(4b) was prepared by the same procedure described above for the preparation of (1,3-dioxolan-2-yl)-*tert*-butyldimethylsilane (4a). The crude product, obtained by Kugelrohr distillation (60 °C (5 mmHg)) could not be purified further by flash chromatography on silica gel because of its instability: crude yield 37%; ^{1}H NMR ($CDCl_3$) δ 0.06 (s, 9 H), 3.72 (t, 2 H), 3.88 (t, 2 H), 4.42 (s, 1 H); HRMS (M − 1) calcd for $C_6H_{13}SiO_2$ 145.0694, found 145.0713.

The 2,4-dinitrophenylhydrazone of formyltrimethylsilane (2b) was obtained in a 46% yield as described above for formyl-*tert*-butyldimethylsilane: mp 141–142 °C; ^{1}H NMR ($CDCl_3$) δ 0.23 (s, 9 H), 7.58 (s, 1 H), 7.94 (d, 1 H), 8.31 (dd, 1 H), 9.05 (d, 1 H), 11.03 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ −2.439, 116.87, 123.24, 128.82, 129.78, 138.09, 144.69, 159.91; HRMS calcd for $C_{10}H_{14}N_4O_4Si$ 282.0784, found 282.0785. Anal. Calcd for $C_{10}H_{14}N_4O_4Si$: C, 42.55; H, 4.97; N, 19.86. Found: C, 42.26; H, 4.91; N, 19.73.

Hydrolysis of (1,3-Dioxolan-2-yl)silanes. Hydrolysis of (1,3-dioxolan-2-yl)-*tert*-butyldimethylsilane (4a) and the corresponding -trimethylsilane (4b) was carried out at 25 °C in one part of 0.5% DCl in D_2O and two parts of acetone-d_6 in an NMR tube. The rates of hydrolysis were determined by following the decrease in the area of the C-4 and C-5 dioxolane protons and the increase in the area of the four ethylene glycol protons with time. The hydrolysis of (1,3-dioxolan-2-yl)-*tert*-butyldimethylsilane also was examined in one part 30% sulfuric acid in water and two parts ethanol at 0 °C. After 70 and 300 min 2,4-dinitrophenylhydrazine reagent was added, and the solutions were allowed to stand at 0 °C overnight. The 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane was isolated in 75% and 50% yield, respectively.

Enzymes and Assays. Bovine liver MAO B was isolated according to the published method.[17] MAO activity was assayed by the method Tabor et al.[18] The percentage of active enzyme was determined by inactivation with [^{14}C]- or [1-^{3}H]pargyline.[19] Protein assays were done with either Pierce BCA protein assay reagent or Pierce Coomassie protein assay reagent using bovine serum albumin for standard curves. All buffers and enzyme solutions were prepared with doubly distilled deionized water.

Formation of Tritiated Aldehydes During Inactivation of MAO by [1-^{3}H](Aminomethyl)-*tert*-butyldimethylsilane. MAO (100 μM, 25 μL) was incubated with 53 mM [1-^{3}H](aminomethyl)*tert*-butyldimethylsilane·HCl in 200 mM Tris-HCl buffer pH 9.0 (475 μL) at 25 °C. A control without inactivator was run simultaneously at one-fifth the scale. The enzyme was assayed after 4 h and was found to be completely inactive. 2,4-Dinitrophenylhydrazine reagent (200 μL) was added directly to the inactivated enzyme and to a nonenzymatic control, and the solutions were allowed to react overnight at room temperature. Water (3 mL) was added to the solutions which were extracted with chloroform (2 × 5 mL). The combined organic extracts were washed with water (2 × 5 mL) and evaporated. Samples were redissolved in acetonitrile and analyzed using analytical reversed-phase HPLC (60:40 acetonitrile/water 0.25 mL/min; FLO-SCINT II scintillation fluid 0.75 mL/min) monitoring the UV absorbance at 360 nm.

Large-Scale Formation of Aldehydes During Inactivation of MAO by (Aminomethyl)-*tert*-butyldimethylsilane. The procedure for the preparation of tritiated aldehydes during inactivation of MAO by [1-^{3}H](aminomethyl)-*tert*-butyldimethylsilane and the subsequent reaction with 2,4-dinitrophenylhydrazine was followed exactly except that (aminomethyl)-*tert*-butyldimethylsilane was substituted for [1-^{3}H]-(aminomethyl)-*tert*-butyldimethylsilane. Preparative reversed-phase HPLC (60:40 acetonitrile/water for 10 min then 100% acetonitrile with a linear gradient for 2 min at 1.4 mL/min) was used to separate compounds in unknown peaks for mass spectral analysis. The product obtained in the peak corresponding to the 2,4-dinitrophenylhydrazone of formyl-*tert*-butyldimethylsilane had a ^{1}H NMR spectrum (Figure 2), a ^{13}C NMR spectrum (data not shown), and mass spectrum (data not shown) the same as those for the synthetic compound. HRMS (EI) calcd for $C_{13}H_{20}N_4O_4Si$ 324.1254, found 324.1269.

Acknowledgment. We are grateful to the National Institutes of Health (GM 32634) for financial support of this research and to Professor Paul Knochel for suggesting the use of (1,3-dioxolan-2-yl)silanes as possible intermediates in the synthesis of formylsilanes.

Registry No. 1, 95452-06-5; 2a, 143370-61-0; 2b, 143370-69-8; 3, 118418-21-6; 4a, 143370-62-1; 4b, 143370-68-7; MAO, 9001-66-5; benzophenone *N*-methylimine, 13280-16-5; (*tert*-butyldimethyl)chlorosilane, 18162-48-6; (aminomethyl)-*tert*-butyldimethylsilane·HCl, 143370-63-2; (aminomethyl)-*tert*-butyldimethylsilane, 143370-64-3; benzophenone, 119-61-9; benzophenone *N*-((*tert*-butyldimethylsilyl)methyl)imine, 143370-65-4; [1-^{3}H]-benzophenone *N*-((*tert*-butyldimethylsilyl)methyl)imine, 143370-66-5; [1-^{3}H](aminomethyl)-*tert*-butyldimethylsilane·HCl, 143370-67-6; 1,3-dithiane, 505-23-7.

(17) Salach, J. I. *Arch. Biochem. Biophys.* **1979**, *192*, 321–327.
(18) Tabor, C. W.; Tabor, H.; Rosenthal, S. M. *J. Biol. Chem.* **1954**, *208*, 645–661.
(19) Chuang, H. Y. K.; Patek, D. R.; Hellerman, L. *J. Biol. Chem.* **1974**, *249*, 2381–2384.

An Improved Synthesis of Naphthoate Precursors to Olivin

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An improved synthesis of olivin synthetic intermediate **3** is described. The synthesis involves the Horner–Wadsworth–Emmons coupling of **14** and **16**, the diastereoselective vinylcuprate addition to enone **20**, and the condensation of isocoumarin **25** and methyl acetate. A parallel sequence starting from allyl ether **26** has provided naphthoate **35** that is suitably differentiated for glycosylation studies.

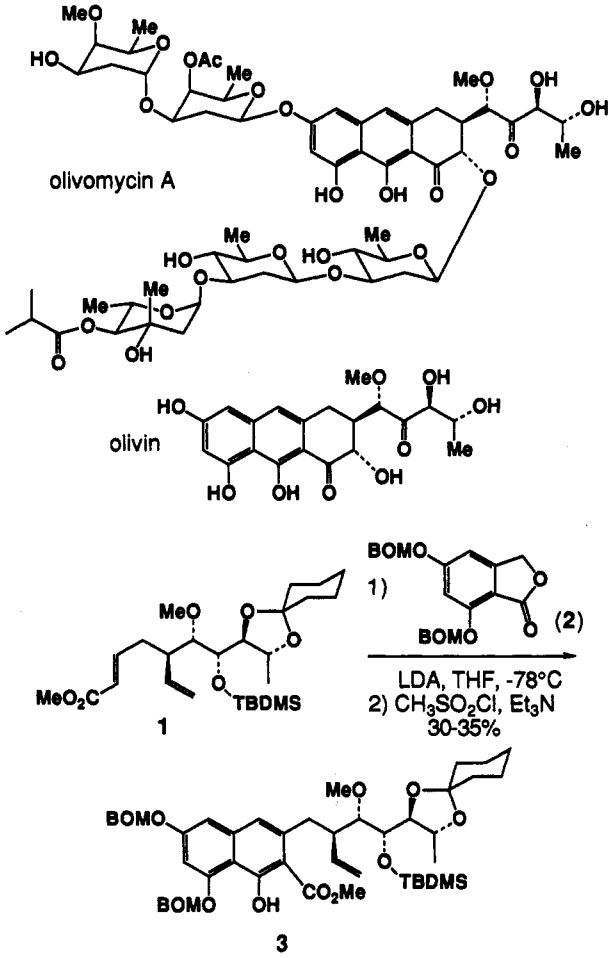
Olivomycin A and other clinically active members of the aureolic acid family of anticancer agents are challenging synthetic targets.[1,2] These compounds are inhibitors of DNA-dependent RNA polymerase, and a recent report suggests that they inhibit transcription of the c-myc protooncogene.[3] Available structure–activity data indicate that the two oligosaccharide chains are essential for bio-

(1) (a) Remers, W. A. *The Chemistry of Antitumor Antibiotics*; Wiley-Interscience: New York, 1979; Chapter 3. (b) Skarbek, J. D.; Speedie, M. K. In *Antitumor Compounds of Natural Origin: Chemistry and Biochemistry*, Aszalos, A., Ed.; CRC Press: Boca Raton, FL, 1981; Chapter 5. (c) Pettit, G. R. *Biosynthetic Products for Cancer Chemotherapy*; Plenum Press: New York, 1977; Vol. 1, p 143.

(2) For a review of synthetic efforts through 1987, see: Franck, R. W.; Weinreb, S. M. In *Studies in Natural Product Chemistry*; Rahman, A. U., Ed.; Elsevier: Amsterdam, 1989; pp 173–208.
(3) Snyder, R. C.; Ray, R.; Blume, S.; Miller, D. M. *Biochemistry* **1991**, *30*, 4290.

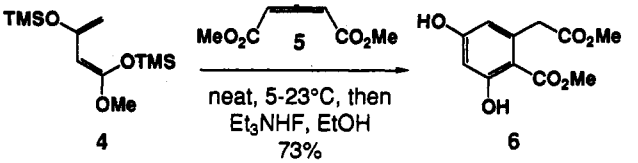
0022-3263/92/1957-6622$03.00/0

logical activity.[1,4] As part of our program directed toward the synthesis of olivomycin A and of potentially less toxic analogues, we required a convenient source of the aglycon olivin for glycosidation studies.[5] Unfortunately, the aromatic annulation sequence (cf., 1 + 2 → 3) utilized in our original synthesis proved unsuitable for scale-up.[5a] We report herein a shorter and more efficient synthesis of naphthoate 3 involving the Horner–Wadsworth–Emmons coupling of 14 and 16, the diastereoselective vinylcuprate addition to enone 20, and the Claisen condensation of isocoumarin 25 and methyl acetate.[6a] This synthesis complements existing methods for the synthesis of highly functionalized isocoumarins.[6b] A parallel sequence has been performed leading to naphthoate 35 that is differentiated for glycosidation studies.

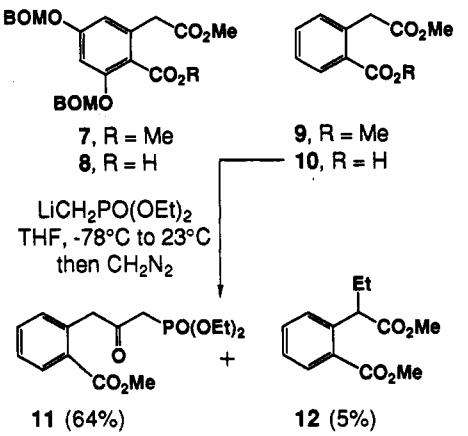


Results and Discussion

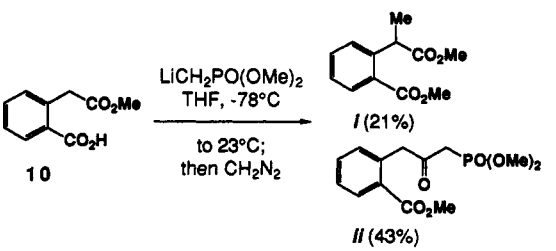
This second generation synthesis of naphthoate 3 commenced with the Diels–Alder reaction[7] of diene 4[8] and allenedicarboxylate 5[9] that provided the known homophthalate 6[10] in 73% yield. Diphenol 6 was the only observed product when the initial Diels–Alder adduct was aromatized by treatment with $Et_3NH^+F^-$ in EtOH.



Our original intention was to proceed by way of di-BOM ether 7. However, treatment of 7 (or other activated acyl derivatives) with $LiCH_2PO(OMe)_2$ under standard conditions provided only very low yields of the desired β-keto phosphonate. Similar problems were encountered in experiments using dimethyl homophthalate (9) as a model system. Competitive enolization of the acidic benzylic methylene appears to be the dominant reaction under these conditions, since quenching the reaction with D_2O led to the recovery of 9 that was partially deuterated at the benzylic position. A solution to this problem presented itself with the discovery that the unwanted enolization was suppressed to a large extent by using monoacid 10 as the substrate.[11] That enolization was still occurring, but to a much lesser extent, was evident by the isolation of 12, which presumably arises from the alkylation of the dianion of 10 with $MePO(OEt)_2$ as the alkylating agent.[12]



Unfortunately, it proved inconvenient to prepare monoacid 8, in part because the BOM group ortho to the



(4) Chromomycin binds in the DNA minor groove as a 2:1 dimer with Mg^{2+}; (a) Gao, X.; Patel, D. J. *Biochemistry* **1989**, *28*, 751. (b) Banville, D. L.; Keniry, M. A.; Kam, M.; Shafer, R. H. *Ibid.* **1990**, *29*, 6521. (c) Banville, D. L.; Keniry, M. A.; Shafer, R. H. *Ibid.* **1990**, *29*, 9294. (d) Gao, X.; Patel, D. J. *Ibid.* **1990**, *29*, 10940. (d) A recent report also establishes that a 1:1:1 complex between chromonycin, Mg^{2+} and DNA occurs under certain conditions: Aich, P.; Sen, R.; Dasgupta, D. *Biochemistry* **1992**, *31*, 2988.

(5) (a) Roush, W. R.; Michaelides, M. R.; Tai, D. F.; Lesur, B. M.; Chong, W. K. M.; Harris, D. J. *J. Am. Chem. Soc.* **1989**, *111*, 2984. (b) Roush, W. R.; Lin, X.-F.; Straub, J. A. *J. Org. Chem.* **1991**, *56*, 1649. (c) Roush, W. R.; Lin, X. *Ibid.* **1991**, *56*, 5740. (d) Sebesta, D. P.; Roush, W. R. *Ibid.* **1992**, *57*, 4799.

(6) For the synthesis of naphthoates from isocoumarins and a summary of methods for isocoumarin synthesis, see: (a) Hauser, F. M.; Pogany, S. A. *J. Heterocycl. Chem.* **1978**, 1535. (b) Hauser, F. M.; Baghdanov, V. M. *J. Org. Chem.* **1988**, *53*, 4676.

(7) (a) Banville, J.; Brassard, P. *J. Chem. Soc., Perkin Trans. I* **1976**, 1852. (b) Danishefsky, S.; Singh, R. K.; Gammill, R. B., *J. Org. Chem.* **1978**, *43*, 379.

(8) Yamamoto, K.; Suzuki, S.; Tsuji, J. *Chem. Lett.* **1978**, 649.

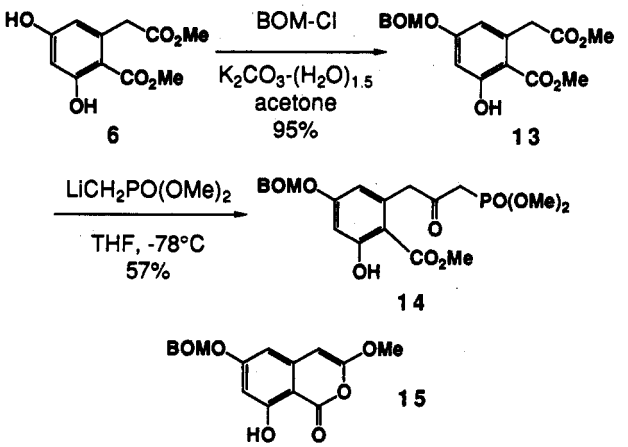
(9) Bryson, T. A.; Dolak, T. M. *Org. Synth.* **1977**, *57*, 62.

(10) Singh, S.; Singh, I. *Indian J. Chem.* **1985**, *24B*, 568.

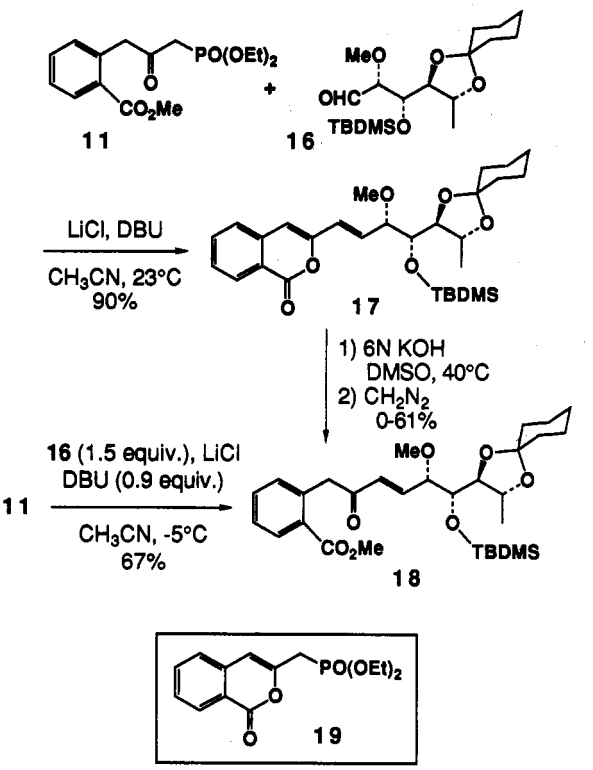
(11) This strategy has been applied to the synthesis of β-keto sulfones from 9: Watanabe, M.; Date, M.; Furukawa, S. *Chem. Pharm. Bull.* **1989**, *37*, 292.

(12) The reaction of 10 and $LiCH_2PO(OMe)_2$ similarly provided the alkylation product i in 21% yield in addition to β-keto phosphonate ii (43%).

carboxylic acid was very labile. As an alternative, we considered the possibility that the benzylic methylene of phenolic diester 13 would also be rendered less acidic than that of 7 owing to phenolate anion formation during the condensation with $LiCH_2PO(OMe)_2$. Thus, treatment of homophthalate 6 with 1 equiv of BOMCl and excess potassium carbonate sesquihydrate in acetone gave phenolic diester 13 in 95% yield.[13] This intermediate indeed proved suitable for conversion to β-keto phosphonate 14 (57%), although considerable diester was also recovered (38%). Quenching this reaction at −78 °C was essential to recover unreacted 13 intact; if the reaction mixture was warmed to 23 °C before workup, a compound believed to be isocoumarin 15 was also isolated.



The Horner–Wadsworth–Emmons (HWE) coupling of model β-keto phosphonate 11 and aldehyde 16[5a] was performed initially by using LiCl/DBU in CH_3CN at 23 °C.[14] Under these conditions, isocoumarin 17 was obtained in 90% yield. Because the subsequent cuprate addition reaction that sets the critical C(3) stereochemistry (olivin numbering) requires an unsaturated ketone, attempts were made to hydrolyze 17. However, forcing conditions (6 N KOH, DMSO, 40 °C) were necessary to achieve any hydrolysis, and nonreproducible results (0–61% yield of 18) were obtained as the intermediate enone acid readily recyclized to 17 during workup.[15] Modified HWE reaction conditions were then developed to avoid isocoumarin formation. Use of the less basic diisopropylethylamine in place of DBU slowed the reaction and provided mixtures of isocoumarin phosphonate 19[23] and isocoumarin 17. Ultimately, we found that performing the HWE reaction at −5 °C with 1.5 equiv of 16 and 0.9 equiv of DBU effectively suppressed cyclization to the isocoumarin and gave a 67% yield of model enone 18.

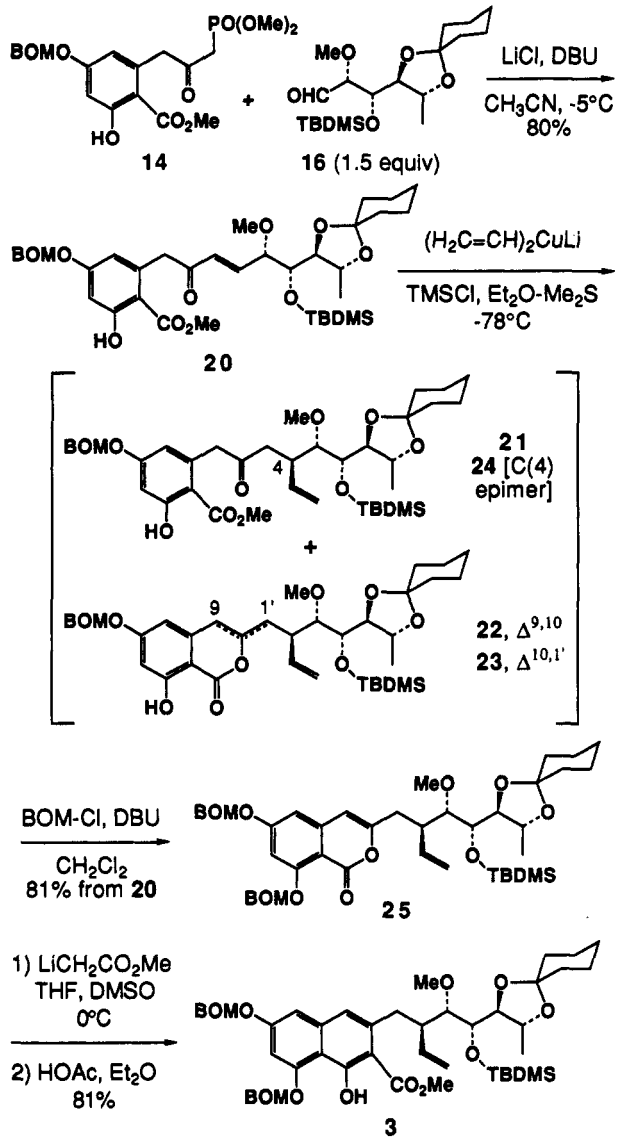


With an initial set of workable HWE reaction conditions in hand, we proceeded with the key coupling of phenolic β-keto phosphonate 14 and aldehyde 16. Attempts to protect 14 as a di-BOM ether prior to the HWE reaction were thwarted by the ease of the cyclization to an isocoumarin analogous to 19. Consequently, 14 was used directly in the HWE reaction without protection of the phenol. Treatment of 14 with excess LiCl, 1.5 equiv of 16, and 1.9 equiv of DBU (the extra equivalent of DBU was added owing to the acidity of the phenol) in CH_3CN at −5 °C provided enone 20 in 80% yield. It should be noted that 20 readily cyclized to an isocoumarin if the reaction mixture was allowed to warm above −5 °C before workup or if 20 was allowed to remain in contact with silica gel for an extended period.

Isocoumarin formation was also a serious complication during attempts to protect the phenolic unit of 20 as a BOM ether prior to the next step. Fortunately, enone 20 proved to be an excellent substrate for the diastereoselective divinylcuprate addition reaction developed in our original olivin synthesis.[5a] Indeed, treatment of 20 with excess $(H_2C{=}CH)_2CuLi$ and TMSCl in 1:1 Et_2O–Me_2S at −78 °C provided a mixture of ketone 21, isocoumarin 22, one isomer of dihydroisocoumarin 23, and a small amount (≤5%) of a compound believed to be 24, the C(4) epimer of 21.[16] Treatment of this unseparated mixture with BOMCl and DBU in CH_2Cl_2 then provided isocoumarin 25 in 81% overall yield from 20. Finally, condensation of 25 with a large excess of the lithium enolate of methyl acetate (generated with LICA at −78 °C) in THF–DMSO at 0 °C followed by aromatization of the crude product by treatment with acetic acid in Et_2O (48 h, 23 °C) provided 3 in 81% yield.[6] Naphthoate 3 so prepared was identical in all respects to samples prepared by the original phthalide coupling sequence.[5a]

This sequence, which is both shorter and more efficient than the original synthesis,[5a] is also ideally suited for preparation of intermediates differentiated for use in

(13) For the selective protection of the p-OH of homophthalates, see: Hurd, R. N.; Shah, D. H. *J. Org. Chem.* **1973**, *38*, 607 (ref 9 therein).
(14) Blanchette, M. A.; Choy, W.; Davis, J. T.; Essenfeld, A. P.; Masamune, S.; Roush, W. R.; Sakai, T. *Tetrahedron Lett.* **1984**, *25*, 2183.
(15) This problem was also observed in a recent total synthesis of monocillin I: Lampilas, M.; Lett, R. *Tetrahedron Lett.* **1992**, *33*, 777.
(16) The reaction of 20 and divinylcuprate did not go to completion unless TMSCl was added. Because divinylcuprate addition to model enone 18 was successful without TMSCl, we surmise that TMSCl is necessary for in situ protection of the phenol in the reaction with 20.
(17) Four, P.; Guibe, F. *Tetrahedron Lett.* **1982**, *23*, 1825.
(18) Still, W. C.; Kahn, M.; Mitka, A. *J. Org. Chem.* **1978**, *43*, 2923.
(19) Hung, S.; Wehner, G. *Synthesis* **1975**, 180.
(20) Spangler, R. J.; Kim, J. H.; Cava, M. P. *J. Org. Chem.* **1977**, *42*, 1697.
(21) Aldehyde 16 was prepared in 85–90% yield from structure 39 of ref 5a ((i) OsO_4, NMO; (ii) $NaIO_4$, THF, H_2O). Aldehyde 16 may also be prepared by ozonolysis of 39 as described in ref 5a.
(22) Vinyllithium was purchased from Organometallics.
(23) ^1H NMR data for 19 (300 MHz, $CDCl_3$): δ 8.25 (d, J = 8.0 Hz, 1 H), 7.69 (t, J = 8.0 Hz, 1 H), 7.50 (t, J = 8.0 Hz, 1 H), 7.39 (d, J = 8.0 Hz, 1 H), 6.52 (d, J_{P-H} = 4.5 Hz, 1 H), 4.18 (q, J = 7.6 Hz, 4 H), 3.11 (d, J_{P-H} = 22 Hz, 2 H), 1.34 (t, J = 7.6 Hz, 1 H).



glycosidation studies. For example, as shown in Scheme I, the monoallyl ether **26** was easily prepared by treatment of homophthalate **6** with allyl bromide and excess potassium carbonate sesquihydrate in acetone (85% yield). Conversion of **26** to enone **28** via phosphonate **27** was successful on modest scales (up to 2 mmol of **27**) using the conditions described for the HWE coupling of **14** and **16** (1.5 equiv of **16**, 1.9 equiv of DBU, −5 °C, 4 h), but on a slightly larger scale (4 mmol of **27**) isocoumarin formation again became significantly problematic. Reliable conditions (ca. 5-mmol scale) were eventually developed by using aldehyde **16** as the limiting reagent. Thus, addition of 1.8 equiv of DBU to a −40 °C solution of **16**, excess LiCl, and 1.5 equiv of **27** in CH_3CN and allowing this reaction to proceed for 24 h at −10 °C provided enone **28** in 71% yield along with 6% of isocoumarin **29**. It should be noted that these conditions have not been applied to the HWE coupling of **14** and **16** but presumably will be called for if this reaction is to be scaled up further. The reaction of **28** and divinylcuprate provided a mixture of ketone **30** and one isomer of dihydroisocoumarin **31** which was treated with DBU and BOMCl to give isocoumarin **32** in 84% from **28**. Differentially protected naphthoate **33** was prepared by condensation of **32** and methyl acetate followed by aromatization. Finally, protection of **33** as the di-BOM ether **34** followed by Pd(0)-catalyzed deprotection[17] of the phenolic allyl ether gave phenol **35** (92% from **33**).

In summary, an improved synthesis of olivin synthetic intermediate **3** and an efficient synthesis of monophenol **35**, which is suitably functionalized for initial glycosylation studies, have been accomplished. Additional progress toward the completion of a total synthesis of olivomycin A will be reported in due course.

Experimental Section

General. *All reactions were conducted in oven-dried* (125 °C) or flame-dried glassware under atmospheres of dry argon or nitrogen. All solvents were purified before use. Ether, THF, and toluene were distilled from sodium benzophenone ketyl. Methylene chloride was distilled from CaH_2.

^1H and ^{13}C NMR spectra were measured on commercially available instruments (300 and 400 MHz for ^1H; 100.6 or 75.4 MHz for ^{13}C). Residual chloroform (δ 7.26 ppm) was used as internal reference for spectra measured in $CDCl_3$. Low and high resolution mass spectra were measured at 70 eV.

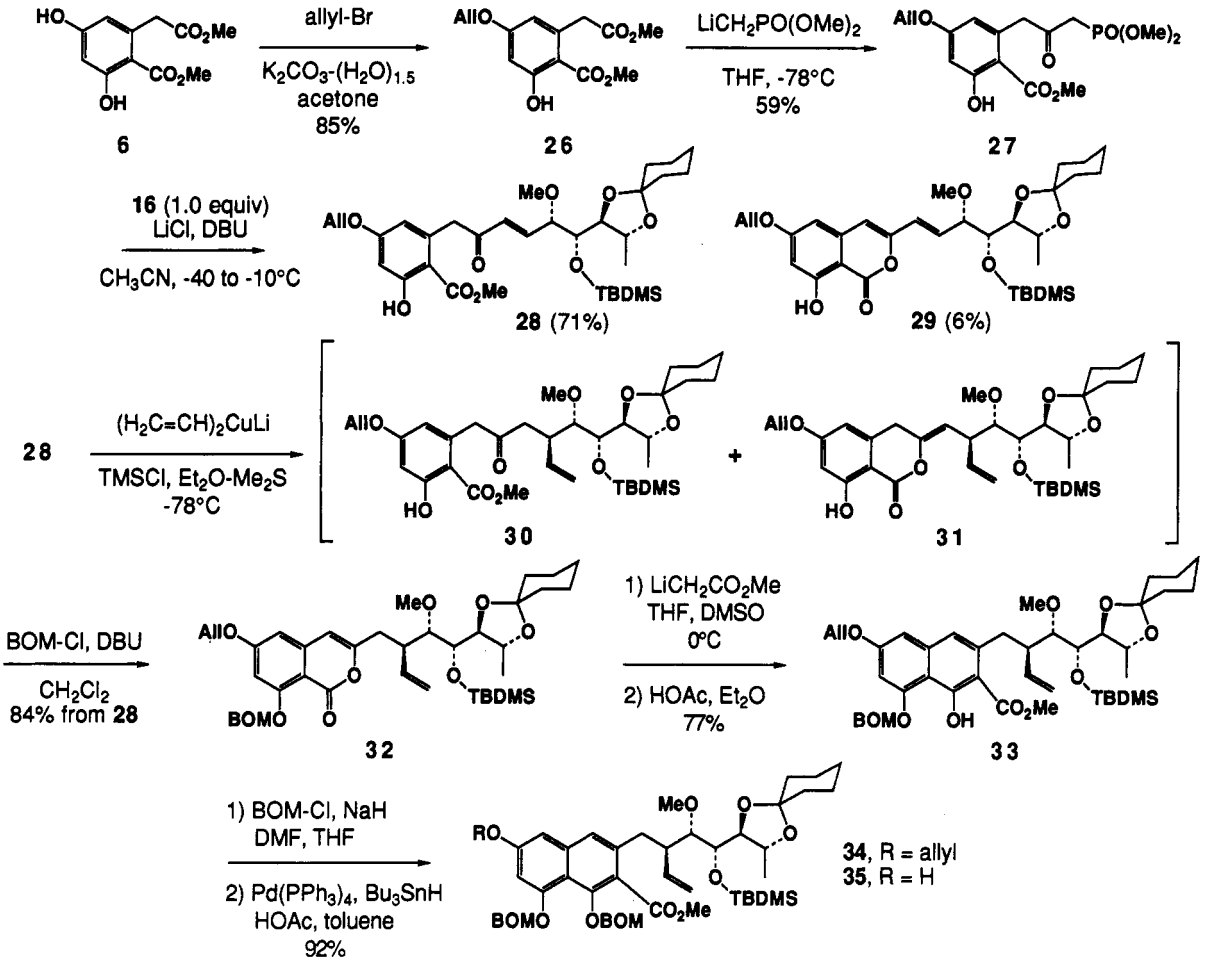
Analytical thin-layer chromatography (TLC) was performed by using 2.5-cm × 10-cm plates coated with a 0.25-mm thickness of silica gel containing PF-254 indicator (Analtech). Preparative thin-layer chromatography was performed by using 20-cm × 20-cm plates coated with a 0.25- or 0.5-mm thickness of silica gel containing PF-254 indicator (Analtech). Flash chromatography was performed as described by Still[18] using silica gel 60 (230–400 mesh). Unless otherwise noted, all compounds purified by chromatography are sufficiently pure (by ^1H NMR analysis) for use in subsequent reactions.

Methyl [3,5-Dihydroxy-2-(methoxycarbonyl)phenyl]acetate (6). Neat diene **4**[8] (34.5 mL, 133 mmol) was added to neat allene **5**[9] (16.0 g, 102 mmol) at 5 °C under nitrogen and the reaction mixture stirred at 23 °C for 20 min. The now red solution was treated with triethylammonium fluoride[19] (25 g, 200 mmol) in 95% ethanol (200 mL) at 23 °C for 10 min. The orange solution was then cooled in an ice bath and diluted with water (200 mL). The mixture was filtered, and the yellow solid was washed with ether and air-dried, giving 13.4 g of crude **6**. The filtrate was extracted with CH_2Cl_2 (3 × 100 mL), and the organic extracts were dried ($MgSO_4$) and concentrated to an orange solid that was purified by flash chromatography (silica gel, 2:1 hexane–EtOAc) to give an additional 6.7 g of **6**. The combined samples of **6** (20.1 g) were recrystallized from acetone to yield 18.0 g (73%) of the known diphenol as white crystals: mp 143.5–144.5 °C (lit.[10] mp 143.5–144.5 °C); R_f 0.53 (1:1 hexane–EtOAc); ^1H NMR (300 MHz) δ 6.32 (d, J = 1.5 Hz, 1 H), 6.20 (d, J = 1.5 Hz, 1 H), 3.85 (s, 3 H), 3.82 (s, 2 H), 3.72 (s, 3 H); IR ($CHCl_3$) 3600, 3500–3100 (br), 1750, 1680, 1645 cm^{-1}.

Methyl [5-[(Benzyloxy)methoxy]-3-hydroxy-2-(methoxycarbonyl)phenyl]acetate (13). A mixture of diphenol **6** (6.4 g, 27 mmol), $K_2CO_3 \cdot H_2O_{1.5}$ (17.7 g, 107 mmol), and BOMCl (3.7 mL, 27 mmol) in acetone (200 mL) was stirred at 30 °C for 2 h. The reaction mixture was cooled to 23 °C, acidified with 1 N HCl, extracted with ether (3×), dried ($MgSO_4$), and concentrated to give 9.8 g of a white solid. Recrystallization of this material from 10:1 hexane–EtOAc (2×) gave 9.1 g (95%) of **13** as fluffy white needles: mp 70–71 °C; R_f 0.64 (3:1 hexane–ethyl acetate); ^1H NMR (400 MHz) δ 11.55 (s, 1 H), 7.3–7.4 (m, 5 H), 6.66 (d, J = 2.6 Hz, 1 H), 6.43 (d, J = 2.6 Hz, 1 H), 5.29 (s, 2 H), 4.71 (s, 2 H), 3.87 (s, 3 H), 3.84 (s, 2 H), 3.69 (s, 3 H); ^{13}C NMR (100.6 MHz) δ 170.6, 169.8, 164.2, 160.6, 137.1, 135.8, 127.4, 127.0, 126.9, 112.3, 105.1, 102.1, 90.8, 69.3, 50.8, 50.7, 41.7; IR ($CHCl_3$) 3680, 1740, 1660, 1620, 1580 cm^{-1}; HRMS, calcd for $C_{19}H_{20}O_7$ 360.1209, found 360.1231. Anal. Calcd for $C_{19}H_{20}O_7$: C, 63.32; H, 5.59. Found: C, 63.29; H, 5.53.

Dimethyl [3-[5′-[(Benzyloxy)methoxy]-2′-(methoxycarbonyl)-3′-hydroxyphenyl]-2-oxopropyl]phosphonate (14). To a solution of *n*-BuLi (3.9 mL of a 2.5 M solution in hexane, 9.7 mmol) in THF (12 mL) at −78 °C under N_2 was added dimethyl methylphosphonate (1.4 mL, 12.4 mmol) dropwise. After being stirred for 10 min at −78 °C, the white mixture was treated with a solution of dimethyl homophthalate **13** (1.0 g, 2.8 mmol) in THF (4 mL), added by cannula. The now yellow reaction mixture was stirred at −78 °C for 3 h, and the reaction was quenched at −78 °C with saturated aqueous NH_4Cl, and the mixture was extracted with Et_2O (3×). The combined organic

Scheme I



extracts were dried ($MgSO_4$) and concentrated to 1.2 g of a yellow syrup. Purification of this material by flash chromatography (silica gel, 1:1 hexane–EtOAc, then 100% EtOAc) gave two fractions: 0.38 g (38%) of recovered **13** and 0.72 g (57%) of β-keto phosphonate **14** as a colorless solid: mp 41–42 °C; R_f 0.26 (EtOAc); ^{1}H NMR (300 MHz) δ 11.44 (s, 1 H), 7.4–7.3 (m, 5 H), 6.66 (d, J = 2.6 Hz, 1 H), 6.40 (d, J = 2.6 Hz, 1 H), 5.28 (s, 2 H), 4.69 (s, 2 H), 4.11 (s, 2 H), 3.86 (s, 3 H), 3.79 (d, J = 11 Hz, 6 H), 3.13 (d, J = 22 Hz, 1 H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 39.5, 40.8, 51.9 (d, J = 27 Hz), 52.9 (d, J = 24 Hz), 70.3, 91.7, 103.1, 106.1, 113.3, 127.8, 128.3, 136.6, 137.7, 161.6, 165.0, 170.4, 198.3 (d, J = 21 Hz); IR ($CHCl_3$) 3420 (br), 1720, 1660, 1640, 1580 cm^{-1}; MS (EI) m/e 452 (M^+), 420, 404, 91. Anal. Calcd for $C_{21}H_{25}O_9P$ + 0.5 mol H_2O: C, 54.66; H, 5.68. Found: C, 54.93; H, 5.71.

If the reaction mixture was warmed to 23 °C before workup, a compound believed to be isocoumarin **15** was also isolated [^{1}H NMR (300 MHz, $CDCl_3$) δ 10.67 (s, 1 H), 7.3–7.4 (m, 5 H), 6.50 (d, J = 2.6 Hz, 1 H), 6.48 (d, J = 2.6 Hz, 1 H), 5.50 (s, 1 H), 5.35 (s, 2 H), 4.72 (s, 2 H), 3.89 (s, 3 H)]. This assignment is consistent with literature NMR data for 3-methoxyisocoumarin.[20]

Methyl 4-[(Benzyloxy)methoxy]-6-[(5′*S*,6′*R*,7′*S*,8′*R*)-6′-[(*tert*-butyldimethylsilyl)oxy]-7′,8′-(cyclohexylidenedioxy)-5′-methoxy-2′-oxonon-3′(*E*)-enyl]-2-hydroxybenzoate (20). A mixture of β-keto phosphonate **14** (20 mg, 0.044 mmol) and LiCl (72 mg, 1.7 mmol) in CH_3CN (0.2 mL) was stirred at 23 °C under N_2 for 30 min and then cooled to −5 °C. A solution of aldehyde **16**[5a,21] (24 mg, 0.066 mmol) in CH_3CN (0.4 mL) was added by cannula and the mixture then treated with DBU (12 μL, 0.084 mmol). After being stirred for 2 h at −5 °C, the mixture was diluted with saturated aqueous NH_4Cl and extracted with Et_2O (3×). The organic extracts were dried (Na_2SO_4) and concentrated to a yellow syrup. Purification of the crude product by flash chromatography (silica gel, 10:1 hexane–Et_2O) gave 25 mg (80%) of enone **20** as a colorless syrup: R_f 0.37 (6:1 hexane–EtOAc); $[\alpha]^{26}_D$ +6.8° (c = 1.5, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 0.10 (s, 6 H), 0.90 (s, 9 H), 1.31 (d, J = 5.6 Hz, 1 H), 1.3–1.5 (m, 2 H), 1.5–1.6 (m, 8 H), 3.33 (s, 3 H), 3.61 (dd, J = 6.4, 7.6 Hz, 1 H), 3.78 (m, 4 H), 3.82 (dd, J = 5.6, 11.2 Hz, 1 H), 4.12 (m, 3 H), 4.70 (s, 2 H), 5.29 (s, 2 H), 6.36 (dd, J = 0.8, 16.8 Hz, 1 H), 6.38 (d, J = 2.4 Hz, 1 H), 6.66 (d, J = 2.4 Hz, 1 H), 6.84 (dd, J = 6.0, 16.0 Hz, 1 H), 7.3–7.4 (m, 5 H), 11.54 (s, 1 H); ^{13}C NMR (100.6 MHz) δ −4.3, −4.2, 18.1, 20.0, 23.7, 25.0, 25.8, 36.5, 36.6, 49.1, 51.7, 57.3, 70.1, 73.8, 75.6, 81.5, 83.5, 91.6, 102.7, 106.1, 108.6, 113.2, 127.7, 127.8, 128.2, 129.8, 136.6, 138.6, 142.8, 161.5, 165.1, 170.5, 195.7; IR ($CHCl_3$) 3620 (sharp), 3300–3600 (br), 1660, 1620, 1580 cm^{-1}; HRMS, calcd for $C_{34}H_{45}O_{10}Si$ ($M^+ - C_4H_9$) 641.2471, found 641.2636. Anal. Calcd for $C_{38}H_{54}O_{10}Si$: C, 62.10; H, 7.95. Found: C, 61.91; H, 7.60.

Methyl 4-[(Benzyloxy)methoxy]-6-[(4′*R*,5′*S*,6′*R*,7′*S*,-8′*R*)-6′-[(*tert*-butyldimethylsilyl)oxy]-7′,8′-(cyclohexylidenedioxy)-5′-methoxy-2′-oxo-4′-vinylnonyl]-6-hydroxybenzoate (21), Isocoumarin 22, and Dihydroisocoumarin 23. A −78 °C mixture of CuBr–DMS (0.27 g, 1.3 mmol) and Me_2S (2.4 mL) in ether (2.4 mL) under N_2 was treated dropwise with vinyllithium[22] (1.2 mL of a 2.0 M solution in THF, 2.4 mmol). After being stirred for 1 h at −78 °C, the yellow-green solution was treated with TMSCl (0.044 mL, 0.35 mmol) followed by dropwise addition of enone **20** (110 mg, 0.16 mmol) in ether (4 mL). The mixture was stirred at −78 °C for 20 min and then poured into a cold mixture of ether and saturated aqueous NH_4Cl. Aqueous NH_4OH was added to the black mixture which was stirred until the aqueous phase was dark blue and the organic phase was colorless and homogeneous (about 2 h). The layers were separated and the aqueous phase was extracted with ether (2×). The combined organic extracts were washed with saturated aqueous NaCl, dried ($MgSO_4$), and concentrated to a yellow syrup (159 mg) which was used directly in the next reaction. The product mixture from a separate experiment was purified by flash chromatography (silica gel, 9:1 hexane–EtOAc) to give ketone **21** as a colorless syrup (46%) and the other products as an inseparable mixture (R_f 0.36). Further fractionation of the latter mixture by preparative TLC (silica gel, 1% acetone/CH_2Cl_2) provided samples

of isocoumarin **22** (R_f 0.83), and a 3:1 mixture of two compounds tentatively identified as one isomer of dihydroisocoumarin **23** and a compound (**24**) thought to be the C(3) epimer of **21**. The latter mixture was not characterized further.

Data for ketone **21**: R_f 0.22 (9:1 hexane–EtOAc); $[\alpha]^{28}_D$ –5.6° (c = 2.5, CH_2Cl_2); ^1H NMR (400 MHz) δ 0.09 (s, 3 H), 0.12 (s, 3 H), 0.90 (s, 9 H), 1.34 (d, J = 6.8 Hz, 1 H), 1.3–1.4 (m, 2 H), 1.5–1.65 (m, 8 H), 2.61 (dd, J = 9.6, 17.2 Hz, 1 H), 2.75 (dd, J = 4.0, 17.2 Hz, 1 H), 3.06 (m, 1 H), 3.21 (dd, J = 4.0, 6.8 Hz, 1 H), 3.42 (s, 3 H), 3.66 (dd, J = J = 6.8 Hz, 1 H), 3.80 (dd, J = 4.8, 6.8 Hz, 1 H), 3.82 (s, 3 H), 3.91 and 3.95 (AB, J = 17.2 Hz, 2 H), 4.11 (dq, J = J = 6.8 Hz, 1 H), 4.50 (s, 2 H), 5.05 (dd, J = 1.6, 10.4 Hz, 1 H), 5.10 (apparent d, J = 17.2 Hz, 1 H), 5.28 (s, 2 H), 5.75 (ddd, J = 8.4, 10.4, 17.2 Hz, 1 H), 6.34 (d, J = 2.6 Hz, 1 H), 7.3–7.4 (m, 5 H), 11.53 (s, 1 H); ^{13}C NMR (100.6 MHz) δ –3.8, –3.6, 18.2, 20.6, 23.9, 25.1, 26.1, 36.9, 37.1, 40.5, 43.2, 51.4, 51.9, 60.3, 70.3, 73.8, 74.7, 82.2, 84.1, 91.7, 102.8, 106.2, 108.9, 113.3, 116.2, 127.8, 127.9, 128.4, 136.8, 138.8, 139.5, 161.6, 165.2, 170.8, 205.4; IR ($CHCl_3$) 3680, 3300–3500 (br), 1720, 1660, 1615, 1530 cm^{-1}; HRMS, calcd for $C_{40}H_{58}O_{10}Si$ 726.3799, found 726.3840. Anal. Calcd for $C_{40}H_{58}O_{10}Si$: C, 66.06; H, 8.04. Found: C, 65.92; H, 7.81.

Partial data for isocoumarin **22**: R_f 0.83 (1% acetone/CH_2Cl_2); ^1H NMR (400 MHz) δ 11.09 (s, 1 H), 7.3–7.4 (m, 5 H), 6.61 (d, J = 2.4 Hz, 1 H), 6.47 (d, J = 2.4 Hz, 1 H), 6.17 (s, 1 H), 5.73 (ddd, J = 9.2, 11.6, 16.0 Hz, 1 H), 5.33 (s, 2 H), 5.03 (dd, J = 1.2, 11.6 Hz, 1 H), 5.02 (dd, J = 1.2, 16.0 Hz, 1 H), 4.71 (s, 2 H), 4.14 (dq, J = J = 6.4 Hz, 1 H), 3.85 (dd, J = 5.6, 6.4 Hz, 1 H), 3.70 (dd, J = J = 6.8 Hz, 1 H), 3.48 (s, 3 H), 3.21 (dd, J = J = 5.6 Hz, 1 H), 2.9–3.0 (m, 2 H), 2.49 (dd, J = 11.2, 15.2 Hz, 1 H), 1.5–1.6 (m, 8 H), 1.3–1.5 (m, 2 H), 1.35 (d, J = 6.4 Hz, 3 H), 0.92 (s, 9 H), 0.13 (s, 3 H), 0.10 (s, 3 H).

6,8-Bis[(benzyloxy)methoxy]-3-[(2′*R*,3′*S*,4′*R*,5′*S*,6′*R*)-4′-[(*tert*-butyldimethylsilyl)oxy]-5′,6′-(cyclohexylidenedioxy)-5′-methoxy-2′-vinylheptyl]benzopyran-1-one (25). A solution of the crude mixture of **21**, **22**, **23**, and **24** prepared in the previous experiment (159 mg) in CH_2Cl_2 (1.6 mL) at 23 °C under N_2 was treated with DBU (0.22 mL, 1.6 mmol) and then BOMCl (0.24 mL, 1.6 mmol). After being stirred for 1 h at 23 °C, the mixture was diluted with saturated aqueous NH_4Cl, extracted with CH_2Cl_2 (3×), filtered through a cotton plug, and concentrated to a yellow syrup (190 mg). Purification of the crude product by flash chromatography (silica gel, 8:1 hexane–EtOAc gradient to 3:1 hexane–EtOAc) gave 104 mg (81% from **20**) of isocoumarin **25** as a white solid. Recrystallization of this material from hexane gave short white needles: mp 77–78.5 °C; R_f 0.29 (5:1 hexane–ethyl acetate); $[\alpha]^{28}_D$ –2.6° (c = 1.0, CH_2Cl_2); ^1H NMR (400 MHz) δ 0.11 (s, 3 H), 0.14 (s, 3 H), 0.92 (s, 9 H), 1.3–1.5 (m, 2 H), 1.36 (d, J = 6.8 Hz, 3 H), 1.5–1.7 (m, 8 H), 2.47 (dd, J = 15.6, 11.6 Hz, 1 H), 2.84–2.88 (m, 2 H), 3.21 (dd, J = J = 5.6 Hz, 1 H), 3.48 (s, 3 H), 3.72 (dd, J = 6.8, 11.6 Hz, 1 H), 3.86 (dd, J = 5.6, 11.6 Hz, 1 H), 4.14 (dq, J = J = 6.8 Hz, 1 H), 4.71 (s, 2 H), 4.81 (s, 2 H), 5.02 (dd, J = 1.4, 10.0 Hz, 1 H), 5.03 (apparent d, J = 17.2 Hz, 1 H), 5.33 (s, 2 H), 5.45 (s, 2 H), 5.75 (ddd, J = 8.8, 10.0, 17.2 Hz, 1 H), 6.08 (s, 1 H), 6.61 (d, J = 2.0 Hz, 1 H), 6.90 (d, J = 2.0 Hz, 1 H), 7.3–7.4 (m, 10 H); ^{13}C NMR (100.6 MHz) δ –3.7, –3.6, 18.3, 20.6, 23.9, 25.2, 26.2, 33.5, 36.9, 37.0, 43.6, 60.9, 70.4, 73.8, 74.3, 82.3, 85.1, 91.9, 92.9, 103.5, 103.7, 104.4, 109.0, 116.7, 127.8, 128.0, 128.3, 128.5, 136.7, 137.0, 138.9, 141.8, 157.5, 158.9, 160.7, 162.6; IR ($CHCl_3$) 1725, 1665, 1605, 1570 cm^{-1}; HRMS, calcd for $C_{46}H_{59}O_9Si$ 783.3930, found 783.3899. Anal. Calcd for $C_{47}H_{62}O_{10}Si$: C, 69.26; H, 7.67. Found: C, 69.27; H, 7.62.

Methyl 6,8-Bis[(benzyloxy)methoxy]-1-hydroxy-3-[(2′*R*,3′*S*,4′*R*,5′*S*,6′*R*)-3′-methoxy-5′,6′-(cyclohexylidenedioxy)-4′-[(*tert*-butyldimethylsilyl)oxy]-2′-vinylheptyl]naphthoate (3). A solution of isopropylcyclohexylamine (0.44 mL, 2.7 mmol) in THF (6 mL) at 0 °C under N_2 was treated with n-BuLi (1.1 mL of a 2.5 M solution in hexanes, 2.7 mmol) for 20 min at 0 °C and 5 min at 23 °C and cooled to –78 °C. Methyl acetate (0.21 mL, 2.7 mmol) was added and then 30 min later the solution of methyl lithioacetate was transferred rapidly by cannula to a solution of isocoumarin **25** (88 mg, 0.11 mmol) in DMSO (3 mL) and THF (3 mL) at 0 °C under N_2. The solution immediately turned yellow. Ten minutes later the mixture was treated with AcOH (5 mL) and stirred at 23 °C for 48 h. The yellow mixture was concentrated in vacuo, diluted with ether, washed with H_2O and saturated aqueous NaCl, dried ($MgSO_4$), and concentrated to a yellow liquid. Purification of the crude product by flash chromatography (10:1 hexane–EtOAc) gave 76 mg (81%) of naphthoate **3** as a colorless oil. Naphthoate **3** so prepared was identical in all respects to samples prepared by the original phthalide coupling sequence.[5a]

Methyl [5-(Allyloxy)-3-hydroxy-2-(methoxycarbonyl)-phenyl]acetate (26). A mixture of diphenol **6** (19.4 g, 81 mmol), $K_2CO_3 \cdot H_2O_{1.5}$ (53 g, 320 mmol), and allyl bromide (7.0 mL, 81 mmol) in acetone (575 mL) was heated at reflux for 6 h. The cooled reaction mixture was acidified with 1 N HCl, and the precipitate was collected by filtration and air-dried to give 23.1 g of crude **26**. This material was crystallized from hexane to yield fluffy white needles, 19.0 g (83%). The filtrate from the reaction mixture was extracted with ether (3×). The combined extracts were dried ($MgSO_4$), combined with the mother liquor from the recrystallization, and concentrated to a white solid. Purification of this material by flash chromatography (silica gel, 10:1 hexane–ether, then 3:1 hexane–EtOAc) gave 1.6 g (6%) of the diallyl ether, R_f 0.09 (10:1 hexane–EtOAc), an additional 0.5 g (2%) of **26**, and 1.2 g (6%) of recovered **6**. The total yield of **26** was 19.5 g (85%): R_f 0.17 (10:1 hexane–EtOAc); mp 83 °C; ^1H NMR (400 MHz) δ 10.62 (s, 1 H), 6.42 (d, J = 2.4 Hz, 1 H), 6.32 (d, J = 2.4 Hz, 1 H), 6.02 (ddt, J = 16.8, 10.4, 5.2 Hz, 1 H), 5.41 (ddt, J = 16.8, 1.6, 1.6 Hz, 1 H), 5.31 (ddt, J = 10.4, 1.6, 1.6 Hz, 1 H), 4.54 (ddd, J = 5.2, 1.6, 1.6 Hz, 1 H), 3.86 (s, 3 H), 3.82 (s, 2 H), 3.69 (s, 3 H); ^{13}C NMR (100.6 MHz) δ 171.6, 170.9, 165.6, 163.1, 138.1, 132.4, 118.0, 113.2, 105.2, 101.0, 68.8, 51.7, 51.6, 42.6; IR ($CHCl_3$) 3500–3200 (br), 1730, 1660, 1620, 1575 cm^{-1}; HRMS, calcd for $C_{14}H_{16}O_6$ 280.0947, found 280.0966. Anal. Calcd for $C_{14}H_{16}O_6$: C, 59.99; H, 5.76. Found: C, 59.82; H, 5.63.

Dimethyl [3-[5′-(Allyloxy)-2′-carbomethoxy-3′-hydroxyphenyl]-2-oxopropyl]phosphonate (27). To a solution of n-BuLi (50 mL of a 2.5 M solution in hexane, 126 mmol) in THF (150 mL) at –78 °C under N_2 was added dimethyl methylphosphonate (17.4 mL, 162 mmol) dropwise. After being stirred for 10 min at –78 °C, the white mixture was treated with a solution of **26** (10.0 g, 36 mmol) in THF (30 mL), added by cannula. After the yellow mixture was stirred at –78 °C for 3 h, the reaction was quenched at –78 °C with saturated aqueous NH_4Cl, and the mixture was extracted with Et_2O (3×). The combined organic extracts were dried ($MgSO_4$) and concentrated to a yellow syrup (16.2 g). Purification of the crude product by flash chromatography (short column of silica gel, 1:1 hexane–EtOAc then neat EtOAc) gave 2.9 g (28%) of recovered **26** and 7.9 g (59%) of β-keto phosphonate **27** as a yellow solid (after being concentrated for 48 h under high vacuum): R_f 0.23 (EtOAc); mp 57–58.5 °C; ^1H NMR (400 MHz) δ 10.55 (s, 1 H), 6.42 (d, J = 2.4 Hz, 1 H), 6.31 (d, J = 2.4 Hz, 1 H), 6.00 (ddt, J = 17.2, 10.4, 5.6 Hz, 1 H), 5.40 (ddt, J = 17.2, 1.4, 1.4 Hz, 1 H), 5.30 (ddt, J = 10.4, 1.4, 1.4 Hz, 1 H), 4.53 (ddd, J = 5.6, 1.4, 1.4 Hz, 2 H), 4.09 (s, 2 H), 3.85 (s, 3 H), 3.81 (s, 3 H), 3.78 (s, 3 H), 3.12 (d, J = 22 Hz, 1 H); ^{13}C NMR (100.6 MHz) δ 198.3 (d, J = 24 Hz), 170.5, 165.4, 163.2, 137.8, 132.2, 118.0, 113.2, 105.3, 101.2, 68.8, 52.9 (d, J = 27 Hz), 51.9 (d, J = 91 Hz), 40.8, 39.6; IR ($CHCl_3$) 3420 (br), 1720, 1660, 1620, 1580; HRMS, calcd for $C_{16}H_{21}O_8P$ 372.0974, found 372.0984. Anal. Calcd for $C_{16}H_{21}O_8P$: C, 51.61; H, 5.67. Found: C, 51.56; H, 5.60.

Methyl 4-(Allyloxy)-6-[(5′*S*,6′*R*,7′*S*,8′*R*)-6′-[(*tert*-butyldimethylsilyl)oxy]-7′,8′-(cyclohexylidenedioxy)-5′-methoxy-2′-oxonon-3′(*E*)-enyl]-2-hydroxybenzoate (28). A –40 °C solution of β-keto phosphonate **27** (2.7 g, 7.2 mmol), LiCl (8.1 g, 288 mmol), and aldehyde **16**[5a,21] (1.8 g, 4.8 mmol) in CH_3CN (19 mL; premixed at 23 °C) was treated with DBU (1.4 mL, 13.0 mmol), added dropwise over a 1-min period. The mixture was allowed to warm to –10 °C over 30 min and then was kept at this temperature for 24 h. The reaction mixture was diluted with saturated aqueous NH_4Cl and extracted with Et_2O (3×). The combined extracts were dried (Na_2SO_4) and concentrated to a yellow syrup. Purification of the crude product by flash chromatography (silica gel, 10:1 hexane–Et_2O) gave 2.09 g (71%) of enone **28** as a white solid, 177 mg (6%) of isocoumarin **29** as a white solid, 260 mg (14%) of recovered aldehyde **16**, and 1.46 g (43%) of recovered phosphonate **27**.

Data for enone **28**: R_f 0.17 (5:1 hexane–Et_2O); mp 52.5–55 °C; $[\alpha]^{23}_D$ +12.6° (c = 2.0, CH_2Cl_2); ^1H NMR (400 MHz) δ 11.63 (s, 1 H), 6.83 (dd, J = 6.0, 16.4 Hz, 1 H), 6.41 (d, J = 2.8, 1 H), 6.34 (d, J = 16.4 Hz, 1 H), 6.01 (ddt, J = 16.0, 10.4, 5.6 Hz, 1 H), 5.40

(dd, J = 16.0, 1.4 Hz, 1 H), 5.29 (dd, J = 10.4, 1.4 Hz, 1 H), 4.53 (d, J = 5.6 Hz, 2 H), 4.06 and 4.10 (AB, J = 17.2 Hz, 2 H), 4.09 (m, 1 H), 3.81 (dd, J = J = 5.6 Hz, 1 H), 3.79 (dd, J = J = 4.8 Hz, 1 H), 3.77 (s, 3 H), 3.60 (dd, J = 6.0, 7.2 Hz, 1 H), 3.32 (s, 3 H), 1.56 (m, 6 H), 1.3–1.55 (m, 2 H), 1.29 (d, J = 6.4, 3 H), 0.89 (s, 9 H), 0.08 (s, 6 H); ^{13}C NMR (100.6 MHz) δ 195.9, 170.8, 165.6, 163.1, 143.0, 138.7, 132.3, 130.0, 118.1, 113.3, 108.9, 100.9, 83.8, 81.8, 75.8, 74.0, 68.8, 57.5, 51.7, 49.3, 36.8, 26.0, 25.2, 23.9, 20.1, 18.3, –4.0, –4.1; IR ($CHCl_3$) 1660, 1620, 1580 cm^{-1}; mass spectrum m/e 618 (M^+), 587 ($M^+ - OCH_3$), 434, 407, 299, 205. Anal. Calcd for $C_{33}H_{50}O_9Si$: C, 64.05; H, 8.14. Found: C, 63.99; H, 7.87.

Partial data for isocoumarin **29**: R_f 0.32 (5:1 hexane–ether); mp 93.5–95.5 °C; ^{1}H NMR (400 MHz) δ 11.09 (s, 1 H), 6.52 (dd, J = 15.6, 6.0 Hz, 1 H), 6.49 (d, J = 2.4 Hz, 1 H), 6.39 (d, J = 2.4 Hz, 1 H), 6.29 (s, 1 H), 6.22 (dd, J = 0.8, 15.6 Hz, 1 H), 6.04 (ddt, J = 17.2, 10.8, 5.2 Hz, 1 H), 5.43 (ddt, J = 17.2, 1.4, 1.4 Hz, 1 H), 5.34 (ddt, J = 10.8, 1.4, 1.4 Hz, 1 H), 4.60 (ddd, J = 5.2, 1.4, 1.4 Hz, 1 H), 4.12 (dq, J = J = 6.0 Hz, 1 H), 3.83 (dd, J = J = 5.6 Hz, 1 H), 3.79 (dd, J = J = 5.2 Hz, 1 H), 3.67 (dd, J = 7.6, 5.6 Hz, 1 H), 3.34 (s, 3 H), 1.5–1.65 (m, 6 H), 1.35–1.45 (m, 2 H), 1.32 (d, J = 6.0 Hz, 1 H), 0.90 (s, 9 H), 0.09 (s, 6 H); IR (CH_2Cl_2) 3600–3100 (br), 3040, 1680, 1620, 1570 cm^{-1}; HRMS, calcd for $C_{32}H_{46}O_8Si$ 586.2962, found 586.2966.

Methyl 4-(Allyloxy)-6-[(4′*R*,5′*S*,6′*R*,7′*S*,8′*R*)-6′-[(*tert*-butyldimethylsilyl)oxy]-7′,8′-(cyclohexylidenedioxy)-5′-methoxy-2′-oxo-4′-vinylnonyl]-6-hydroxybenzoate (30) and Dihydroisocoumarin 31. A –78 °C solution of CuBr–DMS (2.4 g, 11.7 mmol) and Me_2S (22 mL) in ether (22 mL) under N_2 was treated with vinyllithium (10.5 mL of a 2.0 M solution in THF, 21.1 mmol). The yellow solution was stirred for 1 h at –78 °C; then TMSCl (0.39 mL, 3.1 mmol) and, separately, enone **28** (0.87 g, 1.4 mmol) in ether (36 mL) were added dropwise. The mixture was stirred at –78 °C for 20 min and then was poured into a cold mixture of ether and saturated aqueous NH_4Cl. Aqueous NH_4OH was added to the black mixture which was then stirred until the aqueous phase was dark blue and the organic phase was colorless and homogeneous (about 2 h). The layers were separated and the aqueous phase was extracted with ether (2×). The combined organic extracts were washed with saturated aqueous NaCl, dried ($MgSO_4$), and concentrated to a yellow syrup (892 mg), which was used directly in the next reaction. A sample from another run was purified by flash chromatography (silica gel, 7:1 hexane–EtOAc) for characterization purposes: ketone **30** was isolated in 58% yield as a colorless syrup and dihydroisocoumarin **31** was obtained as a colorless syrup in 20% yield.

Data for ketone **30**: R_f 0.50 (5:1 hexane–EtOAc); $[\alpha]^{23}_D$ –6.0° (c = 1.6, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 11.63 (s, 1 H), 6.41 (d, J = 2.4 Hz, 1 H), 6.24 (d, J = 2.4 Hz, 1 H), 6.01 (ddt, J = 17.2, 10.0, 5.4 Hz, 1 H), 5.75 (ddd, J = 17.2, 10.4, 8.4 Hz, 1 H), 5.40 (ddt, J = 17.2, 1.4, 1.4 Hz, 1 H), 5.30 (ddt, J = 10.0, 1.4, 1.4 Hz, 1 H), 5.09 (d, J = 17.2 Hz, 1 H), 5.04 (dd, J = 10.4, 1.6 Hz, 1 H), 4.52 (ddd, J = 5.4, 1.6, 1.6 Hz, 1 H), 4.1 (dq, J = J = 6.8 Hz, 1 H), 3.88 and 3.93 (AB, J = 17.2 Hz, 2 H), 3.81 (s, 3 H), 3.78 (dd, J = 8.4, 6.8 Hz, 1 H), 3.65 (dd, J = J = 6.8 Hz, 1 H), 3.41 (s, 3 H), 3.20 (dd, J = 6.8, 4.4 Hz, 1 H), 3.05 (m, 1 H), 2.73 (dd, J = 13.2, 17.2 Hz, 1 H), 2.58 (dd, J = 8.8, 17.2 Hz, 1 H), 1.5–1.6 (m, 6 H), 1.3–1.4 (m, 2 H), 1.33 (d, J = 6.8 Hz, 3 H), 0.90 (s, 9 H), 0.11 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR (100.6 MHz) δ 205.4, 170.9, 165.6, 163.1, 139.7, 138.9, 132.4, 118.0, 116.1, 113.3, 109.0, 100.9, 84.3, 82.5, 74.8, 74.0, 68.8, 60.3, 57.8, 51.5, 43.2, 40.7, 37.2, 26.2, 25.2, 24.0, 20.7, 18.3, –3.6; IR ($CHCl_3$) 3080 (br), 3020, 1720, 1660, 1620, 1580 cm^{-1}; HRMS, calcd for $C_{35}H_{54}O_9Si$ 646.3537, found 646.3512. Anal. Calcd for $C_{35}H_{54}O_9Si$: C, 64.98; H, 8.41. Found: C, 65.19; H, 8.57.

Partial data for dihydroisocoumarin **31**: R_f 0.58 (5:1 hexane–EtOAc); ^{1}H NMR (400 MHz) δ 10.96 (s, 1 H), 6.36 (d, J = 2.4 Hz, 1 H), 6.26 (d, J = 2.4 Hz, 1 H), 6.01 (ddt, J = 17.6, 10.4, 5.4 Hz, 1 H), 5.88 (ddd, J = 16.8, 9.8, 6.8 Hz, 1 H), 5.56 (ddd, J = 9.6, 1.2, 1.2 Hz, 1 H), 5.40 (ddt, J = 17.6, 1.6, 1.6 Hz, 1 H), 5.32 (ddt, J = 10.4, 1.6, 1.6 Hz, 1 H), 5.08 (ddd, J = 16.8, 1.2, 1.2 Hz, 1 H), 5.07 (ddd, J = 9.8, 1.2, 1.2 Hz, 1 H), 4.55 (ddd, J = 5.4, 1.2, 1.2 Hz, 1 H), 4.04 (dq, J = J = 6.6 Hz, 1 H), 3.6–3.7 (m, 3 H), 3.56 (dd, J = 7.2, 6.8 Hz, 1 H), 3.40 (s, 3 H), 3.31 (m, 1 H), 3.20 (dd, J = 6.8, 4.8 Hz, 1 H), 1.5–1.6 (m, 6 H), 1.3–1.4 (m, 2 H), 1.30 (d, J = 6.6 Hz, 3 H), 0.09 (s, 3 H), 0.03 (s, 3 H); IR ($CHCl_3$) 3160 (br), 1670, 1630, 1580 cm^{-1}.

6-(Allyloxy)-8-[(benzyloxy)methoxy]-3-[(2′*R*,3′*S*,4′*R*,5′*S*,6′*R*)-4′-[(*tert*-butyldimethylsilyl)oxy]-5′,6′-(cyclohexylidenedioxy)-5′-methoxy-2′-vinylheptyl]benzopyran-1-one (32). A solution of the crude mixture of **30** and **31** prepared above (0.89 g) in CH_2Cl_2 (14 mL) was treated with DBU (2.0 mL, 14 mmol) and then BOMCl (1.9 mL, 14 mmol) at 23 °C under N_2. After being stirred for 10 min at 23 °C, the reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted CH_2Cl_2 (3×), filtered through a cotton plug, and concentrated to a yellow syrup (1.08 g). Purification of this material by flash chromatography (silica gel, 7:1 hexane–EtOAc) gave 868 mg (84% frome enone **28**) of isocoumarin **32** as a colorless syrup: R_f 0.42 (5:1 hexane–EtOAc); $[\alpha]^{23}_D$ –4.9° (c = 1.5, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 7.3–7.45 (m, 5 H), 6.78 (d, J = 2.4 Hz, 1 H), 6.37 (d, J = 2.4 Hz, 1 H), 6.06 (s, 1 H), 6.02 (ddt, J = 17.2, 11.6, 5.2 Hz, 1 H), 5.75 (ddd, J = 17.6, 10.0, 8.8 Hz, 1 H), 5.44 (s, 2 H), 5.41 (dd, J = 17.2, 1.4 Hz, 1 H), 5.30 (dd, J = 11.6, 1.4 Hz, 1 H), 5.04 (dd, J = 17.6, 1.4 Hz, 1 H), 5.01 (dd, J = 10.0, 1.4 Hz, 1 H), 4.80 (s, 2 H), 4.57 (ddd, J = 5.2, 1.2, 1.2 Hz, 1 H), 4.14 (dq, J = J = 6.4 Hz, 1 H), 3.87 (dd, J = J = 6.0 Hz, 1 H), 3.72 (dd, J = J = 6.4 Hz, 1 H), 3.48 (s, 3 H), 3.21 (dd, J = J = 5.4 Hz, 1 H), 2.8 (m, 2 H), 2.47 (dd, J = 11.6, 15.6 Hz, 1 H), 1.5–1.7 (m, 6 H), 1.35 (d, J = 6.6 Hz, 3 H), 1.3–1.45 (m, 2 H), 0.92 (s, 9 H), 0.13 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (100.6 MHz), δ 163.9, 160.9, 158.8, 157.6, 141.8, 139.1, 137.2, 137.1, 132.3, 128.4, 128.1, 127.8, 118.2, 116.6, 109.0, 104.3, 102.8, 102.5, 93.2, 85.2, 82.5, 74.4, 74.0 70.5, 69.0, 60.8, 43.7, 37.1, 37.0, 33.7, 26.2, 25.5, 24.0, 20.6, 18.3, –3.6, –3.7; IR ($CHCl_3$) 1720, 1665, 1600, 1570 cm^{-1}; HRMS, calcd for $C_{38}H_{49}O_9Si$ (M – t-Bu) 677.3145, found 677.3122. Anal. Calcd for $C_{42}H_{58}O_9Si$: C, 68.54; H, 7.94. Found: C, 68.53; H, 8.15.

Methyl 6-(Allyloxy)-8-[(benzyloxy)methoxy]-1-hydroxy-3-[(2′*R*,3′*S*,4′*R*,5′*S*,6′*R*)-3′-methoxy-5′,6′-(cyclohexylidenedioxy)-4′-[(*tert*-butyldimethylsilyl)oxy]-2′-vinylheptyl]-naphthoate (33). Methyl acetate (0.75 mL, 9.4 mmol) was added to a solution of lithium isopropylcyclohexylamide (9.4 mmol, prepared from 1.6 mL of isopropylcyclohexylamine and 3.8 mL of a 2.5 M solution of n-BuLi in hexane) and the solution stirred at –78 °C for 30 min. This mixture was then transferred rapidly by cannula to a 0 °C solution of isocoumarin **32** (868 mg, 1.2 mmol) in DMSO (10 mL) and THF (10 mL) under N_2. The solution immediately turned yellow. Ten minutes later the reaction was quenched with AcOH (15 mL) and stirred at 23 °C for 48 h. The mixture was washed with H_2O (2×) and saturated aqueous NaCl (1×), dried ($MgSO_4$), and concentrated to an oil (1.65 g). Purification of this material by flash chromatography (6:1 hexane–EtOAc) gave 719 mg (77%) of **33** as a pale yellow solid which was crystallized from pentane to give short white needles: R_f 0.40 (6:1 hexane–EtOAc, fluorescent blue spot under UV); mp 88–90 °C; $[\alpha]^{27}_D$ + 8 °C (c = 5.0, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 10.18 (s, 1 H), 7.4–7.5 (m, 5 H), 6.96 (s, 1 H), 6.82 (d, J = 2.0 Hz, 1 H), 6.66 (d, J = 2.0 Hz, 1 H), 6.08 (ddt, J = 17.2, 10.8, 5.2 Hz, 1 H), 5.70 (ddd, J = J = J = 10.0 Hz, 1 H), 5.45 (d, J = 17.2 Hz, 1 H), 5.45 (s, 2 H), 5.32 (d, J = 10.0 Hz, 1 H), 4.87 (d, J = 10.8 Hz, 1 H), 4.79 (s, 2 H), 4.76 (d, J = 18.0 Hz, 1 H), 4.59 (d, J = 5.2 Hz, 2 H), 4.15 (dq, J = J = 6.8 Hz, 1 H), 3.98 (s, 3 H), 3.94 (dd, J = J = 5.2 Hz, 1 H), 3.72 (dd, J = 5.2, 6.8 Hz, 1 H), 3.51 (s, 3 H), 3.28 (apparent d, J = 10.0 Hz, 1 H), 3.15 (dd, J = J = 5.2 Hz, 1 H), 2.6–2.8 (m, 2 H), 1.5–1.7 (m, 8 H), 1.3–1.45 (m, 2 H), 1.33 (d, J = 6.8 Hz, 3 H), 0.93 (s, 9 H), 0.14 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR (75.4 MHz) δ 169.6, 157.9, 155.2, 151.2, 139.6, 137.7, 137.6, 136.4, 132.8, 128.5, 128.3, 128.0, 120.1, 117.8, 116.0, 113.7, 109.5, 108.5, 102.1, 101.8, 101.5, 93.4, 85.4, 82.3, 77.2, 76.8, 73.2, 70.7, 68.8, 61.1, 52.0, 47.1, 36.9, 34.1, 26.4, 26.2, 25.2, 23.9, 20.4, 18.2, –3.7, –3.9; IR ($CHCl_3$) 3300–3500 (br), 1720, 1630 cm^{-1}; HRMS, calcd for $C_{45}H_{62}O_{10}Si$ 790.4111, found 790.4170. Anal. Calcd for $C_{45}H_{62}O_{10}Si$: C, 68.32; H, 7.90. Found: C, 68.34; H, 7.95.

Methyl 6-(Allyloxy)-8,9-bis[(benzyloxy)methoxy]-1-hydroxy-3-[(2′*R*,3′*S*,4′*R*,5′*S*,6′*R*)-3′-methoxy-5′,6′-(cyclohexylidenedioxy)-4′-[(*tert*-butyldimethylsilyl)oxy]-2′-vinylheptyl]naphthoate (34). A solution of naphthoate **33** (50 mg, 0.062 mmol) in DMF (0.13 mL) was added to a mixture of NaH (20 mg, 0.5 mmol) in THF (0.7 mL) at 23 °C under nitrogen. After being stirred for 10 min, the mixture was treated with BOMCl (0.043 mL, 0.31 mmol). The yellow mixture was stirred for 15 min at 23 °C, the reaction was quenched with saturated aqueous NH_4Cl, and the mixture was extracted 1:1 hexane–EtOAc,

washed with H_2O (2×) and saturated NaCl (2×), and dried ($MgSO_4$). Concentration of the filtrate provided crude **34** that was used immediately in the next reaction. A sample was purified by flash chromatography (short column of silica gel, 5:1 hexane–ether) for characterization purposes: R_f 0.22 (5:1 hexane–ether); $[\alpha]^{27}_D$ +11° (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 7.25–7.40 (m, 10 H), 6.89 (d, J = 2.4 Hz, 1 H), 6.72 (d, J = 2.4 Hz, 1 H), 6.09 (ddt, J = 17.2, 10.6, 5.4 Hz, 1 H), 5.69 (ddd, J = 8.4, 10.0, 17.4 Hz, 1 H), 5.46 (ddt, J = 17.2, 1.4, 1.4 Hz, 1 H), 5.36 (s, 2 H), 5.32 (ddt, J = 10.6, 1.4, 1.4 Hz, 1 H), 5.21 and 5.22 (AB, J = 6.0 Hz, 2 H), 4.87 (dd, J = 1.4, 10.0 Hz, 1 H), 4.77 (s, 2 H), 4.75 (s, 2 H), 4.75 (dd, J = 1.4, 17.4 Hz, 1 H), 4.60 (ddd, J = 1.2, 1.2, 5.4 Hz, 2 H), 4.15 (dq, J = 6.0, 6.8 Hz, 1 H), 3.93 (dd, J = 5.6, 6.0 Hz, 1 H), 3.90 (s, 3 H), 3.72 (dd, J = 5.2, 6.8 Hz, 1 H), 3.50 (s, 3 H), 3.20 (apparent d, J = 10.4 Hz, 1 H), 3.15 (dd, J = 5.2, 6.0 Hz, 1 H), 2.63–2.70 (m, 2 H), 1.5–1.65 (m, 8 H), 1.3–1.4 (m, 2 H), 1.33 (d, J = 6.0 Hz, 3 H), 0.92 (s, 9 H), 0.13 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR (75.4 MHz) δ 168.8, 157.6, 154.7, 150.2, 139.3, 138.0, 137.8, 137.1, 136.2, 132.9, 128.6, 128.4, 128.3, 128.1, 128.0, 127.8, 127.7, 127.6, 127.5, 125.8, 125.1, 117.9, 116.4, 114.2, 108.6, 103.9, 101.5, 99.6, 93.7, 91.4, 85.3, 82.4, 73.4, 71.6, 70.5, 69.9, 68.8, 63.9, 61.1, 52.1, 46.9, 36.9, 33.3, 26.4, 26.2, 25.5, 23.9, 20.5, 18.3, -3.6, -3.8; IR (CH_2Cl_2) 1725, 1620 cm^{-1}; HRMS, calcd for $C_{53}H_{70}O_{11}Si$ 910.4689, found 910.4671. Anal. Calcd for $C_{53}H_{70}O_{11}Si$: C, 69.86; H, 7.74. Found: C, 69.98; H, 7.48.

Methyl 8,9-Bis[(benzyloxy)methoxy]-1-hydroxy-3-[(2′*R*,3′*S*,4′*R*,5′*S*,6′*R*)-3′-methoxy-5′,6′-(cyclohexylidenedioxy)-4′-[(*tert*-butyldimethylsilyl)oxy]-2′-vinylheptyl]naphthoate (35). Bu_3SnH (20 μL, 0.074 mmol) was added dropwise to a solution of the crude naphthoate **34** (prepared in the previous experiment; theoretically 0.062 mmol), $Pd(PPh_3)_4$ (1.4 mg, 0.001 mmol), and AcOH (3.7 μL, 0.065 mmol) in toluene (0.3 mL) at 23 °C under N_2. Ten minutes later the reaction mixture was diluted with saturated aqueous NH_4Cl, extracted with CH_2Cl_2 (3×), filtered through a cotton plug, and concentrated to a yellow oil (121 mg). Purification of this material by flash chromatography (silica gel, 5:1 hexane–EtOAc) gave 50 mg (92% from naphthol **33**) of **35** that turned yellow on standing: R_f 0.20 (5:1 hexane–EtOAc); $[\alpha]^{27}_D$ +13° (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz) δ 7.25–7.40 (m, 10 H), 7.10 (s, 1 H), 6.83 (d, J = 2.4 Hz, 1 H), 6.66 (d, J = 2.4 Hz, 1 H), 5.65 (ddd, J = 8.4, 10.0, 17.2 Hz, 1 H), 5.59 (s, br, 1 H), 5.34 (s, 2 H), 5.20 and 5.19 (AB, J = 5.6 Hz, 2 H), 4.83 (dd, J = 1.6, 10.0 Hz, 1 H), 4.76 (s, 2 H), 4.72 (s, 2 H), 4.72 (dd, J = 1.6, 17.2 Hz, 1 H), 4.16 (dq, J = 6.0, 6.8 Hz, 1 H), 3.94 (dd, J = J = 5.6 Hz, 1 H), 3.90 (s, 3 H), 3.75 (dd, J = 5.6, 6.8 Hz, 1 H), 3.51 (s, 3 H), 3.18–3.21 (m, 1 H), 2.16 (dd, J = J = 5.6 Hz, 1 H), 2.60–2.71 (m, 2 H), 1.5–1.7 (m, 8 H), 1.3–1.4 (m, 2 H), 1.34 (d, J = 6.0 Hz, 1 H), 0.92 (s, 9 H), 0.13 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (100.6 MHz) δ 169.0, 155.0, 154.9, 150.3, 138.9, 138.0, 137.7, 137.0, 136.1, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 125.4, 124.7, 116.6, 113.6, 108.8, 103.9, 103.2, 99.5, 93.6, 85.3, 82.2, 77.2, 73.5, 73.3, 71.5, 70.4, 61.1, 52.2, 47.0, 36.9, 36.8, 33.4, 26.2, 25.2, 23.9, 20.5, 18.2, -3.6, -3.8; IR (CH_2Cl_2) 3580, 3500–3100 (br), 1720, 1620 cm^{-1}; HRMS, calcd for $C_{50}H_{66}O_{11}Si$ 870.4376, found 870.4343. Anal. Calcd for $C_{50}H_{66}O_{11}Si$: C, 68.93; H, 7.64. Found: C, 68.57; H, 7.88.

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Supplementary Material Available: ^{1}H NMR spectra for **22**, **29**, and **31** (3 pages). This material is contained in many 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.

On the Nature of the Katsuki–Sharpless Asymmetric Epoxidation Catalyst

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The ternary complexes formed by reactions of $Ti_2DIPT_2(O^iPr)_4$ (H_2DIPT = (2*R*,3*R*)-diisopropyl tartrate) with *N*-benzoyl-*N*-phenylhydroxylamine, triethylamine, and diisopropylamine (**3–5**) were examined by NMR spectroscopy in order to link solid-state with solution-state structures and to obtain NMR data for chelating DIPT units lacking ester coordination. The chemical shift differences and the coupling constants between the tartrate skeletal methines in these three complexes were significantly different from those in tartrate complexes previously examined. A linear relation was found between the chemical shift differences at methine positions in various tartrate ester–Ti(IV) alkoxide complexes (i.e. Katsuki–Sharpless catalysts), and the coupling constants ($^3J_{HH}$) between them. The H–C–C–H dihedral angles among the 2:2 complexes were calculated to span about 30°. Parallel changes in the ^{13}C-NMR positions and in the $^1J_{HC}$ and $^2J_{HC}$ values indicated that as the $^3J_{HH}$ values increase, the methines become more and more similar. Further, shielding of one OC*H* by metal-bound carbonyl was deduced to be at the origin of the ^{1}H-NMR chemical shift changes accompanying the angle changes. Along with supporting IR, kinetic, and other evidence, it is argued that these trends reflect a transition between chelating and nonchelating modes of diolate ligation, the latter being stabilized by stronger carbonyl coordination and π donation, and served to confirm that the parent catalyst, $Ti_2DIPT_2(O^iPr)_4$, is best represented by an open, monocyclic structure (A). The pentacoordination implied in A can explain much of the reactivity of $Ti_2DIPT_2(O^iPr)_4$ compared to that of the hexacoordinate complexes of non-tartrate diols. It is argued that the various ester–alkoxide combinations will equilibrate and catalyze epoxidations by the same mechanisms and via the same open structure. Explanations are provided for the success in epoxidation with tartrates, for the lack of success with non-tartrates, and for the epoxidation behavior with two tartrate homologues.

Introduction

The Katsuki–Sharpless (K–S) asymmetric epoxidation (AE) of allylic alcohols by ^{t}BuOOH and the related kinetic resolution of 1(*R*)-substituted allylic alcohols are rare examples of general, catalytic chiral induction processes with predictable outcomes.[1] The major catalytic species in both cases has the formula $Ti_2DIPT_2(O^iPr)_4$[2] (H_2DIPT = (*R*,*R*)-diisopropyl tartrate), but its study is complicated by its fluxional nature and its high reactivity. Early on,[2] $Ti_2DIPT_2(O^iPr)_4$ was assigned structure A in accord with the available NMR and IR evidence and in analogy with the crystal structures of tartrate salts of transition metals.[3]

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