The Chemical Synthesis of C-Ring Aryl Taxoids

K. C. Nicolaou,* Christopher F. Claiborne, Kumarapandian Paulvannan, Maarten H. D. Postema, and Rodney K. Guy

Abstract: We designed and targeted for synthesis the C-ring aryl taxoids **2a–c** in order to develop methods for the construction of the taxoid skeleton and to test their cytotoxicity against tumor cells. Compound **2a** was synthesized by a convergent route from hydrazone **5** and aldehyde **4**. Key steps included a Shapiro reaction to join **5** and **4**, a McMurry coupling to construct the 8-membered ring, a carbonate opening to introduce the 2-benzoate group, and an allylic oxidation followed by side-chain attachment. A similar sequence led to compound **2c**, whereas attempts to attain **2b** were thwarted by the lability of the benzyl group during the carbonate opening. The biological activity of **2a** and **2c** against tumor cells was considerably less than that of taxol.

Keywords
antitumor agents · carbocycles · drug research · taxol

Introduction

Taxol (**1**, Figure 1), originally isolated from the Pacific Yew *Taxus brevifolia*,[1] is an important new anticancer agent that has recently excited both the clinical and basic research communities. The past decade has seen its approval for the treatment of breast and ovarian cancer as well as its clinical evaluation for the management of skin, lung, and head and neck cancers.[2] Taxol functions by interfering with the assembly/disassembly cycle of microtubules, crucial cellular proteins.[3] In vivo, this effect causes the formation of stable bundles of nonfunctional microtubules within cells, arresting the cell cycle and killing the cells.[4] Recently, scientists have expended much effort in attempting to understand the molecular basis of this effect.

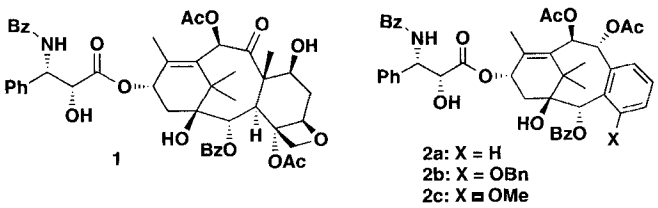

Figure 1. Structures of taxol (**1**) and designed analogues **2a–c**. Bn = benzyl; Bz = benzoyl.

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Chemists working on this problem have concentrated upon probing taxol's structure–activity relationships (SAR), primarily through degradative and semisynthetic methods.[5] The researchers in this area have demonstrated two general principles. First, the so-called "southern" substituents, the phenyl isoserine side chain and the C2 benzoate,[6] are crucial for activity. While either will tolerate subtle alteration, many substitutions or deletions significantly reduce cytotoxicity. On the other hand, the "northern" functionalities at C7,[7] C9,[8] and C10[7a] can be deleted without compromising taxol's effect. Although these studies have produced a large body of information about taxol's SAR, they are necessarily limited in scope. The effects of the less easily manipulated functions such as the C1 hydroxyl, the methyl groups, and the oxetane moiety are less well understood. After resisting for many years, taxol yielded to two groups that published independent total syntheses in early 1994[9, 10] and another one in 1995.[11] These syntheses opened the door for exploration of these previously uncharted areas of taxol's SAR.

One of the key remaining questions about taxol's pharmacophore was the role of the oxetane (D) ring. Kingston's group had shown that cleaving open the oxetane produced a compound that lacked biological activity.[12] However, the manipulations needed to open the oxetane also caused other structural perturbations that make interpreting this result difficult. One could hypothesize that the oxetane serves a purely *structural* role: its presence rigidifies the ABC-ring system to the extent that the taxane core is essentially conformationally inert. Alternatively, one could speculate that the lone pairs of electrons from the oxetane's oxygen might participate actively in hydrogen bonding with taxol's receptor.[12a, 13] Desiring to probe these possibilities, we targeted for synthesis derivatives of the type shown in Figure 1 (**2a–c**) where taxol's C- and D-rings have been replaced by an aromatic moiety. Molecular modeling

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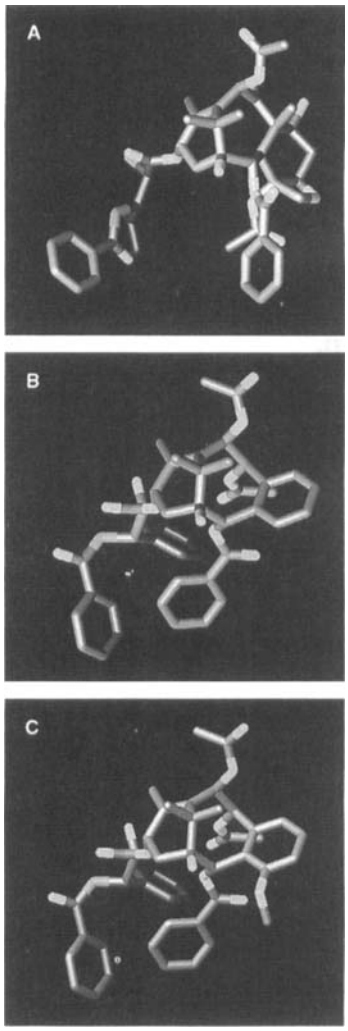


Figure 2. Computer-generated models of taxol (A) and designed taxoids **2a** (B) and **2c** (C).

indicated the possibility of good overlap between such structures and taxol (see Figure 2).

A few similar baccatin III derivatives had been produced previously,[14] but none contained the crucial side-chain and C2 functionalities necessary for biological activity. Thus, we wanted to invent a method that could install both these features and allow the generation of any desired aromatic substitution pattern. At the outset of this project, a convergent strategy for the synthesis of taxol was already in development in these laboratories.[9] It was decided to follow a very similar strategy for these derivatives (Figure 3). Thus, retrosynthetic disconnection of the side chain through known oxidations[15] and esterifications provided a baccatin III analogue whose central B-ring could be imagined to arise from sequential Shapiro[16] and McMurry[17] reactions. This convergent route was perceived to allow high efficiency and flexibility with respect to C-ring substituents.[18]

Abstract in Greek:

Περιληψη: Τα C-δακτυλιου-αρυλοταξοειδη **2a–c**, σχεδιαστηκαν σαν συνθετικοι στοχοι καταλληλοι, αφ' ενος μεν, για την αναπτυξη μεθοδολογιας παρασκευης ταξοειδους σκελετου, αφ' ετερου δε, για τον ελεγχο της τοξικοτητας τους εναντι καρκινικων κυτταρων. Η ενωση **2a** συνετεθη συνδιαζοντας την υδραζονη **5** με την αλδευδη **4**. Τα βασικα σταδια περιελαμβαναν τη συνενωση των **5** με **4** με αντιδραση Sapiro, την δημιουργια του 8-μελους δακτυλιου με συζευξη McMurry, το ανοιγμα του ανθρακικου εστερα για την εισαγωγη του 2-βενζουλεστερα και τελος, μια αλλυλικη οξειδωση, ακολουθουμενη απο προσαρτηση της πλευρικης αλυσιδας. Παρομοια πορεια οδηγησε στην ενωση **2c**, ενω αναλογες προσπαθειες να προσεγγηθει η **2b** εμποδιστηκαν λογω της ασταθειας της βενζυλομαδας στο σταδιο της διανοιξης του ανθρακικου εστερα. Η βιολογικη δραστικοτητα των **2a** και **2c** εναντι καρκινικων κυτταρων ηταν σημαντικα ασθενεστερη της Ταξολης (Taxol).

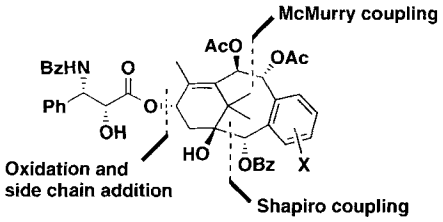
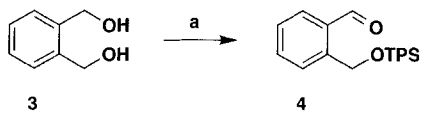


Figure 3. Strategy for the synthesis of C-ring aromatic analogues of taxol.

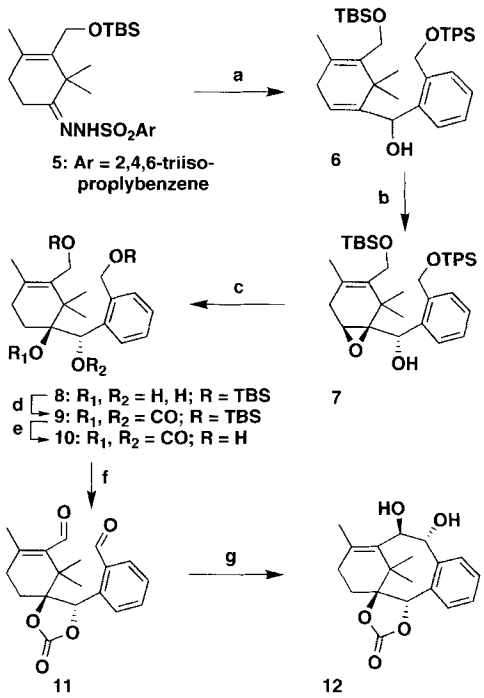
Results and Discussion

A. Synthesis of Aryl C-Ring Taxoid 2a: The synthesis of the aromatic C-ring analogue **2a** was carried out as summarized in Schemes 1 and 2. 1,2-Benzenedimethanol (**3**, Scheme 1) was monosilylated with tBuPh$_2$SiCl and imidazole and thence oxidized with PCC to afford the requisite aldehyde **4** in 67% overall yield. The vinyl anion generated from hydrazone **5**[9] (Scheme 2) by the method of Chamberlin[16b] was condensed



3 4

Scheme 1. Synthesis of the aromatic C-ring **4**. Reagents and conditions: a) TPSCl (0.6 equiv), imidazole (2 equiv), CH_2Cl_2, 25 °C, 2 h; PCC (1.5 equiv), CH_2Cl_2, 25 °C, 1 h; 67% for two steps. TPSCl = t-butyldiphenylsilyl chloride; PCC = pyridinium chlorochromate.



Scheme 2. Synthesis of the ABC-ring system **12**. Reagents and conditions: a) nBuLi (2.1 equiv), THF, −78 → 25 °C, cool to 0 °C and add **4** (1.1 equiv), 0.5 h, 86%; b) tBuOOH (1.1 equiv), [VO(acac)$_2$] (0.05 equiv), benzene, 25 °C, 5 h, 90%; c) LiAlH$_4$ (6.6 equiv), Et$_2$O, reflux, 4 h; TBSCl (2.6 equiv), imidazole (2.7 equiv), CH_2Cl_2, 25 °C, 1 h, 76%; d) CDI (10 equiv), CH_3CN, reflux, 2 h, 95%; e) TBAF (3 equiv), THF, 25 °C, 2 h; f) TPAP (0.05 equiv), NMO (4 equiv), CH_2Cl_2, 25 °C, 1 h, 89%; g) [TiCl$_3$(dme)$_{1.5}$] (7 equiv), Zn·Cu (24 equiv), DME, reflux, 3 h, then add **11** by syringe pump, 1 h addition, then reflux additional 3 h, 53%. TBSCl = t-butyldimethylsilyl chloride; CDI = carbonyldiimidazole; TBAF = tetra-n-butylammonium fluoride; TPAP = tetrapropylammonium perruthenate; NMO = N-methylmorpholine N-oxide.

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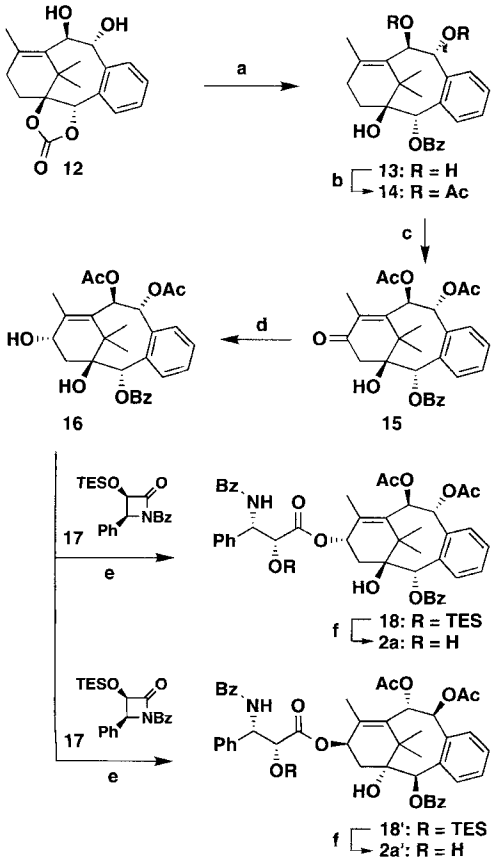
with the TPS-protected benzaldehyde derivative **4** to give alcohol **6** (Scheme 2). Directed epoxidation (90%) by Sharpless' method[19] followed by reductive opening of the resulting epoxide (**7**) with lithium aluminum hydride and reprotection of the primary alcohols (coincidentally desilylated during the reduction) with tBuMe$_2$SiCl and imidazole gave diol **8** in 75% overall yield. A conformation of the molecule perceived to be favorable for the upcoming McMurry reaction was then enforced by rigidifying the C1–C2 bond through formation of a cyclic carbonate. Thus, treatment of **8** with carbonyl diimidazole furnished carbonate **9** in 95% yield. Liberation of the alcohols with nucleophilic fluoride and oxidation with the Griffith–Ley catalyst (TPAP)[20] and *N*-methylmorpholine *N*-oxide (NMO) provided dialdehyde **11** (89% overall yield) via diol **10**. Exposure of this material to the McMurry reagent[17] provided, diastereoselectively, a single cyclic diol (**12**) in racemic form (53% yield). The racemic compound **12** was taken through the synthesis to give two diastereomeric compounds **2a** and **2a′** upon coupling with enantiomerically pure β-lactam **17** (see Scheme 3). At this stage it was also possible to separate the two enantiomers of **12** by formation of their diastereomeric diesters with camphanyl chloride followed by chromatographic separation and cleavage of the chiral auxiliary. Enantiomerically pure diol **12** was characterized by X-ray crystallographic analysis (see ORTEP diagram, Figure 4).



Scheme 3. Synthesis of taxoid **2a**. Reagents and conditions: a) PhLi (6 equiv), THF, −78 °C, 0.5 h, 80%; b) Ac_2O (2.2 equiv), Et_3N (3 equiv), 4-DMAP (0.1 equiv), CH_2Cl_2, 25 °C, 1 h, 100%; c) PCC (46 equiv), Celite, NaOAc (20 equiv), benzene, reflux, 2 h, 55%; d) $NaBH_4$ (excess), MeOH, 0 °C, 20 min, 90% (ca. 8:1 mixture of α to β); e) NaN(SiMe$_3$)$_2$ (3.0 equiv), **17** (2.0 equiv), THF, −78 °C, 0.5 h, 73%; f) HF·pyr (2.0 equiv), THF, 25 °C, 2 h, 90%. 4-DMAP = 4-dimethylaminopyridine; TES = triethylsilyl.

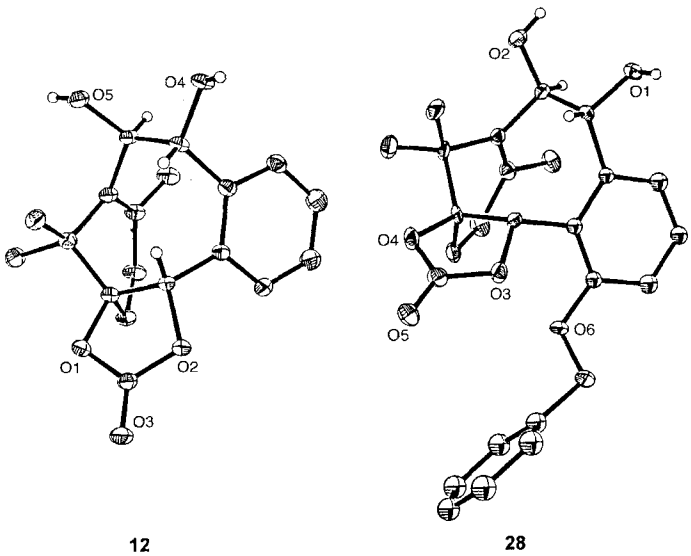


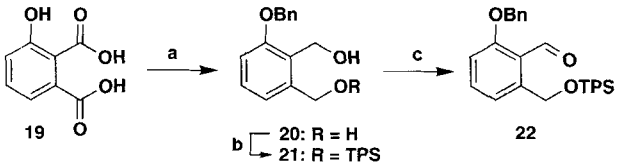
Figure 4. ORTEP drawings of compounds **12** and **28**.

Hydroxybenzoate **13** was formed in a regiospecific manner by treatment of (racemic) **12** with phenyllithium at −78 °C (80% yield) (Scheme 3). Protection of the hydroxyl groups as their acetyl esters (Ac_2O, Et_3N, 4-DMAP, leading to **14**, 100%) followed by allylic oxidation with PCC gave enone **15** (55% yield). Reduction of **15** with sodium borohydride in methanol at 0 °C gave, stereoselectively, allylic alcohol **16** (90% total yield, ca. 8:1 α:β ratio). Finally, side-chain attachment by the Holton–Ojima method[21,22] and β-lactam **17**[22] [NaN(SiMe$_3$)$_2$, −78 to 0 °C] gave two diastereomeric products, **18** and **18′** (37% each), which were chromatographically separated. Desilylation of **18** with HF·pyridine (HF·pyr) furnished the targeted taxoid **2a** (90% yield). Similar treatment of **18′** led to the diastereomeric taxoid **2a′**.

Biological evaluation of **2a** provided interesting results. First, although its level of toxicity was considerably lower than that of taxol, **2a** exhibited significant cytotoxicity against several cell lines, for example:[23] Ovcar-3, $IC_{50} = 2.80 \times 10^{-7}$ M (taxol = 6.2×10^{-10} M); HT-29, $IC_{50} = 1.29 \times 10^{-7}$ M (taxol = 5.1×10^{-9} M); UCLA-P3, $IC_{50} = 2.96 \times 10^{-7}$ M (taxol = 6.4×10^{-9} M). Secondly, the diastereomeric compound **2a′** (in which the side chain is of the correct absolute stereochemistry, but the taxoid framework is antipodal to that of taxol) showed insignificant cytotoxicity against the same cell lines. These results indicated that the major role of the oxetane might be conformational. Taking into consideration the current structural models for taxol,[24] we tried to rationalize the attenuated cytotoxicity through examining missing structural components. We reasoned that perhaps the 4-acetyl group present in taxol might be serving as an anchor for the "hydrophobic collapse" of the C2 benzoyl and C3′ phenyl rings.[25] In order to test this hypothesis, we designed and targeted for chemical synthesis alkoxyaryl derivatives such as **2b** and **2c**, which we expected to provide an ethereal oxygen in approximately the same position as the 4-acyloxy substituent of taxol.

B. Attempted Synthesis of Benzyloxyaryl C-Ring Taxoid 2b: Formation of the required C-ring synthon for the construction

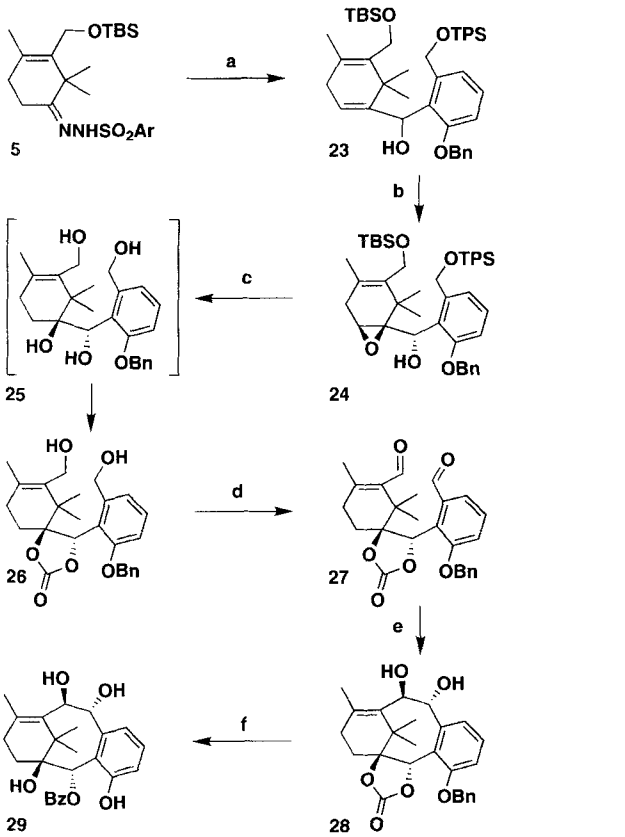
of the benzyloxyaryl taxoid **2b** was carried out by perbenzylation of 3-hydroxyphthalic acid (**19**) (K_2CO_3, BnBr) followed by reduction of the resulting benzyl esters with lithium aluminum hydride to give diol **20** in 75% overall yield (Scheme 4).



Scheme 4. Synthesis of aromatic C-ring **22**. Reagents and conditions: a) BnBr (5.0 equiv), K_2CO_3 (7.0 equiv), DMF, 50 °C, 1.5 h, 75%; $LiAlH_4$ (4.9 equiv), THF, 25 °C, 1.0 h, 81%; b) TPSCl (1.1 equiv), imidazole (1.5 equiv), CH_2Cl_2, 25 °C, 0.5 h, 50% (after separation of isomers); c) PDC (2.0 equiv), 4 Å mol. sieves, CH_2Cl_2, 25 °C, 1.5 h, 82%. BnBr = benzyl bromide; DMF = dimethylformamide; PDC = pyridinium dichromate.

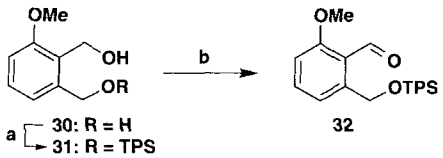
Monoprotection of **20** with *tert*-butyldiphenylsilyl chloride, followed by oxidation of the correctly protected compound **21** (50% yield), provided the required aldehyde **22** (80% yield).

In a manner analogous to that described above, **22** was coupled to the vinyl anion derived from **5** to give allylic alcohol **23** in 86% yield (Scheme 5). Subsequent vanadium-directed[19] epoxidation of **23** yielded epoxide **24** (90% yield). Lithium aluminum hydride reduction of **24** afforded the corresponding tetraol (**25**) by concomitant desilylation. Instead of reprotecting the primary positions as had been done in the case of **6** → **8** (Scheme 2), we treated the tetraol **25** with excess carbonyl diimidazole to construct the carbonate ring as desired at C1 and C2 and allowed the primary hydroxyl groups to form transient urethanes, which were subsequently hydrolyzed selectively to afford **26**. Oxidation of the resulting primary alcohols in **26** with a catalytic amount of TPAP and NMO afforded the required dialdehyde **27** (71% yield). Subjection of dialdehyde **27** to the McMurry coupling cyclization provided diol **28** in modest yield (33%). The stereochemistry of this compound (**28**) was proven by X-ray crystallographic analysis (see ORTEP diagram, Figure 4). Compound **28** proved rather unreactive towards phenyllithium. When forcing conditions (large excess of reagent and HMPA) were used, opening of the carbonate ring was accompanied by concomitant removal of the benzyl group to afford phenolic compound **29** (80% yield). Presumably, this debenzylation reaction proceeds through a single electron transfer (SET) reduction. Triol **29** was not amenable to further convenient manipulations, and the pursuit of **2b** was, therefore, abandoned in favor of a more robust alkoxy group on the aromatic ring.



Scheme 5. Synthesis of the ABC-ring system **29**. Reagents and conditions: a) *n*BuLi (2.1 equiv), THF, −78 → 25 °C, cool to 0 °C and add **22** (1.1 equiv), 0.5 h, 86%; b) *t*BuOOH (1.1 equiv), $[VO(acac)_2]$ (0.05 equiv), benzene, 25 °C, 5 h, 85%; c) $LiAlH_4$ (6.6 equiv), Et_2O, reflux, 4 h; CDI (10 equiv), CH_3CN, reflux, 2 h, 63%; d) TPAP (0.05 equiv), NMO (4 equiv), CH_2Cl_2, 25 °C, 1 h, 71%; e) $[TiCl_3(dme)_{1.5}]$ (7 equiv), Zn-Cu (24 equiv), DME, reflux, 3 h, then add aldehyde **27** by syringe pump, 1 h addition, then reflux for an additional 3 h, 39%; f) PhLi (6.0 equiv), HMPA (6.0 equiv), THF, −78 °C, 0.5 h, 80%. HMPA = hexamethylphosphoramide.

C. Synthesis of Methoxyaryl C-Ring Taxoid 2c: Starting with known intermediate **30**[26] (Scheme 6), the monoprotected intermediate **31** (*t*BuPh$_2$SiCl/imidazole, 45% yield) was oxidized



Scheme 6. Synthesis of aromatic C-ring **32**. Reagents and conditions: a) TPSCl (1.0 equiv), imidazole (1.5 equiv), CH_2Cl_2, 25 °C, 1.0 h, 33% (after separation of isomers); b) PDC (2.0 equiv), 4 Å mol. sieves, CH_2Cl_2, 25 °C, 2 h, 86%.

with PDC in CH_2Cl_2, as with the analogous benzyl ether derivative **21**, to give the required aldehyde **32** (80%). This substrate (**32**) coupled cleanly with the A-ring vinyl anion generated from hydrazone **5** to give alcohol **33** (86% yield, Scheme 7). Epoxidation, followed by reduction, gave the expected tetraol, which was converted to carbonate **35** via epoxide **34** by means of the method described above for compound **26** (Scheme 5). Oxidation of diol **35** (TPAP/NMO, 89% yield) followed by ring closure under McMurry conditions furnished cyclic diol **37** in 33% yield. The stereochemistry of the diol system in this compound was based on NMR comparisons with **12** and **28**, whose structures were firmly established by X-ray crystallography.

Unlike benzyl ether **28**, the methoxy derivative **37** reacted smoothly with phenyllithium under the previously described conditions to afford **38** in 80% yield (Scheme 8). Selective acetylation of the latter compound (**38**) proceeded cleanly to give diacetate **39** (100%), which was oxidized with PCC in the presence of NaOAc in refluxing benzene, furnishing enone **40** (55% yield). Reduction of the carbonyl group of the enone function in **40** with $NaBH_4$ in methanol at 0 °C resulted in the formation of a 1:1 mixture of α and β diastereoisomers (90%

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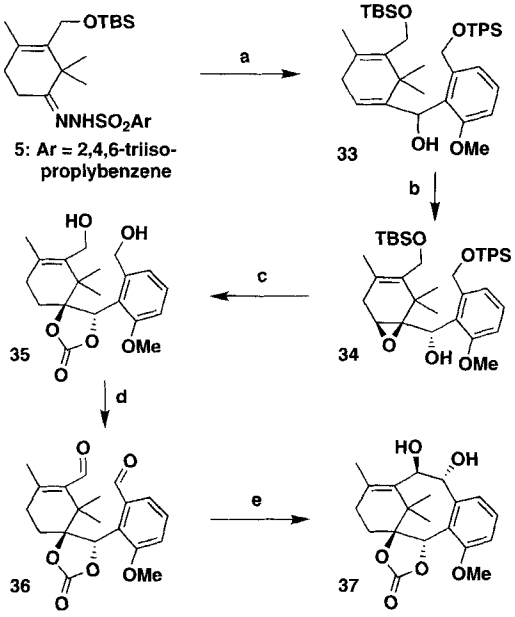
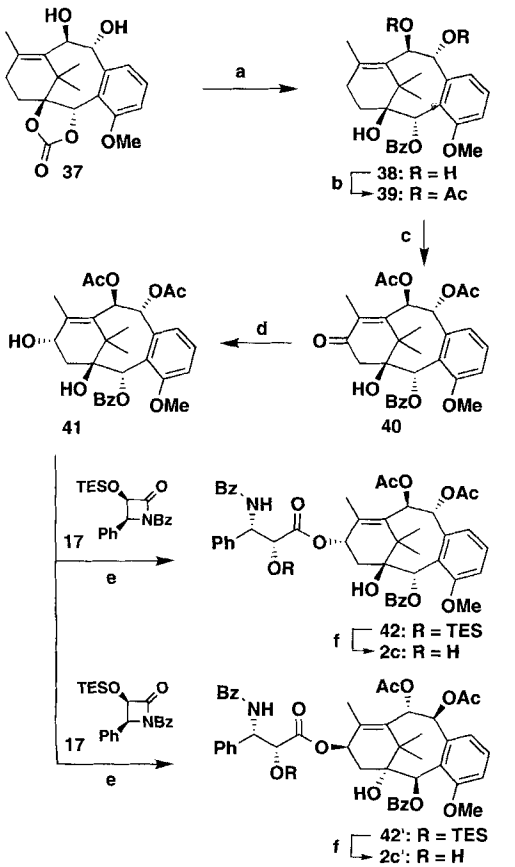


Scheme 7. Synthesis of the ABC-ring system **37**. Reagents and conditions: a) *n*BuLi (2.1 equiv), THF, $-78 \rightarrow 25\,^{\circ}C$, cool to $0\,^{\circ}C$ and add **32** (1.1 equiv), 0.5 h, 86%; b) *t*BuOOH (1.1 equiv), $[VO(acac)_2]$ (0.05 equiv), benzene, $25\,^{\circ}C$, 5 h, 90%; c) $LiAlH_4$ (6.6 equiv), Et_2O, reflux, 4 h, 75%; CDI (10 equiv), CH_3CN, reflux, 2 h, 73%; d) TPAP (0.05 equiv), NMO (4 equiv), CH_2Cl_2, $25\,^{\circ}C$, 1 h, 89%; e) $[TiCl_3(dme)_{1.5}]$ (7 equiv), Zn·Cu (24 equiv), DME, reflux, 3 h, then add aldehyde **36** by syringe pump, 1 h addition, then reflux for an additional 3 h, 33%.



Scheme 8. Synthesis of taxoid **2c**. Reagents and conditions: a) PhLi (6 equiv), THF, $-78\,^{\circ}C$, 0.5 h, 80%; b) Ac_2O (2.2 equiv), Et_3N (3 equiv), 4-DMAP (0.1 equiv), CH_2Cl_2, $25\,^{\circ}C$, 1 h, 100%; c) PCC (46 equiv), Celite, NaOAc (20 equiv), benzene, reflux, 2 h, 55%; d) $NaBH_4$ (excess), MeOH, $0\,^{\circ}C$, 20 min, 90% (ca. 1:1 mixture of α to β); e) $NaN(SiMe_3)_2$ (3.0 equiv), **17** (2.0 equiv), THF, $-78\,^{\circ}C$, 0.5 h, 73%; f) HF·pyr. (2.0 equiv), THF, $25\,^{\circ}C$, 2 h, 90%.

total yield), from which the desired α isomer **41** was isolated by chromatography. The stereochemical outcome of this reduction is somewhat different from that of the corresponding enone leading to the non-oxygenated aromatic taxoid **2a** (see **15** → **16**, ca. 8:1 $\alpha:\beta$ ratio, Scheme 3), suggesting a conformational effect exerted by the aromatic oxygen of **40**. Racemic **41** was then converted to the two taxoids **2c** and **2c'**, via intermediates **42** and **42'**, by attachment of the enantiomerically pure side chain through the Holton–Ojima[21,22] method with β-lactam **17** (Scheme 8). Preliminary biological studies with **2c** and **2c'** indicate low cytotoxicities as compared with taxol.

Conclusion

In this article, a synthetic route to simplified taxoids containing benzenoid systems instead of the CD-ring framework of taxol is described. Although preliminary biological data indicate considerable loss of cytotoxicity, the strategy may prove useful for the synthesis of other designed analogues of taxol that are currently unavailable from natural sources.

Experimental Procedure

General Techniques: Melting points were determined on a Uni-Melt (Thomas Scientific) apparatus and are uncorrected. NMR spectra were recorded on Bruker AMX-500, AMX-400, AM-300, or AM-250 instruments with Me_4Si or $CHCl_3$ (in $CDCl_3$) as internal standard: chemical shift signals (δ) are quoted as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), apt (apparent), b (broad), obs (obscured). IR spectra were recorded on Nicolet 205, Perkin Elmer 1600, or Galaxy 2020 series FT-IR spectrophotometers. Optical rotations were recorded with a Perkin Elmer 241 polarimeter. High-resolution mass spectra (HRMS) were recorded on a VG ZAB-ZSE mass spectrometer, under fast atom bombardment (FAB) or electrospray conditions, at the Scripps Research Institute.

All reactions were monitored by thin-layer chromatography (TLC) carried out on 250 mm Whatman silica gel plates (K 6 F-60 Å) with UV light, *p*-anisaldehyde, or 7% ethanolic phosphomolybdic acid and heat ($200\,^{\circ}C$) as developing agents. E. Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Dry tetrahydrofuran (THF) and ethyl ether were distilled from sodium/benzophenone, methylene chloride was distilled from calcium hydride, and benzene and toluene were distilled from sodium immediately prior to use. All reagents were obtained from Aldrich unless otherwise noted. Solvents used for workup, chromatography, and recrystallizations were reagent grade from Fisher Scientific and were used directly as received. All reactions were carried out under an argon atmosphere with freshly distilled solvents under anhydrous conditions, unless otherwise noted. Yields refer to chromatographically and spectroscopically (^1H NMR) homogenous materials, unless otherwise stated.

Aldehyde 4: *tert*-Butyldiphenylsilyl chloride (1.86 g, 6.77 mmol) was added in one portion to a methylene chloride solution of **3** (850 mg, 6.15 mmol) and imidazole (628 mg, 9.22 mmol) at room temperature, and the resulting solution was stirred for 2 h. The solution was then poured into ether (100 mL) and washed with saturated aqueous ammonium chloride (20 mL) and then brine (20 mL), dried with magnesium sulfate, filtered, and concentrated. The crude alcohol was oxidized in a fashion analogous to the oxidation of **10** to **11** (see below) with tetrapropylammonium perruthenate (20 mg, 57 mmmol), 4-methylmorpholine *N*-oxide (865 mg, 7.38 mmol) and methylene chloride (10 mL) to give **4** as a clear oil (1.54 g, 67%); $R_f = 0.60$ (silica, 30% ether in petroleum ether); FT-IR (film): $\tilde{\nu}_{max} = 2930, 2856, 1669, 1600, 1575, 1471, 1427, 1194, 1113, 1075, 822\ cm^{-1}$; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 10.13$ (s, 1H, CHO), 7.85 (d, $J = 7.5$ Hz, 1H, Ar), 7.81 (dd, $J = 8.0, 2.4$ Hz, 1H, Ar), 7.69–7.65 (m, 4H, Ar), 7.64–7.60 (m, 1H, Ar), 7.47–7.34 (m, 7H, Ar), 5.19 (s, 2H, CH_2O), 1.10 (s, 9H, *t*BuSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 192.9, 143.7, 135.5, 134.0, 133.3, 132.7, 129.7, 127.8, 127.1, 126.9, 63.6, 26.8, 19.4$.

Coupled product 6: *n*-Butyllithium (9.4 mL of a 1.6 M solution in hexanes, 15 mmol) was added dropwise to a solution of the hydrazone **5** (4.0 g, 7.11 mmol) in tetrahydrofuran (30 mL) at −78 °C. After complete addition, a color change from the initial yellow to a bright red was observed. The dry-ice bath was removed and the solution was allowed to warm to 25 °C (gas evolution was observed). The solution of the vinyl anion was then cooled back to 0 °C and aldehyde **4** (2.93 g, 7.82 mmol) was added dropwise as a solution in THF (5 mL). The mixture was stirred for 1 h at 0 °C and was then quenched with aqueous ammonium chloride (15 mL). Ether (100 mL) was added and the mixture was washed with aqueous ammonium chloride (10 mL) and brine (15 mL), and dried over magnesium sulfate. After filtration and concentration, the crude product was purified by flash chromatography (silica) to give **6** as a colorless oil (3.9 g, 86%). $R_f = 0.25$ (silica, 20% ethyl acetate in petroleum ether); FT-IR (film): $\tilde{\nu}_{max} = 3345$, 2956, 1472, 1428 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 7.87-7.78$ (m, 4H, Ar), 7.68 (m, 1H, Ar), 7.55–7.32 (m, 9H, Ar), 5.92 (dd, $J = 3.5$, 3.0 Hz, 1H, HC=C), 5.69 (s, 1H, *H*COH), 5.04 (d, $J = 13.0$ Hz, 1H, CH_2O), 4.79 (d, $J = 13.0$ Hz, 1H, CH_2OSi), 4.28 (s, 2H, CH_2O), 2.96 (s, 1H, OH), 2.81 (dd, $J = 23.0$, 3.0 Hz, 1H, CH_2), 2.74 (dd, $J = 23.0$, 3.5 Hz, 1H, CH_2), 1.87 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.20 (s, 9H, *t*BuSi), 1.01 (s, 9H, *t*BuSi), 0.92 (s, 3H, CH_3), 0.19 (s, 3H, CH_3Si), 0.18 (s, 3H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 143.9$, 141.6, 137.3, 135.6, 135.5, 132.9, 132.8, 129.8, 129.7, 129.0, 128.2, 127.8, 127.7, 127.5, 127.4, 127.3, 69.1, 64.5, 58.8, 38.3, 33.4, 27.9, 27.8, 26.8, 26.3, 26.0, 19.1, 18.3, −5.4; HRMS (FAB): calcd for $C_{40}H_{56}O_3Si_2$ ($[M + Cs^+]$) 773.2822, found 773.2824.

Epoxide 7: *tert*-Butyl hydroperoxide (50 mL of a 3.0 M solution in 2,2,4-trimethylpentane, 0.18 mmol) was added to a solution of the allylic alcohol **6** (100 mg, 0.16 mmol) and vanadium acetylacetonate ($[VO(acac)_2]$) (ca. 2 mg, cat.) in benzene (1 mL) at 0 °C. The solution turned a deep red color and was allowed to warm to 23 °C and stirred for 2 h. The reaction was quenched by dilution with ether (3 mL), followed by addition of aqueous sodium thiosulfate (1 mL), and washed with aqueous sodium bicarbonate (1 mL) and then brine (1 mL). The resulting organic solution was dried over magnesium sulfate, concentrated, and purified by flash chromatography (silica, ether/petroleum ether) to yield **7** as a white foam (95 mg, 90%); $R_f = 0.30$ (silica, 20% ether in petroleum ether); FT-IR (film): $\tilde{\nu}_{max} = 3385$, 2955, 1471, 1427, 1253 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.70$ (d, $J = 7.0$ Hz, 2H, Ar), 7.54 (d, $J = 7.0$ Hz, 1H, Ar), 7.46–7.23 (m, 11H, Ar), 5.28 (s, 1H, *H*COH), 4.90 (d, $J = 13.5$ Hz, 1H, CH_2O), 4.84 (d, $J = 13.5$ Hz, 1H, CH_2O), 4.12 (d, $J = 11.0$ Hz, 1H, CH_2O), 3.09 (s, 1H, H-epoxide), 2.76 (brs, 1H, OH), 2.41 (d, $J = 19.0$ Hz, 1H, $CH_2C=C$), 2.36 (d, $J = 19.0$ Hz, 1H, $CH_2C=C$), 1.67 (s, 3H, CH_3), 1.29 (s, 3H, CH_3), 1.11 (s, 9H, *t*BuSi), 0.88 (s, 9H, *t*BuSi), 0.81 (s, 3H, CH_3), 0.05 (s, 6H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 138.2$, 137.7, 135.6, 135.5, 133.8, 133.1, 133.0, 129.7, 127.9, 127.7, 127.2, 127.0, 126.3, 124.9, 66.2, 66.1, 63.4, 58.8, 58.1, 38.6, 31.7, 26.7, 25.9, 25.8, 22.0, 19.6, 19.2, 18.2, −5.5, −5.6; HRMS (FAB): calcd for $C_{40}H_{56}Si_2O_4$ ($[M + Cs^+]$) 789.2772, found 789.2775.

Disilylether 8: Lithium aluminum hydride (5 mL, 1 M solution in ether, 5.0 mmol) was added dropwise to a solution of epoxide **7** (500 mg, 0.76 mmol) in dry ether (5 mL) at 25 °C. The solution was then refluxed for 4 h, cooled to 0 °C, and quenched with aqueous ammonium chloride (5 mL). The mixture was stirred for 2 h at 25 °C and then diluted with ether (20 mL), washed with aqueous ammonium chloride (10 mL), brine (5 mL), dried over magnesium sulfate, and concentrated. The crude tetraol was carried forward to the next step, where it was reprotected by dissolution in methylene chloride (15 mL) and treatment with *t*-butyldimethylsilyl chloride (300 mg, 2.0 mmol) while being stirred at 25 °C for 30 min. The mixture was quenched with aqueous sodium bicarbonate (5 mL), diluted with ether (15 mL), and dried over magnesium sulfate. The crude product was concentrated and purified by flash chromatography (silica, ether/petroleum ether) to give **8** as a white foam (375 mg, 75%); $R_f = 0.45$ (20% ether in petroleum ether); FT-IR (film): $\tilde{\nu}_{max} = 3384$, 2360 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.33$ (m, 2H, Ar), 7.26 (m, 2H, Ar), 4.98 (brs, 1H, *H*COH), 4.80 (d, $J = 12.5$ Hz, 2H, CH_2OSi), 3.06 (s, 2H, CH_2OSi), 1.90 (m, 2H, $CH_2C=C$), 1.69 (s, 3H, $CH_3C=C$), 1.55 (m, 2H, CH_2), 0.94 (s, 18H, *t*BuSi), 0.12 (s, 12H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 140.65$, 140.6, 138.0, 135.7, 131.2, 127.5, 127.4, 75.9, 59.2, 43.6, 29.0, 27.8, 26.0, 25.9, 25.8, 23.9, 19.2, 18.2, −5.3, −5.4; HRMS (FAB): calcd for $C_{30}H_{54}Si_2O_4$ [M^+] 534.3561, found 534.3545.

Carbonate 9: Carbonyl diimidazole (1.4 g, 8.4 mmol) was added to a solution of diol **8** (450 mg, 0.84 mmol) in dry acetonitrile (10 mL), and the mixture was refluxed for 2 h. The solution was then diluted with petroleum ether (20 mL) and washed with 5% hydrochloric acid (2 × 5 mL), aqueous sodium bicarbonate (10 mL), and brine (10 mL), and dried over magnesium sulfate. Concentration and purification by flash chromatography (silica, ether/petroleum ether) gave **9** as a white foam (447 mg, 95%); $R_f = 0.6$ (silica, 20% ether in petroleum ether); FT-IR (film): $\tilde{\nu}_{max} = 2931$, 2857, 1803, 1456 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 7.43-7.25$ (m, 4H, Ar), 5.95 (s, 1H, *H*COH), 4.77 (d, $J = 13.0$ Hz, 1H, CH_2O), 4.57 (d, $J = 13.0$ Hz, 1H, CH_2O), 4.28 (d, $J = 11.5$ Hz, 1H, CH_2O), 4.19 (d, $J = 11.5$ Hz, 1H, CH_2O), 1.98 (m, 1H, $CH_3C=C$), 1.80 (m, 1H, $CH_3C=C$), 1.62 (s, 3H, $CH_3C=C$), 1.57 (m, 2H, CH_2), 1.34 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 0.92 (s, 9H, *t*BuSi), 0.92 (s, 9H, *t*BuSi), 0.11 (s, 3H, CH_3Si), 0.10 (s, 3H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 155.0$, 138.9, 133.5, 129.0, 127.9, 127.7, 127.3, 90.1, 62.7, 59.2, 42.5, 28.7, 25.8, 25.7, 25.0, 19.1, 18.1, −5.2; HRMS (FAB): calcd for $C_{31}H_{52}O_5SI_2$ [$M + Na^+$] 583.3251, found 583.3250.

Diol 10: Tetra-*n*-butylammonium fluoride (4.8 mL, 1 M solution in THF, 4.8 mmol) was added to a solution of silyl ether **9** (900 mg, 1.6 mmol) in THF (20 mL) at 25 °C. The mixture was stirred for 1 h and quenched with excess aqueous ammonium chloride. Ether (20 mL) was added and the solution was washed with water (5 mL), brine (5 mL), and dried over magnesium sulfate. The combined aqueous layers were extracted with methylene chloride (10 mL) and added to the organic mixture, filtered, and concentrated. The crude product was purified by flash chromatography (silica, ethyl acetate/petroleum ether) to afford diol **10** as a white foam (369 mg, 99%); $R_f = 0.25$ (60% ethyl acetate in petroleum ether); FT-IR (film): $\tilde{\nu}_{max} = 3392$, 2974, 1781 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.38-7.26$ (m, 4H, Ar), 6.07 (s, 1H, $HCOCO_2$), 4.63 (d, $J = 12.5$ Hz, 1H, CH_2O), 4.48 (d, $J = 12.5$ Hz, 1H, CH_2O), 4.21 (d, $J = 11.5$ Hz, 1H, CH_2O), 4.10 (d, $J = 11.5$ Hz, 1H, CH_2O), 1.91 (m, 2H, $CH_3C=C$), 1.63 (s, 3H, $CH_2C=C$), 1.60 (m, 1H, CH_2), 1.33 (m, 1H, CH_2), 1.31 (s, 3H, CH_3), 1.20 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 155.3$, 138.4, 134.0, 133.9, 133.7, 129.5, 129.4, 128.1, 127.8, 89.9, 78.4, 62.1, 58.1, 42.6, 28.6, 24.8, 23.9, 20.9, 19.1; HRMS (FAB): calcd for $C_{19}H_{24}O_5$ [$M + Na^+$] 355.1521, found 355.1520.

Dialdehyde 11: *Tetrapropylammonium perruthenate (14 mg, 0.04 mmol) was* added to a stirred solution of diol **10** (266 mg, 0.801 mmol) and 4-methylmorpholine *N*-oxide (375 mg, 3.20 mmol) in methylene chloride (10 mL) at 23 °C. The solution was stirred for 2 h, diluted with ether (5 mL), filtered through silica gel, and concentrated to give the crude dialdehyde. Purification was carried out by flash chromatography (silica, ethyl acetate/petroleum ether) to afford **11** as a white solid (712 mg, 89%); m.p. 162 °C (from ether/hexanes); $R_f = 0.6$ (silica, 60% ethyl acetate in petroleum ether); FT-IR (film): $\tilde{\nu}_{max} = 2978$, 1798, 1701, 1671 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 10.08$ (s, 1H, CHO), 10.04 (s, 1H, CHO), 7.87 (dd, $J = 7.6$, 1.5 Hz, 1H, Ar), 7.72 (m, 1H, Ar), 7.66 (m, 1H, Ar), 7.51 (d, $J = 7.8$ Hz, 1H, Ar), 6.81 (s, 1H, $HCOCO_2$), 2.36 (m, 1H, $CH_2C=C$), 2.02 (s, 3H, $CH_3C=C$), 1.85 (m, 1H, $CH_2C=C$), 1.52 (s, 3H, CH_3), 1.50 (s, 3H, CH_3), 1.48 (m, 2H, CH_2); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 192.4$, 191.5, 154.7, 153.6, 137.1, 136.4, 135.5, 134.0, 133.6, 129.7, 128.9, 90.7, 76.3, 41.5, 31.5, 24.5, 23.4, 19.7, 8.5; HRMS (FAB): calcd for $C_{19}H_{20}O_5$ [$M + Na^+$] 351.1205, found 351.1210.

McMurry product 12: 1,2-dimethyloxyethane (DME; 30 mL) was added to a flask containing $[TiCl_3(dme)_{1.5}]$ (900 mg, 3.1 mmol) and Zn·Cu couple (930 mg, 7.2 mmol) at 23 °C (reagents were weighed out under inert atmosphere). The solution was heated to reflux with vigorous stirring for 3.5 h and then cooled to 55 °C. Triethylamine (100 μL, 0.72 mmol) was added, followed by a solution of dialdehyde **11** (100 mg, 0.3 mmol in 30 mL DME) from a syringe pump over 1.5 h. After complete addition, the solution was maintained at 55 °C for 2 h, cooled to 0 °C, and poured into a solution of aqueous potassium carbonate (5%, 100 mL) kept at 0 °C. After stirring for 10 min the mixture was allowed to warm to ambient temperature, diluted with ether (100 mL), and filtered through Celite. The organic phase was washed with brine (10 mL), dried over magnesium sulfate, and concentrated. Purification by flash chromatography (silica, 20% ethyl acetate in benzene) afforded **12** (53 mg, 53%) as a crystalline solid (from methylene chloride/hexane), m.p. 251 °C (decomp.); $R_f = 0.20$ (silica, ether); FT-IR (film): $\tilde{\nu}_{max} = 3426$, 2937, 1800, 1457, 1026 cm^{-1}; ^{1}H NMR (500 MHz, [D_6]acetone): $\delta = 7.82$ (m, 1H, Ar), 7.47 (m, 1H, Ar), 7.30 (m, 2H, Ar), 5.91 (s, 1H, $HCOCO_2$), 5.14 (dd, $J = 8.5$, 3.0 Hz, *H*COH), 4.83 (d, $J = 3.0$ Hz, 1H, OH), 4.64 (dd, $J = 8.5$,

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3.0 Hz, 1H, *H*COH), 4.41 (d, J = 3.0 Hz, 1H, OH), 2.37 (m, 1H, CH_2C=C), 2.29 (m, 1H, CH_2C=C), 1.89 (m, 1H, CH_2), 1.72 (s, 3H, CH_3C=C), 1.19 (m, 1H, CH_2), 1.17 (s, 3H, CH_3), 0.79 (3H, CH_3); ^{13}C NMR (125 MHz, [D$_6$]acetone): δ = 154.2, 142.0, 138.0, 133.2, 132.9, 128.2, 127.5, 126.4, 124.1, 93.0, 80.3, 79.2, 75.2, 40.6, 29.5, 23.5, 21.5, 21.1; HRMS (FAB): calcd for $C_{19}H_{22}O_5$ [M + Na$^+$] 353.1365, found 353.1360.

Benzoate diol 13: Phenyllithium (600 µL, 1.2 mmol of a 2 M solution in cyclohexane ether) was added to a stirred solution of diol **12** (65 mg, 0.197 mmol) in THF (17 mL) at −78 °C. The mixture was stirred for 30 min and was then quenched at −78 °C with aqueous ammonium chloride (15 mL). The solution was diluted with ether (50 mL), washed with brine (10 mL), dried over magnesium sulfate, and concentrated. The residue was purified by flash chromatography (silica, ethyl acetate/petroleum ether) to provide **13** as a white solid (64 mg, 80%); R_f = 0.5 (silica, 50% ethyl acetate in petroleum ether); FT-IR (film): $\tilde{\nu}_{max}$ = 3456, 2945, 1704, 1450, 1283 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05 (m, 1H, Ar), 7.58–7.41 (m, 4H, Ar), 7.15 (m, 2H, Ar), 6.31 (s, 1H, HCOBz), 5.41 (d, J = 9.0 Hz, 1H, *H*COH), 4.50 (d, J = 9.0 Hz, 1H, *H*COH), 2.41 (m, 1H, CH_2C=C), 2.28 (m, 1H, CH_2C=C), 1.84 (m, 1H, CH_2), 1.73 (s, 3H, CH_3C=C), 1.36 (s, 1H, CH_2), 1.15 (s, 3H, CH_3), 0.62 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.9, 139.6, 138.5, 138.1, 133.2, 131.4, 129.8, 129.5, 128.4, 126.9, 126.5, 124.4, 123.8, 79.7, 79.2, 74.3, 74.1, 41.5, 29.8, 27.2, 26.1, 20.3, 19.6, 14.1; HRMS (FAB): calcd for $C_{25}H_{28}O_5$ [M + Na$^+$] 431.1834, found 431.1830.

Diacetate 14: Acetic anhydride (26 µL, 0.27 mmol) was added to a stirred solution of diol **13** (50 mg, 0.123 mmol), triethylamine (51 µL, 0.369 mmol), and 4-dimethylaminopyridine (1.5 mg, 0.012 mmol) in methylene chloride (20 mL) at 0 °C. The solution was allowed to warm to 23 °C and stirred for 45 min before quenching with aqueous sodium bicarbonate (10 mL). The reaction mixture was then diluted with ether (10 mL), washed with water (5 mL) and then brine (5 mL), and dried over magnesium sulfate. After concentration, trace impurities were removed by filtration through silica gel (as a solution in 60% ethyl acetate in petroleum ether); this yielded a white foam; R_f = 0.5 (silica, 60% ethyl acetate in petroleum ether); FT-IR (film): $\tilde{\nu}_{max}$ = 3526, 2995, 1733 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.10 (m, 2H, Ar), 7.53 (m, 5H, Ar), 7.20 (m, 2H, Ar), 6.66 (d, J = 10 Hz, 1H, HCOAc), 6.429 (s, 1H, HCOBz), 5.768 (d, J = 10.0 Hz, 1H, HCOAc), 2.51 (brs, 1H, OH), 2.41 (m, 1H, CH_2C=C), 2.325 (m, 1H, CH_2C=C), 2.20 (s, 3H, OAc), 2.13 (s, 3H, OAc), 1.85 (m, 1H, CH_2), 1.73 (s, 3H, CH_3C=C), 1.37 (m, 1H, CH_2), 1.09 (s, 3H, CH_3), 0.83 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.3, 169.5, 165.7, 140.8, 138.9, 136.0, 133.2, 129.8, 129.6, 128.6, 128.4, 128.2, 126.7, 124.7, 124.3, 79.2, 77.5, 74.1, 72.2, 41.4, 29.8, 27.3, 26.1, 21.1, 20.9, 20.2, 19.6; HRMS (FAB): calcd for $C_{29}H_{32}O_7$ [M + Na$^+$] 515.2024, found 515.2050.

Enone 15: To a dry flask were added pyridinium chlorochromate (1.0 g, 4.64 mmol; freshly prepared is best), Celite (1 g), anhydrous sodium acetate (700 mg, 8.53 mmol), benzene (25 mL), and the diacetate **14** (50 mg, 0.1 mmol). The solution was heated to 70 °C and the reaction progress was carefully monitored by thin-layer chromatography (1–2.5 h for completion). The reaction mixture was cooled to 23 °C, diluted with ether (25 mL), and filtered through Florisil. Concentration and purification of the residue by flash chromatography (silica, ether/petroleum ether) gave **15** as a colorless solid (28 mg, 55%); R_f = 0.6 (silica, 80% ether in petroleum ether); FT-IR (film): $\tilde{\nu}_{max}$ = 3502, 2968, 2926, 1749, 1674 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.09 (m, 2H, Ar), 7.64–7.36 (m, 5H, Ar), 7.21 (m, 2H, Ar), 6.81 (d, J = 10.0 Hz, 1H, HCOAc), 6.55 (s, 1H, HCOBz), 5.81 (d, J = 10.0 Hz, 1H, HCOAc), 3.15 (d, J = 19.5 Hz, 1H, CH_3), 2.77 (d, J = 19.5, 1H, CH_2), 2.24 (s, 3H, OAc), 2.20, (s, 3H, OAc), 1.82 (s, 3H, CH_3C=C), 1.22 (s, 3H, CH_3), 1.08 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.6, 170.2, 169.4, 165.7, 150.3, 140.3, 138.1, 134.9, 133.7, 129.7, 129.3, 128.8, 128.7, 127.8, 125.3, 124.4, 77.9, 77.5, 73.5, 70.9, 42.9, 42.8, 32.1, 21.0, 20.9, 19.3, 12.7; HRMS (FAB): calcd for $C_{29}H_{30}O_{38}$ [M + Na$^+$] 529.1838, found 529.1840.

Alcohol 16: Sodium borohydride (excess) was added portionwise to a stirred solution of ketone **15** (50 mg, 0.099 mmol) in methanol (5 mL) at 0 °C, and the resulting mixture was stirred for 45 min and then quenched by dilution with ether (20 mL) and slow addition of aqueous ammonium chloride (5 mL). The aqueous phase was extracted with ether (2 × 5 mL), and the combined organic layers were washed with brine (5 mL), dried over magnesium sulfate, and concentrated. The crude product was found to be a 8:1 mixture of epimers (^{1}H NMR) in favor of the α isomer. Purification by preparative thin-layer chromatography (20% ethyl acetate in benzene) gave alcohol **16** (42 mg, 84%) as a colorless solid; R_f = 0.4 (silica, 30% ethyl acetate in petroleum ether); FT-IR (film): $\tilde{\nu}_{max}$ = 3509, 2926, 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 8.15 (m, 2H, Ar), 7.20–7.70 (m, 7H, Ar), 6.69 (d, J = 10.0 Hz, 1H, HCOAc), 6.47 (s, 1H, HCOBz), 5.81 (d, J = 10.0 Hz, 1H, HCOAc), 4.33 (m, 1H, *H*COH), 2.58 (dd, J = 19.5, 10.0 Hz, 1H, CH_2), 2.27 (brs, 1H, OH), 2.42 (dd, J = 19.5, 3.5 Hz, 1H, CH_2), 2.21 (s, 3H, OAc), 2.14 (s, 3H, OAc), 1.75 (s, 3H, CH_3C=C), 1.09 (s, 3H, CH_3), 1.03 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2, 169.4, 165.5, 142.8, 140.1, 136.5, 133.4, 130.6, 129.6, 129.5, 128.5, 127.8, 127.6, 125.7, 124.1, 77.1, 76.6, 74.05, 71.82, 67.62, 39.7, 29.6, 27.5, 21.0, 20.8, 19.8, 15.3; HRMS (FAB): calcd for $C_{29}H_{32}O_8$ [M + H$^+$] 509.2175, found 509.2175.

Coupled products 18 and 18′: Sodium bis(trimethylsilyl)amide (236 µL, 1 M solution in THF, 0.236 mmol) was added dropwise to a stirring mixture of alcohol **16** (racemic, 40 mg, 0.079 mmol) and the β-lactam **17** (optically pure, 60.0 mg, 0.157 mmol) in THF (2 mL) at −78 °C. The reaction mixture was stirred for 20 min and was then quenched with aqueous ammonium chloride at −78 °C. The biphasic solution was separated and the organic layer was washed with aqueous ammonium chloride (1 mL) and brine (1 mL), and dried over magnesium sulfate. After filtration and concentration, the material was purified by preparative thin-layer chromatography (silica, 50% ether in hexane) to yield the two expected diastereomers (**18**: 19 mg, 37%, and **18′**: 19 mg, 37%).

Analysis of 18: Colorless solid; R_f = 0.45 (silica, 80% ether in petroleum ether); $[\alpha]_D^{22}$ = 26.67 (c 1.5, $CHCl_3$); FT-IR (film): $\tilde{\nu}_{max}$ = 3429, 3956, 1747, 1668 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.27 (d, J = 8.0 Hz, 2H, Ar), 8.13 (d, J = 8.0 Hz, 1H, Ar), 7.87 (m, 2H, Ar), 7.60–7.20 (m, 14H, Ar), 7.14 (d, J = 9.0 Hz, 1H, NH), 6.73 (d, J = 10.0 Hz, 1H, HCOAc), 6.43 (s, 1H, HCOBz), 5.81 (d, J = 10.0 Hz, 2H, HCOAc and *H*CNHBz), 5.64 (m, 1H, HCC=C), 4.33 (d, J = 2.0 Hz, 1H, HCOTES), 2.58 (s, 1H, OH), 2.41 (m, 2H, CH_2), 2.20 (s, 3H, OAc), 2.13 (s, 3H, OAc), 1.73 (s, 3H, CH_3C=C), 1.07 (s, 3H, CH_3), 0.98 (s, 3H, CH_3), 0.71 (t, J = 8.0 Hz, 9H, CH_3CH_2Si), 0.30 (m, 6H, CH_3CH_2Si); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 170.2, 169.4, 167.0, 165.8, 139.4, 139.1, 138.3, 135.6, 134.8, 133.2, 132.0, 131.7, 130.2, 129.5, 128.8, 128.6, 128.4, 128.0, 127.6, 127.1, 127.05, 127.0, 126.2, 124.6, 77.2, 77.7, 75.1, 74.2, 71.9, 70.4, 55.5, 42.2, 35.8, 27.0, 21.1, 21.0, 20.0, 15.3, 6.4, 4.2; HRMS (FAB): calcd for $C_{51}H_{59}O_{11}NSi$ [M + Cs$^+$] 1022.2912, found 1022.2930.

Analysis of 18′: Colorless solid; R_f = 0.32 (silica, 80% ether in petroleum ether); $[\alpha]_D^{22}$ = −24.43 (c 1.4, $CHCl_3$); FT-IR (film): $\tilde{\nu}_{max}$ = 3422, 2955.1, 1746, 1663, 1025 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 (d, J = 7.0 Hz, 2H, Ar), 8.69 (d, J = 7.0 Hz, 2H, Ar), 7.75–7.25 (m, 15H, Ar), 7.09 (d, J = 8.5 Hz, 1H, NH), 6.67 (d, J = 10.0 Hz, 1H, HCOAc), 6.46 (s, 1H, HCOBz), 5.81 (d, J = 10.0 Hz, 1H, HCOAc), 5.54 (m, 1H, HCC=C), 5.18 (d, J = 8.5 Hz, 1H, *H*CNHBz), 4.37 (d, J = 1.5 Hz, 1H, HCOTES), 2.61 (s, 1H, OH), 2.56 (dd, J = 10.3, 6.4 Hz, 1H, CH_2), 2.30 (dd, J = 10.3, 2.7 Hz, 1H, CH_2), 2.20 (s, 3H, OAc), 2.10 (s, 3H, OAc), 1.74 (s, 3H, CH_3C=C), 1.05 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 0.84 (t, J = 8.0 Hz, 9H, CH_3CH_2Si), 0.47 (m, 6H, CH_3CH_2Si); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.4, 170.1, 169.5, 166.5, 165.6, 139.1, 138.9, 138.7, 136.1, 134.2, 133.5, 132.1, 131.6, 129.6, 129.0, 128.7, 128.6, 128.5, 127.7, 127.6, 127.2, 127.0, 126.4, 125.5, 125.3, 76.9, 76.7, 75.3, 74.3, 71.9, 70.6, 55.9, 42.0, 36.6, 27.6, 21.0, 20.9, 19.8, 15.6, 6.5, 4.3; HRMS (FAB): calcd for $C_{51}H_{59}O_{11}NSi$ [M + Cs$^+$] 1022.2912, found 1022.2935.

Taxoids 2a and 2a′: HF·pyr (150 µL) was added to a stirred solution of silyl ether **18** (19 mg, 0.021 mmol; **18′** for taxoid **2a′**) in THF (1 mL) (polyethylene vessel). The reaction mixture was stirred for 30 min and then quenched by being first diluted with ether (3 mL) and then poured into stirred aqueous sodium bicarbonate (5 mL) and allowed to react for 10 min. The organic layer was washed with aqueous sodium bicarbonate (5 mL) and brine (2 mL), and dried over magnesium sulfate. After filtration and concentration, the crude compound was purified by column chromatography (silica, ether) to yield the pure alcohol **2a** (**2a′**).

Properties of 2a: Yield 14 mg, 89%; colorless solid; R_f = 0.43 (silica, ether); $[\alpha]_D^{22}$ = 52.33 (c 0.30, $CHCl_3$); FT-IR (film): $\tilde{\nu}_{max}$ = 3729, 3417, 1654, 1515, 1027 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.30 (d, J = 8.0 Hz, 2H, Ar), 8.18 (d, J = 8.0 Hz, 1H, Ar), 7.84 (d, J = 8.0 Hz, 2H, Ar), 7.60–7.20 (m,

14H, Ar), 6.99 (d, $J = 9.5$ Hz, 1H, NH), 6.73 (d, $J = 10.0$ Hz, 1H, HCOAc), 6.45 (s, 1H, HCOBz), 5.88 (d, $J = 9.5$ Hz, 1H, *H*CNHBz), 5.79 (d, $J = 10.0$ Hz, 1H, HCOAc), 5.72 (m, 1H, HCC=C), 4.47 (s, 1H, *H*COH), 3.26 (brs, 1H, OH), 2.66 (s, 1H, OH), 2.61 (dd, $J = 15.5$, 4.0 Hz, 1H, CH_2), 2.38 (dd, $J = 15.5$, 10.5 Hz, 1H, CH_2), 2.20 (s, 3H, OAc), 2.13 (s, 3H, OAc), 1.75 (s, 3H, CH_3C=C), 1.05 (s, 3H, CH_3), 0.91 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.0$, 170.4, 169.4, 166.9, 139.3, 138.9, 137.8, 135.5, 134.4, 133.3, 132.5, 131.9, 130.2, 129.6, 128.9, 128.8, 128.5, 128.5, 127.9, 126.8, 127.2, 127.1, 127.0, 126.6, 124.7, 77.1, 76.7, 74.2, 73.2, 71.9, 71.7, 54.0, 42.4, 35.4, 27.2, 21.1, 20.9, 20.0, 15.2; HRMS (FAB): calcd for $C_{45}H_{45}O_{11}N$ [$M + Cs^+$] 908.2047, found 908.2058.

Properties of 2a′: Yield 85%; colorless solid; $R_f = 0.32$ (silica, ether); $[\alpha]_D^{22} = -16.00$ (c 0.50, $CHCl_3$); FT-IR (film): $\tilde{\nu}_{max} = 3423$, 2929, 1737, 1658, 1237 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.07$ (d, $J = 8.0$ Hz, 2H, Ar), 7.69 (d, $J = 8.0$ Hz, 2H, Ar), 7.65–7.20 (band, 15H, Ar), 7.00 (d, $J = 9.0$ Hz, 1H, NH), 6.66 (d, $J = 10.0$ Hz, 1H, HCOAc), 6.42 (s, 1H, HCOBz), 5.77 (d, $J = 10.0$ Hz, 1H, HCOAc), 5.59 (brd, $J = 8.0$ Hz, 1H, HCC=C), 5.33 (dd, $J = 9.0$, 2.0 Hz, 1H, *H*CNHBz), 4.50 (dd, $J = 4.0$, 2.5 Hz, 1H, *H*COH), 3.16 (d, $J = 4.0$ Hz, 1H, OH), 2.72 (s, 1H, OH), 2.54 (dd, $J = 15.0$, 10.0 Hz, 1H, CH_2), 2.22 (dd, $J = 15.0$, 3.5 Hz, 1H, CH_2), 2.18 (s, 3H, OAc), 2.11 (s, 3H, OAc), 1.73 (s, 3H, CH_3C=C), 1.04 (s, 3H, CH_3), 0.98 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 171.6$, 170.2, 169.5, 166.6, 165.8, 38.8, 138.7, 138.0, 127.3, 127.0, 126.9, 125.5, 125.2, 76.9, 76.8, 74.2, 73.5, 71.97, 71.9, 54.8, 42.1, 36.4, 27.6, 21.1, 21.0, 19.8, 15.6; HRMS (FAB): calcd for $C_{45}H_{45}O_{11}$ [$M + Cs^+$] 908.2047, found 908.2038.

Diol 20: Benzyl bromide (105 g, 618 mmol) was added to a solution of the diacid **19** (23 g, 123 mmol) and potassium carbonate (119 g, 865 mmol) in dimethylformamide (400 mL) at 25 °C and the solution was then heated to 50 °C for 1.5 h. The dimethylformamide was removed in vacuo and the resulting residue was diluted with ether (500 mL) and washed with water (3 × 100 mL) and brine (100 mL), and dried over magnesium sulfate. After filtration and concentration, the residue was redissolved in ether (800 mL) and cooled to −78 °C. Lithium aluminum hydride (23 g, 600 mmol) was added portionwise and the mixture was allowed to react for 1 h. The mixture was carefully quenched at −78 °C by dilution with ether (500 mL), dropwise addition of water (23 mL), and being warmed to 0 °C and stirred for 30 min. Aqueous sodium hydroxide (3 N, 23 mL) was then added slowly at that temperature, and the reaction mixture was stirred for 1 h at ambient temperature. Water (69 mL) was then added slowly with vigorous stirring; the reaction was allowed to continue for 20 min. The precipitate formed was filtered through silica and the resulting solution was concentrated. Purification (silica, ether/hexane) was carried out by column chromatography to afford compound **20** as a colorless oil (19 g, 73%); $R_f = 0.20$ (60% ether in hexane); IR (film): $\tilde{\nu}_{max} = 3337$, 2881, 1586, 1459, 1263 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.41$ (m, 3H, Ar), 7.35 (m, 1H, Ar), 7.27 (m, 1H, Ar), 6.99 (m, 2H, Ar), 5.17 (s, 2H, CH_2O), 4.89 (d, $J = 6.0$ Hz, 2H, CH_2O), 4.73 (d, $J = 6.0$ Hz, 2H, CH_2O), 2.89 (brs, 1H, OH), 2.78 (brs, 1H, OH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 156.8$, 141.3, 136.7, 129.1, 128.5, 127.9, 127.2, 122.1, 112.3, 70.5, 63.8, 56.1; HRMS (FAB): calcd for $C_{15}H_{16}O_3$ [$M + Cs^+$] 377.0154, found 377.0148.

Monosilyl ether 21: *tert*-Butyldiphenylsilyl chloride (6.8 g, 24.8 mmol) was added to a solution of the diol **20** (5.5 g, 22.5 mmol) and imidazole (2.3 g, 33.8 mmol) in methylene chloride (200 mL) at 0 °C. The reaction mixture was warmed to 25 °C, stirred for 30 min, worked up by addition of ether (200 mL), and washed with H_2O (50 mL) and brine (50 mL). The organic solution was then dried over magnesium sulfate and filtered. Column chromatography (silica, ether/hexane) permitted separation of the mixture (diol and the two monosilyl ethers) to yield the desired monosilyl ether **21** (5.3 g, 49%). Colorless solid, m.p. 54–56 °C (from ether/hexane); $R_f = 0.45$ (50% ether in hexane); IR (film): $\tilde{\nu}_{max} = 3474$, 3067, 2932, 2858, 2360 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.71$ (m, 4H, Ar), 74.6 (m, 4H, Ar), 7.41 (m, 6H, Ar), 7.35 (m, 1H, Ar), 7.22 (m, 1H, Ar), 6.96 (m, 1H, Ar), 6.88 (m, 1H, Ar), 5.15 (s, 2H, CH_2O), 4.85 (d, $J = 6.5$ Hz, 2H, CH_2O), 4.81 (s, 2H, CH_2O), 3.00 (t, $J = 6.5$ Hz, 1H, OH), 1.07 (s, 9H, *t*BuSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 156.9$, 140.0, 136.8, 135.6, 132.8, 129.8, 128.6, 128.1, 127.9, 127.7, 127.2, 121.3, 111.8, 70.4, 64.8, 56.6, 26.7; HRMS (FAB): calcd for $C_{31}H_{34}O_3Si_1$ [$M + Na^+$] 505.2175, found 505.2173.

C-Ring Aldehyde 22: Pyridinium dichromate (8.11 g, 21.6 mmol) was added to a suspension of alcohol **21** (5.2 g, 10.8 mmol) and 4 Å molecular sieves (15 g) in methylene chloride (100 mL) at 0 °C, and the resulting mixture was allowed to reach ambient temperature and stirred for 1.5 h. The reaction mixture was filtered through a pad of silica gel (washed with 200 mL of ether), concentrated, and purified by flash chromatography (silica, ether/hexane) to give the aldehyde **22** (4.2 g, 82%) as a white solid; m.p. 99–101 °C (from ether/hexane); $R_f = 0.70$ (80% ether in hexane); IR (film): $\tilde{\nu}_{max} = 3068$, 2932, 1980, 1585, 1467 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 10.20$ (s, 1H, CHO), 7.73 (m, 2H, Ar), 7.69 (m, 2H, Ar), 7.60 (m, 2H, Ar), 7.38 (m, 11H, Ar), 7.00 (m, 1H, Ar), 5.20 (s, 2H, CH_2O), 5.18 (s, 2H, CH_2O), 1.14 (s, 9H, *t*BuSi); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 191.6$, 162.0, 146.0, 136.0, 135.4, 135.2, 133.4, 129.5, 128.6, 128.2, 127.6, 127.2, 121.2, 118.3, 110.9 70.6, 64.1, 26.8, 19.4; HRMS (FAB): calcd for $C_{31}H_{32}O_3Si$ [$M + H^+$]: 481.2199, found 481.2199.

Coupled product 23: Same procedure as for the preparation of compound **6** (same scale, 86% yield); white foam; $R_f = 0.41$ (silica, 20% ether in hexane); IR (film): $\tilde{\nu}_{max} = 3549$, 2953, 2858, 1585, 1463, 1380 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 87.68$ (m, 4H, Ar), 7.38 (m, 11H, Ar), 7.25 (dd, $J = 8.0$, 8.0 Hz, 1H, Ar), 7.11 (d, $J = 8.0$ Hz, 1H, Ar), 6.97 (d, $J = 8.0$ Hz, 1H, Ar), 5.75 (d, $J = 10.0$ Hz, 1H, HCOH), 5.34 (s, 1H, HC=C), 5.14 (s, 2H, CH_2O), 4.77 (s, 2H, CH_2O), 4.21 (s, 2H, CH_2–O), 4.15 (d, $J = 10.0$ Hz, 1H, *H*COH), 2.57 (d, $J = 22.0$ Hz, 1H, CH_2), 2.40 (d, $J = 22.0$ Hz, 1H, CH_2), 1.74 (s, 3H, CH_3–C=C), 1.29 (s, 3H, CH_3), 1.15 (s, 3H, CH_3), 1.09 (s, 9H, *t*BuSi), 0.94 (s, 9H, *t*BuSi), 0.12 (s, 6H, $(CH_3)_2Si$); HRMS (FAB): calcd for $C_{47}H_{62}O_4Si_2$ [$M + Na^+$] 769.4084, found 769.4070.

Epoxide 24: Same procedure as for the preparation of compound **7** (same scale, 85%); white foam; $R_f = 0.29$ (silica, 20% ether in hexane); IR (film): $\tilde{\nu}_{max} = 3517$, 2932, 2858, 1584, 1465, 1383, 1254 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.68$ (m, 4H, Ar), 7.48 (m, 2H, Ar), 7.42 (m, 2H, Ar), 7.37 (m, 7H, Ar), 7.32 (m, 1H, Ar), 7.24 (m, 1H, Ar), 6.92 (m, 1H, Ar), 5.63 (d, $J = 8.5$ Hz, 1H, *H*COH), 5.10 (dd, $J = 20.5$, 11.5 Hz, 2H, CH_2O), 4.89 (d, $J = 13.0$ Hz, 1H, CH_2O), 4.74 (d, $J = 13.0$ Hz, 1H, CH_2O), 4.29 (d, $J = 8.0$ Hz, 1H, OH), 4.10 (dd, $J = 19.0$, 11.0 Hz, 2H, CH_2O), 2.45 (brs, 1H, HCO), 2.12 (d, $J = 19.0$ Hz, 1H, CH_2), 1.92 (d, $J = 19.0$ Hz, 1H, CH_2), 1.59 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 1.17 (s, 3H, CH_3), 1.09 (s, 9H, *t*BuSi), 0.90 (s, 9H, *t*BuSi), 0.07 (s, 3H, CH_3Si), 0.06 (s, 3H, CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 157.2$, 140.1, 136.7, 135.5, 135.4, 134.3, 132.9, 129.7, 128.5, 128.4, 128.0, 127.7, 127.5, 125.4, 124.7, 120.5, 112.0, 71.1, 69.4, 65.8, 64.1, 58.9, 57.3, 39.4, 31.8, 26.7, 25.9, 24.7, 22.5, 19.6, 19.2, 18.3; HRMS (FAB): calcd for $C_{47}H_{62}O_5Si_2$ [$M + Cs^+$] 895.3190, found 895.3221.

Carbonate diol 26: The hydroxyepoxide **24** was treated with lithium aluminum hydride by the same procedure used for the preparation of compound **8**. The resulting tetraol was then subjected to the following carbonate formation procedure: Carbonyl diimidazole (395 g, 2.43 mmol) was added to a solution of the crude tetraol (100 mg, 0.243 mmol) in dry acetonitrile (8 mL) at 25 °C and the solution was then refluxed for 2 h. The reaction mixture was worked up by dilution with petroleum ether (20 mL) and washing with cold (0–5 °C) 10% aqueous hydrogen chloride (3 × 5 mL; this procedure must be carried out carefully and with TLC monitoring so as to assure complete hydrolysis of the mixed carbonates), aqueous sodium bicarbonate (10 mL), and brine (10 mL). The organic solution was dried over magnesium sulfate and concentrated, and the residue was purified by flash chromatography (silica, ethyl acetate/hexane) to give **26** as a white foam (67 mg, 63%); $R_f = 0.30$ (silica, 50% ethyl acetate in hexane); IR (film): $\tilde{\nu}_{max} = 3386$, 2901, 1779, 1585, 1464 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 7.45$ (m, 2H, Ar), 7.37 (m, 2H, Ar), 7.31 (m, 1H, Ar), 7.23 (m, 1H, Ar), 6.93 (d, $J = 8.5$ Hz, 1H, Ar), 6.89 (d, $J = 8.5$ Hz, 1H, Ar), 6.12 (s, 1H, $CHCO_2$), 5.22 (s, 2H, CH_2O), 4.66 (dd, $J = 13.0$, 7.0 Hz, 1H, CH_2O), 4.52 (dd, $J = 13.0$, 4.5 Hz, 1H, CH_2O), 4.32 (dd, $J = 11.0$, 4.0 Hz, 1H, CH_2O), 4.17 (dd, $J = 11.0$, 4.0 Hz, 1H, CH_2O), 2.53 (m, 1H, OH), 2.15 (m, 1H, CH_2), 2.01 (m, 1H, CH_2), 1.92 (m, 1H, CH_2), 1.83 (m, 1H, OH), 1.66 (s, 3H, CH_3C=C), 1.39 (m, 1H, CH_2), 1.36 (s, 3H, CH_3), 1.23 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 158.0$, 155.8, 140.9, 136.2, 134.6, 133.9, 130.4, 128.5, 127.9, 127.5, 122.1, 121.8, 113.3, 88.0, 78.1, 70.9, 62.6, 58.3, 43.0, 29.4, 23.9, 19.1; HRMS (FAB): calcd for $C_{26}H_{30}O_6$ [$M + Na^+$] 461.1940, found 461.1952.

***Dialdehyde* 27**: Same procedure as for the preparation of compound **11** (same scale, yield 71%); white foam; $R_f = 0.50$ (silica, 50% ethyl acetate in hexane); IR (film): $\tilde{\nu}_{max} = 2981$, 1793, 1672, 1585, 1462, 1264 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 10.10$ (s, 1H, HCO), 10.02 (s, 1H, HCO), 7.53–7.26

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(m, 8H, Ar), 5.28 (s, 1H, $HCOCO_2$), 2.35 (m, 1H, CH_2), 1.99 (s, 3H, $CH_3C{=}C$), 1.98 (m, 1H, CH_2), 1.80 (m, 1H, CH_2), 1.60 (m, 1H, CH_2), 1.44 (s, 3H, CH_3), 1.42 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.8, 191.9, 158.6, 155.4, 153.1, 137.7, 135.5, 131.0, 128.8, 128.5, 128.4, 127.7, 123.6, 119.0, 88.7, 74.4, 71.5, 41.8, 32.0, 28.5, 23.8, 22.1, 20.6, 18.6, 14.2; HRMS (FAB): calcd for $C_{26}H_{26}O_6$ [M + Na^+] 457.1627, found 457.1636.

McMurry product 28: Same procedure as for the preparation of compound **12** (same scale, 39%); white solid; m.p. 190–195 °C (methylene chloride/hexane); R_f = 0.20 (silica, 50% ethyl acetate in hexane); IR (film): $\tilde{\nu}_{max}$ = 3465, 2914, 1786, 1581, 1461 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.48 (m, 2H, Ar), 7.41 (m, 2H, Ar), 7.33 (m, 1H, Ar), 7.25 (m, 2H, Ar), 6.98 (d, J = 8.0 Hz, 1H, Ar), 5.61 (s, 1H, $HCOCO_2$), 5.16 (d, J = 11.5 Hz, 1H, OCH_2Ph), 5.08 (d, J = 8.5 Hz, 1H, $HCOH$), 5.06 (d, J = 11.5 Hz, 1H, $HCOH$), 3.50 (brs, 1H, OH), 2.73 (m, 1H, CH_2), 2.64 (s, 1H, OH), 2.32 (m, 1H, CH_2), 1.82 (m, 1H, CH_2), 1.56 (s, 3H, $CH_3C{=}C$), 1.42 (m, 1H, CH_2), 1.16 (s, 3H, CH_3), 0.79 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 156.1, 154.4, 142.3, 140.0, 136.4, 130.2, 128.9, 128.6, 127.9, 127.1, 120.5, 118.8, 113.5, 93.1, 79.3, 78.8, 74.8, 71.6, 40.5, 29.4, 26.2, 23.9, 21.0, 20.4; HRMS (FAB): calcd for $C_{26}H_{28}O_6$ [M + Na^+] 459.1784, found 459.1762.

Benzoate triol 29: Phenyllithium (600 µL, 1.2 mmol of a 2 M solution in cyclohexane/ether) was added to a stirred solution of diol **28** (65 mg, 0.197 mmol), and HMPA (500 µL) in THF (17 mL) at −78 °C. The resulting mixture was stirred for 30 min and was then quenched at −78 °C with aqueous ammonium chloride (15 mL). The solution was diluted with ether (50 mL), washed with brine (10 mL), dried over magnesium sulfate, and concentrated. The residue was purified by flash chromatography (silica, ethyl acetate–petroleum ether) to afford **29** as a white solid (64 mg, 80%); R_f = 0.5 (silica, 50% ethyl acetate in petroleum ether); IR (film): $\tilde{\nu}_{max}$ = 3456, 2945, 1704, 1450, 1283 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.05 (m, 1H, Ar), 7.58–7.41 (m, 4H, Ar), 7.15 (m, 2H, Ar), 6.31 (s, 1H, HCOBz), 5.41 (d, J = 9.0 Hz, 1H, $HCOH$), 4.50 (d, J = 9.0 Hz, 1H, $HCOH$), 2.41 (m, 1H, $CH_2C{=}C$), 2.28 (m, 1H, $CH_2C{=}C$), 1.84 (m, 1H, CH_2), 1.73 (s, 3H, $CH_3C{=}C$), 1.36 (s, 1H, CH_2), 1.15 (s, 3H, CH_3), 0.62 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.9, 139.6, 138.5, 138.1, 133.2, 131.4, 129.8, 129.5, 128.4, 126.9, 126.5, 124.4, 123.8, 79.7, 79.2, 74.3, 74.1, 41.5, 29.8, 27.2, 26.1, 20.3, 19.6, 14.1; HRMS (FAB): calcd for $C_{25}H_{28}O_5$ [M + Na^+] 431.1834, found 431.1830.

Monosilylether 31: *tert*-Butyldiphenylsilyl chloride (50.72 g, 184.5 mmol) was added to a solution of diol **30** (31.0 g, 184.5 mmol) and imidazole (18.8 g, 276.7 mmol) in methylene chloride (1 L) at 0 °C. The reaction mixture was stirred at this temperature for 1 h and then washed with aqueous sodium bicarbonate (200 mL). The organic layer was dried over magnesium sulfate, concentrated, and purified by flash chromatography (silica, ether/hexane) to give silyl ether **31** (25.0 g, 33%) as a viscous liquid: R_f = 0.46 (silica, 50% ether in hexane); IR (thin film): $\tilde{\nu}_{max}$ = 3451, 2931, 2856, 1588, 1472, 1428, 1390, 1264 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.71 (m, 4H, Ar), 7.45 (m, 2H, Ar), 7.40 (m, 4H, Ar), 7.23 (t, 1H, J = 8.0 Hz, Ar), 6.90 (d, 1H, J = 8.0 Hz, Ar), 6.85 (d, 1H, J = 8.0 Hz, Ar), 4.81 (s, 2H, CH_2), 3.89 (s, 3H, CH_3), 1.04 (s, 9H, *t*BuSi); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.8, 140.0, 135.6, 132.9, 129.9, 128.7, 127.8, 120.9, 110.3, 64.9, 56.4, 26.8; HRMS (FAB): calcd for $C_{25}H_{30}O_3Si$ [M + Na^+] 429.1873, found 429.1862.

Aldehyde 32: Pyridinium dichromate (35.5 g, 94.48 mmol) was added to a suspension of alcohol **31** (19.2 g, 47.24 mmol) and 4 Å molecular sieves (35 g) in methylene chloride (460 mL) at 0 °C, and the mixture was stirred for 30 min at that temperature and then at 25 °C for an additional 2 h. The solution was filtered through a pad of silica gel (washed with 200 mL of ether), concentrated, and purified by flash chromatography (silica, ether/hexane) to give aldehyde **32** (16.43 g, 86%) as a colorless solid; R_f = 0.31 (silica, 20% ether in hexane); IR (thin film): $\tilde{\nu}_{max}$ = 3070, 2958, 2856, 1681 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 10.3 (s, 1H, HCO), 7.69 (m, 5H, Ar), 7.42 (m, 2H, Ar), 7.37 (t, 4H, J = 8.0 Hz, Ar), 6.93 (d, 1H, J = 8.0 Hz, Ar), 5.18 (s, 2H, CH_2), 3.89 (s, 3H, CH_3OAr), 1.14 (s, 9H, *t*BuSi); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 191.6, 162.8, 145.9, 135.4, 133.4, 129.6, 127.7, 120.9, 117.9, 109.5, 64.1, 55.8, 26.9, 19.3; HRMS (FAB): calcd for $C_{25}H_{28}O_3Si$ [M + Cs^+] 537.0873, found 537.0862.

Coupled product 33: Same procedure as for the preparation of compound **6** (same scale, 85%); colorless foam; R_f = 0.45 (silica, 20% ether in hexane); IR (film): $\tilde{\nu}_{max}$ = 2955, 2856, 1684, 1583, 1472 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.67 (m, 4H, Ar), 7.41 (m, 2H, Ar), 7.36 (m, 4H, Ar), 7.25 (t, J = 8.0 Hz, Ar), 7.08 (d, J = 8.0 Hz, 1H, Ar), 6.90 (d, J = 8.0 Hz, 1H, Ar), 5.67 (d, J = 10.5 Hz, 1H, HC=C), 5.29 (brs, 1H, HC=C), 4.74 (s, 2H, CH_2O), 4.22 (d, J = 10.5 Hz, 1H, CH_2O), 4.18 (d, J = 10.5 Hz, 1H, OH), 4.17 (d, J = 10.5 Hz, 1H, CH_2O), 3.85 (s, 3H, CH_3OAr), 2.49 (d, J = 19.5 Hz, 1H, CH_2), 2.38 (d, J = 19.5 Hz, 1H, CH_2), 1.70 (s, 3H, $CH_3C{=}C$), 1.34 (s, 3H, CH_3), 1.07 (s, 12H, CH_3 and *t*BuSi), 0.92 (s, 9H, *t*BuSi), 0.10 (s, 6H, $(CH_3)_2Si$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.4, 143.9, 139.2, 136.4, 135.6, 133.2, 129.6, 129.0, 128.7, 127.7, 121.2, 120.6, 110.6, 69.6, 64.1, 58.9, 55.6, 38.9, 33.5, 27.8, 26.8, 26.0, 25.9, 19.2, 19.1, −5.3; HRMS (FAB): calcd for $C_{41}H_{58}O_4Si_2$ [M + Cs^+] 803.2928, found 803.2956.

Epoxide 34: Same procedure as for the preparation of compound **7** (same scale, 86%); white foam; R_f = 0.45 (silica, 20% ether in hexane); IR (film): $\tilde{\nu}_{max}$ = 3488, 2929, 2856, 1585, 1472, 1256 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.68 (m, 4H, Ar), 7.43 (m, 2H, Ar), 7.37 (m, 4H, Ar), 7.26 (m, 1H, Ar), 7.15 (m, 1H, Ar), 6.87 (m, 1H, Ar), 5.59 (d, J = 8.5 Hz, 1H, $HCOH$), 4.92 (d, J = 13.0 Hz, 1H, CH_2O), 4.74 (d, J = 13.0 Hz, 1H, CH_2O), 4.13 (m, 3H, OH and CH_2O), 3.85 (s, 3H, CH_3OAr), 2.51 (s, 1H, epoxide H), 2.18 (d, J = 19.5 Hz, 1H, CH_2), 2.06 (d, J = 19.5 Hz, 1H, CH_2), 1.61 (s, 3H, $CH_3C{=}C$), 1.45 (s, 3H, CH_3), 1.12 (s, 3H, CH_3), 1.09 (s, 9H, *t*BuSi), 0.91 (s, 9H, *t*BuSi), 0.07 (s, 6H, $(CH_3)_2Si$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.9, 140.0, 135.5, 134.3, 133.0, 129.7, 128.4, 127.7, 125.3, 124.7, 120.3, 110.8, 68.8, 66.1, 64.1, 58.9, 57.5, 56.0, 39.5 32.0, 26.7, 25.9, 24.8, 22.3, 19.6, 19.1, 18.2; HRMS (FAB): calcd for $C_{41}H_{58}O_5Si_2$ [M + Na^+] 709.3721, found 709.3698.

Diol 35: Same procedure as for the preparation of compound **26** (same scale, 61%); white foam; R_f = 0.45 (silica, 20% ether in hexane); IR (film): $\tilde{\nu}_{max}$ = 3388, 2916, 1586, 1468, 1266 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.34 (t, J = 8.0 Hz, 1H, Ar), 6.95 (d, J = 8.0 Hz, 1H, Ar), 6.91 (d, J = 8.0 Hz, 1H, Ar), 6.07 (s, 1H, $HCOCO_2$), 4.64 (dd, J = 13.0, 7.0 Hz, 1H, CH_2OH), 4.31 (dd, J = 11.5, 4.0 Hz, 1H, CH_2OH), 4.15 (dd, J = 11.5, 4.5 Hz, 1H, CH_2OH), 2.36 (m, 1H, OH), 2.11 (m, 1H, $CH_2C{=}C$), 1.96 (m, 1H, $CH_2C{=}C$), 1.79 (m, 1H, CH_2), 1.68 (m, 1H, OH), 1.64 (s, 3H, $CH_3C{=}C$), 1.34 (s, 3H, CH_3), 1.29 (m, 1H, CH_2), 1.20 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.7, 156.5, 143.4, 138.6, 135.9, 133.1, 131.5, 126.3, 122.3, 112.5, 88.9, 78.8, 62.1, 58.4, 56.2, 43.7, 30.7, 29.9, 24.7, 19.3; HRMS (FAB): calcd for $C_{20}H_{26}O_6$ [M + H^+] 385.1627, found 385.1635.

Dialdehyde 36: Same procedure as for the preparation of compound **11** (same scale, 69%); white foam; R_f = 0.45 (silica, 20% ether in hexane); IR (film): $\tilde{\nu}_{max}$ = 2982, 1790, 1668, 1470 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 10.09 (s, 1H, HCO), 10.03 (s, 1H, HCO), 7.63 (t, J = 8.0 Hz, 1H, Ar), 7.44 (d, J = 8.0 Hz, 1H, Ar), 7.28 (d, J = 8.0 Hz, 1H, Ar), 7.09 (s, 1H, $HCOCO_2$), 3.92 (s, 3H, CH_3OAr), 2.34 (m, 1H, $CH_2C{=}C$), 1.97 (s, 3H, $CH_2C{=}C$), 1.86 (m, 1H, $CH_2C{=}C$), 1.75 (m, 1H, CH_2), 1.55 (m, 1H, CH_2), 1.42 (s, 3H, CH_3), 1.41 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 192.8, 191.8, 159.6, 155.5, 153.1, 137.6, 135.4, 131.2, 128.4, 123.4, 117.7, 88.6, 74.5, 56.3, 41.7, 32.0, 23.7, 21.9, 20.9, 18.5; HRMS (FAB): calcd for $C_{20}H_{20}O_6$ [M + Na^+] 359.1495, found 359.1489.

McMurry product 37: Same procedure as for the preparation of compound **12** (same scale, 37%); white foam; R_f = 0.45 (silica, 20% ether in hexane); IR (film): $\tilde{\nu}_{max}$ = 3441, 2937, 1790, 1463 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 7.45 (d, J = 7.5 Hz, 1H, Ar), 7.27 (t, J = 8.0 Hz, 1H, Ar), 6.92 (d, J = 8.0 Hz, 1H, Ar), 5.62 (s, 1H, $HCOCO_2$), 5.08 (dd, J = 9.0, 2.0 Hz, 1H, $HCOH$), 4.62 (dd, J = 9.0, 2.5 Hz, 1H, $HCOH$), 3.86 (s, 3H, CH_3OAr), 2.94 (d, J = 2.0 Hz, 1H, OH), 2.77 (m, 1H, $CH_2C{=}C$), 2.52 (d, J = 2.5 Hz, 1H, OH), 2.38 (m, 1H, $CH_2C{=}C$), 1.91 (m, 1H, CH_2), 1.62 (s, 3H, $CH_3C{=}C$), 1.43 (m, 1H, CH_2), 1.21 (s, 3H, CH_2), 0.80 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 157.3, 154.6, 140.0, 130.3, 129.0, 120.1, 118.5, 112.3, 93.1, 79.4, 78.8, 74.8, 56.6, 40.6, 29.5, 26.2, 23.9, 21.0, 20.5; HRMS (FAB): calcd for $C_{20}H_{24}O_6$ [M + Na^+] 383.1471, found 383.1465.

Benzoate diol 38: Same procedure as for the preparation of compound **13** (same scale, 78%); white foam; R_f = 0.45 (silica, 20% ether in hexane); IR (film): $\tilde{\nu}_{max}$ = 3448, 2963, 1702, 1582, 1459, 1288 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.06 (d, J = 8.0 Hz, 2H, Ar), 7.52 (m, 1H, Ar), 7.40 (m, 3H, Ar), 7.07 (t, J = 7.5 Hz, 1H, Ar), 6.78 (d, J = 8.0 Hz, 1H, Ar), 6.25 (s, 1H, HCOBz), 5.37 (d, J = 9.0 Hz, 1H, $HCOH$), 4.42 (d, J = 9.0 Hz, 1H,

*H*COH), 3.79 (s, 3H, CH_3OAr), 2.85 (m, 1H, $CH_2C{=}C$), 2.30 (s, 1H, $CH_2C{=}C$), 1.77 (m, 1H, CH_2), 1.67 (s, 3H, $CH_3C{=}C$), 1.48 (m, 1H, CH_2), 1.13 (s, 3H, CH_3), 0.61 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.4, 156.6, 142.4, 138.6, 132.9, 131.5, 130.3, 129.8, 128.2, 127.2, 126.6, 117.8, 110.9, 79.7, 79.6, 74.5, 74.4, 60.4, 55.8, 42.2, 30.2, 27.2, 20.2, 19.8; HRMS (FAB): calcd for $C_{26}H_{30}O_6$ [M + Cs^+] 571.1097, found 571.1086.

Benzoate diacetate 39: Same procedure as for the preparation of compound **14** (same scale, 97%); colorless solid; R_f = 0.52 (silica, 50% ethyl acetate in hexane); IR (film): $\tilde{\nu}_{max}$ = 3460, 2920, 1738, 1462, 1372, 1240 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.08 (d, J = 8.0 Hz, 2H, Ar), 7.52 (m, 1H, Ar), 7.41 (dd, J = 8.0, 8.0 Hz, 2H, Ar), 7.18 (m, 1H, Ar), 7.07 (dd, J = 8.0, 8.0 Hz, 1H, Ar), 6.80 (d, J = 7.5 Hz, 1H, Ar), 6.64 (d, J = 10.0 Hz, 1H, HCOAc), 6.35 (s, 1H, HCOBz), 5.68 (d, J = 10.0 Hz, 1H, HCOAc), 3.77 (s, 3H, CH_3OAr), 2.85 (m, 1H, $CH_2C{=}C$), 2.60 (s, 1H, OH), 2.30 (m, 1H, $CH_2C{=}C$), 2.17 (s, 3H, OAc), 2.10 (s, 3H, OAc), 1.78 (m, 1H, CH_2), 1.06 (s, 3H, CH_3), 0.79 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.1, 169.3, 165.5, 156.6, 141.5, 138.3, 132.6, 130.0, 129.5, 128.3, 128.0, 127.3, 126.7, 117.5, 111.5, 79.1, 76.5, 73.9, 72.3, 55.6, 41.7, 30.0, 27.0, 21.0, 20.7, 19.8, 19.6; HRMS (FAB): calcd for $C_{30}H_{34}O_8$ [M + Cs^+] 655.1308, found 655.1323.

Enone 40: Same procedure as for the preparation of compound **15** (25 mg scale, 53%); colorless solid; R_f = 0.44 (silica, 50% ethyl acetate in hexane); IR (film): $\tilde{\nu}_{max}$ = 3506, 2995, 1747 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.08 (m, 2H, Ar), 7.56 (m, 1H, Ar), 7.44 (m, 2H, Ar), 7.21 (m, 1H, Ar), 7.11 (m, 2H, Ar), 6.48 (s, 1H, *H*CNHBz), 5.78 (d, J = 10.0 Hz, 1H, HCOAc), 3.72 (s, 3H, CH_3OAr), 3.71 (d, J = 20.0 Hz, 1H, CH_2), 2.87 (s, 1H, OH), 2.72 (d, J = 20.0 Hz, 1H, CH_2), 2.21 (s, 3H, OAc), 2.15 (s, 3H, OAc), 1.75 (s, 3H, CH_3), 1.20 (s, 3H, CH_3), 1.05 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 199.0, 170.5, 170.2, 169.4, 150.1, 140.1, 137.3, 134.4, 133.3, 129.9, 128.4, 126.0, 120.0, 118.2, 1129, 111.2, 77.9, 73.7, 72.2, 71.4, 56.0, 44.4, 35.7, 31.7, 24.2, 20.7, 19.5, 12.5; HRMS (FAB): calcd for $C_{30}H_{32}O_9$ [M + Cs^+] 669.1101, found 669.1132.

Alcohol 41: Same procedure as for the preparation of compound **16** (10 mg scale, 43%); white foam; R_f = 0.30 (silica, 50% ethyl acetate in hexane); IR (film): $\tilde{\nu}_{max}$ = 3510, 2928, 1716 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.09 (m, J = 8.0 Hz, 2H, Ar), 7.53 (m, 1H, Ar), 7.40 (m, 2H, Ar), 7.15 (m, 1H, Ar), 6.87 (m, 1H, Ar), 6.68 (d, J = 10.0 Hz, 1H, HCOAc), 6.35 (s, 1H, *H*CNHBz), 5.75 (d, J = 10.0 Hz, 1H, HCOAc), 4.39 (br m, 1H, *H*COH), 3.77 (s, 3H, CH_3OAr), 2.90 (dd, J = 15.0, 3.5 Hz, 1H, CH_2), 2.64 (s, 1H, OH), 2.50 (dd, J = 15.0, 10.5 Hz, 1H, CH_2), 2.19 (s, 3H, OAc), 2.11 (s, 3H, OAc), 1.67 (s, 3H, CH_2), 1.00 (s, 3H, CH_3), 0.99 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.1, 169.3, 165.2, 143.0, 138.6, 133.0, 131.0, 129.7, 128.7, 128.3, 128.2, 127.1, 118.7, 118.1, 112.9, 112.1, 74.7, 72.6, 69.8, 68.2, 56.2, 56.3, 42.4, 40.1, 27.1, 21.3, 21.0, 20.1, 15.0; HRMS (FAB): calcd for $C_{30}H_{34}O_9$ [M + Cs^+] 671.1257, found 671.1268.

Coupled product 42: Same procedure as for the preparation of compound **18** (5 mg scale, 37%); colorless solid; R_f = 0.41 (silica, 80% ether in hexane); $[\alpha]_D^{22}$ = −15.91 (c 0.22, $CHCl_3$); IR (film): $\tilde{\nu}_{max}$ = 3510, 2928, 1716 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.13 (m, 2H, Ar), 7.84 (m, 2H, Ar), 7.54–7.15 (m, 14H, Ar), 7.03 (m, 1H, NH), 6.74 (d, J = 10.0 Hz, 1H, HCOAc), 6.37 (s, 1H, HCOBz), 5.91 (dd, J = 11.0, 5.0 Hz, 1H, HCC=C), 5.83 (d, J = 10.0 Hz, 1H, HCOAc), 5.55 (d, J = 8.0 Hz, 1H, *H*CNHBz), 4.34 (d, J = 1.5 Hz, HCOTES), 3.81 (s, 3H, CH_3OAr), 3.25 (s, 1H, OH), 3.10 (dd, J = 15.0, 5.0 Hz, 1H, CH_2), 2.32 (dd, J = 15.0, 11.0 Hz, 1H, CH_2), 2.20 (s, 3H, OAc), 2.12 (s, 3H, OAc), 1.70 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 0.71 (t, J = 8.0 Hz, 9H, CH_3CH_2Si), 0.32 (m, 6H, CH_3CH_2Si); ^{13}C NMR (125 MHz, C_6D_6): δ = 170.0, 169.8, 168.7, 116.8, 165.5, 158.1, 140.3, 139.3, 139.1, 135.1, 132.7, 131.7, 126.6, 77.5, 77.1, 75.5, 74.9, 72.8, 71.7, 71.2, 65.9, 58.6, 55.9, 43.7, 37.2, 26.2, 20.9, 20.6, 14.7, 6.8, 4.6; HRMS (FAB): calcd for $C_{52}H_{61}O_{12}NSi$ [M + Cs^+] 1052.3017, found 1052.3038.

Coupled product 42′: Colorless solid; R_f = 0.41 (silica, 80% ether in hexane); $[\alpha]_D^{22}$ = −12.38 (c 0.21, $CHCl_3$); IR (film): $\tilde{\nu}_{max}$ = 3404, 2943, 1790, 1727 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.10 (m, 2H, Ar), 7.68 (m, 2H, Ar), 7.54–7.27 (m, 13H, Ar), 7.08 (m, 1H, Ar), 6.99 (d, J = 8.5 Hz, 1H, NH), 6.68 (d, J = 10.0 Hz, 1H, HCOAc), 6.39 (s, 1H, HCOBz), 5.80 (d, J = 10.0 Hz, 1H, HCOAc), 5.75 (m, 1H, HCC=C), 5.18 (d, J = 8.5 Hz, 1H, *H*CNHBz), 4.34 (s, 1H, HCOTES), 3.72 (s, 3H, CH_3OAr), 2.95 (dd, J = 15.0, 3.5 Hz, 1H, CH_2), 2.76 (s, 1H, OH), 2.48 (dd, J = 15.0, 10.5 Hz, 1H, CH_2), 2.19 (s, 3H, OAc), 2.08 (s, 3H, OAc), 1.67 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 0.80 (t, J = 6.0 Hz, 9H, CH_3CH_2Si), 0.42 (m, 6H, CH_3CH_2Si); ^{13}C NMR (125 MHz, C_6D_6): δ = 170.4, 170.1, 169.6, 166.3, 165.6, 156.7, 139.4, 139.3, 138.6, 134.1, 133.1, 131.7, 131.6, 130.0, 129.9, 128.6, 128.5, 128.4, 127.7, 127.0, 126.8, 126.4, 118.8, 113.2, 75.4, 74.7, 72.6, 71.1, 56.6, 56.0, 43.0, 37.1, 27.0, 21.0, 20.3, 15.7, 6.5, 4.3; HRMS (FAB): calcd for $C_{52}H_{61}O_{12}NSi$ [M + Cs^+] 1052.3017, found 1052.3059.

Deprotected product 2c: Same procedure as for the preparation of compound **2a** (5 mg scale, 89%); colorless solid; R_f = 0.32 (silica, 80% ether in hexane); $[\alpha]_D^{22}$ = 3.00 (c 0.40, $CHCl_3$); IR (film): $\tilde{\nu}_{max}$ = 3416, 1730, 1644 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.10 (d, J = 8.0 Hz, 2H, Ar), 7.79 (d, J = 8.0 Hz, 2H, Ar), 7.54–7.13 (m, 14H, Ar), 6.89 (d, J = 9.5 Hz, 1H, NH), 6.69 (d, J = 10.0 Hz, 1H, HCOAc), 6.33 (s, 1H, *H*CNHBz), 5.72 (d, J = 10.0 Hz, 1H, HCOAc), 5.67 (m, 1H, HCC=C), 5.63 (m, 1H, *H*CNHBz), 4.56 (br s, 1H, *H*COH), 3.72 (s, 3H, CH_3OAr), 3.07 (dd, J = 15.0, 4.0 Hz, 1H, CH_2), 2.90 (br d, 1H, OH), 2.45 (dd, J = 15.0, 11.0 Hz, 1H, CH_2), 2.18 (s, 3H, OAc), 2.11 (s, 3H, OAc), 1.66 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.54 (s, 3H, CH_3); ^{13}C NMR (125 MHz, C_6D_6): δ = 171.3, 170.4, 169.4, 166.6, 165.4, 156.8, 138.4, 138.2, 137.9, 133.9, 133.2, 132.6, 131.9, 129.9, 128.8, 128.7, 128.3, 128.2, 127.0, 126.9, 126.8, 118.3, 113.3, 74.5, 73.5, 72.5, 72.4, 56.8, 54.9, 42.9, 36.9, 26.9, 21.1, 20.9, 20.2, 14.7; HRMS (FAB): calcd for $C_{46}H_{47}O_{12}N$ [M + Cs^+] 938.2153, found 938.2171.

Deprotected product 2c′: Colorless solid; R_f = 0.23 (silica, 80% ether in hexane); $[\alpha]_D^{22}$ = 18.50 (c 0.40, $CHCl_3$); IR (film): $\tilde{\nu}_{max}$ = 2917, 1714, 1238 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 8.07 (d, J = 7.0 Hz, 2H, Ar), 7.68 (d, J = 7.0 Hz, 2H, Ar), 7.57–7.25 (m, 13H, Ar), 6.87 (m, 2H, Ar and NH), 6.88 (d, J = 10.5 Hz, 1H, HCOAc), 6.35 (s, 1H, HCOBz), 5.78 (d, J = 10.5 Hz, 1H, HCOAc), 5.65 (m, 1H, HCC=C), 5.36 (m, 1H, *H*CNHBz), 4.42 (br s, 1H, HCOTES), 3.61 (s, 3H, CH_3OAr), 3.35 (br s, 1H, OH), 2.93 (dd, J = 15.5, 3.5 Hz, 1H, CH_2), 2.75 (br s, 1H, OH), 2.50 (dd, J = 15.0, 10.5 Hz, 1H, CH_2), 2.19 (s, 3H, OAc), 2.10 (s, 3H, OAc), 1.66 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.98 (s, 3H, CH_3); ^{13}C NMR (125 MHz, C_6D_6): δ = 172.1, 170.2, 169.5, 166.6, 165.4, 156.6, 138.9, 138.5, 133.9, 133.4, 133.2, 132.6, 131.8, 129.9, 129.8, 128.9, 128.6, 128.4, 128.1, 127.0, 126.7, 118.7, 113.2, 74.5, 73.5, 73.1, 72.4, 56.6, 54.8, 42.7, 37.3, 27.2, 21.0, 20.1, 15.5; HRMS (FAB): calcd for $C_{46}H_{47}O_{12}N$ [M + Cs^+] 938.2153, found 938.2175.

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