STRUCTURE OF DIMERIC COMPOUNDS OBTAINED FROM 3β-ACETOXY-21,22-DIOXO-18α,19β*H*-URSAN-28,20β-OLIDE*

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The triterpenoid α-diketone with oxabicyclo[2.2.2]octane system in the ring E (3β-acetoxy-21,22-dioxo-18α,19β*H*-ursan-28,20β-olide (*I*)) gives isopropylidenedioxy derivative *II* and dimeric compounds *V* and *IX* when submitted to chromatography on silica gel in the presence of acetone. Compounds *V* and *IX* were reduced with hydride to hydroxy derivatives *VI*, *X*, and *XI*; on reaction with diazomethane they gave dimeric compounds with a spiroepoxide group at the position 21 (compound *VII*) or 22 (compound *XII*) which reacted further with diazomethane to give monomeric spiroepoxides *VIII*, *XIII*, and *XIV*. The structure of the compounds obtained was derived from their ^{1}H and ^{13}C NMR, IR, and FAB mass spectra.

Recently we have observed[1] that substances of dimeric nature are formed during chromatographical purification of 3β-acetoxy-21,22-dioxo-18α,19β*H*-ursan-28,20β-olide (*I*). The determination of structure of these dimeric compounds and of another compound formed from diketone *I* during chromatography on silica gel is dealt with in the present communication.

Diketone *I* was prepared according to ref.[1] by oxidation of 3β-acetoxy-21-oxo-18α,19β*H*-ursan-28,20β-olide with selenium dioxide in a boiling mixture of acetic acid and dioxane. During chromatography of the raw diketone *I* on silica gel with a petroleum ether–acetone mixture as the eluent there took place an exothermic reaction giving a mixture of four compounds which, in contrast to the yellow diketone *I*, were colourless. The most polar of these compounds was formed in a small quantity only, it was unstable and could be neither characterized nor identified. The other three products (*II*, *V*, and *IX*) could be separated by chromatography and identified without difficulties. Their structure was derived mainly on the basis of their ^{1}H and ^{13}C NMR

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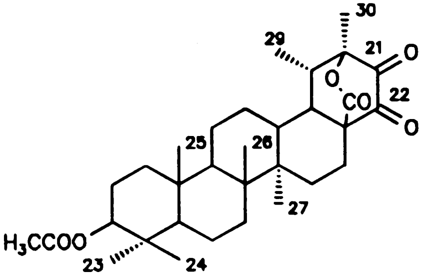
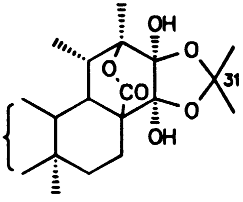
* Part C in the series Triterpenes; Part IC: Collect. Czech. Chem. Commun. 58, 173 (1993).

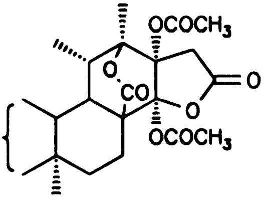
spectra (Tables I – IV), IR spectra in the region of O–H stretching frequencies (Table V), and comparison of the spectral data with those given in refs[2,3] for the starting diketone *I* and for model compounds. For comparison, Table V also presents data for the model compounds *XV* – *XXI* described elsewhere[3,4].



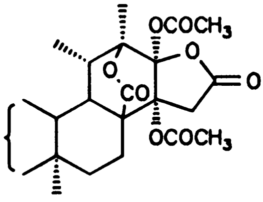
I



II



III



IV

According to the fast atom bombardment mass spectrum (FAB-MS), compound *II* is monomeric, its molecular weight (602) indicating an addition of acetone and water to diketone *I*. In the electron impact mass spectrum (EI-MS) no molecular ion was found, but instead, an ion with *m/z* 542 $[M - CH_3COOH]^{+\bullet}$ and another ion with *m/z* 466 corresponding to elimination of acetic acid, acetone, and water molecules from the molecule *II*. The ^1H NMR spectrum (Table I) – in contrast to that of the starting diketone *I* (ref.[2]) – exhibits two additional singlets of methyl protons of isopropylidenedioxy group in the region of δ 1.3 – 1.6 and two singlets of OH groups whose chemical shifts depend on both temperature and concentration. The ^{13}C NMR spectrum (Table III) exhibits three signals of quaternary carbon atoms of O–C–O type at δ 102.0, 102.2, and 111.1. The IR spectral region of O–H stretching frequencies (measured in dilute tetrachloromethane solution; Table V) has a similar shape like that of the model 21α,22α-diols *XX* and *XXI*. The band of the bonded hydroxyl in compound *II* appears at 3 530 cm^{-1}, which is similar to the cis-diols *XX* and *XXI* and epoxy alcohols *XVIII* and *XIX*. All these facts agree with the structure of the isopropylidenedioxy derivative *II*.

We suggest the structure *II* with β-oriented 1,3-dioxolane ring and α-hydroxyl groups at the positions 21 and 22 on the basis of molecular models; the other possible isomer with 21α,22α-isopropylidenedioxy group is very unlikely because one of the methyl groups at the dioxolane ring would be placed very close to 19α-methyl group and 18α-hydrogen atom. In structure *II*, both methyl groups at the dioxolane ring are oriented out of the molecule and exhibit no nonbonding interactions. In accordance with the structure suggested, the IR spectrum of compound *II* does not contain any band which would be ascribable to intramolecular hydrogen bond of 21-OH group and the ether oxygen atom of the lactone bridge. Such a band (3 589 cm^{-1}, Table V) can be seen in the spectrum of the model compound *XVII* with β-hydroxyl group at C-21 but it is absent from the spectra of 21α-hydroxy derivatives *XV* and *XVI*.

TABLE I
Proton chemical shifts (δ, ppm) and interproton coupling constants (Hz) of compounds *II*, *V* – *VII*. Measured in $CDCl_3$ at 500 MHz; singlets, unless stated otherwise

Parameter	*II*[a]	*V*		*VI*		*VII*[b]	
δ(H-3α)[c]	4.473 m	4.464 m	4.467 m	4.443 m	4.466 m	4.46 m	4.47 m
δ(AcO-3β)	2.050	2.041	2.047	2.049	2.052	2.042	2.046
δ(H-21β)	–	–	–	3.802 dd	–	–	–
J(21β,19β)	–	–	–	1.5	–	–	–
δ(OH-21)	3.85[d]	–	3.79[d]	4.50 d	4.62[d]	–	4.06[d]
δ(OH-22)	4.10[d]	–	4.86[d]	–	5.93[d]	–	5.34[d]
J(21,OH-21)	–	–	–	5.6	–	–	–
δ(Me-23)[e]	0.846	0.843	0.848	0.837	0.849	0.842	0.842
δ(Me-24)[e]	0.838	0.829	0.834	0.831	0.837	0.827	0.832
δ(Me-25)	0.858	0.851	0.858	0.851	0.856	0.842	0.858
δ(Me-26)[f]	0.930	0.882	0.896	0.874	0.898	0.888	0.892
δ(Me-27)[f]	0.937	0.911	0.915	0.904	0.913	0.906	0.936
δ(Me-29)	1.126 d	0.880 d	1.130 d	1.103 d	1.117 d	1.045 d	1.055 d
J(29,19)	7.2	7.1	7.1	7.0	7.0	7.3	7.1
δ(Me-30)	1.555	1.407	1.510	1.436	1.533	1.208	1.519

[a] δ($(CH_3)_2C(O-)_2$): 1.462 and 1.348; δ(H-16α): 2.017 bdt, *J* = 13.4, 13.4 and 4.5; δ(H-16β): 2.091 ddd, *J* = 13.4, 4.5, 2.5. [b] δ(H-31a): 2.974 d, δ(H-31b): 3.758 d, *J*(31a,31b) = 4.6. [c] *J*(3α,2α) + *J*(3α,2β) = 16.2 – 16.5. [d, e, f] The signals with the same symbols may be interchanged.

Next two products (*V* and *IX*) obtained from the chromatography of diketone *I* contain (according to the NMR spectra) two nonidentical triterpenoid parts, and their molecular weight obtained from FAB-MS corresponds to the sum of the molecular weights of two molecules of diketone *I* and one water molecule. The ^{1}H NMR spectra show two singlets of hydroxyl proton, the ^{13}C NMR spectra indicate the presence of two acetate, two lactone, and one ketone carbonyls beside three quaternary carbon atoms of O–C–O type at δ 100 – 106. In this region currently found are the signals of carbon atoms of this substitution type in compounds containing a five-membered ketal or hemi-ketal ring attached to the ring E (e.g. compound *II* and others given in refs[2,3]). These facts allow the dimeric compounds to be represented by the formulas *V* and *IX*: two triterpenoid parts are connected in the rings E by two oxygen atoms which are parts of the 1,3-dioxolane ring. One half of the dimeric molecule (denoted as part A) contains the ketonic group and the other (part B) two hydroxyl groups.

Both the dimeric compounds *V* and *IX* decompose on heating above 300 °C to give a yellow melt corresponding – according to TLC – to diketone *I*. Compounds *V* and *IX* could be purified by recrystallization from a chloroform–heptane mixture without

TABLE II

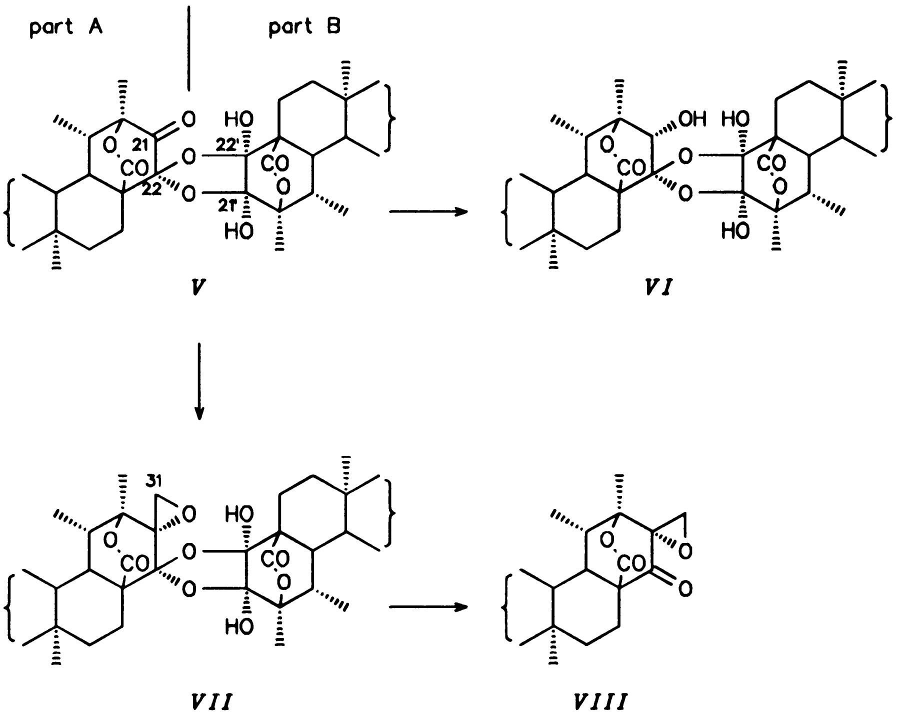
Proton chemical shifts (δ, ppm) and interproton coupling constants (Hz) of compounds *IX* – *XII*. Measured in $CDCl_3$ at 500 MHz; singlets, unless stated otherwise

Parameter	*IX*		X[a]		*XI*[a]		*XII*[b]	
δ(H-3α)[c]	4.463 m	4.474 m	4.46 m	4.46 m	4.46 m	4.46 m	4.47 m	4.47 m
δ(AcO-3β)	2.044	2.044	2.047	2.047	2.045	2.052	2.044	2.044
δ(H-22)	–	–	3.69 d[e]	–	3.83 d	–	–	–
δ(OH-21)	–	3.72[d]	–	5.57[d]	–	4.54[d]	–	4.04[d]
δ(OH-22)	–	4.94[d]	3.62 d[e]	6.33[d]	3.95 bd	6.07[d]	–	5.39[d]
J(22,OH-22)	–	–	2.2	–	3.8	–	–	–
δ(Me-23)[e]	0.846	0.846	[g]		[g]		0.841	0.845
δ(Me-24)[e]	0.832	0.832	[g]		[g]		0.830	0.830
δ(Me-25)	0.854	0.854	[g]		[g]		0.851	0.854
δ(Me-26)[f]	0.868	0.935	[g]		[g]		0.860	0.919
δ(Me-27)[f]	0.929	0.940	[g]		[g]		0.910	0.927
δ(Me-29)	1.083 d	1.120 d	1.022 d	1.136 d	1.081 d	1.102 d	1.208 d	1.122 d
J(29,19)	7.4	7.0	7.3	7.1	7.3	7.3	6.6	7.3
δ(Me-30)	1.412	1.479	1.293	1.502	1.349	1.513	1.425	1.478

[a] The data were obtained from the spectrum of a 2 : 1 mixture of compounds *X* and *XI*. [b] δ(H-31a): 3.08 d, δ(H-31b): 3.61 d, *J*(31a,31b) = 4.4. [c] *J*(3α,2α) + *J*(3α,2β) = 16.3 – 16.7. [d, e, f] The signals with the same symbols may be interchanged. [g] Methyl signals of compounds *X* and *XI* overlap at δ 0.845, 0.848, 0.836, 0.854, 0.908, 0.918, 0.928, 0.932.

decomposition. But the attempt at obtaining crystals suitable for X-ray diffraction failed. Long-term crystallization (several weeks) of compound *V* from the same solvent mixture gave crystals which – according to TLC – represented a ca 1 : 1 : 1 mixture of diketone *I* and both dimeric compounds *V* and *IX*.

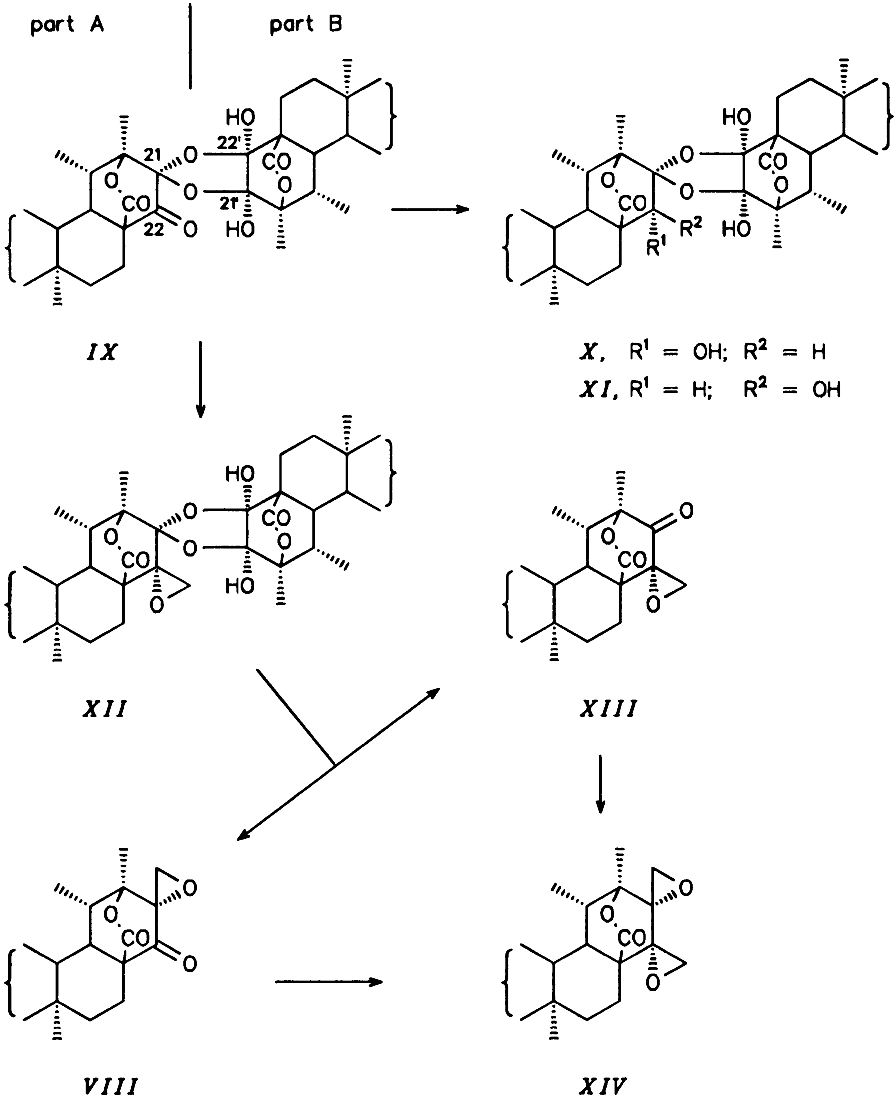
The attempt at acetylation of hydroxyl groups in compounds *V* and *IX* did not bring any information about structure of these dimers: even at very mild conditions (acetanhydride in pyridine at room tempterature) both compounds gave the same (according to TLC) mixture of monomeric products like that formed at the same conditions directly from diketone *I* (see ref.[2]). Two main products – compounds *III* and *IV* containig a γ-lactone ring condensed to the ring E – were separated from the minor products by crystallization and identified by comparison of the ^{1}H and ^{13}C NMR spectra of their mixture with those of pure isomers *III* and *IV* described in ref.[2]. The reduction of the dimeric compound *V* with sodium borohydride (Scheme 1) gave the hydroxy derivative *VI* as the only product, whereas the same reduction of compound *IX* (Scheme 2) gave a mixture of five compounds (according to TLC) in which two compounds of the lowest polarity were highly predominant. Their mixture was separated from the other products chromatographically but the individual components could



SCHEME 1

not be separated in pure state. Therefore they were only identified on the basis of the NMR spectra of the mixture as isomeric hydroxy derivatives *X* and *XI* (vide infra).

The position of ketonic group in compounds *V* and *IX* could be determined on the basis of the reaction with diazomethane which proceeds in two steps. At first, compound *V* gives the dimeric spiroepoxide *VII* which reacts further with excess diazomethane to give a single product – the monomeric compound identical with the spiro-



Scheme 2

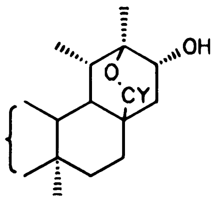
epoxide *VIII* (which was obtained earlier[3] by reaction of diketone *I* with diazomethane). The presence of ketonic group at the position 22 and spiroepoxide group at 21 of epoxide *VIII* was confirmed in the paper[3]. Hence this epoxide is formed by decomposition of the dimeric compound *VII* both directly from part A, which confirms the position of oxo group at C-21 of compound *V*, and from part B by reaction with diazomethane in accordance with the known[2,3] higher reactivity of 21-oxo group in diketone *I*. From compound *IX*, again the dimeric spiroepoxide *XII* is formed in the first step, however, in the subsequent step the reaction is more complex. Monitoring of its course by TLC showed that the dimeric epoxide *XII* gives a mixture of epoxide *VIII* and its isomer *XIII* (which contains[3] the ketonic group at the position 21) on treatment with diazomethane. Compound *XIII* reacts further to give diepoxide *XIV*; prolongation of the reaction time results in gradual removal of epoxide *XIII* from the reaction mixture which finally contains epoxide *VIII* and diepoxide *XIV* in an approximate ratio of 1 : 1 (estimated from TLC). If the reaction was stopped at a suitable moment, it was possible to isolate – beside the dimeric epoxide *XII* – the epoxides *VIII* and *XIII* and diepoxide *XIV* (the ratio of the yield of *VIII* to sum of yields of *XIII* and *XIV* was roughly 1 : 1). The given facts can be interpreted as follows: the 22-oxo group of dimeric compound *IX* reacts with diazomethane to give the dimeric epoxide *XII* which is decomposed, and the part A is converted into epoxide *XIII*. Its 21-oxo group is reactive enough to react further to give diepoxide *XIV*. Part B by the reaction with diazomethane produces epoxide *VIII* which contains the less reactive 22-oxo group: the reaction *VIII* → *XIV* is very slow, which was observed earlier[3]. The configuration of spiroepoxide group in compounds *VII* and *XII* follows from the configurations of the monomeric epoxy derivatives *VIII*, *XIII*, and *XIV* which were derived in paper[3] and agrees with the known fact that reagents preferably attack the less hindered β-side[2,3].

The molecular weights of the dimeric compounds mentioned were confirmed by means of the FAB mass spectra which show the protonated molecular ions $[M + H]^+$ and ions $[M + Na]^+$ (sodium is present as an impurity in the matrix). Moreover, the spectra exhibit the significant ions $[M + H - 60]^+$, which are the most abundant ions in the high-mass region, and the less abundant ions $[M + H - 60 - 16]^+$, $[M + H - 60 - 44]^+$, and $[M + H - 2 \times 60]^+$. In the medium-mass region the important ions are those formed by the decomposition of dimeric molecules into parts A and B connected with a loss of a water molecule. These are the ions $[A + H]^+$ and $[B + H]^+$ and the most abundant ions in this region $[A + H - 60]^+$ and $[B + H - 60]^+$; less abundant are the ions due to the loss of another 44 mass units. With compounds *V* and *IX* these ions correspond to the decomposition to the diketone (from both parts A and B; they also appear in the spectrum of diketone *I*), with the hydroxy derivatives *VI*, *X*, and *XI* they correspond to the decomposition to hydroxy ketone (part A) and diketone (part B), and with the dimeric spiroepoxides *VII* and *XII* they correspond to the decomposition to epoxy ketone (part A; they appear in the spectrum of epoxide *VIII*) and diketone (part B).

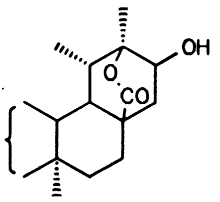
The presence of functional groups in the dimeric compounds *V* – *VII* and *IX* – *XII* follows from the ^{1}H and ^{13}C NMR spectra: the NMR parameters are very similar to those found with the monomeric models having the same functional groups (e.g. *VIII*, *XIII*, *XIV*, *XV*, *XVIII*, *XX* and other similar compounds whose spectral data were published in refs[2,3]). In the ^{13}C NMR spectra (Tables III and IV) the structural assignment of the chemical shifts to individual carbon atoms of the triterpenoid skeleton is based on the APT (attached proton test[5,6]) spectra and on the assignment given for the model substances[2,3]; for the signals of methyl protons in the ^{1}H NMR spectra (Tables I and II) it is based on the same model substances. However, the assignment of most proton and carbon signals to the individual parts A and B was impossible. An exception is formed by the atoms which are immediately connected with the substitution at the positions 21 and 22 (C-21, C-22, H-21, H-22) and in some cases also by the atoms in the closest neighbourhood which are characteristically influenced by the functional groups (C-16, C-17, C-18, C-20 and the protons of the Me-29 and Me-30 groups). These signals can be assigned unambiguously to the part A or B; in Tables I – IV they are given in the left-hand and the right-hand columns for the parts A and B, respectively. For the other signals the assignment to the individual parts is tentative and is based on the comparison with the spectra of the isopropylidenedioxy derivative *II*, which is the nearest model of the part B of all the dimeric compounds. In the case of isomeric hydroxy derivatives *X* and *XI* (Tables II and IV) the data were obtained from the spectra of their mixture (2 : 1). Although some signals of the minor and the major components overlap in the ^{13}C NMR spectrum of this mixture, it was possible (if the signal intensities were taken into account) to find the signals of all the carbon atoms in both the isomers *X* and *XI*. The identification of signals of Me-29 and Me-30 groups in ^{1}H NMR spectra presented no problems either, but the signals of the remaining methyl protons (Me-23 through Me-27) could not be assigned to the individual isomers *X* and *XI* because of their complex overlap (see the footnote *g* in Table II).

The presence of ketonic group at the position 21 in dimeric compound *V* and at 22 in *IX* is confirmed by the following NMR data: the doublet of Me-29 in the ^{1}H NMR spectrum of compound *V* (part A) is shifted upfield (δ 0.88) as compared with the other compounds ($\delta \approx 1.1$). This upfield shift is due to the shielding effect of carbonyl group and was observed[3] with the 21-oxo derivatives; with the isomer *IX* having a 22-oxo group the upfield shift of Me-29 is not observed (δ 1.08). The transformation of 21-ketonic group of compound *V* into the spiroepoxide group of compound *VII* causes an upfield shift of the protons of Me-30 ($\delta(VII) - \delta(V) = -0.199$) similar to that in the monomeric ketone *XIII* ($\delta(XIV) - \delta(XIII) = -0.196$, see ref.[3]). The analogous conversion of 22-ketonic group in *IX* (*IX* → *XII*) does not affect the chemical shift of Me-30. The signal of C-17 is considerably shifted downfield in compound *IX* ($\delta \approx 59$), whereas in the other compounds it appears in the region of δ 46 – 53; according to the conclusions obtained from the model compounds[3], the downfield shift of C-17 is a characteristic feature of the 22-oxo derivatives. The transformation of *IX* into spiroepoxide *XII* causes an upfield shift of C-17 (δ(*XII*) – δ(*IX*) = –12.8) which is the same as that of the model compounds (δ(*XIV*) – δ(*VIII*) = –11). A similar shift (Δδ –10.5) is also observed with both hydroxy derivatives *X* and *XI* after the reduction of ketone *IX*. On the other hand, the transformation of 21-ketone *V* into spiroepoxide *VII* does not affect the chemical shift of C-17, but it causes an upfield shift of C-20 (Δδ –4). The IR spectra also agree with the given position of ketonic group in compounds *V* and *IX*: in the isomer *V* the band of ketonic carbonyl appears about 1 752 cm^{-1}, being overlapped by the bands of lactone carbonyls, in the isomer *IX* it is overlapped by the bands of acetate carbonyls at about 1 720 cm^{-1}. The higher carbonyl frequency is typical of the 21-ketonic group which is in a 1,4-dicarbonyl interaction with lactone carbonyl[3,4].

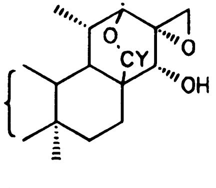
In the ^{1}H NMR spectrum of hydroxy derivative *VI* the proton signal of CH–OH group appears as a doublet of doublets: beside the vicinal coupling with the proton of OH group (^3J = 5.6 Hz) it shows also a long-range coupling (^4J ≈ 1.5 Hz). Out of all possible positions and configurations of this hydrogen atom, only H-21β can exhibit a



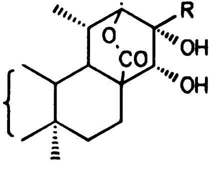
XV, Y = O
XVI, Y = H_2



XVII



XVIII, Y = O
XIX, Y = H_2



XX, R = H
XXI, R = CH_3

TABLE III

Carbon-13 chemical shifts of compounds *II*, *V* – *VII*; measured at 125.7 MHz in $CDCl_3$, for other conditions see Experimental

Carbon	*II*^{a}	*V*		*VI*		*VII*	
1	38.54	38.48	38.48	38.50	38.54	38.44	38.47
2	23.60	23.61	23.61	23.64	23.61	23.63	23.63
3	81.26	80.87	81.01	81.04	81.36	80.92	80.92
4	37.76	37.76	37.76	37.75	37.77	37.74	37.77
5	55.58	55.42	55.45	55.44	55.49	55.41	55.41
6	18.07	18.05	18.05	18.05	18.09	18.10^{b}	18.10
7	33.97	33.73	33.95	33.71	33.96	33.58	33.94
8	40.49	40.45	40.45	40.41	40.48	40.43	40.45
9	50.34	50.21	50.36	50.24	50.37	50.20	50.42
10	37.04	37.03	37.03	37.03	37.03	37.00	37.03
11	21.02	20.93	20.99	20.94	21.00	20.91	20.95
12^{b}	26.08	25.73	25.77	25.81	25.83	25.05	25.91
13	42.63^{b}	42.28	42.77^{b}	42.05^{b}	42.34^{b}	41.64^{c}	42.39^{c}
14	40.93	40.70	40.92	40.75	40.89	40.87	40.99
15^{b}	26.30	25.68	26.30	25.51	26.42	25.62	26.10
16	18.63	18.05	18.39	17.29	18.53	18.07^{b}	18.38
17	53.03	51.80	52.41	50.27	52.02	51.96^{d}	52.28^{d}
18	40.40	43.19	40.63	43.13^{b}	39.97^{b}	41.48^{c}	41.18^{c}
19	42.42^{b}	40.70	42.96^{b}	40.55^{b}	41.61^{b}	41.53^{c}	41.53^{c}
20	83.62	86.64	83.96	84.19	83.71	82.79	83.78
21	102.25^{c}	208.52	103.86^{c}	77.62	102.43^{c}	62.71	103.21^{e}
22	102.00^{c}	104.27^{c}	101.89^{c}	108.98	102.09^{c}	109.47	100.90^{e}
23	27.85	27.93	27.88	27.94	27.92	27.92	27.90
24^{c}	16.47	16.48	16.48	16.49	16.49	16.46	16.48
25^{c}	16.41	16.33	16.44	16.37	16.39	16.34	16.34
26	15.70	15.48	15.53	15.42	15.59	15.47	15.57
27	13.91	13.52	13.81	13.67	13.82	13.75	13.86
28	172.18	169.15	171.16^{d}	171.90	172.63	171.08	171.50
29^{d}	18.32	17.43	17.86	17.50	17.86	17.71	18.22
30^{d}	16.41	16.85	16.37	20.87	16.79	16.91	16.60
31	111.09	–	–	–	–	52.21^{d}	–
AcO:							
C=O	171.49	170.97^{d}	171.07^{d}	171.20	171.61	171.01	171.06
CH_3	21.32	21.30	21.31	21.37	21.34	21.30	21.30

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[a] $(CH_3)_2C(O-)_2$: 29.03 and 26.69. [b, c, d, e] The signals with the same symbols may be interchanged.

TABLE IV
Carbon-13 chemical shifts of compounds *IX* – *XII*; measured at 125.7 MHz in $CDCl_3$, for other conditions see Experimental

Carbon	*IX*		*X*[a]		*XI*[a]		*XII*	
1	38.40	38.45	38.44	38.47	38.47	38.47	38.47	38.47
2	23.58	23.62	23.62	23.62	23.62	23.62	23.63	23.63
3	80.78	80.89	80.95	80.98	81.07	81.12	80.85	80.86
4	37.75	37.75	37.75	37.77	37.75	37.77	37.76	37.76
5	55.38	55.42	55.43	55.43	55.43	55.49	55.43	55.43
6	18.03	18.07	18.08	18.08	18.08	18.08	18.05	18.07
7	34.00	33.86	33.87	34.01	33.87	34.01	34.09	34.04
8	40.56	40.47	40.48	40.48	40.48	40.48	40.45	40.48
9	50.11	50.21	50.22	50.33	50.25	50.33	50.09	50.14
10	37.02	37.02	37.03	37.05	37.03	37.05	37.00	37.02
11	20.85	20.98	20.88	20.98	20.88	20.98	21.00	21.00
12[b]	25.50	25.99	25.35	25.92	25.55	26.04	26.77	26.08
13	42.87[b]	42.56[b]	42.44	42.84	42.95	42.61	43.16[b]	43.61[b]
14	40.78	40.96	41.02	40.97	40.75	40.97	40.24	40.83
15[b]	25.47	26.36	26.64	26.41	26.54	26.41	26.70	26.23
16	18.75	18.69	23.20	18.62	18.08	18.75	19.26	18.76
17	59.07	52.22	48.68	51.81	48.59	52.19	46.28	52.00[c]
18	45.58[b]	40.60[b]	36.81	40.51	44.21	40.42	44.29[b]	40.24[b]
19	41.75[b]	43.49[b]	42.07	41.39	41.95	42.41	45.04[b]	41.45[b]
20	85.75	84.46	86.28	84.31	86.01	84.18	86.47	84.69
21	105.89	102.24[c]	108.14	104.52[b]	108.80	103.02[b]	109.93	102.51[d]
22	207.79	100.67[c]	74.32	99.99[b]	80.01	101.52[b]	64.63	101.88[d]
23	27.91	27.89	27.91	27.91	27.91	27.91	27.90	27.90
24[c]	16.47	16.47	16.48	16.48	16.48	16.48	16.48	16.48
25[c]	16.34	16.38	16.35	16.37	16.35	16.37	16.35	16.39
26	15.60	15.66	15.75	15.62	15.69	15.63	15.65	15.65
27	13.80	13.94	13.80	13.95	14.15	13.80	13.68	13.72
28	167.70	171.72	176.69	172.01	173.67	172.10	172.57	171.74
29[d]	17.02	18.03	17.07	18.25	17.67	17.87	18.59	18.49
30[d]	15.70	16.47	16.22	16.54	16.68	16.44	17.54	16.44
31	–	–	–	–	–	–	51.53[c]	–
AcO:								
C=O	171.06	171.10	171.15	171.18	171.28	171.40	171.04	171.04
CH_3	21.31	21.31	21.32	21.32	21.37	21.32	21.31	21.31

[a] The data were obtained from the spectrum of a 2 : 1 mixture of compounds *X* and *XI*. [b, c, d] The signals with the same symbols may be interchanged.

long-range coupling, viz. with H-19β (see ref.[3]). This confirms not only the position of hydroxy group but also its α-configuration. No such long-range coupling was found in the spectra of hydroxy derivatives *X* and *XI*: H-22 gives a doublet due to vicinal coupling with the OH proton. The configuration at C-22 in compounds *X* and *XI* follows from the ^{13}C NMR spectra: with the derivative *X*, the C-18, which is in γ-position with respect to OH group, appears at δ 36.8 like that in the model compounds *XVIII* – *XXI*, which contain a 22α-OH group (δ 37 – 38, see ref.[3]). In the other isomer *XI* the chemical shift of C-18 (δ 44.2) agrees with that of the model compounds without a 22α-OH group (δ 43 – 49). Also the increments corresponding to the reduction of 22-ketonic group in *IX* to 22α-OH group in *X* for C-18 (Δδ = δ(*X*) – δ(*IX*) = –8.8) and for C-16 (Δδ = +4.5) stand in good accordance with the increments found with the model compounds *VIII* and X*VIII* (Δδ = –8.2 and +4.1, respectively, see ref.[3]).

With regard to the configuration at C-22 (in part A) in the dimeric compound *V* (and similarly at C-21 in *IX*) and at C-21′ and C-22′ (in part B) eight stereoisomers are possible theoretically; four of them can be excluded because only cis annelation is possible between the dioxolane ring and the oxabicyclooctane system in ring E (part B). Two out of the remaining four isomers have the ketonic group (in part A) and hydroxylic groups (in part B) cis oriented with respect to the dioxolane ring, whereas the other two possess the trans orientation of these groups. We tried to differentiate between these possibilities on the basis of IR spectral region of O–H stretching vibrations. The trans isomers should exhibit the bands of both free and intramolecular-bonded hydroxyls of comparable intensities, like those in diols *XX* and *XXI* and in the isopropylidenedioxy derivative *II*, whereas with the cis isomers it is possible to expect additional hydrogen bonds between hydroxyl groups and oxygen atom of ketonic group (*V*, *IX*), epoxy group (*VII*, *XII*), or hydroxyl group (*VI*).

As it can be seen from Table V, the spectra of the given dimeric compounds in tetrachloromethane solutions substantially differ from those of the model dihydroxy derivatives *II*, *XX*, and *XXI*: (i) except for the 21α-hydroxy derivative *VI* they do not contain the band of free hydroxyl (the very weak band about 3 590 cm^{-1} observable with the compounds *V*, *VII*, and *IX* can rather be assigned to a weak intramolecular bond), (ii) even at concentrations about 10^{-4} mol l^{-1} they contain intensive, very broad bands in the region of 3 280 – 3 460 cm^{-1} which are characteristic of intramolecular hydrogen bond (similar broad bands in this region are found in the spectra of crystalline compounds *V*, *VII*, *IX*, and *XII* measured in Nujol; see Experimental). In the keto derivatives *V* and *IX* the intensity of these bands increases with increasing concentration, in the epoxy derivatives *VII* and *XII* and in hydroxy derivative *VI* no perceptible concentration dependence was found in the concentration range used. All these facts indicate that in the tetrachloromethane solutions – even at low concentrations – there exist highly stable intermolecular complexes. It seems likely that these complexes contain two molecules of the dimeric compound connected by hydrogen bonds in

TABLE V

Frequencies and intensities of O–H stretching vibrations in the IR spectra measured in tetrachloromethane. The parameters of overlapping bands were obtained by mathematical separation; f free, b bonded

Compound[a]	ν(OH), cm^{-1}		$\Delta\nu_{1/2}$, cm^{-1}	ε_{rel} [b]	$c \cdot 10^4$, mol l^{-1}
II	f	3 599	25	60	1.8
	b	3 530	41	40	
V	b (or f)	3 589	24	15[c]	0.7
	b	3 541	60	35[c]	
	b	3 461	94	31	
	b	3 371	136	19[d]	
VI	f	3 629	23	4	0.9[e]
	f (or b)	3 605	22	10	
	b	3 530	45	28	
	b	3 451	105	8	
	b	3 348	187	50	
VII	b (or f)	3 590	12	3	1.1[f]
	b	3 492	51	45	
	b	3 312	182	52	
IX	b (or f)	3 590	13	6	1.0
	b	3 537	74	49[c]	
	b	3 464	127	28[d]	
	b	3 354	165	17[d]	
XII	b	3 487	55	19	0.9[e]
	b	3 457	34	31	
	b	3 280	122	50	
XV	f	3 628	14	100	7.7
XVI	f	3 646	19	10	18
	f	3 629	16	90	
XVII	f	3 629	19	23	0.4
	b	3 589	19	77	
XVIII	b	3 529	57	100	11
XIX	b	3 525	59	100	11
XX	f	3 627	23	69	1.1
	b	3 536	50	31	
XXI	f	3 619	30	57	1.7[e]
	b	3 527	58	43	

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[a] The monomeric compounds *II*, *XV* – *XXI* exhibit additional very weak bands at ca 3 450 and 3 490 cm^{-1} due to the carbonyl first overtone of acetate and lactone groups, respectively; in the dimeric compounds *V* – *VII*, *IX*, *XI* these bands are overlapped by strong hydroxyl bands. [b] $\varepsilon_{rel} = 100\varepsilon_i/\Sigma\varepsilon_i$. [c] The intensity decreases with increasing concentration. [d] The intensity increases with increasing concentration. [e] The same spectrum was found at c 1 . 10^{-3} mol l^{-1}. [f] In the range from c 0.5 to 10 . 10^{-4} mol l^{-1} no dependence of spectrum upon concentration was found.

which both the hydroxyl groups of part B and the oxygen atom of the functional group of part A are participating. Such complexes are only possible with the cis arrangement of the participating groups on the dioxolane ring.

For compound *V* two cis isomers can be considered which differ in the orientation of connection of dioxolane ring to part B: from α- or β-side. The α-isomer, which has the parts A and B connected by the bonds 22α-O-22′α and 22β-O-21′α, is very unlikely for sterical reasons (like the α-isomer of compound *II*; vide supra): according to molecular models it has unfavourable nonbonding interactions between the hydrogen atoms at C-16 and 19′α-CH_3 and 18′α-H. No such interactions appear in the β-isomer (the connection 22α-O-21′β and 22β-O-22′β). Similarly, in the case of compound *IX* it is possible to exclude the α-isomer (21α-O-21′α and 21β-O-22′α) because of the interactions between 20α-CH_3 and 19′α-CH_3 and 18′α-H; in the β-isomer (21α-O-22′β and 21β-O-21′β) the two triterpenoid parts A and B are oriented away from each other and do not mutually interact. For the reasons given we formulate the dimeric compounds as β-isomers and suggest the configuration presented in formulas *V* – *VII* and *IX* – *XII*. Judging by the molecular models, all these compounds can form the above-mentioned bimolecular complexes.

In conclusion it can be stated that the α-diketone *I*, which contains the 2-oxabicyclo[2.2.2]octane system in the E ring, is highly reactive and shows a considerable trend to change the hybridization of one or both carbonyl carbon atoms to sp^3: it gives condensation products with acetanhydride in pyridine (compounds *III*, *IV* and others, see ref.[2]), it easily undergoes benzilic rearrangement to give the E-norhydroxy acid[1], during chromatography on silica gel it reacts with water and acetone to give the isopropylidenedioxy derivative *II* or with water to give the dimeric products *V* and *IX*. The FAB-MS shows its high affinity to 3-nitrobenzyl alcohol, which was used as the matrix; the spectrum of diketone *I* exhibits very abundant ions $[M + H + \text{matrix}]^+$, $[M + Na + \text{matrix}]^+$ and $[M + H + \text{matrix} - 60]^+$.

EXPERIMENTAL

The melting points were determined on a Kofler block and are uncorrected. The optical rotations were measured in chloroform (*c* 0.3 to 0.9) on an automatic polarimeter ETL-NPL (Bendix–Ericsson), accuracy ±2°. The IR spectra were recorded in chloroform unless otherwise stated on a PE 684 (Perkin–Elmer) spectrometer with a Data Station Model 3 500. The spectra in the OH stretching region were measured in tetrachloromethane in infrasil cells; thickness 2 cm. To obtain satisfactory signal-to-noise ratios 16 to 80 spectra were accumulated. Mathematical separation of overlapping hydroxyl bands was carried out using a described program[7]. Cauchy (Lorentz) profile function was used for description of the bands, and the background was approximated by a straight line.

The NMR spectra were measured on FT-NMR spectrometer Varian Unity 500 (^1H at 500 MHz, ^{13}C at 125.7 MHz) in deuteriochloroform at 20 °C. 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, using the exponential Lorentz–Gauss function for the resolution enhancement. The carbon-13 chemical shifts were referenced to the signal of solvent and recalculated to tetramethylsilane with the relation $\delta(CHCl_3)$ = 77.00 ppm. The number of directly bonded hydrogen atoms was determined from the proton decoupled "attached proton test" spectra[5,6].

The fast atom bombardment mass spectra (FAB-MS) were obtained on the ZAB-EQ instrument (VG Analytical Ltd., Manchester), supplied with a 8 kV FAB gun. The bombarding particles were xenon atoms, accelerating voltage 8 kV, and resolution 1 100. For each spectrum, approximately 5 – 10 μg sample dissolved in 2 μl chloroform was added into 1 – 2 μl 3-nitrobenzyl alcohol on the probe tip. The electron impact mass spectra (EI-MS) were measured on an INCOS 50 (Finnigan MAT) spectrometer, ionizing electrons energy 70 eV, ion source temperature 150 °C. Samples were introduced from direct exposure probe at heating rate 10 mA/s.

The column chromatography was performed on silica gel Silpearl (Kavalier, Votice). The reaction course was monitored and the purity of samples was checked by thin layer chromatography (TLC) on silica gel G (Merck, detection by spraying with 10% sulfuric acid and heating). For preparative TLC the same silica gel G (Merck) was used with the detection under UV light after spraying with 0.5% methanolic solution of morin. The samples for analyses were dried at 100 °C over phosphorus pentoxide under reduced pressure.

3β-Acetoxy-21,22-dioxo-18α,19β*H*-ursan-28,20β-olide (*I*)

The compound was prepared according to ref.[1]. EI-MS, *m/z* (% rel. int.): 526 (M^+, 0.1), 484 (0.3), 466 (3), 451 (2), 423 (2), 384 (1), 189 (26), 43 (100). FAB-MS, *m/z*: 702 [M + Na + $C_7H_7NO_3$], 680 [M + H + $C_7H_7NO_3$], 620, 527 [M + H], 467, 423.

Preparation of Compounds *II*, *V*, and *IX*

A saturated solution of the raw diketone *I* (1.70 g, 3.20 mmol) in dichloromethane was introduced on a silica gel column (80 g). After the addition of the eluent mixture of petroleum ether–acetone (10 : 1), an exothermic reaction took place on the column. The same mixture with gradually changing ratio from 10 : 1 to 1 : 1 was then used to eluate a mixture of dimeric compounds *V* and *IX* (1.08 g, 49%) followed by compound *II* (0.36 g, 19%) and *I* (0.09 g, 17%). An unstable compound (0.12 g) which was not identified (it gave quantitatively the known[3] epoxide *VIII* by reaction with diazomethane in ether) was eluated with ether containing 5% methanol. The repeated chromatography of the compound mixture *V* and *IX* on silica gel with the mixture of petroleum ether–acetone gave the chromatographically pure components: the less polar compound *IX* and the more polar one *V*.

Isopropylidenedioxy derivative II: m.p. 305 – 308 °C, $[\alpha]_D$ +13°. IR spectrum: 3 586, 3 495, 3 420, 1 755, 1 723, 1 256, 1 104, 1 087, 1 074, 1 030. IR spectrum (Nujol): 3 490, 3 390, 1 765, 1 712, 1 275, 1 221, 1 103, 1 083, 1 030. EI-MS, *m/z* (% rel. int.): 542 (M – 60, 1), 499 (1), 466 (3), 451 (1), 423 (2), 189 (5), 43 (100). FAB-MS, *m/z*: 625 (M + Na), 603 (M + H), 602, 543, 542, 527, 499, 467. For $C_{35}H_{54}O_8$ (602.8) calculated: 69.74% C, 9.03% H; found: 70.03% C, 8.90% H.

Compound V: after recrystallization from a mixture of chloroform–heptane m.p. 319 – 326 °C (decomposition; the melt corresponds to diketone *I* according to TLC), $[\alpha]_D$ +18°. IR spectrum: 3 500, 1 766, 1 752 sh, 1 720, 1 256, 1 105, 1 029, 1 010, 980; ν(OH) ($\Delta\nu_{1/2}$) in Nujol: 3 461 (20), 3 371 (150). FAB-MS, *m/z* (M^+ calculated: 1 070.7): 1 094 (M + Na), 1 072 (M + H), 1 012, 996, 968, 952, 527 (A + H, B + H), 467, 423. For $C_{64}H_{94}O_{13}$ (1 071.5) calculated: 71.74% C, 8.84% H; found: 71.36% C, 8.84% H.

Compound IX: after recrystallization from a mixture of chloroform–heptane m.p. 330 – 336 °C (decomposition; the melt corresponds to diketone *I* according to TLC), $[\alpha]_D$ +3°. IR spectrum: 3 487, 1 760, 1 720, 1 254, 1 063, 1 025, 979; ν(OH) ($\Delta\nu_{1/2}$) in Nujol: 3 450 (115). FAB-MS, *m/z* (M^+ calculated: 1 070.7): 1 094 (M + Na), 1 072 (M + H), 1 012, 996, 968, 952, 527 (A + H, B + H), 467, 423. For $C_{64}H_{94}O_{13}$ (1 071.5) calculated: 71.74% C, 8.84% H; found 71.42% C, 9.01% H.

Reaction of Compound *V* with Diazomethane

a) Compound *V* (30 mg, 0.03 mmol) was treated with an excess solution of diazomethane in ether. After 30 min at room temperature, the solution was evaporated under reduced pressure until dry, and the chromatographically uniform evaporation residue was recrystallized from a chloroform–heptane mixture to give 25 mg (82%) dimeric epoxide *VII*, m.p. 308 – 312 °C (decomposition), $[\alpha]_D$ +9°. IR spectrum: 3 487, 3 310, , 1 760, 1 720, 1 375, 1 254, 1 107, 1 068, 1 030, 979; ν(OH) ($\Delta\nu_{1/2}$) in Nujol: 3 423 (180). FAB-MS, *m/z* (M^+ calculated: 1 084.7): 1 108 (M + Na), 1 086 (M + H), 1 026, 1 090, 982, 966, 541 (A + H), 527 (B + H), 481, 467, 437, 423. For $C_{65}H_{96}O_{13}$ (1 085.5) calculated: 71.92% C, 8.91% H; found: 71.65% C, 8.67% H.

b) Compound *V* (30 mg, 0.03 mmol) was left to stand with an excess solution of diazomethane in ether at room temperature 24 h, whereafter the mixture was treated as sub *a*). The chromatographically uniform product was recrystallized from a chloroform–methanol mixture to give 23 mg (74%) epoxide *VIII* identical with the authentic sample[3] according to TLC and IR spectrum. M.p. 310 – 314 °C (decomposition). FAB-MS, *m/z*: 563 (M + Na), 541 (M + H), 481, 465, 437. Epoxide *VIII* was also obtained by the reaction of dimeric epoxide *VII* with diazomethane at the same conditions.

Reaction of Compound *IX* with Diazomethane

a) Compound *IX* (30 mg, 0.03 mmol) was treated with an excess solution of diazomethane in ether and after 30 min the mixture was worked up in the same way as above in the reaction of compound *V* sub *a*). The chromatographically uniform evaporation residue was recrystallized from a chloroform–heptane mixture to give 23 mg (76%) dimeric epoxide *XII*, m.p. 321 – 331 °C (decomposition), $[\alpha]_D$ +12°. IR spectrum: 3 461, 3 287, 1 753, 1 720, 1 254, 1 069, 1 022; ν(OH) ($\Delta\nu_{1/2}$) in Nujol: 3 460 (120), 3 313 (140). FAB-MS, *m/z* (M^+ calculated: 1 084.7): 1 108 (M + Na), 1 086 (M + H), 1 026, 1 010, 982, 541 (A + H), 527 (B + H), 481, 467. For $C_{65}H_{96}O_{13}$ (1 085.5) calculated: 71.92% C, 8.91% H; found: 72.08% C, 8.72% H.

b) Compound *IX* (30 mg, 0.03 mmol) was left to stand with an excess solution of diazomethane in ether at room temperature 24 h. The same treatment as that for compound *V* sub *a*) above gave a mixture of products which was separated by TLC (silica gel, petroleum ether–acetone–chloroform 7 : 1 : 1) to give the epoxide *XII* (5 mg, 17%), epoxide *VIII* (12 mg, 39%), epoxide *XIII* (7 mg, 23%), and diepoxide *XIV* (5 mg, 16%). According to m.p., TLC, and IR spectra the products were identical with the authentic samples[3].

The dimeric epoxide *XII* was left to stand with an excess solution of diazomethane in ether at room temperature and the reaction course was monitored by means of TLC. After 30 h the mixture contained the monomeric epoxides *VIII*, *XIII*, and *XIV* and after another 20 h it only contained epoxide *VIII* and diepoxide *XIV* in the ratio of ca 1 : 1.

Reduction of Compound *V*

A solution of 40 mg (0.04 mmol) compound *V* in a mixture of 4 ml benzene and 2 ml methanol was treated with 50 mg (1.3 mmol) sodium borohydride. After 4 min, the mixture was diluted with water and ether and acidified with dilute hydrochloric acid. The product was extracted with ether, the ethereal solution was washed with sodium hydrogen carbonate solution, water, and dried with sodium sulfate. The chromatographically uniform evaporation residue of compound *VI* (40 mg, 100%) did not crystallize and formed gels from various solvents. It was dissolved in chloroform and the solution was filtered through a silica gel layer. Chloroform was distilled off and the evaporation residue (m.p. 280 – 290 °C with decomposition) was used for spectral measurements. IR spectrum: 3 495, 3 300, 1 758, 1 720, 1 256, 1 107, 1 028. FAB-MS, *m/z* (M^+ calculated: 1 072.7): 1 096 (M + Na), 1 074 (M + H), 1 014, 998, 970, 954, 529 (A + H), 527 (B + H), 469, 467.

Reduction of Compound *IX*

Compound *IX* (50 mg, 0.05 mmol) was reduced with 50 mg (1.3 mmol) sodium borohydride in a mixture of 4 ml benzene and 2 ml methanol 4 min. The same treatment like that in the above reduction of compound *V* gave a mixture of five compounds; the two least polar ones (*X* and *XI*, 34 mg, 68%) were separated by preparative TLC (silica gel, petroleum ether–chloroform–acetone 5 : 2 : 1). The components *X* and *XI* could not be separated even by repeated chromatography, and their mixture was used for the spectral measurements (according to ^{1}H NMR spectrum the ratio of *X* to *XI* was 2 : 1). IR spectrum: 3 500, 3 320, 1 753, 1 721, 1 256, 1 062, 1 024. FAB-MS, *m/z* (M$^+$ calculated: 1 072.7): 1 096 (M + Na), 1 074 (M + H), 1 014, 998, 970, 954, 529 (A + H), 527 (B + H), 469, 467.

Reaction of Compounds *V* and *IX* with Acetanhydride in Pyridine

Compound *V* (100 mg, 0.09 mmol) was left to stand with 2 ml acetic anhydride–pyridine (1 : 1) mixture at room temperature 24 h. The reaction mixture was decomposed with water and extracted with ether. The extract was washed with dilute hydrochloric acid and with water, dried with sodium sulfate, and evaporated. The evaporation residue was recrystallized from a mixture of chloroform–methanol to give a chromatographically inseparable mixture of lactones *III* and *IV* (82 mg, 65%), m.p. 265 – 270 °C (decomposition), $[\alpha]_D$ +22°. The identity of the products with the lactones *III* and *IV* prepared[2] from diketone *I* was confirmed by the ^{1}H NMR spectrum of the mixture.

The same mixture of lactones *III* and *IV* (62 mg, 62%; m.p. 260 – 265 °C with decomposition, $[\alpha]_D$ +24°) was prepared by the procedure given from 80 mg (0.075 mmol) compound *IX*.

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