A CONTRIBUTION TO PEROXY ACID OXIDATION OF α,β-UNSATURATED KETONES AND LINEARLY CONJUGATED DIENONES: REACTIONS IN THE CHOLESTANE SERIES*

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Oxidation with 3-chloroperoxybenzoic acid of *s-cis* α,β-unsaturated ketones *IX*, *XI* and *s-trans* types *X*, *XII* was compared. The *s-cis* ketones show higher reactivity and furnish a higher yield of the corresponding α,β-epoxy ketones than the *s-trans* ketones. Products of the Baeyer–Villiger reaction are formed only in low yield. The dienone *VI* is oxidized predominantly to *VII* thus violating the rule that linear conjugated dienones are epoxidized at the double bond more distant from the carbonyl group; this result is in accord with the behavior of *s-cis* α,β-unsaturated ketones. ^{1}H NMR and ^{13}C NMR data of the starting compounds and of the products are reported.

It has been well known that conjugation of a double bond with a carbonyl group markedly decreases its reactivity towards peroxy acids[1]. Extensive experience based on a series of examples had led to the generalization that peroxy acids epoxidize linear conjugated dienones on the double bond more distant from the carbonyl group[2–7]. The examples cited in these papers include steroid systems of the types *I*–*IV*.

For synthetic purposes, we needed the 2,3-epoxide derived from *VI* and we attempted to prepare it from the dienone *VI* (ref.[8]) by peroxy acid epoxidation. To our surprise, the action of 3-chloroperoxybenzoic acid on *VI* in benzene solution led to the formation of the epoxide *VII* in 53% yield whereas the epoxide *V* was isolated only in 4% yield. Comparable yields were obtained when dichloromethane was used as a solvent. When the structure of the dienone *VI* is compared with the systems *I*–*IV*, a difference is apparent in the mutual steric relation of the carbonyl group and the adjacent double bond. Whereas in the types *I*–*IV* the arrangement of the double bond to the adjacent carbonyl group is *s-trans*, the same moiety in *VI* is *s-cis*.

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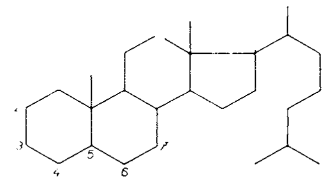
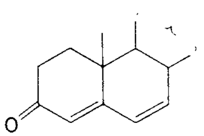
It therefore seemed interesting to compare the reactivity of appropriate model systems differing in these features. As such models we chose α,β-unsaturated ketones *IX*–*XII*. These compounds represent systems with double bonds at positions 4,5 and 5,6 conjugated with an adjacent carbonyl group, so that a pair of *s-cis* (*IX*, *XI*) and a pair of *s-trans* (*X*, *XII*) types are available. They were treated with 3-chloroperoxybenzoic acid under standard conditions (benzene solution, 10% excess of peroxy acid, 22°C, 22 h) and the reaction mixture was subjected to product analysis (TLC, HPLC, preparative chromatography).





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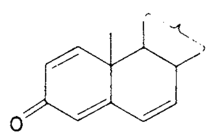

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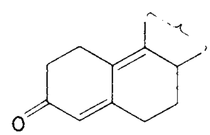

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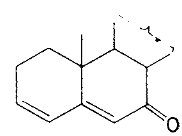

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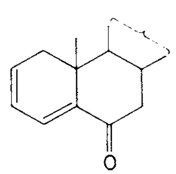

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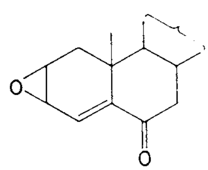

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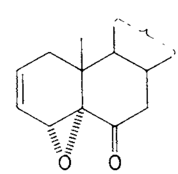

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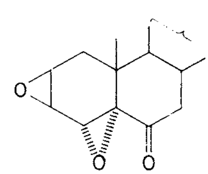

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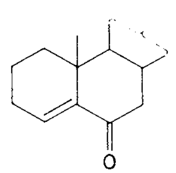

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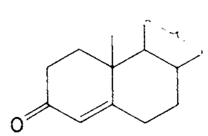

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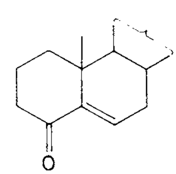

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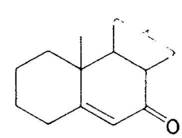


XII

Structure determination of the new compounds, reported in the present paper, is based on spectroscopic measurements (NMR, IR, mass spectra) of which the

NMR data proved most informative. We report not only the ^{1}H and ^{13}C NMR spectra of the new substances but of all reaction products (*V*, *VII*, *VIII*, *XIII*–*XXII*) and of the starting α,β-unsaturated ketones (*VI*, *IX*–*XII*). The aim of the NMR measurements was the structure determination of the new compounds, reporting on the values obtained at higher frequency (200 MHz, in contrast to earlier measurements mostly taken at 60 MHz if reported at all), additional characterization of these compounds by ^{13}C NMR data, as yet mostly unpublished, and estimation of the substitution effects for α,β-unsaturated ketones and epoxy ketones. In the end, we pursued the course of the reaction with 3-chloroperoxybenzoic acid directly in the NMR-tube hoping to obtain some insight into the reaction mechanism. The proton NMR spectra of all investigated compounds (*V*–*XXII*) are given in Table I. Chemical shifts of carbons from ^{13}C NMR spectra are listed in Table II.

The ^{1}H and ^{13}C NMR spectra of the starting unsaturated ketones *VI*, *IX*–*XII* agree with their structures and data available in literature[8–13]. Characteristic are differences between α,β-unsaturated ketones with *s-cis* and *s-trans* arrangement (*VI*, *IX*, *XI* vs *X*, *XII*). Considering rings A and B (if C and D are omitted), the pairs *IX*, *XI* and *X*, *XII* show pseudosymmetry with regard to the plane defined by the atoms C-5, C-10, and C-19 and give closely similar values of the NMR parameters in "symmetrically" equivalent positions. Characteristic values of some ^{1}H and ^{13}C NMR signals for *s-cis* and *s-trans* ketones are shown in Table III. We utilized a comparison of $\delta(C)$ values for unsaturated ketones *VI*, *IX*–*XII* with the values for 5α-cholestane[14] to establish the influence of the "complex" substitution (α,β-unsaturated ketone) in various positions. The substitution effects determined in this manner complete the scarce data in the literature[9] and are listed in Table IV.

The dienone *VI* reacts completely after 18 h to give the epoxide *VII* in 53% (isolated) yield and 4% of the isomeric epoxide *V*. The structure of the major product (*VII*) follows from spectroscopic data (cf. later) corroborated by chemical correlation: hydrogenation of *VII* on $Pd/CaCO_3$ provides the known 5-hydroxy-5α-cholestan-6-one[15]. When the epoxidation was performed in acetonitrile, it proceeded more slowly (16% of unreacted starting compound) with higher yield of the epoxide *V* (13%). This effect is even more pronounced in acetonitrile in the presence of sodium fluoride. ^{1}H and ^{13}C NMR data for *VII* are in full agreement with the structure including the 4α,5α-configuration of the epoxy group. A complete analysis of the signals of all hydrogens on the rings A and B and the values of $J(H, H)$ obtained in hexadeuteriobenzene (better separation of H-1, H-1′, H-2 and H-3) demonstrated the chair conformation of the B-ring ($J(7\alpha,8)$ = 12·2 Hz, $J(7\beta,8)$ = 4·1 Hz) and the long-range couplings of H-1α with 10β-methyl (0·7 Hz), olefinic hydrogen H-3 (3·0 Hz), and epoxide hydrogen H-4 (0·9 Hz), all fully compatible only with 4α,5α-epoxide with partial conformational formula *VII A*.

The second isolated epoxide *V* has a double bond preserved in the position 4,5 (in ^{1}H NMR a single —CH= hydrogen at δ 6·78; in ^{13}C NMR signals CH=C

TABLE I
[1]H NMR parameters of some cholestane derivatives in deuteriochloroform

Compound	H-18[a]	H-19[b]	H-21[c]	H-26[c] H-27[c]	Other protons
V	0·692	1·133 (*J* = 0·6)	0·918	0·862 0·867	H-1: 2·34 dd *J*(1, 1) = 14·8; *J*(1, 2) = 2·2 H-2: 3·63 ddd *J*((2, 1) = 2·2; *J*(2, 1′) = 1·5; *J*(2, 3) = 4·2 H-3: 3·40 t *J*(3, 2) = 4·2; *J*(3, 4) = 4·1 H-4: 6·78 d *J*(4, 3) = 4·1 H-7 and H-7′: 2·58 m and 1·91 m
VI	0·700	1·006	0·923	0·864 0·869	H-1 and H-1′: 2·42 dm and 2·22 dm *J*(1, 1′) = 18·0 H-2 and H-3: 6·06 m H-4: 6·83 m (*W* = 7·4) H-7: 2·56 dd *J*(7, 7′) = 16·2; *J*(7, 8) = 3·6 H-7′: 1·92 dd *J*(7′, 7) = 16·2; *J*(7′, 8) = 12·1
VII	0·710	0·861 (*J* = 0·5)	0·925	0·867 0·871	H-2 and H-3: 5·81–5·99 m H-4: 3·78 dd *J*(4, 3) = 3·7; *J*(4, 2) = 2·0 H-7: 2·48 dd *J*(7, 7′) = 14·3; *J*(7, 8) = 4·4 H-7′: 2·31 dd *J*(7′, 7) = 14·3; *J*(7′, 8) = 11·9
VII[d]	0·627	0·792 (*J* = 0·7)	1·066	1·046 1·046	H-1: 2·07 dm *J*(1, 1′) = 16·3; *J*(1, 2) = 2·0; *J*(1, 3) = 3·0; *J*(1, 4) = 0·9; *J*(1, 19) = 0·7 H-1′: 1·74 dd *J*(1, 1′) = 16·3; *J*(1′, 2) = 6·7 H-2: 5·66 ddt *J*(2, 1) = 2·0; *J*(2, 1′) = 6·7; *J*(2, 3) = 9·7 *J*(2, 4) = 1·8 H-3: 5·78 ddd *J*(3, 1) = 3·0; *J*(3, 2) = 9·7; *J*(3, 4) = 3·8 H-4: 3·99 ddd *J*(4, 1) = 0·9; *J*(4, 2) = 1·8; *J*(4, 3) = 3·8 H-7: 2·52 dd *J*(7, 7′) = 14·4; *J*(7, 8) = 4·1 H-7′: 2·26 dd *J*(7′, 7) = 14·4; *J*(7′, 8) = 11·9

TABLE I
(*Continued*)

Compound	H-18[a]	H-19[b]	H-21[c]	H-26[c] H-27[c]	Other protons
VIII	0·681	0·941 (*J* = 1·0)	0·916	0·862 0·867	H-1: 1·98 d *J*(1, 1′) = 14·7; *J*(1, 2) = 7·1 H-2: 2·95 ddd *J*(2, 1) = 7·1; *J*(2, 1′) = 2·7; *J*(2, 3) = 4·0 H-3: 3·35 dd *J*(3, 2) = 4·0; *J*(3, 4) = 2·7 H-4: 3·94 dd *J*(4, 3) = 2·7; *J*(4, 1′) = 0·4 H-7: 2·47 dd *J*(7, 7′) = 14·4; *J*(7, 8) = 4·1 H-7′: 2·21 dd *J*(7′, 7) = 14·4; *J*(7′, 8) = 12·2
IX	0·701	0·967 (*J* = 0·4)	0·922	0·863 0·868	H-3: 2·12 m H-4: 6·37 dd *J*(4, 3) = 4·7; *J*(4, 3′) = 3·1 H-7 and H-7′: 2·53 m and 1·90 m
X	0·708	1·181	0·910	0·862 0·866	H-4: 5·71 bd *J*(4, 6) = 1·7; *J*(4, 6′) ≠ 0
XI	0·691	0·959	0·921	0·864 0·868	H-3: 2·54 dm *J*(3, 3′) = 16·6 H-6: 6·42 dd *J*(6, 7) = 5·0; *J*(6, 7′) = 2·6 H-7: 2·20 dt *J*(7, 6) = *J*(7, 8) = 5·0; *J*(7, 7′) = 19·4 H-7′: 1·72 ddd *J*(7′, 6) = 2·6; *J*(7′, 7) = 19·4; *J*(7′, 8) = 9·8
XII	0·677	1·177	0·922	0·861 0·865	H-6: 5·63 d *J*(6, 4) = 1·7
XIII	0·685	0·985	0·917	0·865 0·869	H-4: 3·60 d *J*(4, 3) = 4·2; *J*(4, 3′) ~ 0 H-7 and H-7′: 2·34 m (2 H)
XIV	0·702	1·002	0·923	0·866 0·870	H-4: 3·05 t *J*(4, 3) = *J*(4, 3′) = 2·5 H-7 and H-7′: 2·57 m (2 H)
XV	0·709	1·130	0·902	0·863 0·868	H-3 and H-3′: 2·00 m (2 H) H-4: 3·43 dd *J*(4, 3) = 5·2; *J*(4, 3′) = 0·9 H-7a: 2·65 dd *J*(7a, 7a′) = 13·4; *J*(7a, 8) = 11·1 H-7a′: 2·52 dd *J*(7a′, 7a) = 13·4; *J*(7a′, 8) = 2·0 H-8: 1·82 m

TABLE I
(*Continued*)

Compound	H-18[a]	H-19[b]	H-21[c]	H-26[c] H-27[c]	Other protons
XVI	0·696	1·054	0·901	0·864 0·869	H-2: 2·40 ddd $J(2, 1) = 7·6$; $J(2, 1') = 2·0$; $J(2, 2') = 19·6$ H-2': 2·22 ddd $J(2', 1) = 7·4$; $J(2', 1') = 11·2$; $J(2', 2) = 19·6$ H-4: 3·03 s
XVII	0·684	1·145	0·898	0·859 0·865	H-2: 2·31 ddd $J(2, 1) = 6·4$; $J(2, 1') = 2·6$; $J(2, 2') = 19·2$; H-4: 2·97 s
XVIII	0·681	1·100	0·897	0·860 0·865	H-2 and H-2': 2·59 m (2 H) H-4: 6·01 d $J(4, 6) = 1·5$ H-6: 2·20 ddt $J(6, 6') = J(6, 7) = 13·6$; $J(6, 7') = 4·3$; $J(6, 4) = 1·5$
XIX	0·617	0·982	0·891	0·858 0·863	H-3: 2·64 ddd $J(3, 2) = 12·5$; $J(3, 2') = 7·4$; $J(3, 3') = 14·5$ H-3': 2·37 dm $J(3', 2) = 2·4$; $J(3', 2') = 4·3$; $J(3', 3) = 14·5$; $J(3', 1) = 1·4$ H-6: 3·60 d $J(6, 7) = 4·8$; $J(6, 7') \sim 0$ H-7 and H-7': 1·98 m (2 H)
XX	0·651	0·998	0·899	0·860 0·865	H-3 and H-3': 2·60 m and 2·32 m H-6: 3·17 dd $J(6, 7) = 2·4$; $J(6, 7') = 1·0$ H-7: 2·15 ddd $J(7, 6) = 2·4$; $J(7, 7') = 14·4$; $J(7, 8) = 3·8$ H-7': 1·26 ddd $J(7', 6) = 1·0$; $J(7', 7) = 14·4$; $J(7', 8) = 11·0$
XXI	0·694	1·064	0·919	0·865 0·870	H-3 and H-3': 2·89 m and 2·36 m H-6: 5·40 dd $J(6, 7) = 6·5$; $J(6, 7') = 2·2$ H-7: 2·15 dt $J(7, 6) = 5·4$; $J(7, 7') = 17·2$; $J(7, 8) = 4·5$ H-7': 1·71 ddd $J(7', 6) = 2·2$; $J(7', 7) = 17·2$; $J(7', 8) = 10·0$
XXII	0·659	1·003	0·900	0·856 0·860	H-6: 3·02 s

[a] Singlet. [b] Singlet or doublet (if J-value is indicated). [c] Doublet with $J = 6·5$ Hz. [d] Data from hexadeuteriobenzene solution.

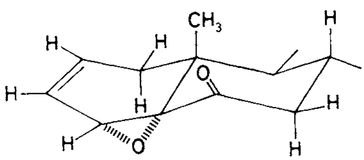
TABLE II

^{13}C NMR chemical shifts of some cholestane derivatives in deuteriochloroform

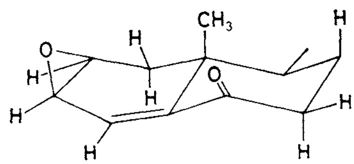
Carbon	*V*	*VI*	*VII*	*VIII*	*IX*	*X*	*XI*	*XII*	*XIII*	*XIV*	*XV*	*XVI*	*XVII*	*XVIII*	*XIX*	*XX*	*XXI*	*XXII*
C-1	35·5	35·9	34·9	32·4	35·5	35·7	36·2	38·8	29·4	30·5	35·1	33·1	26·1	29·7	33·0	37·8	29·5	35·1
C-2	46·5	123·2	122·3	47·7	17·9	33·9	19·3	22·0	15·5	15·3	17·1	28·9	32·5	33·5	20·6	18·8	16·3	20·8
C-3	56·6	128·3	132·4	48·7	25·5	199·3	40·1	26·9	21·9	23·1	25·2	207·1	206·7	173·1	39·4	41·5	32·5	24·9
C-4	128·6	132·8	52·2	51·1	132·4	123·7	203·1	32·7	57·5	60·3	61·1	62·9	62·6	129·4	208·0	208·1	173·5	30·0
C-5	148·4	140·7	69·3	53·7	146·0	171·4	145·4	168·4	68·2	67·5	87·0	70·2	70·2	130·3	68·5	66·2	155·8	68·8
C-6	201·1	200·0	206·4	205·6	203·2	32·9	132·5	124·5	207·6	207·0	173·8	29·1	29·8	29·9	57·0	62·4	113·8	64·1
C-7	46·0	45·5	45·3	45·7	46·0	32·0	31·7	202·3	44·9	46·3	39·6[a]	28·9	30·4	32·8	28·6	31·9	30·1	208·4
C-8	33·6	32·8	36·9	36·5	33·7	35·6	31·1	45·4	37·0	34·9	34·8	35·4	35·0	35·8	29·5	29·6	31·8	43,8
C-9	51·1	50·3	49·4	45·4	51·1	53·8	49·2	50·1	49·1	46·7	51·2	50·7	46·4	51·3	42·5	49·7	43·3	46·9
C-10	39·6	37·8	36·8	38·6	37·7	38·5	38·6	39·2	37·8	38·2	38·2	36·7	37·1	39·7	38·5	38·8	39·2	35·9
C-11	22·0	21·2	20·7	20·5	21·3	21·0	21·3	20·9	20·5	21·2	21·5	21·4	21·5	21·4	21·5	21·4	21·1	21·5
C-12	39·5	39·4	39·3	39·1	39·5	39·6	39·7	39·2	39·3	39·2	39·5	39·7	39·4	41·2	39·4	39·6	39·5	39·7
C-13	42·5	42·4	42·8	42·7	42·6	42·4	42·4	43·1	42·9	42·5	42·8	42·5	42·5	42·5	42·3	42·2	42·4	44·1
C-14	56·7	56·5	56·0	56·0	56·8	55·9	56·6	50·3	56·2	56·4	56·4	55·6	55·8	56·1	56·5	56·2	56·6	51·9
C-15	23·9	24·0	24·0	24·1	23·9	24·1	24·1	26·4	23·9	23·9	24·0	24·2	24·1	24·1	24·0	24·2	24·2	23·9
C-16	28·0	28·0	27·9	27·9	28·0	28·1	28·2	28·6	27·9	27·9	27·6	28·1	28·0	28·2	28·0	28·1	28·2	28·3
C-17	56·0	56·0	56·0	56·0	56·1	56·1	56·1	54·9	56·0	55·9	55·1	56·2	56·0	56·0	55·9	56·1	56·1	55·3
C-18	11·9	11·8	11·9	11·8	11·9	11·9	11·9	12·0	11·9	11·7	11·8	12·0	11·9	12·0	11·9	11·8	11·9	12·1
C-19	24·6	17·8	14·4	15·9	20·3	17·3	21·3	17·3	14·5	18·8	16·7	16·5	18·9	20·1	14·8	18·8	22·9	15·5
C-20	35·7	35·7	35·6	35·7	35·7	35·7	35·7	35·7	35·7	35·5	35·7	35·8	35·7	35·8	35·7	35·7	35·7	35·9
C-21	18·7	18·7	18·6	18·6	18·6	18·6	18·7	18·9	18·6	18·5	18·6	18·6	18·6	18·6	18·6	18·7	18·7	18·7
C-22	36·1	36·1	36·0	36·0	36·1	36·1	36·2	36·2	36·1	35·9	36·0	36·1	36·0	36·1	36·1	36·1	36·2	36·1
C-23	23·8	23·8	23·8	23·8	23·8	23·8	23·8	23·8	23·8	23·7	23·8	23·8	23·8	23·8	23·8	23·8	23·8	23·8
C-24	39·5	39·5	39·4	39·5	39·5	39·5	39·5	39·5	39·4	39·3	39·3	39·5	39·4	39·5	39·5	39·5	39·5	39·4
C-25	28·0	28·0	27·9	28·0	28·0	27·9	28·0	28·0	28·0	27·8	28·0	28·0	27·9	28·0	28·0	28·0	28·0	28·0
C-26	22·6	22·5	22·5	22·5	22·5	22·5	22·5	22·5	22·5	22·4	22·6	22·5	22·5	22·5	22·5	22·5	22·6	22·5
C-27	22·8	22·8	22·8	22·8	22·8	22·8	22·8	22·8	22·8	22·7	22·8	22·8	22·8	22·8	22·8	22·8	22·8	22·8

[a] The value for carbon atom C-7a.

at δ 128·6 and δ 148·4) and an epoxide ring in the 2,3-position (^{1}H NMR: CH—O signals at δ 3·63 and 3·40; ^{13}C NMR: CH—O signals at δ 46·5 and 56·6). The configuration of the epoxide oxygen follows from the detailed analysis of NMR data and molecular models. The low values of $J(1,2)$ and $J(1',2)$ equal to 2·2 and 1·5 Hz, respectively, indicate the gauche arrangement of hydrogens on C(1)—C(2) bond. Such an arrangement together with the geometry allowing for long-range coupling of H-1α with the 10β-methyl group (found J = 0·6 Hz, similar to *VII*) is only possible for β-epoxide which assumes a steric arrangement represented by the partial conformational formula *VA*. The epoxide *V* is unstable on storing; from an older specimen we separated a more polar fraction, the NMR spectrum of which is compatible with the formula *VIII* (mutual coupling of CH—O hydrogens at δ 2·95, 3·35, and 3·94, and ^{13}C NMR spectra (C=O at δ 205·6; three CH—O at 47·7, 48·7, and 51·1 and one quaternary C—O at δ 53·7)). The fact that the diepoxy ketone arises from the monoepoxy ketone *V* (possibly by air oxidation) indicates the same, i.e. β-configuration of the epoxy group at the 2,3-position. Again, a detailed analysis of its ^{1}H NMR spectrum proved a chair form of the B-ring ($J(7α,8)$ = 12·2 and $J(7β,8)$ = 4·1 Hz) and a non-zero long-range coupling of the H-1α to the 10β-methyl group (1·0 Hz, similar to *V* and *VII*) supports this structure. Vicinal couplings in the A-ring ($J(1α,2)$ = 2·7, $J(1β,2)$ = 7·1, $J(2, 3)$ = 4·0, and $J(3, 4)$ = 2·7 Hz) do not permit an unequivocal confirmation of the configurations of both epoxy groups and suggest possible distortions of the real A-ring conformation as compared with the idealized situation on models.



VII A



V A

Typical oxidation products of α,β-unsaturated ketones *IX*–*XI* are the diastereoisomeric pairs of α- and β-epoxy ketones *XIII*, *XIV*, *XVI*, *XVII*, *XIX*, *XX*; only the ketone *XII* furnished the α-epoxy ketone *XXII* exclusively. These substances are known compounds and our NMR data agree with available values reported in the literature[11,12,16–21]. Isolated along with the epoxy ketones were some lactones as products of the Baeyer–Villiger reaction, formally corresponding to the insertion of oxygen between the carbonyl carbon and the double bond (or epoxy group).

4-Cholesten-6-one (*IX*) gave 17% of the unreacted starting compound, 28% of the α-epoxide *XIII* (ref.[16]), 35% of the β-epoxide *XIV* (refs[16,22]), and 4% of the product of the Baeyer–Villiger reaction (*XV*). The structure *XV* was derived from the NMR data. Its ^{13}C NMR spectrum reveals a lactone carbonyl (δ 173·8) and only two C—O carbons (δ 61·1 and 87·0) belonging to the epoxide moiety whereby the second shows a characteristic downfield shift due to a linkage to a further (ether) oxygen of the lactone group. In concord with the structure *XV* a single CH—O hydrogen (δ 3·43 dd, H-4) and a CH_2 group adjacent to carbonyl (δ 2·65 dd and 2·52 dd, H-7a and H-7′a) appear in the ^1H NMR spectrum. However, it is a very difficult task to establish the configuration of the epoxy group in the epoxy lactone *XV* owing to the potential flexibility of the A and B-rings and, particularly, because the second isomer was not isolated. Even though the values of the coupling constants $J(7a,8) = 11{\cdot}1$ and $J(7a', 8) = 2$ Hz define the conformation of the seven-membered B-ring, the models demonstrate that the A-ring assumes both in the α- and β-epoxy lactone two conformations of which at least one accommodates the values of the coupling constants $J(4, 3) \approx 5$ and $J(4,3') \approx 1$ Hz in each case. The values are more similar to those for the α-epoxy ketone *XIII* than for the β-epoxy ketone *XIV*.

Some time ago, Pete and Viriot-Villaume[23] studied the oxidation of 4-cholesten-6-one (*IX*) with 4-nitroperoxybenzoic acid. They obtained two products referred to as compound *A* (m.p. 126–128°C) and compound *B* (m.p. 113–116°C); no optical rotations were given. They considered four possible structures, among them also the structure *XV*, without attributing it specifically to any of the products. The ^1H NMR data reported are scarce and do not permit a reliable comparison. However, closely similar values of the m.p. of the compound *A* and our compound *XV* (128–129°C) permit the assumption that both compounds are identical.

Ahmad and Siddiqui[18] obtained on oxidation of *IX* with peroxybenzoic acid a single epoxy lactone to which they allotted the structure *XXIV*. In our case, we did not isolate it.

TABLE III

Some characteristic NMR parameters of *s-cis* and *s-trans* cholestenones

Parameter	*s-cis* (*IX, XI*)	*s-trans* (*X, XII*)
	^1H NMR	
δ(H-19)	0·96	1·18
δ(—CH=)	6·40	5·70
	^{13}C NMR	
δ(C-19)	21·0	17·3
δ(—CH=)	132·5	124·0
δ(—C=)	146·0	170·0

TABLE IV

^{13}C NMR substituent effects at skeleton carbons in 5α- and 5β-cholestane. Substituent effects are referenced either to 5α-cholestane (A) (ref.[14]) or 5β-cholestane (B) (ref.[9])

Carbon	3-oxo, 4,5-ene (A)	4-oxo, 5,6-ene (A)	6-oxo, 4,5-ene (A)	7-oxo, 5,6-ene (A)	6-oxo, 2,3; 4,5-diene (A)	3-oxo, 4α,5α-ep (A)	3-oxo, 4β,5β-ep (B)	4-oxo, 5α,6α-ep (A)	4-oxo, 5β,6β-ep (B)	6-oxo, 4α,5α-ep (A)	6-oxo, 4β,5β-ep (B)	7-oxo, 5α,6*k*-ep (A)
C-1	−3·1	−2·7	−3·3	0·0	−2·9	−5·7	−11·6	−5·8	0·1	−9·4	−7·2	−3·7
C-2	11·6	−3·0	−4·4	−0·3	100·9	6·6	11·5	−1·7	−2·6	−6·8	−6·1	−1·5
C-3	172·4	13·2	−1·4	0·0	101·4	180·2	179·6	12·5	14·4	−5·0	−4·0	−2·0
C-4	94·5	173·9	103·2	3·5	103·6	33·7	35·3	178·8	180·8	28·3	33·0	0·8
C-5	124·3	98·3	98·9	121·3	93·6	23·1	26·4	21·4	22·4	21·1	23·7	21·7
C-6	3·7	100·3	174·0	95·4	170·8	−0·1	2·2	27·8	34·8	178·4	179·4	34·9
C-7	−0·2	−0·5	13·8	170·1	13·3	−3·3	3·8	−3·6	5·3	12·7	19·7	176·2
C-8	0·0	−4·5	−1·9	9·8	−2·8	−0·2	−1·0	−6·1	−6·4	1·4	−0·7	8·2
C-9	−1·1	−5·7	−3·8	−4·8	−4·6	−4·2	5·8	−12·4	9·1	−5·8	6·1	−8·0
C-10	2·2	2·3	1·4	2·9	1·5	0·4	1·7	2·2	3·4	1·5	2·8	−0·4
C-11	0·1	0·4	0·4	0·0	0·3	0·5	0·6	0·6	0·5	−0·4	0·3	0·6
C-12	−0·6	−0·5	−0·7	−1·0	−0·8	−0·5	−1·0	−0·8	−0·8	−0·9	−1·2	−0·5
C-13	−0·2	−0·2	0·0	0·5	−0·2	−0·1	−0·2	−0·3	−0·5	0·3	−0·2	1·5
C-14	−0·8	−0·1	0·1	−6·4	−0·2	−1·1	−0·9	−0·2	−0·5	−0·5	−0·3	−4·8
C-15	−0·1	−0·1	−0·3	2·2	−0·2	0·0	−0·2	−0·2	−0·1	−0·3	−0·4	−0·3
C-16	−0·2	−0·1	−0·3	0·3	−0·3	−0·2	−0·3	−0·3	−0·2	−0·4	−0·4	0·0
C-17	−0·3	−0·3	−0·3	−1·5	−0·4	−0·2	−0·4	−0·5	−0·3	−0·4	−0·5	−1·1
C-18	−0·3	−0·3	−0·3	−0·2	−0·4	−0·2	−0·2	−0·3	−0·3	−0·3	−0·4	−0·1
C-19	5·1	9·1	8·1	5·1	5·6	4·3	−5·4	2·6	−5·5	2·3	−5·5	3·3

The action of the peroxy acid on 4-cholesten-3-one (*X*) showed an overall lesser reactivity and low tendency of this steroid to give epoxides. Along with unreacted *X* (34%) and unidentified polar fractions (33%) only 3% of the β-epoxide *XVII* (ref.[24]) and 5% of the α-epoxide *XVI* (ref.[25]) could be isolated. This low yield is in sharp contrast with the 63% yield of the epoxides *XIII* and *XIV* obtained from the 6-ketone *IX*. The most abundant individual product (9%) is thus the lactone *XVIII* arising by the Baeyer–Villiger reaction. Its structure follows from NMR data. The ^{13}C NMR spectrum revealed the presence of a lactone carbonyl (δ 173·1), a trisubstituted double bond (δ 129·4 (—CH=) and δ 130·3) (>C=)) and no further carbon of the type C—O. This means that the ether oxygen of the lactone group is at tachedto a =CH— carbon, which conclusion was confirmed by the ^{1}H NMR spectrum in which the olefinic hydrogen (H-4) appears as a doublet at δ 6·01 (split only by allylic long-range coupling with H-6 at δ 2·20) shifted by 0·30 ppm downfield as compared to the starting compound *X*.

A comparatively large proportion of unidentified polar fractions poses an important question of whether or not these fractions are formed by hydrolytic cleavage of the oxirane ring: if so, it would simulate a low yield of epoxidation and lead to an incorrect conclusion. It was thus important to verify the stability of the epoxides *XVI* and *XVII* under the rection and separation conditions. Both compounds were therefore subjected to treatment with 3-chloroperoxybenzoic and 3-chlorobenzoic acid under reaction conditions and with silica gel under the conditions of chromatography. It was found that both epoxides are stable, so that the low yield of the epoxides *XVI* and *XVII* cannot be attributed to their additional conversion into other products; the amount isolated is thus identical with the actual yield.

The next model substances contained a 5,6-double bond. The first one, 5-cholesten-4-one (*XI*, ref.[26]) yielded both 5,6-epoxides[19] *XIX* (29%) and *XX* (22%) along with a small amount (1·6%) of the enol lactone *XXI* whereas the starting material was recovered in a 21% yield. The ^{13}C NMR spectrum proved in the compound *XXI* the presence of a lactone carbonyl (δ 173·5) and a trisubstituted double bond (δ 113·8 (—CH=) and δ 155·8) (>C=)) in the original 5,6-position (^{1}H NMR: δ 5·40 dd, H-6, $J(6,7) = 5{,}4$ and $J(6,7') = 2·2$ Hz). The absence of a further C—O signal and a downfield shift of the sp^2 carbon C-5 toward δ 155·8 demonstrated clearly that the ether oxygen of the lactone group is attached to the position 5.

The last model compound, 5-cholesten-7-one (*XII*, ref.[27]) yielded 5α-cholestan-5,6α-epoxy-7-one *XXII* (27%); the corresponding 5β,6β-isomer was not found. A preparation of the compound *XXII* in 10% yield by alkaline hydrogen peroxide oxidation of *XII* was reported by Kolek and Malunowicz[17] but the m.p. given by the Polish authors differs from ours. The Polish authors report the m.p. 143 – 144·5°C whereas we found m.p. 115 – 116°C, but their ^{1}H NMR data (H-18; 0·66 s; H-19: 1·00 s; H-6: 3·00 s) are in good agreement with ours (Table I), so that the discrepancy is likely to be due to crystal polymorphism.

Along with *XXII* a minute quantity (2%) of a compound was formed which could not be obtained in pure condition and which apparently is not a direct product of the Baeyer–Villiger reaction. In its ^1H NMR spectrum only one signal is shifted from the steroid envelope – a singlet at δ 9·66 (a position typical of aldehyde); it cannot be a hydroxyl since no deuterium exchange occurs after the addition of CD_3OD. The ^{13}C NMR spectrum indicates a lactone carbonyl (δ 171·2), an aldehyde group (δ 201·7), and a C—O carbon (δ 89·8). The compound is most likely *XXIII* but the small quantity did not permit to present unequivocal proof of its structure.

The results of the above oxidations are summarized in Table V. The yields of epoxides and recovered starting compounds obtained by preparative chromatography are compared with analytical data from HPLC. The figures are in excellent agreement except for *XI* where a higher proportion of epoxides was found by the HPLC method.

We also conducted the oxidation of α,β-unsaturated ketones *IX*–*XII* and of the dienone *VI* with 3-chloroperoxybenzoic acid in situ in an NMR tube (Table VI). The original aim – to obtain information of a detailed mechanism of the reaction – could not be achieved. In ^1H and ^{13}C NMR spectra no species could be detected which would correspond to intermediary adducts of peroxy acid to ketone (only signals of 3-chloroperoxybenzoic acid or 3-chlorobenzoic acid could be observed). The experiments were therefore exploited to determine the composition of the reaction mixtures in the course of oxidation of the compounds *IX*–*XII* and *VI*. Such an analysis is conditional upon the existence of characteristic signals for olefinic and CH—O hydrogens in the starting compounds and in the products. Deuteriochloroform was used as solvent, which was particularly convenient since our previous measurements of the starting compounds and products were performed in this solvent and the positions of the relevant signals were thus known; the data occasionally published in the literature refer also to measurements in $CDCl_3$. The results are

TABLE V

Yields of epoxidation established by different analytical methods

Starting compound	Yield of recovered starting compound, %	Yield of epoxides (α + β), %
IX	17[a], 17[b]	63[a], 64[b] (*XIII* + *XIV*)
X	34[a], 37[b]	9[a], 9[b] (*XVI* + *XVII*)
XI	21[a], 21[b]	51[a], 77[b] (*XIX* + *XX*)
XII	59[a], 58[b]	27[a], 28[b] (*XXIII*)

[a] Preparative chromatography; [b] HPLC, conditions cf. Experimental. For analogous data obtained from NMR cf. Table VI.

TABLE VI

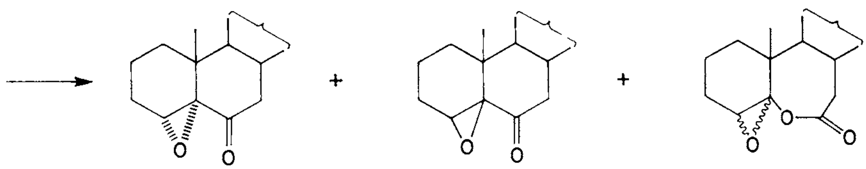
Oxidation of α,β-unsaturated ketones *IX*–*XII* and dienone *VI* with peroxy acid. Starting compound (c. 50 mg) with 20% molar excess of 3-chloroperoxybenzoic acid in 0·5 ml deuteriochloroform; NMR sample tube; composition of reaction mixtures after 48 hours at room temperature as determined by ^{1}H NMR spectra (in parentheses). Only characteristic signals of CH—O and/or —CH= protons used for quantitative estimations are given.

Starting compound recovered, %	Yields, % products				
α,β-unsaturated ketone	α-epoxy-ketone	β-epoxy-ketone	enol-lactone	epoxy-lactone	diepoxy-ketone
IX – 16 (6·40 t, H-4)	*XIII* – 24 (3·61 d, H-4)	*XIV* – 29 (3·07 t, H-4)	11[a] (5·40 t, H-4)	*XV* – 20 (3·44 dd, H-4)	—
X – 44 (5·76 d, H-4)	*XVI* – 4 (3·04 s, H-4)	*XVII* – 1 (2·98 s, H-4)	*XVIII* – 18 (6·00 d, H-4)	28[a] (4·77 s, H-4); 5[a] (4·68 s, H-4)	—
XI – 42 (6·44 dd, H-6)	*XIX* – 20 (3·60 d, H-6)	*XX* – 25 (3·19 m, H-6)	*XXI* – 9 (5·40 dd, H-6)	4[a] (3·39 d, H-6)	—
XII – 45 (5·68 d, H-6)	*XXII* – 29 (3·03 s, H-6)	—	—	26[a] (4·78 s, H-6)	—
VI – 0	*VII* – 75 (5·81–5·99 m, H-2,3; 3·78 dd, H-4)	*V* – 20 (6·79 d, H-4; 3·41 t, H-3; 3·65 m, H-2)	—	—; —	*VIII* – 5 (3·95 dd, H-4; 3·36 dd, H-3; 2·95 m, H-2)

[a] The presence of this compound was suggested only from the ^{1}H NMR spectrum of the reaction mixture but the structure was not confirmed by the isolation and characterization.

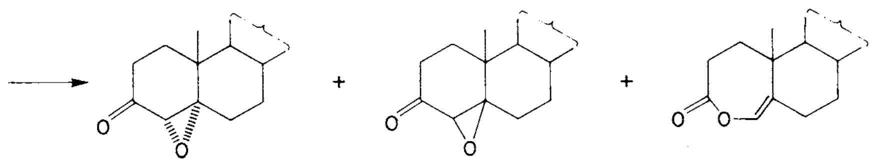
shown in Table VI where the proportion of the individual components is listed together with the characteristic ^{1}H NMR signals used for quantitative evaluation. The differences in comparison with preparative yields may be due to the method itself (no losses caused by isolation) or to a different reaction medium ($CDCl_3$ vs C_6H_6). It is of interest that in some cases the ^{1}H NMR detected further oxidation products not obtained by preparative isolation. They involve compounds of the enol lactone type (from *IX*, cf. ref.[28]) or epoxy lactone type (from *X*, *XI*, and *XII*). Their presence is assumed on the basis of their ^{1}H NMR signals in the positions characteristic of the assumed structures (by analogy and theoretical considerations).

IX



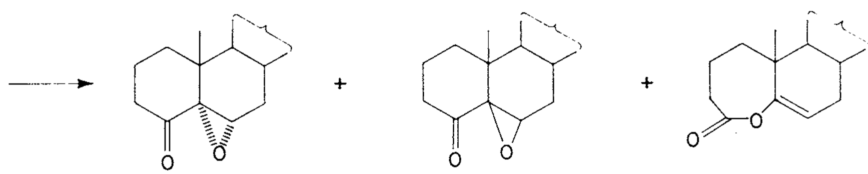
XIII *XIV* *XV*

X



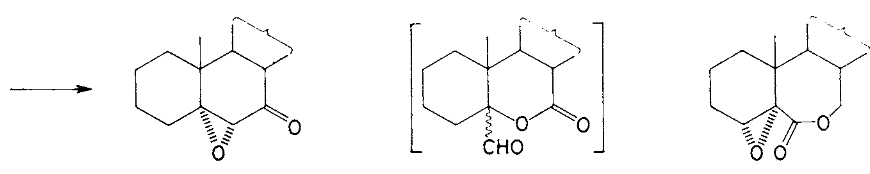
XVI *XVII* *XVIII*

XI



XIX *XX* *XXI*

XII



XXII *XXIII* *XXIV*

On the other hand, in the case of the ketone *XII* we could not detect the product of the hypothetical structure *XXIII* (see above) obtained by chromatographic separation of the reaction mixture. This compound was evidently formed in the course of the workup.

DISCUSSION AND CONCLUSIONS

It is generally believed that treatment of α,β-unsaturated ketones with peroxy acids does not result in epoxidation of the double bond but leads to an attack at the carbonyl group to provide products of the Baeyer–Villiger rearrangement[1]. Exceptions are rare[29,30]. However, in four cases out of five investigated in the present paper, the epoxidation of the double bond is an exclusive or predominant reaction.

A comparison of epoxidation of the compounds *IX*–*XII* shows (Table V) that *s-trans* α,β-unsaturated ketones react more slowly than the *s-cis* types containing the double bond at the same position. The *s-cis* ketones give higher yields of epoxides than the *s-trans* types. This difference in reactivity is probably responsible for the "anomalous" epoxidation of the double bond adjacent to the carbonyl group in the dienone *VI*.

For unsaturated, non-conjugated ketones it has been known that in non-polar solvents the carbonyl function can be hydrogen-bonded and thus direct the attack of the peroxy acid on the double bond. It has also been established that this effect is much less pronounced or virtually absent in polar solvents[31]. It may be considered that the peroxy acid coordinating with the carbonyl group of the α,β-unsaturated ketone would assume an orientation toward the double bond adjacent to carbonyl that is different in the *s-cis* and in the *s-trans* types. This may result in a more ready attack on the double bond in the *s-cis* than in the *s-trans* α,β-unsaturated ketones.

The facts reported in the present paper are in accord with this consideration. The observation that the ratio of *VII* : *V* is higher in less polar benzene than in more polar acetonitrile (also in the presence of NaF)[32] further supports this view.

Our results show that the current belief in preferential reactivity of the double bond more distant from the carbonyl group in linear conjugated dienones is not correct in this general form. Evidently, the validity of this "rule" is limited to aliphatic and cyclic *s-trans* (i.e. *s-trans* arrangement of the carbonyl group and the adjacent double bond) dienones. In *s-cis* dienones the double bond adjacent to carbonyl may react more readily than the distant double bond.

EXPERIMENTAL

Melting points were determined on a Kofler block. Optical activity measurements were carried out in chloroform with an error of ±3°. The UV spectra were measured on a Specord UV VIS spectrometer (Zeiss, Jena, G.D.R.). The infrared spectra were recorded on a Zeiss UR 20 spectrometer. The NMR spectra were measured on an FT-NMR spectrometer Varian XL-200 (^{1}H, 200 MHz; ^{13}C, 50·31 MHz) in deuteriochloroform using tetramethylsilane as internal reference. The chemical shifts and coupling constants of hydrogens were obtained by first order analysis from expanded spectra (1—2 Hz/cm). The type of the carbon atom (C, CH, CH_2, CH_3) corresponding to individual signals was determined from the "attached proton test" spectra[33], intensities of the signals and the chemical shift arguments. The mass spectra were recorded on an AEI MS 902 instrument. All TLC analyses and preparations were conducted on silical gel G (Woelm). The compounds investigated by HPLC were satisfactorily eluted and separated on an octadecyl-silica column (Separon SGX-RPS, 10 μm size, Laboratorní přístroje, Prague, filled into a 250 mm × 4 mm i.d. tube) using pure methanol as the mobile phase. They were detected refractometrically (differential refractometer Type 98·00 from Knauer, Bad Homburg, F.R.G.). All the other parts of the chromatographic equipment were from Spectra-Physics, San Jose, CA, U.S.A.: SP 8 700 solvent delivery system and SP 4 200 computing integrator.

Oxidation of 2,4-Cholestadien-6-one (*VI*)

A) 2,4-Cholestadien-6-one (*VI*, 220 mg) was dissolved in benzene (30 ml), 3-chloroperoxybenzoic acid (82% purity, 150 mg, 24% excess) was added and the solution kept at 22°C. After 18 h the reaction was complete and the solution was washed with H_2O, NaOH, H_2O, dried over $MgSO_4$ and evaporated in vacuo to leave a crystallizing oil (236 mg) which was chromatographed on silica gel.

4α,5-*Epoxy*-5α-*cholest*-2-*en*-6-*one* (VII): Petroleum ether +2% ether eluted the main product (121 mg, 53%) which was crystallized from aqueous acetone to give pure *VII* (112 mg, 49%), m.p. 120—121°C, $[\alpha]_D$ +33° (*c* 2·4). IR spectrum (CCl_4): 1 724 cm^{-1} (CO); 1 682, 1 643, 1 651 sh cm^{-1} (C=C). UV spectrum (EtOH): λ 208 nm (ε 4 800). For $C_{27}H_{42}O_2$ (398·6) calculated: 81·35% C, 10·62% H; found: 81·67% C, 10·72% H.

2β,2β-*Epoxy*-4-*cholesten*-6-*one* (V): Continued elution gave the second product (oil, 10 mg, 4%) crystallizing after treatment with acetone, m.p. 137—139°C, mass spectrum: *m/z* 398 ($M^{+\cdot}$, $C_{27}H_{42}O_2$). IR spectrum (CCl_4): 1 692, 1 619 cm^{-1} (C=C—CO); 1 269, 1 252 cm^{-1} (—O—).

B) 2,4-Cholestadien-6-one (*VI*, 220 mg) was dissolved in boiling acetonitrile (60 ml). The solution was cooled rapidly and NaF (100 mg) and 3-chloroperoxybenzoic acid (150 mg,.82%) were added immediately. After standing at 22°C for 2 h, the solution was poured in water and extracted thoroughly with ether. After washing the solution with water (10 times), Na_2SO_3, K_2CO_3 and water, the residue (246 mg) was chromatographed as under *A*).

4α,5-*Epoxy*-5α-*cholest*-2-*en*-6-*one* (VII): The first fraction gave the compound *VII* (43 mg, 19%) which yielded the pure substance from aqueous acetone (26 mg, 11%, m.p. 117—119°C). The following fraction gave a crystalline material (123 mg, 56%) which after crystallization from aqueous acetone weighed 112 mg (51%), m.p. 127—129°C and was identical (mixture m.p., TLC, IR spectrum) with the starting compound *VI*.

The next fraction (petroleum ether + 10% ether) afforded a compound (18 mg, 8%) identical in TLC migratory aptitude with *V*. Elution with ether furnished unidentified polar fractions (30 mg).

Treatment of the Compounds *IX*—*XII* with 3-Chloroperoxybenzoic Acid

The starting compound was dissolved in benzene and treated with 3-chloroperoxybenzoic acid (82% purity, 10% excess of the theoretical amount at 22°C for 22 h). The solution was then washed with H_2O, K_2CO_3, H_2O and evaporated in vacuo at max. 35°C. The residue was chromatographed on a silica gel column.

Oxidation of 4-Cholesten-6-one (*IX*)

4α,5-*Epoxy*-5α-*cholestan*-6-*one* (XIII): The ketone *IX* (300 mg) was dissolved in benzen (40 ml) and treated with peroxy acid (180 mg). Chromatography on silica gel (20 g) in petroleum ether–ether (2%) gave the epoxy ketone *XIII* (86 mg, 28%) which was crystallized from aqueous acetone to yield the pure compound (71 mg, 23% *XIII*, m.p. 143–144°C, $[\alpha]_D$ +15° (*c* 1·4). Literature[16] reports m.p. 144–145°C, $[\alpha]_D$ +12°). IR spectrum: (CCl_4): 1 725 cm^{-1} (CO), 1 428 cm^{-1} (CH_2 flanked to CO). Mass spectrum: *m/z* 400 ($M^{+\cdot}$). Continued elution furnished an oily fraction (50 mg, 17%) consisting of impure starting material (IR spectrum).

4ξ,5-*Epoxy*-6-*oxa*-B-*homo*-5ξ-*cholestan*-7-*one* (XV): Further elution provided a crystalline compound *XV* (20 mg, 4%) which was purified by TLC (petroleum ether + 30% ether) and crystallization from aqueous acetone, m.p. 128–129°C. IR spectrum (CCl_4): 1 760, 1 250, 1 089 cm^{-1} (lactone); 966, 3 010 sh cm^{-1} (epoxide). Mass spectrum *m/z* 416 ($M^{+\cdot}$). For $C_{27}H_{44}O_3$ (416·6) calculated: 77·84% C, 10·64% H; found: 77·65% C, 10·68% H.

4β,5-*Epoxy*-5β-*cholestan*-6-*one* (XIV): The last fraction (108 mg, 35%) was eluted with petroleum ether–ether (3%). Crystallization from aqueous acetone and heptane provided pure *XIV* (70 mg, 22%), m.p. 135–137°C, $[\alpha]_D$ −16° (*c* 1·3). The IR spectrum (CCl_4) showed identity with an authentic sample. Literature[16,22] gives m.p. 136–137°C, $[\alpha]_D$ −14° and m.p. 139–140°C, $[\alpha]_D$ −8·6°.

Oxidation of 4-Cholesten-3-one (*X*)

The ketone *X* (1 g) was dissolved in benzene (130 ml) and treated with peroxy acid (603 mg). The workup gave an oily product (1·1 g).

4β,5-*Epoxy*-5β-*cholestan*-3-*one* (XVII): Chromatography on silica gel (50 g) in petroleum ether–ether (3%) gave a fraction (30 mg, 3%) which on standing with petroleum ether in a refrigerator provided crystals m.p. 118–119°C, identical, according to TLC, IR spectrum and mixture m.p., with an authetic sample[34] of *XVII*. Literature[24,34] gives m.p. 116–117°C and 118–120°C.

4α,5-*Epoxy*-5α-*cholestan*-3-*one* (XVI): The following fraction was rechromatographed by TLC to yield the crude *XVI* (49 mg, 5%) which after crystallization from petroleum ether furnished the pure product (30 mg, 3%), m.p. 123·5–125·5°C, $[\alpha]_D$ −47° (*c* 1·2). Literature[25,34] gives m.p. 123–124·5°C, $[\alpha]_D$ −44° and m.p. 120–121°C, $[\alpha]_D$ −42·5°. IR spectrum, TLC and mixture m.p. show identity with an authentic sample[34].

4-*Oxa*-A-*homo*-4a-*cholesten*-3-*one* (XVIII): The following fraction (95 mg, 9%) was crystallized twice from petroleum ether to give the pure product *XVIII*, m.p. 83–84°C, $[\alpha]_D$ −3° (*c* 1·2), IR spectrum (CCl_4): 1 766, 1 168, 1 136 cm^{-1} (CO); 3 075, 1 645, 1 653 sh cm^{-1} (C=C). Mass spectrum: *m/z* 400 ($M^{+\cdot}$). For $C_{27}H_{44}O_2$ (400·7) calculated: 80·94% C, 11·07% H; found: 80·95% C, 11·44% H.

The next fraction (340 mg, 34%) was crystallized twice from aqueous acetone to yield the starting compound *X*, m.p. 80–81°C, $[\alpha]_D$ +92° (*c* 2·0). Literature[35] reports m.p. 79–80°C, $[\alpha]_D$ +88·6°. The IR spectrum, mixture m.p. and TLC proved identity with an authentic sample of *X*. Elution with petroleum ether–ether (10%) gave more polar crystalline fractions (330 mg) which were not subjected to further analysis.

Oxidation of 5-Cholesten-4-one (*XI*)

The ketone *XI* (900 mg) was dissolved in benzene (120 ml) and treated with peroxy acid (540 mg).

After the workup, the crude product was chromatographed on silica gel (100 g) in petroleum ether–ether (2%).

5,6α-*Epoxy*-5α-*cholestan*-4-*one* (XIX): The first fraction (272 mg; 29%) was crystallized from aqueous acetone to yield the pure product *XIX* (257 mg, 27%), m.p. 88–89°C, $[\alpha]_D$ −19° (*c* 1·4). Literature[19,23] reports m.p. 86–87°C and m.p. 84–86°C, $[\alpha]_D$ −16°. IR spectrum (CCl_4): 1 728 cm^{-1} (CO), 960, 938 cm^{-1} (—O—). The following fraction (185 mg, 21%) showed the migration rate to be identical with that of the starting compound (*XI*). Crystallization from aqueous acetone gave crystals (150 mg, 17%), m.p. 113·5–114·5°C. Literature[26] reports m.p. 111°C. The compound is identical with the starting compound (mixture m.p., IR).

4a-*Oxa*-A-*homo*-5-*cholesten*-4-*one* (XXI): Continued elution furnished a fraction (37 mg, 4%) which was crystallized from aqueous acetone to give the enol lactone *XXI* (15 mg, 1·6%), m.p. 113–115°C. IR spectrum (CCl_4): 1 760, 1 152, 1 683, 3 035 cm^{-1} (enol lactone). Mass spectrum: *m/z* 400 ($M^{+\bullet}$).

5,6β-*Epoxy*-5β-*cholestan*-4-*one* (XX): Elution with petroleum ether–ether (1 : 1) gave a fraction (206 mg, 22%) which after crystallization from aqueous acetone yielded pure *XX* (155 mg, 16%), m.p. 106–108°C, $[\alpha]_D$ +44° (*c* 1·4). Literature[22] reports m.p. 105–108°C, $[\alpha]_D$ +47°. IR spectrum (CCl_4): 1 720 cm^{-1} (CO), 1 144, 912 (—O—).

Oxidation of 5-Cholesten-7-one (*XII*)

The ketone *XII* (880 mg) was dissolved in benzene (120 ml) and treated with peroxy acid (530 mg). After the workup, the crude product was chromatographed on silica gel (100 g) in petroleum ether–ether (1%).

5,6α-*Epoxy*-5α-*cholestan*-7-*one* (XXII): The first fraction (250 mg, 27%) was crystallized from aqueous acetone to give the compound *XXII* (130 mg, 14%), m.p. 115–116°C, $[\alpha]_D$ +109° (*c* 1·2). IR spectrum (CCl_4): 1 702 cm^{-1} (CO). For $C_{27}H_{44}O_2$ (400·7) calculated: 80·94% C, 11·07% H; found: 80·98% C, 11·27% H. The following fraction (520 mg, 59%) was crystallized from aqueous acetone to give crystals (353 mg, 40%), m.p. 132–133°C identical (IR spectrum, mixture m.p., TLC) with the starting compound (*XII*). The last fraction (22 mg) was obtained only as oil (*XXII*).

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