ELIMINATION REACTION OF ANGULAR HYDROXYMETHYL GROUPS OF 20(29)-LUPENE DERIVATIVES*

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Solvolysis of 28-*p*-toluenesulfonyloxy-20(29)-lupene derivatives *IV*– *VII* proceeds with isomerization of the isopropenyl side chain to the isopropylidene chain and expansion of the ring E to a six-membered ring, containing trisubstituted double bond; for "anhydrobetulin" and its derivatives formulae *VIII*–*XI* with homoconjugated double bonds are suggested. Formation of a conjugated diene system is hindered by steric interactions of the isopropylidene chain with the ring C (with $C_{(12)}$). Only the trisubstituted double bond in the dienes *VIII* and *X* undergoes catalytic reduction, the hydrogen approaching from the α-side (*XII*–*XVI*) as demonstrated by the Cotton effect of trinorketone *XXI* and its 20,20-dibromo derivative *XXIII*.

After elucidation of dehydration (direct or indirect) of 28-lupanol and its derivatives, reported in previous papers[1,2] of this series, we set out to investigate how a 20(29) double bond influences the course of this reaction, *i.e.* dehydration of 20(29)-lupen-28-ol derivatives. Although these eliminations were already studied[3–5], no unequivocal conclusions were reached; the reason being either the use of unsuitable elimination methods or low efficiency of older separation procedures[5]. In this study we prepared "anhydrobetulin" and its derivatives by solvolysis of 28-*p*-toluenesulfonyloxy-20(29)-lupene derivatives *IV*–*VII* obtained by tosylation of the parent hydroxy-derivatives *I*–*III* or oxidation of the hydroxy *p*-toluenesulfonate *V*. The solvolysis was carried out in N,N-dimethylaniline and the formed anhydro derivatives were correlated as usual. This proved *inter alia* that the main product can be isolated from the reaction mixture regardless of polarity of the $C_{(3)}$ substituents. Our present communication does not study solvolysis side-products.

The "anhydro derivatives" can be characterized by the following general features: their formation is accompanied by a marked shift of rotation to the left (ΔM_D = = −702° for *VIII*, −682° for *IX*, −661° for *X* and −669° for *XI*), they are transparent in the UV spectra above 220 nm, and their reaction with peroxybenzoic acid shows the presence of two double bonds. According to the IR and ^{1}H NMR spectra,

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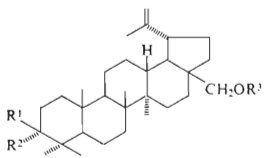
neither of these double bonds corresponds to the original isopropenyl chain of the 20(29)-lupene skeleton; one of them is tetrasubstituted and the other trisubstituted (IR spectrum: 1 674 ± 2 cm^{-1}, ^1H NMR spectrum: one-proton multiplet at δ = = 5·35 ± 0·02 ppm). Their isolated nature follows (beside the UV spectra) also from the signal of a doubly allylic proton in the ^1H NMR spectrum, observed for the anhydro derivatives *VIII* and *X* as a doublet at δ = 2·89 ± 0·02 ppm with coupling constant 11 Hz. ^1H NMR spectra of the anhydro derivatives prove also the presence of two non-equivalent methyl groups bonded to the tetrasubstituted double bond (δ = 1·65 ± 0·01 and 1·69 ± 0·01 ppm). The effect of the double bonds on the shifts of the angular methyl groups cannot be unequivocally evaluated since the trisubstituted double bond must be incorporated at the ring junction, changing thus substantially geometry of the rings. On the basis of these facts we adopted as a working hypothesis the structures *VIII*–*XI* for the anhydro derivatives. Their confirmation was facilitated by substantially different reactivity of the double bonds enabling selective additions to the trisubstituted double bond. Thus, catalytic hydrogenation at room temperature and atmospheric pressure afforded only dihydro derivatives *XII*–*XV* in which the methyl groups, bonded to the tetrasubstituted double bond, appeared to be equivalent (broader singlet at δ = 1·64). Reactions of the remaining, tetrasubstituted, double bond in the dihydro derivatives *XII*–*XV* were restricted to epoxidation and ozonolysis.

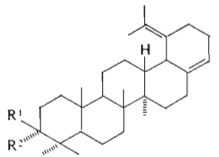
The epoxides, differing in substituents in the position 3, were prepared by epoxidation of the dihydro derivative *XII* and *XIV* or hydrolysis of the epoxy acetate prepared from the acetate *XIV*. Formulae *XVII*–*XIX* were ascribed to them for the following reasons: their IR spectra display characteristic absorption bands at 853 ± 1, 1 086 ± 2 and 1 113 cm^{-1} and in the ^1H NMR spectrum both methyls, originally bonded to the double bond, appear as a six-proton singlet at δ = 1·27. A comparison with ^1H NMR spectra of the corresponding dihydro derivatives *XII*–*XIV* further shows that conversion of the double bond into the epoxide function is accompanied by an upfield shift of the 8β and 14α methyl signals. However, no further structural information could be obtained from these epoxy derivatives since their epoxide function resisted to action of nucleophiles (such as prolonged reflux with tetrahydrofuran solution of lithium aluminium hydride); on the other hand, acid-catalyzed reactions resulted in very facile isomerization. Thus, epoxide *XVII* on treatment with boron trifluoride etherate afforded smoothly a methyl ketone (IR spectrum: 1 357, 1 693 cm^{-1}; ^1H NMR spectrum: δ = 2·125) in which the C-acetyl group is bonded to quaternary carbon atom, bearing methyl group (δ = 1·01); the carbonyl of this acetyl group must be highly hindered, because it cannot be detected by the usual chemical reactions. These facts, together with mechanistic reasons, led us to ascribe formula *XX* to this methyl ketone.

More useful information was obtained from ozonolysis of the dihydro derivative *XII*. The only volatile ozonolysis product was acetone, isolated as 2,4-dinitrophenyl-

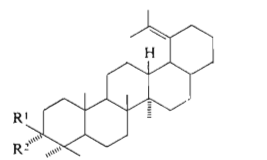
hydrazone. As the non-volatile fragment we found the trinor ketone *XXI* (UV spectrum: 296 nm, log ε 1·90). This compound contains a carbonyl which is part of a six-membered ring (IR spectrum: 1 696 cm^{-1}) and is attached to a methylene



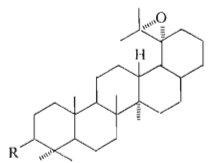
I; $R^1 = R^2 = R^3 = H$
II; $R^1 = OH$, $R^2 = R^3 = H$
III; $R^1 = OAc$, $R^2 = R^3 = H$
IV; $R^1 = R^2 = H$, $R^3 = Ts$
V; $R^1 = OH$, $R^2 = H$, $R^3 = Ts$
VI; $R^1 = OAc$, $R^2 = H$, $R^3 = Ts$
VII; $R^1 + R^2 = O$, $R^3 = Ts$



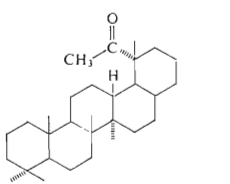
VIII; $R^1 = R^2 = H$
IX; $R^1 = OH$, $R^2 = H$
X; $R^1 = OAc$, $R^2 = H$
XI; $R^1 + R^2 = O$



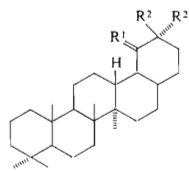
XII; $R^1 = R^2 = H$
XIII; $R^1 = OH$, $R^2 = H$
XIV; $R^1 = OAc$, $R^2 = H$
XV; $R^1 + R^2 = O$
XVI; $R^1 + R^2 = NOH$



XVII; R = H
XVIII; R = OH
XIX; R = OAc



XX



XXI; $R^1 = O$, $R^2 = H$
XXII; $R^1 = NOH$, $R^2 = H$
XXIII; $R^1 = O$, $R^2 = Br$

group (IR spectrum: 1 432 cm^{-1}); its oximation proceeds without difficulties to give oxime *XXII*. Acid-catalyzed bromination of trinorketone *XXI* afforded dibromo derivative *XXIII* with one axial (UV spectrum: $\Delta\lambda = +18{\cdot}5$ nm) and one equatorial (IR spectrum: $\Delta\nu(CO) = +22\ cm^{-1}$) bromine atom. The ^1H NMR spectrum shows that the dibromo ketone *XXIII* does not contain any H—C—Br grouping and thus both the bromine atoms must be geminal. Since, further, the Cotton effect of the dibromo ketone *XXIII* is markedly positive ($a = +108$) whereas the starting trinorketone *XXI* has an expressively negative effect ($a = -86$), the rings D and E must be *cis*-annelated, *i.e.* they must be of 17α, 18α-configuration; moreover the 18α-configuration follows from the coupling constant ($J = 11$ Hz) of the allylic proton formed in the anhydro derivatives *VIII* and *X*.

EXPERIMENTAL

Melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured in chloroform solutions on an ETL-NPL automatic polarimeter (Bendix Ericsson), accuracy ±2°. IR spectra were taken in chloroform on a UR-10 spectrometer, UV spectra on a Unicam SP-700 instrument. ^1H NMR spectra were taken in deuteriochloroform with tetramethylsilane as internal standard on Varian HA-100 (in the text denoted by an asterisk) and Varian HA-60 spectrometers; chemical shifts are given in ppm (δ scale). ORD measurements were carried out on a JASCO-ORD/UV-5 instrument and CD spectra on a Roussel-Jouan 185 dichrographe. Chromatography was performed on neutral alumina (activity II according to Brockmann) and on silica gel (according to Pitra; 30—60 μ). Analytical samples were dried over phosphorus pentoxide at 100°C under reduced pressure (13—130 Pa) for 10 h. Identity of the compounds was determined by mixture melting points, optical rotation, thin-layer chromatography and IR spectra.

Some General Procedures

Tosylations of hydroxy derivatives were carried out with *p*-toluenesulfonyl chloride in pyridine at room temperature for 2—3 days. The reaction mixture was diluted with ether, repeatedly washed with dilute (1 : 4) hydrochloric acid, water and 5% solution of sodium carbonate. After drying over sodium sulfate, the solution was passed through a short column of alumina, the eluate evaporated and the product crystallized or processed in the usual way to give the analytical sample.

Solvolyses of p-*toluenesulfonates* were performed by refluxing 2—3 . 10^{-3} mol of the tosylate in N,N-dimethylaniline (15 ml) for 3·5 h. After cooling, the mixture was diluted with ether and washed as described in the preparation of *p*-toluenesulfonates. The crude product was purified by chromatography.

Catalytic hydrogenation of dienes was carried out in ether over Adams catalyst, prereduced in acetic acid. Epoxidation of dihydro derivatives was performed with a 20—23% excess of peroxybenzoic acid in chloroform. The mixture was set aside for 12 h at 0°C and then washed with 4% solution of sodium carbonate and water. The organic solution was dried over sodium sulfate, filtered and taken down.

p-Toluenesulfonates *IV*– *VII*

Compound *IV* was prepared by tosylation of 20(29)-lupen-28-ol (*I*) as an amorphous product, $[\alpha]_D$ ±0° (*c* 1·1). IR spectrum, cm^{-1}: 819, 844, 857, 960, 1 177, 1 193, 1 605. For $C_{37}H_{56}O_3S$ (580·9) calculated: 76·48% C, 9·71% H, 5·51% S; found: 76·28% C, 9·49% H, 5·48% S.

Compound *V* was obtained by partial hydrolysis of acetate *VI*: a solution of *VI* (1·3 g) in benzene (25 ml) was refluxed with 5% ethanolic potassium hydroxide (25 ml) for 3 h. After the usual work-up procedure, the product was crystallized from ethanol, m.p. 202–203°C, $[\alpha]_D$ +17° (*c* 0·55). IR spectrum, cm^{-1}: 818, 853, 963, 1 177, 1 192, 1 609, 3 610. For $C_{37}H_{56}O_4S$ (599·9) calculated: 74·37% C, 9·74% H, 5·34% S; found: 74·47% C, 9·32% H, 5·37% S.

Compound *VI* was prepared by tosylation of 3-O-acetylbetulin (*III*) and after two crystallizations from ether–hexane melted at 167–169°C; $[\alpha]_D$ +16·5° (*c* 0·55). IR spectrum, cm^{-1}: 818, 850, 960, 1 032, 1 177, 1 190, 1 257, 1 602, 1 645, 1 722 cm^{-1}. For $C_{39}H_{58}O_5S$ (638·9) calculated: 73·31% C, 9·15% H, 5·02% S; found: 73·34% C, 9·22% H, 4·86% S.

Compound *VII*. Jones reagent was added dropwise to a solution of hydroxy derivative *V* (1 g) in benzene (20 ml) and acetone (20 ml) under cooling with ice until the brown coloration persisted. The mixture was concentrated *in vacuo*, diluted with water and the product taken up in ether. After evaporation of ether, the residue (0·85 g) was chromatographed on alumina (20 g). The amorphous oxo derivative *VII* (0·78 g) was eluted with the first 30 ml of benzene; $[\alpha]_D$ +30° (*c* 0·65). IR spectrum, cm^{-1}: 816, 850, 892, 965, 1 176, 1 190, 1 600, 1 640, 1 695.

3-Deoxyanhydrobetulin (*VIII*)

a) Solvolysis of *p*-toluenesulfonate *IV* (1·74 g) gave 1·55 g of product which was chromatographed on alumina (50 g). Elution with benzene–light petroleum (7 : 3) gave 75 mg of a mixture of isomeric olefins (first 150 ml), followed by 1 250 mg of the crude anhydro derivative *VIII* (further 160 ml). This material (1 g) was chromatographed on silica gel, containing 5% silver nitrate (150 g); elution with cyclohexane (80 ml fractions; fractions 2 and 3) afforded 18 mg of hydrocarbon A, m.p. 247·5°C (benzene–ethanol), $[\alpha]_D$ −66° (*c* 0·39). UV spectrum (cyclohexane): 208 nm, log ε 4·14. ^1H NMR spectrum*: 0·80 (CH_3), 0·87 bs (2 × CH_3), 0·97, 1·14 (2 × CH_3), 1·44 and 1·64 ($(CH_3)_2C=$), 2·20 m and 2·80 m (2 and 4 allylic protons, respectively). For $C_{30}H_{48}$ (408·7) calculated: 88·16% C, 11·84% H; found: 88·05% C, 12·00% H. Fractions 8–16 (30 mg) on crystallization from benzene–ethanol gave hydrocarbon B, m.p. 197·5–198·5°C, $[\alpha]_D$ −40° (*c* 0·81). UV spectrum (cyclohexane): 208 nm, log ε 3·98. ^1H NMR spectrum*: 0·80, 0·83, 0·86, 0·935, 0·99 (5 × CH_3), 1·63 and 1·67 ($(CH_3)_2C=$), 5·33 m (H–C=), 2·83 bd (18α H). Fractions 20–22 (680 mg) on crystallization from cyclohexane yielded hydrocarbon C, 3-deoxyanhydrobetulin (*VIII*), m.p. 229·5–230·5°C; $[\alpha]_D$ −172° (*c* 0·37). IR spectrum, cm^{-1}: 836, 857, 1 676. ^1H NMR spectrum: 0·80, 0·83, 0·85, 0·97, 1·13 (5 × CH_3), 1·65 and 1·70 ($(CH_3)_2C=$), 2·88 d, J = 11·5 Hz (18α H), 5·32 m (22-H). For $C_{30}H_{48}$ (408·7) calculated: 88·16% C, 11·84% H; found: 88·08% C, 11·79% H. Consumption of peroxybenzoic acid: 1·92 double bond. Fractions 25–27 (110 mg) afforded hydrocarbon D, m.p. 202–204°C (cyclohexane–ethanol), $[\alpha]_D$ −165° (*c* 0·36). UV spectrum (cyclohexane) 208 nm, log ε 3·95. ^1H NMR spectrum*: 0·87 bs (2 × CH_3), 0·95, 0·99, 1·13 (3 × CH_3), 1·64 and 1·69 ($(CH_3)_2C=$), 2·93 bd (18 or 20-H), 5·36 m (H–C=). For $C_{30}H_{48}$ (408·7) calculated: 88·16% C, 11·84% H; found: 88·10% C, 12·02% H.

b) A solution of ketone *XI* (1·05 g) in benzene (20 ml) was mixed with ethanol (20 ml) and hydrazine hydrate (1·5 ml). After heating to 70°C for 1 h, the solution was concentrated and mixed with diethylene glycol (25 ml) and potassium hydroxide (0·5 g). The temperature was risen during 1 h to 240°C, the mixture was kept at this temperature for another hour, cooled and worked up as usual. Chromatography on alumina as described under *a*), followed by crystallization

from chloroform–methanol, afforded 780 mg of anhydro derivative *VIII*, m.p. 224—225·5°C, $[\alpha]_D$ −169° (*c* 0·95), identical in all respects with the above-described material.

Anhydrobetulin (*IX*)

a) Solvolysis of mono-*p*-toluenesulfonate *V* gave 0·82 g of crude product which was chromatographed on alumina (50 g). Elution with benzene–light petroleum (1 : 1; 180 ml) afforded 25 mg of less polar material, benzene (150 ml) eluted 5 mg of a similar mixture. Anhydrobetulin (*IX*) (770 mg) was eluted with benzene–ether (9 : 1; 250 ml) and crystallized from chloroform–methanol; yield 660 mg of completely pure product, m.p. 251—252·5°C, $[\alpha]_D$ −154° (*c* 1·3). IR spectrum, cm^{-1}: 838, 841, 986, 1 026, 1 670, 3 626. ^1H NMR spectrum: 0·775, 0·84 (2 × CH_3), 0·975—1·00 (2 × CH_3), 1·125 (CH_3), 1·65 and 1·70 ($(CH_3)_2C=$), 5·37 m (H—C=). For $C_{30}H_{48}O$ (434·7) calculated: 84·84%C, 11·39% H; found: 84·82% C, 11·35% H.

b) Acetate *X* (100 mg) was refluxed with 5% solution of potassium hydroxide in benzene–ethanol (1 : 1) for 3 h. The obtained product (82 mg) was crystallized from benzene–ethanol, m.p. 250—251°C, $[\alpha]_D$ −152° (*c* 1·4), and was identical with the compound prepared under *a*).

Anhydrobetulin Acetate (*X*)

a) The crude product (2·2 g), obtained by solvolysis of *p*-toluenesulfonate *VI* (2·75 g), was chromatographed on alumina (150 g) in benzene–light petroleum (2 : 5). The first three fractions (à 30 ml) were combined, evaporated and the residue crystallized from benzene–ethanol, affording a mixture of anhydro acetates (1·65 g), m.p. 202—214°C, $[\alpha]_D$ −68° (*c* 1·2). This mixture (1·5 g) was further separated by chromatography on silica gel, containing 5% of silver nitrate (75 g). Elution with cyclohexane–ether (19 : 1; 50 ml fractions; fractions 6—10) gave 1·1 g of material which on crystallization from cyclohexane yielded 900 mg of pure acetate *X*, m.p. 212—214°C (sealed capillary); $[\alpha]_D$ −113° (*c* 0·58). IR spectrum, cm^{-1}: 984, 1 028, 1 257, 1 677, 1 723. ^1H NMR spectrum: 0·845—0·875 bs (3 × CH_3), 0·97, 1·12 (2 × CH_3), 1·66 and 1·69 ($(CH_3)_2$. .C=), 2·04 (CH_3COO), 2·91 d, J = 10 Hz (18α-H), 4·51 m (3α-H), 5·35 m (22-H). For $C_{32}H_{50}O_2$ (466·7) calculated: 82·34% C, 10·80% H; found: 82·59% C, 10·88% H. Peroxybenzoic acid consumption: 2·11 double bonds.

b) Anhydrobetulin (*IX*) (200 mg) was treated with acetic anhydride (1·5 ml) in pyridine (2 ml) at room temperature for 12 h. The obtained product was twice crystallized from benzene–ethanol and according to its melting point (213—214°C in sealed capillary), specific rotation ($[\alpha]_D$ −115° (*c* 0·55)) and other properties it was identical with the compound prepared according to procedure *a*).

3-Oxo Derivative *XI*

a) Solvolysis of tosylate *VII* (1·49 g) afforded a crude product (0·75 g) which was chromatographed on alumina (50 g). Material eluted with benzene–light petroleum was chromatographed on silica gel containing 5% silver nitrate (30 g) with cyclohexane as eluant (20 ml fractions). Crystallization of the first three fractions from methanol afforded pure oxo derivative *XI*, m.p. 203—205°C, $[\alpha]_D$ −116° (*c* 1·4). IR spectrum, cm^{-1}: 840, 1 703. ^1H NMR spectrum: 0·93, 1·00, 1·03, 1·08, 1·13 (5 × CH_3), 1·64 and 1·69 ($(CH_3)_2C=$), 5·37 m (22-H). For $C_{30}H_{46}O$ (422·7) calculated: 85·24% C, 10·97% H; found: 85·03% C, 10·95% H.

b) A solution of chromium trioxide (200 mg) in pyridine (7 ml) was added portionwise to a solution of hydroxy derivative *IX* (500 mg) in pyridine (5 ml). After standing for 24 h at room tem-

perature, the mixture was worked up as usual. Chromatography of the neutral fraction (460 mg) on alumina (30 g) in benzene afforded (first 60 ml) 430 mg of product which on crystallization from ethyl acetate gave oxo derivative *XI*, identical with the compound prepared by procedure *a*).

Dihydro Derivative *XII*

Crude anhydro derivative *VIII* (65 mg; before chromatography on silica gel with silver nitrate) was hydrogenated till the hydrogen uptake ceased. The product was chromatographed on silica gel with 10% silver nitrate (10 g) in cyclohexane (5 ml fractions). Crystallization of the product (fraction 8) from ethyl acetate afforded pure dihydro derivative *XII* (48 mg), m.p. 251·5–252°C; $[\alpha]_D$ −70° (*c* 1·2). ^{1}H NMR spectrum: 0·80 (CH_3), 0·84–0·86 (2 × CH_3), 1·01, 1·03 (2 × CH_3), 1·63–1·65 bs ($(CH_3)_2C=$). For $C_{30}H_{50}$ (410·7) calculated: 87·73% C, 12·27% H; found: 87·80% C, 12·21% H.

Dihydro Acetate *XIV*

Hydrogenation of acetate *X* (1·4 g), followed by two crystallizations from benzene–hexane, afforded 0·97 g of dihydro derivative *XIV*, m.p. 262–265°C; $[\alpha]_D$ −22° (*c* 0·85). IR spectrum, cm^{-1}: 981, 1 028, 1 255, 1 722. ^{1}H NMR spectrum: 0·84–0·87 bs (3 × CH_3), 0·99, 1·03 (2 × × CH_3), 1·63–1·65 bs ($(CH_3)_2C=$), 2·04 (CH_3COO), 4·49 m (3αH). For $C_{32}H_{52}O_2$ (468·7) calculated: 81·99% C, 11·18% H; found: 82·12% C, 11·08% H. Compound *XIV* (800 mg) was hydrolyzed by reflux with 5% ethanolic potassium hydroxide for 4 h to give hydroxy derivative *XIII* (610 mg), m.p. 205–206°C (acetone). $[\alpha]_D$ −44° (*c* 1·1). IR spectrum, cm^{-1}: 985, 1 025, 1 070, 3 625. ^{1}H NMR spectrum: 0·77, 0·85, 0·98, 1·00, 1·03 (5 × CH_3), 1·63–1·65 bs ($(CH_3)_2$. .C=). For $C_{30}H_{50}O$ (426·7) calculated: 84·44% C, 11·81% H; found: 84·51% C, 11·78% H. The hydroxy derivative *XIII* (600 mg) was oxidized in pyridine (100 ml) with chromium trioxide (300 mg). After standing for 2 days at room temperature, the crude product was worked up in the usual manner and chromatographed on alumina (50 g). Benzene fractions were combined, taken down and the residue crystallized from chloroform–methanol, affording 390 mg of oxo derivative *XV*, m.p. 215–217°C; $[\alpha]_D$ −11° (*c* 1·1). IR spectrum, cm^{-1}: 1 423, 1 692. ^{1}H NMR spectrum: 0·94, 1·01, 1·03 (3 × CH_3), 1·07–1·08 (2 × CH_3), 1·63–1·65 bs ($(CH_3)_2C=$). Oxime of dihydro ketone *XVI* was prepared by heating *XV* and hydroxylamine hydrochloride in pyridine on a water bath for 2 h. The usual isolation procedure followed by crystallization from chloroform–methanol afforded *XVI* which sublimed even in sealed capillary. For $C_{30}H_{49}NO$ (439·7) calculated: 81·94% C, 11·23% H, 3·19% N; found: 81·80% C, 11·44% H, 3·21% N.

Epoxide *XVII*

Hydrocarbon *XII* (770 mg) was epoxidized as described above and the product was crystallized twice from chloroform–methanol, yielding 640 mg of epoxide *XVII*, m.p. 227–228°C, $[\alpha]_D$ −19° (*c* 1·0). IR spectrum, cm^{-1}: 852, 1 084, 1 114. ^{1}H NMR spectrum: 0·80 (CH_3), 0·85–0·87 bs (2 × CH_3), 0·93, 1·06 (2 × CH_3), 1·26–1·275 bs ($(CH_3)_2C-O$). For $C_{30}H_{50}O$ (426·7) calculated: 84·44% C, 11·80% H; found: 84·54% C, 11·84% H.

Epoxide *XIX*

Epoxidation of acetate *XIV* (220 mg) and two crystallizations of the product from chloroform–methanol gave 120 mg of epoxide *XIX*, m.p. 288–292°C. IR spectrum, cm^{-1}: 854, 1 023, 1 032, 1 089, 1 113, 1 138, 1 254, 1 723. ^{1}H NMR spectrum: 0·86 (2 × CH_3), 0·89, 0·925, 1·07 (3 × × CH_3), 1·29 bs ($(CH_3)_2C-O$), 2·05 (CH_3COO), 4·46 m (3αH). For $C_{32}H_{52}O_3$ (484·7) cal-

culated: 79·28% C, 10·81% H; found: 79·12% C, 10·83% H. The product *XIX* (100 mg) on reflux with 5% solution of potassium hydroxide in benzene–ethanol (1 : 1) for 3 h afforded hydroxy derivative *XVIII* which after two crystallizations from chloroform–methanol weighed 82 mg and melted at 252–255°C. IR spectrum, cm^{-1}: 853, 1 085, 1 113, 3 625. ^1H NMR spectrum: 0·77, 0·87, 0·92, 0 975, 1·06 (5 × CH_3), 1·26–1·275 bs ($(CH_3)_2C$—O). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·18% C, 11·35% H.

Isomerization of Epoxide *XVII*

Boron trifluoride etherate (0·2 ml) was added to a solution of epoxide *XVII* (150 mg) in ether (20 ml). After standing at room temperature for 12 h, the mixture was washed with water, 5% sodium carbonate solution, dried over sodium sulfate and taken down. The residue (131 mg) was chromatographed on alumina (20 g). After elution with light petroleum (40 ml) and light petroleum–benzene (9 : 1; 60 ml), the main product (110 mg) was eluted with light petroleum–benzene (7 : 3; 40 ml). Crystallization from light petroleum–acetone afforded 110 mg of methyl ketone *XX*, m.p. 222·5–223·5°C; $[\alpha]_D$ +22° (*c* 0·85). IR spectrum, cm^{-1}: 1 357, 1 693. UV spectrum (ethanol): λ_{max} 289 nm, log ε 1·56. ^1H NMR spectrum: 0·79–0·84 (3 × CH_3), 0·98, 1·07 (2 × CH_3), 1·01 (19β-CH_3), 2·125 (CH_3CO—C). For $C_{30}H_{50}O$ (426·7) calculated: 84·44% C, 11·80% H; found: 84·30% C, 11·76% H.

Trinorketone *XXI*

Ozone (3–3·5%) was introduced into a solution of hydrocarbon *XII* (820 mg) in chloroform (300 ml), cooled with dry ice and the reaction was monitored by thin-layer chromatography on alumina in benzene. After 2 3/4 h no starting hydrocarbon was detectable. The solution was taken down *in vacuo* at low temperature, the residue was dissolved in 80% acetic acid (10 ml) and zinc dust (1 g) was added. After stirring at 50°C for 2 h, the mixture was taken down under slightly diminished pressure and the distillate was introduced into a saturated solution of 2,4-dinitrophenylhydrazine in 2M-HCl. The crystalline precipitate (12 mg) which separated on standing at +5°C overnight melted at 122–125°C and according to paper chromatography[6] corresponded to acetone 2,4-dinitrophenylhydrazone. The non-volatile portion of the ozonolysis mixture was dissolved in ether (150 ml), the acidic material was removed by washing with 5% sodium carbonate solution (3 × 50 ml) and the etheral layer was taken down. The neutral residue (690 mg) was chromatographed on alumina (50 g) in benzene (20 ml fractions). Fractions 4–7 after crystallization from benzene–ethanol afforded 490 mg of trinorketone *XXI*, m.p. 237–239°C; $[\alpha]_D$ −67° (*c* 0·99). UV spectrum (ethanol): λ_{max} 296 nm, log ε 1·90. IR spectrum, cm^{-1}: 1 432, 1 696. ORD (dioxane, *c* 0·08): $(\phi)_{325} = -3\,910°$, $(\phi)_{305} = 0°$, $(\phi)_{278} = 4\,700°$, $a = -86$. CD (dioxane, *c* 0·065): λ_{max} ($\Delta\varepsilon$) = 305 nm (−2·34) and 298 nm (−2·38). ^1H NMR spectrum: 0·81 (CH_3), 0·86 (2 × CH_3), 0·94, 1·08 (2 × CH_3). For $C_{27}H_{44}O$ (384·6) calculated: 84·31% C, 11·07% H; found: 84·36% C, 11·21% H. Oxime *XXII* was prepared by heating of the ketone *XXI* (60 mg) and hydroxylamine hydrochloride (40 mg) in pyridine (5 ml) in a water bath for 2·5 h. The usual work-up procedure and crystallization from benzene–cyclohexane afforded 40 mg of oxime *XXII*, m.p. 236–239°C. For $C_{27}H_{45}NO$ (399·6) calculated: 3·51% N; found: 3·48% N.

Dibromo Ketone *XXIII*

A solution of bromine (93 mg) in acetic acid (5 ml) was added to a solution of ketone *XXI* (150 mg) in acetic acid (5 ml). After standing in the dark at room temperature overnight, the separated crystals (80 mg) were crystallized from cyclohexane to give dibromo ketone *XXIII*, m.p. 231 to 232·5°C; $[\alpha]_D$ +51·6° (*c* 0·66). UV spectrum (cyclohexane): λ_{max} 314·5 nm, log ε 1·68. IR spec-

trum, cm^{-1}: 811, 976, 1 718. ORD (dioxane, c 0·08): $(\phi)_{344} = 5\,360°$, $(\phi)_{320} = 0°$, $(\phi)_{291} = -5\,455°$, $a = +108$. For $C_{32}H_{42}Br_2O$ (526·4) calculated: 61·60% C, 8·04% H, 30·36% Br; found: 61·70% C, 8·22% H, 29·34% Br.

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