# The Radiation-Induced Addition Reaction of Alcohols to 1,2-Dichlorotetrafluorocyclobutene and 1,2-Dichlorohexafluorocyclopentene

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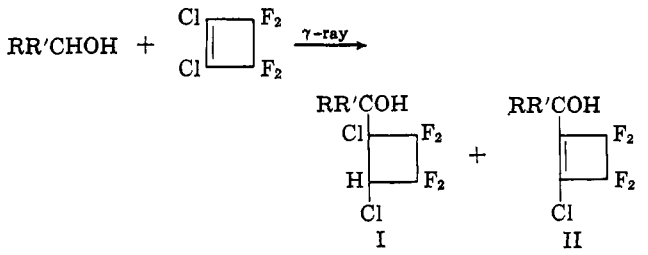
Various alcohols containing polyfluorocycloalkyl or polyfluorocycloalkenyl groups have been synthesized by the addition reaction of alcohols, such as methanol, ethanol, and 1- and 2-propanol, to 1,2-dichlorotetrafluorocyclobutene and 1,2-dichlorohexafluorocyclopentene under $\gamma$-ray irradiation. While only the polyfluorocyclopentenylcarbinols were obtained in the addition to the halocyclopentene, the addition of alcohols to the halocyclobutene gave both the 1:1 adduct and the dehydrochlorinated 1:1 adduct, whose molar ratio varied markedly with the structure of the alcohols.

Reports on the synthesis of the alcohols containing polyfluorocycloalkyl or polyfluorocycloalkenyl groups have been meager. Barrick and co-workers[1] synthesized (2,2,3,3-tetrafluorocyclobutyl)carbinol and (3,3,-4,4-tetrafluoro-1-cyclobutenyl)isopropylcarbinol by the cycloaddition reactions of tetrafluoroethylene with allyl alcohol and ethynylisopropylcarbinol, respectively. Several substituted perfluorocyclobutanols[2] were prepared by the reaction of perfluorocyclobutanone and a variety of unsaturated compounds such as propylene, methylacetylene, and allene. Polyfluorocyclobutenyldimethylcarbinols[3] were recently obtained in the reaction of tetrafluoroethylene or trifluorochloroethylene with 3-methyl-1-butyn-3-ol.

In a previous report,[4] the addition reaction of alcohols to various chlorofluoroethylenes under $\gamma$-ray irradiation was reported to take place to give the 1:1 adducts in appreciable yields. The addition reactions of alcohols, such as methanol, ethanol, and 1- and 2-propanol, have been further extended to 1,2-dichlorotetrafluorocyclobutene and 1,2-dichlorohexafluorocyclopentene to obtain the polyfluorocycloalkyl- and polyfluorocycloalkenylcarbinols. These carbinols are potential intermediates for the synthesis of versatile derivatives of polyfluorocycloalkanes and polyfluorocycloalkenes.

Mixtures of the halocyclobutene or halocyclopentene and an alcohol in a molar ratio of 1:3 were irradiated in a glass tube at a rate of $0.59 \times 10^5$ r./hr. for a period of about 3 weeks at room temperature. The products from the addition of alcohols to 1,2-dichlorotetrafluorocyclobutene were found to be a mixture of the 1:1 adduct I and the dehydrochlorinated 1:1 adduct II as shown in thee quation. The molar ratios of I to II varied markedly with the structure of the alcohols. The results are shown in Table I with the yields.




*cis* and *trans*

R = H or $CH_3$; R' = H, $CH_3$, or $C_2H_5$

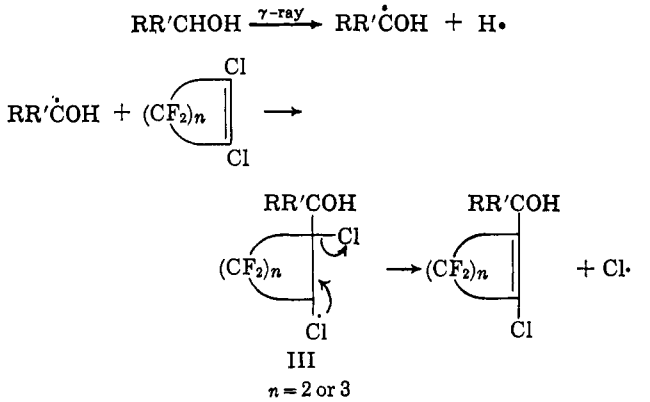
TABLE I

ADDITION OF ALCOHOLS TO 1,2-DICHLOROTETRAFLUOROCYCLOBUTENE

| Expt. no. | Alcohols | Total dosage $\times 10^6$, r. | Total yield of 1:1 adducts,[a] % | Composition of 1:1 adducts, % I | II |
|---|---|---|---|---|---|
| 1 | $CH_3OH$ | 33 | 21 | 57 | 43 |
| 2 | $C_2H_5OH$ | 30 | 61 | 74 | 26 |
| 3 | $C_2H_5OH$ | 31 | 71 | 75 | 25 |
| 4 | $n$-$C_3H_7OH$ | 22 | 19 | 54 | 46 |
| 5 | $n$-$C_3H_7OH$ | 29 | 23 | 52 | 48 |
| 6 | $i$-$C_3H_7OH$ | 22 | 49 | 7 | 93 |
| 7 | $i$-$C_3H_7OH$ | 38 | 64 | 7 | 93 |

[a] Based on the amount of the halocyclobutenes added.

From these results, it seems that two factors, ease of the hydrogen abstraction from the alcohols and steric interference of alkyl groups of the alcohols, effect the ratio of I to II. The ratio is almost independent of the total dosage applied. The dehydrochlorinated 1:1 adducts are thought to be formed by a mechanism similar to that proposed for the addition reaction of ethers[5] to halocyclobutenes and halocyclopentenes.




The radical dechlorination of III would compete with the abstraction of a hydrogen from the alcohol to give the 1:1 adduct I. Therefore, the more reactive alcohol, whose $\alpha$-hydroxyalkyl radical formed by the hydrogen abstraction was stabilized by resonance, would be expected to give predominantly I. It was found in the radical addition of ethers[4] that the ratio of the 1:1 adduct to the dehydrochlorinated 1:1 adduct increased

(1) D. D. Coffman, P. L. Barrick, R. D. Cramer, and M. S. Raasch, *J. Am. Chem. Soc.*, **71**, 490 (1949); P. L. Barrick, U. S. Patent 2,462,345 (1949).

(2) D. C. England, *J. Am. Chem. Soc.*, **83**, 2205 (1961).

(3) J. D. Park and W. C. Frank, *J. Org. Chem.*, **29**, 1445 (1964).

(4) H. Muramatsu, *ibid.*, **27**, 2325 (1962).

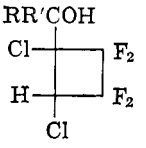
(5) H. Muramatsu and K. Inukai, *ibid.*, **30**, 544 (1965).

with the apparent reactivity of the ethers. The difference of the molar ratio of I to II between methanol and ethanol may be explained by the above reasoning. The increase of the ratio from the case of ethanol to that of 2-propanol, however, would be due to the steric effect of the alkyl groups in the alcohols.

The gas chromatogram of the 1:1 adducts I exhibited the presence of *cis* and *trans* forms in the halocyclobutyl group. Some of these isomers were separated using a preparative gas chromatograph. Both isomers gave the same 2-chlorotetrafluorocyclobutenylalkylcarbinol on treatment by alcoholic potassium hydroxide. The ratios of the both stereoisomers were calculated from the area of their peaks and the result is shown in Table II, The isomer A has a slightly lower boiling point and a smaller retention time compared with the isomer B. When R and R′ in I were bulky groups, the steric interference with the neighboring groups was shown by molecular models to be larger in the isomer where the chlorine atoms are *trans*. From the results of Table II, therefore, the isomer A would be the *trans* form and the isomer B the *cis* form.

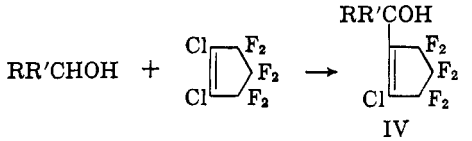
TABLE II

COMPOSITION OF STEREOISOMERS IN THE 1:1 ADDUCTS




| Expt. no. | 1:1 adducts R | R′ | Isomer A, % | Isomer B, % |
|---|---|---|---|---|
| 1 | H | H | 51 | 49 |
| 2 | H | $CH_3$ | 33 | 67 |
| 3 | H | $CH_3$ | 36 | 64 |
| 4 | H | $C_2H_5$ | 32 | 68 |
| 5 | H | $C_2H_5$ | 36 | 64 |
| 6 | $CH_3$ | $CH_3$ | 7 | 93 |
| 7 | $CH_3$ | $CH_3$ | 5 | 95 |

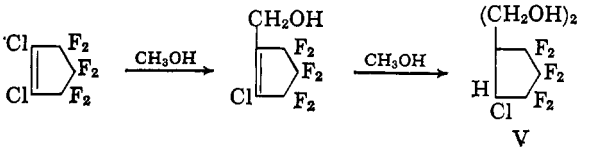
The addition of the alcohols to 1,2-dichlorohexafluorocyclopentene gave almost exclusively the corresponding dehydrochlorinated 1:1 adducts IV as occurred in the additions of ethers.[5] In the addition




IV

R = H or $CH_3$; R′ = H, $CH_3$, or $C_2H_5$

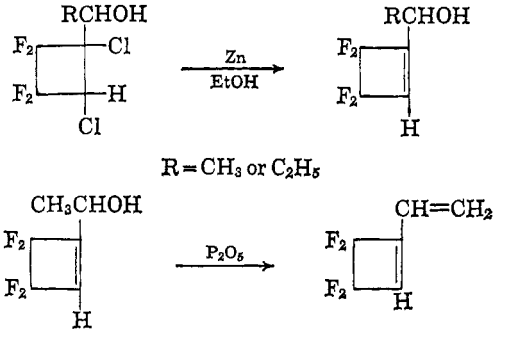
of methanol, a small amount of a compound, white needle crystals of m.p. 103°, was obtained along with the chlorohexafluorocyclopentenylcarbinol, and its structure was tentatively assigned as V from elemental analysis and the infrared spectrum. The physical




V

properties and results of analyses of the 1:1 adducts and the dehydrochlorinated 1:1 adducts are listed in Tables III, IV, and V.

The dechlorination of methyl- and ethyl(1,2-dichlorotetrafluorocyclobutyl)carbinols with zinc dust gave the corresponding alkyl(tetrafluoro-1-cyclobutenyl)carbinols. The methyl(tetrafluoro-1-cyclobutenyl)carbinol thus obtained was dehydrated with phosphoric anhydride to yield 3,3,4,4-tetrafluoro-1-cyclobutenylethylene which is known to be synthesized by the cycloaddition of tetrafluoroethylene and ethynylethylene.[1] The physical properties of the alkyl(tetrafluoro-1-cyclobutenyl)carbinols are shown in Table VI.




## Experimental[6]

**Addition Reactions of Alcohols to 1,2-Dichlorotetrafluorocyclobutene.**—A mixture of 95 g. (0.49 mole) of 1,2-dichlorotetrafluorocyclobutene and 81 g. (1.76 moles) of ethanol was added to a glass tube, 20 × 5 cm. (*ca.* 300-ml. capacity). The reaction tube was then sealed and received γ-irradiation at room temperature to a total dosage $3.1 \times 10^7$ r. for a period of 564 hr. Distillation of the irradiation products, after the removal of the unchanged olefin (21 g.) and ethanol, gave 18 g. (0.087 mole, 18% yield) of methyl(2-chloro-3,3,4,4-tetrafluoro-1-cyclobutenyl)carbinol, b.p. 96–98° (48 mm.), 63 g. (0.26 mole, 53% yield) of methyl(1,2-dichloro-3,3,4,4-tetrafluorocyclobutyl)carbinol, b.p. 103–106° (48 mm.), and *ca.* 3 g. of a viscous residue. The infrared spectrum of the methylhalocyclobutenylcarbinol exhibited a free OH band at 2.79 μ (sh), a broad hydrogen-bonded OH band at 2.98 μ, and a C=C band at 6.06 μ. The gas chromatogram[7] of methyl(dichlorotetrafluorobutyl)carbinol obtained showed two peaks with retention times of 4.9 and 5.8 min., indicating the existence of the two stereoisomers. Both the stereoisomers were separated using preparative gas chromatography and were treated with alcoholic potassium hydroxide to give the same methyl(2-chlorotetrafluoro-1-cyclobutenyl)carbinol. The isomer with the retention time of 4.9 min. melted at 41–45° and had infrared absorption bands at 2.86 (m), 3.34 (w), 3.38 (w), 7.05 (m), 7.31 (vs), 7.70 (m), 7.80 (m), 7.88 (m), 8.06 (m), 8.44 (s), 8.62 (s), 8.96 (m), 9.32 (m), 9.59 (m), 10.33 (w), 10.76 (m), 11.17 (m), 11.96 (vs), 13.19 (m), and 14.75 (w) μ. The other isomer with the retention time of 5.8 min. melted at 48–49° and had infrared absorption bands at 3.00 (m), 3.36 (w), 3.42 (w), 6.90 (w), 7.09 (m), 7.19 (m), 7.35 (vs), 7.78 (m), 7.92 (m), 8.06 (m), 8.37 (s), 8.47 (vs), 8.83 (w), 8.97 (m), 9.12 (w), 9.36 (m), 9.55 (w), 10.36 (m), 10.55 (m), 11.12 (w), 11.90 (vs), 12.20 (s), and 13.28 (w) μ.

The addition reaction of methanol and 1- and 2-propanol to 1,2-dichlorotetrafluorocyclobutene was done under the same conditions mentioned above. The yields and physical properties of the 1:1 adducts and the dehydrochlorinated 1:1 adducts are summarized in Tables I, III, and IV.

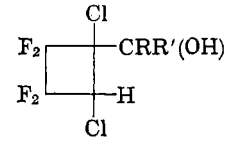
**Addition Reactions of Alcohols to 1,2-Dichlorohexafluorocyclopentene.**—A mixture of 99 g. (1.65 moles) of 2-propanol and 114.4 g. (0.47 mole) of 1,2-dichlorohexafluorocyclopentene was sealed in a glass tube and irradiated at room tem-

(6) All temperature readings are uncorrected. 1,2-Dichlorotetrafluorocyclobutene and 1,2-dichlorohexafluorocyclopentene were obtained from the Peninsular Chem Research, Inc., and used without further purification.

(7) A Hitachi-KGL-2 was employed using helium as the carrier gas at a flow rate of 54 cc./min. and a column temperature of 129°; a 2-m. column packed with 25% Silicone DC-550 was used.

TABLE III

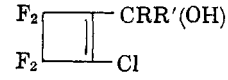
DICHLOROTETRAFLUOROCYCLOBUTYLCARBINOLS



| R | R′ | B.p., °C. (mm.) | $n^{20}D$ | $d^{20}_4$ | MRD Calcd. | MRD Found | Fluorine, % Calcd. | Fluorine, % Found | Chlorine, % Calcd. | Chlorine, % Found |
|---|---|---|---|---|---|---|---|---|---|---|
| H | H | 101–102 (69) | 1.4180 | 1.651 | 34.67 | 34.65 | 33.5 | 33.2 | 31.2 | 31.0 |
| $CH_3$ | H | 106–107 (50) | 1.4211 | 1.550 | 39.29 | 39.44 | 31.5 | 31.3 | 29.4 | 29.1 |
| $C_2H_5$ | H | 104–105 (33) | 1.4233 | 1.464 | 43.91 | 44.39 | 29.8 | 30.0 | 27.8 | 25.9 |
| $CH_3$ | $CH_3$ | 98–100 (51) | 1.4173 | 1.427 | 43.91 | 44.97 | 29.8 | 31.9 | 27.8 | 25.8 |

TABLE IV

CHLOROTETRAFLUOROCYCLOBUTENYLCARBINOLS

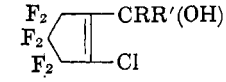


| R | R′ | B.p., °C. (mm.) | $n^{20}D$ | $d^{20}_4$ | MRD Calcd. | MRD Found | Fluorine, % Calcd. | Fluorine, % Found | Chlorine, % Calcd. | Chlorine, % Found | $\nu_{C=C}$, $\mu$[a] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| H | H | 96–98 (69) | 1.4023 | 1.555 | 29.34 | 29.85 | 39.9 | 39.6 | 18.6 | 18.7 | 6.03 |
| $CH_3$ | H | 89–90 (52) | 1.4025 | 1.445 | 33.95 | 34.51 | 37.2 | 37.2 | 17.3 | 17.2 | 6.06 |
| $C_2H_5$ | H | 92–94 (41) | 1.4090 | 1.381 | 38.57 | 39.13 | 34.8 | 33.7 | 16.2 | 17.3 | 6.06 |
| $CH_3$ | $CH_3$ | 87–88 (52) | 1.4070 | 1.381 | 38.57 | 38.96 | 34.8 | 34.8 | 16.2 | 16.6 | 6.09 |

[a] $\nu_{C=C}$ of 1,2-dichlorotetrafluorocyclobutene, 6.12 $\mu$.

TABLE V

CHLOROHEXAFLUOROCYCLOPENTENYLCARBINOLS

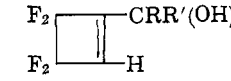


| R | R′ | B.p., °C. (mm.) | $n^{20}D$ | $d^{20}_4$ | MRD Calcd. | MRD Found | Fluorine, % Calcd. | Fluorine, % Found | Chlorine, % Calcd. | Chlorine, % Found | $\nu_{C=C}$, $\mu$[a] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| H | H | 104–105 (90) | 1.3910 | 1.656 | 34.11 | 34.52 | 47.4 | 47.1 | 14.7 | 14.6 | 6.03 |
| $CH_3$ | H | 89–90 (45)[b] | | | | | 44.8 | 44.4 | 13.9 | 13.9 | 6.07 |
| $C_2H_5$ | H | 102 (45) | 1.3997 | 1.482 | 43.35 | 43.92 | 42.4 | 42.2 | 13.2 | 13.5 | 6.075 |
| $CH_3$ | $CH_3$ | 90 (45) | 1.4001 | 1.494 | 43.35 | 43.60 | 42.4 | 42.9 | 13.2 | 13.1 | 6.14 |

[a] $\nu_{C=C}$ of 1,2-dichlorohexafluorocyclopentene, 6.12 $\mu$. [b] M.p. 60.5–61.5°.

TABLE VI

TETRAFLUOROCYCLOBUTENYLCARBINOLS



| R | R′ | B.p., °C. (mm.) | $n^{20}D$ | $d^{20}_4$ | MRD Calcd. | MRD Found | Fluorine, % Calcd. | Fluorine, % Found | $\nu_{C=C}$, $\mu$ |
|---|---|---|---|---|---|---|---|---|---|
| $CH_3$ | H | 104–105 (100) | 1.3873 | 1.376 | 29.09 | 29.12 | 44.7 | 43.7 | 6.135 |
| $C_2H_5$ | H | 99–100 (50) | 1.3952 | 1.307 | 33.70 | 33.79 | 41.3 | 41.0 | 6.14 |

perature to a total dosage $3.1 \times 10^7$ r. for a period of 545 hr. After the recovery of the unchanged alcohol (89 g.) and halocyclopentene (16 g.), distillation of the irradiation products gave 101.5 g. (0.38 mole, 81% yield) of (2-chlorohexafluoro-1-cyclopentenyl)dimethylcarbinol, b.p. 89–91° (45 mm.), and 2 g. of a tarry residue. The infrared spectrum of the dimethylhalocyclopentenylcarbinol showed a free OH absorption band at 2.78 $\mu$ (sh), a broad hydrogen-bonded OH band at 2.92 $\mu$, and a sharp C=C absorption band at 6.14 $\mu$.

Using the same procedure, ethanol and 1-propanol added to 1,2-dichlorohexafluorocyclopentene in yields of 46 and 28%, respectively. In the addition of methanol (76 g., 2.32 moles) to the dichlorohexafluorocyclopentene (146.5 g., 0.60 mole), 8 g. of a fraction of b.p. 100–105° (8 mm.) was obtained along with 41.2 g. (0.17 mole, 29% yield) of (2-chlorohexafluoro-1-cyclopentenyl)carbinol, b.p. 103–106° (90 mm.). When the fraction was allowed to remain at room temperature, white needle crystals precipitated which were filtered and recrystallized from benzene. The crystalline material melted at 103° and was slightly soluble in carbon tetrachloride and freely soluble in methanol. Its infrared spectrum showed OH absorption at 3.06 $\mu$ and no C=C absorption band. The structure of the crystals was tentatively assigned as 1,1-bis(hydroxymethyl)-2-chloro-3,3,4,4,5,5-hexafluorocyclopentane.

*Anal.* Calcd. for $C_7H_7ClF_6O_2$: Cl, 13.0; F, 41.8. Found: Cl, 13.1; F, 42.4.

The physical properties of the dehydrochlorinated 1:1 adducts, alkyl(2-chlorohexafluorocyclopentenyl)carbinols, are listed in Table V.

**Dechlorination of Alkyl(1,2-dichlorotetrafluorocyclobutyl)carbinols.**—To 12 g. (0.18 g.-atom) of zinc dust in 50 ml. of ethanol was added dropwise 29 g. (0.12 mole) of methyl(1,2-dichlorotetrafluorocyclobutyl)carbinol (a mixture of *cis* and *trans* form) for 15 min. The reaction mixture was heated at about 100° for 4 hr. and filtered. Dilute hydrochloric acid was added to the filtrate and the organic layer was separated and dried. Distillation gave 16.3 g. (0.096 mole, 80% yield) of methyl(3,3,4,4-tetrafluoro-1-cyclobutenyl)carbinol, b.p. 103–105° (100 mm.).

The infrared spectrum of the carbinol showed a free OH band at 2.79 μ (sh), a broad hydrogen-bonded OH band at 3.00 μ, and C=C band at 6.135 μ.

Using the same procedure, 16.7 g. (0.066 mole) of ethyl(1,2-dichlorotetrafluorocyclobutyl)carbinol with 7 g. (0.11 g.-atom) of zinc dust gave 9.4 g. (0.051 mole, 78% yield) of ethyl (3,3-4,4-tetrafluoro-1-cyclobutenyl)carbinol, b.p. 98–100° (50 mm.).

**Dehydration of Methyl(3,3,4,4-tetrafluoro-1-cyclobutenyl)-carbinol.**—To 19 g. (0.13 mole) of phosphoric anhydride was added dropwise 15 g. (0.09 mole) of the carbinol and the reaction mixture was heated at 140° for 40 min. and distilled. Redistillation of the product gave 8.5 g. (0.056 mole, 63% yield) of 3,3,4,4-tetrafluoro-1-cyclobutenylethylene, b.p. 99–100°, $n^{20}D$ 1.3820. $d^{20}_4$ 1.260 (lit.[1] b.p. 98–99°, $n^{25}D$ 1.3742, $d^{25}_4$ 1.2588).

*Anal.* Calcd. for $C_6H_4F_4$: F, 50.0. Found: F, 49.7.

The tetrafluorocyclobutenylethylene was polymerized easily upon standing in the air or by peroxide treatment to give a transparent polymer.

# Synthesis of 6β-(2,6-Dichlorobenzoyloxy)-2,4-cholestadiene and Related Compounds[1a]

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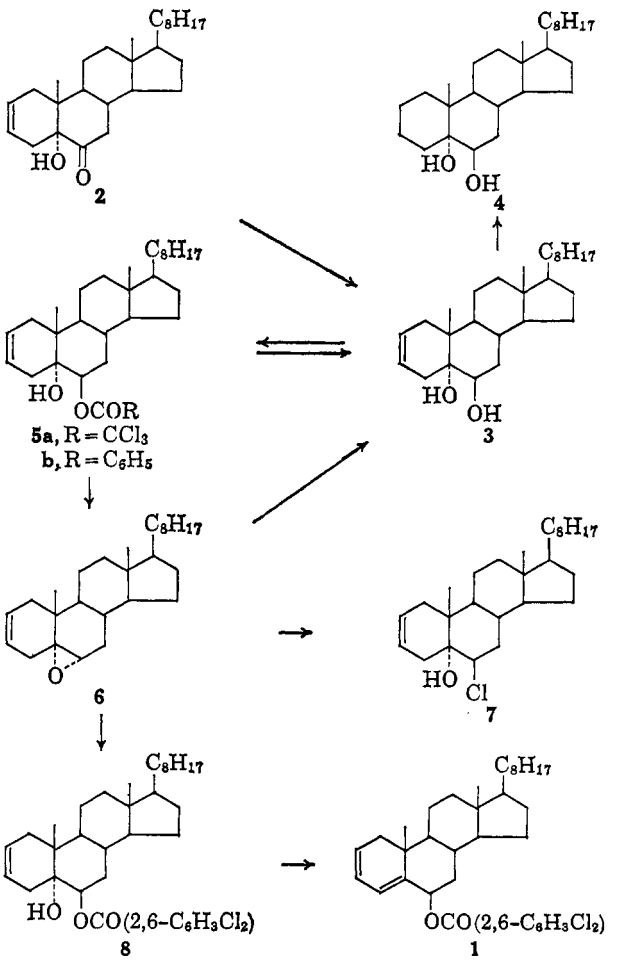
The preparations of 2-cholestene-5α,6β-diol (**3**) and two 6β ester derivatives are described. Treatment of the latter compounds with base yields 5α,6α-epoxy-2-cholestene, which may be converted to **3**, to 6β-chloro-2-cholsten-5α-ol, and to 6β-(2,6-dichlorobenzoyloxy)-2-cholesten-5α-ol. The latter ester, whose preparation by esterification of **3** with 2,6-dichlorobenzoyl chloride was unsuccessful, may be dehydrated to yield the title compound. Some aspects of the spectra of these compounds are discussed.

In connection with investigations of the direct and solvolytic nucleophilic displacement reactions of some conjugated dienes bearing suitable leaving groups in an allylic position, we required a convenient synthesis of 6β-(2,6-dichlorobenzoyloxy)-2,4-cholestadiene (**1**). This compound seems to be an appropriate substrate for observing long-range allylic rearrangements in a stereochemically well-defined system. The success of Summers, *et al.*,[2a,b] Wallis and Becker,[2c] and Young, *et al.*,[2d] in preparing 6β-substituted 4-cholestenes by dehydration of the corresponding 5α-cholestanols with thionyl chloride in pyridine prompted our investigation of the same reaction in the 2-cholestene series. The preparation and therapeutically interesting biological activities of $\Delta^2$ steroids bearing appropriate substituents elsewhere in the molecule have been the subjects of recent reports.[3]

2-Cholesten-5α-ol-6-one (**2**) has been described by Reich, Walker, and Collins,[4] and appeared to be an appropriate entry to the desired system. We have repeated their preparation on a larger scale and have shown that material of adequate quality for our purposes may be obtained by crystallization rather than chromatography.

Treatment of the ketone **2** with lithium aluminum hydride afforded 2-cholestene-5α,6β-diol (**3**) (see Chart I) in excellent yield as a nicely crystalline solid. The assignment of the β configuration to the 6-hydroxyl group thus introduced is analogous to an example reported by Wallis and Becker[2c] who prepared cholestane-5α,6β-diol by lithium aluminum hydride reduction of cholestan-5α-ol-6-one. While lithium aluminum hydride reduction of 6-keto steroids gives predominantly the 6β-hydroxy steroid it is usually possible to isolate some of the 6α epimer.[5] In the present case, as in that of the corresponding reduction of cholestan-5α-ol-6-one,[2c] the normal preference for attack on the less hindered side is probably reinforced

CHART I




(1) (a) This work was supported by funds administered by the Research Committee, The Graduate School, Washington State University. (b) To whom communications should be addressed.

(2) (a) A. J. Fudge, C. W. Shoppee, and G. H. R. Summers, *J. Chem. Soc.*, 958 (1954); (b) D. N. Jones, J. R. Lewis, C. W. Shoppee, and G. H. R. Summers, *ibid.*, 2876 (1955); (c) E. J. Becker and E. S. Wallis, *J. Org. Chem.*, **20**, 353 (1955); (d) R. E. Ireland, T. I. Wrigley, and W. G. Young, *J. Am. Chem. Soc.*, **80**, 4604 (1958).

(3) For some recent examples and references to earlier work, see J. A. Edwards, P. G. Holton, J. C. Orr, E. Necoechea, A. de la Roz, E. Segovia, R. Urquiza, and A. Bowers, *J. Med. Chem.*, **6**, 174 (1963).

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