Short Preparation of (*S*)-(*E*)-1-(*O*-Methylmandeloxy)butadiene

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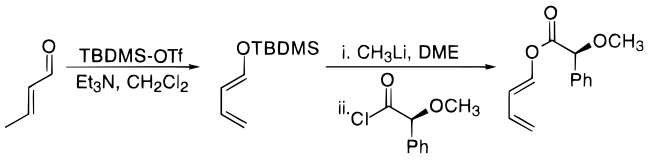
Diene **3** is a synthetically useful and theoretically interesting compound. Synthetically, high levels of diastereoselectivity have been observed in Diels−Alder reactions using **3**.[1] Thus, **3** provides an alternative to the more common motif of placing the chiral auxiliary in the dienophile. The ability to control asymmetry occurs despite the flexibility of the ester linkage and the distance between the forming and existing chiral centers. These characteristics have prompted theoretical studies[2] to probe the roles and relative importance of the ester conformation and π-stacking in the transition state. Such studies, along with empirical observations, have led to a new model for asymmetric induction that does not invoke $\pi-\pi$ interactions between the phenyl and dienyl groups.



1 **2** **3**

Despite the usefulness of diene **3**, a simple preparation has not been available. Any useful preparation of diene **3** must control the olefin geometry and proceed without racemization of the mandelate. The existing route[1] proceeds in seven steps from the cycloadduct of cyclopentadiene and maleic anhydride. The length of this preparation is probably responsible for the lack of routine application of diene **3**. Here we present a simple two-step synthesis of **3** from crotonaldehyde with complete control of stereochemistry.

It was recognized that lithium enolates can be generated by the action of methyllithium on the corresponding silyl enol ethers without loss of the olefin geometry.[3] Quenching the enolate corresponding to **1** with acid chloride **2** would provide diene **3** with retention of the enol ether geometry. The silyl enol ether geometry is, in turn, dictated by use of a bulky silylating agent. Thus, diene **1** was prepared[4] by heating a solution of crotonaldehyde, triethylamine, and *tert*-butyldimethylsilyl triflate in dichloromethane for 36 h at reflux. The product was obtained in 91% yield as a single isomer after distillation. The enolate was generated from **1** over a 6 h period in DME. Replacing DME with THF gave only a small amount of the enolate even at long reaction times (24 h). Enolate acylation proceeded smoothly when freshly distilled acid chloride was used. Diene **3** was obtained as a 97:3 mixture of *E:Z* isomers (GC) in 63% overall yield from crotonaldehyde. HPLC with a chiral solid phase[5] showed only a trace amount of the enantiomer (>99% ee). A detailed experimental follows.

Experimental Section

(*E*)-1-(*tert*-Butyldimethylsiloxy)butadiene (1). Freshly distilled crotonaldehyde (5.03 g, 71.8 mmol) and triethylamine (9.95 g,98.3 mmol) were dissolved in dichloromethane (30 mL). To this solution was added *tert*-butyldimethylsilyl triflate (15 mL, 65.3 mmoL) dropwise at 0 °C. The resulting red solution was heated at reflux for 36 h. The room temperature solution was diluted with Et_2O (120 mL) and extracted with cold $NaHCO_3$ (saturated aqueous, 2 × 50 mL) and brine (5 mL). The organic phase was dried over $MgSO_4$ and the solvent removed *in vacuo*. The residue was distilled (12 mmHg, 76−80 °C) to give the title compound as a colorless oil (10.96 g, 59.5 mmol, 91%).

(*S*)-*O*-Methylmandeloyl Chloride (2). Thionyl chloride (15 mL) was distilled directly into a flask containing (*S*)-methoxyphenylacetic acid (3.0 g, 18 mmol). The resulting solution was aged at room temperature for 1 h, and the volatiles were removed *in vacuo*. Kugelrohr distillation (∼5 mmHg, 110 °C) of the residue gave the title compound (2.4 g, 72%) as a colorless oil (stored at 4 °C and used within 12 h after distillation).

(*S*)-(*E*)-1-(*O*-Methylmandeloxy)butadiene (3). To (*E*)-1-(*tert*-Butyldimethylsiloxy)butadiene (**1**) (0.54 g, 2.9 mmol) in DME (5 mL) at room temperature was added methyllithium in ether (1.4 M, 2.1 mL, 2.9 mmol). The solution was stirred for 6 h or until more than 90% of the enol ether was consumed (aliquot quenched and GC with tetradecane as internal standard). The cloudy solution was transferred via cannula to a 0 °C THF (2 mL) solution of acid chloride (0.88 g, 4.8 mmol) and warmed to room temperature. The resulting clear solution became cloudy after being stirred 5 min. After 15 min, water (10 mL) and ether (30 mL) were added. The phases were separated, and the organic layer was extracted with NaOH (10% aqueous, 3 × 10 mL) and brine (1 × 10 mL). The organic phase was dried over $MgSO_4$, and the solvent was removed *in vacuo*. The resulting yellow oil was chromatographed with EtOAc:hexane (3:97) to give the title compound as a colorless oil (0.44 g, 2.0 mmol, 69%), $[\alpha]^{28}_D$ +7.91° (c = 2.17, CH_2Cl_2).[5]

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(1) (a) Trost, B. M.; O'Krongly, D.; Belletire, J. L. *J. Am. Chem. Soc.* **1980**, *102*, 7595−7596. (b) Siegel, C.; Thornton, E. R. *Tetrahedron: Asymmetry* **1991**, *2*, 1413−1428.

(2) (a) Maddaluno, J. F.; Gresh, N.; Giessner-Prettre, C. *J. Org. Chem.* **1994**, *59*, 793−802. (b) Tucker, J. A.; Houk, K. N.; Trost, B. M. *J. Am. Chem. Soc.* **1990**, *112*, 5465−5471. (c) Siegel, C.; Thornton, E. R. *Tetrahedron Lett.* **1988**, *29*, 5225−5228.

(3) (a) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324−2336. (b) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4464−4465.

(4) (a) Prepared according to the following modified method: Mander, L. N.; Sethi, S. P. *Tetrahedron Lett.* **1984**, *25*, 5953−5956. (b) Full characterization: Kozlowski, M. C.; Bartlett, P. A. *J. Am. Chem. Soc.* **1991**, *113*, 5897−5898 (supplementary material).

(5) Chiralpak AD column using 99.9:0.1 heptane−2-propanol as eluent. Note that the observed rotation is significantly lower than the reported rotation (see ref 1a), even though the chiral HPLC column indicates >99% ee. We have no explanation for this discrepancy.

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