OXIDATION RATES OF TRITERPENOID SECONDARY ALCOHOLS WITH CHROMIC ACID*

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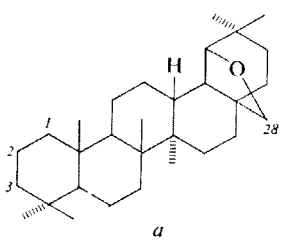
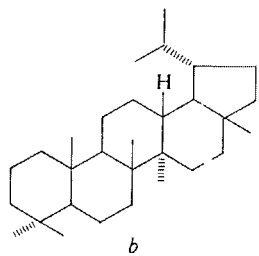
Oxidation rates with chromic acid were measured of alcohols *I*—*VI* derived from the skeletons *a*, *b*, *c* and *d* with a hydroxyl group in the position 1, 2, and 3, as well as of some additional triterpenoid alcohols. The results are discussed in terms of the effect of steric factors of neighbouring substituents and the effect of conformational transmission. Some of the derivatives of 19β,28-epoxy-18α-oleanane (*a*) and lupane (*b*) were newly prepared.

In continuation of our studies of sterical relationships in ring A of triterpenoid derivatives we measured the oxidation rates of hydroxy derivatives with chromic acid; it is known that these rates reflect very sensitively the steric situation in the neighbourhood of the oxidized hydroxyl group (for main references see[1,2]). In this



a



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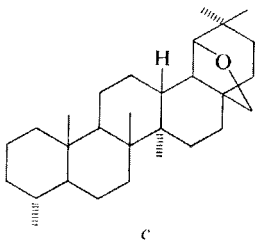

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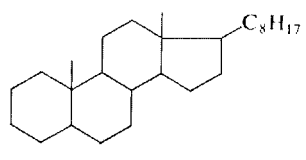

d

I, 1α-OH
II, 1β-OH
III, 2α-OH
IV, 2β-OH
V, 3α-OH
VI, 3β-OH

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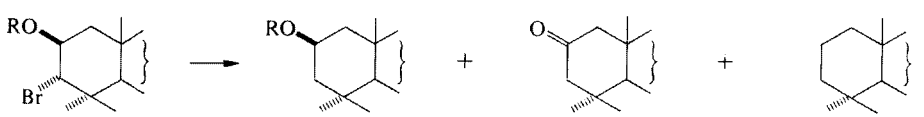
paper oxidation rates of axial and equatorial alcohols *I* – *VI* are compared, which contain a hydroxy group on the A ring and which are derived from 19β,28-epoxy--18α-oleanane (*a*) and lupane (*b*). In order to determine the effect of the methyl groups in the position 4 the study was completed in the case of 3-hydroxy derivatives *V* and *VI* by derivatives 19β,28-epoxy-24-nor-18α-oleanane (*c*) and 5α-cholestane (*d*), and, for the sake of comparison, by some additional triterpenoid alcohols.

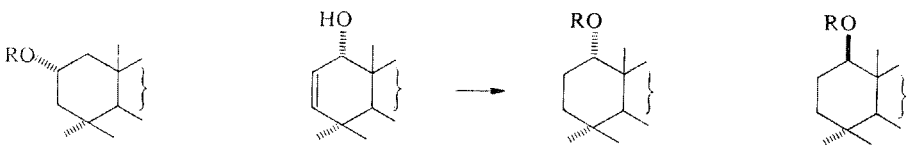
The preparation of 1- and 3-hydroxy derivatives *Ia*, *IIa*, *Va* and *VIa* in the 19β,28--epoxy-18α-oleanane series (*a*) and of 3-hydroxy derivatives *Va* and *VIa* in the 19β,28--epoxy-24-nor-18α-oleanane series (*c*) has already been described in preceding papers[3–5]. For further completion of this series of hydroxy derivatives we prepared now both isomeric 19β,28-epoxy-18α-oleanan-2-ols (*IIIa* and *IVa*). As starting material 2β-hydroxy-3α-bromo derivative *VIIa* was used, as well as its formate *VIIIa* and 2-oxo derivative *Xa*; the latter was prepared from bromohydrin *VIIa* in the described manner[6]. On reduction of ketone *Xa* with sodium in ethanol 2α-hydroxy derivative *IIIa* was obtained, while reduction with tritert-butoxylithium aluminum hydride gave 2β-hydroxy derivative *IVa*, as could be expected in analogy with the steroid series[7]. In both cases reduction took place very stereospecifically; according to thin layer chromatography the second isomer is formed in trace amounts only. Hydroxy derivatives *IIIa* and *IVa* were further characterized as acetates *XIIa* and *IXa*. In an attempt at the preparation of the 2β-isomer *IVa* directly from bromohydrin *VIIa* by catalytic debromination with hydrogen in the presence of 5% palladium on charcoal hydroxy derivative *IVa* was obtained in a 17% yield only; ketone *Xa* was the main product (78%). A similar course of catalytic debromination has also been observed in analogous steroidal bromohydrins[8] and very probably, it is characteristic just of 2β-hydroxy-3α-halogen derivatives. 2β-Hydroxy derivative *IVa* was obtained from 2β-formyloxy-3α-bromo derivative *VIIIa* on reaction with hydrogen on palladium and subsequent alkaline hydrolysis in 45% yield. It is true that in this case the formation of ketone *Xa* is suppressed (7%), but in addition to this hydrogenolysis of the formate group also takes place under formation of derivative *XIa* (43%).



VIIa, R = H *IVa*, R = H *Xa* *XIa*
VIIIa, R = CHO *IXa*, R = CH_3CO

In the lupane series (*b*) isomeric 1- and 3-hydroxy derivatives *Ib*, *IIb*, *Vb* and *VIb* have been described earlier[9–13]; since we have prepared some of them by procedures different from those in the literature cited, and since we found for some of them

constants which do not agree with those published, we describe their preparation and properties here shortly. 1α-Hydroxy derivative *Ib* was obtained by hydrogenation of the unsaturated alcohol[14] *XIIIb*, and 1β-hydroxy derivative *IIb* by hydrogenation of 2-lupen-1-one, according to[9,11]. 3α-Hydroxy derivative *Vb* was prepared by reduction of 2α,3α-epoxylupane[9-11] (*XVIb*) with lithium aluminum hydride, while the 3β-isomer *VIb* by hydrogenation of lupeol according to[12]. The disagreement in melting points may be caused by polymorphy (in substances *Vb* and *VIb*), but in the case of derivatives *Ib* and *Vb* optical rotation values also differ considerably from those published[9,10]. However, our values agree with the differences of molecular rotations between the series *a* and *b*. Hydroxy derivatives *Ib*, *IIb* and *Vb* were further characterized as acetates *XIVb*, *XVb* and *XVIIb*, in which a good agreement of their constants with the literature data was found so far as they have been described. The conformation of the acetoxyl group was further confirmed by the ^{1}H-NMR spectra of these acetates; in axial acetoxy derivatives *XIVb* and *XVIIb* the signal of the methine proton in the CH—$OCOCH_3$ group appears as a narrow triplet and the sum of the vicinal coupling constants is $\sum J = 5{\cdot}5$ Hz, while in the equatorial acetoxy derivative *XVb* the triplet is broad, with $\sum J = 15$ Hz.



IIIa, R = H; *XIIa*, R = CH_3CO — *XIIIb* — *Ib*, R = H; *XIVb*, R = CH_3CO — *IIb*, R = H; *XVb*, R = CH_3CO

Kinetic measurements of the oxidation with chromic acid were carried out under conditions similar to those used by Grimmer for the oxidation of steroidal alcohols[15], *i.e.* in 99·67% acetic acid, in the presence of N-methylmorpholine. Under its effect the oxidations were slowed so that their half-times ranged from 6 to 60 minutes. The rate constants of the 2nd order reaction are given in Table I,* and the courses of these oxidations agreed with this order up to 80–90% conversion.

It is generally accepted[1,2,17-20] that the oxidation of secondary alcohols with chromic acid takes place *via* the intermediate chromate ester and the rate determining step is its decomposition, involving breaking of the bond to the carbinol hydrogen.

* Oxidation rates of alcohols *Ia*, *IIa*, *Va* and *VIa* have also been measured in paper[16], but under different conditions; in the paper mentioned the values of absolute rate constants were given incorrectly. In order to obtain correct values the tabulated data should be multiplied by the factor $4{\cdot}89 \cdot 10^5$.

The rate is the greater the more the hydroxyl group is hindered. In agreement with this in all pairs of epimeric alcohols given in Table I the axial alcohol reacts more rapidly than the equatorial one. In the case of 5α-cholestan-3-ols *Vd* and *VId* the ratio of the reaction rates observed under our experimental conditions ($k_{Vd}/k_{VId} = 2{\cdot}5$) is very close to the value obtained by Schreiber and Eschenmoser[17] (3·0). From the comparison of 3-hydroxy derivatives in the series *a*, *c* and *d* it is evident that the influence of the methyl groups in the position 4 is important. A gradual introduction of the methyl groups in both epimers *V* and *VI* leads to an increase in the reaction rate (about 1·2–1·7 times for each methyl group). This increase is more pronounced in equatorial alcohols *VI* than in axial alcohols *V*, so that with an increasing number of methyl groups the ratio of the rates of the axial and the equatorial epimer (k_V/k_{VI}) gradually decreases. Since the ratio of oxidation rates of epimeric alcohols may be considered an approximate measure of their free energy difference (see[1,19] and the references therein), it may indicate that with increasing substitution in the position 4 the energy difference between 3α and 3β-hydroxy derivatives gradually decreases.

From the comparison of isomeric 1-, 2- and 3-hydroxy derivatives *I*–*VI* in the triterpenoid series *a* it is evident that the 2α-isomer *IIIa* having the least hindered hydroxy group reacts most slowly; on the other hand, it is the 2β-isomer *IVa* which of all the studied alcohols reacts fastest. The ratio of rates of the axial and the equatorial 2-epimer ($k_{IVa}/k_{IIIa} \sim 13$) is comparable with the rate for 5α-cholestan-2-ols ($k_{IVd}/k_{IIId} \sim 15$) from literature[17] in spite of the fact that in 2β-derivative *IVa* two

TABLE I

Relative Oxidation Rates of Alcohols *I*–*VI* with Chromic Acid

Derivative	OH-group		Rate constants[a]			
			a	*b*	*c*	*d*
I	1α	ax	10·1	5·28	—	—
II	1β	eq	4·89	3·40	—	—
III	2α	eq	1·46	—	—	—
IV	2β	ax	19·9	—	—	—
V	3α	ax	3·84	3·57	3·21	2·50
VI	3β	eq	2·22[b]	2·35[b]	1·69	1·00

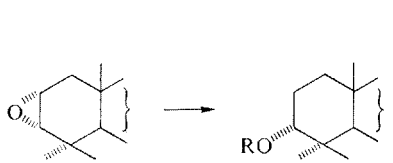
[a] Referred to 5α-cholestan-3β-ol *VId*; its absolute rate constant is 9·48 l mol^{-1} min^{-1}. [b] The following relative rate constants were observed for 3β-hydroxy derivatives *VI* derived from 13β,28-epoxylupane (2·28), 19β,28-epoxy-lupane (2·05), methyl ester of 28-lupanoic acid (2·12), 18α-oleanan-28,20β-olide (2·14), 20β,28-epoxy-18α,19β*H*-ursane (2·39), 20β,28-epoxy-18α,19β*H*--ursan-20-one (2·22).

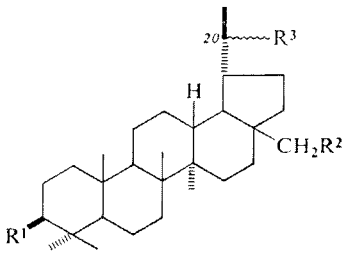
1,3-*syn*-axial interactions OH/CH_3 (with the 4β- and 10β-methyls in the chair form), appear, while in 5α-cholestan-2β-ol *IVd* there is only a single such interaction (with the 10β-methyl group). For example 5α-pregnan-11β-ol which has two *syn*-axial interactions OH/CH_3 reacts more than 64 times faster than its 11α-epimer and more than 900 times faster than 3β-hydroxy derivative *VId* (see[1,17]). In comparison with these steroid alcohols the oxidation rate of triterpenic 2β-hydroxy derivative *IVa* is relatively low. Since according to our earlier results[21] the A ring of derivative *IVa* is partly in boat form (about 60% in non-polar solvents), it is possible that the decrease of the rate is caused by the fact that in the boat form the oxidation rate is much lower than in the chair form; in the boat form the infavourable interaction between the hydroxyl group and the methyl groups vanishes. A further possibility is that due to the strong steric hindrance of the 2β-hydroxyl in the chair form the rate of formation of the chromate ester decreases to such an extent that it becomes the rate-determining step. This phenomenon has been observed in sterically strongly hindered alcohols[18,20], for example in triterpenoid 6β-hydroxy derivative[18].

In order to determine whether the long-range effects caused by structural changes in more remote rings[1] will become evident we comprized in our study in addition to derivatives of the *a* and *b* series, further triterpenoid derivatives. They were compounds having in ring E or D an ether or lactone bridge or a carbonyl group, derived from lupane, 18α-oleanane and 18α,19β*H*-ursane skeleton (see note[b] in Table I). However, the oxidation rates of all these 3β-hydroxy derivatives *VI* differ negligibly; neither in the case of 3α-isomers *V* did we observe important differences between the series *a* and *b*. This indicates that the oxidation rate of the hydroxyl group in the position 3 is very little sensitive to the effects of remote substituents. It is also interesting that in the case of axial and equatorial 1-hydroxy derivatives *I* and *II* considerable differences in reactivity appear between the series *a* and *b*; both lupan-1-ols *Ib* and *IIb* react more slowly than the corresponding derivatives of 19β,28-epoxy-18α-oleanane *Ia* and *IIa* (1·8 times and 1·5 times, respectively). These differences may be attributed to the conformational transmission effect[1], having its origin in the deformations of the triterpenoid skeleton, caused by structural changes in the E ring. The higher sensitivity of 1-hydroxy derivatives toward long range effects may be caused by the fact that deformations of rings A, B and C change the steric situation in the neighbourhood of the hydroxyl groups more than in 3-hydroxy derivatives; the hydroxyl groups on $C_{(1)}$ are in the vicinity of the rings B and C and especially in the proximity of the 11-methylene group, while the hydroxyl groups on $C_{(3)}$ are oriented out of the molecule.

Finally, we also compared the oxidation rates of lupane derivatives *XVIII*–*XX* which have a hydroxyl group in the side chain and differ in configuration at $C_{(20)}$. The rates of $C_{(20)}$ epimeric 30-nor-20-ols differ only very little, while 20*R*-epimers react more rapidly (*XVIII*: 2·86, *XIX*: 2·52) than 20*S*-epimers (*XVIII*: 2·28, *XIX*: 2·16), similarly as in the case of pregnan-20-ols (see[15]); this trend is still more pro-

nounced during the oxidation of primary alcohols *XX* where oxidation up to acids takes place (20*R*: 1·77; 20*S*: 0·80). The rate constants of oxidation of $C_{(20)}$ epimeric 30-nor-20-lupanol (*XVIII*, *XIX*) or 29-lupanol (*XX*) derivatives respectively, will be discussed elsewhere in connection with the equilibration of these systems.





XVIb

Vb, R = H
XVIIb, R = CH_3CO

XVIII, $R^1 = R^2 = H$, $R^3 = OH$
XIX, $R^1 = CH_3COO$, $R^2 = H$, $R^3 = OH$
XX, $R^1 = R^2 = CH_3COO$, $R^3 = CH_2OH$

EXPERIMENTAL

The melting points were measured on a Kofler block. Optical rotations were measured in chloroform (*c* 0·5—1·0) 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) spectrophotometer. ^{1}H-NMR spectra were measured at 100 MHz on a Varian HA-100 instrument in deuteriochloroform, using tetramethylsilane as internal standard. Chemical shifts are given in p.p.m. in δ-scale. For column chromatography alumina (Reanal, activity II) was used, for thin-layer chromatography silica gel according to Stahl (type 60). Acetyl derivatives were prepared with acetic anhydride in pyridine at room temperature. Samples for analysis and for kinetic measurements were dried over phosphorus pentoxide at 100°C and 0·1—1 Torr for 8—24 hours.

Acetic acid used for kinetic measurements were purified by 24 hours' boiling with 2% of chromium trioxide and rectification on a column with 60 TP. The water content was adjusted to 0·33% on the basis of aquametric determination. N-Methylmorpholine was prepared by reductive methylation of morpholine with formaldehyde according to[22]. The product was rectified on a column of 20 TP and only the medium fraction of b.p. 115°C was collected. All samples of hydroxy derivatives used for kinetic measurements were crystallized from solvents free of hydroxyl group (hexane, cyclohexane, light petroleum, ether or acetonitrile).

19β,28-Epoxy-18α-oleanan-2α-ol (*IIIa*)

2-Oxo derivative *Xa* (150 mg, see[6]) was reduced with sodium (3·5 g) in ethanol (150 ml), by boiling for 30 minutes. The mixture was diluted with water, acidified with dilute hydrochloric acid and extracted with ether. The ethereal extract was washed with water and dried over sodium sulfate, then filtered and evaporated. The residue contained according to thin-layer chromatography a small amount of the 2β-isomer *IVa*. Chromatography on alumina (15 g; elution with a benzene–ether mixture) and crystalization from chloroform–methanol gave 2α-hydroxy derivative *IIIa* (80 mg), m.p. 236—237·5°C. The analytical sample, prepared by preparative thin layer chromato-

graphy on silica gel (elution with light petroleum–ether mixture (6 : 4) and crystallization from chloroform–hexane had m.p. 238–239°C, $[\alpha]_D$ +50°. IR spectrum: 3620, 3450 (OH), 1032 (COC) cm^{-1}. For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·39% C, 11·58% H.

Acetyl derivative XIIa had after crystallization from methanol and from hexane m.p. 205 to 207°C, $[\alpha]_D$ +23°. IR spectrum: 1729, 1265 (CH_3COO), 1032 (COC) cm^{-1}. For $C_{32}H_{52}O_3$ (484·7) calculated: 79·28% C, 10·81% H; found: 79·44% C, 11·11% H.

19β,28-Epoxy-18α-oleanan-2β-ol (*IVa*)

A) Tri-tert-butoxylithium aluminum hydride (200 mg) was added to a solution of 2-oxo derivative *Xa* (140 mg) in ethyl acetate (50 ml) and the mixture was allowed to stand at room temperature for 24 hours. Water was then added followed by dilute hydrochloric acid. The organic layer was washed with water and dried over sodium sulfate, and ethyl acetate was distilled off. The residue which contained according to thin-layer chromatography traces of 2α-isomer *IIIa* was dissolved in benzene and the solution was filtered through alumina (5 g). After crystallization from benzene derivative *IVa* was obtained (90 mg), m.p. 266–268°C, $[\alpha]_D$ +80°. IR spectrum: 3620, 3440 (OH), 1035 (COC) cm^{-1}. For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·13% C, 11·41% H. After crystallization from chloroform–methanol the acetyl derivative *IXa* had m.p. 239–241°C, $[\alpha]_D$ +65°. IR spectrum: 1732, 1264 (CH_3COO), 1035 (COC) cm^{-1}. For $C_{32}H_{52}O_3$ (484·7) calculated: 79·28% C, 10·81% H; found: 79·41% C, 11·07% H.

B) 2β-Formyloxy-3α-bromo derivative *VIIIa* (360 mg, see[6]) was dissolved in boiling ethanol (150 ml). After cooling of the solution to 20°C, 5% palladium on charcoal (0·40 g) and powdered calcium carbonate (0·20 g) were added and the mixture was shaken under hydrogen for 28 hours. Additional catalyst (0·40 g) and calcium carbonate (0·20 g) were added and the mixture was shaken with hydrogen for another 15 hours. The solution was filtered, the filtrate was alkalized with 1·5 g of potassium hydroxide and the mixture was allowed to stand at room temperature for 16 hours. After dilution with water it was acidified with hydrochloric acid and extracted with chloroform. The extract was washed with water and dried over sodium sulfate. Chloroform was distilled off and the residue dissolved in benzene and chromatographed on alumina (30 g). Benzene (100 ml) eluted 19β,28-epoxy-18α-oleanane (*XIa*, 120 mg), m.p. 232–233°C (chloroform–methanol), $[\alpha]_D$ +50°. Identity with an authentic sample[23] was proved by mixture melting point determination. Further 50 ml of benzene eluted 2-oxoderivative *Xa* (20 mg) with m.p. 242–244°C (methanol), identical according to its IR spectrum and mixture melting point with an authentic sample[6]. Benzene–ether mixture 4 : 1 (100 ml) eluted 2β-hydroxy derivative *IVa* (130 mg), identical with the sample, described under *A*) m.p. 268–270°C.

C) A solution of bromohydrin *VIIa* (550 ml, see[6]) in ethanol (150 ml) was shaken under hydrogen and in the presence of 5% palladium on charcoal (1 g) as catalyst and calcium carbonate (0·5 g) for 27 hours. The solution was filtered and ethanol distilled off under reduced pressure. Chromatography of the residue as under *A*) gave gradually a non-polar fraction (10 mg), which was not identified, then 2-oxo derivative *Xa* (360 mg), and finally 2β-hydroxy derivative *IVa* (80 mg).

1α-Lupanol (*Ib*)

2-Lupen-1α-ol (*XIIIb*, 60 mg, see[14]) and platinum dioxide (160 mg) in ether (50 ml) was shaken under hydrogen for 4 hours. The catalyst was filtered off and ether was distilled off. Derivative *Ib*

was obtained (50 mg), m.p. 215–216°C (chloroform–methanol), $[\alpha]_D$ −6°. Ref.[9] gives m.p. 212–213°C, $[\alpha]_D$ +38°. For $C_{30}H_{52}O$ (426·7) calculated: 84·04% C, 12·23% H; found: 83·85% C, 12·05% H. Acetyl derivative *XIVb* had after crystallization from chloroform–methanol m.p. 193–196°C, $[\alpha]_D$ +6°. IR spectrum: 1723, 1262, 1042 (CH_3COO) cm^{-1}. ^{1}H-NMR spectrum: 0·75, 0·84 (2 × CH_3); 0·91 (2 × CH_3); 0·94, 1·05 (2 × CH_3); 0·75 d (J = 6·9 Hz) and 0·84 d (J = 7 Hz) ($CH.(CH_3)_2$); 2·09 (CH_3COO); 4·73 bt (ΣJ = 5·5 Hz, 1β-H). For $C_{32}H_{54}O_2$ (470·8) calculated: 81·64% C, 11·56% H; found: 81·38% C, 11·40% H.

1β-Lupanol (*IIb*)

Hydrogenation of 2-lupen-1-one (250 mg) was carried out according to lit.[9] in a mixture of acetic acid and dioxane 1 : 1 (120 ml) in the presence of platinum dioxide (200 mg). After chromatography on alumina (30 g; elution with a mixture of benzene and light petroleum, and benzene–ether) 140 mg of derivative *IIb*, were obtained, m.p. 227–229°C (chloroform–methanol), $[\alpha]_D$ −27°. Lit.[9] gives m.p. 222–223°C, $[\alpha]_D$ −29·5°.

Acetyl derivative XVb had m.p. 177–178°C (ether–cyclohexane–methanol), $[\alpha]_D$ −20°. Ref.[9] gives m.p. 170°C, $[\alpha]_D$ −20°. IR spectrum: 1720, 1262, 1030 (CH_3COO) cm^{-1}. ^{1}H-NMR spectrum: 0·75, 0·82, 0·85, 0·92, 1·02, 1·04 (6 × CH_3); 0·75 d (J = 6·9 Hz) and 0·83 d (J = 6·8 Hz) ($CH(CH_3)_2$); 2·00 (CH_3COO); 4·54 bt (ΣJ = 15 Hz, 1α-H).

3α-Lupanol (*Vb*)

A mixture of 2α,3α-epoxylupane (*XVIb*, 150 mg; prepared according to ref.[9]), lithium aluminum hydride (75 mg) and ether (30 ml) was refluxed for 5 hours, then poured into ethyl acetate, washed with diluted hydrochloric acid and water and dried over sodium sulfate. The solvents were distilled off and the residue chromatographed on a thin layer of silica gel (elution with benzene–light petroleum 1 : 1). Derivative *Vb* (100 mg) was obtained, m.p. 141–143°C and, after solidification, 173–176°C (ether–acetonitrile). M.p. depends on the heating rate: when heating is slow the change of modification takes place without an observable melting and the sample melts then at 174–176°C. $[\alpha]_D$ −25°. Lit.[10] gives m.p. 160·5–163°C, $[\alpha]_D$ −4·3°. For $C_{30}H_{52}O$ (428·7) calculated: 84·04% C, 12·23% H; found: 83·90% C, 12·01% H.

Acetyl derivative XVIIb had m.p. 146–149°C (ethyl acetate–methanol), $[\alpha]_D$ −46·5°. Lit.[9] gives m.p. 145–147°C, $[\alpha]_D$ −48·6° and −46·5°. IR spectrum: 1721, 1263, 1040 (CH_3COO) cm^{-1}. ^{1}H-NMR spectrum: 0·76, 0·84 (2 × CH_3); 0·88 (2 × CH_3); 0·99, 1·05 (2 × CH_3); 0·76 d (J = 6·9 Hz) and 0·84 d (J = 7 Hz) ($CH(CH_3)_2$); 2·07 (CH_3COO), 4·62 t (ΣJ = 5·5 Hz; 3β-H).

3β-Lupanol (*VIb*)

Hydrogenation of lupeol in acetic acid in the presence of platinum dioxide (according to ref.[12]) gave derivative *VIb*, m.p. 190–191°C, and after solidification, 206–207°C (chloroform–ethanol), $[\alpha]_D$ −15°. Lit.[12,13] gives m.p. 201–202°C, $[\alpha]_D$ −18°.

Kinetic Measurements

Approximately 0·5 mg of hydroxy derivative were weighed in a quartz cell of 1 cm thickness and dissolved in 0·5 ml of 99·67% acetic acid containing N-methylmorpholine (3 μl/ml). After

heating of the cell in the aluminum block of the cell space of the Unicam SP-700 spectrophotometer at 25°C the solution was additioned under stirring with 2 ml of equally temperated chromium trioxide solution in 99·67% acetic acid containing about 0·3 mg of CrO_3. The time dependence of the absorbance of chromium trioxide at 28330 cm^{-1} was recorded. The second order rate constants (k) were calculated using the equation

$$k = \frac{2{\cdot}303}{t(a-b)} \cdot \log \frac{b(a-x)}{a(b-x)},$$

where t is time, a absorbance at the beginning of the reaction, b decrease in absorbance after the end of the reaction, x decrease in absorbance at time t. During the oxidation of the hydroxyl group a certain consumption of the oxidizing reagent takes place under the effect of side reactions (oxidation of the substance under investigation apart from its hydroxy group, oxidation of the solvent mixture). From the control experiments with analogous ketones under the same conditions it followed that the rate of side reactions attains maximally 10% of the oxidation rate of the most difficulty oxidized hydroxyl group in the series of the substances investigated. The time dependence of the decrease in absorbance of chromium trioxide caused by parasitic oxidations was substituted by a linear dependence, from which the corrections for the values b and x were obtained. The rate constants given in Table I are average values obtained from at least three measurements. Reproducibility of the results was ±5%.

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