DMR8015658 and 8241625). We also acknowledge the assistance provided by Bristol Laboratories, Syracuse, NY, in performing all of the elemental analyses reported herein. Drs. C. Hussey and T. M. Laher for the cyclic voltammograms of the products, and Dr. R. M. Metzger for the conductivity measurements on the charge-transfer salts.

Registry No. **1a**, 1758-25-4; **1b**, 10538-49-5; **2a**, 87145-73-1; **2b**, 87145-74-2; **3a**, 87145-75-3; **4a**, 87145-76-4; **4b**, 87145-77-5; **5a**, 87145-78-6; **5b**, 87145-79-7; **6a**, 87145-80-0; **6a**·TTF, 87145-81-1; **6b**, 87145-82-2; **6b**·TTF, 87145-83-3; **7a**, 87145-84-4.

Supplementary Material Available: Cyclic voltammograms of products **6a,b** (1 page). Ordering information is given on any current masthead page.

Stereocontrolled Synthesis of (*E*)- and (*Z*)-3-Deuteriophosphoenolpyruvate

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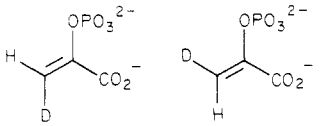
Phosphoenolpyruvate (PEP) derivatives which are stereospecifically labeled at the methylene position with hydrogen isotopes are important substrates for probing the stereochemistry of a number of enzymatic transformations.[1,2] These materials are currently available by an enzymatic synthesis developed by Rose.[3] In connection with model studies of the chorismate-to-prephenate rearrangement,[1,4] we required substantial quantities of stereoselectively deuterated PEP (1) and were therefore led to develop an alternative nonenzymatic synthesis.

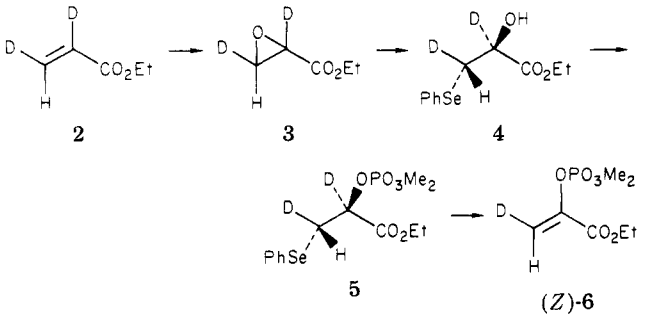


(*E*)-1 (*Z*)-1

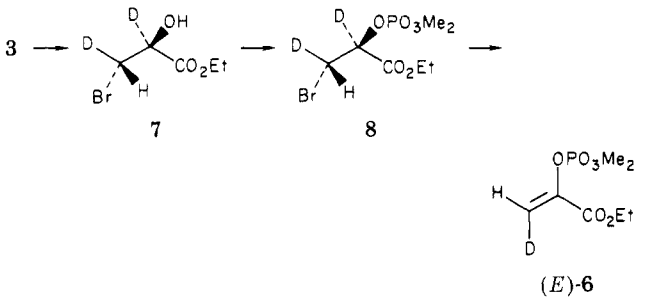
Ethyl (*E*)-2,3-dideuterioacrylate (**2**) is prepared by the method of Hill and Newkome,[5] involving catalytic deuterogenation of the anthracene–propiolate Diels–Alder adduct followed by pyrolysis. Of the material produced by this route, 96% is the desired isomer. Epoxidation of **2** with 3,5-dinitroperoxybenzoic acid[6] affords the labeled glycidate **3** with no apparent stereoisomerization.

Conversion of **3** to the *Z* isomer of **1** (Scheme I) involves opening of the epoxide ring with diisobutylaluminum phenylselenide in hexane, leading to a 3:1 mixture of phenylselenide **4** and its regioisomer. A number of reagents were investigated for accomplishing this conversion, including the alkali metal salts of phenylselenide in both protic and aprotic solvents, and the diisobutylaluminum derivative proved to be the most regioselective. After chromatographic purification, **4** is converted to the lithium

Scheme I



Scheme II



salt and phosphorylated with dimethyl phosphorochloridate at low temperature. Hydrogen peroxide oxidation of **5** and concomitant selenoxide elimination afford the triester of (*Z*)-3-deuteriophosphoenolpyruvate, (*Z*)-**6**. This material is hydrolyzed by a two-step procedure using bromotrimethylsilane[7] followed by aqueous potassium hydroxide, and the desired product is isolated as the crystalline cyclohexylammonium salt after ion-exchange chromatography. The overall yield from acrylate **2** to (*Z*)-**1** is 27%, and the stereochemical purity is comparable to that of the starting acrylate.

A complementary route, leading to the *E* isomer of **1** via an anti elimination process, is depicted in Scheme II. In this instance the epoxide moiety of **3** is opened with bromotrimethylsilane catalyzed by zinc bromide to give the bromohydrin **7** in 92% yield along with <5% of its regioisomer. A number of other catalysts, including triphenylphosphine and zinc iodide, were investigated in order to optimize the regioselectivity of this ring-opening process as well. Zinc bromide was the most selective and the easiest to remove from the reaction mixture.

Conversion of bromohydrin **7** to the *E* isomer of **6** is carried out in a single pot. Dimethyl phosphate **8** is formed at −78 °C by deprotonation with lithium diisopropylamide and addition of dimethyl phosphorochloridate; subsequent warming of the basic reaction mixture to room temperature effects the desired anti elimination and provides (*E*)-**6** in quantitative yield. Hydrolysis and purification according to the procedure described above gives the monocyclohexylammonium salt of (*E*)-**1** in 66% overall yield from **2** and with undiminished stereochemical purity.

Experimental Section

Unless otherwise noted, IR spectra were recorded in $CHCl_3$ solution on a Perkin-Elmer Model 1420 spectrophotometer. ^1H NMR spectra were recorded on the UCB-250 FT instrument, operating at a field strength of 250 MHz. Chemical shifts are reported in parts per million on the δ scale relative to internal tetramethylsilane; data are presented as follows: chemical shift (multiplicity, number of protons, coupling constants in hertz).

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The NMR solvent was $CDCl_3$. The workup of each reaction culminated in drying the organic phase over $MgSO_4$, filtering, and removing the solvent at reduced pressure on a rotary evaporator. Unless otherwise noted, distillations were bulb-to-bulb distillations performed with a Kugelrohr oven at the temperature and pressure indicated. Microanalyses were performed by the Microanalytical Laboratory of the College of Chemistry, University of California, Berkeley.

Ethyl (*Z*)-2,3-Dideuterioacrylate (2). The starting material was prepared as described by Hill and Newkome[5] and was shown by high-field NMR to contain 96% of the desired isomer.

Ethyl (2*R,3*S**)-2,3-Dideuterioepoxypropanoate (3).** A solution of 2.5 g (24.5 mmol) of the deuterioacrylate **2** and 12.3 g (54 mmol) of 3,5-dinitroperoxybenzoic acid[6] in 50 mL of $CHCl_3$ was heated at reflux for 8 h. The mixture was cooled to 0 °C, diluted with CH_2Cl_2, and filtered. The precipitate was washed with CH_2Cl_2, and the combined filtrates were washed with 20% aqueous $NaHSO_3$ and two portions of saturated aqueous $NaHCO_3$, dried, and distilled through a short-path apparatus to afford **3**: 1.98 g (68% yield); bp 76–80 °C (30 torr); IR (film) 1741, 1420, 1390, 1255, 1201, 1030 cm^{-1}; NMR δ 1.31 (t, 3, J = 7), 3.0 (s, 1), 4.25 (dq, 2, J = 2.2, 7). Anal. Calcd for $C_6H_6D_2O_3$: C, 51.72; H, 6.95. Found: C, 51.49; H, 6.88.

Ethyl (2*R,3*S**)-2,3-Dideuterio-2-hydroxy-3-(phenylseleno)propanoate (4).** A solution of diisobutylaluminum phenylselenide in hexane was prepared by the addition of 1.32 g (4.25 mmol) of diphenyl selenide to 6.0 mL of a 1.41 M solution (8.5 mmol) of diisobutylaluminum hydride in hexane. This reagent was added to a solution of 1.0 g (8.5 mmol) of glycidate **3** in 60 mL of hexane at −78 °C, and the solution was stirred for 2 h and then allowed to warm to 21 °C over an 8-h period. The mixture was washed with phosphate buffer (pH 3), and the aqueous layer was back-extracted with three portions of CH_2Cl_2. The combined organic layers were washed with saturated aqueous $NaHCO_3$, dried, and concentrated, and the crude product was purified by chromatography (ether/hexane, 1:1) to give **4**: 1.5 g (64% yield); IR 3560, 1730, 1480, 1080, 905 cm^{-1}; NMR δ 1.19 (t, 3, J = 7.1), 3.14 (s, 1), 3.33 (s, 1), 3.97 (dq, 1, J = 7.13, 7.15), 4.12 (dq, 1, J = 7.09, 7.14), 7.2–7.6 (m, 5). Anal. Calcd for $C_{11}H_{12}D_2O_3Se$: C, 48.36; H, 5.17. Found: C, 48.19; H, 5.13.

Ethyl (2*R,3*S**)-2,3-Dideuterio-2-[(dimethoxyphosphinyl)oxy]-3-(phenylseleno)propanoate (5).** To a solution of 0.98 g (3.56 mmol) of selenoalcohol **4** in 100 mL of THF at −78 °C was added a solution of 3.56 mol of lithium diisopropylamide in 25 mL of THF. After 15 min at −78 °C, 0.57 g (3.96 mmol) of dimethyl phosphorochloridate was added, and the mixture was allowed to warm to 21 °C over a 12-h period. After addition of 25 mL of saturated aqueous NH_4Cl, the aqueous layer was extracted four times with CH_2Cl_2, and the combined organic layers were washed with 2.5 N HCl and saturated $NaHCO_3$, dried, and evaporated to give 1.3 g (95% yield) of **5**, which was of sufficient purity to be carried on to the next step: IR 1750, 1270, 1045, 1020 cm^{-1}; NMR δ 1.25 (t, 3, J = 7.1), 3.36 (s, 1), 3.77 (d, 3, J = 18.1), 3.81 (d, 3, J = 18.2), 4.16 (m, 2), 7.2–7.6 (m, 5). A sample was purified for analysis by preparative TLC (silica gel; EtOAc/hexane, 70:30). Anal. Calcd for $C_{13}H_{17}D_2O_6PSe$: C, 40.96; H, 5.02; P, 8.12. Found: C, 40.93; H, 5.12; P. 8.01.

Ethyl (*Z*)-3-Deuterio-2-[(dimethoxyphosphinyl)oxy]-propenoate ((*Z*)-6). To a solution of 1.3 g (3.4 mmol) of phosphate ester **5** in 140 mL of CH_2Cl_2 at 21 °C was added 1.0 mL (8.8 mmol) of 30% H_2O_2. The mixture was stirred vigorously for 1 h, diluted with CH_2Cl_2, and washed with $NaHCO_3$. The organic layer was dried and evaporated to give *Z* enol ester **6**: 0.714 g (94% yield); IR 1730, 1635, 1310, 1280, 1170, 1040, 1005, 850, 820 cm^{-1}; NMR δ 1.34 (t, 3, J = 7.1), 3.88 (d, 6, J = 11.2), 4.29 (q, 2, J = 7.1), 5.97 (d, 1, J = 2.5). A sample was purified for analysis by preparative TLC (silica gel; EtOAc/hexane, 70:30). Anal. Calcd for $C_7H_{13}O_6P$: C, 37.51; H, 5.85; P, 13.82. Found: C, 37.35; H, 5.94; P, 13.64.

Cyclohexylammonium (*Z*)-3-Deuteriophosphoenolpyruvate ((*Z*)-1). A solution of 0.71 g (3.17 mmol) of triester (*Z*)-**6** and 1.05 mL (7.9 mmol) of bromotrimethylsilane in 25 mL of CH_2Cl_2 was kept at 21 °C for 2 h. After evaporation at reduced pressure, the residue was dissolved in 16 mL of 1 N KOH, washed with CH_2Cl_2, and desalted by elution through a column of Dowex 50W-X8 resin in the H^+ form. Addition of 0.33 mL (3.17 mmol) of cyclohexylamine to the eluant, lyophilization, and recrystallization from 1:1 methanol/ether gave 0.59 g (69% yield) of colorless product, mp 153–154 °C dec (lit.[8] mp 144–146 °C). Analysis of the olefinic proton signals at δ 5.76 (*E* isomer) and δ 6.06 (*Z* isomer) (CD_3OD solvent) indicated that this material was contaminated by less than 8% of the *E* isomer.

Ethyl (2*R,3*S**)-2,3-Dideuterio-3-bromo-2-hydroxypropanoate (7).** To a solution of 0.90 g (7.63 mmol) of labeled glycidate **3** and 1.0 mL (9.1 mmol) of bromotrimethylsilane in 75 mL of CH_2Cl_2 at −78 °C was added 0.174 g (0.76 mmol) of zinc bromide. The mixture was stirred at −78 °C for 6 h and then allowed to warm to 21 °C over a 12-h period. After hydrolysis of the trimethylsilyl ether with 2.8 mL of 2.5 N HCl, the mixture was partitioned between additional CH_2Cl_2 and saturated aqueous $NaHCO_3$, and the organic layer was dried and evaporated to give the bromohydrin **7** as analytically pure, colorless crystals: 1.39 g (92% yield); mp 49–50 °C; IR 3400, 1730, 1390, 1320, 1240, 1060 cm^{-1}; NMR δ 1.33 (t, 3, J = 7), 3.24 (br s, 1), 3.66 (s, 1), 4.30 (q, 2, J = 7). Anal. Calcd for $C_5H_7D_2BrO_3$: C, 30.48; H, 4.60; Br, 40.55. Found: C, 30.33, H, 4.50; Br, 40.78.

Ethyl (*E*)-3-Deuterio-2-[(dimethoxyphosphinyl)oxy]-propenoate ((*E*)-6). To a solution of 1.19 g (5.98 mmol) of bromohydrin **7** in 150 mL of THF at −78 °C was added a solution of 5.98 mmol of LDA in 30 mL of THF. After 15 min, 0.72 mL (6.58 mmol) of dimethyl phosphorochloridate was added, and the solution was allowed to warm to −20 °C over 14 h. After 3 h at 0 °C, the reaction mixture was partitioned between saturated aqueous NH_4Cl and CH_2Cl_2. The aqueous layer was washed twice with CH_2Cl_2, and the combined organic layers were washed with 2.5 N HCl and saturated $NaHCO_3$, dried, and evaporated to give the *E* enol phosphate (*E*)-**6**: 1.36 g (quantitative yield); NMR δ 1.34 (t, 3, J = 7.1), 3.88 (d, 6, J = 11.5), 4.29 (q, 2, J = 7.1), 5.61 (d, 1, J = 2.48).

Cyclohexylammonium (*E*)-3-Deuteriophosphoenolpyruvate ((*E*)-1). A 1.345 g sample of the *E* triester (*E*)-**6** was hydrolyzed and purified as described above for the *Z* isomer to give (*E*)-**1**: 1.15 g (72% yield); mp 150–151 °C dec. NMR analysis indicated that less than 6% of the *Z* stereoisomer was present.

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Registry No. (*E*)-**1**, 87115-14-8; (*Z*)-**1**, 87115-16-0; **2**, 87115-17-1; **3**, 87115-18-2; **4**, 87115-19-3; **5**, 87115-20-6; (*E*)-**6**, 87115-21-7; (*Z*)-**6**, 87115-22-8; **7**, 87115-23-9; **8**, 87115-24-0.

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(Arene)chromium Tricarbonyl Complexes in Organic Synthesis: Stereoselective Synthesis of *cis*- and *trans*-7-Hydroxycalamenenes[1]

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In the previuos papers, we have reported that nuclear lithiation of some arene compounds can be controlled regiochemically by complexation of the arene ring with chromium tricarbonyl group.[2,3] For example, (η^6-7-methoxy-1-tetralol)chromium tricarbonyl and the related

(1) Dedicated to Emeritus Prof. Takeo Sakan on the 70th anniversary of his birth.

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