21,22-DISUBSTITUTED 18α,19βH-URSANE DERIVATIVES WITH OXABICYCLOOCTANE SYSTEM IN RING E*

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Dedicated to Professor Václav Horák on the occasion of his 70th birthday.

Reaction of 3β-acetoxy-21,22-dioxo-18α,19βH-ursan-28,20β-olide (*IIIa*) and 20β,28-epoxy-21,22-dioxo-18α,19βH-ursan-3β-yl acetate (*IIIb*) with diazomethane afforded derivatives *XII – XIV* with spiroepoxide group in position 21 or 22, which were further converted into hydroxy derivatives *XV* and *XVII*. Ethylene ketals *VIII – X* were also prepared. In connection with the determination of position and configuration of the functional groups at C(21) and C(22), the ^{1}H and ^{13}C NMR spectral data of the prepared compounds are discussed. Complete analysis of two four-spin systems in the ^{1}H NMR spectrum of bisethylenedioxy derivative *Xb* led to the proton–proton coupling constants from which the structure with two 1,4-dioxane rings condensed with ring E, and their conformation, was derived.

As reported in our previous paper[1], the triterpenoid 21,22-diketone *IIIa*, derived from 3β-acetoxy-18α,19βH-ursan-28,20β-olide (*Ia*), is easily transformed (e.g. during chromatography) into products of dimeric character which complicate its purification and further use in the preparation of 21,22-seco acids. During attempts to determine their structure we observed[2,3] an anomalous course of several reactions with these dimeric compounds as well as with the starting diketone *IIIa* and its analogue *IIIb* derived from 20β,28-epoxy-18α,19βH-ursan-3β-yl acetate (*Ib*). The dimeric compounds contain[3] a diol system, a keto group and a 1,3-dioxolane ring in positions 21 and 22. The elucidation of their structure is based on the course of reaction of the keto groups with diazomethane, on their reduction with sodium borohydride and particularly on the comparison of their ^{1}H and ^{13}C NMR spectra with those of monomeric model

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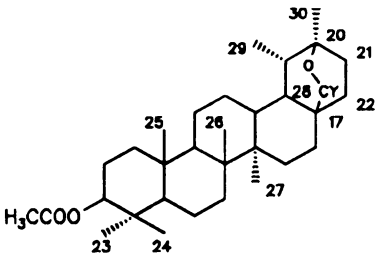
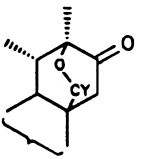
compounds[3]. This paper concerns the preparation of these monomeric models, further the reaction of 21,22-diketones *IIIa* and *IIIb* with diazomethane and summarizes the ^1H and ^{13}C NMR data of the prepared compounds. Most of the reactions were carried out concurrently in two series: with compounds containing a lactone bridge (series *a*, 28,20β-olides) and with compounds having an ether bridge in the ring E (series *b*, 20β,28-epoxy compounds). The spectral study also includes 21α-hydroxy and acetoxy derivatives *IV* and *V* whose preparation was already published[4].

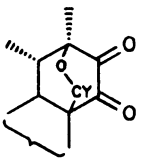
Reduction of diketone *IIIa* with sodium borohydride afforded 21α,22α-dihydroxy derivative *VIa* as the sole product which was then converted into acetate *VIIa*. The ethylenedioxy derivatives were prepared by prolonged heating of the appropriate keto-



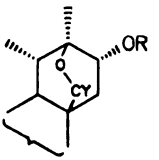
Ia, Ib



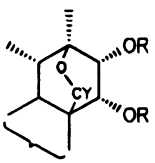
IIa, IIb



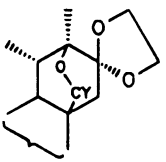
IIIa, IIIb



IVa, IVb, R = H
Va, Vb, R = CH_3CO



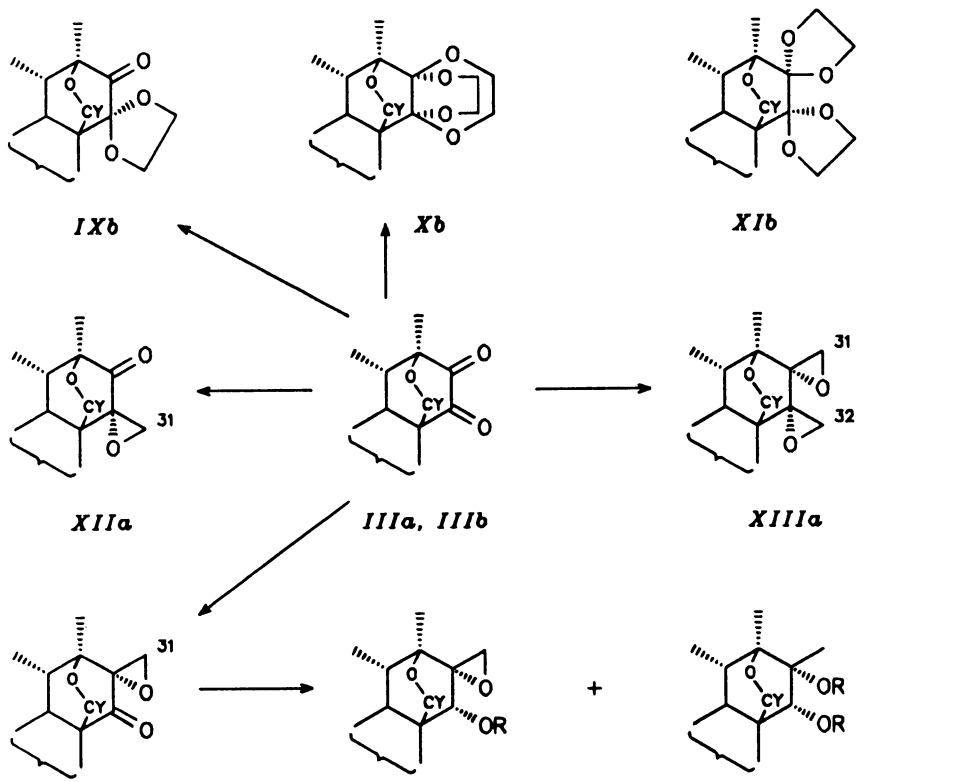
VIa, R = H
VIIa, R = CH_3CO



VIIIa, VIIIb

In formulae *I* – *VIII*: *a*, Y = O; *b*, Y = H_2

ne with ethylene glycol in benzene using *p*-toluenesulfonic acid as catalyst. Because the reaction was accompanied by partial deacetylation in position 3β, the obtained product mixtures were reacetylated with acetic anhydride in pyridine. This procedure afforded ethylenedioxy derivative *VIIIb* (63%) from *IIb* (ref.[4]); the yield of ethylenedioxy derivative *VIIIa* from keto lactone *IIa* (ref.[4]) was lower (40%) due to formation of side products which were not identified. With 21,22-diketones *IIIa* and *IIIb* the reaction course was still more complex: in the lactone series *a* complex mixture of products arose from which no defined compounds could be obtained even after various modifications of the reaction conditions. In the ether series *b* the reaction of diketone *IIIb* with ethylene glycol gave a mixture containing bisethylenedioxy derivative *Xb* (32%) as the principal product; as a minor product we isolated 21-oxo-22-ethylenedioxy derivative *IXb* (6%).



Diketone *IIIa* reacted with ethereal diazomethane at room temperature, giving after 24 h the 22-keto epoxide *XIVa* as principal product (73%). As minor products we isolated the isomeric 21-keto epoxide *XIIa* (6%) and the diepoxide *XIIIa* (5%). The diepoxide *XIIIa* was also obtained from the keto epoxides *XIIa* and *XIVa* by prolonged treatment with diazomethane. Reaction of diketone *IIIb* with diazomethane gave keto epoxide *XIVb*. Interestingly enough, ketones *IIa* and *IIb* did not react under the same conditions, although a similar diterpenoidal keto lactone is reported to react with diazomethane[5]. Reduction of the keto epoxide *XIVb* with sodium borohydride afforded 22α-hydroxy derivative *XVb* as the sole product whereas reduction of the keto epoxide *XIVa* under the same conditions gave, in addition to the 22α-hydroxy derivative *XVa*, also the 21α,22α-diol *XVIIa*.

The position and configuration of the functional groups in compounds *VI*, *VII*, *XII* – *XVIII* has been suggested on the basis of the known[2] higher reactivity of a keto group in position 21, assuming that the reagent approaches from the less hindered β-side, and the results were confirmed by spectral measurements (vide infra).

The characteristic parameters of ^{1}H NMR spectra of the prepared compounds are summarized in Tables I – III. In the case of hydroxy derivatives *XVa*, *XVb* and *XVIIa*, Table III also contains data for the corresponding trichloroacetylcarbamoyl (TAC) derivatives *XVIa*, *XVIb* and *XVIIIa* which were prepared by in situ reaction[6,7] with trichloroacetyl isocyanate (TAI). The assignment of the methyl proton signals is based on the reasoning published in ref.[8] for lactone *Ia*, on mutual comparison of the spectra of the above-mentioned compounds in the series *a* and *b*, and on comparison with the spectra of compounds *I* – *III* and other ones whose spectral data are published[2]. Chemical shifts of ^{13}C signals are summarized in Tables IV and V. The assignment of signals to individual carbon atoms follows from the APT (attached proton test[9,10]) spectra and from comparison with data published[2] for similar compounds.

Both the ^{1}H and ^{13}C NMR spectra clearly confirm the presence of the corresponding functional groups in compounds *IV* – *XVIII*. Thus, e.g., all the derivatives that contain the spiroepoxide grouping (*XII* – *XVI*) show in their ^{1}H NMR spectra an AB system of the epoxide methylene group at δ 2.4 – 3.1 with geminal coupling constant J(AB) = 4 – 6.5 Hz. In the ^{13}C NMR spectra the carbon signal of the epoxide CH_2 group is located in the region δ 47 – 50 and the signal of the quaternary carbon atom of this group appears at δ 57 – 60. The $O-CH_2-CH_2-O$ protons in the ethylenedioxy derivatives *VIII* – *X* give rise to a complex multiplet in the region δ 3.7 – 4.5 and signals of carbon atoms in these groupings in *VIII* and *X* appear at δ 56 – 66. In the following text we shall comment only on those cases in which the NMR data lead to confirmation of the position and configuration of the groups in question.

For configurational assignment at C(21) and C(22), e.g. in hydroxy derivatives, one can use with advantage the signal splitting due to the long-range coupling of the E-ring protons whose four bonds form a W-system (see Fig. 1). In the 20β,28-epoxy deriva-

tives of the series *b* the long-range coupling is exhibited by the C(28)H_2 protons (see refs[2,11,12]): H-28(*exo*) which appears upfield (δ 3.1 – 3.8) is coupled with H-18α, whereas H-28(*endo*), shifted downfield (δ 4.0 – 4.5), is coupled with H-22α. Both in the ether series *b* and in the lactone series *a* there is also a long-range splitting of H-21β due to the coupling with H-19β. The range of the long-range coupling constants (^4J) observed in the compounds described in this paper and ref.[2] is given in Fig. 1.

TABLE I
Proton NMR parameters of compounds *IV* – *VIII* (measured in $CDCl_3$ at 200 MHz, unless stated otherwise; for conditions – see Experimental). Chemical shifts (ppm), multiplicities[a] and coupling constants (Hz)

Parameter	*IVa*	*IVb*	*Va*[b]	*Vb*[c]	*VIa*[d,e]	*VIIa*[d,f]	*VIIIa*[g]	*VIIIb*[g]
δ(H-3α)[h]	4.47 m	4.48 m	4.47 m	4.48 m	4.45 m	4.48 m	4.47 m	4.48 m
δ(Ac-3β)	2.043	2.045	2.043	2.041	2.052	2.049	2.040	2.045
δ(H-21β)	3.87 bm	3.85 bddd	4.75 ddd	4.78 ddd	3.72 ddd	4.98 dd	–	–
δ(H-22α)	1.52 dd	[i]	1.42 dd	[i]	–	–	1.78 d	1.53 dd
δ(H-22β)	2.15 dd	2.00 dd	2.30 dd	2.12 dd	3.76 dd	4.96 d	1.95 d	1.70 d
J(21β,19β)	[i]	1.8	2.0	1.9	1.9	1.7	–	–
J(21β,22α)	5.6	5.4	5.5	5.4	–	–	–	–
J(21β,22β)	10.0	9.9	10.1	10.1	8.6	8.6	–	–
J(22α,22β)	13.5	13.3	14.0	13.6	–	–	13.9	13.6
δ(Me-23)[j]	0.847	0.846	0.845	0.841	0.841	0.850	0.842	0.843
δ(Me-24)[j]	0.835	0.839	0.835	0.841	0.841	0.838	0.831	0.839
δ(Me-25)[k]	0.847	0.874	0.854	0.876	0.858	0.856	0.848	0.873
δ(Me-26)	0.927	0.982	0.930	0.983	0.954[j]	0.925[j]	0.924	0.984
δ(Me-27)	0.927	0.925	0.916	0.915	0.933[j]	0.901[j]	0.906	0.908
δ(H-28en)	–	4.07 dd	–	4.09 dd	–	–	–	4.11 dd
δ(H-28ex)	–	3.20 dd	–	3.25 dd	–	–	–	3.31 dd
J(28en, 28ex)	–	8.7	–	8.7	–	–	–	8.7
J(28en, 22α)	–	2.8	–	2.7	–	–	–	2.6
J(28ex, 18α)	–	1.4	–	1.4	–	–		1.5
δ(Me-29)	1.205 d	1.073 d	1.181 d	1.045 d	1.114 d	1.135 d	1.131 d	0.997 d
J(29, 19)	7.3	7.3	7.4	7.3	7.5	7.0	7.2	7.3
δ(Me-30)	1.440	1.202	1.374	1.113	1.476	1.350	1.302	1.080

[a] Singlets, unless stated otherwise; [b] δ(AcO-21α) 2.078; [c] δ(AcO-21α) 2.041; [d] measured at 500 MHz; [e] δ(OH-21α) 3.14 d, *J*(21β,OH-21α) = 6.2; δ(OH-22α) 3.46 d, *J*(22β,OH-22α) = 4.8; δ(H-16α) 2.03 dt, *J* = 13, 13 and 5; δ(H-16β) 1.16 ddd, *J* = 13.4, 4.4 and 2.7; δ(H-15α) 1.81 ddd, *J* = 13.6, 4.8 and 2.7; δ(H-15β) 1.75 ddd, *J* = 13.4, 13.4 and 4.4; [f] δ(Ac-21α) and δ(Ac-22α) 2.052 and 2.146; [g] δ(O-CH_2-CH_2-O) 3.85 – 4.00 m; [h] *J*(3α,2α) + *J*(3α,2β) = 16.0 – 16.5; [i] parameter not found; [j] tentative assignment, signals may be interchanged; [k] broad singlet or doublet with $J \leq 0.5$.

TABLE II

Proton NMR parameters of compounds *IX*, *X*, *XII* – *XIV* (measured in $CDCl_3$ at 200 MHz, unless stated otherwise; for conditions – see Experimental). Chemical shifts (ppm), multiplicities[a] and coupling constants (Hz)

Parameter	*IXb*[b]	*Xb*[b]	*XIIa*	*XIIIa*	*XIVa*	*XIVb*
δ(H-3α)[c]	4.48 m	4.49 m	4.47 m	4.47 m	4.47 m	4.48 m
δ(Ac-3β)	2.048	2.047	2.044	2.045	2.042	2.048
δ(Me-23)[d]	0.852	0.845	0.848	0.844	0.853	0.852
δ(Me-24)[d]	0.846	0.839	0.840	0.836	0.841	0.847
δ(Me-25)[e]	0.890	0.878	0.870	0.860	0.871	0.895
δ(Me-26)	1.011	0.976	0.964	0.936	0.965	1.033
δ(Me-27)	0.930	0.917	0.896	0.905	0.904	0.911
δ(H-28en)	4.27 d	4.07 d	–	–	–	4.39 d
δ(H-28ex)	3.78 dd	3.63 dd	–	–	–	3.61 dd
J(28en, 28ex)	9.1	9.2	–	–	–	9.8
J(28ex, 18α)	1.6	1.5	–	–	–	1.4
δ(Me-29)	0.785 d	1.080 d	0.941 d	1.127 d	1.079 d	0.939 d
J(29, 19)	7.0	7.0	7.2	7.0	7.2	7.2
δ(Me-30)	1.125	1.157	1.453	1.257	1.332	1.071
δ(H-31)	–	–	3.09[f]	2.47 d[d]	2.96 d	2.96 d
δ(H-31′)	–	–	3.09[f]	2.90 d[d]	3.00 d	2.90 d
J(31,31′)	–	–	[f,g]	4.6	6.3	6.5
δ(H-32)	–	–	–	2.50 d[d]	–	–
δ(H-32′)	–	–	–	2.93 d[d]	–	–
J(32,32′)	–	–	–	3.9	–	–

[a] Singlets, unless stated otherwise; [b] measured at 500 MHz, for parameters of $O-CH_2-CH_2-O$ see Table VI; [c] $J(3\alpha,2\alpha) + J(3\alpha,2\beta) = 16.0 - 16.6$; [d] tentative assignment, signals may be interchanged; [e] broad singlet or doublet with $J \leq 0.5$; [f] in the mixture of $CDCl_3 + C_6D_6$ (1 : 2): δ(H-31) 2.51 d, δ(H-31′) 2.66 d, *J*(31,31′) = 5.8; [g] undeterminable value.

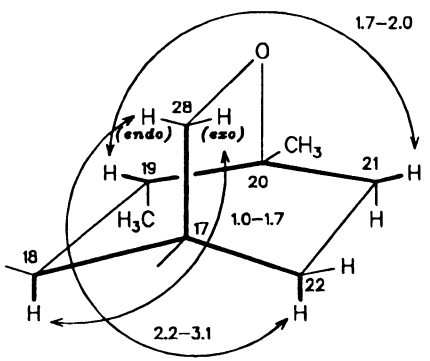


FIG. 1

Long-range coupling constants (^4J, in Hz) of the ring E protons in 20β,28-epoxy compounds (series *b*)

The value of $^4J(21\beta,19\beta)$ (about 1.8 Hz) in the spectra of diol *VIa* and diacetate *VIIa* confirms β-configuration of the proton and thus α-configuration of the hydroxy and acetoxy groups on C(21). The high vicinal coupling constant $J(21\beta,22\beta)$ (8.6 Hz) shows *cis*-configuration of both the oxygen functionalities in positions 21 and 22. Spectrum of the diol *VIa* exhibits coupling of H-21β and H-22β with the corresponding protons of the OH groups. The assignment was confirmed by two-dimensional H,H-COSY spectrum of *VIa* which further enabled us to identify signals of all the four protons in positions 15 and 16 (see note *e* in Table I). In accord with the presence of the 22α-OH group (and 1,3-*syn*-axial interaction with it), the signal of the axial H-16α proton is shifted downfield (δ 2.03) compared with protons of other methylene groups (δ 1.0 – 1.8). In the ^{13}C NMR spectra the effect of the 21α-OH and OAc groups in derivatives *VIa* and *VIIa* manifests itself by an upfield shift of the C(16) and C(18)

TABLE III
Proton NMR parameters of compounds *XV* – *XVIII* (measured in $CDCl_3$ at 200 MHz). Chemical shifts (ppm), multiplicities[a] and coupling constants (Hz)

Parameter	*XVa*[b]	*XVb*[c]	*XVIa*[d]	*XVIb*[e]	*XVIIa*[f]	*XVIIIa*[g]
δ(H-3α)[h]	4.47 m	4.48 m	4.47 m	4.48 m	4.45 m	4.45 m
δ(Ac-3β)	2.043	2.044	2.046	2.047	2.048	2.040
δ(H-22β)	3.62 d	3.50	4.93	4.83	3.69 bd	5.18
δ(Me-23)[i]	0.850	0.849	0.848	0.848	0.841	0.835
δ(Me-24)[i]	0.838	0.844	0.839	0.848	0.841	0.835
δ(Me-25)[j]	0.862	0.885	0.867	0.890	0.859	0.853
δ(Me-26)	0.946	1.003	0.949	1.016	0.936[i]	0.926[i]
δ(Me-27)	0.954	0.960	0.989	0.983	0.943[i]	0.835[i]
δ(H-28en)	–	4.22 d	–	4.28 d	–	–
δ(H-28ex)	–	3.25 dd	–	3.39 bd	–	–
J(28en, 28ex)	–	9.4	–	10.0	–	–
J(28ex, 18α)	–	1.4	–	≈1.0	–	–
δ(Me-29)	1.050 d	0.935 d	1.094 d	0.963 d	1.154 d	1.298 d
J(29, 19)	7.1	7.1	7.3	7.1	7.3	7.3
δ(Me-30)	1.197	0.931	1.193	0.926	1.416	1.565
δ(H-31)	2.64 d	2.62 d	2.87 d	2.84 d	1.246[k]	1.749[k]
δ(H-31')	3.09 d	2.99 d	2.91 d	2.80 d	–	–
J(31,31')	4.3	4.5	5.2	5.4	–	–

[a] Singlets, unless stated otherwise; [b] δ(OH-22α) 2.32 d, J(22β, OH-22α) = 2.2; [c] δ(OH-22α) 2.40 bs; [d] δ(NH) 8.35 bs; [e] δ(NH) 8.33 bs; [f] δ(OH-21α) 3.09 s, δ(OH-22α) 3.23 d, J(22β, OH-22α) = 5.4; [g] δ(NH) 8.27 s and 8.54 s; [h] $J(3\alpha,2\alpha) + J(3\alpha, 2\beta) = 16.0 - 16.2$; [i] signals may be interchanged; [j] broad singlet or doublet with $J \leq 0.5$; [k] Me-31.

TABLE IV
Carbon-13 chemical shifts of compounds *IV* – *VIII* (measured in $CDCl_3$ at 50.31 MHz, unless stated otherwise; for conditions – see Experimental)

Carbon	*IVa*	*IVb*	*Va*	*Vb*	*VIa*[a]	*VIIa*	*VIIIa*[b]	*VIIIb*[c]
1	38.47	38.47	38.45	38.50	38.48	38.52	38.46	38.48
2	23.65	23.66	23.61	23.66	23.59	23.64	23.63	23.65
3	80.93	80.90	80.84	80.87	81.46	80.86	80.87	80.87
4	37.77	37.77	37.73	37.78	37.74	37.79	37.75	37.77
5	55.46	55.44	55.43	55.48	55.50	55.49	55.44	55.45
6	18.09	18.10	18.05	18.09	18.08	18.06	18.08	18.10
7	33.84	33.83	33.81	33.84	33.84	33.86	33.83	33.83
8	40.54	40.69	40.52	40.71	40.46	40.50	40.54	40.70
9	50.41	50.54	50.34	50.55	50.41	50.44	50.37	50.55
10	37.05	37.06	37.02	37.08	37.06	37.07	37.02	37.05
11	20.94	21.22	20.88	21.22	20.96	20.92	20.93	21.19
12	25.05	25.42	25.14	25.55	25.33	25.25	25.32	25.52
13	42.74	39.65	42.72	39.70	42.04	41.94	42.68	39.44
14	41.08	41.35	41.02	41.33	41.02	40.93	41.08	41.37
15	26.99	26.65	26.85	26.59	26.68	26.41	26.91	26.48
16	27.32	29.48	27.14	29.30	23.81	23.40	27.29	29.26
17	41.77	32.95	41.57	32.73	47.92	46.46	42.77	33.43
18	48.56	47.01	48.23	46.85	37.54	38.82	47.85	46.77
19	41.73	42.02	41.87	42.18	40.85	40.85	42.12	42.25
20	84.11	73.37	82.91	72.20	83.92	82.57	85.90	75.43
21	72.11	73.42	72.51	74.50	70.30[d]	69.29[d]	108.24	108.99
22	41.86	45.93	39.88	43.91	67.35[d]	67.97[d]	47.68	50.76
23	27.92	27.90	27.89	27.91	27.88	27.91	27.90	27.89
24[d]	16.47	16.48	16.44	16.46	16.46	16.45	16.45	16.46
25[d]	16.33	16.40	16.30	16.40	16.36	16.38	16.32	16.39
26	15.69	15.76	15.65	15.76	15.67	15.64	15.68	15.77
27	14.17	14.23	14.09	14.20	14.22	13.89	14.10	14.17
28	176.42	67.84	175.49	67.97	175.28	172.66	175.42	67.32
29[e]	18.64	20.19	18.41	19.79	17.71	17.34	18.31	19.76
30[e]	21.10	21.54	20.92[d]	21.63[d]	21.38	20.82[e]	16.70	17.32
OAc-3β:								
CH_3	21.32	21.31	21.27	21.29	21.31	21.31	21.28	21.29
CO	171.08	171.03	170.97	170.97	171.68	171.05	170.98	170.96
OAc-21,22:								
CH_3	–	–	21.13[d]	21.22[d]	–	20.45[e]	–	–
CO	–	–	169.66	170.12	–	168.72	–	–
CH_3	–	–	–	–	–	20.32[e]	–	–
CO	–	–	–	–	–	169.44	–	–

[a] Measured at 125.7 MHz; [b] $O-CH_2-CH_2-O$: 65.94, 63.93; [c] $O-CH_2-CH_2-O$: 65.50, 63.58; [d,e] signals may be interchanged.

TABLE V

Carbon-13 chemical shifts of compounds *X*, *XIII* – *XV* and *XVII* (measured in $CDCl_3$ at 50.31 MHz, unless stated otherwise; for conditions – see Experimental)

Carbon	*Xb*[a]	*XIIIa*	*XIVa*	*XIVb*	*XVa*	*XVb*	*XVIIa*
1	38.51	38.53	38.44	38.49	38.62	38.50	38.50
2	23.67	23.70	23.60	23.64	23.74	23.63	23.63[b]
3	80.91	80.88	80.77	80.80	80.98	80.88	81.30
4	37.78	37.84	37.75	37.79	37.87	37.78	37.76
5	55.47	55.52	55.40	55.43	55.60	55.45	55.50
6	18.10	18.14	18.04	18.08	18.20	18.12	18.12
7	34.05	33.85	33.82	33.84	34.03	33.91	33.93
8	40.59	40.55	40.58	40.75	40.65	40.66	40.50
9	50.44	50.47	50.24	50.47	50.57	50.58	50.38
10	37.05	37.14	37.05	37.10	37.19	37.09	37.07
11	21.39	20.98	20.91	21.23	21.10	21.32	21.01
12	26.11	25.13	25.55	25.71	25.71	26.08	25.85
13	39.87	42.57	42.84	39.08	42.45	39.57	42.59
14	40.90	40.93	40.88	41.10	41.12	41.23	41.00
15	26.89	26.35	25.69	25.66	26.78	26.28	26.70
16	20.04	19.89	18.88	20.58	22.95	24.78	23.66[b]
17	43.13	46.43	57.42	48.64	[e]	37.89	48.44
18	44.09	43.34[b]	46.00	43.32[b]	37.81	36.97	37.36
19	40.59	41.92[b]	43.23	43.18[b]	43.57	43.68	43.34
20	78.40	83.33	83.03	76.07	82.10	72.16	85.25
21	94.11[b]	59.74[c]	60.05	58.60	59.14	60.31	71.73
22	94.36[b]	57.20[c]	201.46	[e]	68.87	72.98	75.10
23	27.89	27.96	27.89	27.92	27.98	27.91	27.91
24[b]	16.49	16.50	16.46	16.50	16.50	16.49	16.48
25[b]	16.49	16.37	16.33	16.50	16.40	16.49	16.39
26	15.76	15.69	15.62	15.79	15.78	15.77	15.75
27	13.97	14.10	14.02	14.14	14.04	14.07	14.12
28	64.97	173.29	169.07	64.26	174.08	67.27	175.11
29[c]	19.78	17.48	17.34	18.82	17.39	18.93	18.72
30[c]	18.10	17.83	17.05	17.92	17.93	18.62	18.80
31	–	48.37[d]	49.04	47.65	49.75	49.51	26.35
32	–	47.41[d]	–	–	–	–	–
OAc-3β:							
CH_3	21.29	21.27	21.26	21.31	21.22	21.32	21.37
CO	170.96	170.91	170.94	170.97	170.87	170.96	171.45

[a] 2 × O-CH_2-CH_2-O: 63.86, 62.22, 57.88, 56.12; [b,c,d] signals may be interchanged; [e] signal not found.

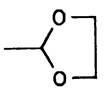
signals (Δδ about −4 and −10, respectively) and a downfield shift of the C(17) signal (Δδ about +5) as compared with the alcohol *IVa* and acetate *Va*.

The structure with free keto group in position 21 for the ketal *IXb* is based on the significant upfield shift (δ 0.785) of the 29-methyl group doublet in the ^{1}H NMR spectrum. A similar shift has also been found in the 21-ketone *IIb* (δ 0.77) and in further compounds of the series *b* with an oxo group or an exocyclic double bond in position 21 (see ref.[2]). This is obviously due to a magnetic anisotropy of the C=O and C=C bonds: as seen from molecular models, the 29-methyl protons are in a shielding cone of these double bonds. In case of the isomeric structure with the ethylenedioxy group in position 21 one would expect the value of δ to be about 1.0 (see the value for the ketal *VIIIb* in Table I).

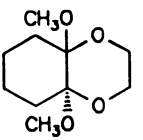
For the bisethylenedioxy derivative, prepared from the diketone *IIIb*, the following two structures were possible: *Xb* with two 1,4-dioxane rings and *XIb* with two 1,3-dioxolane rings. We decided between these two structures on the basis of geminal, and also vicinal, coupling constants of protons in the $O-CH_2-CH_2-O$ bridges. These 8 protons form two ABCD systems that overlap in the region δ 3.75 – 4.30 and form a complex multiplet containing moreover also a doublet of the H-28(*endo*) proton. In the 200 MHz ^{1}H NMR spectrum these two ABCD systems could not be identified and analyzed; however, a two-dimensional H,H-COSY 500 MHz spectrum enabled identification of signals in each of the two ABCD systems and an approximate assessment of their chemical shifts. Even the 500 MHz spectrum could not be analyzed as a spectrum of the first order; however, a simulation-iterative procedure successfully led to final values of parameters δ and *J* which are summarized in Table VI (the individual ABCD systems are denoted as the 1st and 2nd system). A comparison of the observed and calculated spectra (after addition of the H-28(*endo*) doublet) is demonstrated in Fig. 2. The correctness of analysis of these two four-spin systems is confirmed by the fact that using the parameters δ and *J*, obtained from the 500 MHz spectrum, in simulation of the 200 MHz spectrum led to a complete agreement with the observed 200 MHz spectrum in this region. For comparison, Table VI shows values of δ and *J*, obtained by complete analysis of the ABCD system of the ethylenedioxy protons in the 500 MHz spectrum of derivative *IXb*, which contains a five-membered ketal ring, and also coupling constants available in the literature for simple model compounds such as 2-methyl-1,3-dioxolane[13] (*XIX*), bicyclic diketal *XX* with a 1,4-dioxane ring[14] and *trans*- and *cis*-bicyclic derivatives *XXI* and *XXII* (ref.[15]).

In the case of compounds *IXb* and *Xb* it is not possible to ascribe the δ-values to individual protons in the ethylenic bridges and, moreover, for the compound *Xb* one cannot decide which of the ABCD systems belongs to the 21α,22α- and which to the 21β,22β-ethylenedioxy group. However, on the basis of vicinal coupling constants and their comparison with those of the model compounds *XIX* – *XXII* these constants could be ascribed to the pairs of *cis*- and *trans*-hydrogen atoms (see Table VI). The values of

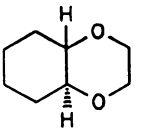
geminal coupling constants in derivative *IXb* (^2J about −7.5 Hz) correspond to a five-membered ring[13,15] and agree with those found for 2-methyl-1,3-dioxolane (*XIX*). Also the vicinal coupling constants (^3J) in both compounds are very similar. On the other hand, the values of ^2J in both ABCD systems of the bisethylenedioxy derivative *Xb* (about −11.5 Hz) exclude the presence of five-membered ketal rings and indicate the presence of 1,4-dioxane rings in this derivative. Similar values of ^2J (−11 to −12.5 Hz) were found in compounds *XX* – *XXII* and other 1,4-dioxane derivatives[15]. It is worth notice that in the ^{13}C NMR spectrum of derivative *Xb* the signals of both quaternary bridgehead atoms (C(21) and C(22)) appear at δ about 94 whereas in compounds *VIIIa* and *VIIIb* (with five-membered ketal ring) at δ 108 – 109. Also quaternary-type carbon atoms with two C–O bonds in similar compounds containing a five-membered ring annelated to the ring E exhibit signals in the region δ 104 – 109 (ref.[2]).



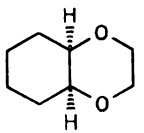
XIX



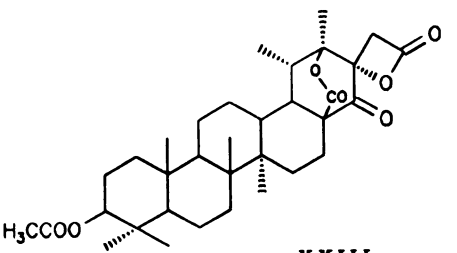
XX



XXI



XXII



XXIII

The bisethylenedioxy derivative *Xb* is interesting also from the viewpoint of conformation of both the dioxane rings. The values of ^3J(*cis*) (about 3.2 Hz) in the 1st ABCD system agree with the analogous constants in the model compounds *XX* – *XXII* and correspond to a chair conformation of this ring (a half-chair form or a conformation between these extrema can also be considered). However, one of the ^3J(*trans*) constants is somewhat higher (3.7 Hz) whereas the other one is lower (9.4 Hz) than the values found for the models *XX* and *XXI* which have the chair form fixed by *trans*-annelation of the rings. These differences may be explained by a rapid interconversion of two unequally populated chair (or half-chair) conformations. The population of these conformations can be estimated taking as standards the ^3J(*trans*) values of the diketal *XX* which seems to be the closest model: for the coupling constant of diequatorial

protons we took the value 0.8 Hz and for that of diaxial protons 12.4 Hz. Both the $^3J(trans)$ values in the 1st spin system of derivative *Xb* (3.7 and 9.4 Hz) lead to the same result: 25% of one and 75% of the other chair form. The high values of all four ^3J constants in the 2nd spin system of *Xb* (6.4 – 8.3 Hz) are compatible with neither a chair nor a half-chair conformation and indicate that the second dioxane ring exists predominantly in one of the possible boat forms.

Although the spiroepoxide derivatives *XIV* – *XVI*, which had been prepared in both series *a* and *b*, were not chemically intercorrelated, their structural similarity follows from comparison of the ^1H and ^{13}C NMR spectra. The corresponding derivatives exhibit very similar spectral characteristics and also chemical shift differences between both series agree with differences found for other compounds of series *a* and *b* listed in Tables I – V and in the literature[2]. In accord with the presence of 21-keto group, the doublet due to 29-methyl group in the ^1H NMR spectrum of keto epoxide *XIIa* is shifted upfield (δ 0.94) compared with the 22-keto isomer *XIVa* (δ 1.08). In the spectrum of keto epoxide *XIVb* this doublet appears at δ 0.94 whereas for the isomeric

TABLE VI

Calculated proton NMR parameters of ABCD systems of $O-CH_2-CH_2-O$ fragments in compounds *IXb*, *Xb* (coupling constant values in model compounds *XIX* – *XXII* taken from literature are given for comparison)

Parameter	*IXb*[a]	*Xb*[a]		*XIX*[b]	*XX*[c]	*XXI*[d]	*XXII*[d]
		1st system	2nd system				
		Chemical shifts (ppm)					
δ(A)	4.040	3.920	4.034				
δ(B)	4.079	4.182	4.079				
δ(C)	4.300	4.223	3.840				
δ(D)	4.371	3.962	3.978				
		Coupling constants (Hz)					
$J(A,B) = {}^3J(cis)$	6.6	3.2	6.6	7.2	3.8	3.1	3.2
$J(A,C) = {}^2J(gem)$	−7.4	−11.7	−11.0	−7.6	−11.2	−12.3	−12.0
$J(A,D) = {}^3J(trans)$	5.7	3.7	6.4	6.0	0.8	2.1	6.6
$J(B,C) = {}^3J(trans)$	5.9	9.4	6.6	6.0	12.4	11.7	6.6
$J(B,D) = {}^2J(gem)$	−7.3	−11.4	−11.4	−7.6	−11.2	−12.3	−12.0
$J(C,D) = {}^3J(cis)$	7.2	3.3	8.3	7.2	3.8	3.1	3.2

[a] Obtained by full simulation-iteration analysis of four spin systems in 500 MHz spectra; [b] ref.[13]; [c] ref.[14]; [d] ref.[15].

21-keto derivative one would expect a δ value of about 0.78 (vide supra). In the infrared spectrum of compound *XIIa* the ketone stretching vibration band is located at 1 754 cm^{-1} and is partially overlapped by the lactone carbonyl band, whereas in the spectrum of isomer *XIVa* it is overlapped by the acetate carbonyl band at about 1 731 cm^{-1}. Such an increase of the carbonyl frequency is characteristic of just 21-ketones of the series *a* and is caused by a 1,4-dicarbonyl interaction with the lactone carbonyl (see ref.[4]).

The ^{13}C NMR chemical shifts for the keto epoxide *XIVa* are almost identical with those found[2] for the β-lactone *XXIII* which contains 22-ketone group except, naturally, the signals of carbon atoms in the β-lactone and epoxide ring, including the C(21) atom. The structure of lactone *XXIII* was proved by X-ray diffraction analysis[2]. In the ^{13}C NMR spectra, the most characteristic for the presence of a 22-keto group is a downfield shift of the C(17) signal: in the lactone series *a* the values for 22-ketones *IIIa*, *XIVa* and *XXIII* range between δ 57 and 63 whereas for compounds without a 22-keto group they are in the region δ 41 – 49; in the ether series *b* the respective values are δ 46 – 49 (for *IIIb*, *XIVb* and other 22-ketones) and δ 32 – 38 (see Tables IV and V and tables in ref.[2]).

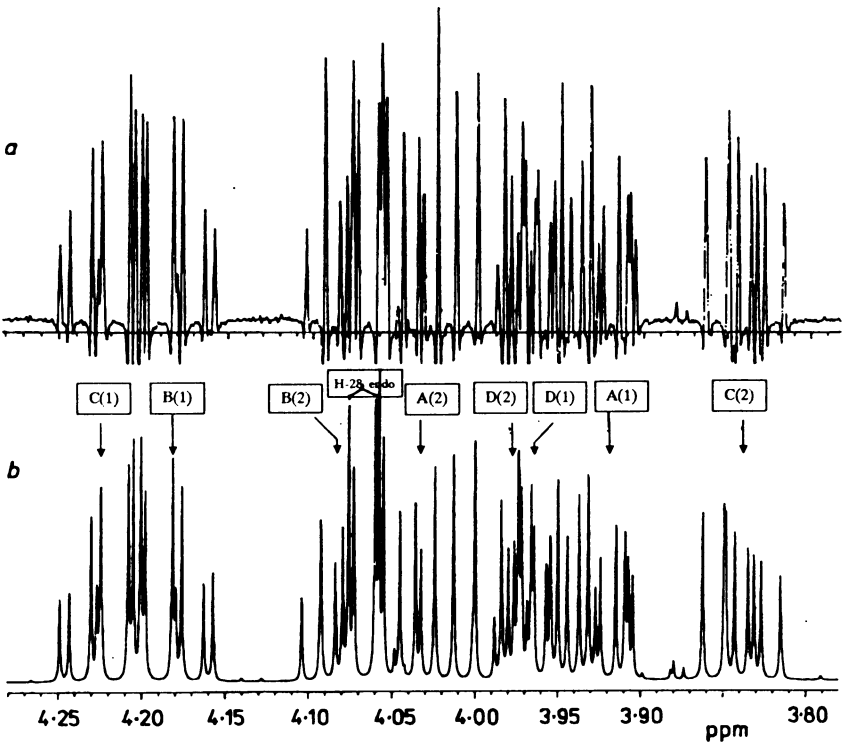


FIG. 2
Part of the ^{1}H NMR spectrum of bisethylenedioxy derivative *Xb* in deuteriochloroform at 500 MHz; *a* observed spectrum, *b* calculated spectrum

Further information on the structure of the epoxy derivatives can be gained from ^{1}H NMR spectra of the hydroxy derivatives *XV* and *XVII* and their TAC derivatives *XVI* and *XVIII*. In accord with the presence of hydroxyl at C(22), the introduction of the TAC-group in derivatives *XVIa* and *XVIb* has only a negligible effect on chemical shift of the Me-29 and Me-30 signals, whereas the presence of 21α-OTAC group in compound *XVIIIa* results in a downfield shift of proton signals of both these methyl groups (Δδ about +0.15). The CH–OR proton in hydroxy derivatives *XVa*, *XVb* and *XVIIa* appears as a singlet or a doublet (caused by vicinal coupling with the OH proton), in the TAC derivatives *XVIa*, *XVIb* and *XVIIIa* as a sharp singlet. The absence of long-range splitting of this signal, and particularly of the H-28(*endo*) signal, in compounds of the series *b* (*XVb*, *XVIb*) confirms that the secondary hydroxyl group is in position 22α (see Fig. 1). In the ^{13}C NMR spectra, the effect of the 22α-OH group manifests itself particularly by an upfield shift of the C(18) γ-carbon atom, which in the spectra of hydroxy derivatives *XVa*, *XVb* and *XVIIa* appears at δ 37 – 38, similarly to diol *VIa*; in compounds without a 22α-OH (or OAc) group this carbon atom resonates at δ 43 – 49. Infrared spectra of hydroxy epoxides *XVa* and *XVb* and diols *VIa* and *XVIIa*, measured in dilute tetrachloromethane solutions, exhibit a strong band of intramolecularly bonded hydroxyl in the region 3 525 – 3 540 cm^{-1} (for more detailed data see ref.[3]) proving thus the *cis*-configuration of the functional groups.

It is obvious from the mentioned spectral data that the attack by hydride at the 21- and 22-keto group and by diazomethane at the 21-keto group takes place from the β-side. The same sterical approach may be assumed also for the reaction of diazomethane with the 22-keto group, therefore in compounds *XIIa* and *XIIIa* the CH_2 group of the epoxide should have the 22β-configuration and the epoxide oxygen atom the 22α-configuration.

In the mass spectra, most of the prepared compounds exhibit molecular ions of low abundance. In some cases, the ions of highest *m/z* already correspond to loss of acetic acid or carbon monoxide from the original molecule. In all cases we observed the ion of *m/z* 189, typical[16] of the rings A and B in 3β-acetoxy derivatives of pentacyclic triterpenes, and also the usual[17] fragments arising by loss of ions *m/z* 60, 15, and 28. In addition, in some compounds there is a significant fission of the C(20)–C(21) and C(17)–C(22) bonds which has already been observed[18] in analogous derivatives. In this way we may explain the formation of ions *m/z* 60 from diol *VIa* and ions *m/z* 74 from diol *XIIa*. Cleavage of the mentioned bonds in both 21-ethylenedioxy derivatives *VIIIa* and *VIIIb* affords relatively abundant (about 20%) ions *m/z* 86 and the corresponding less abundant ions [M – 86]$^{+\bullet}$ (*m/z* 470 and 456, respectively). Similarly, bisethylenedioxy derivative *Xb* gives rise to ions *m/z* 144 and [M – 144]$^{+\bullet}$. The analogous fragmentation of ethylenedioxy ketone *IXb* is accompanied by transfer of hydrogen radical, the charge remaining with the triterpenic moiety (*m/z* 456 and 457).

EXPERIMENTAL

The melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured in chloroform (c 0.3 – 0.9) on an automatic polarimeter ETL-NPL (Bendix–Ericsson), accuracy ±2 °. Infrared spectra were recorded in chloroform on a PE 684 (Perkin–Elmer) spectrometer, wavenumbers are given in cm^{-1}.

NMR spectra were measured on FT–NMR spectrometers Varian XL–200 (^1H at 200 MHz, ^{13}C at 50.31 MHz) and Varian UNITY-500 (^1H at 500 MHz, ^{13}C at 125.7 MHz) in deuteriochloroform. Tetramethylsilane was used as the internal reference for proton chemical shifts. The values of proton chemical shifts (ppm, δ-scale) and interproton coupling constants (in Hz) were obtained by the first order analysis, unless stated otherwise, from the expanded spectra (2 Hz/cm) using the double exponential Lorentz–Gauss function for the resolution enhancement. Homonuclear correlated ^1H–^1H 2D-COSY experiments were run at 500 MHz using pulse sequence RD – P_1 – t_1 – PW – AT with the following parameters: pulses P_1 = PW = 14.4 μs (90°), acquisition time AT = 0.204 s, spectral width 2 506 Hz, 256 evolution time t_1 increments, relaxation delay RD = 1 s, data matrix 1 024 × 1 024 points, sine-bell weighting in both dimensions. The trichloroacetylcarbamoyl derivatives were prepared in NMR tubes by addition of a slight excess of trichloroacetyl isocyanate to a solution of the alcohol in deuteriochloroform[6,7]. Carbon-13 chemical shifts were referenced to the signal of solvent and recalculated to tetramethylsilane using the relation $\delta(CDCl_3) = 77.0$ ppm. The number of directly bonded hydrogen atoms was determined from the proton decoupled "attached proton test" spectra[9,10] (APT).

Mass spectra were measured on an INCOS 50 (Finnigan MAT) spectrometer, energy of ionizing electrons 70 eV, ion source temperature 150 °C, direct inlet, heating rate 10 mA/s.

The reaction course and sample purity were checked by thin-layer chromatography on silica gel G (Merck, detection by spraying with 10% sulfuric acid and heating). Preparative thin-layer chromatography was carried out on the same silica gel (detection by UV light after spraying with 0.2% methanolic solution of morin). Analytical samples were dried at 100 °C over phosphorus pentoxide under diminished pressure. The preparation of compounds *IIa*, *IIb*, *IVa*, *IVb*, *Va* and *Vb* is described in ref.[4], compounds *IIIa* and *IIIb* were prepared according to reference[1].

Reaction of Ketones with Ethylene Glycol

A) Reaction of ketone IIa. A mixture of ketone *IIa* (200 mg, 0.4 mmol), ethylene glycol (1.5 ml), *p*-toluenesulfonic acid (20 mg) and benzene (8 ml) was heated to reflux for 10 h. After cooling, the solution was filtered through a layer of alumina, concentrated and the residue was extracted with ether. The solvent was evaporated and the crude product was acetylated with a mixture of acetic anhydride and pyridine (1 : 1) at room temperature. The mixture was decomposed with water and the product was taken up in ether. The ethereal solution was washed successively with dilute hydrochloric acid, a solution of sodium hydrogen carbonate and with water, and dried over anhydrous sodium sulfate. Preparative thin-layer chromatography on silica gel in benzene–ether (3 : 1) afforded ethylenedioxy derivative *VIIIa* (86 mg, 40%), m.p. 346 – 349 °C (decomp.) (chloroform–methanol), $[\alpha]_D$ +16°. IR spectrum: 1 746, 1 723, 1 256, 1 063, 1 031. Mass spectrum, *m/z* (%): 556 (M^+; 0.3), 496 (3), 481 (2), 470 (0.1), 453 (7), 189 (5), 86 (18), 43 (100). For $C_{34}H_{52}O_6$ (556.8) calculated: 73.35% C, 9.41% H; found: 73.16% C, 9.52% H.

B) Reaction of ketone IIb. A mixture of ketone *IIb* (100 mg, 0.2 mmol), ethylene glycol (1 ml), *p*-toluenesulfonic acid (10 mg) and benzene (5 ml) was heated to reflux for 15 h and then it was processed and acetylated as described under *A*). The residue after evaporation of ether was crystallized from chloroform–methanol and afforded 68 mg (63%) of ethylenedioxy derivative *VIIIb*, m.p. 305 – 309 °C, $[\alpha]_D$ +20°. IR spectrum: 1 720, 1 256, 1 029. Mass spectrum, *m/z* (%): 542 (M^+; 6), 483 (1), 456 (2), 301 (2), 189 (3), 86 (22), 43 (100). For $C_{34}H_{54}O_5$ (542.8) calculated: 75.23% C, 10.03% H; found: 75.57% C, 10.90% H.

C) Reaction od diketone IIIb. A mixture of diketone *IIIb* (100 mg, 0.2 mmol), ethylene glycol (1 ml), *p*-toluenesulfonic acid (10 mg) and benzene (6 ml) was heated to reflux for 7 h and then it was processed and acetylated as described under *A*). Preparative thin-layer chromatography on silica gel in benzene–ether (7 : 3) afforded bisethylenedioxy derivative *Xb* (38 mg, 32%), m.p. 344 – 353 °C (decomp.) (chloroform–ether), $[\alpha]_D$ +4°. IR spectrum: 1 721, 1 256, 1 110. Mass spectrum, *m/z* (%): 600 (M^+; 1.2), 540 (0.4), 510 (4), 485 (2), 456 (0.5), 189 (3), 144 (7), 43 (100). For $C_{36}H_{52}O_7$ (600.8) calculated: 71.97% C, 9.39% H; found: 71.94% C, 9.52% H.

The second product obtained was the ethylenedioxy derivative *IXb* (7 mg, 6%), not melting up to 366 °C (ether), $[\alpha]_D$ +34°. IR spectrum: 1 747, 1 724, 1 257, 1 062, 1 043. Mass spectrum, *m/z* (%): 528 (M^+ – 28; 2), 485 (0.5), 457 (13), 456 (4), 384 (0.6), 189 (4), 43 (100). For $C_{34}H_{52}O_6$ (556.8) calculated: 73.35% C, 9.41% H; found: 73.20% C, 9.54% H.

Reaction of Ketones with Diazomethane

A) Reaction of diketone IIIa. Diketone *IIIa* (140 mg, 0.27 mmol) was dissolved in ethereal solution of diazomethane and allowed to stand at room temperature for 24 h. The crystals which separated were collected on filter and crystallized from chloroform–methanol to give 90 mg (63%) of keto epoxide *XIVa*, m.p. 312 – 314 °C (decomp.), $[\alpha]_D$ +4°. IR spectrum: 1 765, 1 731, 1 254. Mass spectrum, *m/z* (%): 480 (M^+ – 60; 4), 465 (1), 452 (0.5), 437 (4), 189 (6), 43 (100). For $C_{33}H_{48}O_6$ (540.7) calculated: 73.30% C, 8.95% H; found: 73.06% C, 9.01% H.

After evaporation of diazomethane from the first filtrate, the products were separated by chromatography on a thin layer of silica gel in benzene–ether (3 : 1) which afforded another portion of the keto epoxide *XIVa* (14 mg, 10%), and the isomeric keto epoxide *XIIa* (8 mg, 6%), m.p. 302 – 308 °C (ether), $[\alpha]_D$ +10°. IR spectrum: 1 754, 1 766 shoulder, 1 724, 1 255. Mass spectrum, *m/z* (%): 480 (M^+ – 60; 3), 465 (1.5), 437 (3), 189 (7), 43 (100). For $C_{33}H_{48}O_6$ (540.7) calculated: 73.30% C, 8.95% H; found: 73.10% C, 9.07% H.

As further product was obtained diepoxide *XIIIa* (8 mg, 5%), m.p. 287 – 295 °C (ether), $[\alpha]_D$ +15°. IR spectrum: 1 749, 1 720, 1 254. Mass spectrum, *m/z* (%): 494 (M^+ – 60; 3), 479 (1), 451 (4), 189 (5), 43 (100). For $C_{34}H_{50}O_6$ (554.8) calculated: 73.61% C, 9.08% H; found: 73.40% C, 9.26% H.

B) Reaction of diketone IIIb. Diketone *IIIb* (100 mg, 0.2 mmol) was dissolved in ethereal solution of diazomethane and allowed to stand at room temperature for 24 h. After distilling off the diazomethane solution, the residue was subjected to preparative thin-layer chromatography on silica gel in light petroleum–ether (7 : 3) which afforded the principal product *XIVb* (30 mg, 29%), m.p. 296 – 300 °C (decomp.) (chloroform–methanol), $[\alpha]_D$ 0°. IR spectrum: 1 725, 1 256. Mass spectrum, *m/z* (%): 526 (M^+; 2), 466 (2), 451 (1), 423 (1), 384 (1), 189 (7), 43 (100). For $C_{33}H_{50}O_5$ (526.8) calculated: 75.25% C, 9.57% H; found: 75.02% C, 9.64% H.

C) Reaction of keto epoxide XIVa. Keto epoxide *XIVa* (10 mg) was dissolved in chloroform (0.5 ml) and the solution was mixed with an excess of ethereal solution of diazomethane. After standing at room temperature for 4 days, the solvents were evaporated and the product was separated from the starting keto epoxide by thin-layer chromatography on silica gel. According to its IR spectrum, the obtained diepoxide *XIIIa* (2 mg, 20%) was identical with an authentic specimen (vide supra).

D) Reaction of keto epoxide XIIa. Under conditions described in procedure *C*), the keto epoxide *XIIa* was quantitatively converted within 2 days into diepoxide *XIIIa* which was identical with an authentic sample (according to IR spectrum).

Reduction of Keto Derivatives with Sodium Borohydride

A) Reduction of diketone IIIa. Sodium borohydride (100 mg, 2.6 mmol) was added to a suspension of diketone *IIIa* (100 mg, 0.19 mmol) in a mixture of benzene (5 ml) and methanol (5 ml). After stirring for

5 min at room temperature, the reaction mixture was diluted with water and acidified with dilute hydrochloric acid. The product was taken up in ether, the ethereal extract was washed successively with water, a solution of sodium hydrogen carbonate, water, and dried over sodium sulfate. The solvent was evaporated, the residue dissolved in chloroform and filtered through a layer of silica gel. Crystallization from chloroform–methanol afforded 62 mg (62%) of 21α,22α-dihydroxy derivative *VIa*, m.p. 335 – 339 °C, $[\alpha]_D$ +20°. IR spectrum: 3 616, 3 450, 1 730, 1 715. Mass spectrum, *m/z* (%): 470 (M^+ – 60; 4), 427 (4), 411 (0.5), 189 (5), 60 (3), 43 (100). For $C_{32}H_{50}O_6$ (530.8) calculated: 72.42% C, 9.50% H; found: 72.19% C, 9.59% H.

Acetate *VIIa* was prepared from *VIa* by treatment with a 1 : 1 mixture of acetic anhydride and pyridine at room temperature for 24 h; m.p. 310 – 312 °C (chloroform–methanol), $[\alpha]_D$ –15°. IR spectrum: 1 758, 1 724, 1 248. Mass spectrum, *m/z* (%): 544 (M^+; 3), 539 (1), 511 (5), 189 (4), 43 (100). For $C_{36}H_{54}O_8$ (614.8) calculated: 70.33% C, 8.85% H; found: 70.05% C, 8.98% H.

B) Reduction of epoxy ketone XIVa. Sodium borohydride (150 mg, 4.0 mmol) was added portionwise to a solution of epoxy ketone *XIVa* (100 mg, 0.19 mmol) in a mixture of benzene (5 ml) and methanol (5 ml). After standing at room temperature for 1 h, the reaction mixture was worked up as described under *A*) and the products were separated by thin-layer chromatography on silica gel in benzene–ether (4 :1) which afforded hydroxy derivative *XVa* (56 mg, 56%), m.p. 330 – 334 °C (chloroform–heptane), $[\alpha]_D$ +15°. IR spectrum: 3 526, 1 746, 1 721, 1 256. Mass spectrum, *m/z* (%): 482 (M^+ – 60; 4), 467 (1), 439 (5), 189 (5), 43 (100). For $C_{33}H_{50}O_6$ (542.8) calculated: 73.03% C, 9.29% H; found: 73.20% C, 9.18% H.

Rechromatography of the more polar product on a thin layer of silica gel in chloroform–benzene–acetone (4 : 3 : 3) afforded compound *XVIIa* (16.5 mg, 16%), m.p. 342 – 353 °C (decomp.) (chloroform–cyclohexane), $[\alpha]_D$ +27°. IR spectrum: 3 616, 3 530, 1 738, 1 719, 1 255. Mass spectrum, *m/z* (%): 484 (M^+ – 60; 2), 469 (1), 441 (3), 189 (5), 74 (13), 43 (100). For $C_{33}H_{52}O_6$ (544.8) calculated: 72.76% C, 9.62% H; found: 72.53% C, 9.70% H.

C) Reduction of epoxy ketone XIVb. Under conditions described for the reduction of epoxy ketone *XIVa* (see procedure *B*)), the epoxy ketone *XIVb* (70 mg, 0.13 mmol) was converted into compound *XVb* (45 mg, 63%), m.p. 300 – 313 °C (decomp.) (chloroform–cyclohexane), $[\alpha]_D$ +30°. IR spectrum: 3 506, 1 720, 1 255. Mass spectrum, *m/z* (%): 528 (M^+; 1), 468 (3), 453 (1), 425 (1), 264 (2), 189 (14), 43 (100). For $C_{33}H_{52}O_5$ (528.8) calculated: 74.96% C, 9.91% H; found: 75.12% C, 10.04% H.

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