that in the spectra of N_a-methyldihydroindole alkaloids the highest field aromatic carbon signal at 107 ± 2 ppm represents C-12.[6,14] By analogy with methyl substitution effects on simple indole models[15] a C-12′ linkage as depicted in **2** should strongly deshield this carbon and slightly shield C-9′ while not significantly influencing the other aromatic sites. The shift contrast between the aromatic carbon signals of the decarbomethoxy 14′,15′-dihydro-(19*S*)-vindolinine part of **2** and those of N'_a-methyl-(19*R*)-vindolinine (**7**) was in perfect agreement with a C-12′ attachment of the monomers. The second site of linkage is of course through the N'_a-CH'_2 carbon of the alkaloid. Two possibilities had then to be considered. The close shifts of C-7 of villalstonine (**3**)[9] and C-7 of **2** strongly suggested similar environments for this carbon in both compounds and was in consonance with previous conclusions.[2] The stereochemistry of this cis linkage could not be ascertained by NMR spectroscopy and has been put forward by analogy with all other related bisindole alkaloids having 2,7-dihydropleiocarpamine as a constituent part.[16] Based on the arguments presented above, structure **2** is proposed for 14′,15′-dihydropycnanthine.

Registry No.—2, 21400-49-7.

References and Notes

(1) Résonance Magnétique Nucléaire du ^{13}C de Produits Naturels et Apparentés. XXI. For part XX see S. Ōmura, A. Nakagawa, A. Neszmelyi, S. D. Gero, A.-M. Sepulchre, F. Piriou, and G. Lukacs, *J. Am. Chem. Soc.*, **97**, 4001 (1975).

(2) A. A. Gorman, N. J. Dastoor, M. Hesse, W. von Philipsborn, V. Renner and H. Schmid, *Helv. Chim. Acta*, **52**, 33 (1969).

(3) F. Markgraf and P. Boiteau, *Adansonia*, **12**, 223 (1972).

(4) The prime symbols are applied for convenience to the (19*R*)- and (19*S*)-vindolinine carbons both in the dimers and in the monomers.

(5) C. Djerassi, M. Cereghetti, H. Budzikiewicz, M.-M. Janot, M. Plat, and J. Le Men, *Helv. Chim. Acta*, **47**, 827 (1964).

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(8) P. Rasoanaivo, N. Langlois, and P. Potier, *Tetrahedron Lett.*, 3669 (1974).

(9) B. C. Das, J.-P. Cosson, G. Lukacs, and P. Potier, *Tetrahedron Lett.*, 4299 (1974).

(10) Spectra were recorded in $CDCl_3$ solution at 22.63 MHz on a Bruker HX 90E Fourier transform spectrometer. Chemical shifts in Table I are given with respect to Me_4Si used as internal standard.

(11) J. B. Stothers, "Carbon-13 NMR Spectroscopy," Academic Press, New York, N.Y., 1972.

(12) Inspection of the data presented in Table I shows practically identical resonance positions for C-21′ of **2** and **8**. This can be rationalized in view of the strained piperideine system in **8**. The absence of any significant homoallylic endocyclic effect[13] was already demonstrated on the C-21′ shift of (19*R*)-vindolinine (**5**) compared to the resonance of the same carbon in 14′,15′-dihydro-(19*R*)-vindolinine (**6**).[6]

(13) E. Wenkert, D. W. Cochran, E. W. Hagaman, F. M. Schell, N. Neuss, A. S. Katner, P. Potier, C. Kan, M. Plat, M. Koch, H. Mehri, J. Poisson, N. Kunesch, and Y. Rolland, *J. Am. Chem. Soc.*, **95**, 4990 (1973).

(14) G. Lukacs, M. de Bellefon, L. Le Men-Olivier, J. Lévy, and J. Le Men, *Tetrahedron Lett.*, 487 (1974).

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The Dianion of Adipoin. A Model Study for the C Ring of Phorbol

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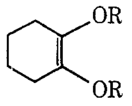
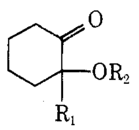
Received June 30, 1975

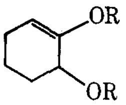
The *acyloin condensation* is a valuable method for ring formation and has been the subject of a recent reinvestigation[1] and review.[2] Although some details of the mechanism may be in question, enediolate **1a** is generally accepted as the stable species which on protonation gives adipoin **2a** or on silylation[3] gives bis silyl ether **1b**. The reverse reaction, however, i.e., treatment of an acyloin with base (**2a** → **1a**), is not so well known.



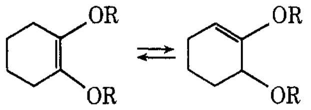
1a, R = Li
b, R = Me_3Si



2a, $R_1 = R_2 = H$
b, $R_1 = CH_3$; $R_2 = H$
c, $R_1 = CH_2CH_2CN$; $R_2 = H$
d, $R_1 = CH_2OH$; $R_2 = H$
e, $R_1 = H$; $R_2 = Me_3Si$
f, $R_1 = H$; $R_2 = Li$



3a, R = Li
b, R = Me_3Si



1a,b **2a,b**

A number of groups have reported the alkylation[4a-h] of acyloins on carbon (e.g., **2a** → **2b**), Michael addition[5a-c] (e.g., **2a** → **2c**), and aldol condensations[6] (e.g., **2a** → **2d**).

All published reports thus far on acyloin dianions, with one exception[7] (vida infra), however, evoke the structure of the well-known enediolate **1a**. We have determined that **1a** is in fact the "thermodynamic" enolate dianion and that compound **3a** is a readily accessible "kinetic" enolate dianion.[8]

When a THF solution of freshly distilled monomeric[9] adipoin **2a** is added dropwise to an excess of 2 equiv of lithium diisopropyl amide or 2,2,6,6-tetramethylpiperidide, a dianion is formed which on silylation gives predominantly the kinetic enolate cyclohexene-2,3-diol bis(trimethylsilyl) ether[13,14] (**3b**) in 73% yield (see Table I). This compound possesses the expected vinyl proton multiplet at δ 4.88 and methine adjacent to oxygen at δ 3.95.

If adipoin **2a** is refluxed in DMF with Me_3SiCl–Et_3N, conditions under which a "thermodynamic" mixture is to be expected,[15] the more stable bis silyl ether **1b** is the predominant bis silyl ether formed. These results are consistent with the observed site of reaction of acyloins which were conducted under equilibrating conditions.[4,5,6]

The observation[7] that enediolate **5**, obtained from acyloin condensation of ethyl butyrate, condenses with ethyl acetate to give a product derived from **7** can be best explained by the equilibrium in Scheme I. Condensation with

Scheme I

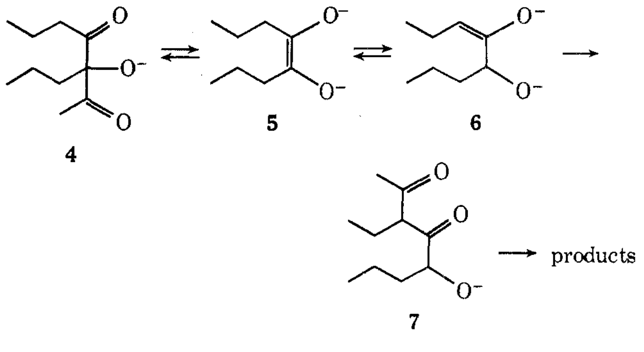


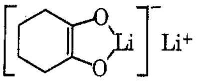
Table I
The Adipoin Dianions[a]

Entry	Conditions	% "thermodynamic" (1b)	% "kinetic" (3b)	% yield
1	Acyloin condensation (Na, Me_3SiCl)	89	11	68
2	Equilibrium (Et_3N, Me_3SiCl)	67	33	53
3	Kinetic (LDA)[b]	16	84	73
4	Kinetic (lithium 2,2,6,6-tetramethylpiperidide)	15	85	67

[a] Percentages determined by VPC. [b] Lithium diisopropylamide.

enediolate **5** gives a nonenolizable β-diketone which would revert to **5** in the presence of excess ethoxide. Some equilibrium concentration of enolate dianion **6** would eventually lead to product.

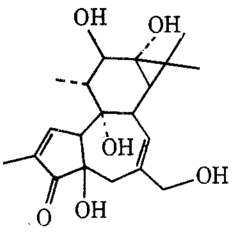
Under kinetic conditions the initially formed OLi group in salt **2f** hinders the approach of a second mole of base to that side of the carbonyl, thus yielding **3a.** The stability of the enediolate **1a** is presumably due to increased delocalization possible in structures such as **8.**



8

We have also repeated Rühlmann's[16] acyloin synthesis of **1b.** Our product contains ca. 10% of the "kinetic" enolate[17] **3b** which was isolated and fully characterized. This compound could arise by base-catalyzed equilibration of **1b** under the reaction conditions or may imply an alternative mechanism for the acyloin condensation.[1]

Our initial interest in acyloin dianions stemmed from model studies directed toward the construction of the C ring system of phorbol (**9**).[18] The interesting C ring of phorbol contains an unusual cyclopropyl-cyclopropylcarbinyl diol moiety. To develop a synthetic route to this diterpene we required a method for the construction of the 1,2-norcaranediol system **10a.**[19]



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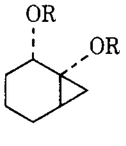
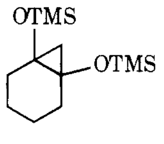


10a, R = H
b, R = Me_3Si



11

The synthesis of **10b** is easily achieved by the reaction of **3b** with a sixfold excess of Simmons–Smith[20,21] reagent in ether at room temperature, giving 83% of **10b** despite a report by Conia[13a] that attempted reaction of a similar system with Simmons–Smith reagent led to rearrangement. Compound **10b** possessed cyclopropane multiplets at δ 0.52 and 0.73 and methine adjacent to oxygen at δ 4.03. (The known[21] **11** was present as an impurity.)

The chemical shifts[22] of the cyclopropane hydrogens suggest that the methylene has been transferred as expected[23] from the side opposite the allylic $OSiMe_3$ grouping. Thus the various methods[11] available for the introduction of a hydroxyl α to carbonyl makes the 1,2-norcaranediol ring system accessible in three steps from a ketone via the heretofore unknown adipoin kinetic enolate dianion.[24]

Experimental Section

Infrared spectra were recorded on a Perkin-Elmer 237B spectrometer; ^1H NMR spectra were taken at 220 MHz in dilute $CDCl_3$ solution on a Varian HR220 referenced to Me_4Si (via residual $CHCl_3$). Mass spectra were obtained on Varian MAT CH-7 and AEI MS-9 mass spectrometers. Microanalyses were obtained from Spang Microanalytical Laboratory, Ann Arbor, Mich. VPC analyses were carried out on a Varian 920: column A is 5 ft × 0.25 in., 15% Carbowax 20M on Chromosorb W and column B is 5 ft × 0.25 in., 1.5% OV101 on Chromosorb P.

Cyclohexene-2,3-diol Bis(trimethylsilyl) Ether. A solution of lithium diisopropylamide in dry THF was prepared in the usual way under argon from 4.34 ml of *n*-butyllithium in hexane (2.3 *m*, Alfa) and 1.46 ml of diisopropylamine (distilled from CaH). The solution was then cooled to −76° and 0.32 g (2.8 mmol) of freshly distilled adipoin was added dropwise in THF. After stirring at −76° for 30 min 1.28 g (10 mmol) of trimethylsilyl chloride was added and the mixture allowed to warm to room temperature over 1 hr. The reaction mixture was then poured into cold $NaHCO_3$ and pentane.

After drying, the pentane was removed by rotavap and the residual oil distilled at 74° (1.1 mm) to give 0.53 g (73%) of bis silyl ethers **1b** and **3b.**

VPC analysis (column A, 110°C) showed only two components: compound **1b** (16%, t_R 1.9 min) and compound **3b** (84%, 2.2 min). Only a trace of the monosilyl ether **2e** (3.4 min) was detected. Column B at 85° showed **1b** (16%, t_R 8.1 min) and **3b** (84%, 9.5 min). Each component was purified by preparative VPC.

Compound **3b** showed ir 1653 cm^{-1}; NMR δ 4.88 (1 H, t), 3.95 (1 H, t), 1.0–2.2 (6 H, m), 0.23 (9 H, s), 0.16 (9 H, s); MS *m/e* (rel intensity) 258 (18), 230 (12), 215 (11), 169 (20), 168 (51), 147 (64), 75 (31), 73 (100).

Anal. Calcd for $C_{12}H_{26}O_2Si_2$: C, 55.81; H, 10.08; mol wt, 258.1473. Found: C, 55.91; H, 10.01; mol wt, 258.1480.

Compound **1b** showed ir 1689 cm^{-1}; NMR δ 1.95–2.35 (4 H, m), 1.65–1.85 (4 H, m) 0.2 (18 H, s); MS *m/e* (rel intensity) 258 (85), 146 (90), 75 (30), 73 (100).

Anal. Calcd for $C_{12}H_{26}O_2Si_2$: mol wt, 258.14713. Found: mol wt, 258.14925.

Norcarane-1,2-diol Bis(trimethylsilyl) Ether. In a 250-ml three-neck flask with magnetic stir bar was added 25 mg of AgOAc and 25 ml of glacial acetic acid. The vigorously stirred solution was heated with a microburner almost to reflux. Then 3.27 g (50 mmol, 20 mesh granular) of Zn was added in one portion. The solution was heated to reflux for 1 min, then cooled to room temperature in a water bath. The acetic acid was decanted and the Zn/Ag couple washed once with glacial acetic acid and six times with ether. The couple was then dried under vacuum for 1 hr. To the couple prepared above was added 45 ml of dry ether and a bit of silver wool. Then 3.86 ml (50 mmol) of CH_2I_2 was added and the mixture refluxed under argon for 2 hr, at which time most of the zinc had dissolved.

Two grams (7.74 mmol) of cyclohexene-2,3-diol bis(trimethylsilyl) ether (**3b**) was added and the reaction stirred at room temperature for 17 hr. At this time pyridine (about 10 ml) was added to the flask until no more precipitate formed. The precipitate was removed by filtration and an equal volume of benzene added. The solvents were evaporated on the rotavap and the residual oil distilled to give 1.75 g (83%) of a colorless liquid, bp 100° (6 mm). VPC (column A, 128°) showed compound **10b** (85%, 1.5 min) and the isomeric cyclopropane **11** (15%, 1.8 min).[21] Compound **10b** has ir no carbonyl or double bond; NMR δ 4.03 (1 H, m), 1.0–2.3 (6 H, m), 0.73 (2 H, m), 0.52 (1 H, m), 0.07 (9 H, s), 0.05 (9 H, s); MS *m/e* (rel intensity) 272 (14), 182 (15), 156 (17), 146 (66), 93 (14), 75 (43), 73 (100).

Anal. Calcd for $C_{13}H_{28}O_2Si_2$: C, 57.35; H, 10.29; mol wt, 272.1629. Found: C, 57.36; H, 10.29; mol wt, 272.1630.

"Thermodynamic" Enolate Mixture. To 0.5 g (4.4 mmol) of freshly distilled adipoin was added 1.24 g (10.5 mmol) of Me_3SiCl, 1.06 g (10.5 mmol) of triethylamine, and 50 ml of DMF. The mixture was refluxed under argon with stirring for 2 days. After cooling the mixture was poured into 100 ml of ice-cold saturated $NaHCO_3$ and rapidly extracted with 100 ml of ice-cold pentane. The pentane solution was dried over Na_2SO_4–K_2CO_3 and distilled to afford a single fraction, bp 104–106° (140 mm), 618 mg (54%) of a mixture of silyl ethers. VPC analysis showed (column B, 110°)

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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(1) J. J. Bloomfield, D. C. Owsley, C. Ainsworth, and R. E. Robertson, *J. Org. Chem.*, **40,** 393 (1975).

(2) J. J. Bloomfield, D. C. Owsley, and J. M. Nelke, *Org. React.*, in press.

(3) For a good review of the acyloin condensation conducted in the presence of Me_3SiCl see K. Rühlmann, *Synthesis*, 236 (1971).

(4) (a) M. S. Kharasch, E. Sternfield, and F. R. Mayo, *J. Org. Chem.*, **5,** 362 (1940); (b) J. C. Speck and R. W. Bast, *ibid.*, **11,** 788 (1946); (c) J. Colonge and P. Brison, *Bull. Soc. Chim. Fr.*, 175 (1962); (d) J. H. van de Sande and K. R. Kopecky, *Can. J. Chem.*, **47,** 163 (1969); (e) H. Heine, *Justus Liebigs Ann. Chem.*, **735,** 56 (1970); (f) F. Chen, R. E. Robertson, and C. Ainsworth, *J. Chem. Eng. Data*, **16,** 121 (1971); (g) T. Wakamatsu, K. Akasaka, and Y. Ban, *Tetrahedron Lett.*, 3879 (1974); (h) Y. Ueno and M. Okawara, *Synthesis*, 268 (1975).

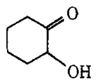
(5) (a) J. Szmuszkovicz and H. Born, *J. Am. Chem. Soc.*, **75,** 3350 (1953); (b) J. Colonge and P. Brison, *Bull. Soc. Chim. Fr.*, 96 (1962); (c) J. Colonge and P. Brison, *ibid.*, 175 (1962).

(6) J. Colonge and Y. Vaginay, *Bull. Soc. Chim. Fr.*, 3140 (1965).

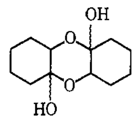
(7) R. B. Woodward and E. R. Blout, *J. Am. Chem. Soc.*, **65,** 562 (1943), footnote 12.

(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



i



ii

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).

(11) G. M. Robottom, M. A. Vazquez, and D. R. Pelegrina, *Tetrahedron Lett.*, 4319 (1974).

(12) "Handbook of Chemistry and Physics", 51st ed, Chemical Rubber Publishing Co., Cleveland, Ohio, 1970.

(13) To our knowledge there is only one such "kinetic" acyloin dianion bis silyl ether in the literature: H. Teichmann and V. Prey, *Justus Liebigs Ann. Chem.*, **732,** 121 (1970). Two acyloin dianion bis(trimethylsilyl) ethers substituted at the 2 position and consequently unable to form an enediolate have been reported: (a) J. P. Barnier, B. Garnier, C. Girard, J. M. Denis, J. Salaun and J. M. Conia, *Tetrahedron Lett.*, 1747 (1973); (b) P. Y. Johnson and M. A. Pries, *J. Am. Chem. Soc.*, **96,** 5618 (1974).

(14) All new compounds possessed satisfactory spectral and analytical data.

(15) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34,** 2324 (1969).

(16) U. Schrapler and K. Rühlmann, *Chem. Ber.*, **97,** 1383 (1964).

(17) A similar compound and mechanism for its formation was proposed by Rühlmann (ref 3, p 247) as a possible side product in the acyloin condensation, although it was not detected.[24]

(18) E. Hecker and R. Schmidt, *Fortschr. Chem. Org. Naturst.*, **31,** 378 (1974).

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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).

(22) W. G. Dauben and W. T. Wipke, *J. Org. Chem.*, **32,** 2976 (1967).

(23) H. E. Simmons, T. L. Cairns, S. A. Vladuchick, and C. M. Hoiness, *Org. React.*, **20,** 1 (1973).

(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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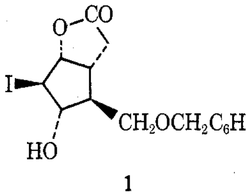
Received August 13, 1975

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



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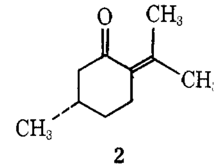
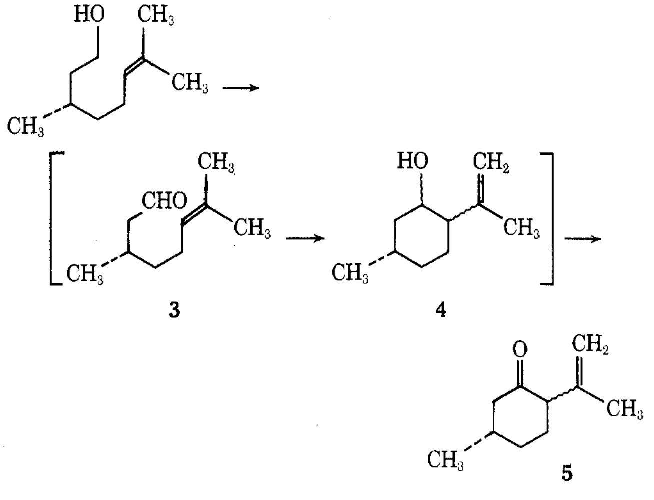


2

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]



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-