PARTICIPATION BY SOME OXYGEN CONTAINING GROUPS IN HYPOBROMOUS ACID ADDITION TO DOUBLE BOND*

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$5(O)^n$ and $6(O)^{\pi,n}$ participations by some oxygen containing functional groups in the course of reaction with hypobromous acid have been studied on olefinic models of steroid type (*I* and *II*). The ability of these groups to participate has been compared on the basis of their relative reactivity with water (as externally attacking nucleophile) competing with participation. The results of the product analysis show that the ability to react with $5(O)^n$ participation decreases in the order $HO > CH_3O \simeq CH_3OCH_2O > CH_3CO_2 > HCO_2 > CH_3SO_3 \geqq (C_2H_5O)_2PO_2 > C_6H_5CO_2 > O_2NO \gg CF_3CO_2$, $C_2H_5OCO_2$; in the last two functional groups is this ability completely suppressed. The $6(O)^{\pi,n}$ participation comes in consideration only for compounds of the type *II* bearing the groups with the —X=O moiety which are ordered in the following sequence: $C_2H_5OCO_2 \simeq CH_3CO_2 \geqq (C_2H_5O)_2PO_2 > HCO_2 > C_6H_5CO_2$. The remaining functional groups (CF_3CO_2, O_2NO and CH_3SO_3) do not undergo this process. Generally, it is valid that introduction of electron-withdrawing substituents into a participating group impedes or completely suppresses its ability to participate.

The neighboring group participation may substantially influence the course of electrophilic additions as has been demonstrated on a variety of examples[1-3]. Purpuseful introduction of a neighboring group as a control element can result in remarkable regio- and stereo-selectivity and electrophilic addition may be thus utilized to introduction of a substituent into the defined position. This application has also been demonstrated on a series of examples[4-12]. On the other hand, it sometimes may become desirable to suppress the participation[13,14] or, in case of competition of several neighboring groups, to favor one of them at the expense of the second group[15,16].

In our previous papers[6-9,17-21] we were mainly concerned with participation of hydroxyl, methoxyl and acetoxyl groups and their mutual competition[15,16] in electrophilic additions to a double bond located in the steroid skeleton. We demonstrated occurrence of $5(O)^n$, $6(O)^n$, $6(O)^{\pi,n}$, $6(O)^{\pi,n}$ and $7(O)^{\pi,n}$ participations of these groups[8,9-23] (for notation *cf.* ref.[6]) and we defined steric, electronic and stereoelectronic factors[8,19-25] controlling reactivity of the individual groups as well as selection of the reaction route by an ambident ester group (*cf.* also ref.[6,19,20,26]).

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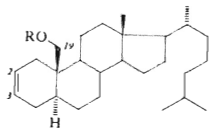
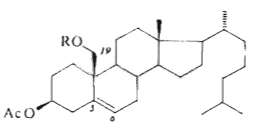
In this paper, we present a test for participation abilities of some other oxygen containing functional groups on two representative types of olefinic substrates.

In preceding papers, we investigated the reactivity of the OR groups in standard location at $C_{(19)}$ while the position of the double bond was changed systematically[6-8,17,18,21]. We thus prepared 19-substituted olefins with a double bond located successively in positions 1,2; 2,3; 3,4; 4,5; 5,6; and 6,7. Topologically, this series may be divided into compound with participating functionality in homoallylic (containing the double bond in steroid position 1,2; 4,5 and 5,6) and in bishomoallylic position (2,3-; 3,4; and 6,7-unsaturated substances). We found a remarkable difference in the reactivity of the both groups. As representatives of these groups we chose derivatives (Scheme 1) with a double bond in the position 2,3 (type *I*)





Ia, R = H
Ib, R = CH_3
Ic, R = CH_3OCH_2
Id, R = CHO
Ie, R = CH_3CO
If, R = CF_3CO
Ig, R = C_6H_5CO
Ih, R = C_2H_5OCO
Ii, R = CH_3SO_2
Ij, R = NO_2
Ik, R = $(C_2H_5O)_2PO$

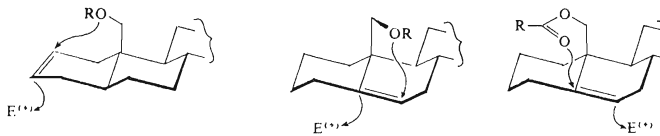
IIa, R = H
IIb, R = CH_3
IIc, R = CH_3OCH_2
IId, R = CHO
IIe, R = CH_3CO
IIf, R = CF_3CO
IIg, R = C_6H_5CO
IIh, R = C_2H_5OCO
IIi, R = CH_3SO_2
IIj, R = NO_2
IIk, R = $(C_2H_5O)_2PO$

SCHEME 1

and 5,6 (type *II*) which are most readily accessible by synthesis. In cases of OH and OCH_3 groups both types prefer $5(O)^n$ participation (somewhat more pronounced in the first type) leading to the formation of a cyclic bromo ether (Scheme 2)[6]. The acetoxy group show a notable qualitative difference: The 2,3-unsaturated derivative of the type *I* reacts predominantly with $5(O)^n$ participation in the same manner as does the corresponding alcohol or methyl ether. The competing $7(O)^{\pi,n}$ process and attack by water as external nuceophile occurs to a small extent only[19]. By contrast, the type *II* prefers $6(O)^{\pi,n}$ participation to $7(O)^{\pi,n}$ process and to external attack; $5(O)^n$ participation does not occur at all[6,19]. It appeared thus tempting to test further oxygenated functional groups with different distribution of electron density and dif-

ferent steric requirement and show their relative abilities to participate in the course of electrophilic additions.

Starting from the alcohols *Ia* (ref.[27]) and *IIa* (ref.[28]) we prepared their methyl ethers[24], methoxymethyl ethers, formates (*IId cf.* ref.[5]), acetates[6,29], trifluoroacetates, benzoates (*IIg*, *cf.* ref.[30]), ethoxycarbonates (ref.[6]), mesylates (*IIi cf.* ref.[31]), nitrates and diethyl phosphates (Scheme 1). These compounds were successively treated with hypobromous acid (generated in situ from N-bromoacetamide and perchloric acid) in aqueous dioxane and the products (Scheme 3 and 4, Table I and II) were



I 5(O)^n *II* 5(O)^n *II* 6(O)$^{\pi,n}$

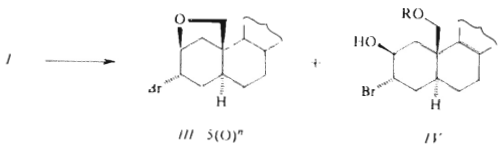
SCHEME 2

TABLE I

Yields and products of hypobromous acid addition to the model olefins *Ia*—*Ik*

Starting compound	Neighboring group	Mode of reaction, % of the total yield			Total yield %	Ref.
		5(O)^n	(product) external[a]	other		
Ia	HO	100 (*III*)	—	—	95	27
Ib	CH_3O	100	—	—	96	24
Ic	CH_3OCH_2O	100	—	—	92	—
Id	HCO_2	84	16 (*IVd*)[b]	—	98	—
Ie	CH_3CO_2	88	12 (*IVe*)[b]	—	90	6
If	CF_3CO_2	—	90 (*IVa*)	—	78	—
Ig	$C_6H_5CO_2$	38	62 (*IVg*)[b]	—	97	—
Ih	$C_2H_5OCO_2$	—	52 (*IVh*)[b]	48 (*IX*)[c]	87	6
Ii	CH_3SO_3	55	45 (*IVi*)	—	85	—
Ij	O_2NO	32	68 (*IVj*)	—	93	—
Ik	$(C_2H_5O)_2PO_2$	56	44 (*IVk*)	—	71	—

[a] Attack by external nucleophile. [b] The product may be (in part) formed also by 7(O)$^{\pi,n}$ participation for discussion *cf.* ref.[19,20]). [c] The bromohydrin *IVe* is formed by two mechanism: by attak of water as an external nucleophile (20%) and by 7(O)$^{\pi,n}$ participation (80%) (ref.[19]).



SCHEME 3: For R *cf.* SCHEME 1

isolated and subjected to spectroscopic analysis. Structures of the new compounds were established by means of their ^{1}H NMR (Tables III and IV), IR and mass spectra.

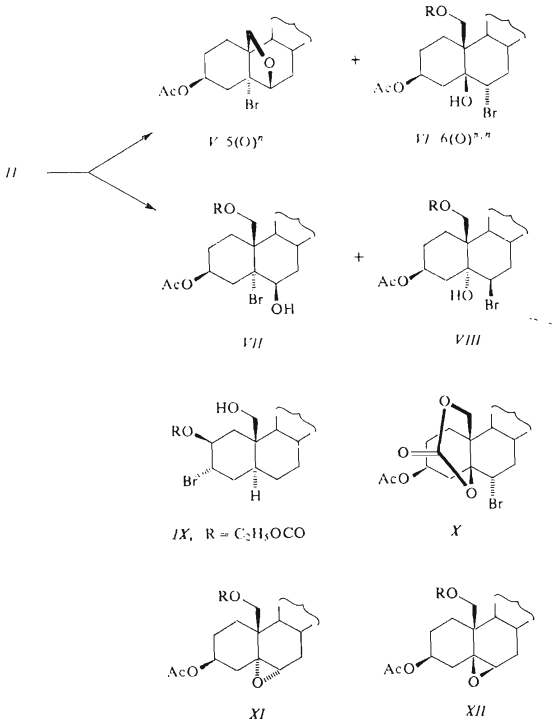
TABLE II

Yields and products of hypobromous acid addition to the model olefins *IIa*–*IIk*

Starting compound	Neighboring group	Mode of reaction, % of the total yield (Product)				Total yield %	Ref.
		5(O)ⁿ	6(O)$^{\pi,n}$	external[a]	β-Br-ion[b]		
IIa	HO	100 (*V*)	—	—	—	97	27
IIb	CH_3O	65 (*V*)	—	—	35 (*XIb*)	88	24
IIc	CH_3OCH_2O	79 (*V*)	—	21	—	92	—
IId	HCO_2	—	71 (*VId*)	[c]	[c]	87	5
IIe	CH_3CO_2	—	78 (*VIe*)	12 (*VIIe*)[d]	10 (*XIe*)	86	6
IIf	CF_3CO_2	—	—	75 (*VIIf*)	—	70	—
IIg	$C_6H_5CO_2$	—	65 (*VIg*)	21 (*VIIg*)[c]	14 (*XIg*)	96	—
IIh	$C_2H_5OCO_2$	—	53 (*VIh*) + 29 (*X*)	6 (*VIIh*)[c]	12 (*XIh*)	91	6
IIi	CH_3SO_3	68 (*V*)	—	—	32 (*XIi*)	87	—
IIj	O_2NO	—	—	73 (*VIIj*)	27 (*XIj*)	86	—
IIk	$(C_2H_5O)_2PO$	—	74 (*VIk*)	26 (*XIIk*)[c,f]	—	71	—

[a] Attack by water as an external nucleophile. [b] Product arising from 5β,6β-bromonium ions. [c] Not estimated. [d] The bromohydrin *VIIa* is formed by two mechanisms: by attack of water as an external nucleophile (67%) and by 7(O)$^{\pi,n}$ participation (33%). [e] The product may be formed (in part) also by 7(O)$^{\pi,n}$ participation (for discussion *cf.* ref.[19,20]). [f] The product may be a priori formed by the route described under *e*, and also by cyclization from *VIk*.

The 2,3-unsaturated derivatives provide two types of products: cyclic ethers *III* (*cf.* ref.[27]) arising by $5(O)^n$ participation and bromohydrins of the type *IV* (Table I). In one case only, *i.e.* in the ethyl carbonate *Ih*, the ester group is also transferred into the position 2 to form the derivative *IX*. With the trifluoroacetate *If* the addition is accompanied by saponification. With the alcohols *Ia* and ethers *Ib* and *Ic* the reaction proceeds with exclusive $5(O)^n$ participation. With the formate *Id* and acetate *Ie* the preference of this process is somewhat decreased in favor of a competing attack by water as external nucleophile and $7(O)^{n,n}$ process (*cf.* ref.[19,20]). This decrease



SCHEME 4: For *a*—*k* *cf.* SCHEME 1

can be explained by diminished nucleophilicity of the ether oxygen in the ester group due to the effect of the carbonyl oxygen. Further decrease in the nucleophilicity of the other oxygen in the ester group may be achieved by introducing fluorine atoms (the trifluoroacetoxy group in *If* does not participate at all) or aromatic ring (for the benzoate *Ig* the ratio of $5(O)^n$ to other processes is rather lower than for the acetate *Ie*). The same tendency is shown by the ethyl carbonate *Ih* where the $5(O)^n$ participation is completely suppressed. The mesylate *Ii* and the diethyl phosphate *Ik* show practically identical tendency to $5(O)^n$ participation, the nitrate *Ij* reacts in similar manner as the benzoate *Ig*. The best groups for $5(O)^n$ participation are thus hydroxyl and alkoxyl. Esterification of the hydroxyl may disfavor or completely suppress this participation.

Examination of the extent of suppression of $5(O)^n$ participation appeared particularly interesting for derivatives possessing a seven-membered ring B (*XIII*, Scheme 5) in which the stereoelectronic conditions for the $5(O)^n$ process are even more favorable[8] than in 2,3-unsaturated compounds of the type *I*. Starting from the alcohol *XIIIa* (ref.[8]), we prepared the corresponding trifluoroacetate *XIIIf* and the mesylate *XIIIi* and subjected them to treatment with hypobromous acid. It turned out that in the trifluoroacetate *XIIIf* the participation is, once again, completely sup-

TABLE III

^{1}H NMR Data of the products of hypobromous acid addition to the olefins *Ia*–*Ik*

Compound	18-H	19-H (*J*)[a]	2-H (*W*)	3-H (*W*)	Others
IVa	0·67	3·82 m (10)	4·17 m (20)	4·35 m (15)	—
IVd	0·64	4·35 and 4·64 d (12)	4·21 m (12)	4·34 m (7)	8·15 s (HCO_2)
	0·65[b]	4·17 and 4·91 d (12)[b]	5·20 m (12)[b]	4·48 m (10)[b]	
IVg	0·61	4·56 + 4·70 d (12)	4·22 m (8)	4·37 m (7)	—
		4·34 d[b]	5·18 m[b]	4·52 m[b]	
IVi	0·69	4·53 + 4·61 d (10)	4·23 m (8)	4·34 m (7)	3·02 s (CH_3SO_3)
IVj	0·65	4·69 + 4·81 d (10)	4·22 m (9)	4·32 m (8)	—
			5·23 m[b]	4·46 m[b]	
IVk	0·67	4·20 m[c]	4·42 m (15)[c]		1·34 t and 4·13 p (*J* = 7; CH_3CH_2OP)

[a] AB system. [b] The values obtained after treatment with trichloroacetyl isocyanate. [c] Overlapped by other signals.

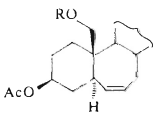
TABLE IV

^{1}H/NMR Data of the product of hypobromous acid addition to olefins *IIa - IIk*

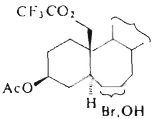
Compound	18-H	19-H (*J*)[a]	3-H (*W*)	6-H (*J* or *W*)	Others
VIg	0·53	4·63 brd s	5·27 m (13)	4·65 m (22)	2·07 s (CH_3CO_2)
VIk	0·63	4·33 brd s	4·82 m (15)	4·63 dd (5 + 12)	2·07 s (CH_3CO_2), 1·35 t and 4·13 p (J = 7·5; CH_3 CH_2 OP)
VIIc	0·73	3·84 + 4·25 d (11)	5·11 m (35)	3·95 dd (4·1 + 2·7) 5·24[b]	2·03 s (CH_3CO_2), 3·43 s (CH_3O) 4·64 + 4·69 d (J = 7, O—CH_2—O)[a]
VIIf	0·65	4·75 + 5·02 d (12)	5·45 m (30)	4·13 m (10)	2·02 s (CH_3CO_2)
VIIg	0·63	4·85 brd s	3·50 m (30)	4·18 m (9)	2·00 s (CH_3CO_2)
VIIj	0·67	4·92 + 5·07 d (12)	5·49 m (30)	4·16 m (7)	2·04 s (CH_3CO_2)
XIg	0·53	4·60 brd s	5·05 m (30)	3·03 d (3)	1·97 s (CH_3CO_2)
XIi	0·65	4·43 + 4·51 d (11)	4·99 m (32)	3·01 d (4)	2·02 s (CH_3CO_2); 3·06 s (CH_3SO_3)
XIIk	0·65	4·35 brd s	4·55 m (30)	2·99 m (6)	2·08 s (CH_3CO_2); 1·32 t and 4·10 p (J = 7, CH_3CH_2OP)

[a] AB system. [b] The values obtained after treatment with trichloroacetyl isocyanate.

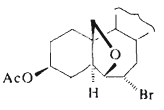
pressed and according to mass and ^{1}H NMR spectra the bromohydrin *XIV* is the sole product; its structure was not investigated in detail. On the other hand, the mesylate *XIIIi* gave the known[8] cyclic ether *XV* in practically quantitative yield. It can be thus concluded that even under particularly favorable stereoelectronic conditions the 5(O)^n participation of the hydroxyl group can be completely suppressed by trifluoroacetylation. Mesylation can do it only to a certain extent and under stereoelectronic conditions favorable for participation this effect does not occur.



XIIIa, R = H
XIIIf, R = CF_3CO
XIIIi, R = CH_3SO_2



XIV



XV

SCHEME 5

The situation is somewhat more complicated for 5,6-unsaturated derivatives *I*, due to occurence of two parallel 5(O)^n and 6(O)$^{\pi,n}$ processes which are, moreover, accompanied by the facile formation of epoxides from some intermediary bromohydrins[6]. As a result, the reaction mixture is usually more complex in this than in the first series. The alcohol *IIa* reacts with hypobromous acid in close analogy to its counterpart *Ia* and gives solely the cyclic ether *V* as a product of 5(O)^n participation (Table II). Contrasting with the first series in the methyl ether *IIb* is the 5(O)^n participation already slightly suppressed (discussion *cf.* ref.[8,24,25]); the same situation is observed with the methoxymethyl ether *IIc*. In both cases, the by-products are due to cleavage of the 5β,6β-bromonium ions. The formyloxy (*IId*) and acetoxy (*IIe*) derivatives react with predominant formation of diequatorial bromohydrins *VI* as products of 6(O)$^{\pi,n}$ participation that are accompanied by a smaller amount of compounds arising by attack of water as external nucleophile or by cleavage of a 5β,6β-bromonium ion (*VII*, *XIe*; Table II). The 5(O)^n participation is completely suppressed.

In the similar manner as in 5(O)^n participation, the 6(O)$^{\pi,n}$ process can be more or less suppressed by decreasing the nucleophilicity of the participating oxygen: thus in the trifluoroacetate *IIf* participation is completely suppressed; the only isolated product is here the bromohydrin *VIIf*. Introduction of an aromatic ring into the ester grouping (benzoate *IIg*) also results in a moderate decrease of propensity for 6(O)$^{\pi,n}$ participation. Contrasting with the negative effect on 5(O)^n process which

exerts introduction of an additional oxygen into an ester function (Table I), this structural modification tends to have a positive effect on $6(O)^{\pi,n}$ participation. The ethyl carbonate *IIh* gives rise to two products of $6(O)^{\pi,n}$ participation, namely the

TABLE V

Analytical and physical data of products of hypobromous acid addition to olefins *Ia*–*Ik*, *IIa*–*IIk*

Compound	Formula (m.w.)	Calculated/Found			M.p., °C $[\alpha]_D^{20}$
		% C	% H	% Br	
IVa	$C_{27}H_{47}BrO_2$	67·06	9·80	16·52	144–146
	(483·6)	66·85	9·92	16·39	+40°
IVd	$C_{28}H_{47}BrO_3$	65·74	9·26	15·62	102–103
	(511·6)	65·60	9·31	15·42	+27°
IVg	$C_{34}H_{51}BrO_3$	69·49	8·75	13·60	160–162
	(587·7)	69·53	8·80	13·32	+51°
IVi	$C_{28}H_{49}BrO_4S$	59·88	8·79	14·23	146–147
	(561·7)	59·63	8·85	14·39	+38°
IVj	$C_{27}H_{46}BrNO_4$	61·35	8·77	15·12	102–103
	(528·6)	61·20	8·84	15·37	+70°
IVk	$C_{31}H_{56}BrO_5P$	60·09	9·11	12·90	166–167
	(619·7)	59·84	9·06	12·72	+32°
VIg	$C_{36}H_{53}BrO_5$	66·96	8·28	12·38	oil
	(645·7)	67·15	8·19	12·70	+29°
VIk	$C_{33}H_{58}BrO_7P$	58·49	8·63	11·79	oil
	(677·7)	58·21	8·46	11·48	+12°
VIIc	$C_{31}H_{53}BrO_5$	63·58	9·12	13·64	oil
	(585·7)	63·79	9·27	13·38	−31°
VIIf	$C_{31}H_{48}BrF_3O_5$	58·40	7·59	12·53	154–156
	(637·6)	58·16	7·72	—	−23°
VIIg	$C_{36}H_{53}BrO_5$	66·96	8·28	12·38	oil
	(645·7)	66·78	8·35	12·26	+6°
VIIj	$C_{29}H_{48}BrNO_6$	59·38	8·25	13·62	108–109
	(586·6)	59·23	8·36	13·40	−20°
XIg	$C_{36}H_{52}O_5$	76·56	9·28	—	oil
	(564·8)	76·43	9·35	—	−31°
XIi	$C_{30}H_{50}O_6S$	66·88	9·35	—	oil
	(538·8)	66·64	9·28	—	−48°
XIIk	$C_{33}H_{57}O_7P$	66·42	9·63	—	oil
	(596·8)	66·29	9·80	—	−11°

bromohydrin *VIh* and the cyclic carbonate *X* (ref.[6]) whereas the external attack and formation of the 5β,6β-bromonium ion occurs here only to a small extent (similar to the acetate *IIe*). Surprisingly, the mesylate *IIi* gives an appreciable amount of a product of $5(O)^n$ participation. In the nitrate *IIj* any participation is completely suppressed, whereas for the diethyl phosphate *IIk* the contribution of the $6(O)^{n,n}$ process is comparable with that of the acetoxy group.

Generally it follows from the above mentioned facts that participation of oxygen containing groups can be more or less suppressed by introducing the electron-withdrawing substituents. The order of reactivity for $5(O)^n$ participation is then as follows: $HO > CH_3O \simeq CH_3OCH_2O > CH_3CO_2 > HCO_2 > CH_3SO_3 \geqq (C_2H_5O)_2PO_2 < C_6H_5CO_2 < O_2NO \gg CF_3CO_2$, $C_2H_5OCO_2$. Whereas in alcohols of our series the $5(O)^n$ participation is quantitative, it is completely suppressed in the trifluoroacetate and diethyl carbonate. The above order is not followed by ambident ester groups where concomitant $6(O)^{n,n}$ participation by the same group may occur. Then the selection of the reaction routes is controlled by a variety of additional factors (for discussion *cf.* ref.[6,8,19-23]). For $6(O)^{n,n}$ process the following order applies: $C_2H_5OCO_2 \simeq CH_3CO_2 \geqq (C_2H_5O)_2PO_2 > HCO_2 > C_6H_5CO_2$. The remaining functional groups do not undergo $6(O)^{n,n}$ participation.

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 50°C/26 Pa (0·2 Torr). Optical rotations were measured in chloroform with an error of ± 3°. The infrared spectra were recorded on a Zeiss UR 20 spectrometer in tetrachloromethane unless otherwise stated. The ^{1}H NMR spectra were recorded on a Varian XL-200 apparatus (FT mode) and on a Tesla BS 476 instrument (60 MHz) in deuteriochloroform at 30°C with tetramethylsilane as internal reference. Chemical shifts are given in ppm. Apparent coupling constants were obtained from the first order analysis. The mass spectra were recorded on a Jeol JMS D 100 spectrometer operating at 14–75 eV. The samples were introduced using a direct inlet at lowest temperature enabling evaporation. The elemental composition of ions was determined by accurate mass measurements. The identity of the samples prepared by different routes was checked by micture melting point determination, by thin-layer chromatography (TLC) and by infrared and ^{1}H NMR spectra. Usual work up of an ethereal solution means washing the solution with 5% aqueous hydrochloric acid, water, a 5% aqueous potassium hydrogen carbonate solution, water, drying with sodium sulfate and evaporation of the solvent *in vacuo*.

19-Methoxy-5α-cholest-2-ene (*Ic*)

The alcohol *Ia* (210 mg) was dissolved in benzene (7 ml) and stirred with N,N-dimethylaniline and chloromethyl ether (0·15 ml) at room temperature for three days. The mixture was then diluted with ether and water and the ethereal layer was worked up as usual. The residue was dissolved in a mixture of light petroleum and benzene (5 : 1) and the solution was filtered through a column of aluminum oxide. The eluate was evaporated to afford the oily ether *Ic* (165 mg), $[\alpha]_D^{20}$ +53° (*c* 2·0). For $C_{29}H_{50}O_2$ (430·7) calculated: 80·87% C, 11·70% H; found: 80·64% C, 11·56% H.

5α-Cholest-2-en-19-ol 19-Formate (*Id*)

The alcohol *Ia* (200 mg) was treated with formic acid (6 ml) at 70°C for 1 h. The mixture was cooled, diluted with water and the product was extracted with ether. The ethereal phase was washed with water, a 5% aqueous potassium hydrogen carbonate solution, water, dried with sodium sulfate and the solvent evaporated. The residue was crystallized from a mixture of methanol, acetone and water to yield the formate *Id* (155 mg) m.p. 67–68°C. ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 4·13 (1 H, d, J = 12 Hz, 19-H), 4·42 (1 H, d, J = 12 Hz, 19-H), 5·62 (2 H, m, W = = 8 Hz, 2-H and 3-H), 7·80 (1 H, s, HCO_2). For $C_{28}H_{46}O_2$ (414·7) calculated: 81·10% C, 11·18% H; found: 80·99% C, 11·25% H.

5α-Cholest-2-en-19-ol Trifluoroacetate (*If*)

The alcohol *Ia* (200 mg) was dissolved in pyridine (3 ml) and treated with trifluoroacetic anhydride (0·3 ml) at 0°C for 2 h. The mixture was then poured onto ice, the product was extracted with ether, the ethereal phase was washed 10 times with water, dried with sodium sulfate and evaporated to yield the crude unstable trifluoroacetate *Id* (*c.* 200 mg) which was immediately used in further preparation. ^{1}H NMR spectrum: 0·63 (3 H, s, 18-H), 4·33 (1 H, d, J = 12 Hz, 19-H), 4·58 (1 H, d, J = 12 Hz, 19-H), 5·63 (2 H, m, W = 9 Hz, 2-H and 3-H).

5α-Cholest-2-en-19-ol Benzoate (*Ig*)

The alcohol *Ia* (220 mg) was dissolved in pyridine (4 ml) and treated with benzoyl chloride (0·4 ml) at 0°C for 2 h and then at room temperature for 1 h. The mixture was decomposed with ice and water, the product was taken up into ether and the ethereal layer was worked up as usual. The residue was dissolved in light petroleum and filtered through a column of aluminum oxide. The eluate was evaporated to yield the oily benzoate *Ig* (185 mg). $[\alpha]_D^{20}$ +30° (*c* 4·1). ^{1}H NMR spectrum: 0·57 (3 H, s, 18-H), 4·32 (1 H, d, J = 12 Hz, 19-H), 4·58 (1 H, d, J = 12 Hz, 19-H), 5·67 (2 H, m, W = 9 Hz, 2-H and 3-H). For $C_{34}H_{50}O_2$ (490·8) calculated: 83·21% C, 10·27% H; found: 83·06% C, 10·34% H.

5α-Cholest-2-en-19-ol Methansulfonate (*Ii*)

The alcohol *Ia* (220 mg) was dissolved in pyridine (3 ml) and treated with methanesulfonyl chloride (0·2 ml) at 0°C for 30 min. The mixture was then decomposed with ice and water, the product was extracted with ether and the ethereal phase was worked up as usual to yield the oily mesylate *Ii* (*c.* 210 mg) $[\alpha]_D^{20}$ +36° (*c* 2·3). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 2·97 (3 H, s, CH_3SO_3), 4·15 (1 H, d, J = 10 Hz, 19-H), 4·45 (1 H, d, J = 10 Hz, 19-H), 5·67 (2 H, m, W = 8 Hz, 2-H and 3-H). For $C_{28}H_{48}O_3S$ (464·8) calculated: 72·36% C, 10·41% H, 6·90% S; found: 71·12% C, 10·58% H, 6·79% S.

5α-Cholest-2-en-19-ol Nitrate (*Ij*)

A solution of the alcohol *Ia* (200 mg) in chloroform (5 ml) was added to a reagent from acetic anhydride (1·2 ml) and 65% nitric acid (0·3 ml) at −30°C over a period of 15 min, the mixture was stirred at −30°C for 3 h and at −10°C for 2 h, then poured onto ice and aqueous ammonium hydroxide and stirred for 1 h. The product was extracted with ether and the ethereal phase was worked up as usual. The residue was dissolved in light petroleum and filtered through a column of aluminum oxide. The eluate was evaporated *in vacuo* to afford the oily nitrate *Ij* (180 mg), $[\alpha]_D^{20}$ +50° (*c* 2·1). ^{1}H NMR spectrum: 0·65 (3 H, s, 18-H), 4·42 (1 H, d, J = 11 Hz, 19-H),

4·65 (1 H, d, J = 11 Hz, 19-H), 5·65 (2 H, m, W = 9 Hz, 2-H and 3-H). For $C_{27}H_{45}NO_3$ (431·7) calculated: 75·13% C, 10·51% H, 3·24% N; found: 74·96% C, 10·28% H.

5α-Cholest-2-en-19-ol Diethyl Phosphate (*Ik*)

A 1·6M solution of n-butyllithium (0·6 ml) was added to a solution of the alcohol *Ia* (270 mg) in tetrahydrofuran (9 ml) at 0°C and the mixture was stirred for 15 min. Then a solution of diethyl chlorophosphate(150 mg) in tetrahydrofuran (3 ml) was added at 0°C during a period of 10 min and the mixture was then stirred at room temperature for 30 min. The mixture was poured into a 2M aqueous solution of ammonium chloride, the product was taken up into ether and the ethereal phase was worked up as usual. The residue was dissolved in a mixture of benzene and light petroleum (4 : 1) and filtered through a column of aluminum oxide. The filtrate was evaporated to yield the oily phosphate *Ik* (215 mg), $[\alpha]_D^{20}$ −34° (*c* 1·9). ^{1}H NMR spectrum: 0·70 (3 H, s, 18-H), 1·33 (3 H, t, J = 7 Hz, CH_3CH_2), 4·15 (m, overlapped by other signal, 19-H), 4·12 (p, J = Hz, CH_3CH_2), 5·65 (2 H, m, W = 14 Hz, 2-H and 3-H). For $C_{31}H_{55}O_4P$ (522·8) calculated: 71·23% C, 10·61% H; found: 71·09% C, 10·78% H).

19-Methoxymethoxy-5-cholesten-3β-ol 3-Acetate (*Ic*)

The alcohol *IIa* (400 mg) was dissolved in benzene (15 ml) and stirred with N,N-dimethylaniline (0·48 ml) and chloromethyl methyl ether (0·28 ml) at room temperature for three days. The mixture was then diluted with ether and water and the ethereal layer was worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to give the ether *IIc* (320 mg), m.p. 80–81°C, $[\alpha]_D^{20}$ −42° (*c* 1·8). ^{1}H NMR spectrum: 0·70 (3 H, s, 18-H), 2·01 (3 H, s, CH_3CO_2), 3·33 (3 H, s, CH_3O), 3·42 (1 H, d, J = 10 Hz, 19-H), 3·72 (1 H, d, J = 10 Hz, 19-H), 4·57 (2 H, s, O—CH_2—O), 4·58 (1 H, m, W = 30 Hz, 3α-H), 5·58 (1 H, W = 11 Hz, 6-H). For $C_{31}H_{52}O_4$ (488·8) calculated: 76·18% C, 10·72% H; found: 76·02% C, 10·77% H.

5-Cholesten-3β,19-diol 3-Acetate 19-Trifluoroacetate (*IIf*)

The alcohol *IIa* (500 mg) was dissolved in pyridine (5 ml) and treated with trifluoroacetic anhydride (0·5 ml) at 0°C for 2 h. The mixture was then poured onto ice and water, the product was extracted with ether and the ethereal phase was washed 10 times with water, dried and evaporated to yield the oily trifluoroacetate *IIf* (*c.* 450 mg), which was immediately used in further experiments. ^{1}H NMR spectrum: 0·67 (3 H, s, 18-H), 2·00 (3 H, s, CH_3CO_2), 4·20 (1 H, d, J = 12 Hz, 19-H), 4·72 (1 H, m, W = 30 Hz, 3α-H), 4·80 (1 H, d, J = 12 Hz, 19-H), 5·68 (1 H, m, W = = 13 Hz, 6-H).

5-Cholesten-3β,19-diol 3-Acetate 19-Nitrate (*IIj*)

A solution of the alcohol *IIa* (2 g) in chloroform (20 ml) was introduced into a reagent prepared from acetic anhydride (12 ml) and 65% nitric acid (3 ml) at −30°C in the period of 30 min, the mixture was then stirred at −30 to −20°C for 3 h, then poured onto a mixture of ice and aqueous ammonium hydroxide and stirred for 1·5 h. The product was extracted with ether and the ethereal layer was worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to afford the nitrate *IIj* (1·48 g), m.p. 144–145°C, $[\alpha]_D^{20}$ −71° *c*(2·1). ^{1}H NMR spectrum: 0·69 (3 H, s, 18-H), 2·02 (3 H, s, CH_3CO_2), 4·38 (1 H, d, J = 11 Hz, 19-H), 4·58 (1 H, m, W = 30 Hz, 3α-H), 4·72 (1 H, d, J = 11 Hz, 19-H), 5·68 (1 H, m, W = 13 Hz: 6-H). IR spectrum: 852, 1 239, 1 279, 1 638, 1 735 cm^{-1}. For $C_{29}H_{47}NO_5$ (489·7) calculated, 71·13% C, 9·67% H; found: 70·96% C, 9·80% H.

5-Cholesten-3β,19-diol 3-Acetate 19-Diethyl Phosphate (*IIk*)

A 1·6 mol l^{-1} solution of n-butyllithium in hexane (3·7 ml) was added dropwise to a stirred solution of the alcohol *IIa* (1·95 g) in tetrahydrofuran (10 ml) at 0°C over a period of 5 min, and the mixture was stirred at room temperature for 10 min. A solution of diethyl chlorophosphate (0·91 g) in tetrahydrofuran (3 ml) was added at 0°C over a period of 10 min, the mixture was stirred at room temperature for 30 min, poured into a 2 mol l^{-1} aqueous solution of ammonium chloride, the product was extracted with ether and the ethereal phase was worked up as usual. The residue was dissolved in a mixture of benzene and light petroleum (3 : 1) and filtered through a column of aluminum oxide. The filtrate was evaporated and the residue was chromatographed on a column of silica gel using a mixture of light petroleum, ether and acetone (88 : 10 : 2), which eluted lipophilic impurities, and then with a mixture of the same solvents (85 : 10 : 5) which eluted the desired oily phosphate *IIk* (720 mg), $[\alpha]_D^{20}$ −38° (*c* 2·1). ^{1}H NMR spectrum: 0·68 (3 H, s, 18-H), 1·33 (t, J = 7 Hz, CH_3CH_2), 2·03 (3 H, s, CH_3CO_2), 4·05 (m, overlapped by other signal, 19-H), 4·10 (p, J = 7 Hz, CH_3CH_2—OP), 4·15 (1 H, m, W = 30 Hz, 3α-H), 5·65 (1 H, m, W = 11 Hz, 6-H). For $C_{35}H_{59}O_7P$ (622·8) calculated: 67·50% C, 9·55% H; found: 67·32% C, 9·43% H.

The elemental analyses were carried out in the Analytical Laboratory of this Institute (head Dr J. Horáček). The IR *spectra were recorded and interpreted by Dr S. Vašíčková. The* ^{1}H NMR *spectra were recorded by Mrs J. Jelínková and Mrs M. Snopková and interpreted by Dr J. Zajíček. Mass spectra were recorded and interpreted by Drs V. Hanuš, and F. Tureček.*

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