Taxane Synthesis through Intramolecular Pinacol Coupling at C-1−C-2. Construction and Oxidative Transformations of a C-Aromatic Taxane Diene

Charles S. Swindell,* Madhavi C. Chander, Julia M. Heerding, Peter G. Klimko, Leera T. Rahman, J. Venkat Raman, and Hemalatha Venkataraman

Department of Chemistry, Bryn Mawr College, 101 North Merion Avenue, Bryn Mawr, Pennsylvania 19010-2899

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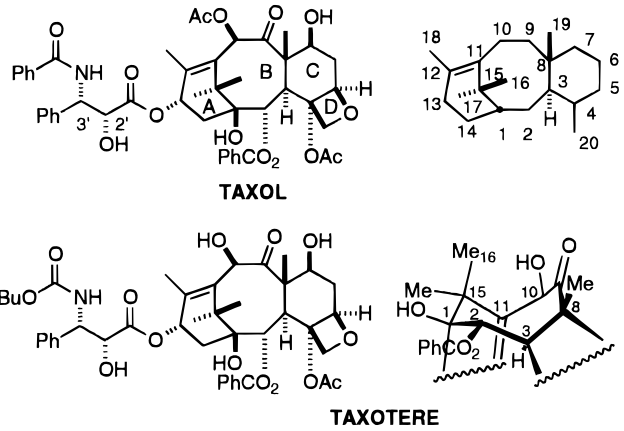
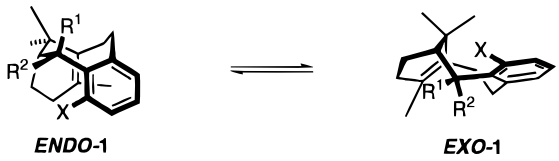
A ten-linear-step construction of C-aromatic taxane diene **14** from ethyl isopropyl ketone, acryloyl chloride, and commercially available **8** is reported. This sequence concludes with an intramolecular pinacol coupling carried out on **13**. **14** is oxidized by *m*-chloroperbenzoic acid and dimethyldioxirane to give **17** through intermediate epoxide **20** and by $VO(acac)_2$−*t*-BuOOH and $Mo(CO)_6$−*t*-BuOOH to give **13**. **17** is converted efficiently into **22** upon treatment with $Mo(CO)_6$−*t*-BuOOH, apparently through an unusual equilibration with isomeric **20**, which is converted irreversibly to **22**. While these oxidative transformations highlight some of the peculiar reactivity patterns characteristic of taxane-related structures, the formation of **14** through an intramolecular pinacol coupling that joins C-1 and C-2 demonstrates the potential of this strategy for stereoselectively delivering advanced taxane synthesis intermediates.

Introduction

The clinically effective antitumor agent taxol[1] possesses an eight-membered B-ring that adheres closely to the conformational ideal.[2] An examination of the X-ray crystallographic structure[3] of the related semisynthetic analog Taxotere[4] reveals the B-ring to adopt the typically favored boat-chair conformation, with the C-2 benzoyloxy substituent disposed equatorially and thereby avoiding contact with the axial C-16 methyl group. Planar trigonal carbons are located at sites associated either with large substituent A-values (C-9) or with severe transannular interactions (C-11). The transannular contact with C-11 that remains is minimized to involve hydrogen by the configuration of C-3. Furthermore, C-8 occurs at a boat-chair site characterized by negligible substituent *A*-values, a situation advantageous for geminal disubstitution.

The endo conformation of the structurally complex natural taxanes possesses the face-to-face relationship of the A- and C-rings typified by structurally simple *endo*-**1**. In his investigations of C-aromatic taxane conformations, Shea demonstrated, for example, that *endo*-**1** was favored for R^1,R^2 = carbonyl, X = H[5] and for R^1 = H, R^2 = OH, X = OMe[6] but that *exo*-**1** was more stable for R^1 = OH, R^2 = H, X = OMe[6] and for the simple structure (not shown) lacking the A-ring methyl groups and having R^1,R^2 = carbonyl, X = H.[5]





One of the chemical challenges posed by the taxanes is to define how these structural features can productively influence synthetic processes expected to form the eight-membered B-ring, especially those that lead to advanced tricyclic intermediates and create one or more of the B-ring stereogenic centers under kinetic control. The most fundamental issue is whether endo or exo[7] transition structures obtain. To the extent that starting material and/or product ground state structure can suggest mediating transition structure, endo transition structures are often encountered (Figure 1). Thus, in-

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(1) Isolation: (a) Wani, M. C.; Taylor, H. L.; Wall, M. E.; Coggon, P.; McPhail, A. T. *J. Am. Chem. Soc.* **1971**, *93*, 2325−2327. Synthesis: (b) Holton, R. A.; *et al. J. Am. Chem. Soc.* **1994**, *116*, 1597−1598, 1599−1600. (c) Nicolaou, K. C.; *et al. J. Am. Chem. Soc.* **1995**, *117*, 624−633, 634−644, 645−652, 653−659. Recent reviews: (d) Kingston, D. G. I.; Molinero, A. A.; Rimoldi, J. M. In *Progress in the Chemistry of Organic Natural Products;* Herz, W., Kirby, G. W., Moore, R. E., Steglich, W., Tamm, Ch., Eds.; Springer-Verlag: Vienna, 1993; Vol. 61, pp 1−206. (e) Nicolaou, K. C.; Dai, W.-M.; Guy, R. K. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 15−44. (f) Boa, A. N.; Jenkins, P. R.; Lawrence, N. J. *Contemp. Org. Synth.* **1994**, *1*, 47−75.

(2) For an excellent discussion of some aspects of medium ring conformational analysis, see: Still, W. C.; Galynker, I. *Tetrahedron* **1981**, *37*, 3981−3996.

(3) Guéritte-Voegelein, F.; Guénard, D.; Mangatal, L.; Potier, P.; Guilhem, J.; Cesario, M.; Pascard, C. *Acta Crystallogr.* **1990**, *C46*, 781−784.

(4) Mangatal, L.; Adeline, M.-T.; Guénard, D.; Guéritte-Voegelein, F.; Potier, P. *Tetrahedron* **1989**, *45*, 4177−4190.

(5) Shea, K. J.; Gilman, J. W. *Tetrahedron Lett.* **1984**, *25*, 2451−2454.

(6) Jackson, R. W.; Higby, R. G.; Gilman, J. W.; Shea, K. J. *Tetrahedron* **1992**, *48*, 7013−7032.

(7) In this context, the terms endo and exo are used in the sense defined by *endo*-**1** and *exo*-**1**.

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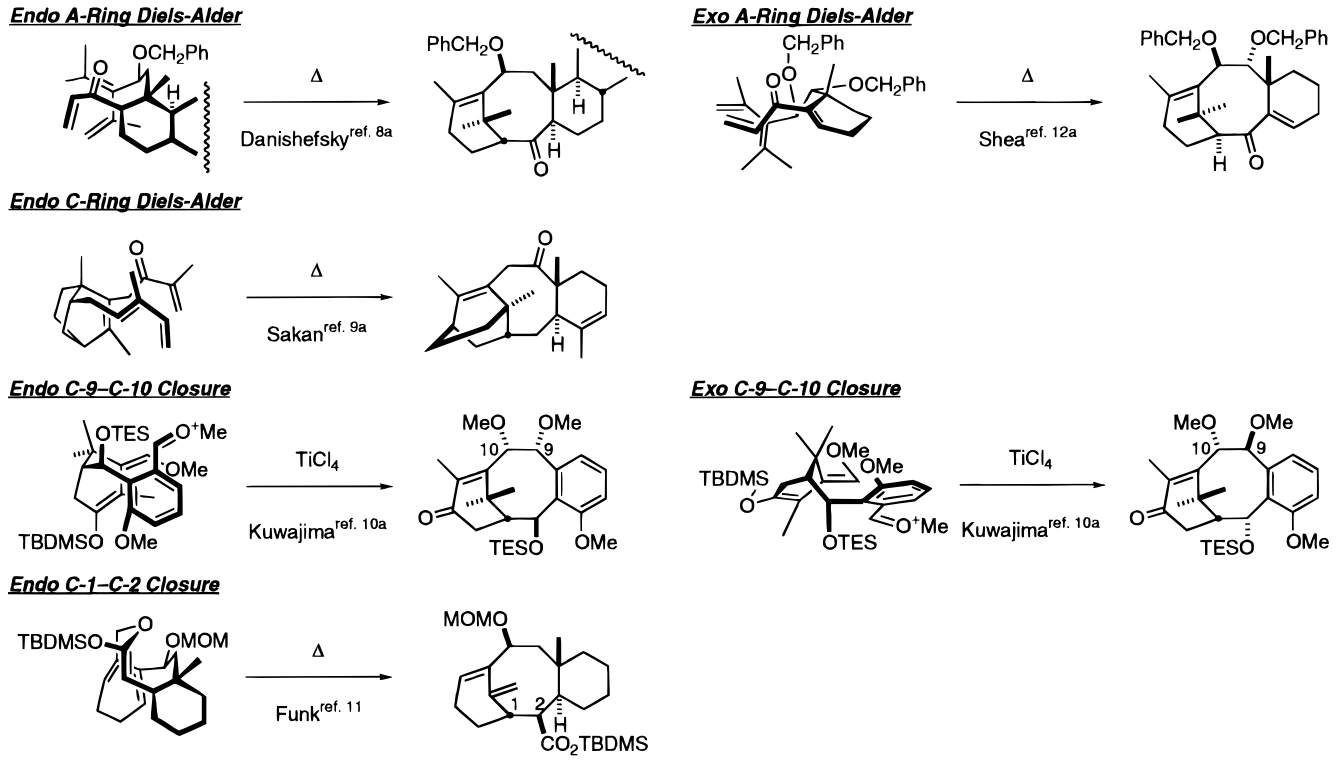
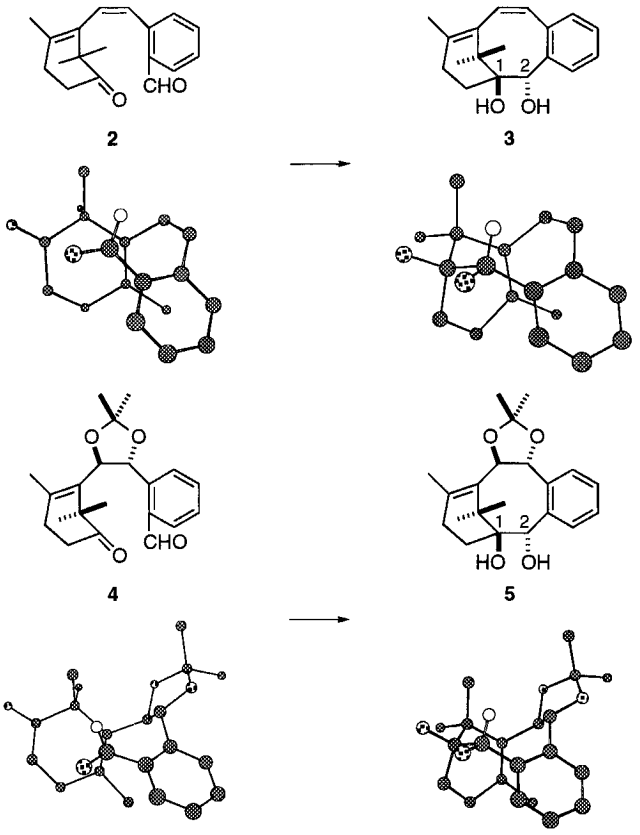


Figure 1. Examples of endo and exo modes of taxane B-ring formation.

tramolecular Diels−Alder cycloadditions that form the taxane A-ring[8] and the C-ring,[9] cationic cyclizations at C-9−C-10,[10] and an Ireland−Claisen rearrangement that joins C-1−C-2[11] apparently can proceed through the endo manifold. On the other hand, counterexamples of exo-mode intramolecular A-ring Diels−Alder cycloadditions[12] and C-9−C-10 cationic cyclizations[10a] have been reported, as well. Indeed, conflicts between the transition structure requirements of the reaction types chosen to implement B-ring-forming strategies and the conformational and stereochemical features of the intended taxane products have complicated much work in this area.

Our plan for constructing the taxanes focuses on formation of the B-ring to yield tricyclic intermediates by closure of the C-1−C-2 bond. Were this bond to be formed through an intramolecular pinacol coupling carried out on C-aromatic intermediate **2** (Scheme 1), the foregoing conformational considerations and the involvement of an endo transition structure would suggest the formation of **3** with an equatorial 2-OH group.[13] Likewise, stereochemically complicated acetonide **4** would be

Scheme 1



expected to provide analogous tricycle **5** in which the newly created C-1 and C-2 stereogenic centers would be correctly induced by those preexisting at C-9 and C-10, all such sites bearing equatorial oxygen substituents in **5**. Herein[14] and in the following article we describe our construction of substances related to **3** and **5**, as well as

(8) (a) Park, T. K.; Kim, I. J.; Danishefsky, S. J.; de Gala, S. *Tetrahedron Lett.* **1995**, *36*, 1019−1022. See also: (b) Shea, K. J.; Gilman, J. W. *J. Am. Chem. Soc.* **1985**, *107*, 4791−4792. (c) Bonnert, R. V.; Jenkins, P. R. *J. Chem. Soc., Perkin Trans. 1* **1989**, 413−418. (d) For a related Diels−Alder cycloaddition, see: Winkler, J. D.; Kim, H. S.; Kim, S. H. *Tetrahedron Lett.* **1995**, *36*, 687−690.

(9) (a) Sakan, K.; Craven, B. M. *J. Am. Chem. Soc.* **1983**, *105*, 3732−3734. (b) For a related Diels−Alder cycloaddition, see: Lu, Y. F.; Fallis, A. G. *Tetrahedron Lett.* **1993**, *34*, 3367−3370.

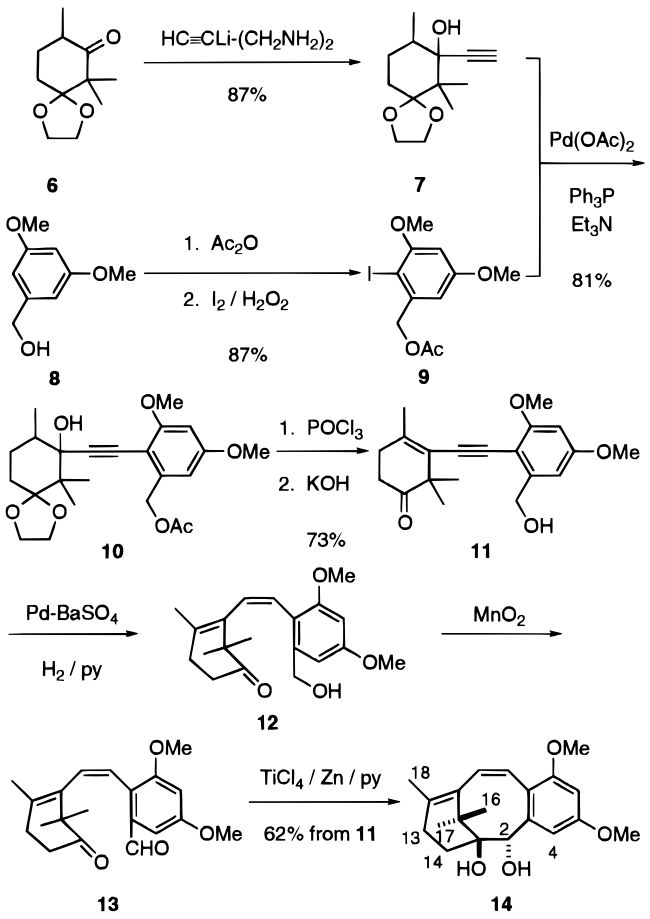
(10) (a) Seto, M.; Morihira, K.; Horiguchi, Y.; Kuwajima, I. *J. Org. Chem.* **1994**, *59*, 3165−3174. (b) For a related pinacol coupling, see ref 1c.

(11) Funk, R. L.; Dailey, W. J.; Parvez, M. *J. Org. Chem.* **1988**, *53*, 4141−4143.

(12) (a) Jackson, R. W.; Shea, K. J. *Tetrahedron Lett.* **1994**, *35*, 1317−1320. See also: (b) Alaimo, C. A.; Coburn, C. A.; Danishefsky, S. J. *Tetrahedron Lett.* **1994**, *35*, 6603−6606. (c) Kim, I. J.; Park, T. K.; Danishefsky, S. J. *Tetrahedron Lett.* **1995**, *36*, 1015−1018.

(13) For an analysis of stereoselective medium and large ring formation through the pinacol coupling, see: McMurry, J. E.; Siemers, N. O. *Tetrahedron Lett.* **1993**, *34*, 7891−7894.

Scheme 2



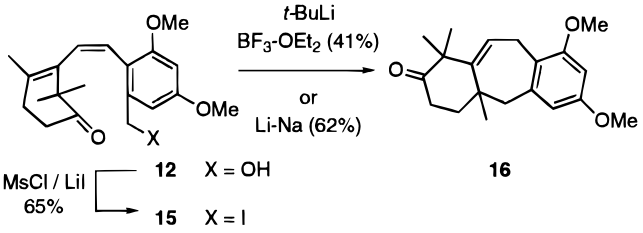
transformations relevant to their utility as synthesis intermediates for the preparation of the complex natural taxanes.

Results and Discussion

Our initial goal was the preparation of C-aromatic taxane diene **14** (Scheme 2). Birch reduction and subsequent elaboration of its C-ring, perhaps preceded by the introduction of oxygen functionality at C-9 and C-10, would enable **14** to function as an intermediate for the synthesis of the complex taxanes of interest. Monoacetal **6**,[15] available in three simple operations from ethyl isopropyl ketone and acryloyl chloride, is an ideal structurally uncomplicated progenitor for the taxane A-ring. The conversion of **6** into propargylic alcohol **7** could be carried out with commercial lithium acetylide−ethylenediamine complex; **10** was then available through the indicated Pd-induced coupling of **7** and **9**. The *Z*-selective partial reduction of the triple bond of **11** and related substances proved difficult to implement and was bypassed initially[14a] through a cumbersome sequence that involved photoisomerization of an *E* relative of **12**. We eventually discovered conditions for the partial reduction of **11** in which both the Pd−$BaSO_4$ catalyst and the free hydroxyl are crucial. An unidentified contaminant accompanied the **12** so produced, but it proved convenient to convert unpurified **12** to **14** through intermediate keto aldehyde **13**, probably because alternative keto aldehyde byproducts fail to undergo efficient pinacol cyclization. When the pinacol coupling step[16] was carried out with pure **13**, **14** was formed in 86% yield.[14a] The sequence illustrated in Scheme 2 provides **14** in ten linear steps from commercially available materials.

The endo conformation and relative stereochemistry at C-1 and C-2 of **14** (see model **3**, Scheme 1) rest on several NOE experiments involving protons at key sites. The NOE relationship between H-4 (δ 6.88) and H-13 and H-14 (δ 2.17−2.31) defines the endo conformation of **14**. This conformational assignment is further supported by the anomalously high field signal for Me-18 (δ 0.80) due to shielding by the aromatic C-ring.[17] This signal fails to exhibit an NOE of either of the remaining carbon-bound methyl singlets. Me-17 (δ 1.14) was identified by its NOE relationship with H-13 and H-14, leaving the singlet at δ 1.20 to be assigned to Me-16. The NOE relationship between H-2 (δ 4.74) and Me-16 then defines the relative stereochemistry of **14**. The existence of atropisomers was not indicated for **14**. While we cannot rule out unequivocally a rapid equilibration with an undetectable exo component, the ^{1}H NMR spectral data and NOE experiments could be interpreted in a straightforward fashion in terms of **14** having a single nonfluxional endo conformation.

Before examining the pinacol cyclization of **13**, we converted **12** into iodide **15** to investigate the closure of the C-1−C-2 bond through Barbier chemistry. SmI_2[18] and Zn−Cu[19] couple transformed **15** into complex mixtures. However, exposure of **15** to either *tert*-butyllithium or lithium−sodium dispersion indeed caused cyclization to occur but to give 6-7-6 ring system **16**[20] through the attachment of the iodomethyl carbon to the conjugated diene substructure.



Our expectation that **14** could serve as an intermediate for complex taxane synthesis was predicated on the hypothesis that the double bond at C-9−C-10, positions that are sterically hindered and unreactive in the natural taxanes, would be susceptible to oxidation intended to introduce appropriate functionality. The encumbered bridgehead double bond was anticipated to focus attack at C-9 and C-10, and the sterically undemanding aromatic C-ring, particularly the absence of the angular

(14) For preliminary reports of this work, see: (a) Swindell, C. S.; Chander, M. C.; Heerding, J. M.; Klimko, P. G.: Rahman, L. T.; Raman, J. V.; Venkataraman, H. *Tetrahedron Lett.* **1993**, *34*, 7005−7008. (b) Swindell, C. S.; Chander, M. C. *Tetrahedron Lett.* **1994**, *35*, 6001−6004.

(15) (a) Hargreaves, J. R.; Hickmott, P. W.; Hopkins, B. J. *J. Chem. Soc. C* **1968**, 2599−2603. (b) Detering, J.; Martin, H. D. *Angew. Chem., Intl. Ed. Engl.* **1988**, *27*, 695−698.

(16) (a) Mukaiyama, T.; Sato, T.; Hanna, J. *Chem. Lett.* **1973**, 1041−1044. (b) Kato, N.; Takeshita, H.; Kataoka, H.; Ohbuchi, S.; Tanaka, S. *J. Chem. Soc., Perkin Trans. 1* **1989**, 165−174.

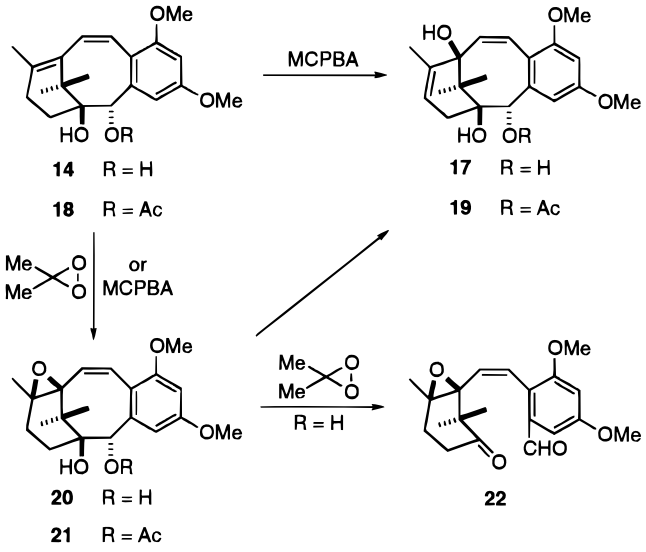
(17) Shea, K. J.; Gilman, J. W.; Haffner, C. D.; Dougherty, T. K. *J. Am. Chem. Soc.* **1986**, *108*, 4953−4956.

(18) (a) Molander, G. A.; Etter, J. B.; Zinke, P. W. *J. Am. Chem. Soc.* **1987**, *109*, 453−463. (b) Molander, G. A.; McKie, J. A. *J. Org. Chem.* **1991**, *56*, 4112−4120.

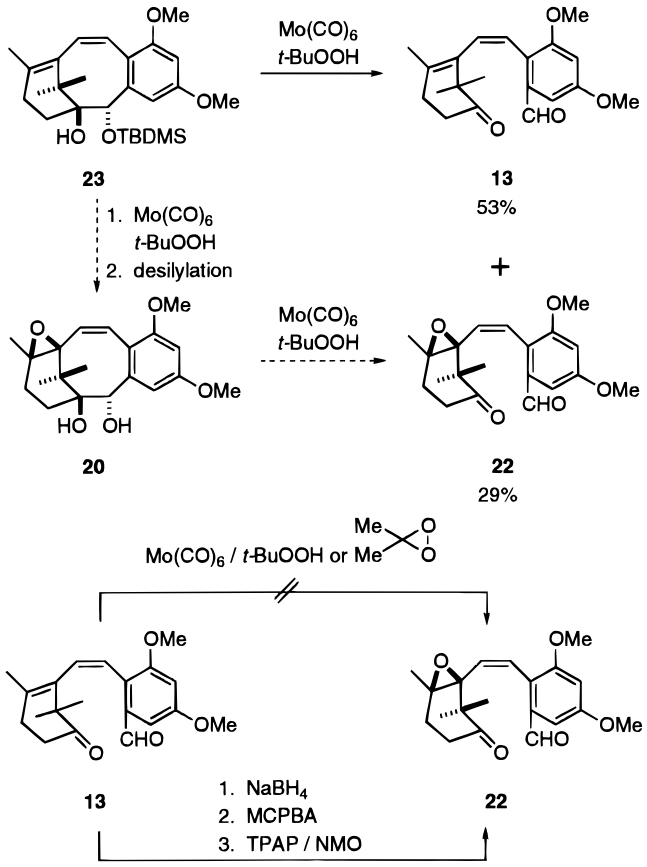
(19) Wang, Z. Y.; Warder, S. E.; Perrier, H.; Grimm, E. L.; Bernstein, M. A.; Ball, R. G. *J. Org. Chem.* **1993**, *58*, 2931−2932.

(20) It is noteworthy that **16** is structurally related to the rearranged abietane diterpenes exemplified by barbatusol: Kelecom, A. *Tetrahedron* **1983**, *39*, 3603−3608.

Scheme 3

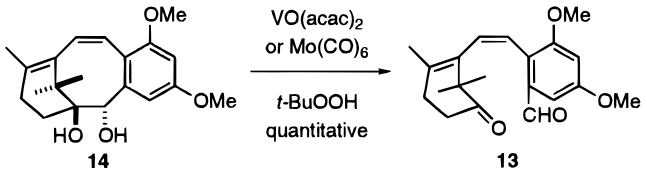


Scheme 4



methyl group, was expected to permit sufficient reactivity.[21] However, exposure of **14** to *m*-chloroperbenzoic acid delivered in 81% yield **17** with its B-ring olefinic bond intact (Scheme 3). Presumably, it is the methoxy group at C-7 that is responsible for shielding the α face of the C-9−C-10 olefin, whereas the β face of this substructure is inherently inaccessible owing to the conformation of the eight-membered ring. A repetition of this experiment with acetate **18** afforded analogous **19** in 79−86% yield after column chromatography, but when this reaction mixture was purified by radial chromatography, or when the oxidation was carried out by dimethyldioxirane,[22] epoxide **21** could be isolated in 70% or quantitative yields, respectively.[23] The appearance of the acetyl group on the C-2 oxygen evidently confers on **21** a degree of stability toward isomerization.[24] Nevertheless, **21** could be readily isomerized into **19**, for example, upon more prolonged exposure to silica gel. Thus, **20** must mediate the transformation of **14** into **17**. It seems likely that the crowded conformation that results from the C-11 sp^3 bridgehead in **20** and **21** is alleviated by the introduction of the A-ring-flattening double bond in **17** and **19**, an effect that might provide the driving force for the formation of the latter isomerization products. An attempt to force diepoxidation of the A- and B-ring double bonds of **14** through exposure to dimethyldioxirane resulted in the low-yield (29%) formation of **22** (Scheme 3).

The facile cleavage of the C-1−C-2 bond reappeared when **14** was subjected to attempted epoxidations involving $VO(acac)_2$ or $Mo(CO)_6$ and *t*-BuOOH. In both cases, quantitative formation of keto aldehyde **13** resulted instead. The action of these reagents on **14** as well as the cleavage of **20** by dimethyldioxirane, which are uncharacteristic of these oxidants,[22,25] are probably manifestations of the strain of the ring system and the favorable stereoelectronic alignment of the C-1−C-2 bond broken and the aromatic π-system; the C-1−C-2−C-3−C-4 dihedral angle for **14** is calculated (MM2) to be approximately 90°.



Given the reactivity of **14** toward oxidative vicinal diol cleavage, the C-2 hydroxyl was masked in **23** and the latter material subjected to reaction with $Mo(CO)_6$−*t*-BuOOH (Scheme 4). Nonetheless, **13** predominated again owing to *in situ* desilylation and subsequent oxidative vicinal diol cleavage. Accompanying **13** was its apparent epoxidation product **22**.[26] However, control experiments indicated **13** to be reactive neither to $Mo(CO)_6$−*t*-BuOOH nor to dimethyldioxirane. To remove all doubt regarding the structure of **22** produced through the chemistry of Scheme 3 (*vide supra*) and Scheme 4 (and Scheme 5; *vide infra*), it was independently derived from **13** as indicated in Scheme 4. Thus, **22** must be formed in the $Mo(CO)_6$−*t*-BuOOH reaction through the initial epoxidation of **23** followed by desilylation and vicinal diol cleavage. Under the conditions of the $Mo(CO)_6$−*t*-BuOOH reaction, strained intermediate **20** manifests its anomalous reactivity in a more rapid vicinal diol

(21) For an early preparation of a taxane diene related to **14**, see: Kende, A. S.; Johnson, S.; Sanfilippo, P.; Hodges, J. C.; Jungheim, L. N. *J. Am. Chem. Soc.* **1986**, *111*, 8277−8279.

(22) For reviews, see: (a) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205−211. (b) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187−1201.

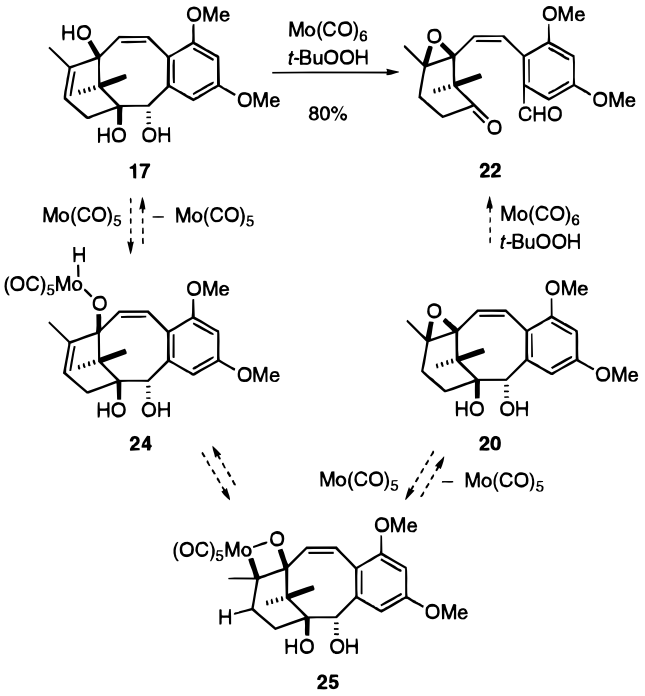
(23) For related observations, see: Holton, R. A. In *Strategies and Tactics in Organic Synthesis*; Lindberg, T., Ed.; Academic Press: San Diego, 1991; Vol. 3, Chapter 5.

(24) Silyl ether **23** behaves similarly. Chander, M. C., unpublished results.

(25) For reviews, see: (a) Sharpless, K. B.; Verhoeven, T. R. *Aldrichimica Acta* **1979**, *12*, 63−74. (b) Jorgensen, K. A. *Chem. Rev.* **1989**, *89*, 431−458.

(26) Treatment of **23** with $VO(acac)_2$−*t*-BuOOH produces in 60% yield the secondary *tert*-butyldimethylsilyl derivative of **17**. Chander, M. C., unpublished results.

Scheme 5



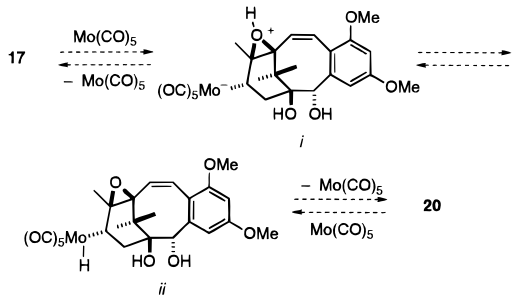
cleavage similar to that experienced by **14** above, rather than rearrangement to **17**, as occurs in the *m*-chloroperbenzoic acid-involving process of Scheme 3.

Among our further attempts to functionalize the B-ring of intermediates derived from **14** was the reaction of **17** with $Mo(CO)_6$−*t*-BuOOH (Scheme 5). Surprisingly, this experiment produced previously encountered **22** in substantial yield. Neither $Mo(CO)_6$ nor *t*-BuOOH alone was able to effect this transformation. From the experience described above, this observation implies the intermediacy of epoxide **20**, which must be produced through an equilibrium between isomers **17** and **20** established by $Mo(CO)_6$. We are unaware of a similar transformation induced by $Mo(CO)_6$. Since the experiments portrayed in Scheme 3 demonstrate that **17** is the dominant equilibrium partner, it is only due to the fortuitous irreversible $Mo(CO)_6$−*t*-BuOOH-induced transformation of **20** into **22** that the low equilibrium concentration of **20** present in this reaction medium is reported. A mechanistic explanation for the equilibration of **17** and **20** induced by thermally generated $Mo(CO)_5$ is presented in Scheme 5.[27]

Conclusion

We have synthesized C-aromatic taxane diene **14** through an efficient sequence that has allowed the investigation of its oxidative chemistry and that of several of its relatives. Such procedures focus reactivity on the A-ring and/or lead to the facile oxidative cleavage of the C-1−C-2 vicinal diol, the latter transformation occurring under unconventional conditions. An unusual $Mo(CO)_6$-mediated isomerization of an allylic alcohol into an epoxide was detected in the conversion of **17** into **22**. These observations highlight some of the peculiar reactivity patterns characteristic of taxane-related structures. Most importantly, however, the formation of **14** through an intramolecular pinacol coupling that joins C-1 and C-2 demonstrates the potential of this strategy for stereoselectively delivering advanced taxane synthesis intermediates. The development of this approach in the context of routes that install C-9 and C-10 oxygenation at an early stage is the subject of the following article.

(27) Among the alternatives is the following. It is unappealing since in the direction **20** → **17** it requires the insertion of Mo into an unactivated carbon−hydrogen bond.



Experimental Section

In general, reactions were carried out under N_2. "Chromatography" refers to flash chromatography conducted with Merck silica gel (230−400 mesh; 60 Å) with elution carried out with ethyl acetate−hexanes. Radial chromatography was conducted with Analtech precast rotors (silica gel GF) with elution again carried out with ethyl acetate−hexanes. Melting points were determined on a capillary apparatus and are uncorrected. ^{1}H NMR spectroscopy at 300 MHz and ^{13}C NMR spectroscopy at 75 MHz were carried out on $CDCl_3$ solutions using TMS as internal standard ($\delta = 0$); coupling constants are reported in hertz.

Propargylic Alcohol 7. To 90% lithium acetylide−ethylenediamine complex (25.80 g, 252.5 mmol) in 180 mL of THF under a nitrogen atmosphere was added dropwise a solution of ketal ketone **6** (20 g, 101 mmol) in 150 mL of THF. The reaction mixture was stirred for 48 h at ambient temperature and then cautiously poured into 600 mL of a 1:1 mixture of ether−saturated aqueous NH_4Cl. The aqueous layer was extracted with ether (2 × 500 mL), and the combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated. Chromatography of the residue gave **6** (19.68 g, 87%) as a white, crystalline solid: mp 92−93 °C; ^{1}H NMR δ 3.99−3.85 (m, 4H), 3.80 (s, OH), 2.40 (s, 1H), 2.02−1.95 (m, 1H), 1.79 (dt, J = 5.65, 13.20, 1H), 1.61−1.43 (m, 3H), 1.24 (s, 3H), 1.13 (s, 3H), 1.10 (d, J = 6.7, 3H); ^{13}C NMR δ 122.71, 84.90, 78.43, 72.42, 65.78, 64.36, 45.72, 35.90, 30.01, 26.27, 22.30, 17.12, 16.55; IR ($CHCl_3$) 3500, 2120 cm^{-1}. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.51; H, 9.01.

3,5-Dimethoxybenzyl Acetate. To 39.0 g (232 mmol) of **8** in 100 mL of CH_2Cl_2 containing 26.4 g (334 mmol) of pyridine was added dropwise a solution of 22.1 g (281 mmol) of acetyl chloride in 100 mL of CH_2Cl_2. After the addition was complete, a thick white precipitate formed. The reaction mixture was then poured into 500 mL of 1:1 ether−5 M HCl. The layers were separated, and the aqueous layer was extracted with ether (2 × 100 mL). The combined organic layers were washed successively with 5 M HCl (2 × 100 mL) and saturated aqueous $NaHCO_3$ (2 × 100 mL). The organic layer was dried ($MgSO_4$) and concentrated to afford 45 g (93%) of the title compound as an oil: ^{1}H NMR δ 6.48 (d, J = 2.4, 2H), 6.41 (t, J = 2.4, 1H), 5.02 (s, 2H), 3.79 (s, 6H), 2.11 (s, 3H).

2-Iodo-3,5-dimethoxybenzyl Acetate (9). To 3,5-dimethoxybenzyl acetate (49.99 g, 238.1 mmol) in a 1000 mL Erlenmeyer flask open to the air containing 200 mL of acetic acid and iodine (48.34 g, 190.4 mmol) was added a 30% w/w solution of H_2O_2 in water (29.38 g, 259.3 mmol) in one portion. The reaction mixture was stirred until GC analysis indicated that all of the starting material had been consumed (5−8 h). The mixture was then poured into 500 mL of 1:1 ethyl acetate−saturated aqueous $Na_2S_2O_5$ to discharge the dark brown color of the remaining iodine. After separation of the two layers, the aqueous layer was extracted with ethyl acetate (2 × 200 mL) and the combined organic layers were washed twice with water, then saturated aqueous $NaHCO_3$, water, and brine. Drying (Na_2SO_4) and concentration provided **9** (74 g, 94%) as

an ivory solid: mp 74−75 °C; ^{1}H NMR δ 6.62 (d, J = 2.4, 1H), 6.40 (d, J = 6.4, 1H), 5.14 (s, 2H), 3.88 (s, 3H), 3.82 (s, 3H), 2.16 (s, 3H). Anal. Calcd for $C_{11}H_{13}IO_4$: C, 39.31; H 3.90. Found: C 39.52; H 4.06.

Propargylic Alcohol 10. To 100 mL of triethylamine, which had been sparged with N_2 for 20 min, were added **7** (9.58 g, 42.8 mmol), **9** (10.1 g, 30 mmol), $Pd(OAc)_2$ (560 mg, 2.5 mmol), and PPh_3 (920 mg, 3.5 mmol). The solution was heated to a gentle reflux and gradually turned black. After 3.5 h, the solution was cooled to 25 °C and poured into 300 mL of 1:1 ether−saturated aqueous NH_4Cl. The aqueous layer was extracted with ether (2 × 100 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the amber residue afforded **10** (11.0 g, 85%) as a white crystalline solid: mp 97 °C; ^{1}H NMR δ 6.51 (d, J = 2.1, 1H), 6.38 (d, J = 2.1, 1H), 5.23 (s, 2H), 4.05−3.88 (m, 4H), 2.11 (s, 3H), 1.92−1.75 (m, 1H), 1.63−1.47 (m, 3H), 1.32 (s, 3H), 1.22 (s, 3H), 1.20 (d, J = 6.6, 3H); ^{13}C NMR δ 170.6 (C), 162.0 (C), 160.3 (C), 139.8 (C), 112.8 (C), 104.7 (CH), 104.6 (C), 98.6 (C), 97.6 (CH), 79.1 (C), 77.5 (C), 65.6 (CH_2), 64.9 (CH_2), 64.2 (CH_2), 55.7 (CH_3), 55.3 (CH_3), 46.1 (C), 36.3 (CH), 30.1 (CH_2), 26.3 (CH_2), 22.4 (CH_3), 20.1 (CH_3), 17.3 (CH_3), 16.5 (CH_3); IR (neat) 3470, 2220, 1720 cm^{-1}. Anal. Calcd for $C_{24}H_{32}O_7$: C, 66.65; H 7.46. Found: C, 66.79; H 7.30.

Enyne 11. To a solution of **10** (37 g, 85.7 mmol) in 300 mL of benzene was added 40 mL of pyridine followed by the dropwise addition of $POCl_3$ (32.83 g, 214.1 mmol) in 200 mL of benzene. After being stirred for 18 h at ambient temperature, the reaction mixture was cautiously poured into 600 mL of 1:1 ether−saturated aqueous $NaHCO_3$. The two layers were separated, and the aqueous layer was extracted with ether (2 × 200 mL). The combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated. Chromatography of the residue gave transparent, cubic crystals of the acetate ester of **11** (25.5 g, 80%): mp 93−94 °C; ^{1}H NMR δ 6.56 (d, J = 2.12, 1H), 6.42 (d, J = 2.12, 1H), 5.25 (s, 2H), 3.86 (s, 3H), 3.84 (s, 3H), 2.62−2.48 (m, 4H), 2.11 (s, 3H), 2.09 (s, 3H), 1.37 (s, 3H); ^{13}C NMR δ 213.39, 170.29, 161.14, 160.02, 138.96, 138.84, 123.59, 104.67, 104.58, 97.46, 94.46, 86.54, 64.58, 55.47, 55.05, 46.27, 35.19, 30.88, 24.90, 21.80, 20.52; IR ($CHCl_3$) 2240, 1730, 1715 cm^{-1}. Anal. Calcd for $C_{22}H_{26}O_5$: C, 71.33; H, 7.07. Found: C, 71.23; H, 7.10.

Treatment of the acetate ester of **11** (21 g, 56.8 mmol) with 2 g of KOH (86% w/w) in 250 mL of 1:2:1 THF−MeOH−water for 5 h at ambient temperature was followed by the addition of the reaction mixture to 600 mL of 1:1 ether−saturated aqueous NH_4Cl, extraction of the aqueous layer with ether (2 × 150 mL), and drying (Na_2SO_4) of the combined organic layers. Concentration afforded **11** as fluorescent crystals (17 g, 91%): mp 117−119 °C; ^{1}H NMR δ 6.62 (d, J = 2.04, 1H), 6.36 (d, J = 2.04, 1H), 4.80 (d, J = 6.20, 2H), 3.83 (s, 3H), 3.82 (s, 3H), 2.56−2.48 (m, 4H), 2.06 (s,3H), 1.94 (t, J = 6.20, 1H), 1.35 (s, 6H); ^{13}C NMR δ 213.69, 161.49, 160.67, 144.68, 139.13, 123.88, 103.28, 103.18, 97.33, 94.81, 87.08, 64.06, 55.77, 55.37, 46.59, 35.51, 31.17, 25.30, 22.19; IR ($CHCl_3$) 3636, 2240, 1720 cm^{-1}. Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15; H, 7.37. Found: C, 72.96; H, 7.54.

***Z*-Diene 12.** A mixture of **11** (7.00 g, 21.3 mmol) and Pd−$BaSO_4$ (1.5 g, 20% w/w) in 50 mL of pyridine was shaken for 6 h in an atmosphere of hydrogen (60 psi) in a Parr apparatus. The reaction mixture was filtered through Celite and concentrated to give crude **12**. A purified sample yielded the following data: mp 86−87 °C; ^{1}H NMR δ 6.66 (d, J = 2.38, 1H), 6.38 (d, J = 12.01, 1H), 6.35 (d, J = 2.38, 1H), 6.12 (d, J = 12.01, 1H), 4.58 (d, J = 3.52, 2H), 3.82 (s, 3H), 3.68 (s, 3H), 2.44 (t, J = 6.76, 2H), 2.24 (app t, J = 6.74, 2H), 1.60 (br s, OH), 1.27 (s, 6H), 1.13 (s, 3H); ^{13}C NMR δ 215.59, 159.59, 157.17, 140.12, 134.99, 130.35, 129.19, 124.75, 118.36, 102.86, 97.44, 62.99, 60.12, 55.15, 54.95, 47.01, 35.89, 30.17, 24.73, 21.24; IR (CH_2Cl_2) 3610, 1715 cm^{-1}. Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.58; H, 7.65.

***Z*-Keto Aldehyde 13 from 12.** To a solution of crude **12** (7.00 g, 21.2 mmol) in 60 mL of dry benzene was added in one portion activated MnO_2 (18.43 g, 212 mmol), and the resulting slurry was stirred at ambient temperature for 30 min. Filtration through Celite and concentration gave a mixture of aldehydes of which **13** was the major component. A sample purified by radial chromatography yielded the following data: mp 79−81 °C; ^{1}H NMR δ 10.03 (s, 1H), 6.92 (d, J = 2.53, 1H), 6.69 (d, J = 2.53, 1H), 6.66 (d, J = 12.39, 1H), 6.37 (dd, J = 12.39, 1.02, 1H), 3.86 (s, 3H), 3.84 (s, 3H), 2.37 (br t, J = 6.68, 2H), 2.35 (br t, J = 6.68, 2H), 1.24 (s, 6H), 1.08 (s, 3H); ^{13}C NMR δ 215.13, 192.40, 159.74, 158.17, 134.58, 133.05, 132.86, 132.33, 125.14, 123.65, 104.47, 100.71, 55.76, 55.54, 47.29, 36.05, 30.32, 29.68, 25.08, 21.40; IR ($CHCl_3$) 1715, 1690 cm^{-1}. Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.15; H, 7.37. Found: C, 72.96; H, 7.53.

Tricyclic Diol 14. To 500 mL of THF cooled to 0 °C was added cautiously $TiCl_4$ (23 mL, 205 mmol). The ice bath was removed, and activated Zn (28 g, 430 mmol) and pyridine (17 mL, 208 mmol) were added sequentially. To this mixture at ambient temperature was added over 4.5 h via syringe pump a solution of crude **13** (7 g, 21.3 mmol) in 300 mL of THF. The reaction mixture was stirred for an additional 30 min and then treated for 10 min with 300 mL of 10% aqueous K_2CO_3. This mixture was extracted three times with ether, and the combined organic layers were washed twice with water and brine, dried (Na_2SO_4), and concentrated to give crude **14** estimated by NMR and GC to be 70% pure. Purification by chromatography gave **14** as white crystals (4.8 g, 62% from **12**): mp 116−118 °C; ^{1}H NMR δ 6.88 (d, J = 2.40, 1H), 6.52 (d, J = 10.30, 1H), 6.41 (dd, J = 10.30, 1.21, 1H), 6.33 (d, J = 2.40, 1H), 4.74 (s, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.28 (br s, OH), 2.93 (br s, OH), 2.31−2.17 (m, 2H), 1.59 (dt, J = 3.30, 13.10, 1H), 1.32−1.20 (m, 1H), 1.20 (s, 3H), 1.14 (s, 3H), 0.80 (s, 3H); ^{13}C NMR δ 158.52, 157.73, 144.59, 134.59, 134.32, 133.21, 127.04, 119.89, 103.55, 96.50, 78.95, 71.62, 55.74, 55.25, 38.79, 28.68, 26.34, 23.46, 21.41, 20.54; HRMS calcd for $C_{20}H_{26}O_4$ 330.1831, found 330.1845. Anal. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found: C, 72.88; H, 7.83.

Iodide 15. To a solution of **12** (1.09 g, 3.3 mmol) in 10 mL of dry DMF were added sequentially LiI (490 mg, 3.6 mmol), diisopropylethylamine (870 μL, 5 mmol), and methanesulfonyl chloride (510 μL, 6.6 mmol), and the mixture was stirred for 6.5 h at ambient temperature. At this point, additional LiI (3 mmol), diisopropylethylamine (8.2 mmol), and methanesulfonyl chloride (6.6 mmol) were added and the mixture was stirred for an additional 1 h, poured into 40 mL of saturated aqueous $NaHSO_3$, and extracted with ethyl acetate (3 × 40 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give **15** (940 mg, 65%): ^{1}H NMR δ 6.50 (d, J = 2.4, 1H), 6.36 (d, J = 12.4, 1H), 6.33 (d, J = 2.4, 1H), 6.26 (d, J = 12.4, 1H), 4.38 (s, 2 H), 3.80 (s, 3 H), 3.64 (s, 3 H), 2.43 (t, J = 7.1, 2H), 2.24 (t, J = 7.1, 2H), 1.28 (s, 6 H), 1.16 (s, 3 H); ^{13}C NMR δ 215.0 (C), 159.4 (C), 157.6 (C), 137.7 (C), 135.2 (C), 130.3 (C), 129.7 (CH), 124.6 (CH), 119.6 (C), 105.6 (CH), 98.6 (CH), 55.2 (CH_3), 55.0 (CH_3), 47.0 (C), 35.9 (CH_2), 30.2 (CH_2), 24.8 (CH_3), 21.5 (CH_3), 5.8 (CH_2).

Tricycle 16. To a solution of **15** (650 mg, 1.5 mmol) in 50 mL of 2:3 ether−THF at −78 °C was added freshly distilled boron trifluoride etherate (200 μL, 230 mg, 1.63 mmol). The mixture was stirred for 20 min, at which time a solution of *tert* -butyllithium in pentane (1.7 M, 1.9 mL, 2.23 mmol) was added dropwise over 2 min. The mixture became red and was stirred for 50 min and poured into 150 mL of 1:1 ether−saturated aqueous NH_4Cl, the aqueous layer was extracted with ether (2 × 75 mL), and the combined organic layers were dried ($MgSO_4$) and concentrated. Chromatography of the residue gave **16** (193 mg, 41%).

Alternatively the following procedure could be employed. To a Li−Na dispersion (21 mg of a 30% dispersion in mineral oil; 5% Na) suspended in THF (2 mL) under Ar was added solid **15** (100 mg, 0.23 mmol). The mixture was stirred at ambient temperature for 3 h, and then 1 mL of 10% aqueous NH_4Cl was added via syringe. The mixture was poured into 50 mL of 1:1 10% aqueous NH_4Cl−ethyl acetate, the aqueous layer was extracted with ethyl acetate (40 mL), and the organic layers were combined, dried ($MgSO_4$), and concentrated. Purification, as above, gave **16** (44 mg, 62%): ^{1}H NMR δ 6.53 (d, J = 2.3, 1H), 6.30 (d, J = 2.3, 1H), 5.74 (dd, J = 8.1, 4.1, 1H), 3.80 (s, 6H), 3.61 (dd, J = 17.4, 8.1 Hz, 1H), 3.29 (dd, J = 17.4, 4.1, 1H), 3.17 (d, J = 13.3, 1H), 2.70−2.40 (m, 3H),

2.26−2.10 (m, 2H), 1.24 (s, 3H), 1.18 (s, 3H), 0.81 (s, 3H); ^{13}C NMR δ 216.96 (CO), 158.22 (C), 156.18 (C), 150.65 (C), 140.71 (C), 121.65 (C), 120.65 (CH), 106.98 (CH), 96.08 (CH), 55.57 (CH_3), 55.23 (CH_3), 49.75 (C), 47.61 (CH_2), 38.22 (C), 35.28 (CH_2), 33.66 (CH_2), 30.16 (CH_3), 27.63 (CH_3), 23.97 (CH_3), 22.60 (CH_2); IR ($CHCl_3$) 1715 cm^{-1}; HRMS cald for $C_{20}H_{26}O_3$ 314.1882, found 314.1893.

Triol 17. To a solution of **14** (33 mg, 0.1 mmol) in 3 mL of CH_2Cl_2 at −15 °C was added *m*-chloroperbenzoic acid (17.30 mg, 0.10 mmol). The reaction mixture was stirred at this temperature for 30 min and then slowly brought to room temperature over a period of 2 h, diluted with 20 mL of CH_2Cl_2, washed with 20% aqueous $NaHSO_3$, 10% aqueous $NaHCO_3$, water, and brine, dried (Na_2SO_4), and concentrated. Chromatography of the residue provided triol **17** (28 mg, 81%), as white crystals: mp 149−153 °C; ^{1}H NMR δ 6.71 (d, J = 2.25, 1H), 6.52 (d, J = 12, 1H), 6.32 (d, J = 2.25, 1H), 5.68 (d, J = 12, 1H), 4.96 (s, 1H), 4.74−4.72 (m, 1H), 3.83 (s, 3H), 3.78 (s,3H), 3.35 (br s, OH), 3.26 (br s, OH), 2.25 (dd, J = 17.38, 6.02, 1H), 2.04 (d, J = 17.38, 1H), 1.70 (br s, OH), 1.15 (s,3H), 1.14 (s, 3H), 1.08 (s, 3H); ^{13}C NMR δ 157.96, 154.58, 142.88, 136.93, 133.55, 121.05, 120.50, 115.02, 100.99, 94.52, 77.95, 73.62, 67.04, 53.55, 53.19, 41.53, 31.88, 19.97, 16.74, 15.32; IR ($CHCl_3$) 3500 cm^{-1}. Anal. Calcd for $C_{20}H_{26}O_5$: C, 69.34; H, 7.57. Found: C, 69.44; H, 7.55.

Acetate 18. To a solution of **14** (66 mg, 0.2 mmol) in 3 mL of CH_2Cl_2 at ambient temperature were added DMAP (3 mg), triethylamine (40 μL, 0.3 mmol), and acetic anhydride (23 μL, 0.24 mmol). After being stirred for 30 min, the reaction mixture was poured into 40 mL of 1:1 ethyl acetate−10% aqueous NH_4Cl. The aqueous layer was extracted twice with ethyl acetate, and the combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated. Filtration of the residue through silica gel provided **18** (72 mg, 96%) as a white solid: mp 133−136 °C; ^{1}H NMR δ 6.64 (d, J = 2.33, 1H), 6.60 (d, J = 10.33, 1H), 6.48 (d, J = 10.33, 1H), 6.35 (d, J = 2.33, 1H), 5.96 (s, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 2.34−2.20 (m, 2H), 2.09 (s, 3H), 1.73 (dt, J = 13.69, 4.01, 1H), 1.36−1.22 (m, 1H), 1.28 (s, 3H), 1.15 (s, 3H), 0.82 (s, 3H); ^{13}C NMR δ 171.50, 158.35, 158.04, 142.11, 135.55, 134.58, 133.08, 127.16, 120.04, 103.55, 96.50, 78.99, 74.82, 55.74, 55.28, 38.80, 28.68, 26.38, 23.64, 21.41, 21.23, 20.58; IR ($CHCl_3$) 3540, 1730 cm^{-1}. Anal. Calcd for $C_{22}H_{28}O_5$: C, 70.95; H, 7.58. Found: C, 70.98; H, 7.64.

Acetate 19. To a solution of **18** (100 mg, 0.27 mmol) in 5 mL of CH_2Cl_2 at 0 °C was added *m*-chloroperbenzoic acid (93 mg, 0.54 mmol). After being stirred at this temperature for 20 min, the reaction mixture was diluted with 50 mL of CH_2Cl_2, washed with 20% aqueous $NaHSO_3$, 10% aqueous $NaHCO_3$, water, and brine, dried (Na_2SO_4), and concentrated. Chromatography of the residue gave **19** (82 mg, 79%). Alternatively, when the reaction was carried out in 6 mL of 1:1 CH_2Cl_2−saturated aqueous $NaHCO_3$, **19** was obtained in 86% yield: IR ($CHCl_3$) 3510, 1730 cm^{-1}; ^{1}H NMR δ 6.66 (d, J = 11.97, 1H), 6.46 (d, J = 2.19, 1H), 6.32 (d, J = 2.19, 1H), 6.12 (s, 1H), 5.76 (d, J = 11.97, 1H), 4.76−4.74 (m, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 2.52 (br s, OH), 2.30 (dd, J = 17.39, 5.29, 1H), 2.13 (s, 3H), 2.09 (d, J = 17.39, 1H), 1.80 (br s, OH), 1.22 (s, 3H), 1.20 (s, 3H), 1.14 (s, 3H).

Epoxide 21. To a solution of **18** (100 mg, 0.27 mmol) in 5 mL of CH_2Cl_2 at 0 °C was added a solution of freshly prepared dimethyldioxirane in acetone (approximately 0.1 M, 4.4 mL, 0.44 mmol). After 10 min, concentration and purification of the residue by radial chromatography provided **21** (103 mg, quantitative) as white crystals. Alternatively, radial chromatography of the reaction mixtures above that otherwise led to **19** allowed the isolation of **21**: mp 118−120 °C; ^{1}H NMR δ 6.86 (d, J = 11.07, 1H), 6.72 (d, J = 2.17, 1H), 6.34 (d, J = 2.17, 1H), 6.00 (d, J = 11.07, 1H), 5.96 (s, 1H), 3.84 (s, 3H), 3.77 (s, 3H), 2.36 (br s, OH), 2.29 (ddd, J = 11.40, 5.67, 2.65, 1H), 2.10 (s, 3H), 1.89 (app dt, J = 12.06, 5.67, 1H), 1.57 (app t, J = 12.06, 1H), 1.36 (s, 3H), 1.34−1.23 (m, 1H), 1.02 (s, 3H), 0.14 (s, 3H); ^{13}C NMR δ 206.85, 169.49, 160.16, 158.54, 139.75, 129.66, 125.97, 120.11, 103.98, 96.09, 75.18, 74.62, 66.27, 61.90, 55.37, 55.17, 39.57, 27.45, 25.92, 22.63, 21.28, 20.85; IR ($CHCl_3$) 3500, 1730 cm^{-1}. Anal. Calcd for $C_{22}H_{28}O_6$: C, 68.02; H, 7.27. Found: C, 67.97; H, 7.40.

Epoxy Keto Aldehyde 22 from 20. To a solution of **14** (66 mg, 0.2 mmol) in 1 mL of CH_2Cl_2 at 0 °C was added in aliquots until **14** was consumed a solution of freshly prepared dimethyldioxirane in acetone (approximate 0.1 M). Concentration and radial chromatography gave **22** (20 mg, 29%): mp 107−109 °C; ^{1}H NMR δ 10.08 (s, 1H), 7.02 (d, J = 2.34, 1H), 6.74 (d, J = 12.59, 1H), 6.62 (d, J = 2.34, 1H), 6.16 (d, J = 12.59, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 2.38−2.06 (m, 4H), 1.26 (s, 3H), 1.23 (s, 3H), 1.09 (s, 3H); ^{13}C NMR δ 211.20, 191.17, 159.44, 157.59, 134.84, 128.25, 126.43, 123.02, 103.36, 99.87, 68.45, 61.46, 55.03, 54.99, 47.50, 32.90, 26.95, 22.61, 20.30, 18.22; IR ($CHCl_3$) 1715, 1700 cm^{-1}. Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.75 ; H, 7.02. Found: C, 69.72 ; H, 7.19.

***Z*-Keto Aldehyde 13 from 14.** To a solution of **14** (40 mg, 0.12 mmol) and $VO(acac)_2$ (0.5 mg) in 3 mL of benzene at ambient temperature was added dropwise a solution of *tert*-butyl hydroperoxide in 2,2,4-trimethylpentane (3 M, 48 μL, 0.15 mmol). After being stirred for 2 h, the reaction mixture was diluted with water and extracted three times with ether. The combined organic layers were washed with water and brine, dried (Na_2SO_4), and concentrated to furnish **13** in quantitative yield.

To a solution of **14** (33 mg, 0.1 mmol) and $Mo(CO)_6$ (2 mg) in 2.5 mL of benzene was added dropwise a solution of *tert*-butyl hydroperoxide in 2,2,4-trimethylpentane (3 M, 40 μL, 0.12 mmol). No reaction was observed at ambient temperature, but upon heating to reflux for 1.5 h, **14** was converted to **13**, which was obtained in quantitative yield after workup as above.

Silyl Ether 23. To a solution of **14** (850 mg, 2.6 mmol), imidazole (352 mg, 5.2 mmol), and DMAP (10 mg) in 16 mL of DMF was added *tert*-butyldimethylsilyl chloride (467 mg, 3.09 mmol), and the mixture was heated to 60 °C and stirred for 2 h. The reaction mixture was cooled, diluted with 20 mL of water, and extracted three times with ether. The organic layers were combined, washed three times with water and brine, dried (Na_2SO_4), and concentrated. Chromatography of the residue gave **23** (900 mg, 82%): ^{1}H NMR δ 6.74 (d, J = 2.29, 1H), 6.53 (d, J = 10.22, 1H), 6.46 (app dd, J = 10.22, 1.23, 1H), 6.30 (d, J = 2.29, 1H), 4.76 (s, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 2.28−2.07 (m, 2H), 1.67 (dt, J = 13.16, 3.15, 1H), 1.29−1.17 (m, 1H), 1.22 (s, 3H), 1.15 (s, 3H), 0.87 (s, 9H), 0.79 (s, 3H), −0.10 (s, 3H), −0.34 (s, 3H); ^{13}C NMR δ 158.34, 157.72, 145.17, 135.36, 135.19, 133.56, 126.77, 119.73, 104.32, 96.67, 77.72, 77.23, 73.78, 55.77, 55.25, 38.77, 28.99, 27.29, 25.81, 25.72, 23.80, 21.65, 20.76, 18.18, −4.96, −5.71.

Reaction of 23 with $Mo(CO)_6$−*t*-BuOOH. To a mixture of **23** (88 mg, 0.2 mmol), $Mo(CO)_6$ (2 mg), and solid Na_2HPO_4 (100 mg) in 10 mL of benzene was added dropwise *tert*-butyl hydroperoxide (70% in water, 23 μL, 0.24 mmol). The reaction mixture was heated to reflux for 6 h and cooled, and solid Na_2SO_3 was added, followed by dilution with water. The aqueous layer was extracted three times with ether, and the combined organic layers were washed with 10% aqueous $NaHCO_3$, water, and brine, dried (Na_2SO_4), and concentrated. Chromatography of the residue gave **13** (35 mg, 53%) and **22** (19 mg, 29%).

Epoxy Keto Aldehyde 22 from 13. To a solution of **13** (300 mg, 0.92 mmol) in 10 mL of ethanol at 0 °C was added solid $NaBH_4$ (35 mg, 0.9 mmol). After being stirred for 30 min, acetone and water were added sequentially. The reaction mixture was extracted three times with ether, and the organic layers were combined, washed with water and brine, dried (Na_2SO_4), and evaporated. Chromatography of the residue gave the related diol (220 mg, 73%): ^{1}H NMR δ 6.65 (d, J = 2.31, 1H), 6.39 (d, J = 2.31, 1H), 6.32 (d, J = 11.89, 1H), 6.23 (d, J = 11.89, 1H), 4.63 ($^1/_2$ ABq, J = 12.56, 1H), 4.46 ($^1/_2$ ABq, J = 12.56, 1H), 3.62−3.53 (m, 1H), 2.51−2.30 (m, 1H), 2.15−2.02 (m, 1H), 1.93−1.83 (m, 1H), 1.77−1.62 (m, 1H), 1.16 (s, 3H), 1.14 (s,3H), 1.06 (s, 3H).

To a solution of the above diol (200 mg, 0.6 mmol) in 3 mL of 1:1 CH_2Cl_2−saturated aqueous $NaHCO_3$ at 0 °C was added *m*-chloroperbenzoic acid (155 mg, 0.9 mmol). The reaction mixture was stirred for 40 min and then diluted with 30 mL of CH_2Cl_2, and the organic layer was washed with 20% aqueous

$NaHSO_3$, 10% aqueous $NaHCO_3$, water, and brine, dried (Na_2SO_4), and concentrated. Chromatography of the residue gave the related epoxy diol (120 mg, 57%): ^{1}H NMR δ 6.69 (d, J = 2.40, 1H), 6.50 (d, J = 12.05, 1H), 6.33 (d, J = 2.40, 1H), 5.93 (d, J = 12.05, 1H), 4.55−4.34 (m, 2H), 3.84 (s, 3H), 3.77 (s, 3H), 3.30−3.12 (m, 1H), 2.40−2.28 (m, 1H), 2.25−2.10 (m, 1H), 1.89−1.78 (m, 1H), 1.70−1.53 (m, 1H), 1.39 (s, 3H), 1.21 (s, 3H), 1.08 (s, 3H).

To a solution of the above epoxy diol (60 mg, 0.17 mmol) in 10 mL of CH_2Cl_2 at ambient temperature were added 4 Å molecular sieves (1 g), tetrapropylammonium perruthenate (2 mg), and *N*-methylmorpholine *N*-oxide (35 mg, 0.262 mmol). The reaction mixture was stirred for 30 min, filtered through silica gel with the aid of ethyl acetate, and concentrated to provide **22** in quantitative yield.

Reaction of 17 with $Mo(CO)_6$−*t*-BuOOH. To a solution of **17** (20 mg, 0.06 mmol) and $Mo(CO)_6$ (3 mg) in 6 mL of 2:1 benzene−CH_2Cl_2 was added dropwise *tert*-butyl hydroperoxide (70% in water, 16 μL, 0.14 mmol). The reaction mixture was refluxed for 10 h and then cooled. Workup and purification as above for the reaction of **23** with $Mo(CO)_6$−*t*-BuOOH gave **22** (16 mg, 80%).

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