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REACTIONS IN DRY MEDIA: REACTIONS OF CHOLESTEROL AND CHOLESTANES ON SILICA BOUND FERRIC CHLORIDE

CHOLESTANE—DIACHOLESTENE REARRANGEMENT

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Abstract—Reaction of cholesterol with silica bound $FeCl_3$ resulted in a mixture of 3β-cholesteryl chloride and dicholesteryl ether.

5-Cholestene and hydroxy- and halogeno-substituted cholestane derivatives gave on heating at 100° with this reagent a 1:1 mixture of 20-epimeric diacholestenes. The 20(*R*)-isomer gave with *meta*-chloroperbenzoic acid 20(*R*)-α-epoxide, while the 20(*S*)-gave a mixture of 20(*S*)-α- and 20(*S*)-β-epoxides.

5α,6β-Dihydrocholestane reacted with the $FeCl_3/SiO_2$ under milder conditions (50°) to give 6β-hydroxy-20(*R*)-diacholestene, which was converted to the 20(*R*)-diacholestene.

We have recently shown that $FeCl_3$ adsorbed on silica gel acts as Lewis-type reagent for dehydrations or rearrangements of t-alcohols.[1] We now describe reactions of cholesterol and other cholestane derivatives with this reagent. The steroid system was chosen since its behaviour in acidic media is well documented.[2,3]

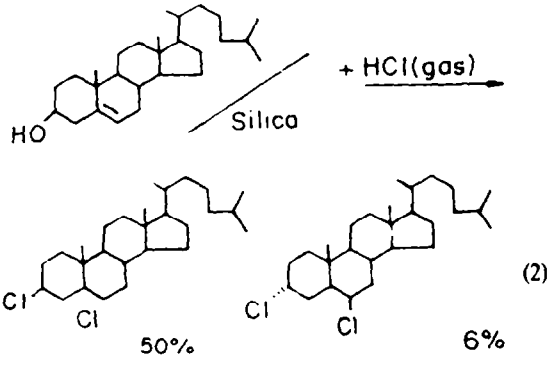
The $FeCl_3$ reagent was prepared by dissolving an appropriate amount of $FeCl_3.6H_2O$ in a solvent (preferably acetone) and mixing it with chromatographic type silica gel and evaporating the solvent in a rotatory evaporator (*ca.* 30 torr) and at high vacuum (0.1 torr). We have used silica gel containing *ca.* 7.5% $FeCl_3$, ("inactive $FeCl_3/SiO_2$ reagent") which was activated by heating with constant mixing at 100° for *ca.* 1 hr. This treatment converted the yellow powder into a brownish one ("active $FeCl_3/SiO_2$ reagent") which was strongly acidic. Its acid content was determined as a function of heating time at 100° and was found to be the highest after 1 hr, corresponding to 0.07 mM HCl per gram reagent (0.26%).[4]

The reactions of steroids were performed either by mixing the substrate dissolved in methylene chloride with the reagent, or by heating after removing the solvent under reduced pressure.

Cholesterol (1) reacted in solution with the active $FeCl_3/SiO_2$, as evidenced by the development of a violet-brown color when its solution in methylene chloride was mixed with the active-reagent. The method chosen for this reaction was adsorbing a concentrated solution of the substrate in a 1:1 mixture of methylene chloride–ether on a chromatographic column filled with the reagent, followed by elution with methylene chloride. Two products were isolated: cholesteryl chloride (52%) and dicholesteryl ether (28%) (eqn 1).

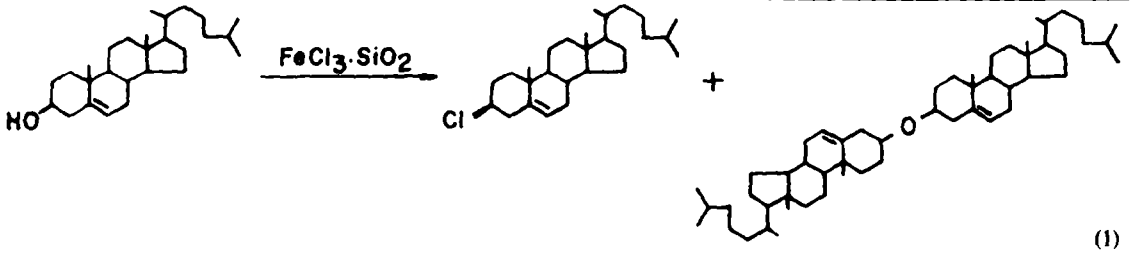
$FeCl_3$ binds to the OH group of cholesterol creating a good leaving group whose dissociation is facilitated by double bond participation. The cholesteryl cation formed in this way undergoes substitution at C-3 either by a chloride ion or by the free cholesterol forming cholesteryl chloride and dicholesteryl ether respectively.

It was observed that cholesterol did not react either when mixed with silica gel in solution, or when heated at 100° with dry silica gel. Cholesterol was also recovered unchanged (98%) when its solution was passed through a column of silica gel saturated with HCl. On the other hand, passing dry HCl for 2 hr through silica gel containing adsorbed cholesterol (2%) gave as a major product 3β,5α-dichlorocholestane (50%) and as a minor one 3α,6β-dichlorocholestane (6%) (eqn 2).



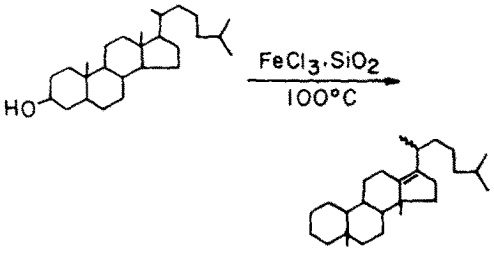
(2)

Cholestanol (2) did not react with the "active" $FeCl_3/SiO_2$ at room temperature, either in solution, or in the adsorbed state when left standing for 2 days.



(1)

However, when the dry powder (containing 2% of the substrate) was heated at 100°, a non polar material was formed (in 60% yield, after 45 min heating). Separation on either $AgNO_3$ coated TLC silica plates, or by GC gave a 1:1 ratio of 20(*R*)- and 20(*S*)-diacholestenes[5] (**3**) and (**4**) (eqn 3). Their structure was established by ^{13}C NMR[6] and by interrelation with a known compound obtained by a different route (*vide infra*).



(3)

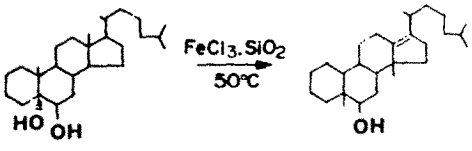
Epoxidation of 20(*R*)-diacholestene (**3**) with *meta*-chloroperbenzoic acid gave one product, the 13α,17α-epoxide (**5**) and that of the 20(*S*)-olefin (**4**) two products, 13α,17α-and 13β,17β-epoxides (**6**) and (**7**). Since the mixture of **5**, **6** and **7** can be readily separated on tlc plates (5% ether/hexane, silica), the epoxidation may be utilized as a method for the identification of the 20-epimeric diacholestenes.

When the reaction of cholestanol (**2**) was conducted at lower temperature (90°) the diacholestenes were formed in 10% yield only, the major product being 2-cholestene. We have also found that other monosubstituted cholestanes rearrange under similar conditions to the same mixture of diacholestenes **3** and **4**. The following compounds were submitted to this treatment: 2α-cholestanol, 5β-cholestan-3α-ol, 5α-cholestanol, 5α-cholestene, 3α-chlorocholestane, 3β-chlorocholestane and 3α-bromocholestane.

The rearrangement of 3β-chlorocholestane was investigated in more detail. Thus when the reaction was interrupted after 10 min, the products consisted of 20(*R*)- and 20(*S*)-diacholestenes (**3** and **4**, in a 4:3 ratio) (59%), 2-cholestene (15%) and a mixture of 3β-chloro, 3α-chloro and 2α-chlorocholestanes (25%).

No reaction was observed upon refluxing the substrates with a solution of $FeCl_3$ in dimethylformamide or upon heating the adsorbed material on silica gel as above.

As anticipated the rearrangement of cholestane-5α,6β-diol (**8**) occurred under milder conditions.[7] Heating of this compound adsorbed on $FeCl_3/SiO_2$ at 50° for 20 min resulted in 35% yield of diacholesten-6β-ol (**9**) having the natural configuration at C-20 (eqn 4).

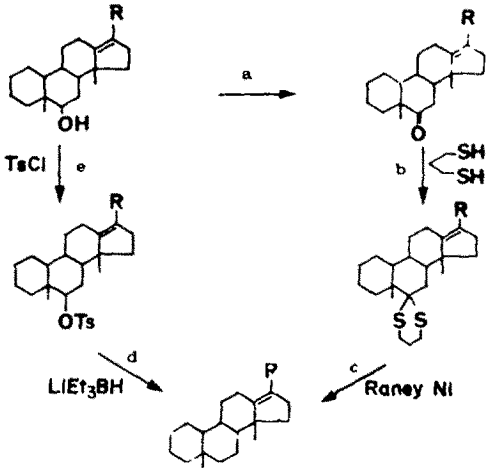


(4)

It is of interest to note that the free OH at C-6 survived the reaction conditions.

Alcohol **9** was converted by two different methods (Scheme 1) into 20(*R*)-diacholestene, identical with that obtained by the direct rearrangement of ring A substituted cholestanes (**3**).

The cholestane–diacholestane rearrangement probably involves the intermediacy of a C-5 carbonium ion. This species is formed either by the protonation of the double bond in 5-chloestene or, in the case of ring A substituted cholestane derivatives, by acid catalyzed elimination and addition reactions.



Scheme 1.

Scheme 1. (a) Pyridinium chlorochromate, room temp, 2 hr. (b) 1. 1,3-Propanedithiol + BF_3.etherate, 10 min. 2. KOH/methanol. (c) Raney nickel W-4/MeOH, reflux, 8 hr. (d) Tosyl chloride + pyridine, 0°, 24 hr. (e) 1. $LiEt_3BH$/tetrahydrofuran ("super hydride"), 0°. 2. room temp, 20 hr 3. 3N NaOH + 30% H_2O_2.

According to current views[2b,c,d] the C-5 cation isomerizes by a series of 1,2-H and Me shifts to give, after loss of the proton at C-17 the thermodynamically stable diacholestene system. The initially formed 20(*R*)-product (**3**) may isomerize further to a 1:1 mixture of the C-20 epimers (**3** and **4**).[8]

The presence of free HCl adsorbed on the silica (formed on heating of the silica bound $FeCl_3$) is necessary for the cholestane–diacholestene rearrangement. Thus, wetting the silica gel with solvents leaches the acid out, thus deactivating free reagent.

The transformation of cholestane derivatives to diacholestenes was also accomplished by Nafion H[9] (perfluorosulfonic acid resin) replacing $FeCl_3/SiO_2$. Thus heating Nafion H preadsorbed with 1% 5-cholestene at 100° for 1 hr led to the two epimeric 20-diacholestenes (**3** and **4**) in 90% yield. Similar treatment of 3β-cholestanol (**2**) gave the same products, in 30% yield; the remainder of the starting material was unchanged.

The use of solid phases appears to be an easy way to perform the cholestane–diacholestene rearrangement.

It should be pointed out that the rearrangement of 3β-cholestanol adsorbed on montmorillonite to a mixture of diacholestenes (20%) was previously reported to occur on heating under vacuum at 146° for 16 hr.[10]

EXPERIMENTAL

^1H NMR spectra of $CDCl_3$ solns were recorded on a Bruker WH-270 at 270 MHz, a Bruker HFX-10 at 90 MHz and a Varian FT-80A spectrometer at 80 MHz, with TMS as internal standard. ^{13}C NMR spectra of $CDCl_3$ solns were determined with a Bruker WH-270 at 67.9 MHz, a Bruker WH-90 at 22.6 MHz and a Varian CFT-20 spectrometer at 20 MHz with the same internal standard. All the chemical shifts are in δ(ppm) units. Mass spectra were measured using an Atlas CH-4 mass-spectrometer. All m.ps are uncorrected.

The diacholestenes were analyzed by GC on a Varian Aerograph, Series 1400 gas chromatograph-flame ionization detector, He at 60 psi, with a SE-30 10% on Chromosorb P AW, 60-

80 Mesh, 2 m × 1/8", stainless steel column, at 200°, injector 220°, detector 230°. The GC preparative separations of these compounds were performed using an Aerograph A 90-P gas chromatograph-thermal conductivity detector, He at 60 psi, with a SE-30 12% on Chromosorb P, 30–60 Mesh, 4 m × 3/8", aluminium column at 180°, filament current 100 mA.

Preparation of $FeCl_3/SiO_2$ *reagents.* Acetone soln (600 ml) of $FeCl_3.6H_2O$ (50 g, or anhyd $FeCl_3$, 30 g) and chromatographic grade silica gel (500 g, Merck Kieselgel 60, 70–230 Mesh ASTM) were stirred at room temp in a rotary evaporator until dry and then in high vacuum (0.1 torr) for 3 hr resulting in the "inactive" $FeCl_3/SiO_2$ reagent (yellow, containing 7.5% $FeCl_3$).

This powder was heated for 1 hr at 100° in a rotary evaporator to give a brownish powder ("active" $FeCl_3/SiO_2$ reagent).

Reaction of cholesterol (1) *with the "active"* $FeCl_3/SiO_2$

A conc soln of 1 (1 g) in CH_2Cl_2-ether (1:1) was placed on top of a chromatographic column (internal dia. 25 mm) filled with a layer of silica gel (80 ml) below a layer of the "active" $FeCl_3/SiO_2$ reagent (80 ml). Elution with CH_2Cl_2 (0.5l) gave 3β-cholesteryl chloride (545 mg, 52%), m.p. 87–89° (lit[11] 90°) and dicholesteryl ether (274 mg, 28%), m.p. 201–202° (lit[12] 203°). MS: *m/e* (rel. intensity) no M^+ detectable, but 369 (100%) and 385 (10%) stem from C–O fragmentation. ^1H NMR: δ 5.22 (2H, d, J = 12 Hz, H-C6), 3.24 (2H, m, H-C3), 1.00 (6H, s, H-C19), 0.86 (12H, d, J = 6 Hz, H-C26, 27) and 0.67 (6H, s, H-C18).

Reaction of cholesterol (1) *adsorbed on silica with* HCl *gas*

A stream of dry HCl was passed for 2 hr through silica gel (50 g) preadsorbed with 1 (1 g). The excess HCl was flushed out with N_2 and the products were eluted with ether (600 ml). The residue (1.1 g) was chromatographed on silica gel with gradient elution hexane–ether to give: 3β,5α-dichlorocholestane (571 mg, 50%), m.p. 115° (lit[13] 117°). ^1H NMR: δ 4.46 (1H, broad m, H-C3), 1.06 (3H, s, H-C19), 0.89 (3H, d, J = 6 Hz, H-C21), 0.86 (6H, d, J = 6 Hz, H-C26, 27) and 0.64 (3H, s, H-C18). MS: *m/e* (rel. intensity) 444 (12%), 442 (61%), 440 (100%, M^+), 405 (56%, M^+-Cl), 404 (41%, M^+-HCl), 384 (16%, M^+-HCl-CH_3), 368 (30%, M^+-2HCl), 301 (16%, M^+-HCl-C_8H_{17}), 285 (60%, $C_{16}H_{23}Cl_2^+$), 265 (19%, M^+-2HCl-C_8H_{17}), and 3α,6β-dichlorocholestane (69 mg, 6%), m.p. 124–125° (lit[14] 128°). ^1H NMR: δ 4.58 (1H, sharp m, H-C3), 4.14 (1H, sharp m, H-C6), 1.05 (3H, s, H-C19), 0.86 (6H, d, J = 6 Hz, H-C26, 27), 0.71 (3H, s, H-C18). MS: *m/e* (rel. intensity) 444 (2%), 442 (14%), 440 (18%, M^+), 425 (6%, M^+-CH_3), 404 (6%, M^+-HCl), 287 (21%, $C_{16}H_{25}Cl_2^+$), 285 (31%, $C_{16}H_{23}Cl_2^+$), 265 (26%, M^+-2HCl-C_8H_{17}).

Backbone rearrangement of 3β-*cholestanol* (2) *with* $FeCl_3/SiO_2$

(1) A soln of 2 (0.5 g) in CH_2Cl_2 (50 ml), and "inactive" $FeCl_3/SiO_2$ reagent (25 g) were mixed at room temp in a rotary evaporator until dryness and then heated in the evaporator at 100° for 45 min during which the yellow powder turned brown. This brown powder was placed on top of a short column containing silica gel (25 g). The material was eluted with CH_2Cl_2 (250 ml) and the solvent was evaporated. The residue was chromatographed on silica gel with hexane to give a mixture consisting mainly of 20(*R*) and 20(*S*)-diacholestenes (3 and 4) (285 mg, 60%) which separated on an analytical GC column into two major components in a 1:1 ratio, their retention times relative to 2-cholestene (1.00) being: 20(*R*)-3 0.54 and 20(*S*)-4 0.44. Preparative separation was accomplished on a silver nitrate coated silica gel chromatographic column using hexane as an eluent. The first fraction (74 mg, 26%) consisted of unidentified olefins. The second fraction gave 20(*S*)-olefin (4) (91 mg, 32%) gum. The third fraction gave 20(*R*)-olefin 3 (120 mg, 42%) gum. For ^1H and ^{13}C NMR data of 3 and 4, see Ref. [5].

(2) A similar experiment carried out at 90° resulted in 10% of a mixture of the rearranged olefins 3 and 4, the rest consisting of 2-cholestene.

Epoxidation of olefins 3 *and* 4

A soln of 4 (20 mg) in CH_2Cl_2 (5 ml) was treated with a soln of *m*-chloroperbenzoic acid (20 mg) in the same solvent (5 ml). After 2 hr at room temp $NaHSO_3$ aq was added and the products were isolated by conventional methods and chromatographed on silica gel (with 3% ether in hexane) to give: 20(*S*) α-epoxide 6 (9 mg, 43%). MS: *m/e* (rel. int.) 388 (1%), 387 (6%), 386 (23%, M^+), 371 (9%, M^+-CH_3), 234 (100%, $C_{16}H_{26}O^+$), and 20(*S*) β-epoxide 7 (9 mg, 43%) m.p. 105–107°. MS: *m/e* (rel. int.) 387 (4%), 386 (10%, M^+), 385 (10%, M^+-H), 371 (5%, M^+-CH_3), 234 (43%, $C_{16}H_{26}O^+$), 139 (100%, $C_9H_{15}O^+$).

Epoxidation of 20(*R*)-olefin 3 (25 mg) was carried out as above to give the 20(*R*) α-epoxide 5 (22 mg, 84%). ^1H and ^{13}C-NMR data of epoxides 5–7, see Ref. [5].

Backbone rearrangement of 2α-*cholestanol,* 5β-*cholestan*-3α-*ol,* 5α-*cholestanol,* 5-*cholestene,* 3α-*chlorocholestane and* 3α-*bromocholestane with* $FeCl_3/SiO_2$

Each of the title compounds (15 mg) was heated separately with yellow $FeCl_3/SiO_2$ (1 g) at 100° for 60 min and the products isolated as above. Chromatographic separation on silica gel using hexane as eluent resulted in mixtures of 20(*R*)- and 20(*S*)-olefins (3 and 4) in *ca.* 1:1 ratio (GC, ^1H NMR).

Backbone rearrangement of 3β-*chlorocholestane with* $FeCl_3/SiO_2$

The title compound (0.22 g) adsorbed on the "inactive" $FeCl_3/SiO_2$ (11 g) prepared as described above was heated at 100° for 60 min. Elution with CH_2Cl_2 and chromatography of the residue on silica gel with hexane gave a non-polar material (126 g, 60%) which consisted mainly of a mixture of 20(*R*)- and 20(*S*)-olefins (3 + 4) as indicated by its ^1H NMR spectrum, which was similar to that of the non-polar fraction obtained from 3β-cholestanol (2).

Their identity was established by: (1) analysis on a GC column which gave two peaks (with retention times of 0.54 (for 3) and 0.44 (for 4) relative to 2-cholestene (1.00) when co-chromatographed with 3 and 4 isolated above. (2) Separation on analytical tlc plates coated with $AgNO_3$. (3) Epoxidation with *m*-chloroperbenzoic acid which gave three epoxides (5, 6 and 7). After separation by chromatography (3% ether/hexane, silica) they were found to be identical (^1H NMR, ^{13}C NMR and tlc) to epoxides 5, 6 and 7 obtained from 2.

When the reaction was stopped in an early stage (10 min) the products which were separated by chromatography on silica with hexane as eluent gave three fractions: (1) a *ca.* 1:1 mixture of 3 and 4 (118 mg, 59% gum. MS: *m/e* (rel. int.) 370 (11%, M^+), 355 (26%, M^+-CH_3), 258 (22%, M^+-C_8H_{16}), 257 (100%, M^+-C_8H_{17}).

Preparative GC separation gave two major compounds (3 and 4) as gums, identical to those obtained from 2. (2) 2-Cholestene (30 mg, 15%) m.p. 74–75° (lit[10] 75–76°). ^1H NMR: δ 5.61 (2H, sharp m, H-C2, 3), 0.86 (6H, d, J = 6 Hz, H-C26, 27), 0.76 (3H, s, H-C19) and 0.67 (3H, s, H-C18). ^{13}C NMR: δ 126.0 (C3) and 125.9 (C2) (see Ref. 15). (3) A mixture of three chlorocholestanes (55 mg, 25%) consisting, according to ^1H NMR (270 MHz) of 3α-chlorocholestane (δ 4.50 ppm, sharp m), 2α-chlorocholestane (δ 4.06 ppm, t of t) and 3β-chlorocholestane (δ 3.86 ppm, t of t).

Backbone rearrangement of cholestane-5α,6β-*diol* (8) *with* $FeCl_3/SiO_2$

The title compound 8 was prepared from 1 according to the following sequence: 1 was treated at room temp with PCl_5 to give 3β-cholesteryl chloride. This product was dehydrochlorinated by sodium in n-amyl alcohol; the 5-cholestene thus obtained was epoxidized with *m*-chloroperbenzoic acid to 5α,6α-epoxycholestane and the latter was hydrolysed with periodic acid dihydrate at room temp to give 8. m.p. 123° (hexane) (lit[16] 125.5°).

A soln of 8 (0.5 g) in CH_2Cl_2 (50 ml) and the "inactive" $FeCl_3/SiO_2$ reagent (25 g) were mixed at room temp in a rotary evaporator until dryness and then for 20 min at 50°. Elution with wet ether and chromatography of the residue on silica gel with hexane–ether gave 20(*R*)- 9 (168 mg, 35%) m.p. 97–100° (acetone) (lit[2c] 97–99°). $[\alpha]_D$: +15° (lit[2b] +20°). For ^1H and ^{13}C NMR see Ref. [5]. MS: *m/e* (rel. int.) 386 (4%, M^+).

20(R)-*Diacholesten*-6-*one*

A soln of 9 (113 g) in CH_2Cl_2 (50 ml) and pyridinium chlorochromate (100 mg) were mixed at room temp for 2 hr. MeOH

(0.1 ml) was added and the title compound was obtained (40 mg, 36%) gum, by filtration, evaporation and chromatography on silica (5% ether in hexane). $[\alpha]_D$ +52° (lit[2c] + 54°). ^{1}H NMR: δ 1.12 (3H, s, H-C19), 0.96 (3H, s, H-C18) and 0.83 (6H, d, J = 6 Hz, H-C26, 27). ^{13}C NMR: see Ref. [5]. MS: *m/e* (rel. int.) 385 (16%), 384 (54%, M^+), 369 (44%, M^+-CH_3).

6-(1',3'-Propylenedithioketal)-20(R)-diacholestene

Diacholesten-6-one (205 mg) was treated with 1,3-propandithiol (0.25 ml) and BF_3-etherate (0.25 ml) at room temp until the appearance of an orange color (*ca.* 10 min). A methanolic KOH was added and after several extractions with ether–water the mixture was chromatographed on silica (5% ether in hexane) to give the desired dithian (191 mg, 76%) as a gum. ^{1}H NMR: δ 2.74 (4H, J = 4.5 Hz, $-CH_2-S$), 0.94 (3H, d, J = 7 Hz, H-C21), 0.91 (6H, s, H-C19) and 0.83 (6H, d, J = 6 Hz, H-C26, 27). ^{13}C NMR: see Ref. [5]. MS: *m/e* (rel. int.) 476 (11%), 475 (25%), 474 (75%, M^+), 400 (26%, M^+-C_3H_6S), 367 (14%, M^+-$C_3H_7S_2$), 267 (100%, M^+-$C_{15}H_{27}$).

Catalytic hydrogenation of 6 - (1',3' - propylenedithioketal) - 20(R) - diacholestene.

A methanolic soln (12 ml) of the title compound (34 mg) was treated with freshly prepared Raney Ni W-4 (0.7 g) and heated under reflux for 8 hr. The products were isolated by a conventional method and were separated by flash-chromatography on silver nitrate coated silica gel 60 (230–400 mesh) with hexane as eluent. The first fraction gave 20(*R*)-olefin (3) (20 mg, 75%) (tlc on Ag-silica, ^{1}H NMR). Treatment of it with *m*-chloroperbenzoic acid resulted in 20(*R*)-α-epoxide identical with 5 (tlc, ^{1}H NMR and ^{13}C NMR).

β-Tosyloxy-20(R)-diacholestene

Pyridine soln (25 ml) of 9 (1.2 g) was treated with tosyl chloride (1.3 g, m.p. 67–70°) at 0° for 24 hr. Conventional work-up and flash-chromatography onsilica gel using CH_2Cl_2 and hexane (20:80) resulted in the title compound (475 mg, 28%). ^{1}H NMR: 7.30, 7.77 (4H, AB, J_{AB} = 8.5 Hz, arom.), 4.19 (1H, d of d, J-9.5, 6.0 Hz, H-C6), 0.94 (3H, d, J = 7 Hz, H-C21, collapsed to singlet at 0.94 ppm when irradiated at 2.39 ppm), 0.85 (3H, s, H-C19), 0.83 (3H, s, H-C18) and 0.82, 0.83 (6H, 2d, J = 6.5 Hz, H-C26, 27).

Reduction of 6β-tosyloxy-20(R)-diacholestene with lithium triethylborohydride

A dry soln (4 ml) of the 6β-tosylate (300 mg) in THF was treated with 1 M soln of $LiEt_3BH$ ("super hydride") at 0° and then at room temp for 20 hr. 3N NaOH (2 ml) and 30% H_2O_2 (2 ml) were added and the product was isolated by extraction with pentane. Chromatography on silica gel with hexane gave 20(*R*)-diacholestene (24 mg, 12%) identical with 3 (obtained from 2) (tlc on Ag-silica, ^{1}H NMR and ^{13}C NMR). Treatment with *m*-chloroperbenzoic acid gave 20(*R*)-α-epoxide identical with 5 (tlc, ^{1}H NMR, ^{13}C NMR).

The second fraction gave 20(*R*)-diacholesta-6,13(17)-diene (20 mg, 10%). ^{1}H NMR: δ 4.74 (2H, m, H-C6, 7), 0.95 (3H, d, J = 7 Hz, H-C21), 0.88 (6H, s, H-18, 19) and 0.84 (6H, d, J = 6.5 Hz, H-C26, 27).

Attempts to reduce the rearranged tosylate with LAH afforded only alcohol 9 without traces of 3.

Reactions with Nafion H resin[9]

Rearrangement of 3β-cholestanol (2). A soln of 2 (12.5 mg) in CH_2Cl_2 (10 ml) was mixed with Nafion H powder (1.25 g) in a rotatory evaporator at room temp until dry and then at 100° for an additional 1 hr. The powder was washed with CH_2Cl_2 and the soln evaporated until dryness and the residue chromatographed on silica gel with hexane. The first fraction (3.6 mg, 30%) consisted of a *ca.* 1:1 mixture of 3 and 4 (GC, ^{1}H NMR); the second fraction gave 2-cholestene (1.5 mg, 13%). Further elution with ether gave 6.9 mg (55%) of the starting material.

Rearrangement of 5-cholestene. The title compound (12.5 mg) was reacted with Nafion H (1.25 g) at 100° as described above. Chromatography on silica resulted in a 1:2 mixture of 4 and 3 (11.3 mg, 90%) and the starting material (1.3 mg, 10%).

No reaction was observed when the substrate was treated either with Nafion K at 100° for 60 min or with Nafion H at room temp for 44 hr.

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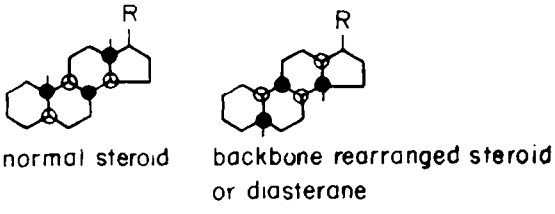

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[9]Nafion is a trademark of the DuPont Co. to whom we extend thanks for a sample of the potassium salt of Nafion 501 resin. The active H form was generated from this salt by treatment with HNO_3, washing with water, and drying in high vacuum at 70–90°.

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