REACTIONS OF SOME DIBROMOSTEROIDS WITH SILVER SALTS IN THE PRESENCE OF WATER

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The transformation of vicinal dibromides under the effect of aqueous solutions of silver salts in the presence of water was investigated. The structures of the products were solved using IR, mass and ^{1}H-NMR spectrometry, which showed that diequatorial dibromides give rise to hydroxy derivatives, while the axial dibromides gave a mixture of epoxides in which β-isomer predominated.

The preparation of epoxides from vicinal dihalogenides has been described by Greene[1], but it has been only sporadically[2] used preparatively. In this study our aim was to check the utilizability of this method for further steroidal dibromides.

We prepared the starting dibromides from olefins by addition of bromine, which – in some cases – was followed by isomerization[3]. The physico-chemical data of these substances were either in agreement with the literature data, or – in the case of as yet undescribed substances – with the values expected for the given structures (see Table I and Experimental). For comparison we prepared α-epoxides by oxidation of the same olefins with 3-chloroperbenzoic acid. The corresponding β-epoxides were obtained by chromatography of the mother liquors after crystallization of α-epoxides, or by addition of hypobromous acid and dehydrobromination of the bromohydrins thus formed (Table I).

The reaction itself was carried out by mixing a substrate solution in tetrahydrofuran with an aqueous silver fluoride solution at room temperature. After working up the reaction mixture we isolated chromatographically substances identical to authentic epoxides in their polarity. Their structure was proved by comparison of their IR spectra and mixture melting points. Thus, in the transformation of 1α,2β-dibromide[4] *I* we obtained β-epoxide *II* in 50% yield, from 2β,3α-dibromide[3] *VI* we obtained 80% of β-epoxide[5] *VII* and 5% of α-epoxide[5] *VIII*. Under these conditions 3α,4β-dibromide[3] *IX* changed slowly to a mixture of products among which 3,4-epoxides[6] *X* and *XII* could not be detected in spite of the fact that under these conditions bromohydrin *XI* is converted smoothly to β-epoxide *X*. The reaction of

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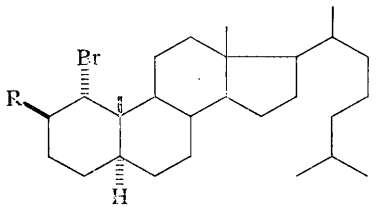
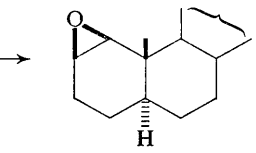
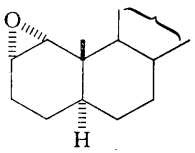


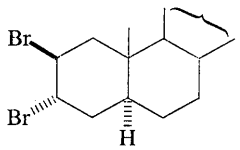
I, R = Br
III, R = OH
IV, R = F



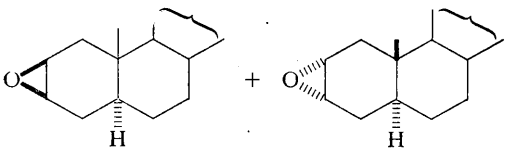
II



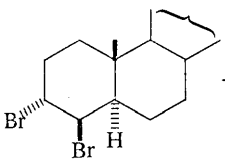
V



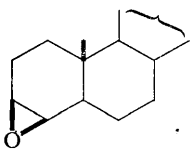
VI



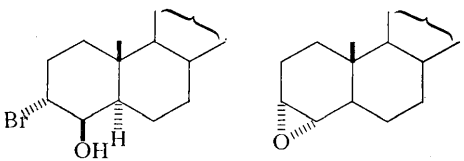
VII + *VIII*



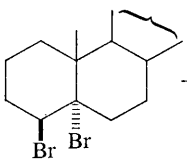
IX



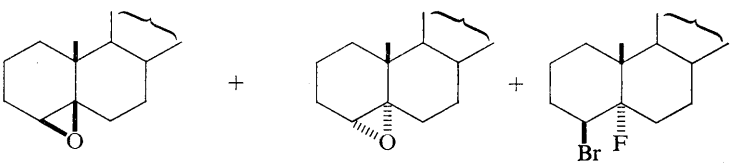
X



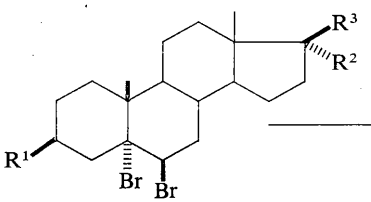
XI + *XII*

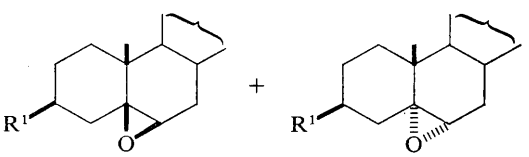


XIII



XIV + *XV* + *XVI*





XVII, $R^1 = R^2 = H$, $R^3 = i\text{-}C_8H_{17}$
XX, $R^1 = OH$, $R^2 + R^3 = O$
XXIII, $R^1 = OH$, $R^2 = H$, $R^3 = i\text{-}C_8H_{17}$

XVIII, $R^1 = R^2 = H$, $R^3 = i\text{-}C_8H_{17}$
XXI, $R^1 = OH$, $R^2 + R^3 = O$

XIX, $R^1 = R^2 = H$, $R^3 = i\text{-}C_8H_{17}$
XXII, $R^1 = OH$, $R^2 + R^3 = O$

TABLE I

^{1}H-NMR Data on m,n-Disubstituted Steroids

The spectra were measured in deuteriochloroform using tetramethylsilane as internal reference and a Varian HA-100 (100 MHz) instrument. Chemical shifts are in δ-units (p.p.m..) and the coupling constants in Hz. The spectra of some of the listed substances have been discussed earlier (see references in the first column).

Compound	C_m—H	C_n—H	C_{19}—H[a]	C_{18}—H[b]	C_{21}—H[c]	$C_{26,27}$—H[c]
Dibromides						
I	4·64[d]	4·99[e]	1·36	0·66	0·90	0·87
VI[22,23]	— 4·60[f]	—	1·12	0·64	0·88	0·84
IX	4·43[h]	4·86[g]	1·09	0·65	0·90	0·86
XIII	4·96[i]	—	1·41	0·64	0·89	0·85
XVII[10,22]	—	4·88[j]	1·41	0·71	0·91	0·86
XXIV	4·63[k]	4·47[k]	1·06	0·72	0·89	0·86
XXVIII	4·61[l]	4·41[m]	0·80	1·16	—	—
XXXII[22,23]	3·85 to	4·45[f]	0·86	0·64	0·90	0·87
XXXIII	— 4·13[f]	—	0·89	0·65	0·89	0·86
XXXV[ae]	— 4·43[n]	—	0·90	0·65	0·91	0·86
Fluorobromides						
IV	4·24[o]	5·00[p]	1·08[q]	0·65	0·89	0·85
XVI	4·11[r]	—	1·30	0·65	0·90	0·86
Bromohydrins						
III	4·20[d]	4·40[e]	1·19	0·67	0·91	0·87
XI	4·43[h]	3·86[s]	1·02	0·65	0·91	0·86
XXVI	3·89[k]	4·23[k]	1·00	0·71	0·91	0·86
XXX	— 4·70[f]	—	0·80	1·05	—	—
Epoxides						
II	— 3·08[f]	—	0·89	0·70	0·91	0·87
V	2·99[t]	3·05[u]	0·89	0·66	0·90	0·86
VII[24]	— 3·12[f]	—	0·84	0·64	0·90	0·86
VIII[24]	— 3·10[f]	—	0·76	0·64	0·90	0·86
X	3·08[v]	2·92[w]	0·94	0·64	0·89	0·86

TABLE I
(*Continued*)

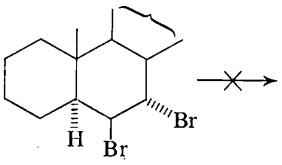
Compound	C_m—H	C_n—H	C_{19}—H[a]	C_{18}—H[b]	C_{21}—H[c]	$C_{26,27}$—H[c]
XII[25]	3·13[e]	2·67[t]	0·76	0·64	0·89	0·85
XIV[26,27]	2·89[x]	—	0·98	0·67	0·90	0·85
XV[26,28]	2·91[x]	—	1·04	0·68	0·90	0·85
XVIII[27]	—	2·99[y]	0·98	0·65	0·89	0·86
XIX[28]	—	2·87[q]	1·04	0·61	0·89	0·86
XXI[29]	—	3·11[y]	1·03	0·85	—	—
XXII[29]	—	2·93[q]	1·09	0·82	—	—
XXV	— 2·89[f]	—	0·89	0·70	0·90	0·86
XXVII	2·68[t]	3·02[z]	0·72	0·68	0·88	0·84
XXIX	3·45[aa]	3·13[ab]	0·81	0·77	—	—
XXXI	3·31[ac]	3·06[ad]	0·79	0·72	—	—

[a] Singlet, with the exception of compound *IV*; [b] singlet; [c] doublet with $J = 6-6,5$ Hz; [d] broad singlet, $W_{1/2} = 5$ Hz; [e] multiplet, $W_{1/2} = 9$ Hz; [f] overlapping signals; [g] doublet of triplets, $J = 2·2$ and $2·5$ Hz; [h] multiplet, $W_{1/2} = 7$ Hz; [i] broad doublet, $J = 4·2$ Hz; [j] quartet, $J = 4$ and $1·8$ Hz; [k] triplet, $J = 2·8$ Hz; [l] broad triplet, $J = 1·5$ and 8 Hz; [m] doublet, $J = 1·5$ Hz; [n] quartet, 2 protons; [o] broad doublet, $J = 8$ Hz; [p] broad doublet, $J_{H,F} = 48·5$ Hz; [q] doublet, $J = 4·5$ Hz; [r] broad doublet, $J_{H,F} = 9$ Hz, $J_{4,3\alpha} + J_{4,3\beta} = 6$ Hz; [s] multiplet, $W_{1/2} = 6$ Hz; [t] doublet, $J = 4$ Hz; [u] multiplet partly overlapping the neighbouring signal; [v] broad triplet, $J = 4$ Hz; [w] broad doublet, $J = 4$ Hz; [x] triplet, $J = 2·2$ Hz; [y] doublet, $J = 3$ Hz; [z] doublet of doublets, $J = 4$ and 2 Hz; [aa] triplet, $J = 3·2$ Hz; [ab] doublet, $J = 3·2$ Hz; [ac] broad doublet, $J = 3·1$ Hz; [ad] doublet, $J = 3·1$ Hz; [ae] further signals: 0·94 (d, *J* 6 Hz, 3 H), 1·99 (s, 3 H), 4·69 (mt, 1 H), 5·39 (mt, 2 H), p.p.m.

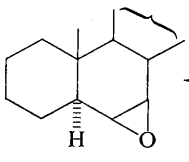
4β,5α-dibromide[7] *XIII* again afforded a mixture of several components, in which β-epoxide[8] *XIV* prevailed over α-epoxide[8] *XV* (44% and 5%, resp.). The transformation of 5α,6β-dibromides[9,10] *XVII* and *XX* gave 29% of β-epoxides[11,12] *XVIII* and *XXI* and 6% od α-epoxides[12,13] *XIX* and *XXII* (transformation of dibromide *XXIII* was described in detail in ref.[2]). From the reaction of 6β,7α-dibromide *XXIV* we did not obtain any of the 6,7-epoxides notwithstanding the fact that the corresponding bromohydrin *XXVI* is converted smoothly to β-epoxide *XXV* under the same conditions. In the case of 16β,17α-disubstituted substrates and the reaction with silver fluoride epoxides cannot be prepared either from dibromide *XXVIII* or bromohydrin *XXX*. This reaction is also quite useless in the case of diequatorial dibromides[2,3] *XXXII* to *XXXIV* and 22,23-dibromide[14] *XXXV* which are rather stable under the

reaction conditions; the use of more drastic conditions did not lead to the formation of epoxides either.

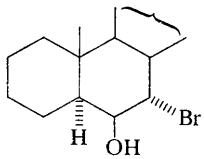
The by-products were not analysed in greater detail, but on the basis of their polarity and IR spectra the conclusion may be drawn that in the majority of cases they are unsaturated hydroxy steroids and dienes. Among the by-products attention was paid to only those containing fluorine. We found that the products did not contain detectable amounts of fluorohydrins (mass spectrometry), but small amounts of fluorobromides were isolated. To substance *IV* the structure of 1α-bromo-2β-fluoro--5α-cholestane was assigned on the basis of mass spectrometry and ^{1}H-NMR spec-



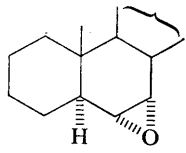
XXIV



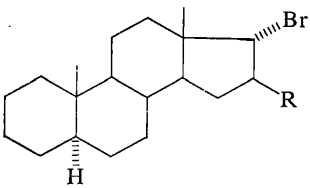
XXV



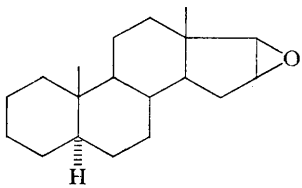
XXVI



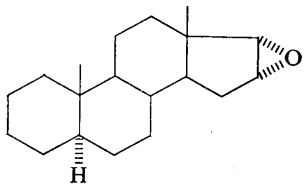
XXVII



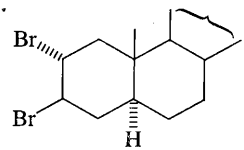
XXVIII, R = Br
XXX, R = OH



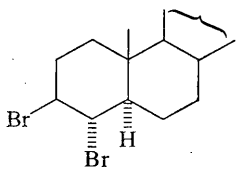
XXIX



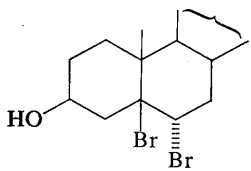
XXXI



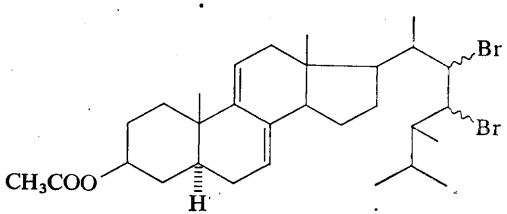
XXXII



XXXIII



XXXIV



XXXV

troscopy (longe-range interactions of C_{19}-protons with fluorine in β-position[15]). In a similar manner the structure of 4β-bromo-5-fluoro-5α-cholestane was assigned to substance *XVI* (coupling constants of the $C_{(4)}$-proton are compatible with the values for an equatorial proton in geminal position with respect to the bromine atom, but not to the fluorine atom; the singlet of the $C_{(10)}$-methyl group excludes the position of fluorine at 4β or 5β.

When the reaction was carried out with an aqueous suspension of silver oxide or an aqueous solution of silver perchlorate in the presence of pyridine, the result of the reaction was analogous (with the exception of fluorobromide formation), but in some instances the reaction product contained a larger fraction of skeletal rearrangement products[2].

When rationalizing these results we base our considerations on the idea of the solvolysis of one of the bromine atoms, assisted by the second bromine atom. Further reactions then take place *via* the carbonium or epibromonium ions[16]. The last mentioned pathway is more probable in cases when the formation of the corresponding epibromonium ion is less demanding on energy then the formation of the corresponding carbonium ion in which 1,3-diaxial interactions of the second bromine atom persist. Supposing that the conformational change of the ring (and thus also of the rest of the molecule) caused by the formation of the epibromonium ion is close to the conformational change caused by the introduction of the corresponding double bond, the highest yields of the epibromonium ion and thus also of the epoxides may be expected in positions corresponding to the olefins with lowest heats of hydrogenation. This supposition was corroborated in a series of diaxial disecondary dibromides where the yields of epoxides decrease in an order ($VI > I > XXIV = IX$) inverse to the order of heats of hydrogenation of 5α-cholestenes[17] ($\Delta^2 < \Delta^1 < \Delta^6 < \Delta^3$).

Higher yields of β-epoxides in the cases mentioned can be explained by primary solvolysis of that bromine atom which is exposed to 1,3-diaxial interactions with bulkier substituents, in our case with the $C_{(10)}$-methyl group. The epibromonium ions thus formed undergo diaxial opening with water[18], under formation of diaxial bromohydrins. The configuration of the hydroxyl group and the epoxide formed in the subsequent step is identical with the configuration of the primarily reacting bromine atom. In secondary-tertiary dibromides *XIII*, *XVII* and *XXIII* the relative yields of α-epoxides increased in accordance with the better conditions for a preferential solvolysis of the α-bound bromine atom.

Under the given conditions epoxides are not formed from diequatorial dibromides *XXXII* and *XXXIV*, or from *trans*-dibromides with both halogens on a five-membered ring (*XXVIII*) or in the side chain (*XXXV*), which is probably due to the difficulties with which these systems assume conformations which are favourable for the formation of epibromonium intermediates, *i.e.* antiperiplanar arrangement of both atoms of bromine. In systems which do not oppose the formation of epibromonium ions from dibromides the transformation of dibromides under the effect of silver

fluoride in the presence of water may represent a further utilisable method of the preparation of steroidal β-epoxides[19-21].

EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. The analytical samples were dried at room temperature and 0·2 Torr for 8 hours over phosphorus pentoxide. The IR spectra were measured in tetrachloromethane, unless otherwise stated. The specific rotations were measured in chloroform.

Epoxidation of 5α-Cholest-1-ene

50 mg of 3-chloroperbenzoic acid were added to a solution of 86 mg of 5α-cholest-1-ene[4] in 4 ml of chloroform at −10°C and the mixture was allowed to stand for 30 minutes at room temperature. The reaction mixture was washed with a potassium hydrogen carbonate solution, evaporated and the residue was separated on a thin-layer of silica gel. The non-polar fraction represents 1α,2α-epoxide *V* (60 mg) which after crystallization from ethanol had m.p. 96−97°C, $[\alpha]_D^{20}$ +12° (*c* 0·9). The polar component is 1β,2β-oxido-5α-cholestane (*II*, 12 mg), m.p. 94−95°C (methanol), $[\alpha]_D^{20}$ +34° (*c* 1·1); IR spectrum: 848 and 939 cm^{-1}. For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·97% H; found: 83·71% C, 12·01% H.

1β,2β-Oxido-5α-cholestane (*II*)

Bromohydrin *III* (140 mg) was added to a suspension of silver oxide (1 g) in 5 ml of tetrahydrofuran and the mixture was stirred at room temperature for 5 hours. After additional 18 hours standing the inorganic material was filtered off and washed with tetrahydrofuran. The extract was evaporated and purified on a silica gel thin layer (benzene). The product (109 mg) melted at 94−95°C (methanol), undepressed on admixture of a sample prepared by epoxidation of 5α-cholest-1-ene.

Reaction of 1α,2β-Dibromo-5α-cholestane with Silver Fluoride

A solution of 50 mg of 1α,2β-dibromide[4] *I* in 2 ml of tetrahydrofuran was stirred with silver fluoride in water (0·3 ml) for 21 hours and the mixture was diluted with chloroform, washed with water, dried over anhydrous sodium sulfate and concentrated. The residue was chromatographed on a silica gel thin-layer with light petroleum. The zone was eluted yielding 5 mg of 1α-bromo-2β-fluoro-5α-cholestane (*IV*), m.p. 103−106°C (methanol), $[\alpha]_D^{20}$ +34° (*c* 0·8), mass spectrum: M^+/e 468; benzene–light petroleum (1 : 1) mixture eluted 1β,2β-oxido-5α-cholestane (*II*, 19·5 mg), m.p. 94−95°C (methanol), undepressed on admixture of a sample prepared by epoxidation of 5α-cholest-1-ene.

6β,7β-Oxido-5α-cholestane (*XXV*)

Bromohydrin *XXIV* (84 mg) was refluxed with a solution of 800 mg of KOH in 30 ml of methanol. After two hours the mixture was concentrated to half its volume and the product was precipitated with water. 6β,7β-Oxide *XXV* (40 mg) melted at 106−109°C and after crystallization from methanol at 111−112°C, $[\alpha]_D^{20}$ −13° (*c* 0·7). For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·73% C, 12·04% H.

Oxidation of 5α-cholest-6-ene with 3-chloroperbenzoic acid gave after crystallization 6α,7α-epoxide *XXVII* and another epoxide of unknown structure; for the preparation of the 6β,7β-epoxide oxidation with peracid is unsuitable because both 6,7-epoxides are inseparable by common chromatographic methods.

3α-Bromo-5α-cholestan-4β-ol (*XI*)

a) *From* 5α-*cholest*-3-*ene*: 2 ml of water were added under stirring to a solution of 200 mg of 5α-cholest-3-ene[31] in 15 ml of dioxan, followed by 0·9 ml of 9% perchloric acid and 150 mg of N-bromosuccinimide. After one hour's standing at room temperature the mixture was decomposed by pouring it into 50 ml of a sodium sulfite solution and the product was extracted with ether. The extract was washed three times with a saturated aqueous sodium chloride solution dried over sodium sulfate and evaporated. The residue was applied onto a thin layer of silica, gel and developed with benzene. The zone of R_F 0·5 was eluted with ether, yielding 73 mg of *XI*, m.p. 184—186°C (ether, methanol), $[\alpha]_D^{20}$ +7° (*c* 0·6); IR spectrum: 3630, 1056 and 977 cm^{-1}. For $C_{27}H_{47}BrO$ (467·6) calculated: 69·35% C, 10·13% H; found: 69·27% C, 10·22% H.

b) *From* 3β,4β-*oxido*-5α-*cholestane* (X): A solution of 10 mg of epoxide *X* in 1 ml of ether was shaken with 0·15 ml of 48% hydrobromic acid at room temperature for one hour. The mixture was diluted with benzene, the organic layer was washed with potassium carbonate solution and water and dried over sodium sulfate. The residue melted at 185°C, R_F value (0·54 in benzene) and the IR spectrum confirm the identity with bromohydrin *XI*.

7α-Bromo-5α-cholestan-6β-ol (*XXVI*)

5α-Cholest-6-ene[30] (267 mg) was converted to bromohydrin using N-bromosuccinimide and perchloric acid, as in the case of the preparation of compound *XI*. Chromatography on silica gel (10% benzene in light petroleum) gave 140 mg of compound *XXVI*, $[\alpha]_D^{20}$ −17° (*c* 1·8). IR spectrum: 3630, 1051, 1021 cm^{-1}. For $C_{27}H_{47}BrO$ (467·6) calculated: 69·35% C, 10·13% H; found: 69·01% C, 10·22% H.

17α-Bromo-5α-androstan-16β-ol (*XXX*)

5α-Androst-16-ene[32] (280 mg) was converted to a bromohydrin as in the preceding case. Chromatography on silica gel in benzene gave compound *XXX* (123 mg), m.p. 46—48°C (methanol, −60°C), $[\alpha]_D^{20}$ −17° (*c* 1·3). For $C_{19}H_{31}BrO$ (355·4) calculated: 64·21% C, 8·79% H, 22·49% Br; found: 64·39% C, 8·99% H, 22·90% Br.

6β,7α-Dibromo-5α-cholestane (*XXIV*)

A solution of 68 mg of bromine in 0·8 ml of tetrachloromethane was added dropwise and under stirring and cooling at 0°C to a solution of 138 mg of 5α-cholest-6-ene[30] in 5 ml of tetrachloromethane. After ten minutes the solution was evaporated in a vacuum to dryness and the residue was chromatographed on silica gel with light petroleum (10 g). From the first 20 ml of the eluate 150 mg of dibromide *XXIV* were isolated, which after crystallization from ether and methanol melted at 123—127°C (120 mg). Further crystallization increased the melting point to 125—127°C (110 mg), $[\alpha]_D^{20}$ −18° (*c* 1·1). For $C_{27}H_{46}Br_2$ (530·5) calculated: 61·13% C, 8·74% H, 30·13% Br; found: 60·96% C, 8·58% H, 30·41% Br.

16β,17β-Dibromo-5α-androstane (*XXVIII*)

5α-Androst-16-ene[32] (358 mg) was converted to a dibromide under the conditions used for the preparation of compound *XXIV*. Chromatography on silica gel with light petroleum gave compound *XXVIII*, m.p. 102–103°C (ether, methanol, 170 mg), $[\alpha]_D^{20}$ +18° (*c* 1·1). For $C_{19}H_{30}Br_2$ (418·3) calculated: 54·56% C, 7·23% H, 38·21% Br; found: 54·57% C, 6·84% H, 38·18% Br.

TABLE II

Reaction of Dibromides and Bromohydrins with Silver Salts in the Presence of Water

Starting compound	Reagent	Reaction time h	Reaction products (yield,%)
I	AgF	21	*II* (54), *IV* (11)
III	Ag_2O	18	*II* (94)
VI[a]	AgF	48	*VII* (66), *VIII* (4), *XXXII* (10)
VI[b]	$AgClO_4$	24	*VII* (23), *XXXII* (9)
VI[c]	Ag_2O	24	*VII* (58), *XXXII* (10)
IX[d]	AgF	40	*X* (0), *XII* (0)
XI	AgF	20	*X* (87)
XIII	AgF	2	*XIV* (44), *XV* (5), *XVI* (5)
XVII[e]	AgF	1	*XVIII* (29), *XIX* (6)
XX	AgF	4	*XXI* (28), *XXII* (6)
XXIV[f]	AgF	48	*XXV* (0), *XXVII* (0)
XXVI[g]	AgF	6	*XXV* (12)
XXVIII[h]	AgF	120	*XXIX* (0), *XXXI* (0)
XXX[i]	AgF	120	*XXIX* (0)

[a] 18% of the starting compound was regenerated; [b] 25% of the starting compound was regenerated, compound *VIII* was overlapped with two undefined hydroxycholestenes; [c] 11% of the starting compound regenerated; [d] 55% of the starting compound was isolated together with 3 and 16% of substances of the same polarity as epoxides *X* and *XII*, resp., but the IR spectrum did not confirm identity with authentic samples; [e] 35% of an unseparable mixture of both epoxides was isolated, m.p. 68–72°C. The composition of the mixture was determined on the basis of specific rotation $[\alpha]_D^{20}$ −9° (*c* 1·2) and the intensity of the $C_{(6)}$—H signal in the ^{1}H-NMR spectrum; [f] 68% of the starting dibromide was isolated, as well as 12 and 5% of substances of similar polarity as epoxides *XXV* and *XXVII*, resp., but the substances did not display absorption maxima for hydroxyl groups in the IR spectra; [g] 73% of the starting compound was isolated; [h] 40% of the starting compound was isolated; [i] all starting compound was consumed, the main product was an unidentified substance with a rearranged skeleton.

Reaction of Dibromides and Bromohydrins with Silver Salts

a) A solution of bromo steroid (100 mg) in tetrahydrofuran (2 ml) was stirred with an aqueous silver fluoride solution (0·7 ml, $c = 1{\cdot}5$ g/ml) at room temperature for 30 minutes to 120 hours. The mixture was diluted with chloroform, washed with water, filtered through a column of sodium sulfate, evaporated, and the residue was chromatographed on a thin layer of silica gel with light petroleum. The starting or the isomeric dibromocholestanes were then isolated, while after development with benzene epoxycholestanes were obtained (in the conversion of more polar substrates, such as *XX*, ether–benzene mixture was used for development). The yields listed in Table II are based on the weighing of the products isolated, and the structures were determined after crystallization of these products (comparison of the melting points and the IR spectra with those of authentic samples).

b) A solution of dibromide (100 mg) in tetrahydrofuran (2 ml) and pyridine (0·3 ml) was mixed and stirred with a solution of silver perchlorate in water (0·6 ml, $c = 1{\cdot}6$ g/ml). When the reaction was complete (control by thin-layer chromatography) the mixture was worked up as in case *a*).

c) A solution of bromo derivative (50 mg) in tetrahydrofuran (2 ml) was stirred with fresh silver oxide prepared from 350 mg of silver nitrate. When the reaction was over the mixture was diluted with chloroform (50 ml), the inorganic material was eliminated by filtration over sodium sulfate and the products were isolated as in case *a*).

1α-Fluoro-2β-bromo-5α-cholestane (*IV*)

A solution of 1α,2β-dibromide[4] *I* (50 mg) was allowed to react with silver fluoride under standard conditions for 21 hours. Chromatography of the product was submitted to thin-layer chromatography in light petroleum, affording 5 mg of compound *IV*, m.p. 103—106°C (methanol), $[\alpha]_D^{20}$ +34° (*c* 0·8), mass spectrum: M^+/e 468.

4β-Bromo-5-fluoro-5α-cholestane (*XVI*)

A solution of 44 mg of dibromide *XIII* was allowed to react with silver fluoride under standard conditions for 2 hours. Chromatography of the product on a silica gel thin layer, using light petroleum for development, gave 1·8 mg of compound *XVI*, m.p. 99—101°C (dichloromethane, methanol), $[\alpha]_D^{20}$ +49° (*c* 1·0), M^+/e 468. For $C_{27}H_{46}BrF$ (469·5) calculated: 69·06% C, 9·88% H; found: 68·93% C, 10·01% H.

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