line 1-oxide, mp 238—240°. This sample was identified with an authentic specimen described by Okamoto.[10]

**Reaction of 4-Methylsulfonylquinoline 1-Oxide with 1N Sodium Hydroxide**——4-Methylsulfonylquinoline 1-oxide (190 mg) was dissolved in N sodium hydroxide (20 ml) and gently warmed on a water bath. The reaction mixture began to be colored and muddy precipitate appeared. After heating for 1 hr at 70°, the precipitate was dissolved in water and examined by paper chromatography (solvent: water pH 10). A spot ($Rf$=0.86) corresponding to 4-hydroxyquinoline 1-oxide was observed as the main product, accompanied with two ($Rf$=0.56, 0.42) minor spots.

**Reaction of 4-Methylsulfonylquinoline 1-Oxide with Sodium Hydrogen Sulfide**——Into a solution of sodium hydrogen sulfide, an ethanol solution of 4-methylsulfonylquinoline 1-oxide (45 mg) was added. The resulting mixture was refluxed for 3 hr and evaporated to dryness. The red colored residue was taken up in small amount of water and acidified with acetic acid to pH 2—3. Then, precipitated material was collected and recrystallized from methanol. Orange-yellow needles. mp 140—141°. This sample was identified by mixed melting point test and IR absorption measurement with authentic specimen.

**Reaction of 4-Alkyl- or Arylsulfonylquinoline 1-Oxide with Alkyl- or Arylmercaptan**——Into an ethanol solution of sodium alkyl- or arylmercaptide, an ethanol solution of 4-alkyl- or arylsulfonylquinoline 1-oxide (1 equivalent) was combined. The solution was refluxed gently for 1 hr on an oil bath. Precipitated inorganic salt was removed by filtration, water was added and the product extracted with chloroform. The organic layer was dried over anhydrous magnesium sulfate and evaporated to dryness. The product was washed thoroughly with ether and recrystallized from methanol or acetone. This sample was identified with the specimen obtained from 4-chloroquinoline 1-oxide by mixed melting point test and or IR absorption measurement. $\gamma_{max}^{KBr}$ 700—800 $cm^{-1}$, 1350 $cm^{-1}$(-SR), 1295—1300 $cm^{-1}$ (heteroaromatic N-oxide).

**Reaction of 4-Methylsulfonylquinoline 1-Oxide with Hydrazine Hydrate**——To a solution of 4-methylsulfonylquinoline 1-oxide (190 mg) dissolved in 5 ml of ethanol, 5 ml of 80% hydrazine hydrate was added and the mixture was gently refluxed for 1 hr. Yellowish green needles were precipitated, filtered, and washed with ether and recrystallized from boiling ethanol. Yield 128 mg. mp 168—170° (decomp.). This sample was identical with authentic specimen of 4-hydrazinoquinoline 1-oxide described by Itai and Kamiya.[11]

**Reaction of 4-Methylsulfonylquinoline 1-Oxide with Sodium Azide**——A mixture of 4 methylsulfonyl quinoline 1-oxide (190 mg), sodium azide (198mg) and 10 ml of acetonitrile was refluxed for 6 hr. After cooling, insoluble salt was filtered off and the filtrate and washings were combined and solvent was removed under reduced pressure. The brown viscous residue was taken up in chloroform and dried over anhydrous magnesium sulfate and solvent was evaporated off. Recrystallization from acetone gave pale brown crystal. Yield 98 mg. mp 141—143° (decomp.). This sample was identical with the specimen of 4-azidoquinoline 1-oxide described by Itai and Kamiya.[11]

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# Chemistry of 3-Phenylcholestan-3-ols[1]

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In the preceding paper one of the authors reported that the structure of the Zimmermann complex derived from cholestan-3-one was elucidated to be 2α-(2,4-dinitrophenyl)cholestan-

1) This paper constitutes Part XVII of the series entitled "Analytical Chemical Studies on Steroids"; Part XVI: *J. Chromatog.*, **31**, 535 (1967).
2) Location: *Kita-4-bancho, Sendai.*

3–one on the basis of nuclear magnetic resonance spectra.[3] An interest in stereochemistry of aryl–substituted oxosteroid prompted us to prepare cholestan–3–one having phenyl group at $\alpha$–position. The present paper deals with some observations during the attempt to synthesize the above compound.

Reaction of 2$\alpha$, 3$\alpha$–epoxycholestane with phenylmagnesium bromide in tetrahydrofuran and subsequent chromatographic separation on alumina gave a crystalline material as main product. This substance appeared to have empirical formula $C_{33}H_{52}O$ and to bear hydroxyl group, which was resistant to usual acetylation and chromium trioxide oxidation. On brief exposure to thionyl chloride in pyridine it was readily dehydrated to afford phenylcholestene, whose conjugated system exhibited absorption maximum at 250 m$\mu$ (log $\varepsilon$ 4.12). All these results together indicated that the product obtained would be 3–phenylcholestan–3–ol. Hence the authors prepared the epimeric 3–phenylcholestan–3–ols from cholestanone by the known method.[4] Upon comparison with the authentic sample thus obtained, the product proved to be 3$\beta$–phenylcholestan–3$\alpha$–ol (I). It is now to be noted that cleavage of the epoxide with Grignard reagent takes a sterically anomalous course providing no *trans*–diaxial opening product.[5,6] This unusual reaction appears to proceed in such a manner as illustrated in Chart 1.

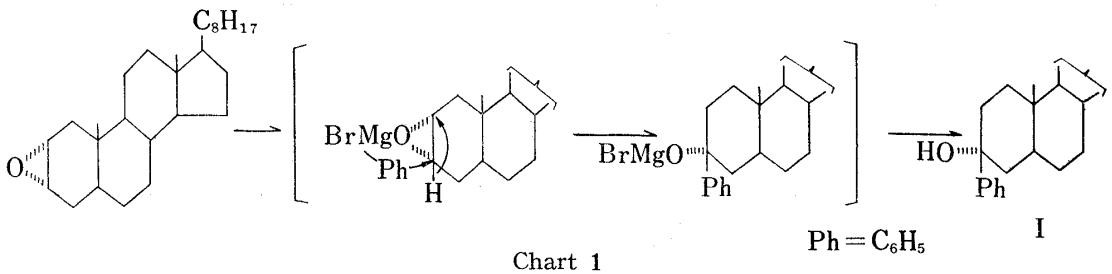


Chart 1

During the preparation of the authentic samples mentioned above, it was unexpectedly found that on treatment with chromium trioxide in acetic acid 3$\alpha$–phenylcholestan–3$\beta$–ol (II) could be readily isomerized to its C–3–epimer (I), whereas the reverse did not proceed. It is obvious that the relative ease, with which epimerization takes place, is ascribable to the presence of the phenyl group. In actuality isomerization did not occur between the two epimeric 3–methylcholestan–3–ols[7] under the same conditions. Furthermore no epimerization arose unless chromium trioxide was added.

Based upon these facts the reaction mechanism can be at present tentatively explained as follows (see Chart 2). 3$\alpha$–Phenylcholestan–3$\beta$–ol is first converted to chromic acid ester,[8] and

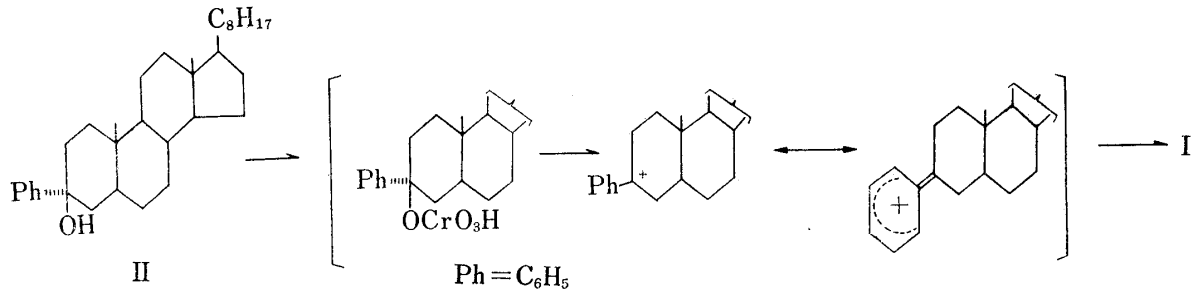


Chart 2

3) T. Nambara and M. Katō, *Chem. & Ind.* (London), **1967**, 1090.
4) J.A. Zderic, M.E.C. Rivera, and D.C. Limón, *J. Am. Chem. Soc.*, **82**, 6373 (1960).
5) J.A. Zderic and D.C. Limón, *J. Am. Chem. Soc.*, **81**, 4570 (1959).
6) C. Djerassi, "Steroid Reactions," Holden–Day, Inc., San Francisco, 1963, p. 631.
7) J.L. Beton, T.G. Halsall, E.R.H. Jones, and P.C. Phillips, *J. Chem. Soc.*, **1957**, 753.

then to carbonium ion with loss of chromate, which is stabilized by the delocalization of the positive charge towards benzene nucleus. This in turn combines with chromate ion to form the thermodynamically more stable epimer.[9,10] In this novel epimerization the phenyl group may play roles of stabilizing the intermediate as well as of exerting greater preference for the equatorial bond than hydroxyl group.

## Experimental[11]

**Reaction of 2α,3α-Epoxychloestane with Phenylmagnesium Bromide**——To anhydrous tetrahydrofuran (THF) (40 ml) containing Mg turning (0.4 g) was added bromobenzene (2.8 g) in THF (8 ml). Upon completion of Grignard reagent formation 2α,3α-epoxycholestane (1 g) dissolved in THF (30 ml) was added. After being refluxed for 15 hr, saturated aq. $NH_4Cl$ solution (20 ml) was added to the reaction mixture to decompose the Grignard complex. The resulting solution was extracted with AcOEt (70 ml×4), washed with $H_2O$ and dried over anhydrous $Na_2SO_4$. After evaporation of solvent the residue obtained was chromatographed on $Al_2O_3$ (60 g). Elution with hexane and hexane–benzene (9:1) gave unchanged 2α,3α-epoxycholestane (107 mg). The subsequent eluate (550 mg) with hexane–benzene (9:1) was rechromatographed on $Al_2O_3$ (30 g). Elution with hexane–benzene (9:1 to 8:2) and recrystallization of the eluate from aq. acetone gave 3β-phenylcholestan-3α-ol (300 mg) as colorless needles. mp 162—165°, $[\alpha]_D^{20}$ +21.4° ($c$=0.10). *Anal.* Calcd. for $C_{33}H_{52}O$: C, 85.28; H, 11.28. Found: C, 84.95; H, 11.24. Mixed mp on admixture with the authentic sample showed no depression, and infrared (IR) spectra of two samples were identical.

**Reaction of Cholestan-3-one with Phenylmagnesium Bromide**——According to the procedure of Zderic, *et al.*,[4] cholestan-3-one (1 g) was submitted to Grignard reaction with $C_6H_5MgBr$, and the crude product obtained was chromatographed on $Al_2O_3$ (30 g). Elution with hexane and hexane–benzene (9:1 to 7:3) and recrystallization of the eluate from acetone gave 3β-phenylcholestan-3α-ol (350 mg) as colorless needles. mp 162—165°. Elution with hexane–benzene (6:4) and ether and recrystallization of the eluate from aq. acetone gave 3α-phenylcholestan-3β-ol (350 mg) as colorless needles. mp 110—111°, $[\alpha]_D^{20}$ +20.4° ($c$=0.12) (reported mp 76—78°/100—103°). *Anal.* Calcd. for $C_{33}H_{52}O$: C, 85.28; H, 11.28. Found: C, 85.01; H, 11.32.

**3-Phenylcholest-2-ene**——To a solution of I (220 mg) in pyridine (3 ml) was added $SOCl_2$ (0.3 ml) and the resultant solution was allowed to stand at 0° for 5 min. The mixture was poured into ice–water and extracted with $CHCl_3$. On usual work-up the crude product obtained was recrystallized from acetone to give 3-phenylcholest-2-ene as colorless needles. mp 132—133°, $[\alpha]_D^{20}$ +42.3° ($c$=0.15) (reported mp 126—127°).[4] *Anal.* Calcd. for $C_{33}H_{50}$: C, 88.72; H, 11.28. Found: C, 88.92; H, 11.24. Mixed mp on admixture with the authentic sample showed no depression and IR spectra of two samples were identical.

**Epimerization of 3α-Phenylcholestan-3β-ol**——To a solution of II (100 mg) in glacial AcOH (6 ml) was added 2% $CrO_3$ in 98% AcOH solution (3 ml), and the resulting solution was allowed to stand at room temperature for 3 hr. After addition of MeOH to decompose $CrO_3$, the reaction mixture was diluted with $H_2O$ and extracted with ether. On usual work-up the crude product (80 mg) obtained was chromatographed on $Al_2O_3$ (4 g). Elution with hexane and recrystallization of the eluate from EtOH–ether gave I (27 mg) as colorless needles. mp 163—165°. Mixed mp on admixture with the authentic sample showed no depression and IR spectra of two samples were identical.

**Reaction of Cholestan-3-one with Methylmagnesium Bromide**——According to the procedure of Beton, *et al.*[7] cholestan-3-one (450 mg) was submitted to Grignard reaction with $CH_3MgBr$. The crude product obtained was chromatographed on $Al_2O_3$ (20 g). Elution with hexane–benzene (7:3 to 6:4) and recrystallization of the eluate from MeOH gave 3β-methylcholestan-3α-ol as colorless needles. mp 124—126° (reported mp 128—129°). Elution with hexane–benzene (5:5) and ether and recrystallization of the eluate from aq. acetone gave 3α-methylcholestan-3β-ol as colorless needles. mp 148—150.5° (reported mp 148—150°).

Epimerization was attempted with each one of these epimers under the above-mentioned conditions, but the unchanged material was quantitatively recovered.

**Acknowledgement** The authors are grateful to Mrs. Reiko Imanari for her technical assistance. Thanks are also due to all the staff of central analysis laboratory of this Institute for elemental analyses and IR spectral measurements.

8) L.F. Fieser, *J. Am. Chem. Soc.*, **75**, 4377 (1953).
9) N.L. Allinger, J. Allinger, M.A. DaRooge, and S. Greenberg, *J. Org. Chem.*, **27**, 4603 (1962).
10) E.W. Garbisch, Jr. and D.B. Patterson, *J. Am. Chem. Soc.*, **85**, 3228 (1963).
11) All melting points were taken on a micro hot-stage apparatus and are uncorrected. Optical rotations were measured in $CHCl_3$.