Synthesis of an Enantiomerically Pure Intermediate Containing the CD Substructure of Taxol

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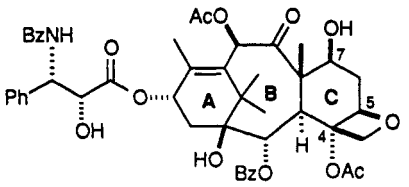
A straightforward conversion of the (*R*)-(−)-Hajos–Parrish ketone **5** to oxetane **13** is reported. It is anticipated that intermediates related to this compound could be useful for the total synthesis of taxol.

The anticancer diterpenoid taxol (**1**), by virtue of its unique structural features, potent biological activity,[1] unprecedented mechanism of action,[2] and limited availability, has attracted a great deal of attention from the synthetic organic community.[3] A number of synthetic



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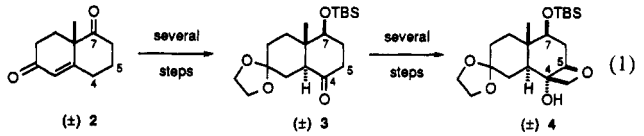
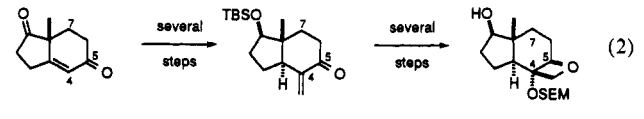
Taxol

approaches toward taxol have been described.[4] In principle, total synthesis could be helpful in increasing the availability of the drug, though this would be a daunting challenge. Another incentive for carrying out such studies is the hope of finding simpler versions of the molecule which still manifest useful activity. At the purely academic level, the rather intriguing structural complexity of the molecule has made it a formidable and thus far elusive target. In a recent paper[4a] we described the synthesis of a potentially useful intermediate **4** containing the CD ring substructure of taxol (eq 1). Our starting material was



(±) **2** (±) **3** (±) **4** (1)



(-) **5** (-) **8** (-) **14** (2)

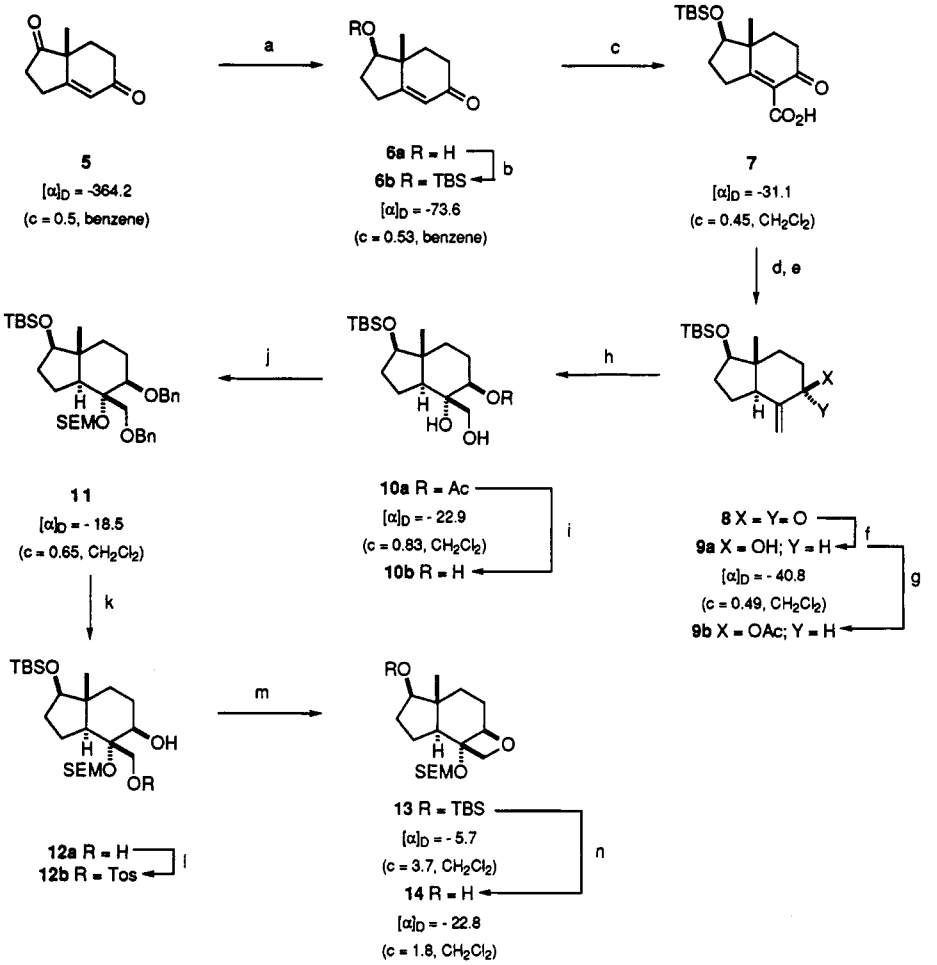
the racemic Wieland–Miescher ketone (**2**) which was transformed to **3** *en route* to **4**. In this paper we wish to disclose an oxetane construction which is complementary in design in that it proceeds in a completely different manner from a ketone **8** as the progenitor of C-5 of taxol (eq 2).[5] The synthesis described here commences with enantiomerically pure (*R*)-(−)-Hajos–Parrish ketone **5**. The terminal compound described is **14** which is a possible intermediate for reaching the 7-desoxytaxane series or analogues thereof.

Enantiomerically pure (*R*)-(−)-Hajos–Parrish ketone **5**[6] was converted by known protocols to the *exo*-methylene ketone **8** (Scheme I). Reduction of **8** with $NaBH_4$ in the presence of $CeCl_3$ in methanol[7] at 0 °C gave exclusively equatorial allylic alcohol **9a**. Solubility problems complicated direct osmylation of this substrate necessitating its conversion to acetate **9b**. Dihydroxylation of the double bond with catalytic osmium tetraoxide and *N*-methylmorpholine *N*-oxide[8] then proceeded from the α face to give essentially a single diol **10a**. With the requisite oxygens suitably disposed, we addressed the matter of oxetane formation. It was found necessary to protect the tertiary hydroxyl group with a nonmigratable protecting group.[9] This problem was solved as follows. The acetate was hydrolyzed giving triol **10b** which upon treatment with excess KH followed by catalytic $^nBu_4NI$ and 2 equiv of BnBr (until both the primary and secondary hydroxyl groups had been benzylated as evidenced by TLC) and then 2 equiv of SEM-Cl gave directly compound **11**. Hydrogenolysis of both benzyl groups then gave diol **12a**. Selective monotosylation followed by exposure to NaH in THF at 45 °C afforded the desired oxetane **13** in 58%

(1) Chabner, B. A. *Princ. Prac. Onc.* **1991**, *5*, 1.
(2) (a) Schiff, P. B.; Fant, J.; Horwitz, S. B. *Nature* **1979**, *277*, 665. (b) Schiff, P. B.; Horwitz, S. B. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 1561. (c) Parness, J.; Horwitz, S. B. *J. Cell Biol.* **1981**, *91*, 479.
(3) For reviews see: (a) Swindell, C. S. *Org. Prep. Proc. Int.* **1991**, *23*, 465. (b) Kingston, D. G. I. *Pharmac. Ther.* **1991**, *52*, 1. (c) Blechert, S.; Guénard, D. *Taxus* Alkaloids. In *The Alkaloids*; Brossi, A., Ed.; Academic Press: San Diego, **1990**; Vol. 39, p 195.
(4) In addition to the work reviewed in ref 3, more recent contributions include: (a) Magee, T. M.; Bornmann, W. G.; Isaacs, R. C. A.; Danishefsky, S. J. *J. Org. Chem.* **1992**, *57*, 3274. (b) Queneau, Y.; Krol, W. J.; Bornmann, W. G.; Danishefsky, S. J. *J. Org. Chem.* **1992**, *57*, 4043. (c) Wender, P. A.; Mucciaro, T. P. *J. Am. Chem. Soc.* **1992**, *114*, 5878. (d) Nicolaou, K. C.; Hwang, C.-K.; Sorensen, E. J.; Clairborne, C. F. *J. Chem. Soc., Chem. Commun.* **1992**, 1117. (e) Nicolaou, K. C.; Liu, J. J.; Hwang, C.-K.; Dai, W.-M.; Guy, R. K. *J. Chem. Soc., Chem. Commun.* **1992**, 1118.
(5) In addition to ref 4a,e, for previous oxetane constructions see: (a) Berkowitz, W. F.; Amarasekara, A. S.; Perumattam, J. J. *J. Org. Chem.* **1987**, *52*, 1119. (b) Lin, J.; Nikaido, M. M.; Clark, G. *J. Org. Chem.* **1987**, *52*, 3745. (c) Ettouati, L.; Ahond, A.; Poupat, C.; Potier, P. *Tetrahedron* **1991**, *47*, 9823.
(6) Preparation of the (*S*)-(+) Hajos–Parrish ketone, $[\alpha]_D = +367$ (c = 1; C_6H_6), has been reported. See: (a) Micheli, R. A.; Hajos, Z. G.; Cohen, N.; Parrish, D. R.; Portland, L. A.; Sciamanna, W.; Scott, M. A.; Wehrli, P. A. *J. Org. Chem.* **1975**, *40*, 675. (b) Hajos, Z. G.; Parrish, D. R. Organic Syntheses; Wiley: New York, 1990; Collect. Vol. VII, p 363. The procedure involves the L-(−)-proline-catalyzed Robinson annelation of the product of the Michael addition reaction between 2-methyl-1,3-cyclopentanedione and methyl vinyl ketone, followed by acid-catalyzed elimination of water. We prepared the (*R*)-(−)-Hajos–Parrish ketone, $[\alpha]_D = -364.2$ (c = 0.5; C_6H_6) by substituting D-(+)-proline in the same sequence of reactions.
(7) Gemal, A. L.; Luche, J.-L. *J. Am. Chem. Soc.* **1981**, *103*, 5454.
(8) Van Rheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.
(9) Failure to do so resulted in spiroepoxide formation during the act of activating the primary hydroxyl group to promote oxetane formation.

0022-3263/93/1958-3938$04.00/0

Scheme I[a]



[a] Reagents: (a) $LiAl(O^tBu)_3H$, 0 °C; (b) TBS-Cl, imidazole, 54% overall; (c) magnesium methyl carbonate, DMF, 125 °C, 74%; (d) H_2, 10% Pd–$BaSO_4$, 0 °C; (e) H_2CO, catalytic piperidine, DMSO; (f) $NaBH_4$, $CeCl_3$, 57% from **7**; (g) Ac_2O, pyridine, catalytic DMAP; (h) catalytic OsO_4, NMO, 89% from **9a**; (i) K_2CO_3, MeOH; (j) xs KH, 0 °C, and then 2 equiv of BnBr, catalytic $^nBu_4NI$ and then 2 equiv of SEM-Cl; 98%; (k) H_2, 10% Pd–C, EtOH, catalytic AcOH, 69%; (l) Tos_2O, pyridine, catalytic DMAP; 70%; (m) NaH, THF, 45 °C, 74%; (n) 1 equiv of TBAF, THF, rt 89%.

overall yield (three steps). Selective removal of the TBS group in the presence of the SEM group to give **14** was then accomplished by exposure to 1 equiv of TBAF in THF at rt.

To summarize, we have converted the enantiomerically pure (*R*)-(−)-Hajos–Parrish ketone **5** in 14 steps to oxetane **13**. In terms of directness of the route from bicyclic enones (derivable from Robinson annulation) to the cyclic domains containing hydroxyoxetane, the methodology described herein is superior to that of our previous disclosure.[4a] Access to relevant enantiomerically pure starting material is also much improved. At the moment, functionality to install the C7 oxygen has not been included. We are currently exploring this chemistry as a route to taxol analogues.

Experimental Section

General. Air- and/or moisture-sensitive reactions were conducted under an atmosphere of dry nitrogen using flame-dried glassware and standard syringe/septa techniques. Methylene chloride was distilled from calcium hydride immediately prior to use. Likewise, THF was distilled from sodium benzophenone ketyl. Anhydrous DMF in Sure Seal bottles was purchased from Aldrich. All other reagents are commercial reagent grade and were purchased from their suppliers and used without further purification. Melting points were measured using an Electrothermal IA 9100 digital melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded with a Perkin-Elmer 1600 series fourier-transform (FT) spectrometer. NMR spectra were recorded using a Bruker AMX-400 spectrometer. Optical rotations were measured with a JASCO DIP-370 digital polarimeter. Concentrations pertaining to such rotations are given in grams/100 mL. Flash chromatography was performed using EM Science silica gel 60 (230-400 mesh).

Silyl Ether 6b. Lithium tri-*tert*-butoxyaluminum hydride (76 mL, 1.0 M in THF, 76.0 mmol) was added in a dropwise manner over 30 min to a solution of diketone **5** (5.02 g, 30.5 mmol) in THF (60 mL) at 0 °C. Stirring was maintained for 10 min, and then acetone (10 mL) was added followed shortly thereafter by ice–water (50 mL). After being stirred at 0 °C for 1 h, the resulting suspension was acidified to pH 5–6 with 10% sulfuric acid, and the bulk of the THF was then removed by rotary evaporation. The residue was diluted with brine (150 mL) and extracted alternately with two portions each of ether (200 mL) and ethyl acetate (200 mL). The combined extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the alcohol **6a** as a white solid.

The crude alcohol thus obtained was dissolved in DMF (30 mL) and treated successively with imidazole (5.5 g, 80.8 mmol) and TBSCl (6.5 g, 43.1 mmol). After being stirred for 8 h at room temperature, the reaction mixture was diluted with water (250 mL) and extracted with ether (3 × 200 mL). The combined extracts were washed with water (3 × 100 mL), dried over $MgSO_4$, filtered, and concentrated to give a residue which was purified by flash chromatography (9:1 hexanes–ethyl acetate). This

yielded 4.6 g, 54%, of silyl ether **6b** as a colorless oil, $[\alpha]^{25}_D$ −73.6° (*c* 0.53, benzene). TLC (3:2 hexane–ethyl acetate): R_f = 0.54. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.76 (br s, 1H); 3.72–3.77 (dd, 1 H, *J* = 7.5, 10 Hz); 2.64–2.72 (m, 1H); 2.46–2.56 (m, 1H); 2.31–2.42 (m, 2H); 1.93–2.06 (m, 2H); 1.65–1.85 (m, 2H); 1.10 (s, 3H); 0.89 (s, 9H); 0.05 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 199.3, 175.1, 123.3, 110.6, 80.7, 45.6, 34.4, 33.4, 29.6, 25.7, 18.0, 15.2, −4.5, −4.9. IR (film): 1671 (s), 1251 (m), 1110 (s) cm^{-1}. HRMS: *m/z* (M^+ + H) for $C_{16}H_{28}O_2Si$ calcd 281.1937, found 281.1942.

Keto Acid 7. Magnesium methyl carbonate (6.4 mL, 2.0 M in DMF, 12.8 mmol) was added to a solution of enone **6b** (1.02 g, 3.62 mmol) in DMF (21 mL), and the reaction was heated at 125 °C while a stream of nitrogen was maintained bubbling through the solution. Initially, vigorous evolution of carbon dioxide was observed, and after 2 h the reaction was complete. The mixture was cooled to room temperature and most of the DMF removed under reduced pressure. Water (20 mL) was added, and with cooling in an ice bath the reaction mixture was acidified with concentrated HCl. The resulting yellow solution was extracted with ether (3 × 20 mL). Throughout the workup, ice was frequently added to the separatory funnel to minimize hydrolysis of the silyl ether under the strongly acidic conditions. The combined organic extracts were dried over $MgSO_4$ and concentrated to give the acid **7** as a yellow oil. This was chromatographed on SiO_2, eluting with 4:1 hexane–EtOAc containing 1% AcOH and then recrystallized from hexane to give 871.8 mg, 74%, of unsaturated keto acid **7** as white fluffy needles, mp 91.5–92.5 °C, $[\alpha]^{25}_D$ −31.1° (*c* 0.45, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 13.1 (s, 1H); 3.82–3.85 (dd, 1 H, *J* = 7.5, 10 Hz); 3.14–3.35 (m, 2H); 2.73–2.85 (m, 1H); 2.62–2.69 (m, 1 H) 2.01–2.11 (m, 2H); 1.76–1.94 (m, 2H); 1.19 (s, 3H); 0.90 (s, 9H); 0.08 (s, 3 H); 0.06 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.7, 195.8, 164.1, 120.7, 79.9, 49.0, 33.5, 32.0, 31.1, 30.0, 25.7, 18.0, 15.8, −4.5, −5.0. IR (film): 3065 (w), 1739 (s), 1624 (s), 1252 (s), 1019 (m) cm^{-1}. HRMS: *m/z* (M^+ + H) for $C_{17}H_{28}O_4Si$ calcd 324.1757, found 324.1759.

Allylic Alcohol 9a. A solution of the enone acid **7** (451.9 mg, 1.39 mmol) was dissolved in methanol[10] (10 mL) and cooled to 0 °C, and 10% Pd on $BaSO_4$ (65 mg) was added. The mixture was stirred at the same temperature under a balloon of hydrogen during which time the catalyst separated from the support. Hydrogenation was complete within 2 h. The reaction mixture was filtered through Celite and concentrated (bath temp ≤10 °C).[11] Final pumping *in vacuo* was also conducted at about 10 °C. This gave the saturated β keto acid as a pale yellow oil.

The crude keto acid was dissolved in DMSO (4 mL) at room temperature and then treated with 37% aqueous formaldehyde (0.6 mL, 7.39 mmol) and piperidine (14 μL, 0.14 mmol). After a very brief induction period there was evolution of carbon dioxide. Stirring was conducted at room temperature for 1.5 h after which time a 1:1 mixture of water and brine (20 mL) was added. After being stirred for 5 min, the mixture was extracted with ether (2 × 25 mL). The combined organic extracts were then washed with water (2 × 15 mL) and brine (15 mL) and dried ($MgSO_4$). Concentration gave the *exo*-methylene ketone **8** as a pale yellow oil.

The crude *exo*-methylene ketone was immediately dissolved in methanol (20 mL) and the resulting solution cooled to 0 °C whereupon $CeCl_3 \cdot 7H_2O$ (0.6 g, 1.6 mmol) was added. Once dissolution was complete, sodium borohydride (217.7 mg, 5.75 mmol) was then added carefully in small portions. Stirring was conducted for 30 min at which time saturated NaCl was added to the slurry followed by 1 M HCl until a homogeneous solution was obtained. This mixture was extracted with ether (3 × 30 mL), and the organic extracts were pooled and washed with saturated $NaHCO_3$ (15 mL), water (15 mL), and brine (15 mL) and then dried ($MgSO_4$). Filtration and concentration gave a residue which was purified by flash chromatography eluting with 9:1 hexane–ethyl acetate. This gave allylic alcohol **9a** (235.3 mg; 57% from enone **7**), $[\alpha]^{25}_D$ −40.8° (*c* 0.49, CH_2Cl_2) as a viscous pale yellow oil. TLC (4:1 hexane–ethyl acetate): R_f = 0.29. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.05 (s, 1H); 4.63 (s, 1H); 3.96–4.00 (m, 1H); 3.70 (t, 1H, *J* = 8.6 Hz); 1.96–2.10 (m, 3H); 1.85–1.90 (m, 1H); 1.65–1.75 (m, 2H); 1.35–1.60 (m, 3H); 1.19–1.30 (m, 1H); 0.85 (s, 9H); 0.06 (s, 3 H); 0.01 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 150.7, 102.1, 81.5, 73.2, 48.5, 45.9, 35.2, 33.0, 31.3, 25.8, 25.8, 20.9, 11.3, −4.5, −4.9. IR (film): 3370 (br, s), 1256 (s), 1119 (s) cm^{-1}. HRMS: *m/z* (M^+) for $C_{17}H_{32}O_2Si$ calcd 296.2172, found 296.2175.

Diol 10a. Allylic alcohol **9a** (230.0 mg, 0.78 mmol) was dissolved in methylene chloride (5 mL) and treated sequentially with pyridine (0.25 mL, 3.1 mmol), a catalytic quantity of DMAP, and acetic anhydride (88 μL, 0.93 mmol). The resulting mixture was stirred at room temperature for 2.5 h. Water (10 mL) was then added and the reaction mixture extracted with ether (3 × 25 mL). The combined extracts were then washed with water (15 mL), 10% $CuSO_4$ (2 × 20 mL), and brine (10 mL) and dried ($MgSO_4$). Concentration gave acetate **9b**.

The crude acetate **9b** was dissolved in 8:1 acetone–water (9 mL), and NMO (187.0 mg, 1.59 mmol) was added followed by osmium tetraoxide (0.4 mL, 0.08 M in 2-methyl-2-propanol, 32 μmol). After the solution had stirred for 12 h, saturated $NaHSO_3$ (15 mL) was added. The resulting mixture was stirred for 30 min and then poured into saturated NaCl (25 mL). Extraction with ethyl acetate (5 × 25 mL), drying over $MgSO_4$, and concentration gave a pale orange oil. Gradient elution flash chromatography (9:1, 4:1, 7:3 hexane–ethyl acetate) gave acetate diol **10a** as a white crystalline solid, mp 93.5–94.5 °C (256.3 mg, 89%), $[\alpha]^{25}_D$ −22.9° (*c* 0.83, CH_2Cl_2). TLC (3:2 hexane–ethyl acetate): R_f = 0.22. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 4.69 (dd, 1H, *J* = 4.8, 11.5 Hz); 3.99–4.02 (m, 1H); 3.78 (m, 1H); 1.96–2.10 (m, 2H); 2.15–2.20 (m, 1H); 2.08 (s, 3H); 1.90–2.00 (m, 2H); 1.50–1.75 (m, 5H); 1.35–1.50 (m, 1H); 1.15 (m, 1H); 0.86 (s, 9H); 0.08 (s, 3H); 0.01 (s, 6H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 170.8, 83.7, 81.3, 74.0, 61.4, 51.3, 43.7, 34.5, 30.6, 26.4, 25.8, 21.3, 19.3, 18.0, 12.1, −4.5, −4.9. IR (film): 3453 (br, s), 1732 (s), 1251 (s) cm^{-1}. HRMS: *m/z* (M^+) for $C_{19}H_{36}O_5Si$ calcd 373.2411, found 373.2410.

Compound 11. A solution of the acetate diol **10a** (256.3 mg, 0.78 mmol) in methanol (3 mL) was treated with an excess of solid K_2CO_3. The resulting suspension was stirred at room temperature for 30 min at which point saturated NH_4Cl (2 mL) was added, and the reaction mixture was then concentrated. Water (2 mL) and brine (10 mL) were added to the residue, and the resulting mixture was then extracted with methylene chloride (3 × 15 mL). The extracts were dried over $MgSO_4$ and the concentrated to give triol **10b**.

A solution of the crude triol **10b** (168.7 mg, 0.51 mmol) in THF (6 mL) was added via cannula over a 5-min period to a suspension of hexane-washed KH (108.7 mg, 2.71 mmol) in THF (4 mL) at 0 °C. The mixture was stirred for 10 min, and then tetra-*n*-butylammonium iodide (47.6 mg, 0.13 mmol) and benzyl bromide (0.12 mL, 1.01 mmol) were added. The reaction mixture was allowed to warm gradually to room temperature and stirred there for 11 h. At this point dibenzylation was complete (TLC analysis) and SEM-Cl (0.18 mL, 1.02 mmol) was added. After 4 h the reaction mixture was cooled to 0 °C, quenched with saturated NH_4Cl, poured into brine (15 mL), and extracted with ether (3 × 25 mL). The extracts were dried ($MgSO_4$) and concentrated, and the resulting residue was chromatographed (19:1 petroleum ether–ether) to give compound **11** (322.1 mg, 98%), $[\alpha]^{25}_D$ −18.5° (*c* 0.65, CH_2Cl_2). TLC (4:1 petroleum ether–ether): R_f = 0.65. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27–7.35 (m, 10H); 5.09 (d, 1H, *J* = 6.7 Hz); 5.01 (d, 1H, *J* = 6.7 Hz); 4.79 (s, 1H); 4.63 (br s, 2H); 4.56 (d, 1H, *J* = 11.7 Hz); 4.45 (d, 1H, *J* = 11.7 Hz); 4.15 (d, 1H, *J* = 11.7 Hz); 3.97 (d, 1H, *J* = 11.7 Hz); 3.60–3.72 (m, 3H); 3.45–3.55 (m, 2H); 2.35–2.45 (m, 1H); 1.40–2.00 (m, 5H); 0.95–1.10 (m, 3H); 0.95 (s, 3H); 0.89 (s, 9H); 0.04 (s, 3H); 0.02 (s, 3H); −0.04 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.0, 138.6, 128.2, 127.44, 127.32, 127.28, 127.24, 127.2, 91.5, 90.5, 85.7, 81.9, 81.8, 73.6, 72.4, 72.1, 65.1, 51.9, 44.3, 35.2, 30.8, 26.8, 25.8, 21.6, 18.1, 11.3, −1.5, −4.5, −4.9. IR (film): 2951 (s), 1249 (s), 1110 (s) cm^{-1}. HRMS: *m/z* (M^+) for $C_{37}H_{60}O_5Si_2$ calcd 640.3979, found 640.3980.

Oxetane 13. A solution of the dibenzyl ether **11** (175.2 mg, 0.27 mmol) in 19:1 ethanol–acetic acid (10 mL) containing a spatula tip of 10% Pd/C was stirred at room temperature under a balloon of hydrogen for 3 h. The reaction mixture was filtered through Celite and concentrated. The resulting residue was

(10) Anhydrous MeOH in Sure Seal bottles from Aldrich was used.
(11) Care should be taken here since above 10 °C spontaneous decarboxylation of this β keto acid takes place.

chromatographed (4:1 hexane–ethyl acetate) to give pure diol **12a** (87.1 mg; 69%).

The diol **12a** (87.1 mg, 0.19 mmol) was dissolved in dry methylene chloride (2 mL), cooled to 0 °C, and treated sequentially with dry pyridine (80 μL, 0.99 mmol), a catalytic amount of DMAP, and *p*-toluenesulfonic anhydride (74.0 mg, 0.23 mmol). The reaction was allowed to warm gradully to room temperature overnight. The reaction mixture was concentrated, and the residue was chromatographed (9:1 hexane–ethyl acetate) to give the desired monotosylate **12b** (80.8 mg, 70%).

Tosylate **12b** (69.0 mg, 0.11 mmol) was dissolved in dry THF (0.5 mL) and transferred via cannula to a suspension of NaH (14.5 mg, 0.60 mmol) in dry THF (0.5 mL) at rt. The reaction was stirred at 45 °C for 19 h. It was then cooled to rt, quenched with brine (5 mL), and extracted with ether (3 × 15 mL). The combined extracts were dried over $MgSO_4$, filtered, and concentrated. Chromatography (9:1 petroleum ether–ether) gave pure oxetane **13** as a colorless oil (36.8 mg, 74%), $[\alpha]^{25}_D$ −5.7° (*c* 3.7, CH_2Cl_2). TLC (9:1 petroleum ether–ether): R_f = 0.43. ^1H NMR ($CDCl_3$, 400 MHz): δ 4.95 (d, 1H, *J* = 5.6 Hz); 4.84 (d, 1H, *J* = 7.5 Hz); 4.74 (d, 1H, *J* = 7.5 Hz); 4.53 (d, 1H, *J* = 7.3 Hz); 4.40 (d, 1H, *J* = 7.3 Hz); 3.64–3.68 (m, 1H); 3.60 (t, 1H, *J* = 8.2 Hz); 1.75–2.1 (m, 5H); 1.5–1.7 (m, 4H); 1.15 (s, 3H); 0.89–0.93 (m, 2H); 0.89 (s, 9H); 0.02–0.03 (d, 6H); 0.02 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 90.0, 85.5, 82.0, 80.3, 74.1, 65.5, 45.1, 43.5, 32.6, 29.7, 27.2, 25.8, 19.9, 18.1, 18.0, 10.5, −1.4, −4.4, −4.8. IR (film): 2954 (s), 1250 (m), 1116 (m) cm^{-1}. HRMS: *m/z* (M^+) for $C_{23}H_{46}O_4Si_2$ calcd 442.2935, found 442.2921.

Alcohol 14. Silyl ether **13** (36.8 mg, 83 μmol) was dissolved in dry THF (1 mL), cooled to 0 °C, and treated with TBAF (83 μL, 1.0 M in THF, 83 μmol). The ice bath was removed, and the mixture was allowed to stir at room temperature for 11 h. The solvent was then removed under reduced pressure and water (5 mL) added to the residue. It was then extracted with ether (2 × 15 mL). The organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Chromatography (3:2 hexane–ethyl acetate) afforded pure alcohol **14** as a colorless oil (24.4 mg, 89%), $[\alpha]^{25}_D$ −22.8° (*c* 1.8, CH_2Cl_2). TLC (3:2 hexane–ethyl acetate): R_f = 0.27. ^1H NMR ($CDCl_3$, 400 MHz): δ 4.97 (d, 1H, *J* = 6.3 Hz); 4.84 (d, 1H, *J* = 7.5 Hz); 4.74 (d, 1H, *J* = 7.5 Hz); 4.56 (d, 1H, *J* = 7.3 Hz); 4.38 (d, 1H, *J* = 7.3 Hz); 3.63–3.70 (m, 3H); 1.80–2.10 (m, 4H); 1.50–1.70 (m, 5H); 1.23–1.26 (m, 1H); 1.19 (s, 3H); 0.88–0.92 (m, 2H); 0.016 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 90.0, 85.3, 82.1, 80.0, 73.9, 65.5, 45.5, 43.1, 32.1, 29.4, 27.0, 19.7, 18.1, 10.4, −1.4. IR (film): 3428 (s), 2951 (s), 1249 (s), 1060 (s) cm^{-1}. HRMS: *m/z* (M^+) for $C_{17}H_{32}O_4Si$ calcd 329.2149, found 329.2133.

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Supplementary Material Available: Spectra of obtained compounds (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.