4, and 5 (28:2:1)[7a] in 150 ml of ethanol. This stirred mixture was hydrogenated at 25° and 1 atm for 5 hr. After filtration through Dicalite and evaporation of the solvent, glc[7a] analysis indicated the presence of only 5.

Wolff–Kishner Reduction of 7 to a Mixture of 8 and 9.—The apparatus and procedure used has been described[10a] except that the product was isolated by ether extraction. From 16.2 g (0.05 mol) of 7 was isolated 14.5 g of crude crystalline reaction products. These products were taken up in petroleum ether[14] and subjected to column chromatography using acidic and basic alumina with petroleum ether[14] as the eluent. Concentration of the eluate gave white crystals (12.9 g) which were shown by glc[7b] to be a mixture of 8:9 (3:7).

Base-Catalyzed Cleavage of 7.—The reaction vessel was a 25-ml, one-necked, flat-bottomed, stainless steel flask equipped with a Dean–Stark trap. A ball joint on the trap fitted with a Teflon O-ring provided a seal with the flask. The top of the trap directly above the reaction flask was threaded and fitted with a screw cap containing a glass tube which constituted a helium inlet. The tube was sealed to the screw with silicone rubber. The glass joint above the stopcock of the trap was fitted with a straight-bore glass condenser which acted as the helium outlet. A 0.25-g (0.77 mmol) sample of 7, 0.3 g of KOH pellets, 0.3 g of NaOH pellets, and 10 ml of diethylene glycol were added to the flask and the assembled system was purged for several minutes with a fast stream of helium. The flow was lessened to maintain a slight positive pressure and the flask was lowered into a preheated (250°) Wood's metal bath. After 3 hr of heating, the reaction mixture was allowed to cool under a helium atmosphere. The resulting brown reaction mixture was extracted with ether. The ethereal extracts were combined, washed with water, dried (Na_2SO_4), and concentrated, giving a dark brown oil. The oil was taken up in petroleum ether[14] and subjected to column chromatography using a silica gel, neutral alumina column, and petroleum ether as the eluent. Concentration of the eluate gave a faint yellow oil which crystallized on trituration with petroleum ether.[14] Recrystallization from 95% ethanol gave 150 mg (70%) of 9 as white crystals: mp 95–96° (lit.[18] mp 95°).

Clemmensen Reduction of 7.—Two grams (6.2 mmol) of 7 was reduced using the conditions of procedure A. After 4 days, less than 10% of 7 had reacted to give 8:9 (15:1) as determined by glc analyses.[7b] However, addition of powdered zinc amalgam resulted in 95% reduction in an additional 24 hr to give 1.1 g (54% combined yield) of a mixture of 8:9 (15:1).[7b]

Wolff–Kishner Reduction of 7 to 8.—By use of procedure A,[11] 0.65 g (2 mmol) of 7 gave 0.55 g (88%) of 8.

Isolation and Reduction of 6.—Steam distillation of the products from the reduction of 25 g (0.15 mol) of 1, using procedure C, gave 12 g of nonvolatile residue. This residue was triturated with hot petroleum ether[14] and the liquid was decanted leaving crude 6. Recrystallization from 1:1 chloroform–ethanol gave 1.1 g (4.5%) of white, crystalline 6: mp 182–184° (lit.[17a,19] mp 184°); ir ($CHCl_3$) 2.80, 6.25, and 8.88 μ; mass spectrum (70 eV) *m/e* (rel intensity) 281 (9), 172 (25), 171 (31), 155 (10) 127 (13), and 43 (100); nmr ($CDCl_3$) δ 7.96–7.13 (m, 14, ArH), 2.30 (s, 2, –OH), 1.65 (s, 6, $-CH_3$); nmr (CD_3COCD_3) δ 8.03–7.23 (m, 14, ArH), 2.04 (broad s, 2, –OH), 1.63 (s, 6, $-CH_3$); uv max (95% EtOH) 219 nm (log ϵ 5.42), 232 (5.43), 269 (4.09), and 277 (4.01).

Anal. Calcd for $C_{24}H_{22}O_2$: C, 84.17; H, 6.47. Found: C, 83.94; H, 6.36.

The reduction of 0.24 g (0.7 mmol) of 6 using procedure A gave 7:8:9 (5:1:1) as shown by glc analysis.[7b]

Reduction of 1-Acetonaphthone (15).—The reduction of 8.5 g (0.05 mol) of 15 using procedure A gave 1-ethylnaphthalene in 82% yield as shown by glc analysis.[7a] Three other volatile hydrocarbons were also observed by glc analysis (combined yield 5%); they had retention times like those of 3, 4, and 5. The nonvolatile fraction showed three major components in a ratio of 1:1.25:1.50, which were similar in retention times to 7, 8, and 9.

6-Ethyl-1,2,3,4-tetrahydronaphthalene (11).—This compound was prepared as outlined previously[6] except that nitroethane was used as solvent: mass spectrum (70 eV) *m/e* (rel intensity) 160 (41), 145 (35), 132 (27), 131 (100), 117 (21), and 115 (20); nmr (CCl_4) δ 6.91–6.59 (m, 3, ArH), 2.99–2.27 (broad m, 6, $ArCH_2$–), 2.01–1.52 (broad m, 4, $-CH_2$–nonbenzylic), 1.17 (t, 3, $-CH_3$). The boiling point, ir, and uv agreed with reported values.[6]

1-(2-Naphthyl)ethanol (12).—A 75.6-g (0.44 mol) sample of 1 was reduced with diisobutylaluminum hydride[20] to give 69.6 g (95%) of crude 12 which, when recrystallized twice from petroleum ether,[14] gave 67.1 g (88%) of pure 12, mp 70–72° (lit.[21] mp 71–72°).

2-Vinylnaphthalene (13).—A sample of 13 was prepared from 12 in 41% yield as described.[22] Conversion of the crude product to picrate and its recrystallization from methanol gave yellow needles, mp 90–92° (lit.[22] mp 91–92°). Chromatographic regeneration gave 2.5 g (35%) of 13, mp 64–66° (lit.[21,22] mp 65–66°). Glc analysis indicated the purity of 13 to be 98%.[7a]

Registry No.—1, 93-08-3; 3, 31861-77-5; 4, 31861-78-6; 5, 32367-54-7; 6, 32298-43-4; 7, 32298-44-5; 8, 32298-45-6; 9, 32298-46-7.

Acknowledgments.—We are grateful to the National Science Foundation and the American Petroleum Institute for partial support. We thank Dr. O. C. Dermer for reading the manuscript.

(19) (a) M. S. Newman, *J. Org. Chem.*, **26**, 582 (1961); (b) R. S. Davidson, P. F. Lambeth, and F. H. Younis, *J. Chem. Soc. C*, 2203 (1969). These authors report melting points of 158–171° and 165–171°, respectively, for mixtures of *meso*- and (±)-6.

(20) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967, p 260.

(21) S. Yura, Y. Yamamoto, H. Hara, and R. Oda, *J. Soc. Chem. Ind. Jap.*, **45**, 575 (1942).

(22) L. H. Klemm, J. W. Sprague, and H. Ziffer, *J. Org. Chem.*, **20**, 182 (1955).

Cholesterol 26-Hydroperoxide[1]

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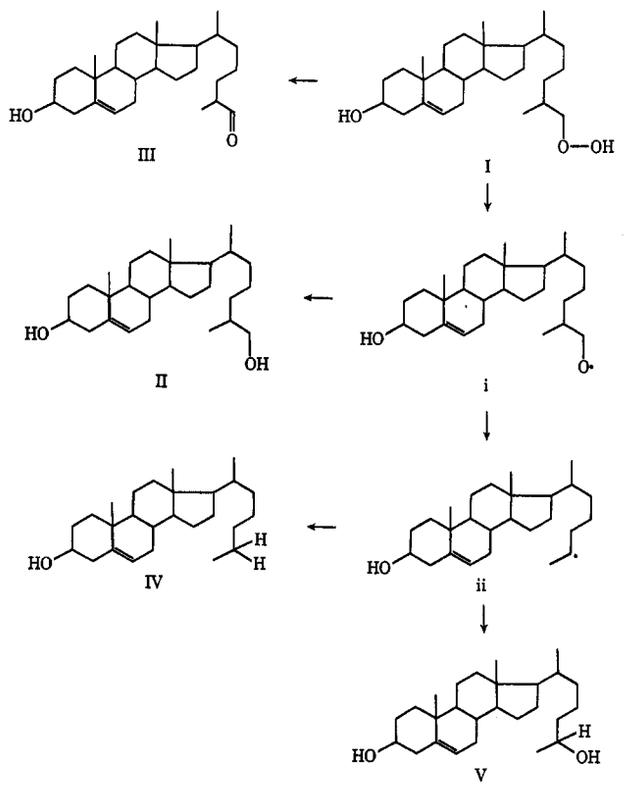
Recent investigations have shown that the autoxidation of cholesterol proceeds *via* hydroperoxide formation at the tertiary 20α and 25 positions as well as the secondary 24 position of the side chain.[2] The present communication reports the isolation of another cholesterol hydroperoxide identified as 3β-hydroxy-5-cholestene 26-hydroperoxide (I). Upon sodium borohydride reduction of the hydroperoxide I, a single diol was obtained which was identified as 5-cholestene-3β,26-diol (II) by comparison of its chromatographic and physical properties with those of an authentic sample. Further proof of the structure of compound I was obtained from its infrared absorption at 3610 and 3540 cm^{-1}, characteristic of the OH stretching of the hydroxyl and hydroperoxyl groups, respectively; from its proton magnetic resonance spectra which shows the C_{27}-methyl protons as a three-proton doublet at δ 0.94 and the C_{26}-methyl protons as a two-proton multiplet at δ 3.92, deshielded 2.05 ppm by the 26-hydroperoxyl group; and from its high-resolution mass spectral analysis. The four major thermal decomposition products of the compound I were identified by their chromatographic and spectral properties as 5-cholestene-3β,26-diol (II), 3β-hydroxy-5-cholesten-26-al (III),

(1) (a) Supported by the Medical Research Council of Canada (Grant MA-4051) and the Conseil de la Recherche Médicale du Québec. (b) Presented at the 14th Annual Meeting of the Canadian Federation of Biological Societies, Toronto, June 1971, Abstract 367.

(2) (a) J. E. van Lier and L. L. Smith, *J. Org. Chem.*, **35**, 2726 (1970); (b) *ibid.*, **36**, 1007 (1971); (c) *Steroids*, **15**, 4 (1970).

27-nor-5-cholesten-3β-ol (IV), and 27-nor-5-cholestene-3β,25ξ-diol (V). The decomposition followed a similar pattern as observed for the 20α-, 24-, and 25-hydroperoxy derivatives of cholesterol[2] and may be viewed as to proceed *via* homolysis of the peroxide oxygen–oxygen bond to produce the 26-alkoxy radical i or *via* dehydration of the 26-hydroperoxy group to afford the 26-aldehyde III.[3]



The recombination of i with a hydrogen radical afforded the 26-alcohol II while β scission of the C_{25}–C_{26} bond in the 26-alkoxy radical i yielded the norcholestene 25-alkyl radical ii, which upon recombination with a hydrogen radical led to the formation of compound IV, and which upon recombination with a hydroxy radical led to the formation of compound V. Because of their scarce availability and the lack of authentic samples, the absolute configurations at the 25 positions in both compounds II and V will await future experimentation. Products II, III, IV, and V as well as the putative intermediate radicals i and ii were revealed in the mass spectrum of the 26-hydroperoxide I by *m/e* 402 (36), 400 (12), 372 (59), 388 (25), 401 (36), and 371 (19), respectively. The low intensity of the molecular ion *m/e* 418 (2.5) reflects the instability of the 26-hydroperoxide I at elevated temperatures.[5] Since thermal decomposition or prolonged storage of the 26-hydroperoxide I gave the 26-alcohol II as a major product, the presence of II in commercial cholesterol samples[6] must be regarded as a result of air oxidation and not of animal origin. Our present finding also does not support the earlier proposed enzymic origin of the 26-hydroxycholesterol isolated from lipid deposits of the human atherosclerotic aorta.[7]

(3) The formation of an aldehyde from a primary hydroperoxide may not involve a radical mechanism. The thermal decomposition of organic hydroperoxides has recently been reviewed.[4]

(4) D. Swern, "Organic Peroxides," Vol. I, Wiley-Interscience, New York, N. Y., 1970.

(5) In the mass spectra of the 20α-, 24-, and 25-hydroperoxy derivatives of cholesterol[2c] only the 24- and 25-hydroperoxides revealed a molecular ion.

(6) J. E. van Lier and L. L. Smith, *Lipids*, **6**, 2 (1971).

Experimental Section[8]

3β-Hydroxy-5-cholestene 26-Hydroperoxide (I).—One kilogram of cholesterol was kept for a total period of 3 months at 70° in the dark and was recrystallized in ethanol every 4 weeks. The pooled mother liquor was stored at −20° while pending for chromatographic separation. Finally, column chromatography of the mother liquor on silica gel in toluene–ethyl ether (20:1, v/v) gave five major fractions (A–E).[8] Most sterol hydroperoxides of our interest were located in fraction C, including the major cholesterol 25-hydroperoxide, together with small amounts of the 24-, 20α-, and the new 26-hydroxyperoxy derivatives of cholesterol. Fraction C was chromatographed on a column of Sephadex LH-20 (60 × 2.5 cm) developed in methylene chloride–ethanol (100:1, v/v). Fractions of 950 drops (15 ml) were collected and analyzed by tlc. Traces of cholesterol were located in fractions 10–13, which was followed by some unidentified minor hydroperoxides (fractions 26–30). The major constituent of fraction C, the cholesterol 25-hydroperoxide, was obtained in fractions 30–39 and the 26-hydroperoxide I in fractions 43–50. Some unidentified compounds were also detected in fractions 51–62. The cholesterol 26-hydroperoxide I was finally recrystallized from toluene–hexane (1:1, v/v) to give 140 mg of white needles: mp 153–155°; ir (CCl_4) 3610 (OH), 3540 cm^{-1} (OOH); pmr ($CDCl_3$) δ 0.68 (s, 3 H, C_{18} protons), 0.94 (d, 3 H, J = 6 Hz, C_{27} protons), 0.96 (d, 3 H, J = 6 Hz, C_{21} protons), 1.01 (s, 3 H, C_{19} protons), 3.56 (m, 1 H, $W_{1/2}$ = 16 Hz, 3α proton), 3.92 (m, 2 H, C_{26} protons), and 5.42 (d, 1 H, J = 4 Hz, C_6 vinyl proton); mass spectrum (70 eV) *m/e* (rel intensity) 418 (2.5), 403 (42), 402 (38), 401 (36), 400 (22), 398 (24), 388 (25), 387 (45), 384 (100), etc. By gas chromatographic analysis the thermal decomposition of this compound gave the following products: 27-nor-5-cholesten-3β-ol (IV, 19%), 27-nor-5-cholestene-3β,25-diol (V, 11%), 3β-hydroxy-5-cholesten-26-al (III, 27%), and 5-cholestene-3β,26-diol (II, 24%). Prolonged storage of the 26-hydroperoxide I in solution resulted also in its partial decomposition to give 26-hydroxycholesterol II as the major product as shown by tlc.

Anal. Calcd for $C_{27}H_{46}O_3$: mol wt, 418.3446. Found: mol wt, 418.3473.

(7) (a) G. Steel, C. J. W. Brooks, and W. A. Harland, *Biochem. J.*, **99**, 51P (1966); (b) *Biochem. Biophys. Acta*, **125**, 620 (1966); (c) J. E. van Lier and L. L. Smith, *Biochemistry*, **6**, 3269 (1967).

(8) Cholesterol was purchased from Sigma Chemical Co., St. Louis, Mo., and purified *via* several crystallizations from chloroform–methanol. Purified cholesterol was kept for periods of 4 weeks at 70° in the dark, followed by crystallization from ethanol in order to harvest the autoxidation products. Isolation of oxidized sterols from the accumulated mother liquors was conducted using the slight modification of previously described procedures.[2a] Thus, mild acid and alkaline extractions were avoided and instead the mother liquor was chromatographed directly on silica gel columns (Baker analytical grade, 60–200 mesh) developed in toluene containing 0–5% ethyl ether. Eluents were pooled upon thin layer and gas chromatographic analyses, such as to give five major fractions: (A) compounds more mobile than cholesterol; (B) cholesterol and sterols of similar polarity; (C) sterols less mobile than cholesterol, but more mobile than 25-hydroxycholesterol; (D) 25-hydroxycholesterol and sterols of similar polarity; (E) polar sterols, possibly sterol triols and sterol acids. Selected fractions were further separated *via* chromatography on Sephadex LH-20 (Pharmacia, Uppsala, Sweden) developed in methylene chloride containing 1% ethanol, as previously described.[2a] Thin layer chromatography (tlc) and preparative gas chromatography (gc) were performed in the same manner as previously described.[2a,9a] Steroid mobilities R_c (tlc) and r_T (gc) are given in terms of cholesterol as unity.

Infrared absorption (ir) spectra were recorded with a Perkin-Elmer Model 357 spectrophotometer equipped with a beam condensor. Steroids were either incorporated in KBr pellets 1.5 mm in diameter or dissolved in carbon tetrachloride or deuteriochloroform in a 1.0-mm path cell. Proton magnetic resonance (pmr) spectra were obtained with a Varian T-60 spectrometer in deuteriochloroform solution using tetramethylsilane as internal standard. High-resolution mass spectral measurements were obtained with an AEI MS-9 mass spectrometer, and medium-resolution mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6E instrument (70 eV). Melting points were determined on a calibrated Kofler block and are corrected.

(9) (a) J. E. van Lier and L. L. Smith, *J. Chromatogr.*, **41**, 37 (1969); (b) *ibid.*, **36**, 7 (1968).

5-Cholestene-3β,26-diol (II). A. From Sodium Borohydride Reduction of Cholesterol 26-Hydroperoxide (I).—Compound I (10 mg) in 5 ml of methanol was cooled to 0° and sodium borohydride (50 mg) was added. After 5 min the excess sodium borohydride was destroyed by the addition of a few drops of acetic acid. The mixture was stirred with 10 ml of water and the product was extracted with methylene chloride. The methylene chloride extract was dried ($MgSO_4$) and concentrated to afford 4.0 mg of 5-cholestene-3β,26-diol (II): mp 169–170° [*cf.* mp 168–173° for (25*RS*)-26-hydroxycholesterol,[10] mp 169–171°[6]]; ir (KBr) 3300 cm^{-1} (OH); R_c 0.47 (magenta); r_T 3.18 and 2.27 on 3% QF-1 and 3% OV-1, respectively, identical with the r_T of an authentic sample of (25*RS*)-26-hydroxycholesterol.[6]

B. From Thermolysis of I.—Samples of 100–200 μg of the 26-hydroperoxide I in 10 μl of ethanol were injected into the flash heater zone (270°) of the gas chromatograph (6 mm i.d., 3% OV-1). The decomposition products were collected in glass capillaries by methods described earlier.[9b] After five successive collections sufficient materials were accumulated for further chromatographic and spectral identification purposes. Thus the least mobile sterol with R_c 0.47 (magenta), r_T 3.18 and 2.27 on 3% QF-1 and 3% OV-1, respectively, was identified as 5-cholestene-3β,26-diol (II) by comparison of its chromatographic data with those of an authentic sample. The structure was further confirmed by mass spectral analysis, which gave the correct molecular ion at *m/e* 402 (10).

3β-Hydroxy-5-cholesten-26-al (III).—Preparative gas chromatography of cholesterol 26-hydroperoxide gave in addition to 26-hydroxycholesterol II a comparatively more mobile component, R_c 0.87 (orange-red), r_T 3.83 and 1.88 on 3% QF-1 and 3% OV-1, respectively. The reverse mobile behavior of this compound on the selective 3% QF-1 column suggested the presence of a carbonyl group. By analogy with the thermal decomposition of cholesterol 24-hydroperoxide which afforded the 24-keto sterol as the major product[2b] this component was tentatively assigned as 3β-hydroxy-5-cholesten-26-al (III). This structural assignment was further supported by its mass spectral data which gave the expected molecular ion at *m/e* 400 (70), and by ir spectroscopy (KBr) 1720 cm^{-1} (CHO).

27-Nor-5-cholestene-3β,25ξ-diol (V). A. From Thermolysis of I.—A third major thermal decomposition product of the 26-hydroperoxide I, obtained from preparative gas chromatography, was identified as 27-nor-5-cholestene-3β,25ξ-diol (V) by comparison of its chromatographic data with those of an authentic sample: R_c 0.47 (magenta); r_T 2.30 and 1.53 on 3% QF-1 and 3% OV-1, respectively. Its mass spectrum showed the molecular ion at *m/e* 388 (8).

B. From 27-Nor-3β-hydroxy-5-cholesten-25-one.—Nor-25-ketocholesterol (4.0 mg) dissolved in 0.5 ml of methanol was treated with an excess of sodium borohydride (25 mg). The course of the reduction was followed by tlc. After all the starting material had disappeared a few drops of acetic acid was added followed by 10 ml of water. The product was extracted with methylene chloride, dried ($MgSO_4$), and concentrated to give a colorless product. Recrystallization of the product from hexane–ethyl ether gave 1.8 mg of 27-nor-5-cholestene-3β,25-diol (V): mp 159–169° (*cf.* lit.[11] mp 158–168°); R_c 0.47 (magenta); r_T 2.30 and 1.53 on 3% QF-1 and 3% OV-1, respectively; ir (KBr) 3300 cm^{-1} (OH).

27-Nor-5-cholesten-3β-ol (IV). A. From Thermolysis of I.—The most mobile thermal decomposition product of the 26-hydroperoxide I, isolated *via* preparative gas chromatography, was identified as 27-nor-5-cholesten-3β-ol (IV) by comparison of its spectral and chromatographic properties with those of an authentic sample: R_c 0.97 (magenta); r_T 0.86 and 0.84 on 3% QF-1 and 3% OV-1, respectively. Mass spectral analysis gave a molecular ion at *m/e* 372 (100).

B. From 27-Nor-5-cholestene-3β,25-diol (V).—Nor-5-cholestene-3β,25-diol (3.0 mg) was selectively converted to the 25-monotosylate upon treatment with 20 mg of *p*-toluenesulfonyl chloride in 0.5 ml of dry pyridine. The reaction was monitored by tlc and when most of the starting material had disappeared, anhydrous ether (3 ml) was added followed by lithium aluminum hydride (200 mg). The mixture was refluxed for 5 hr, followed by the addition of 10 ml of water. The product was extracted with methylene chloride. Gas chromatographic analysis of the methylene chloride extract revealed the presence of two major components, 27-norcholesterol (IV, 50%) and 27-nor-5-cholestene-3β,25-diol (V, 30%), together with a small amount of norcholestene.[12] The product mixture was separated by preparative tlc and recrystallization from hexane–ethyl ether to afford 1.2 mg of 27-nor-5-cholesten-3β-ol (V): mp 127–131° (*cf.* lit.[11] mp 132°); R_c 0.97 (magenta); r_T 0.86 and 0.84 on 3% QF-1 and 3% OV-1 respectively; ir (KBr) 3300 cm^{-1} (OH).

Registry No.—I, 23652-97-3; II, 13095-61-9; III, 32557-11-2; IV, 4420-91-1; V, 7548-79-0.

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(10) P. D. G. Dean and M. W. Whitehouse, *Biochem. J.*, **98**, 410 (1966).

(11) J. Jacques, H. Kagan, and G. Ourisson, "Tables of Constants of Numerical Data," Vol. 14, S. Allard, Ed., Pergamon Press, Oxford, 1965.

(12) H. Schmid and P. Karrer, *Helv. Chim. Acta*, **32**, 1371 (1949).

Poly-α,α,2,3,5,6-hexafluoro-*p*-xylylene

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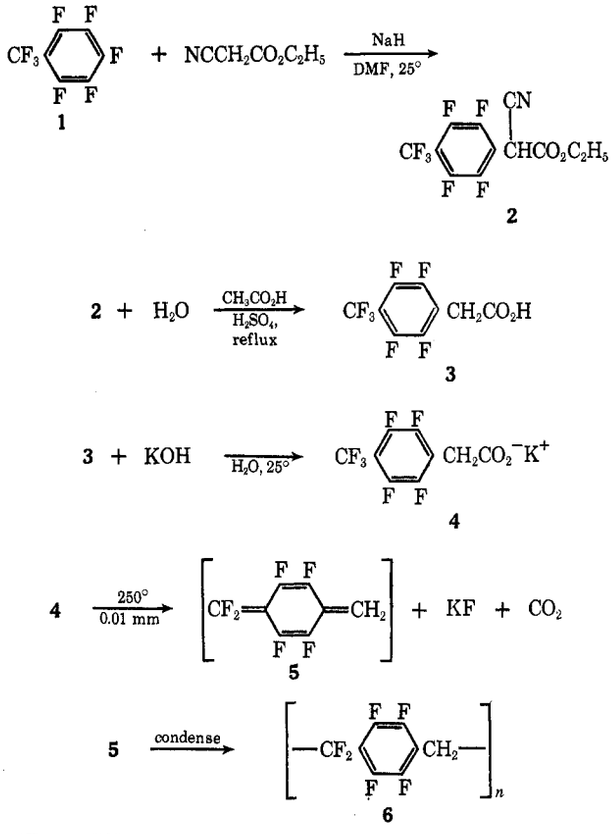
Poly-α,α,2,3,5,6-hexafluoro-*p*-xylylene (**6**) is formed by pyrolyzing potassium (4-trifluoromethyl-2,3,5,6-tetrafluorophenyl)acetate (**4**) under vacuum. The highly reactive intermediate, α,α,2,3,5,6-hexafluoro-*p*-xylylene (**5**), is transported, in the gas phase, to a cool surface where it condenses and immediately polymerizes.[1] The polymer was obtained as a clear



(1) Poly-*p*-xylylenes are commonly prepared by generating the monomeric *p*-xylylenes in the gas phase and condensing them to give polymers: L. A. Errede and M. Szwarc, *Quart. Rev., Chem. Soc.*, **12**, 301 (1959); W. F. Gorham, *J. Polym. Sci.*, **4**, 3027 (1966).