Canadian Journal of Chemistry

Published by THE NATIONAL RESEARCH COUNCIL OF CANADA

VOLUME 46 JANUARY 1, 1968 NUMBER 1

Reaction mechanism studies. 4. The diaxial → diequatorial rearrangement of β-chlorothioethers

J. F. KING,[1] K. ABIKAR, DONNA M. DEAKEN, AND R. G. PEWS[2]

Department of Chemistry, University of Western Ontario, London, Ontario

Received August 23, 1967

Benzenesulfenyl chloride adds diaxially to 5α-cholest-2-ene (**1**) yielding 2β-chloro-3α-(phenylthio)-5α-cholestane (**3**). Assuming that the reaction proceeds via the episulfonium ion (**2**), this allows the inclusion of these species within the scope of the diaxial opening rule. On heating, **3** undergoes rearrangement to 3β-chloro-2α-(phenylthio)-5α-cholestane (**4**). This reaction is the first instance of a diaxial → diequatorial rearrangement of β-halothioethers.

Mild oxidation of **3** gives a mixture of the two sulfoxides epimeric at the sulfur atom (**16***a* and **16***b*). On heating, both sulfoxides suffer pyrolytic elimination, without any sign of diaxial → diequatorial rearrangement. A major product of the elimination, evidently 2-chloro-5α-cholest-2-ene (**18**), was found to be formed a little more readily from the *S*-sulfoxide (**16***b*) than from the *R*-isomer (**16***a*). This observation is in accord with the conclusion of previous investigators that the elimination of the sulfenic acid from an alkyl sulfoxide involves bond formation between the hydrogen and sulfinyl oxygen during the rate determining stage (cf. **19**).

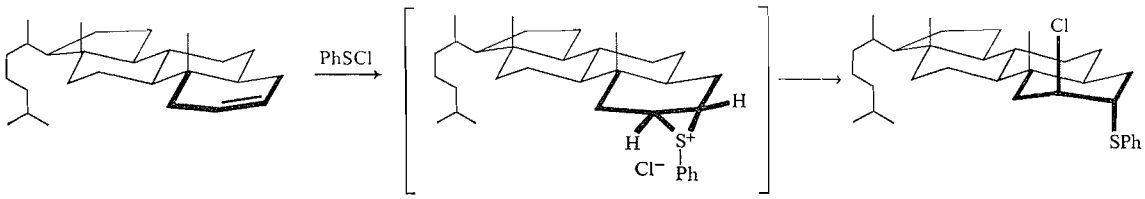
Canadian Journal of Chemistry, 46, 1 (1968)

The diaxial → diequatorial rearrangement (1) has been shown to take place with dihalides (2–4), and carboxylic (1, 5) and sulfonic esters (6) of halohydrins. Our interest in this reaction has led us to consider the possibility of such rearrangement with other types of compounds, not only to discover the full scope of the reaction but also with an eye to elucidating details of its mechanism (cf. (7)). From the examples already known it appeared that a sufficient—though not necessarily exclusive—requirement for the rearrangement was the presence in a 1,2-diaxial relationship of a good leaving group and a function capable of neighboring group participation. We therefore expected that β-halothioethers should be capable of undergoing the diaxial → diequatorial rearrangement. In addition, these species possess structural features which we hoped would be helpful to us in our general study (and which are discussed, in part, in the following paper), and we set out to make 2β-chloro-3α-(phenylthio)-5α-cholestane (**3**) as an appropriate substrate with which to test these notions. This account describes the preparation of this compound, its thermal rearrangement, and the proof of structure of these materials, together with some observations on the corresponding sulfoxides. The following paper outlines experiments designed to shed light on the mechanism of this reaction, and upon the diaxial → diequatorial rearrangement in general.

Electrophilic attack on 5α-cholest-2-ene is well known to take place preferentially from the α face, which is presumably less hindered than the β face because of the absence of angular methyl groups. As it is believed that sulfenyl chlorides react with simple olefins with initial formation of an episulfonium ion (8–10), it was therefore anticipated that the reaction of 5α-cholest-2-ene with benzenesulfenyl chloride would lead first to the episulfonium ion (**2**). It would further be expected that **2** would open according to the "diaxial opening rule" giving the corresponding diaxial compound, 2β-chloro-3α-(phenylthio)-5α-cholestane (**3**). This expectation is based on

[1]Fellow of the Alfred P. Sloan Foundation, 1966–1968.

[2]Holder of a Dow Chemical of Canada Limited Postgraduate Fellowship, 1961–1962, and a National Research Council of Canada Studentship, 1962–1963. Present address: Dow Chemical Co., Midland, Michigan, U.S.A.



1 2 3

analogy with the observed behavior of other three-membered ring species, such as epoxides (11), halonium ions (12), and ethylenimines (13), and not on any direct evidence from episulfonium ions themselves. Therefore, when the reaction was in fact found to yield a 1:1 adduct, the compound was subjected to careful scrutiny in order to be entirely certain the structure was indeed **3**.

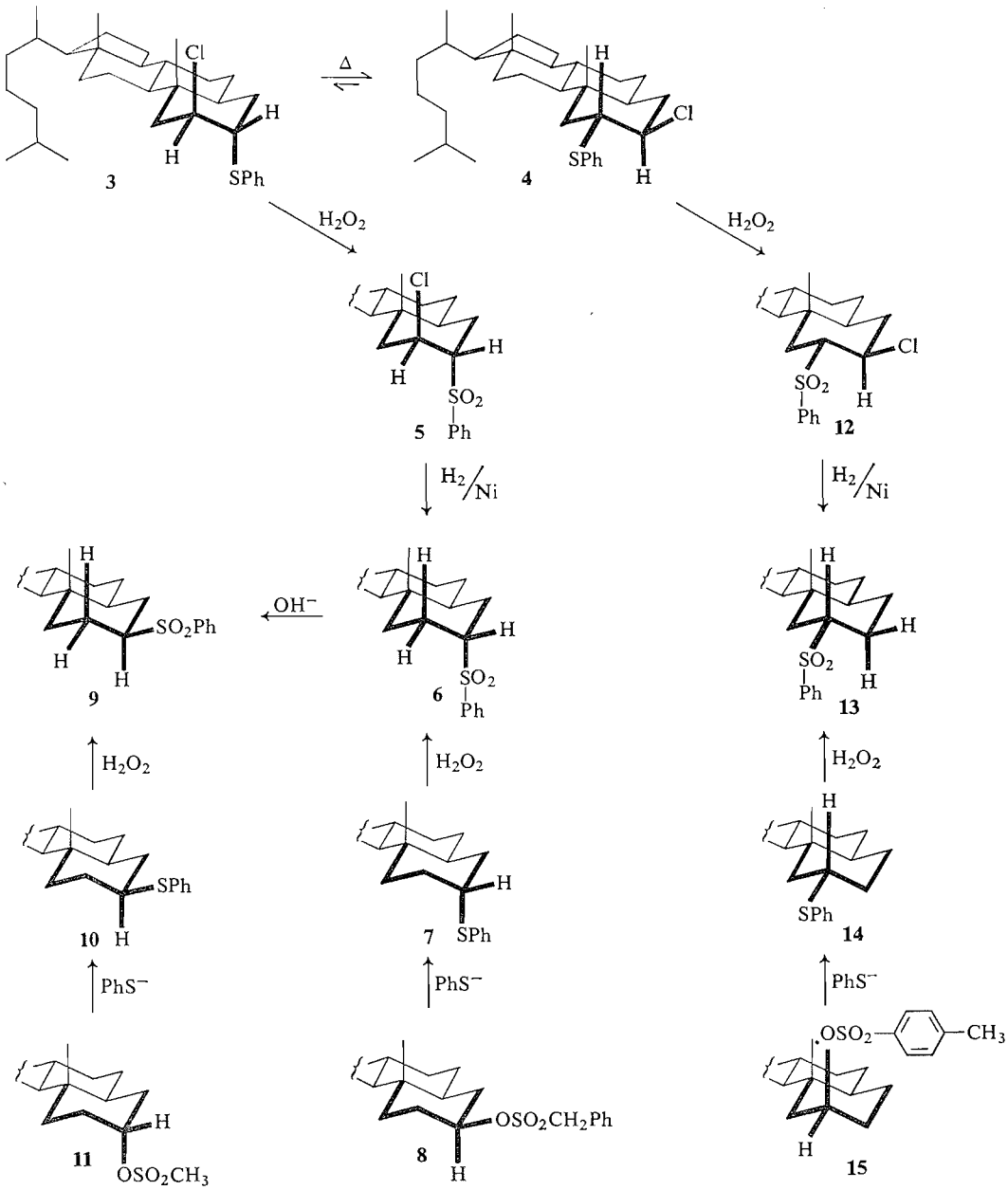
As the usefulness of the compound to us depended on whether or not it would undergo diaxial → diequatorial rearrangement, it was immediately subjected to the appropriate conditions and found to isomerize. Among the dozen examples of diaxial → diequatorial rearrangement reported with 2,3-disubstituted 5α-cholestane derivatives (4–7), the molecular rotation difference ($[\phi]_{Eq} - [\phi]_{Ax}$) varies from −290° to −730°, with most in the range of roughly −400° to −550°. The difference in the present instance is −410°, in excellent agreement with the expectation that the 5α-cholest-2-ene – benzenesulfenyl chloride adduct is in fact diaxial, and rearranging to a diequatorial isomer.

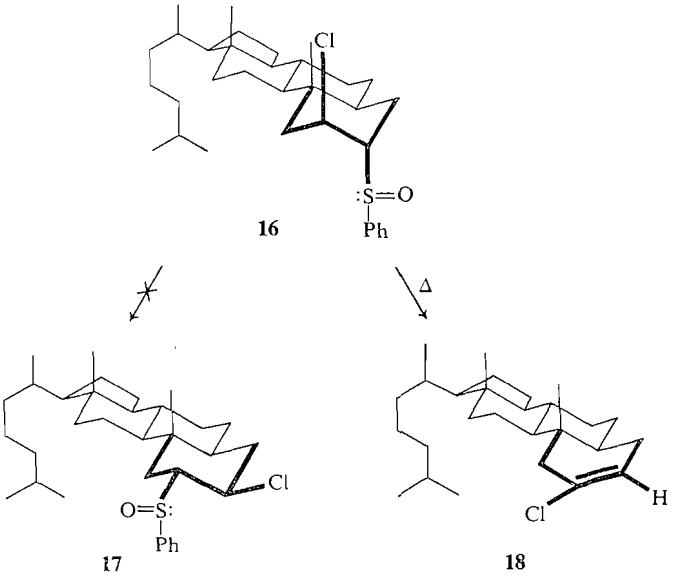
Comparison of the nuclear magnetic resonance (n.m.r.) spectra of the two compounds confirmed this. The diaxial isomer showed bands centered near 4.4 and 3.75 p.p.m. and assigned to the methine protons on C-2 and C-3 respectively.[3] Both bands showed as unresolved humps with widths measured at one-half their heights ("half-widths") of less than 9 c.p.s. Hassner and Heathcock (15) have examined the spectra of a number of analogous steroids and have found that such methine hydrogen atoms when equatorial have half-widths of from 5 to 12 c.p.s., whereas axial protons, presumably because of the greater coupling with vicinal axial protons, show much broader bands, viz. from 15 to 30 c.p.s. The rearranged compound (**4**) showed only a single broad band (half-width > 40 c.p.s.) around 4.4 p.p.m. but the picture was somewhat clearer with the sulfone (**12**), obtained by oxidation of **4**. The spectrum of **12** has broad bands centered around 3.9 and 3.25 p.p.m. with half-widths of about 15 and 20 c.p.s. respectively, clearly indicating that the protons at C-2 and C-3 in the sulfone (**12**) and hence in the rearranged thioether (**4**) are axial.

The above argument establishes that the 5α-cholest-2-ene – benzenesulfenyl chloride adduct is diaxial and rearranges thermally to a diequatorial isomer. No data, however, have been presented to show that the compound is in fact **3**, and not the diaxial compound in which the positions of the substituents are reversed, i.e. 3α-chloro-2β-(phenylthio)-5α-cholestane. The required evidence was obtained from a sequence of reactions beginning with the oxidation of **3** to the corresponding sulfone (**5**). Hydrogenation of **5** in the presence of Raney nickel gave the dechloro-sulfone (**6**), together with a somewhat larger amount of 5α-cholestane. The structure of the dechloro-sulfone was established by independent synthesis from 5α-cholestan-3β-yl phenylmethanesulfonate (**8**) as in the reaction scheme. The assignment of the stereochemistry of 7 (and hence of **6**) follows from the well-known predilection of thiophenoxide ions to attack with inversion of configuration at carbon atoms bearing easily displaced groups, as in the closely related example of the 4-*t*-butylcyclohexyl tosylates studied by Eliel and Ro (16). As a check on this point 5α-cholestan-3α-yl mesylate (**11**) was treated with sodium thiophenoxide and the product (**10**) oxidized to the sulfone (**9**). This material was clearly different from **6** but could be obtained from **6** by treatment with strong base, which allows the phenylsulfonyl group to epimerize to the less compressed equatorial position.

As a final check that the diaxial compound (**3**)

[3]This assignment, rather than the reverse, is made on the basis of (*i*) the greater deshielding effect of chlorine as compared with sulfur (14), and (*ii*) the observation that the band at 3.75 p.p.m. is shifted to 3.95 p.p.m. in the *p*-nitro analogue of **3** (see J. F. King and K. Abikar, Can. J. Chem. This issue.) while the 4.4 p.p.m. band is unchanged.

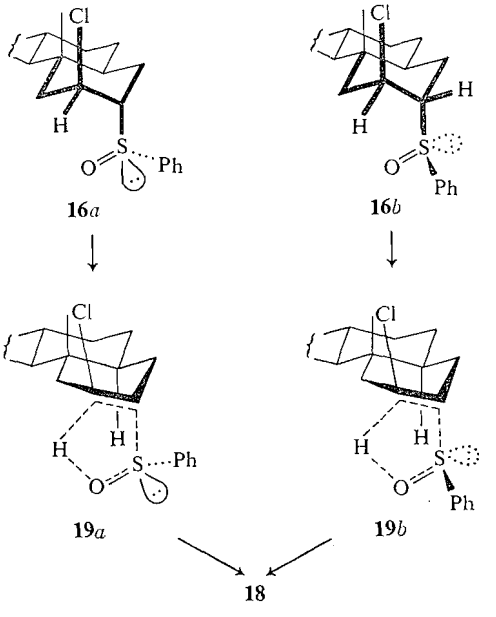




was in fact, undergoing a diaxial → diequatorial rearrangement, the product (**4**) was oxidized to **12** which was then hydrogenolyzed giving 2α-(phenylsulfonyl)-5α-cholestane (**13**). Sulfone **13** was synthesized from 5α-cholestan-2β-yl tosylate (**15**) via the sulfide (**14**) in a manner similar to the preparation of **6** and **9**. In agreement with the assigned stereochemistry, **13** was stable to the conditions under which **6** isomerized to **9**.

The above results, coupled with the recent discovery of neighboring group participation by sulfinyl groups (17), prompted us to determine whether or not the corresponding β-chlorophenylsulfoxides would undergo diaxial → diequatorial rearrangement. Accordingly sulfides **3** and **4** were subjected to mild oxidation to yield the corresponding sulfoxides. The material from **3** was found to be a roughly 2:1 mixture of the two sulfoxides epimeric at the sulfur atom, and which proved to be separable on thin-layer chromatography. The major component melted at 125° and showed a strong positive Cotton effect ($a = +300$). Following the work of Mislow and co-workers on optically active aryl alkyl sulfoxides (18, 19), it was assigned the *R* configuration at the sulfur atom, as in **16***a*. The other diaxial sulfoxide (m.p. 160°) showed a very strong negative Cotton effect ($a = -1432$) and was accordingly formulated as the *S*-isomer (**16***b*). Further oxidation of the original mixture of the two epimeric sulfoxides gave a virtually quantitative yield of sulfone **5**. The diequatorial chloro-sulfide (**4**) was also oxidized under mild conditions giving what appeared from its sharp melting point and chromatographic behavior to be a single product (**17**), though no very serious attempts were made to determine whether or not the product was in fact composed of epimeric materials.

On heating, neither **16***a* nor **16***b* gave any detectable quantity of **17**. The major isolated



product (in 40–50% yield) from the sulfoxide mixture was evidently derived from pyrolytic elimination of the elements of benzenesulfenic acid (PhSOH). The presence of one olefinic hydrogen (at 5.7 p.p.m.) and the known propensity of sulfoxides to undergo cis elimination (20) indicate the vinyl chloride structure (**18**) for the pyrolysis product.

Kingsbury and Cram (20) have suggested that such eliminations proceed via a transition state in which the hydrogen becomes bonded to the *oxygen* atom of the sulfinyl group rather than the sulfur atom, and two recent papers supply stereochemical support for this idea (21, 22). For the pyrolysis of **16***a* and **16***b*, these transition states may be formulated as in **19***a* and **19***b*, respectively. On such a basis it would be expected that the *S*-sulfoxide (**16***b*) would form **18** more readily than the *R*-sulfoxide (**16***a*), because **19***b* lacks the non-bonding repulsion between the phenyl group and the 5α-hydrogen present in **19***a* (and which is probably not present in the starting material (**16***a*)). This expectation was, in fact, realized. Upon heating a toluene solution of each sulfoxide at 95° for a number of hours, taking samples at intervals for assay by thin-layer chromatography, we found in each sample that the *S*-sulfoxide (**16***b*) produced more **18** than did the *R*-isomer (**16***a*). Accompanying **18** in the pyrolysis and running at only slightly slower rate on the chromatogram, was a second material which appeared to be formed in larger amount from the *R*-sulfoxide than from the *S*-compound. No attempt was made to characterize this material owing to the small quantities at hand. The observation, however, raises the interesting possibility that the material is 2-chloro-5α-cholest-3-ene, an allylic isomer of **18**, which for a reason similar to that given for the relative ease of forming **18**, might be expected to be produced more readily from **16***a* than from **16***b*.

Experimental

Melting points were determined on a Kofler hot stage and are uncorrected. Infrared spectra were obtained with a Beckman IR-7 instrument equipped with sodium chloride optics. Nuclear magnetic resonance spectra were measured on a Varian A-60 instrument with tetramethylsilane as internal standard. Optical rotations at the D line were determined with a Rudolph model 80 polarimeter using approximately 1% solutions in chloroform; all other rotations were obtained using a Jasco ORD/UV-5-CD spectropolarimeter.

Petroleum ether refers to the fraction of boiling range 35–60°. Thin-layer chromatography was carried out on Camag Kieselgel DF 5. A multiple development technique was employed to separate compounds with very similar R_f values. In these cases the plate was developed using solvent which gave a low R_f value, then air-dried and redeveloped, the procedure being repeated until the desired separation had been achieved.

2β-Chloro-3α-(phenylthio)-5α-cholestane (3)

5α-Cholest-2-ene was prepared by the method of Alt and Barton (4), and benzenesulfenyl chloride by chlorination of diphenyl disulfide (23). A solution of 5α-cholest-2-ene (**1**) (2.7 mmole) in methylene chloride (60 ml) was cooled in an ice bath. Benzenesulfenyl chloride (3.0 mmole) in methylene chloride (30 ml) was added with stirring over a period of 15 min. The brownish-red color of the sulfenyl chloride disappeared rapidly as long as there was any unreacted cholest-2-ene; the conversion of all of the olefin was marked by persistence of the color. The reaction mixture was quickly washed with two 50 ml portions of water, the methylene chloride layer dried with sodium sulfate, and the solvent evaporated under reduced pressure. The product (1.35 g, 90%) crystallized in the flask immediately. Recrystallization from acetone gave needles melting at 109–110°, $[\alpha]_D$ +20.5°.

Anal. Calcd. for $C_{33}H_{51}SCl$: C, 76.92; H, 9.98; S, 6.22; Cl, 6.88. Found: C, 76.98; H, 9.96; S, 6.29; Cl, 6.87.

3β-Chloro-2α-(phenylthio)-5α-cholestane (4)

2β-Chloro-3α-(phenylthio)-5α-cholestane (**3**) (0.90 g) was dissolved in 1-butanol and heated at 80° for 1½ h. The solvent was removed under reduced pressure and the residue chromatographed on silica gel. The fraction (651 mg) eluted with petroleum ether was recrystallized from ether–methanol; m.p. 74°, $[\alpha]_D$ −57°.

Anal. Calcd. for $C_{33}H_{51}SCl$: C, 76.92; H, 9.98; S, 6.22; Cl, 6.88. Found: C, 76.94; H, 10.01; S, 6.38; Cl, 6.63.

2β-Chloro-3α-(phenylsulfonyl)-5α-cholestane (5)

2β-Chloro-3α-(phenylthio)-5α-cholestane (**3**) (100 mg) in acetic acid (10 ml) was heated at 91° with excess 30% hydrogen peroxide (~1 ml) for 2 h. The reaction mixture was poured into water and extracted with chloroform. The chloroform extract was washed successively with dilute NaOH, dilute HCl, and water. The solvent was removed under reduced pressure leaving a product (96 mg) which was then recrystallized from acetone. The compound melted at 154°, solidified and melted again at 165°; $[\alpha]_D$ +53°.

Anal. Calcd. for $C_{33}H_{51}SO_2Cl$: C, 72.43; H, 9.40; S, 5.86; Cl, 6.48. Found: C, 72.62; H, 9.38; S, 6.08; Cl, 6.62.

3α-(Phenylthio)-5α-cholestane (7)

5α-Cholestan-3β-yl phenylmethanesulfonate (**8**) was prepared by the reaction of cholestan-3β-ol, phenylmethanesulfonyl chloride, and triethylamine, as described by Durst (24). A portion (250 mg) of the sulfonate was added to a solution prepared by mixing benzenethiol (0.50 g), metallic sodium (40 mg), 95% ethanol (2 ml) with tetrahydrofuran (10 ml), and the mixture refluxed in a nitrogen atmosphere for 9 h. The reaction mixture was then poured into dilute aqueous NaOH and extracted with chloroform. The extract was washed with dilute

HCl and water and dried over Na_2SO_4. The crude product (256 mg) obtained on evaporation of the solvent was purified by thin-layer chromatography giving a material (174 mg, 81%) which on recrystallization from ether–ethanol melted at 105–106°, $[\alpha]_D$ +19.5°.

Anal. Calcd. for $C_{33}H_{52}S$: C, 82.44; H, 10.90; S, 6.66. Found: C, 82.18; H, 10.65; S, 6.94.

3α-(Phenylsulfonyl)-5α-cholestane (6)

3α-(Phenylsulfonyl)-5α-cholestane was prepared by oxidation of 3α-(phenylthio)-5α-cholestane (**7**) with hydrogen peroxide as already described in the preparation of 2β-chloro-3α-(phenylsulfonyl)-5α-cholestane (see above). The yield was virtually quantitative. The analytical specimen was obtained by recrystallization from ether–ethanol, m.p. 159–160°, $[\alpha]_D$ +17.5°.

Anal. Calcd. for $C_{33}H_{52}SO_2$: C, 77.29; H, 10.22; S, 6.24. Found: C, 77.17; H, 9.79; S, 6.24.

Hydrogenation of 2β-Chloro-3α-(phenylsulfonyl)-5α-cholestane

2β-Chloro-3α-(phenylsulfonyl)-5α-cholestane (**5**) (157 mg) was dissolved in 2-methoxyethanol and shaken with hydrogen at atmospheric pressure in the presence of Raney nickel catalyst (ca. 3.3 g) and calcium carbonate (200 mg). The crude product obtained after filtration and evaporation of the solvent from the filtrate, was separated by thin-layer chromatography into two components. The major component (85 mg) was shown to be cholestane and the minor component (23 mg) to be 3α-(phenylsulfonyl)-5α-cholestane (**6**), in each case by comparison of specific rotation, infrared spectrum, melting point, and mixture melting point with that of an authentic specimen.

3β-(Phenylthio)-5α-cholestane (10)

3β-(Phenylthio)-5α-cholestane was prepared in 76% yield from 5α-cholestan-3α-yl methanesulfonate (**11**) by the method given for 3α-(phenylthio)-5α-cholestane (see above), m.p. 79–80°, $[\alpha]_D$ +18°. The reaction mixture also contained a small amount (12%) of 5α-cholest-2-ene.

Anal. Calcd. for $C_{33}H_{52}S$: C, 82.44; H, 10.90; S, 6.66. Found: C, 82.23; H, 11.21; S, 7.05.

3β-(Phenylsulfonyl)-5α-cholestane (9)

Oxidation of 3β-(phenylthio)-5α-cholestane (**10**) with hydrogen peroxide as described above in the preparation of 2β-chloro-3α-(phenylsulfonyl)-5α-cholestane gave a 70% yield of crude 3β-(phenylsulfonyl)-5α-cholestane. Recrystallization from methylene chloride – ethanol gave the pure material, m.p. 182°, $[\alpha]_D$ +20.5°.

Anal. Calcd. for $C_{33}H_{52}SO_2$: C, 77.29; H, 10.22; S, 6.24. Found: C, 77.54; H, 9.88; S, 6.59.

Epimerization of 3α-(Phenylsulfonyl)-5α-cholestane

3α-(Phenylsulfonyl)-5α-cholestane (**6**) (25 mg) was heated with potassium hydroxide (135 mg) in distilled dimethyl sulfoxide at ~75° for 16 h. The reaction mixture was poured into water and extracted with chloroform. The extract was washed with dilute hydrochloric acid and water, dried, and the solvent evaporated. The material (21 mg, 84%), melting at 182–183°, obtained on recrystallization from ether–ethanol, was shown by infrared spectrum and mixture melting point to be identical to 3β-(phenylsulfonyl)-5α-cholestane obtained by hydrogen peroxide oxidation of 3β-(phenylthio)-5α-cholestane (see above).

2α-(Phenylthio)-5α-cholestane (14)

Benzenethiol (2.0 ml) and tetrahydrofuran (80 ml) were added to a solution (5 ml) of sodium ethoxide (from 300 mg of sodium) in ethanol. 5α-Cholestan-2β-yl tosylate (865 mg) was added and the mixture refluxed under nitrogen for 6 h. It was then poured into dilute NaOH, extracted with methylene chloride, and the extract washed with dilute HCl and water, and dried over sodium sulfate. The crude product, which was contaminated with phenyl disulfide, was subjected to thin-layer chromatography using cyclohexane–ether (9:1) and developing two or three times. The purified material (136 mg) so obtained, was recrystallized from ether–methanol and acetone–methanol; m.p. 85–86°.

Anal. Calcd. for $C_{33}H_{52}S$: C, 82.44; H, 10.90; S, 6.66. Found: C, 82.15; H, 10.66; S, 6.90.

2α-(Phenylsulfonyl)-5α-cholestane (13)

2α-(Phenylthio)-5α-cholestane was oxidized in good yield with hydrogen peroxide as in the preparation of 2β-chloro-3α-(phenylsulfonyl)-5α-cholestane (see above). The product was chromatographed and then recrystallized from ether–methanol giving an analytical sample melting at 167–168°; $[\alpha]_D$ +9°.

Anal. Calcd. for $C_{33}H_{52}O_2S$: C, 77.29; H, 10.22; S, 6.24. Found: C, 77.47; H, 10.15; S, 6.39.

Hydrogenation of 3β-Chloro-2α-(phenylsulfonyl)-5α-cholestane

3β-Chloro-2α-(phenylsulfonyl)-5α-cholestane (**12**) (317 mg) was dissolved in 2-methoxyethane (50 ml) and shaken with hydrogen in the presence of Raney nickel catalyst (~1.0 g) and lithium carbonate (0.2 g) for 46 h. On thin-layer chromatography the crude product (270 mg) was separated into unreacted **12** (116 mg), cholestane (72 mg, 53% yield, on the basis of unrecovered starting material), and 2α-(phenylsulfonyl)-5α-cholestane (**13**) (45 mg, 24% yield, on the basis of unrecovered starting material) identified by melting point, mixture melting point, and specific rotation.

2β-Chloro-3α-(phenylsulfinyl)-5α-cholestane (R- and S-isomers, 16a and 16b)

2β-Chloro-3α-(phenylthio)-5α-cholestane (**3**) (682 mg, 1.32 mmoles) was suspended in glacial acetic acid (200 ml) and 30% hydrogen peroxide solution (2.0 ml) added. The solid particles were scratched with a glass rod to aid dissolution, and the reaction mixture was then let stand for 2 h at room temperature. The material was then poured into water (ca. 300 ml) and the mixture extracted with methylene chloride. The extracts were washed successively with dilute NaOH, water, dilute HCl, and water again. The methylene chloride layer was then dried with anhydrous $MgSO_4$ and the solvent evaporated giving the crude product (701 mg). On recrystallization from ether–methanol a crystalline product (591 mg) melting from 115 to 130° was obtained. This material was used directly in both the preparative pyrolysis forming **18**, and the oxidation to sulfone **5**. It showed only one spot on thin-layer chromatography with a number of solvents, but was found to be resolved into two components with cyclohexane–ether (3:1). A portion (200 mg) of the recrystallized sulfoxide mixture was placed on thin-layer plates and developed two or three times with the cyclo-

hexane–ether mixture. The front-running material (63 mg) melted at 160° after recrystallization from ether–methanol. The n.m.r. spectrum showed unresolved peaks at 3.1 and 4.9 p.p.m. with widths at half-heights of 8 c.p.s. each. The optical rotatory dispersion (o.r.d.) curve of an ethanol solution showed a trough at 270 mμ, [φ] −9202°, and a peak at 221 mμ, [φ] +20770°, ([α]$_D$ −4° in chloroform); on the basis of the work of Mislow *et al.* (18), it was assigned the *S* configuration at the sulfur atom.

Anal. Calcd. for $C_{33}H_{51}ClOS$: C, 74.61; H, 9.68; Cl, 6.68; S, 6.04. Found: C, 74.33; H, 9.64; Cl, 6.72; S, 5.91.

The slower-running component (139 mg) was recrystallized from ether–methanol, m.p. 125°. The n.m.r. spectrum showed humps at 3.0 and 4.1 p.p.m., half-widths roughly 10 c.p.s. each. The o.r.d. curve (ethanol) showed a peak at 270 mμ, [φ] +24 980°, and a trough at 221 mμ, [φ] −118 200° ([α]$_D$ +118° in chloroform); it was assigned the *R*-configuration at the sulfur atom.

Anal. Calcd. for $C_{33}H_{51}ClOS$: C, 74.61; H, 9.68; Cl, 6.68; S, 6.04. Found: C, 74.60; H, 9.86; Cl, 6.45; S, 6.01.

*Pyrolysis of 2β-Chloro-3α-(phenylsulfinyl)-5α-cholestane (**16**)*

The diaxial sulfoxide (**16**, mixture of epimers at the sulfur atom) (250 mg) was heated in a mixture of nitromethane (8 ml) and chloroform (2 ml) for 21 h at 98 ± 2°. The solution was evaporated to dryness. Thin-layer chromatography of the residue showed no material corresponding to either the starting material (**16**) or the diequatorial sulfoxide (**17**); most of the product appeared to run near the front and only slightly more slowly than 5α-cholest-2-ene. A benzene solution of the residue was filtered through silica gel and the solvent evaporated. This material was chromatographed on alumina (grade I); elution with petroleum ether yielded 80 mg of a product which after four recrystallizations from ether–methanol melted at 122°; [α]$_D$ +71°. The n.m.r. spectrum showed unresolved humps at ~5.7 p.p.m. and 2.1 p.p.m. in addition to the complex absorption from 0.5 to 2.0 p.p.m.

Anal. Calcd. for $C_{27}H_{45}Cl$: C, 80.04; H, 11.19; Cl, 8.75. Found: C, 80.47; H, 11.21; Cl, 8.44.

To determine the relative ease with which each of the two sulfoxides (**16***a* and **16***b*) formed the compound melting at 122° (**18**), 6 mg samples of each sulfoxide were dissolved in dry toluene (5 ml) and each solution divided into five ampoules. Each ampoule was flushed with dry nitrogen, sealed, and heated in a water bath at 95°. An ampoule of each sulfoxide was opened after 1 h, 2 h, and 4 h and the remaining two after 10½ h. In each case the solvent was removed with a stream of nitrogen, and a portion of the residue analyzed by thin-layer chromatography. Development with cyclohexane–ether (3:1) showed the reaction to be nearly complete after 10½ h, and that there was no detectable amount of material running at the same rate on the chromatogram as 3β-chloro-2α-(phenylsulfinyl)-5α-cholestane (**17**) in any of the samples. Development with petroleum ether showed a material from each sulfoxide with the same R_f value as **18**; for each pair of samples the intensity of that spot from the *S*-sulfoxide (**16***b*, m.p. 160°) was distinctly greater than that from the *R*-sulfoxide (**16***a*, m.p. 125°). In the chromatogram of each reaction product there appeared another spot immediately following that corresponding to **18**. The intensity of this spot in the material from the *R*-sulfoxide was greater than that of the corresponding spot from the *S*-sulfoxide. From the *R*-sulfoxide the spots due to **18** and the slower moving material appeared to be of very similar intensities, whereas from the *S*-sulfoxide the spot due to **18** was a good deal more intense than that of the slower moving material.

*Oxidation of the 2β-Chloro-3α-(phenylsulfinyl)-5α-cholestane Mixture (**16**)*

The crystalline mixture of the two sulfoxides epimeric at the sulfur atom (100 mg) was dissolved in glacial acetic acid (10 ml). Hydrogen peroxide solution (30%, 1.0 ml) was added and the mixture heated for 2 h at 91°. It was then poured into water and extracted with chloroform. The extract was washed with dilute NaOH, water, dilute HCl, and water, respectively, and dried over $MgSO_4$. The solvent was evaporated giving the crude product (96 mg). Recrystallization from acetone gave the pure product, melting at 165° with a transition at 154°. Its infrared spectrum was identical to that of the material obtained directly by oxidation of the diaxial chlorosulfide (**3**).

*3β-Chloro-2α-(phenylsulfinyl)-5α-cholestane (**17**)*

3β-Chloro-2α-(phenylthio)-5α-cholestane (**4**) was oxidized in good yield with hydrogen peroxide in glacial acetic acid in a manner similar to that used in the preparation of 2β-chloro-3α-(phenylsulfinyl)-5α-cholestane (**16**). On recrystallization from methylene chloride – methanol the product melted at 201–202°; [α]$_D$ −184°.

Anal. Calcd. for $C_{33}H_{51}ClOS$: C, 74.61; H, 9.68; Cl, 6.68; S, 6.04. Found: C, 74.56; H, 9.65; Cl, 6.78; S, 6.18.

Acknowledgments

This work was supported by grants-in-aid from the Ontario Research Foundation and the Department of University Affairs of the Province of Ontario, and by the National Research Council of Canada.

1. D. H. R. Barton. *In* Theoretical organic chemistry papers presented to the Kekule Symposium. Butterworths, London. 1959. p. 127.
2. D. H. R. Barton and E. Miller. J. Am. Chem. Soc. **72**, 1066 (1950).
3. K. Hattori and T. Kawasaki. Yakugaku Zasshi, **57**, 115 (1937).
4. G. H. Alt and D. H. R. Barton. J. Chem. Soc. 4284 (1954).
5. D. H. R. Barton and J. F. King. J. Chem. Soc. 4398 (1958).
6. J. F. King, R. G. Pews, and R. A. Simmons. Can. J. Chem. **41**, 2187 (1963).
7. J. F. King and R. G. Pews. Can. J. Chem. **43**, 847 (1965).
8. N. Kharasch. *In* Organic sulfur compounds. Vol. 1. *Edited by* N. Kharasch. The Pergamon Press, Ltd., London. 1961. p. 375.
9. D. J. Pettit and G. K. Helmkamp. J. Org. Chem. **29**, 2702 (1964).

10. W. H. MUELLER and P. E. BUTLER. J. Am. Chem. Soc. **88**, 2866 (1966).
11. A. FURST and P. A. PLATTNER. Intern. Congr. Pure and Appl. Chem., 12th Congr., New York. 1951. Abstracts of papers. p. 409.
12. D. H. R. BARTON and R. C. COOKSON. Quart. Rev. London, **10**, 44 (1956).
13. A. HASSNER and C. HEATHCOCK. Tetrahedron Letters, 393 (1963); *also* J. Org. Chem. **30**, 1748 (1965).
14. L. M. JACKMAN. Applications of nuclear magnetic resonance spectroscopy in organic chemistry. The Pergamon Press, Ltd., London. 1959. p. 53.
15. A. HASSNER and C. HEATHCOCK. J. Org. Chem. **29**, 1350 (1964).
16. E. L. ELIEL and R. S. RO. J. Am. Chem. Soc. **79**, 5995 (1957).
17. H. HOGEVEEN, G. MACCAGNANI, and F. MONTANARI. Bull. Sci. Fac. Chim. Ind. Bologna, **21**, 257 (1963).
18. K. MISLOW, M. M. GREEN, P. LAUR, J. T. MELILLO, T. SIMMONS, and A. L. TERNAY, JR. J. Am. Chem. Soc. **87**, 1958 (1965).
19. P. BICKART, M. AXELROD, J. JACOBUS, and K. MISLOW. J. Am. Chem. Soc. **89**, 697 (1967).
20. C. A. KINGSBURY and D. J. CRAM. J. Am. Chem. Soc. **82**, 1810 (1960).
21. D. N. JONES and M. A. SAEED. Proc. Chem. Soc. 81 (1964).
22. S. I. GOLDBERG and M. S. SAHLI. Tetrahedron Letters, 4441 (1965).
23. H. LECHER. Ber. **58**, 409 (1925).
24. T. DURST. Ph.D. Thesis, University of Western Ontario, London, Ontario. 1964.