compound **2e** (trace, 2.8 min), compound **1b** (66%, 5.7 min), and compound **3b** (34%, 6.3 min). Compound **2e** was isolated by preparative VPC and showed ir 1720 cm^{-1}; NMR δ 4.39 (1 H, t), 1.3–2.6 (8 H, m), 0.2 (9 H, s); MS (70 eV) *m/e* (rel intensity) 186 (<0.1), 171 (42), 148 (18), 129 (23), 75 (100); MS (20 eV) 186 (<0.1), 171 (100), 148 (40), 129 (23), 75 (66), 73 (15).

Anal. Calcd for $C_9H_{18}O_2Si$: mol wt, 186.1056. Found: mol wt, 186.1056.

Acyloin Condensation of Diethyl Adipate. A 25-g sample of diethyl adipate was cyclized according to Rühlmann[16] to give after distillation 23.4 g of bis silyl ethers (68%). VPC analysis (column A, 110°) showed compound **1b** (89%, 1.9 min) and compound **3b** (11%, 2.2 min). Column B (110°) showed compound **1b** (89%, 5.7 min) and compound **3b** (11%, 6.3 min).

Registry No.—**1b,** 6838-67-1; **2a,** 533-60-8; **2e,** 53638-19-0; **3b,** 57173-86-1; **10b,** 57173-87-2; trimethylsilyl chloride, 75-77-4; diethyl adipate, 141-28-6.

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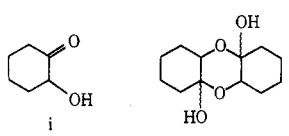
(7) R. B. Woodward and E. R. Blout, *J. Am. Chem. Soc.*, **65**, 562 (1943), footnote 12.
(8) The terms "thermodynamic" and "kinetic" enolate are used as defined by H. O. House, "Modern Synthetic Reactions", W. A. Benjamin, Menlo Park, Calif., 1972, p 502.
(9) Pure adipoin (i) is a mobile liquid of bp 194°. On standing for several hours i dimerizes[10] to a mixture of hemiacetals Ii of mp 93–113°. Thus



comparison of melting points[11] of this dimer is probably not valid. This error has also been perpetrated in various compilations.[12]
(10) J. C. Sheehan, R. C. O'Neill, and M. A. White, *J. Am. Chem. Soc.*, **72**, 3376 (1950).
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(15) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34**, 2324 (1969).
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(20) J. M. Denis, C. Girard, and J. M. Conia, *Synthesis*, 549 (1972).
(21) Compound **1b** has been cyclopropanated and this isomeric 1,6-norcaranediol bis(trimethylsilyl) ether (**11**) is present as an impurity of 15% in compound **10b:** M. Audidrand, R. Le Goaller, and P. Arnaud, *C. R. Acad. Sci.*, **268**, 2322 (1969).
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(24) Since the submission of this manuscript another report has appeared [C. M. Cookson and G. H. Whitham, *J. Chem. Soc., Perkin Trans. 1*, 806 (1975) describing the isolation of the silylated "kinetic" enolate dianion from the modified acyloin condensation of ethyl acetate.

A Convenient Synthesis of (*S*)-(−)-Pulegone from (−)-Citronellol

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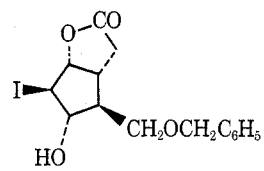
In connection with studies which have led to an efficient asymmetric synthesis of the levorotatory iodolactone **1**,[1] it became necessary to have a convenient source of (*S*)-(−)-pulegone (**2**). (*S*)-(−)-Pulegone occurs in the volatile oils of



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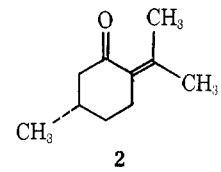
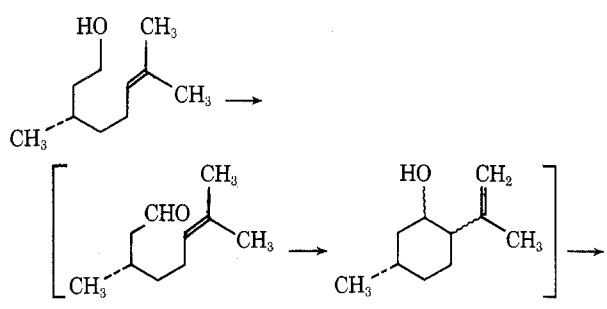


2

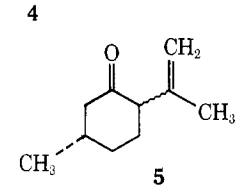
numerous plants;[2] however, there are at present no commercial suppliers.

The classical cation–olefin cyclization of citronellal to a mixture of isopulegols followed by oxidation offered a method for the preparation of **2** from (−)-citronellal;[3] however, the optical purity of (−)-citronellal isolated from natural sources is low.[4] A more convenient starting material appeared to be (−)-citronellol,[5] which is available by high-temperature hydroalumination of (+)-pinane, followed by oxidation of the acyclic organoaluminum compound.[6]

Treatment of (−)-citronellol, $[\alpha]^{20}D$ −4.1° (neat) (88% optically pure), with 2.5 equiv of pyridininum chlorochromate[7] in dry methylene chloride gave isopulegone (**5**) in one step via the intermediates citronellal (**3**) and the isopulegols (**4**). Treatment of **5** with ethanolic sodium hydroxide gave (−)-pulegone, $[\alpha]^{20}D$ −20° (neat), which was isolated in 70% overall yield.[8]



3 4



5

That pyridinium chlorochromate is sufficiently acidic to cause the cyclization of **3** to **4** was suggested by the observation that cis allylic alcohols are oxidized by the reagent to trans aldehydes.[7]

Optically pure (−)-**2** was prepared by recrystallization of its semicarbazone from ethanol. Treatment of the fully resolved semicarbazone (crystallized three times from ethanol), $[\alpha]^{22}D$ −65.2°,[9] with excess pyruvic acid[10] in glacial acetic acid gave (*S*)-(−)-pulegone, $[\alpha]^{23}D$ −22.5° (neat).[11]

Experimental Section

Preparation of (−)-Pulegone (2). To a suspension of 160 g (0.8 mol) of pyridinium chlorochromate in 1 l. of dry methylene chlo-

ride was added 40.0 g (0.26 mol) of (−)-citronellol, $[\alpha]^{23}D$ −4.1° (neat).[12] The slurry was stirred at 25° for 36 hr.[13] The mixture was filtered through Celite and the solids were washed thoroughly with methylene chloride. The solution was evaporated to ca. 500 ml and washed with 10% hydrochloric acid, 10% sodium bicarbonate, and water. The methylene chloride solution was evaporated to give a mobile oil (43 g). The oil was taken up in 300 ml of ethanol and treated with 600 mg (15 mmol) of sodium hydroxide. The solution was heated for 1 hr, then the ethanol was evaporated under reduced pressure and the residue was partitioned between 200 ml of ether and 100 ml of water. The ether was washed with 10% hydrochloric acid and then brine. Evaporation of the solvent and distillation of the residue gave 28 g (0.184 mol, 71%) of (−)-pulegone, bp 104–106° (18 mm), $[\alpha]^{22}D$ −20° (neat), homogeneous by gas chromatographic analysis.

Preparation of (*S*)-(−)-Pulegone Semicarbazone. To a solution of 35 g (230 mmol) of (−)-pulegone, $[\alpha]^{22}D$ −20° (neat), in 400 ml of ethanol and 200 ml of water cooled to 0° was added 55 g (404 mmol) of sodium acetate trihydrate and 40 g (359 mmol) of semicarbazide hydrochloride. The solution was stirred at 0° for 2 hr and then at 20° for 36 hr. The precipitated solid (53 g) was separated by filtration and was extracted three times with 200 ml of chloroform. Evaporation of the chloroform and recrystallization of the residue from ethanol gave 47 g (225 mmol, 98%) of the semicarbazone, mp 169–171°. This material was recrystallized twice from ethanol to afford 40.2 g (192 mmol, 83%), of pure semicarbazone: mp 170–171°; $[\alpha]^{23}D$ −65.2° (*c* 2.2, $CHCl_3$);[9] ir (CCl_4) 3522, 3489, 3419, 3200 (NH), 1689 (C=O), 1510 cm^{-1} (C=N); NMR ($CDCl_3$) δ 8.73 (1 H, s, NNH), 5.88 (2 H, bs, NH_2), 2.83–0.88 (16 H, m), 1.87 (3 H, s, allylic CH_3), 1.74 (3 H, s, allylic CH_3), 1.00 (3 H, d, J = 5.5 Hz, CH_3).

Regeneration of Optically Pure (−)-Pulegone (2). To 40 g (191 mmol) of (−)-pulegone semicarbazone dissolved in 100 ml of hot glacial acetic acid was slowly added (ca. 30 min) 35 g (398 mmol) of freshly distilled pyruvic acid. The solution was heated on a steam bath for 2 hr. The volume was reduced to ca. 50 ml under reduced pressure and the residue was partitioned between 200 ml of water and 400 ml of ether. The ether layer was washed with 200 ml of water, 200 ml of saturated sodium bicarbonate, and 50 ml of brine. The ether solution was dried ($MgSO_4$), evaporated, and distilled to give 25 g (164 mmol, 86%) of (−)-pulegone, bp 104–108° (22 mm), $[\alpha]^{23}D$ −22.5° (neat).[11,14]

Registry No.—**2**, 3391-90-0; **2** semicarbazone, 57237-90-8; (−)-citronellol, 7540-51-4; semicarbazide hydrochloride, 18396-65-1.

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(4) E. Guenther, "The Constituents of Essential Oils", Vol. II, Van Nostrand, Princeton, N.J., 1949.
(5) The reported values for the rotation of (−)-citronellol range from $[\alpha]D$ −2.24° [Y. R. Naves, G. Brus, and J. Allard, *C. R. Acad. Sci.*, **200**, 1112 (1935)] to $[\alpha]D$ −4.20° [F. Tiemann and R. Schmidt, *Ber.*, **29**, 923 (1896)].
(6) R. Rienacker and G. Ohloff, *Angew. Chem.*, **73**, 240 (1961); K. Ziegler, F. Krupp, and K. Zozel, *Justus Liebigs Ann. Chem.*, **629**, 241 (1960); U.S. Patent 2,961,452.
(7) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975); this reagent is available from the Aldrich Chemical Co.
(8) The conversion of citronellol to pulegone using "conventional" reagents [i.e., (1) $CrO_3 \cdot 2C_5H_5N$; (2) *p*-TsOH–CH_2Cl_2; (3) Jones oxidation; (4) EtOH–KOH] gave pulegone in ca. 38% yield.
(9) For lit. mp 171–172° and $[\alpha]^{20}D$ +61.7° (*c* 4.0, $CHCl_3$) for the semicarbazone of (+)-pulegone, see ref 3c; we observed mp 170–171° and $[\alpha]^{23}D$ +66° (*c* 2.05, $CHCl_3$).
(10) E. B. Hershberg, *J. Org. Chem.*, **13**, 542 (1948).
(11) E. Beckmann and M. Pleissner, *Justus Liebigs Ann. Chem.*, **262**, 1 (1891), report $[\alpha]D$ +22.53°, and J. Doeuvre and H. Perret, *Bull. Soc. Chim. Fr.*, **2**, 298 (1935), report $[\alpha]D$ +22.58° for (+)-pulegone.
(12) Kindly supplied by Firmenich, Inc. (courtesy of Mr. Charles C. Bryan); see ref 5 and 6.
(13) The reaction can easily be followed by TLC (silica gel, methylene chloride). R_f values: citronellol, 0.17; citronellal, 0.65; isopulegols, 0.27 and 0.35; isopulegone, 0.41; pulegone, 0.36.
(14) This work was supported in part by a grant from the National Science Foundation.

Reactions of Cholesteryl Substrates with Chloride Ion in Aprotic Solvents. Synthesis of Epicholesteryl Chloride

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Shoppee,[2] after a review of the literature, concluded that, owing to homoallylic participation by the 5,6 π bond,[2,3] the hydroxyl group of cholesterol invariably undergoes replacement by chlorine with retention of configuration. Epicholesteryl chloride (3-α-chlorocholest-5-ene, **1**) was subsequently prepared by a variety of methods,[4,5] all of which involved replacement, with inversion, of a 3-α-hydroxyl group by chlorine prior to introduction of the 5,6 π bond by dehydration of a 5- or 6-ol. Column and thin layer chromatography were used to separate it from cholesta-3,5-diene (**2**). Recently, it has been shown that reaction of cholesterol with triphenylphosphine–carbon tetrachloride reagent does give rise to a small (~8%) amount of **1** within the product mixture.[6]

Since dipolar aprotic solvents are excellent media for SN2 reactions,[7] it might be possible to utilize them to prepare **1** by direct attack of chloride ion upon a suitable cholesteryl substrate. Several bimolecular inversions at C-3 of cholesteryl derivatives have been documented.[8] Plausible products from chloride-ion attack are indicated in Scheme I.

Reaction of cholesteryl *p*-toluenesulfonate (**3a**) with lithium chloride in refluxing acetone[9] was found to lead to a crude product, mp 91–92°, which after recrystallization gave pure cholesteryl chloride (3-β-chlorocholest-5-ene, **3b**), mp 95°. Unfortunately, neither crude nor purified yields are given but, from the small increase in melting point after recrystallization, it would appear that the reaction gave almost entirely substitution products, formed with retention of configuration. However, when the same reaction was carried out in refluxing acetonitrile,[6] a crude product was obtained which on chromatographic analysis yielded 8% **1**, 71% **3b**, and 18% **2**.

Scheme I