under formation of ion *d* (*m/e* 373 or 415, resp., in both instances their relative abundance is about 5%). The los of radical C_3H_5O can be formulated

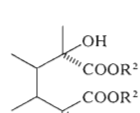


SCHEME 1

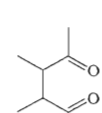
more easily on the basis of structure *XXXII* than of *XXXIII*. Further relatively abundant ions (*m/e* 221, 208 and 140 in 3-hydroxy and 3-acetoxy derivative) belong to fragments with the D and E rings. The mass spectra of other substances with a bicycloheptane and bicyclooctane arrangement in the E ring are given in ref.[3].



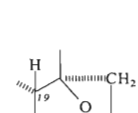
XXVII



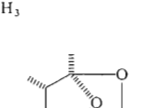
XXVIII, $R^1 = R^2 = H$
XXIX, $R^1 = H$, $R^2 = CH_3$
XXX, $R^1 = Ac$, $R^2 = CH_3$



XXXI



XXXII



XXXIII

The mentioned oxidation of ketolactone *II* in alkaline medium, as well as the reactivity of the product of this reaction show a close analogy with keto ether *I* and the products of its oxidation[1], with the difference that in the oxidation of ketolactone *II* the product od benzilic rearrangement with the original lactone ring preserved prevails considerably, while the products of oxidative cleavage of the $C_{(21)}$—$C_{(22)}$ bond (*i.e.* E-secodiacid, its anhydride or decarboxylation product), formed from keto ether *I* in a 50% yield, are completely lacking. The properties of E-nor derivatives with a lactone and epoxide bridge are identical in those cases where the lactone ring is not attacked. The differences were found in the migration ability of the carbon atoms $C_{(17)}$ and $C_{(20)}$ in the oxidation of ketolactone *XV*, and, to a certain extent, in the reactivity of their keto group.

EXPERIMENTAL

The melting points were determined on a Kofler block. Specific rotations were measured in chloroform using an automatic polarimeter, ETL-NPL (Bendix–Ericsson), with a $\pm 2°$ accuracy. The infrared spectra were measured in chloroform on UR-10 and UR-20 instruments (Zeiss, Jena). The ^{1}H-NMR spectra were measured on a Varian HA-100 instrument, (if not stated otherwise) in deuteriochloroform, with tetramethylsilane as internal reference; The chemical shifts are

given in ppm, δ-scale. The mass spectra were measured using a Varian MAT-311 spectrometer and the energy of the ionizing electrons was 70 eV, ionizing electron current was 1 mA, the temperature of the ion source was 200°C, and the temperature of the direct inlet system 130 to 200°C. The composition of the ions for which it is given was measured on the basis of high resolution technique, with an error not exceeding 5 ppm. The discussed geneses of the ions were confirmed using the Direct Analysis of Daughter Ions technique. The purity of the samples was checked by thin-layer chromatography (silica gel according to Stahl, type 60). Samples for analysis were dried over phosphorus pentoxide at 100°C and 13—130 Pa pressure for 8 h. Silica gel for chromatography according to Pitra had 30—60 μ particle size.

Preparation of the acetates was carried out in pyridine–acetic anhydride mixture 1 : 1 at room temperature for about 12 h. Methyl esters were prepared with ethereal diazomethane. Under "conventional working up of the reaction mixture" a triple extraction of the aqueous layer with ether, washing of the extract with 5% hydrochloric acid and water till neutrality is understood.

Oxidation of Ketolactone *II*

A suspension of ketolactone *II* (4 g) in benzene (150 ml) was added to a solution of potassium tert-butylate (4 g of potassium in 150 ml of tert-butyl alcohol). The mixture was saturated with oxygen at 50—60°C under stirring for 16 h. After cooling the mixture was acidified with 5% hydrochloric acid and extracted with ether. The ethereal phase was washed with water and ether was evaporated under reduced pressure. The residue (3·8 g) was extracted with benzene repeatedly and insoluble hydroxy acid *VI* (2·8 g) was thus obtained, m.p. 280—290°C under decomp. For $C_{30}H_{46}O_6$ (502·7) calculated: 71·68% C, 9·22% H; found: 71·65% C, 9·18% H.

From the extract benzene was evaporated and the residue (1·0 g) was acetylated as usual. The mixture of acetates obtained was separated by chromatography on silica gel. Elution with benzene gave a ketolactone (see ref.[3]; 0·75 g), m.p. 335—340°C (chloroform–heptane), $[\alpha]_D$ +73° (*c* 0·68). Ether eluted diacetate *VII* (0·2 g), m.p. 265—267°C (decomp.; ether), $[\alpha]_D$ —85° (*c* 0·46). IR spectrum: 3600, 3520, 1795, 1760, 1730, 1260 cm^{-1}. For $C_{34}H_{50}O_8$ (586·7) calculated: 69·59% C, 8·59% H; found: 69·18% C, 8·69% H.

Methyl ester diacetate IX: m.p. 237—240°C (chloroform–heptane), $[\alpha]_D$ —89° (*c* 0·58). IR spectrum: 1795, 1755, 1730, 1260 cm^{-1}. ^{1}H-NMR spectrum: 0·852 (3 × CH_3); 0·993, 0·896, 1·385 (3 × CH_3); 1·129 d, $J \sim 6{\cdot}5$ Hz (19α-CH_3); 2·06, 2·18 (2 × CH_3COO); 3·78 (—$COOCH_3$); 4·49 m (3α-H) ppm. For $C_{35}H_{52}O_8$ (600·8) calculated: 69·97% C, 8·72% H; found: 69·80% C, 8·83% H.

Methyl ester VIII: does not melt up to 360°C (residue after evaporation of ethereal diazomethane; poorly soluble). For $C_{31}H_{48}O_6$ (516·7) calculated: 72·06% C, 9·36% H; found: 72·40% C 9·42% H.

Acetate X: m.p. 287—290°C (chloroform–heptane), $[\alpha]_D$ +34° (*c* 0·56). IR spectrum: 3600, 3520, 1790, 1730, 1260 cm^{-1}. For $C_{33}H_{50}O_7$ (558·7) calculated: 70·93% C, 9·02% H; found: 70·71% C, 8·95% H.

Pentol XI

A mixture of diacetoxy acid *VII* (0·3 g) and lithium aluminum hydride (0·5 g) in dioxane (20 ml) was refluxed for 2 h, decomposed with water and acidified with 5% hydrochloric acid. The product was extracted with a mixture of ethyl acetate and ether and further worked up in the conventional manner. The crude product *XI* (0·3 g) was characterized as acetate *XII*: m.p. 283—287°C (chloro-

form–heptane), $[\alpha]_D$ —18° (*c* 0·53). IR spectrum: 3620, 3600—3420, 1730, 1260, 1030 cm^{-1}. For $C_{36}H_{58}O_8$ (618·1) calculated: 69·87% C, 9·45% H; found: 69·81% C, 9·32% H. Mass spectrum: *m/e* (%): 600 (1·5), 558 (2), 540 (4), 498 (20), 467 (7), 438 (14), 189 (50), 43 (100).

Oxidation: A suspension of pentol *XI* (0·1 g) and sodium periodate (0·1 g) in a mixture of tert-butyl alcohol (100 ml) and water (3 ml) was allowed to stand at room temperature for 3 weeks. The reaction mixture was diluted with water, the separated product (0·1 g) filtered off and characterized as acetate *XIII*: m.p. 332—334°C (ether), $[\alpha]_D$ +37° (*c* 0·27). According to thin-layer chromatography and mixture melting point it was identical with a preparation obtained earlier[1]. Literature[1] gives for lactone *XIII* m.p. 338—341°C, $[\alpha]_D$ +43°.

3β-Acetoxy-22-oxo-E(21)-nor-18α,19β*H*-ursan-28→20β-olide (*XV*)

a) *Diacetate* VII (0·1 g) was heated under argon at 270°C for 5 min. The product (0·08 g) was dissolved in benzene and filtered through silica gel. On crystallization from a mixture of chloroform and methanol E-nor-ketolactone *XV* was obtained, m.p. 336—338°C, $[\alpha]_D$ +18° (*c* 0·35). IR spectrum: 1820, 1770, 1730, 1260 cm^{-1}. ^{1}H-NMR spectrum: 0·857 (3 × CH_3), 0·921, 1·000, 1·377 (3 × CH_3); 0·935 d, J = 7·1 Hz (19-CH_3); 2·04 (CH_3COO); 4·49 m (3α-H). For $C_{31}H_{46}O_5$ (498·7) calculated: 74·66% C, 9·30% H; found: 74·40% C, 9·11% H.

b) *Oxidation of hydroxy acid* VI: A solution of *VI* (0·1 g) and lead tetraacetate (0·1 g) in acetic acid (15 ml) was heated on a water bath for 2 h. After 2 days standing at room temperature ethylene glycol (1 ml) and water (20 ml) were added. The separated product (0·1 g) was suction-dried, chromatographed on silica gel and characterized as acetate *XV* (0·06 g): m.p. 333—336°C (benzene–heptane), $[\alpha]_D$ +18° (*c* 0·46). According to IR spectrum, TLC and mixture melting point it was identical with the above acetate *XV*.

Oxime XVI: a solution of E-nor-ketolactone *XV* (0·01 g) and hydroxylamine hydrochloride (0·02 g) in pyridine (10 ml) was heated on a water bath for 3 h, cooled, diluted with water and worked up in the conventional manner. Triple crystallization from chloroform–methanol gave oxime *XVI*, poorly soluble in organic solvent: m.p. 290—292°C. IR spectrum (nujol): 3420, 1800, 1755, 1730, 1260, 1025 cm^{-1}. For $C_{31}H_{47}NO_5$ (513·7) calculated: 72·48% C, 9·22% H, 2·73% N; found: 72·62% C, 9·06% H, 2·93% N.

Reduction of E-Nor-ketolactone *XV*

A solution of E-nor-ketolactone *XV* (0·12 g) and sodium borohydride (0·2 g) in pyridine (6 ml) was allowed to stand at room temperature for 3 days, diluted with water and the solid product (0·1 g) was suction-dried, dissolved in chloroform and filtered through silica gel. Crystallization from chloroform–benzene gave substance *XXI*, m.p. 329—331°C, $[\alpha]_D$ +41° (*c* 0·68). IR spectrum: 3630, 1780, 1730, 1260 cm^{-1}. For $C_{31}H_{48}O_5$ (500·7) calculated: 74·36% C, 9·66% H; found: 74·23% C, 9·70% H.

Acetate XXII: m.p. 270—272°C (ether), $[\alpha]_D$ —25° (*c* 0·26). IR spectrum: 1790, 1760, 1730, 1260 cm^{-1}. ^{1}H-NMR spectrum (Tesla 80): 0·862 (3 × CH_3); 0·90, 0·94, 1·34 (3 × CH_3); 1·00, d, $J \approx 7{\cdot}5$ Hz (19-CH_3); 1·99, 2·075 (2 × CH_3COO); 4·44 m (3α-H); 4·75 (22 β-H). For $C_{33}H_{50}O_6$ (542·7) calculated: 73·03% C, 9·29% H; found: 72·75% C, 9·28% H.

3β-Acetoxy-E(21)-nor-18α,19β*H*-ursane-28→20β,22→20α-diolide (*XVIII*)

a) A solution of E-nor-ketolactone *XV* (0·02 g) and lead tetraacetate (0·08 g) in acetic acid (10 ml) was heated on a water bath for 6 h. When cooled a product crystallized out (0·015 g)

which was filtered off under suction and washed with water. Crystallization from chloroform–heptane gave compound *XVIII* that would not melt up to 360°C, $[\alpha]_D$ +40° (*c* 0·58). IR spectrum: 1805, 1770, 1730, 1260 cm^{-1}. ^{1}H-NMR spectrum: 0·857 (3 × CH_3); 0·949 (2 × CH_3); 1·694 (CH_3); 1·107 d, J = 6·9 Hz (19-CH_3); 2·04 (CH_3COO); 4·47 m, (3α-H). For $C_{31}H_{46}O_6$ (514·7) calculated: 72·34% C, 9·01% H; found: 72·65% C, 9·11% H.

b) A solution of hydroxy acid *VI* (0·19 g) and lead tetraacetate (0·3 g) in pyridine (10 ml) was allowed to stand overnight at room temperature. After addition of glycerol the mixture was worked up in the conventional manner. The residue (0·2 g) was dissolved in chloroform and filtered through a layer of alumina. Crystallization from chloroform–heptane mixture gave dilactone *XVII*, m.p. 300—308°C (decomp.), $[\alpha]_D$ +33° (*c* 0·52). IR spectrum: 3620, 1805, 1770 cm^{-1}. For $C_{29}H_{44}O_5$ (472·7) calculated: 73·69% C, 9·38% H; found: 73·89% C, 9·48% H.

Acetate XVIII: it does not melt up to 360°C (chloroform–heptane), $[\alpha]_D$ +42° (*c* 0·43). According to IR spectra and TLC it is identical with dilactone *XVIII* obtained earlier.

c) A solution of hydroxy acid *VI* (0·1 g) and lead tetraacetate (0·1 g) in acetic acid (10 ml) was heated on a water bath for 20 h. After cooling to room temperature the reagent was decomposed with glycerol and the mixture diluted with water. The separated product (0·07 g) was filtered off under suction and characterized as acetate *XVIII* which did not melt up to 360°C (chloroform–heptane), $[\alpha]_D$ +40° (*c* 0·38). According to IR spectrum and TLC analysis it is identical with dilactone *XVIII* obtained earlier.

Oxidation of E-Nor-ketolactone *XV* with 3-Chloroperoxybenzoic Acid

A solution of E-nor-ketolactone *XV* (0·08 g) and 3-chloroperoxybenzoic acid (0·1 g) in chloroform (5 ml) was allowed to stand at room temperature for 24 h. It was then filtered through alumina, yielding 0·06 g of product *XXIV* which would not melt up to 360°C (chloroform–heptane), $[\alpha]_D$ +40° (*c* 0·74). IR spectrum: 1780, 1730, 1260 cm^{-1}. ^{1}H-NMR spectrum: 0·859 (3 × CH_3); 0·945, 1·009, 1·568 (3 × CH_3); 1·009 d, J = 7·0 Hz (19-CH_3); 2·04 (CH_3COO); 4·48 m (3α-H). For $C_{31}H_{46}O_6$ (514·7) calculated 72·34% C, 9·01% H, found: 72·69% C, 9·26% H. Further elution of alumina with chloroform–ether gave 0·01 g of compound *XVIII*. It does not melt up to 360°C (ether) $[\alpha]_D$ +41° (*c* 0·26). According to IR spectrum and TLC it is identical with dilactone *XVIII* obtained earlier.

Reduction of Dilactone *XVIII* with Lithium Aluminum Hydride

A mixture of dilactone *XVIII* (0·04 g) and lithium aluminum hydride (0·08 g) in benzene (10 ml) and tetrahydrofuran (6 ml) was refluxed for 10 h. After cooling it was diluted with methanol, acidified with 5% hydrochloric acid and extracted with a mixture of ethyl acetate and ether. Further work-up was done in the conventional manner. Poorly soluble product *XIX* was obtained and characterized after acetylation and subsequent chromatography as a mixture of isomeric acetates *XX* (0·015 g), m.p. 60—80°C (residue from light petroleum), $[\alpha]_D$ +27° (*c* 0·50). IR spectrum: 1725—1735, 1260, 1030 cm^{-1}. For $C_{37}H_{60}O_8$ (632·8) calculated: 70·22% C, 9·56% H; found: 70·21% C, 9·77% H. Mass spectrum: *m/e* (%): M^+ 632 (1·5), 572 (4), 512 (11·5), 452 (5), 392 (3), 189 (47), 43 (100).

Reduction of Lactone *XIII* with Lithium Aluminum Hydride

Lactone *XIII* (0·12 g) was extracted into a suspension of lithium aluminum hydride (0·1 g) in ether (60 ml) and the mixture was refluxed for 5 h. After cooling it was decomposed with

water, acidified with hydrochloric acid and extracted with a mixture of ethyl acetate and ether. After washing the organic extract with water a product crystallized out (0·08 g) which was washed with ether and had m.p. 268—275°C; according to TLC identical with product *XIX* obtained in the preceding experiment.

Acetate XX: m.p. 75—91°C (residue after evaporation of pentane). According to TLC, IR spectrum, and mass spectrum identical with acetate *XX* obtained earlier.

Reduction of Dilactone *XXIV* with Lithium Aluminum Hydride

A mixture of dilactone *XXIV* (0·05 g), lithium aluminum hydride (0·07 g) and dioxane (6 ml) was refluxed for 4 h, decomposed with ice, acidified with 5% hydrochloric acid, diluted with ethyl acetate and worked up in the conventional manner. The residue (0·05 g) was acetylated; on chromatography on a thin layer of silica gel and extraction with heptane (washing out of impurities) product *XXVI* was obtained, m.p. 90—95°C, $[\alpha]_D$ +28° (*c* 0·46). IR spectrum: 3 610, 3 550—3 430, 1 735—1 725, 1 260, 1 035 cm^{-1}. ^{1}H-NMR spectrum: 0·846 (2 x CH_3); 0·868, 1·014, 1·066, 1·256 (4 × CH_3); 1·048 d, J = 7 Hz (19-CH_3); 2·03, 2·095, 2·105 (3 x CH_3COO); 3·89 d and 4·03 d, J_{gem} ~ 11·5 Hz (—CH_2—O—); 3·97 d and 4·36 d, J_{gem} ~ 11 Hz (CH_2—O—); 4·47 m (3α-H). Trichloroacetylcarbamoyl derivative: 0·85 (2 × CH_3); 0·87, 1·01 ~ 1·10, 1·57 (4 × CH_3); ~1·05 d, J ~ 7 Hz (19-CH_3); 2·03 (CH_3COO); 2·07 (2 × CH_3COO); ~4·57 d and ~4·37 d (overlapped, 2 × —CH_2—O—); 8·45 and 8·80 (2 × NH). For $C_{35}H_{58}O_8$ (606·8) calculated: 69·27% C, 9·63% H; found: 69·36% C, 9·46% H. Mass spectrum *m/e* (%): 588 (1), 515 (18), 455 (5·5), 189 (11), 57 (100), 43 (83).

Oxidation of Pentol *XXV* with Sodium Periodate

A solution of pentol *XXV* (0·13 g) in ethanol (10 ml), dioxane (10 ml) and tert-butyl alcohol (2 ml) was allowed to stand at room temperature with excess sodium periodate for 5 days. After dilution with water it was worked up in the conventional manner. On triple crystallization from ether product *XXXII*/*XXXIII* (3β-OH) was obtained, m.p. 255—258°C. IR spectrum: 3 630, 1 040 cm^{-1}. For $C_{28}H_{46}O_3$ (430·6) calculated: 78·09% C, 10·77% H; found: 78·23% C, 10·71% H. Mass spectrum *m/e* (%): M^+ 430 ($C_{28}H_{46}O_3$, 80), 415 ($C_{27}H_{43}O_3$, 12), 412 ($C_{28}H_{44}O_2$, 11), 400 (*a*, $C_{27}H_{44}O_2$, 50), 373 (*d*, $C_{25}H_{41}O_2$, 5), 247 (*b*, $C_{17}H_{27}O$, 42), 229 (*c*, $C_{17}H_{25}$, 20), 221 ($C_{14}H_{21}O_2$, 28), 208 ($C_{13}H_{20}O_2$, 66), 207 ($C_{14}H_{23}O$, 100), 189 ($C_{14}H_{21}$, 84), 140 ($C_8H_{12}O_2$, 100).

Acetate: m.p. 290—292°C (chloroform–heptane), $[\alpha]_D$ +49° (*c* 0·48). IR spectrum: 1 730, 1 260 cm^{-1}. ^{1}H-NMR spectrum (Jeol FX-60): 0·85, 0·91, 1·41 (3 × CH_3); 0·96 (3 × CH_3); 1·19 d, J ~ 7 Hz (19-CH_3); 2·04 (CH_3COO); 3·24 d and 3·85 d, J_{gem} ~ 7 Hz (—CH_2—O—); 4·47 m (3α-H) ppm. Mass spectrum *m/e* (%): M^+ 472 ($C_{30}H_{48}O_4$, 71), 457 ($C_{29}H_{45}O_4$, 5), 454 ($C_{30}H_{46}O_3$, 3), 442 (*a*, $C_{29}H_{46}O_3$, 50), 415 (*d*, $C_{27}H_{43}O_3$, 5) 412 ($C_{28}H_{44}O_2$, 7·5), 397 ($C_{27}H_{41}O_2$, 11) 289 (*b*, $C_{19}H_{29}O_2$, 15), 229 (*c*, $C_{17}H_{25}$, 10), 221 ($C_{14}H_{21}O_2$, 15), 208 ($C_{13}H_{20}O_2$, 34), 189 ($C_{14}H_{21}$, 62), 140 ($C_8H_{12}O_2$, 88), 43 (100). For $C_{30}H_{48}O_4$, (472·7) calculated: 76·22% C, 10·24% H; found: 75·98% C, 10·07% H. The mother liquors after crystallization of the acetate were chromatographed on a thin layer of silica gel and two so far unidentified compounds were obtained: *1*) 0·03 g of a compound with m.p. 281—283°C (chloroform–light petroleum), $[\alpha]_D$ +81° (*c* 0·44). IR spectrum: 1 730, 1 260 cm^{-1}; *2*) 0·02 g of a compound melting at 268—270°C (ether–light petroleum), $[\alpha]_D$ +25° (*c* 0·20). IR spectrum: 3 570, 1 730, 1 260, 1 030 cm^{-1}.

Hydrolysis of Dilactone *XXIV*

A solution of dilactone *XXIV* (0·09 g) and potassium hydroxide (0·4 g) in benzene (10 ml) and methanol (10 ml) was refluxed for 2 h and part of the solvents distilled off. The residue was diluted with water and neutralized with dilute hydrochloric acid. The solution was extracted with chloroform and the organic layer worked up in the conventional manner. The residue was treated with ethereal diazomethane solution. From this solution a part of product *XXIX* (0·06 g) crystallized out, m.p. 264—267°C (decomp.; chloroform–heptane), $[\alpha]_D$ +14° (*c* 0·52). IR spectrum: 3630, 3550, 1730 cm^{-1}; $\nu_{(OH)}$ (tetrachloromethane): 3628, 3608, 3527, 3440 cm^{-1}. For $C_{31}H_{52}O_7$ (536·6) calculated: 69·37% C, 9·77% H; found: 69·21% C, 10·01% H.

Acetate XXX: m.p. 210—215°C, it solidifies again and does not melt up to 360°C (chloroform–ether–heptane), $[\alpha]_D$ +22° (*c* 0·45). IR spectrum: 3600, 3540, 3400, 1730, 1260 cm^{-1}; $\nu_{(OH)}$ (tetrachloromethane); 3603, 3527, 3448 cm^{-1}. ^{1}H-NMR spectrum (Tesla 80): 0·84 (2 × × CH_3), 0·86, 1·40, 1·01 (3 × CH_3); 0·93 d, $J \sim 7{\cdot}5$ Hz (19-CH_3); 2·00 (CH_3COO); 4·47 m (3α-H); 3·60, 3·64 (2 × $COOCH_3$); 3·95 bs (2 × OH). For $C_{33}H_{54}O_8$ (578·8) calculated: 68·48% C, 9·40% H, found: 68·41% C, 9·60% H. After separation of dimethyl ester *XXIX* ether was distilled off from the filtrate and the residue was chromatographed on a thin layer of silica gel, affording a further amount of dimethyl ester *XXIX* (0·01 g) and 3-hydroxydilactone *XXIII*, m.p. ~200°C, resolidifies and remelts at 258—265°C (chloroform–heptane), $[\alpha]_D$ +34° (*c* 0·42). IR spectrum: 3620, 1780 cm^{-1}. Acetate *XXIV*: does not melt up to 360°C (chloroform–heptane), $[\alpha]_D$ +43° (*c* 0·53). According to IR spectrum and TLC it was identical with an authentic sample of *XXIV*.

Pyrolysis of Methyl Ester *XXIX*

Methyl ester *XXIX* (0·03 g) was heated at 300°C for 1 min, cooled and dissolved in chloroform and the solution filtered through alumina. Double crystallization from chloroform–heptane gave 3-hydroxy dilactone *XXIII*, m.p. 155—160°C, resolidification and remelting at 240—250°C, $[\alpha]_D$ +31° (*c* 0·36). According to TLC and IR spectrum the product is identical with preparation *XXIII* obtained hydrolytically.

Acetate XXIV: does not melt up to 360°C (chloroform–heptane), identical according to IR spectrum and TLC with dilactone *XXIV* obtained earlier.

Oxidation of Hydroxy Acid *XXVIII* with Lead Tetraacetate

A solution of dilactone *XXIV* (0·1 g) in a mixture of benzene and methanol (1 : 1) was refluxed with potassium hydroxide (0·4 g) for 2 h, the solvents were distilled off under reduced pressure and the residue dissolved in pyridine (10 ml) and treated with lead tetraacetate (0·4 g) and acetic acid (10 ml) which was added until the originally formed precipitate dissolved. After 12 h standing at room temperature ethylene glycol and water were added dropwise to the mixture. After working up in the conventional manner the residue (0·09 g) was chromatographed on silica gel; after crystallization from heptane 0·04 g of diketone *XXXI* were obtained, m.p. 173—180°C (decomp.), $[\alpha]_D$ +10° (*c* 0·67). IR spectrum: 3630, 1710, 1368 cm^{-1}. In ^{1}H-NMR spectrum a singlet of the CH_3COO group was present at 2·13 ppm. Mass spectrum *m/e* (%): M^+ 416 ($C_{27}H_{44}O_3$, 6), 398 (18), 383 (9), 373 (6), 345 (83), 327 (27), 309 (10), 207 (47), 189 (50), 43 (100). The sample decomposes both on heating or standing at room temperature in chloroform.

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