STEREOCHEMISTRY OF SOME 5-METHYL-19-NOR-5β-CHOLEST-9-ENE DERIVATIVES*

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Hydride reduction and bromination of isomeric ketones of the Westphalen type *I*, *X* and *XVII* were investigated. Chemical behavior, physical properties and stereochemistry of the products and related substances were studied. Depending on substitution, the B-ring may assume one of two possible B_1 or B_2 half-chair conformations.

In one of our earlier papers[1] we described the preparation of the ketones *I*, *X*, and *XVII* derived from 5-methyl-19-nor-5β-cholest-9-ene. We now report the chemical and physical properties of these ketones and their derivatives. Stereochemistry of the compounds investigated constitutes a comparatively complex problem since conformations of both the A- and B-ring have to be considered. As indicated by inspection of Dreiding models the B-ring in Westphalen type steroids may exist in one of the three following steric arrangements: One boat (B_3) and two half-chair (B_1 or B_2) conformations (Fig. 1). As a matter of fact, all three forms have been successively advanced by several authors[2-5]. In most cases investigated in the present paper, conclusions may be made concerning ring- and substituent-stereochemistry.

Hydride Reduction of Ketones

The ketone *I* undergoes reduction with both lithium aluminium hydride and sodium borohydride to give two epimeric alcohols in about 1 : 1 proportion (Table I). The compound melting at 133–134°C was identified as the known[1,6] 3β-epimer *II*. This finding, by exclusion, leads to 3α-formulation *III* for the remaining epimer. Both epimers are convertible to the parent ketone *I* by oxidation. It is of interest to note that the analogous 6β-acetoxy-5-methyl-19-nor-5β-cholest-9-en-3-one is reported[7] to furnish the corresponding 3β-hydroxy derivative in 96% yield on sodium borohydride reduction in the presence of boric acid. Spectral data (Table II) show the 3β and 3α hydroxyls in *II* and *III* to be axial and equatorial, respectively. This is in agreement with a chair conformation of the A-ring (Fig. 1). It is pertinent to note

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that the chair conformation of the A-ring does not depend on the conformation of the B-ring: None of the possible conformations of the B-ring ($B_1 - B_3$) forces the A-ring to change its stable conformation.

TABLE I
Reduction of Ketones

Starting ketone	Products (% of the total yield)		Total yield %
I	*II* (49)	*III* (51)	94[a]
I	*II* (54)	*III* (46)	97[b]
X	*XI* (>99)	–	96[a]
X	*XI* (>99)	–	95[b]
XVII	*XIX* (30)	*XX* (70)	94[a,c]

[a] Reduction with sodium borohydride; [b] reduction with lithium aluminium hydride; [c] the ratio was determined by integration of 5β-methyl signals in ^{1}H-NMR spectrum.

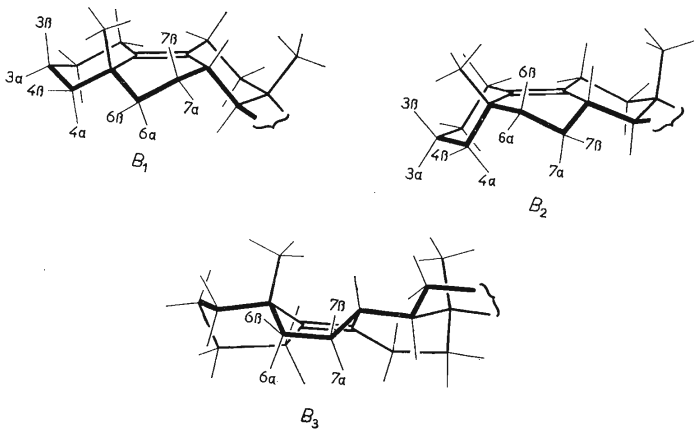
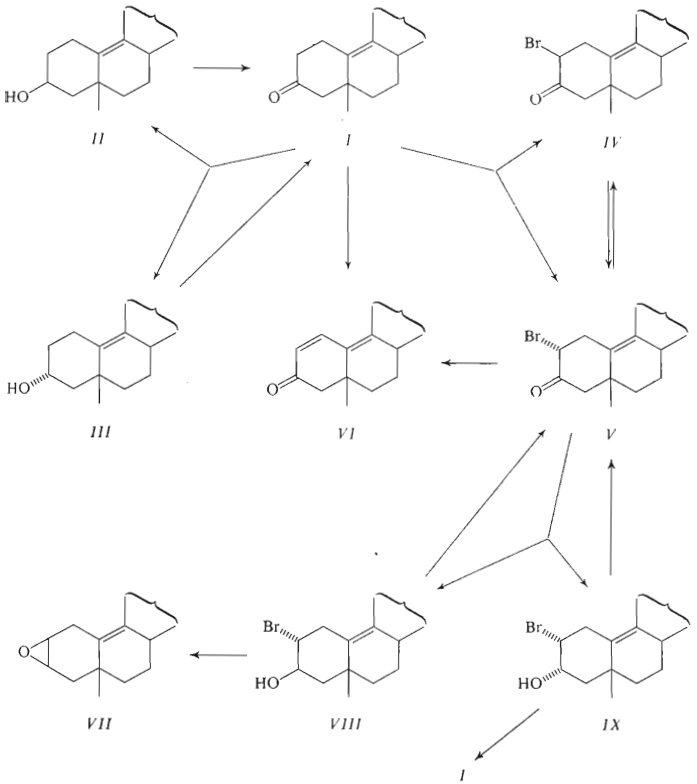
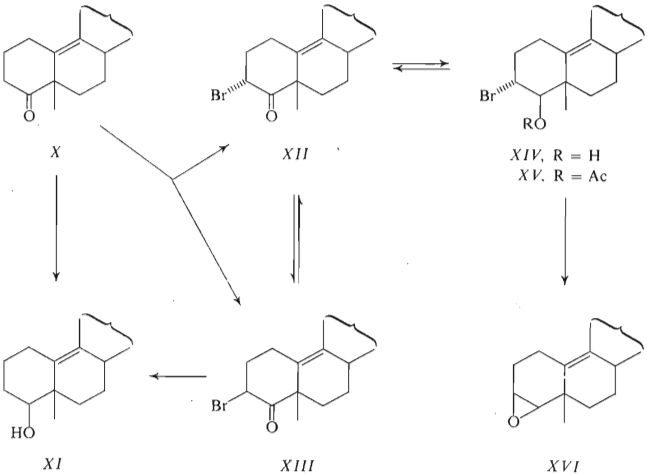


FIG. 1
Conformations of the B-Ring in Westphalen Type Steroids



Both lithium aluminum hydride and sodium borohydride reduction of the 4-oxo derivative *X* proceeds stereospecifically to yield the known[1,8] 4β-hydroxy derivative *XI* (Table I). This result is in accordance with strong steric shielding of the β-side by the adjacent 5β-methyl group and good accessibility of the α-side. The physical data (Table II) show that 4β-hydroxyl in *XI* is equatorial, again demonstrating the A-ring to be in the chair form.

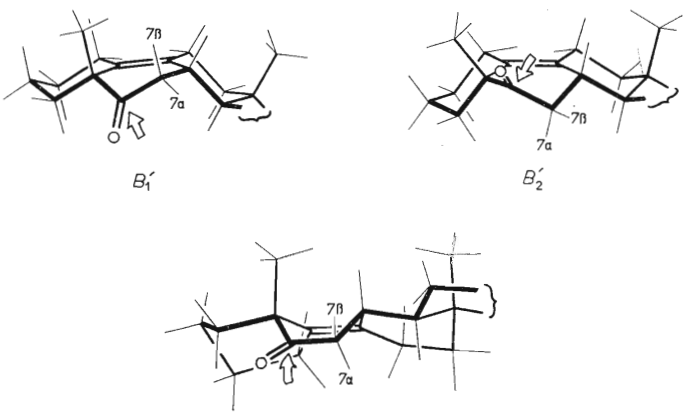


On the other hand, sodium borohydride reduction of the ketone *XVII* yields a mixture of both epimeric alcohols *XIX* and *XX*, the α-epimer *XX* being preponderant (Table I). This result differs considerably from a similar case of 4-ketone *X* with exclusive formation of a β-epimer. When comparing both cases, two points should be considered: The presence of a double bond in the B-ring and three possible conformations (B'_1, B'_2, and B'_3; Fig. 2) of the B-ring in which the 6-ketone *XVII* could react. These features are not operative in the A-ring of the 4-ketone *X*, where the double bond is absent and the A-ring assumes a normal chair conformation A_1. In the conformation B'_1 of the ketone *XVII* the approach of the reagent to the carbonyl group is shielded by the 5β-methyl group analogously as in the case of the 4-ketone. Inspection of Dreiding models shows that flattening of the B-ring by the double bond cannot influence this hindrance and that the α-side of the molecule is well accessible. Thus, high yield or exclusive formation of the β-epimer is predictable. The same argument is also valid for the boat conformation B'_3 of the B-ring. A different situation arises when the conformation B'_2 is considered. The 5β-methyl is bent away and access to the reaction center at $C_{(6)}$ from the α-side is more difficult due to interaction with 4α- and 7α-hydrogen atoms. Formation of both 6α and 6β epimers with possible predominance of the 6α-epimer *XX* may be therefore expected for this conformation. Actual formation of the both alcohols *XIX* abd *XX* (as a minor

TABLE II

^{1}H-NMR Spectra of Alcohols and Bromohydrins

Compound	18-H	19-H	Other protons (*J*, Hz)
II	0·78	1·24	3α-H: 4·10 m
III	0·76	0·92	3β-H: 4·55 m
VIII	0·80	1·20	2β-H: 4·08 m 3α-H: 4·30 m
IX	0·80	1·06	2β-H: 4·69 m ($J_{2\beta,1\xi} = 3{\cdot}5$, $J_{2\beta,1\xi} = 2{\cdot}0$, $J_{2\beta,3\beta} = 3{\cdot}5$) 3β-H: 3·74 ($J_{3\beta,2\beta} = 3{\cdot}5$, $J_{3\beta,4\beta} = 5{\cdot}5$, $J_{3\beta,4\alpha} = 11{\cdot}0$)
XI	0·79	1·00	4α-H: 3·48 ($J_{4\alpha,3\alpha} = 5{\cdot}5$, $J_{4\alpha,3\beta} = 10$)
XIV	0·78	1·02	3β-H: 4·33 ($(J_{3,2\xi} + J_{3,2\xi}) = 18$, $J_{3\beta,4\alpha} = 9{\cdot}7$) 4α-H: 3·48 ($J_{4\alpha,3\beta} = 9{\cdot}7$)
XIX	0·81	1·24	6α-H: 3·56 ($J_{6\alpha,7\alpha} = 4$, $J_{6\alpha,7\beta} = 11$)
XX	0·78	1·43	6β-H: 3·50 ($J_{6\beta,7\alpha} = 11$, $J_{6\beta,7\beta} = 3$)
XXIII	0·77	1·46	6β-H: 3·57 ($J_{6\beta,7\beta} = 3{\cdot}2$) 7β-H: 4·50 ($J_{7\beta,6\beta} = 3{\cdot}2$, $J_{7\beta,8\beta} = 3{\cdot}0$)



B_1' B_2' B_3'

FIG. 2

Conformations of the B-Ring in 6-Oxo Derivatives

and major product, respectively) indicates decisive role of the B_2' conformation in the reduction process.

The ^{1}H-NMR spectra demonstrate (Table II) the 6β-hydroxyl group in *XIX* to be equatorial and are only compatible with the half-chair conformation B_1 for the B-ring. This is in agreement with the conclusion made on analogous compounds[3,4]. Similar reasoning was applied to the epimeric 6α-hydroxy derivative *XX*. The coupling of the 6β-H is practically the same as in the 6β-hydroxy derivative thus proving equatorial conformation for the hydroxyl. The conformation of the B-ring must therefore be represented by the half-chair B_2. Moreover, in both 6-hydroxy derivatives the values of the coupling constants of 6-protons rule out a boat conformation B_3 for the ring *B*.

Bromination of Ketones

Bromination of the ketone *I* with Jacques' reagent (trimethylphenylammonium bromide perbromide) gives rise to epimeric bromo ketones *IV* and *V* (Table III). The 2-position of the bromine atom in these compounds follows from the presence of a multiplet of the CHBr in the ^{1}H-NMR spectrum. In addition, dehydrobromination of both these bromo ketones gives the dienone *VI* identical with the dehydrobromination product of *I* obtained on treatment with 2,3-dichloro-5,6-dicyanobenzoquinone. Axial conformation of the bromine substituent in *V* and equatorial one in *IV* (Fig. 3) was derived from IR and CD data (Table IV). The conformation of the A-ring in *V* remains unchanged in a variety of solvents as was demonstrated by CD measurements (Table IV).

Bromination of the 4-ketone *X* with the same reagent gives rise to two epimeric bromo ketones *XII* and *XIII* (Table III). The IR spectrum (Table IV) of the bromo ketone *XIII* in tetrachloromethane indicates equilibrium of the conformers with axial (1711 cm^{-1}) and equatorial (1734 cm^{-1}) bromine in 3 : 2 relation. Similarly, the CD spectrum in cyclohexane shows a single abnormally broad band with a maximum

TABLE III
Bromination of Ketones

Starting ketone	Products (% of the total yield)		Total yield %
I	*IV* (5)	*V* (95)	92
X	*XII* (56)	*XIII* (44)	93
XVII	*XXI* (2)	*XXII* (98)	88

TABLE IV

Physical Data of Ketones and Bromo Ketones

Compound	IR	CD		^{1}H-NMR		
	ν(C=O)	$\Delta\varepsilon$	λ, nm	5β-CH_3	CH-Br	(J, Hz)
I	1 713	−0·4	290[a]	1·02		
IV	1 734	−4·1	306[c]	0·97	4·59 m	
V	1 719	−5·1	310[a]	0·93	4·29 m	
		−5·7	317[b]			
		−4·7	314[c]			
X	1 711	+1·7	304[a]	1·25		
XII	1 728	+2·7	305[a]	1·29	4·94 dd	($J_{3\beta,2\alpha}$ = 10·5, $J_{3\beta,2\beta}$ = 5·5)
XIII	1 711	+2·8	313[a]	1·38	4·60 t	
	1 734	+1·7	338[a]			
		+6·5	324[b,d]			
		+4·7	309[c]			
		+2·1	338[c]			
XVII	1 714	−2·5	295[a]	1·46		
	1 720	−2·4	299[b]			
		−2·5	296[c]			
XXI		−2·1	325[b]			
		−1·9	325[c]			
XXII	1 719	+0·8	319[a]	1·44	4·28 d	($J_{7\beta,8\beta}$ = 2·5)
		+1·5	323[b]			
		0·96	323[c]			

[a] In methanol; [b] in cyclohexane; [c] in acetonitrile; [d] superposition of two equally intense bands at 310 and 338 nm.

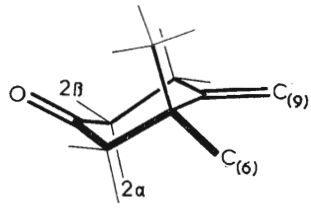


FIG. 3

Conformations of Epimeric 2-Bromo-3-oxo Derivatives *IV* and *V*

at 324 nm arising by superposition of two equally intense bands at 310 and 338 nm. Thus, this finding also indicates the presence of two conformers. In polar solvents (acetonitrile and methanol) there is a pronounced maximum at 309 and 313 nm resp., (equatorial Br) with a shoulder at 338 nm (axial Br). In these solvents, mutual proportion of the conformers is in favor of the equatorial conformer. The dependence of conformation on the polarity of the solvent is attributed to flipping of the chair form with an axial bromine atom in cyclohexane to a twisted boat form with an equatorial bromine in acetonitrile and methanol. If the B-ring is in conformation B_1, then the A-ring may occupy two twist boat conformations A_2 (axis of symmetry $C_{(2)}-C_{(5)}$) and A_3 (axis of symmetry $C_{(3)}-C_{(10)}$) (Fig. 4). The conformation A_3 can be excluded since the dihedral angle between C—Br linkage and C=O grouping is nearly 90°, a feature not compatible with IR spectrum. If conformation B_2 is presumed for the B-ring, the A-ring is forced into twist-boat conformation A_4 (axis of symmetry $C_{(1)}-C_{(4)}$). This conformation cannot be excluded on the basis of available data.

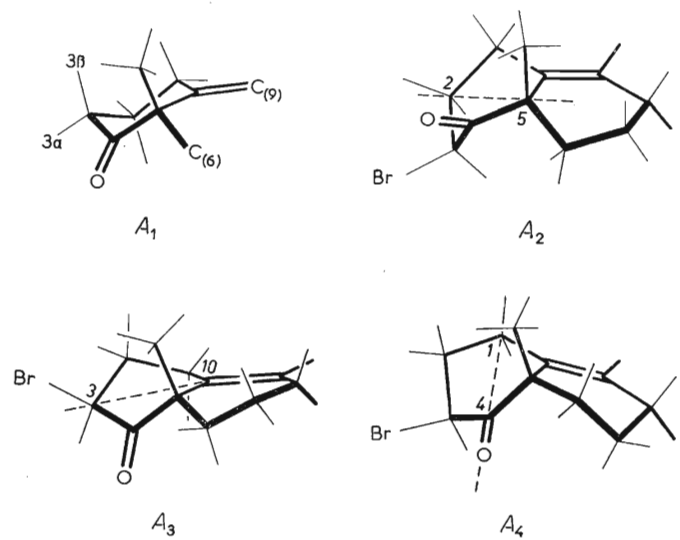
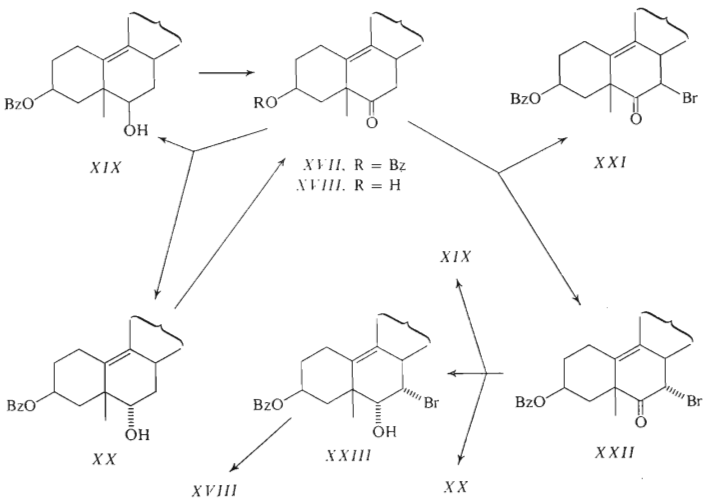


FIG. 4

Conformations of Epimeric 3-Bromo-4-Oxo Derivatives *XII* and *XIII*

Equatorial conformation of the bromine atom in *XII* is suggested by a negligible downfield shift of the 5β-methyl signal and is confirmed by the coupling constants of the 3β-H (Table IV) corresponding to coupling with 2α-H ($\emptyset_{aa} = 180°$) and 2β-H ($\emptyset_{ac} = 60°$). Equtorial conformation for the bromine atom follows also from a shift of the C=O maximum by 17 cm^{-1} in the IR spectrum and from the position of the CD maximum (Table IV). The A-ring in this epimer therefore adopts the chair conformation A_1.



Bromination of the 6-ketone *XVII* yields two bromo ketones (Table III). The bromine atom in the major product *XXII* is axial as was demonstrated by a negligible shift of the carbonyl band in the IR spectrum and by a sign and shift of the maximum by 28 nm in the CD spectrum as compared with the parent ketone (Table IV). Comparison with the parent ketone *XVII* furthermore shows no shift in the 5β-methyl protons signal and this fact is indicative of α-configuration of the bromine atom. The same conclusion can be drawn from the coupling of the 7-H (Table IV). All these facts are only compatible with the structure *XXII* with the B-ring in conformation B'_2 since in the half chair conformation B'_1 the bromine would be equatorial, and in the boat form B'_3 the $J_{7\alpha,8\beta}$ should be about 5–6 Hz (in contrast with the actual value of $J = 2{\cdot}5$ Hz). Inspection of a Dreiding model shows that the 7α-bro-

mine atom would be in strong nonbonded interaction with the 15α-hydrogen in the conformation B_1'.

The second bromo ketone could only be isolated in a very poor (c. 2%) yield. Also in this case, spectroscopic evidence demonstrates the bromine atom to be axial (Table IV). In view of the small quantity and instability of this compound, it could not be studied in detail. Presumably, this compound is the epimeric bromo ketone *XXI*.

Hydride Reduction of Bromo Ketones

Both sodium borohydride and lithium aluminum hydride reduction of the bromo ketone *V* gives a mixture of bromohydrins *VIII* and *IX* with the latter preponderating (Table V). After reduction, the configuration of the bromine atom remains unaffected since reoxidation of both *VIII* and *IX* gives the parent bromo ketone *V*. On treatment with methanolic potassium hydroxide the bromohydrin *VIII* is converted into the epoxide *VII*. The IR spectrum shows in *VIII* the absence of an intramolecular hydrogen bond; two narrow multiplets at 4·08 and 4·30 in the ^{1}H-NMR spectrum are associated with protons at positions 2 and 3 and indicate diaxial conformation of the bromine and hydroxyl; the hydroxyl group therefore has the β-configuration. The epimeric bromohydrin *IX* yields the ketone *I* upon the action of methanolic potassium hydroxide. This experiment demonstrates the 3α-configuration of the hydroxyl group.

Reduction of the bromo ketone *XII* with lithium aluminum hydride or sodium borohydride yields only the bromohydrin *XIV*. The configuration of the bromine atom in this product remains unchanged, as was demonstrated by its reoxidation

TABLE V
Reduction of Bromo Ketones

Starting compound	Products (% of the total yield)			Total yield %
V	*VIII* (19)	*IX* (81)		91[a]
V	*VIII* (22)	*IX* (78)		93[b]
XII	*XIV* (99)	—		90[a], 95[b]
XIII	*XI* (99)	—		92[a], 95[b]
XXII	*XIX* (5)	*XX* (15)	*XXIII* (80)	95[a,c]

[a] Reduction with sodium borohydride; [b] reduction with lithium aluminum hydride; [c] the ratio of alcohols *XIX* and *XX* was determined by integration of 5β-methyl signals in ^{1}H-NMR spectrum.

to *XII*. The β-configuration of the hydroxyl group follows from the formation of the epoxide *XVI* on treatment with methanolic potassium hydroxide. Axial conformations of 3β-H and 4α-H follow from the corresponding coupling constants (Table II).

Similar reduction of the bromo ketone *XIII* proceeds with loss of the bromine atom and yields the alcohol *XI* (ref.[1,8]) as the sole product.

Sodium borohydride reduction of the bromo ketone *XXII* proceeds to a small extent with loss of the bromine atom to yield a mixture of 6-epimeric alcohols *XIX* and *XX*. The mutual proportion of these components (Table V) is about the same as in the reduction of the ketone *XVII* with the same reagent. The main product, however, is the bromohydrin *XXIII* the formation of which is due to stereospecific reduction of the keto group. The configuration of the bromine atom in *XXIII* was confirmed by reoxidation to the parent bromo ketone *XXII* and the *cis*-configuration of the hydroxy group and the bromine atom was proved by alkali treatment of *XXIII* leading to the ketone *XVIII*. Of the two possible half-chair conformations of the B-ring, the dihedral angle between 7β-H and 8β-H is c. 30° and 60° in the chair conformations B_1 and B_2, respectively. The value of the corresponding coupling constant $J_{7\beta,8\beta}$ (3 Hz) is in agreement with the conformation B_2. The conformation B_1 is less favorable due to the presence of a strong non-bonded interaction between the 7α-bromine atom and the 15α-hydrogen. In addition, interactions of 6α-hydroxyl with 4α-H and 14α-H are also present. In the conformation with the B-ring in the boat form B_3, the bromine atom and the hydroxy group, as well as 6β and 7β protons would be eclipsed. The value of the $J_{6\beta,7\beta}$ was found to be 3·2 Hz and is not in accord with this conformation.

CONCLUSION

It was claimed by Jones and Summers[2] that the B-ring in Westphalen diol possesses the B_2 conformation. This statement was later disproved by Narayanan and Iyer[3] and Mousseron–Canet and Guilleux[4] who were able to prove the existence of the B_1 conformation for Westphalen diol and some of its derivatives.

Our results prove the existence of alternative half-chair conformations B_1 and B_2 in B-ring substituted compounds; which alternative is present in each particular case depends on the given structural features. French authors[5] later found the B-ring in some 6β-fluoro derivatives to be in the boat conformation B_3. Owing to the small size of the fluorine atom, the results of the French authors indicate that 9(10)-unsaturated 5β-methyl-19-nor-steroids lacking substitution in the B-ring might generally adopt boat conformation B_3 of the B-ring. In B-ring substituted compounds investigated in the present paper a B-ring boat was not found; presumably, this is due to substitution of the B-ring differing from that present in the substances of the French authors.

EXPERIMENTAL

Melting points were determined on a Kofler block. Analytical samples were dried at 50°C/0·2 Torr. Optical measurements were carried out in chloroform with an error of ±1°. 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 HA-100 instrument 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 an AEI MS 907 mass spectrometer. The CD spectra were recorded on a Dichrographe II (Jouan–Roussel) in methanol cyclohexane and acetonitrile. The identity of samples prepared by different routes was checked by mixture 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, 5% aqueous potassium hydrogen carbonate solution, water, drying with sodium sulfate and evaporation of the solvent *in vacuo*.

Bromination of Ketones *I*, *X* and *XVII*

The ketone (200 mg) was dissolved in 1,2-dimethoxyethane (3 ml) and treated with Jacques' reagent (200 mg) for 5 min at room temperature while stirring. The mixture was diluted with ether and water, the ethereal solution was washed with water, 5% aqueous potassium hydrogen carbonate solution, 5% aqueous sodium thiosulfate solution, water, dried and evaporated. The residue was chromatographed on four preparative silica gel plates (20 × 20 cm) with a mixture of light petroleum and benzene (1 : 1) as eluent. The lipophilic components were β-bromo ketones, the polar ones were α-bromo ketones. Yields of products are given in Table III, analytical and physical data in Table VI.

Reduction of Ketones *I*, *X*, *XVII* and Bromo ketones *V*, *XII*, *XIII*, *XXII*

Method A: The ketone (100 mg) was dissolved in ethanol (2—5 ml) and reduced with sodium borohydride (50 mg) at room temperature overnight. The mixture was decomposed with acetic acid, diluted with ether and water, and the organic layer was worked up as usual. The residue was chromatographed on two preparative silica gel plates (20 × 20 cm) using a mixture of benzene and ether (95 : 5) as eluent. The corresponding zones were collected, eluted with ether and evaporated. The results are given in Tables I and V. Analytical and physical data are given in Table VI.

Method B: The ketone (100 mg) was dissolved in ether (3 ml) and reduced with lithium aluminum hydride (50 mg) at room temperature overnight. The mixture was decomposed with saturated sodium sulfate solution, the product extracted with ether and the ethereal solution was worked up as usual. The residue was chromatographed as given under *A*.

5-Methyl-19-nor-5β-cholest-9-en-6-one (*I*)

a) *From* 5-*methyl*-19-*nor*-5β-*cholest*-9-*en*-3α-*ol* (III): The alcohol *III* (25 mg) was dissolved in acetone (3 ml) and treated with excess of Jones' reagent at room temperature for 5 min. The excess oxidizing agent was decomposed with methanol, ether was added and the solution was washed with water, 5% aqueous potassium hydrogen carbonate solution, water, dried and the solvent evaporated to give the noncrystalline ketone *I* (21 mg), $[\alpha]_D^{20}$ +21° in accordance with the literature[1].

b) *From* 2α-*bromo*-5-*methyl*-19-*nor*-5β-*cholest*-9-*en*-3α-*ol* (IX): A solution of the bromohydrin *IX* (200 mg) and potassium hydroxide (200 mg) in methanol (15 ml) and benzene (10 ml) was refluxed for 3 h. Solvents were distilled off under reduced pressure, the residue was treated with ether and water, the organic layer was washed with water, dried and evaporated to yield the noncrystalline ketone *I* (125 mg), $[\alpha]_D^{20}$ +18°.

2α-Bromo-5-methyl-19-nor-5β-cholest-9-en-3-one (*V*)

a) *From* 2α-*bromo*-5-*methyl*-19-*nor*-5β-*cholest*-9-*en*-3β-*ol* (VIII): The bromohydrin *VIII* (11 mg) was dissolved in acetone (1 ml) and treated with excess of Jones' reagent for 5 min at room

TABLE VI

Analytical and Physical Data of Products of Bromination of Ketones and Reduction of Ketones and Bromo Ketones

Compound	Formula (m.w.)	Calculated/Found %C	% H	% Br	M.p., °C $[\alpha]_D^{20}$
III	$C_{27}H_{46}O$	83·87	11·99	—	oil
	(386·7)	83·71	11·93		+29°
IV	$C_{27}H_{43}BrO$	69·96	9·35	17·24	—
	(463·6)	69·82	9·31	—	—
V	$C_{27}H_{43}BrO$	69·96	9·35	17·24	101—102
	(463·6)	69·87	9·37	17·48	−144°
VIII	$C_{27}H_{45}BrO$	69·66	9·74	17·16	oil
	(465·6)	69·52	9·70	17·35	+25°
IX	$C_{27}H_{45}BrO$	69·66	9·74	17·16	oil
	(465·6)	69·53	9·70	17·31	+40°
XII	$C_{27}H_{43}BrO$	69·96	9·35	17·24	128—129
	(463·6)	69·81	9·23	17·50	+13°
XIII	$C_{27}H_{43}BrO$	69·96	9·35	17·24	oil
	(463·6)	69·89	9·31	17·35	+121°
XIV	$C_{27}H_{45}BrO$	69·66	9·74	17·16	oil
	(465·6)	69·51	9·75	17·30	−31°
XXI	$C_{34}H_{47}BrO_3$	69·97	8·12	13·69	oil
	(583·7)	69·85	8·01	—	—
XXII	$C_{34}H_{47}BrO_3$	69·97	8·12	13·69	oil
	(583·7)	69·74	8·12	13·82	+55°
XXIII	$C_{34}H_{49}BrO_3$	69·73	8·43	13·64	oil
	(585·7)	69·58	8·37	13·81	+25°

temperature. The excess oxidizing agent was decomposed with methanol, the mixture treated with ether and water, the organic layer was washed with water, 5% aqueous potassium hydrogen carbonate solution, water, dried and the solvent evaporated. The residue was crystallized from a mixture of acetone, methanol and water to yield the bromo ketone *V* (4 mg), m.p. 98—100°C.

b) *From 2α-bromo-5-methyl-19-nor-5β-cholest-9-en-3α-ol* (IX): The bromohydrin *IX* (30 mg) was oxidized with Jones' reagent in acetone (1 ml) as given under *a*). Crystallization of the crude reaction product gave the bromo ketone *V* (14 mg), m.p. 101—102°C.

5-Methyl-19-nor-5β-cholest-1,9-dien-3-one (*VI*)

a) *From 5-methyl-19-nor-5β-cholest-9-en-3-one* (I): A stirred solution of the ketone *I* (230 mg) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (200 mg) in toluene (7 ml) was refluxed under nitrogen for 8 h. The mixture was filtered, the filtrate was diluted with ether, and the ethereal solution was worked up as usual. The residue was chromatographed on three preparative silica gel plates (20 × 20 cm) using a mixture of light petroleum and benzene (1 : 1) as eluent. Corresponding zones were worked up to yield the noncrystalline dienone *VI* (140 mg), $[\alpha]_D^{20}$ +178° (*c* 2·7). IR spectrum: 1611, 1678 cm^{-1}. ^{1}H-NMR spectrum: 0·84 (3 H, s, 18-H), 1·11 (3 H, s, 5β-methyl). For $C_{27}H_{42}O$ (382·6) calculated: 84·75% C, 11·06% H; found: 84·60% C, 11·12% H.

b) *From 2α-bromo-5-methyl-19-nor-5β-cholest-9-en-3-one* (V): The bromo ketone *V* (100 mg) was refluxed in *sym*-collidine (2 ml) for 4 h. The mixture was treated with ether and 5% aqueous hydrochloric acid solution, and the ethereal layer was worked up as usual. The residue was chromatographed on one preparative plate of silica gel (20 × 20 cm) with benzene as eluent. The corresponding zone was eluted to yield the dienone *VI* (49 mg), $[\alpha]_D^{20}$ +175° (*c* 2·0).

3α-Bromo-5-methyl-19-nor-5β-cholest-9-en-4-one (*XII*)

The bromohydrin *XIV* (20 mg) in acetone (1·5 ml) was oxidized with excess of Jones' reagent for 5 min at room temperature. The mixture was worked up as given for *V* and the residue crystallized from a mixture of acetone, methanol and water to afford the bromo ketone *XII* (12 mg), m.p. 127—128°C.

3α-Bromo-5-methyl-19-nor-5β-cholest-9-en-4β-ol 4-acetate (*XV*)

The bromohydrin *XIV* (80 mg) was dissolved in pyridine (1 ml) and acetylated with acetic anhydride (0·6 ml) at room temperature overnight. The mixture was decomposed with ice, the product was taken up in ether and the ethereal solution was worked up as usual. The residue was crystallized from a mixture of acetone, methanol and water to yield the acetate *XV* (67 mg), m.p. 137—138°C, $[\alpha]_D^{20}$ +38° (*c* 1·6). IR spectrum: 1236, 1747 sh, 1756 cm^{-1}. ^{1}H-NMR spectrum: 0·77 (3 H, s, 18-H), 1·03 (3 H, s, 5β-methyl), 2·11 (3 H, s, CH_3COO—), 4·25 (1 H, m, 3β-H), 5·02 (1 H, d, $J_{4\alpha,3\beta}$ = 11 Hz, 4α-H). For $C_{29}H_{47}BrO_2$ (507·6) calculated: 68·62% C, 9·33% H, 15·74% Br; found: 68·70% C, 9·33% H, 15·88% Br.

3β,4β-Epoxy-5-methyl-19-nor-5β-cholest-9-ene (*XVI*)

A solution of bromohydrin *XIV* (20 mg) and potassium hydroxide (100 mg) in methanol (5 ml) was refluxed for 2 h. The solvents were distilled off under reduced pressure, the residue was treated with ether and water, the organic layer was washed with water, dried and evaporated to yield the noncrystalline epoxide *XVI* (14 mg) $[\alpha]_D^{20}$ +127° (*c* 1·4). ^{1}H-NMR spectrum: 0·80

(3 H, s, 18-H), 1·16 (3 H, s, 5β-methyl), 3·23 (1 H, s, 3α-H), 2·74 (1 H, $J_{4\alpha,3\alpha} = 3·6$ Hz, 4α-H). For $C_{27}H_{44}O$ (384·7) calculated: 84·31% C, 11·53% H; found: 84·42% C, 11·57% H.

3β-Hydroxy-5-methyl-19-nor-5β-cholest-9-en-6-one (*XVIII*)

a) *From* 3β-*benzoyloxy*-5-*methyl*-19-*nor*-5β-*cholest*-9-*en*-6-*one* (XVII): A solution of the benzoate *XVII* (130 mg) and potassium hydroxide (100 mg) in methanol (10 ml) was refluxed for 1 h. The solvents were distilled off under reduced pressure, the residue was treated with ether and water, the ethereal layer was washed with water, dried and evaporated to yield the hydroxy ketone *XVIII* (73 mg), m.p. 70–72°C. ^{1}H-NMR spectrum: 0·75 (3 H, s, 18-H), 1·45 (3 H, s, 5β-methyl). For $C_{27}H_{44}O_2$ (400·7) calculated: 80·94% C, 11·07% H; found: 80·81% C, 11·09% H.

b) *From* 7α-*bromo*-5-*methyl*-19-*nor*-5β-*cholest*-9-*en*-3β,6α-*diol* 3-*monobenzoate* (XXIII): a solution of the bromohydrin *XXIII* (30 mg) and potassium hydroxide (100 mg) in methanol (6 ml) was refluxed for 2 h. The mixture was worked up as given under *a*) to yield the hydroxy ketone *XVIII* (14 mg), m.p. 69–71°C.

3β-Benzoyloxy-7α-bromo-5-methyl-19-nor-5β-cholest-9-en-6-one (*XXII*)

The bromohydrin *XXIII* (25 mg) was dissolved in acetone (1 ml) and treated with excess of Jones' reagent for 5 min at room temperature. The mixture was worked up as given for *V* to yield the noncrystalline bromo ketone *XXII* (22 mg), $[\alpha]_D^{20}$ +21° (*c* 2·0).

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