(6) (1% incorporation) were synthesized from [^{14}C]tryptamine and secologanin.[15] [Ar-^{3}H]Geissoschizine was metabolized into ajmalicine (7.7%) and several other alkaloids, the identities of which are under investigation. The formation of akuammicine and stemmadenine was not detected under these conditions.

The following conclusions can be drawn from the data of Table I. (a) A complete system of soluble enzymes is present in the 37000*g* supernatant fraction which catalyzes the formation of the *Corynanthé* alkaloids from tryptamine and secologanin in presence of NADPH, thiols, and Tris buffer. (b) The necessary reductive step between the postulated intermediate (**4a**) (derived in turn from vincoside (**4**)) and ajmalicine (**5**) or geissoschizine (**6**) and the later members appears to depend on NADPH. (c) The role of tryptamine and secologanin as true precursors has been established at the cell-free level. (d) The use of callus tissue allows the isolation of a particularly active synthetase mixture and offers considerable advantages over young seedlings as the source of biological material; cf. the relative incorporations of tryptamine into ajmalicine (preparation A, 1%; preparation B, 18%) and of geissoschizine (**6**) into ajmalicine (whole plants, 0.12%,[16] 0.22%;[5c] preparation B, 7.7%). (e) Large scale, high yielding incubations can now be used to define (by isolation) the chemical structure of the various intermediates and metabolites already detected by autoradiography. (f) Purification and immobilization of selected enzymes of the pathway are now feasible.

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References and Notes

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(4) S. A. Brown, *Biosynthesis*, **1**, 1 (1972).
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(8) In a provocative and critical memoir, J. W. Cornforth (*Chem. Soc. Rev.*, **2**, 1 (1973)) has emphasized such problems as bioconversion of unnatural substrates, shunt metabolism, and true enzyme specificity in attempting to answer the question "what are the criteria for intermediacy in a biochemical pathway?"
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(10) A. I. Scott, P. B. Reichardt, M. B. Slaytor, and J. G. Sweeny *Bioorg. Chem.*, **1**, 157 (1971) (see footnote 8).
(11) E.g., J. E. Sherwin, *Plant Cell Physiol.*, **11**, 865 (1970), in cucumber seedlings. C. Baxter and M. Slaytor, *Phytochemistry*, **11**, 2763 (1972) in *Phalaris tuberosa*. Tryptophan decarboxylase in *C. roseus* has been partially purified by ammonium sulfate precipitation and gel filtration in our laboratory.
(12) Cell-free studies with other classes of alkaloid, e.g., hemlock, sparteine, *Solanum* are in progress,[5a,b] but demonstration of the synthesis of complex alkaloids of tryptophan–iridoid derivation in homogenized systems has until now been thwarted by the release of polyphenol oxidase and other inhibitors of indole alkaloid synthesis.[1,10]
(13) Calluses were grown in SH medium according to Schenk and Hildebrandt[14] with slight modifications.
(14) R. U. Schenk and A. C. Hildebrandt, *Can. J. Bot.*, **50**, 199 (1972).
(15) Percentage incorporations of cell-free incubations were based on the radioactivity incorporated. Therefore experiments 2 and 3 are not strictly comparable due to the different specific activities of the substrates. Variation is also expected for different collections of the callus tissue.
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Preparation of an Optically Active Prostaglandin Intermediate via Asymmetric Induction

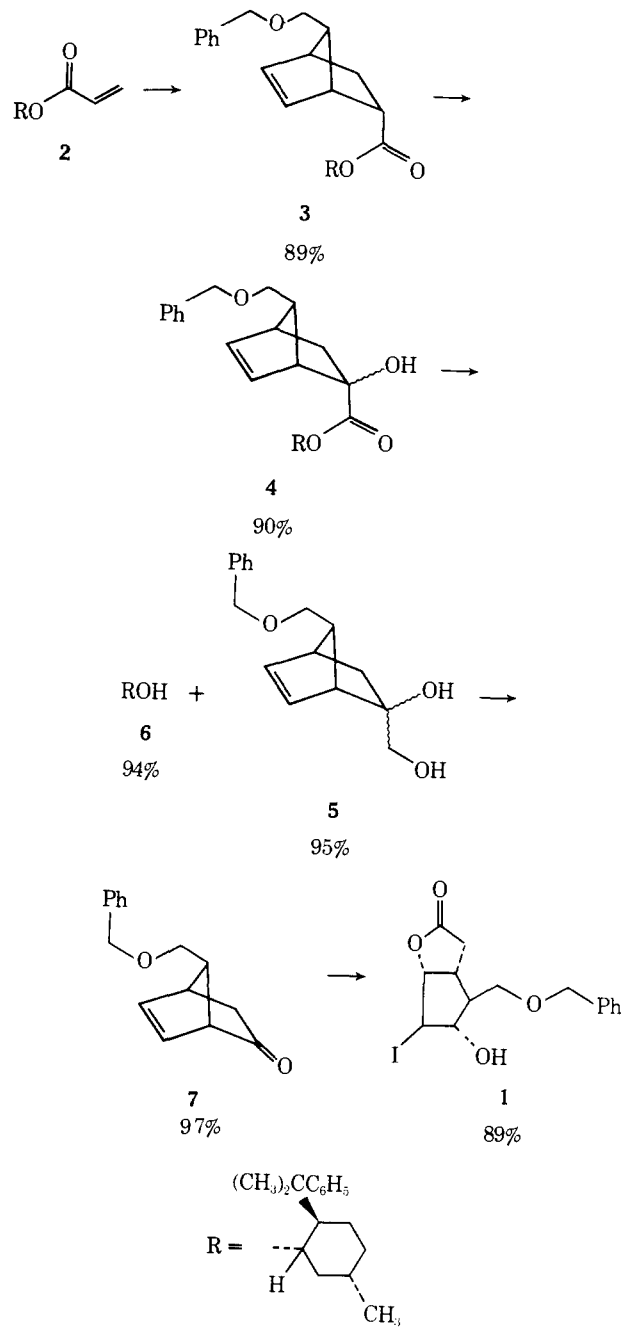
Sir:

We describe herein an improved method for the preparation of the key prostaglandin intermediate **1**[1] in optically pure form *without resolution* by a process which utilizes a new, readily accessible, recyclable, and efficient chiral controlling group (Scheme I).

Treatment of the optically pure acrylate **2**, $[\alpha]^{23}D$ +16.21° (*c* 1.68, CH_2Cl_2), with 0.7 equiv of aluminum chloride[2] in methylene chloride at −55° for 1 hr followed by the addition of 2.5 equiv of 5-benzyloxymethylcyclopentadiene[1a] at −55°[3] affords an 89% yield of the endo adduct **3**[4,5] as an oil, $[\alpha]^{23}D$ −21.3° (*c* 2.2, $CHCl_3$).

That the absolute configuration of **3** is as shown has been proven by conversion to the known, optically active iodolactone (**1**) and agrees with the stereochemical prediction made on the basis of Walborsky's work with *R*-(−)-men-

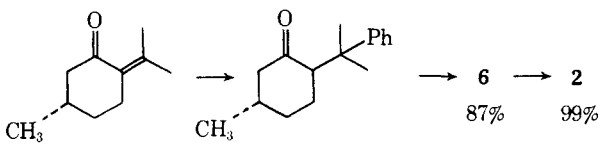
Scheme I



thyl acrylate.[2b] The addition of the enolate of **3** (1.1 equiv of lithium diisopropylamide, −78 to 0° for 1 hr) to an oxygenated solution of THF at −78° containing 2 equiv of triethylphosphite[6] produced the α-hydroxy esters (**4**) as an oil (ca. 2:1 mixture of exo- and endo-hydroxyl). The hydroxy esters (**4**) were directly reduced with excess lithium aluminum hydride to a mixture of endo and exo diols (**5**) and the alcohol (**6**). Filtration of the crude reaction mixture through a tenfold amount of silica gel gave the optically pure alcohol (**6**) (eluted with benzene:ether, 20:1) as an oil, $[\alpha]^{23}D$ +26.3° (*c* 2.02, EtOH), and a mixture of endo- and exo-diols (**5**) (eluted with ether:ethanol, 20:1) as an oil. Since **6** is recovered pure and in high yield, it can efficiently be recycled. Treatment of **5** with 1.4 equiv of sodium metaperiodate in aqueous *tert*-butyl alcohol (buffered to pH 7) gave the optically active ketone **7** as an oil, $[\alpha]^{23}D$ −365° (*c* 1.29, $CHCl_3$).[7,8]

The ketone **5** was converted to the known, optically active iodolactone[1d] by treatment with basic hydrogen peroxide[9] to give the acid-sensitive hydroxy acid which was treated with 2.5 equiv of potassium triiodide in aqueous sodium bicarbonate (24 hr, 0°) to give optically pure **1**, mp 120–121° (from methylene chloride–hexane), $[\alpha]^{23}D$ −33.3° (*c* 1.3, $CHCl_3$),[10] 89% yield from **7**.

The optically pure acrylate (**2**) was prepared in 71% yield from optically pure (−)-pulegone.



8

85%

S-(−)-Pulegone was treated with 1.2 equiv of phenylmagnesium bromide in the presence of cuprous chloride to give a kinetic mixture (ca. 1:1) of cis and trans ketones (**8**). Equilibration with ethanolic potassium hydroxide gave the expected[11] 85:15 mixture which was directly reduced with sodium–isopropyl alcohol in refluxing toluene.[12] Since the more stable *trans*-**8** is reduced to the equatorial alcohol more rapidly than *cis*-**8**, equilibration occurs, and one obtains almost entirely the all equatorial alcohol (**6**).[13] The acrylate (**2**) was prepared by treatment of **6** with 1.5 equiv of triethylamine and 1.2 equiv of acryloyl chloride.

The (−)-pulegone used was prepared by treatment of (−)-citronellol,[14] $[\alpha]^{20}D$ −4.1° (neat), with 2.5 equiv of pyridinium chlorochromate[15] in dry methylene chloride for 40 hr.[16] Treatment of the isopulegone with ethanolic potassium hydroxide and distillation gave a 70% yield of *S*-(−)-pulegone, $[\alpha]^{20}D$ −20° (neat).[17]

Optically pure (−)-pulegone was prepared by recrystallization of its semicarbazone from ethanol. Treatment of the fully resolved semicarbazone, mp 170–171° (recrystallized three times from ethanol), $[\alpha]^{22}D$ −65.23°[18] (*c* 2.2, $CHCl_3$), with excess pyruvic acid in glacial acetic acid gave *S*-(−)-pulegone, bp 104–106° (22 mm), $[\alpha]^{23}D$ −22.5°.[19]

The chiral alcohol **6** (or, equivalently, its enantiomer (−)-**6**, prepared from (+)-pulegone) is dramatically superior to (−)-menthol in chiral directing ability. For example, Hamer[2a] reports the stannic chloride catalyzed Diels–Alder reaction of (−)-menthyl acrylate with cyclopentadiene at 4° in toluene gave, after lithium aluminum hydride reduction and vapor phase chromatography, *endo*-bicyclo[2.2.1]hept-2-enecarbinol, $[\alpha]^{25}D$ +31.4° (ethanol).[20] Under identical conditions (+)-*endo*-bicyclo[2.2.1]hept-2-enecarbinol, $[\alpha]^{22}D$ +76.1° (*c* 0.9, ethanol), was obtained from the reaction of (−)-**2** with cyclopentadiene.[21,22]

References and Notes

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(2) For Lewis-acid catalysis in asymmetric Diels–Alder reactions, see (a) R. F. Farmer and J. Hamer, *J. Org. Chem.*, **31**, 2418 (1966); (b) H. M. Walborsky, L. Barash, and T. C. Davis, *Tetrahedron*, **19**, 2333 (1963); (c) J. Sauer and J. Kredel, *Tetrahedron Lett.*, 6359 (1966).

(3) Higher temperatures cause total polymerization of the diene.

(4) A small amount (ca. 7%) of the exo adduct is formed. No evidence for other isomers of **3** was found.

(5) Satisfactory NMR, ir, and high resolution mass spectra were obtained for all compounds reported herein.

(6) This in situ formation and reduction of the α-hydroperoxy ester was found to be superior to other methods. See D. S. Watt and S. J. Selikson, *J. Org. Chem.*, **40**, 267 (1975); H. H. Wasserman and B. H. Lipshutz, *Tetrahedron Lett.*, 1731 (1975).

(7) The ORD curve of **7** is similar to that of other β,γ-unsaturated ketones. $(\phi)_{3190}$ = −22300°, $(\phi)_{3010}$ = 0°, $(\phi)_{2790}$ = +20100° (c 0.0342, EtOH). See K. Mislow and J. G. Berger, *J. Am. Chem. Soc.*, **84**, 1945 (1962); A. Moscowitz, K. Mislow, M. A. W. Glass, and C. Djerassi, *ibid.*, **84**, 1956 (1962).

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(10) Lit.[1d] mp 120–122°, $[\alpha]^{25}D$ −34.0° (c 1.1, $CHCl_3$); prepared by resolution of the precursor unsaturated acid as the (+)-amphetamine salt.

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(12) Sukh Dev, *J. Indian Chem. Soc.*, **33**, 769 (1956).

(13) The small amount (ca. 7%) of alcohol produced from *cis*-**8** must be removed by silica gel chromatography, since it would produce the enantiomer of **7** in the above scheme.

(14) Kindly supplied by Firmenich. For preparation see R. Rienäcker and G. Ohloff, *Angew. Chem.*, **73**, 240 (1961).

(15) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975).

(16) One can monitor the appearance and consumption of the intermediates citronellal, isopulegol, and isopulegone conveniently by TLC (methylene chloride). See E. J. Corey, H. E. Ensley, and J. W. Suggs, *J. Org. Chem.*, in press, for details.

(17) 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 much lower yield.

(18) Lit. mp 171–172°, $[\alpha]^{20}D$ +61.7° (c 4.0, $CHCl_3$) for semicarbazone of (+)-pulegone: Y. Naves and P. Ochsner, *Helv. Chim. Acta*, **47**, 51 (1964). In our hands, mp 170–171°, $[\alpha]^{23}D$ +66° (c 2.05, $CHCl_3$).

(19) Lit. bp 81° (5 mm), $[\alpha]^{22}D$ +23.56°: W. J. Houlihan, *J. Org. Chem.*, **27**, 4096 (1962).

(20) Reported maximum rotation of (−)-*endo*-bicyclo[2.2.1]hept-2-enecarbinol, $[\alpha]D$ −76.6° (ethanol). J. A. Berson, J. S. Walia, A. Remanick, S. Suzuki, P. Reynolds-Warnhoff, and D. Willner, *J. Am. Chem. Soc.*, **83**, 3986 (1961).

(21) We are grateful to Dr. Jasjit S. Bindra (Chas. Pfizer and Co.) for encouraging us to undertake this project and for helpful suggestions and discussions.

(22) This investigation was assisted financially by the National Science Foundation.

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An Aryltrialkoxysulfurane Prepared from a Cyclic Sulfenate. Polarity Rules and Sulfurane Reactivity[1]

Sir:

We report the synthesis of the first cyclic sulfenate, sultene **1**, and its conversion to aryltrialkoxysulfurane **2**, which appears to exist in a conformation with a five-membered diequatorial ring. This sulfurane, in contrast to well-studied diaryldialkoxysulfurane **3**,[2f-h] reacts with several bifunctional alcohols to give stable spirosulfuranes with five and six-membered rings.

No sultenes have ever been reported, although cyclic sulfenates have been proposed as reactive intermediates[3] and suggested to explain mass spectral fragmentation.[4] Sultene **1** is prepared in 85% yield in CCl_4 by the reaction of **4** with bromine and pyridine at −5°. Recrystallization from pen-