Cycloaddition−Fragmentation as a Route to Bicyclic Ring Systems. Use of the Intermolecular Diyl Trapping Reaction

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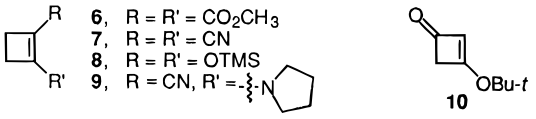
A route to bicyclo[*n*.3.0] ring systems ($n = 5-7$) has been devised. Key transformations include an intermolecular diyl trapping reaction (**1** + **3** → **4**), and fragmentation of the resulting tricyclic cycloadduct **4** (**4** → **5**). A variety of diylophiles were examined, including electron deficient (**6**, **7**, **21**, **29**, **30**, **31**), electron rich (**8**), and push-pull cycloalkenes (**9**, **10**, **19**, **20**).

Introduction

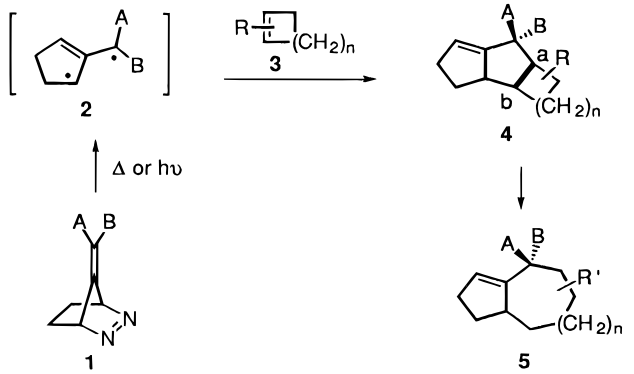
Bicyclo[*n*.3.0] ring systems are found in many naturally occurring materials.[1] One route to this framework involves the assembly and subsequent fragmentation of a tricyclic system.[2] In this paper, we report the results of our efforts to use the *inter*molecular diyl trapping reaction as a reasonably rapid entry to the bicyclo[*n*.3.0] assembly, in cases where $n = 5-7$. As shown in Scheme 1, our approach calls for either a thermally or a photochemically induced extrusion of nitrogen from diazene **1** to afford a 2-alkylidenecyclopentane-1,3-diyl **2**,[3,4] interception of the diyl to afford the tricyclic cycloadduct **4**, and scission of the σ bond, C_a-C_b, to provide the desired ring system **5**.

Results and Discussion

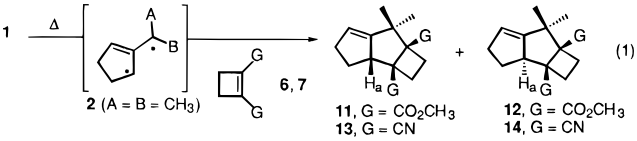
Bicyclo[5.3.0] Framework. In an effort to assemble this system, we examined cyclobutenes **6**−**10** as potential diylophiles. Given that electron deficient olefins are excellent trapping agents,[4] we anticipated that **6** and **7** would function admirably. It was not clear, however, whether **8**, **9**, or **10** would be useful, given the presence of both an electron-withdrawing and an electron-donating substituent in **9** and **10**, and two donating groups in **8**. In practice, cyclobutenes **8**-**10** all failed to intercept the electron rich diyl **2** (A = B = CH_3). Diyl dimerization occurred instead.



Scheme 1



Cycloaddition readily occurred using each of the electron deficient alkenes **6** and **7** (see eq 1). While the yields were high, stereoselectivity was not. Determination of the ring junction stereochemistry in compounds **11**−**14** was aided by the fact that when the allylic methine proton, H_a, is cis to the electron-withdrawing groups, as in compounds **11** and **13**, it consistently appears downfield of the signal for the corresponding methine in the stereoisomer. The chemical shift difference at 500 MHz varies from ∼0.1 ppm for **13** and **14**, to ∼0.2 ppm for the diesters **11** and **12**, to ∼0.3 ppm for the anhydrides **22** and **23**, yet to be discussed. The nitriles **13** and **14** were converted to the corresponding diesters **11** and **12** to confirm their structure and add credibility to the ^{1}H NMR correlations.



G	cis,syn/cis,anti ratio	yield (%)	conditions*
CO_2CH_3	4.5:1 (**11**/**12**)	94	neat diylophile (5-fold excess), 75 °C, 80 min
CN	1.3:1 (**13**/**14**)	89	3-fold excess diylophile (1.67M), CH_3CN, reflux

* While an excess of diylophile is used, it can easily be recovered and reused.

The conversion of tricyclic diesters **11** and **12** to the desired bicyclo[5.3.0]decane framework was accomplished by reducing a mixture of the diastereomers with lithium in liquid ammonia (see eq 2).[5] Quenching the resulting

[⊗] Abstract published in *Advance ACS Abstracts,* February 1, 1996.

(1) (a) Fraga B. M. *Nat Prod. Rep.* **1992**, *9*, 217. (b) Petasis, N. A.; Patane, M. A. *Tetrahedron* **1992**, *48*, 5757. (c) Roxburgh, C. J. *Tetrahedron* **1993**, *49*, 10749. (d) Kozikowski, A. P.; Jung, S. H. *Tetrahedron Lett.* **1986**, *27*, 3227. (e) Wender, P. A.; Ihle, N. C.; Correia, C. R. D. *J. Am. Chem. Soc.* **1988**, *110*, 5904. (f) Devon, T. K.; Scott, A. I. *Handbook of Naturally Occurring Compounds Volume II Terpenes*; Academic: New York, 1972. (g) Jakupovic, J; Schuster, A; Bohlmann, F.; Ganzer, U.; King, R. M.; Robinson, H. *Phytochemistry* **1989**, *28*, 543.

(2) (a) Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091. (b) Trost, B. M.; Parquette, J. R. *J. Org. Chem.* **1994**, *59*, 7568. (c) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 3705. (d) Ghosh, S.; Karpha, A.; Saha, G. Patra, D. *Tetrahedron Lett.* **1992**, *33*, 2363. (e) Lautens, M.; Kumanovic, S. *J. Am. Chem. Soc.* **1995**, *117*, 1954. (f) Lange, G. L.; Gottardo, C. *J. Org. Chem.* **1995**, *60*, 2183. (g) Resse, C. B.; Sanders, H. P. *Synthesis* **1981**, 276. (h) Fujiwara, T.; Tomaru, J.; Suda, A.; Takeda, T. *Tetrahedron Lett.* **1992**, *33*, 2583. (i) Batroff, V.; Flitsch, W. *Liebigs Ann. Chem.* **1987**, 621. Also, see refs 5, 10, 13, 15, 18, and 26.

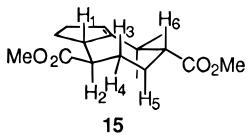
(3) (a) Dowd, P. *Acc. Chem. Res.* **1972**, *5*, 242. (b) Little, R. D. *Chem. Rev.*, in press.

(4) Berson, J. A. *Diradicals*; Borden, W. T. Ed.; John Wiley & Sons: New York, 1982; Chapter 4.

(5) (a) Coates, R. M.; Senter, P. D.; Baker, W. R.; *J. Org. Chem.* **1982**, *47*, 3597. (b) Baker, W. R.; Senter, P. D.; Coates, R. M. *J. Chem. Soc., Chem. Commun.* **1980**, 1011. (c) Saha, G.; Bhattacharya, A.; Roy, S. S.; Ghosh, S. *Tetrahedron Lett.* **1990**, *31*, 1483. (d) Gassman, P. G.; Creary, X. *J. Chem. Soc., Chem. Commun.* **1972**, 1214. (e) Bloomfield, J. J.; Martin, R. A.; Nelke, J. M. *J. Chem. Soc., Chem. Commun.* **1972**, 96.

0022-3263/96/1961-1787$12.00/0

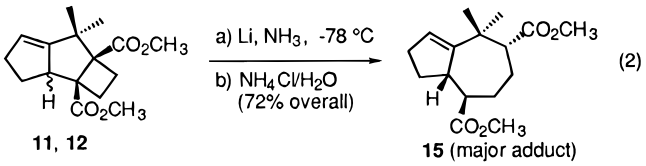
Table 1. Result of NOE Experiments (% NOE)



15

	irradiate				
observe	H_1	H_2	H_3	H_4	H_5
H_4					6.8
H_5		2.9		4.4	
H_6	2.3		3.4		

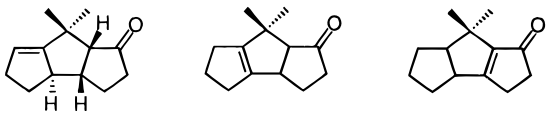
intermediate at low temperature with saturated aqueous ammonium chloride produced a 27:4:2:1 mixture of diastereomeric diesters in a combined yield of 72%. Attempts to improve selectivity and yield by using other proton donors were unsuccessful.[6]



11, 12 **15** (major adduct) (2)

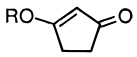
The diastereomers were separated, and the stereochemistry of the major adduct **15** was determined from extensive decoupling and NOE experiments (Table 1). The stereochemistry corresponds to one where both esters occupy pseudoequatorial orientations about the seven-membered ring. Molecular mechanics calculations place this diastereoisomer more than 2 kcal/mol lower in energy than any of the alternatives.[7]

Bicyclo[6.3.0] Framework. We intended to use the previously characterized tricyclic enone **16** as an entry point to this system.[8] The plan was simply to move the trisubstituted C−C π bond to either of the tetrasubstituted positions portrayed in structures **17** and **18** and then cleave it to afford an eight-membered ring. Unfortunately, we were unable to cleanly effect the isomerization using rhodium trichloride in ethanol at reflux[9] or at 145 °C in a sealed tube.



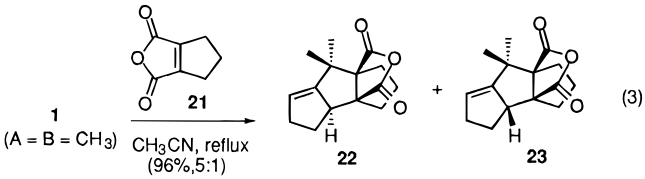
16 **17** **18**

We also attempted to access the ring system *via* cycloaddition to 3-methoxy-2-cyclopenten-1-one (**19**) and 3-acetoxy-2-cyclopenten-1-one (**20**), followed by the application of well-established retroaldol methodology to generate the eight membered ring.[10] Unfortunately, neither enone proved to be an effective diylophile. This was particularly surprising with the acetoxy enone **20**, as we reasoned that the acetyl group would sufficiently attenuate the electron-donating ability of the substituent to allow cycloaddition to occur more rapidly than dimerization. AM1 calculations corroborated this notion, placing the LUMO energy for **20** well below that of **19**.



19, R = CH_3
20, R = $COCH_3$

The desired bicyclo[6.3.0] framework was eventually obtained *via* cycloaddition using the bicyclic anhydride **21**, followed by reduction of the C−C π bond, hydrolytic opening of the anhydride, and oxidative cleavage (note eq 3 and Scheme 2). Like maleic anhydride, **21** proved to be a reactive diylophile.[4] Thus, the portionwise addition over 3 h, of a 0.8 M solution of the diazene **1** (A = B = CH_3) to a 0.8 M solution of the anhydride in



22 **23** (3)

acetonitrile at reflux, afforded a 96% yield of a 5:1 mixture (by ^{1}H NMR) of propellanes **22** and **23**. In this case, we found it convenient to use a 20% excess of diazene because it proved simpler to remove dimer rather than excess diylophile.

The major adduct, **22**, corresponded to that resulting from the endo mode of cycloaddition. We have previously encountered a similar result in the cycloaddition of the dimethyl diyl **2** (A = B = CH_3) to cyclopentenone.[8] This outcome is reminiscent of the endo-selectivity which is often associated with kinetically controlled Diels−Alder reactions. It is possible that bonding secondary orbital interactions between the diyl and diylophile could play a role in determining the stereochemical outcome of the diyl trapping cycloaddition. However, one must exercise caution in applying this concept to both types of reactions, for exceptions exist.[11]

Since the stereochemical difference between compounds **22** and **23** is removed in the sequence of reactions leading to **27** (Scheme 2), the materials were combined and subjected to catalytic hydrogenation. The anhydride was opened hydrolytically, and the resulting diacids **24** were subjected to oxidative cleavage. This afforded a mixture of dione **27** and the regioisomeric β-lactones, **25** and **26**, resulting from carboxylate capture of the intermediate formed during oxidation with lead tetraacetate.[12] It proved straightforward to convert the lactones to

(6) A 9:2:1:0.2 diastereomeric ratio was obtained when quenching with Et_3NHOAc: Lombardo, L.; Mander, L. N.; Turner, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 6626. A 8:3:1:0.1 diastereomeric ratio was obtained when quenching with chiral proton donor (−)-1-[5-chloro-2-(methylamino)phenyl]-1,2,3,4-tetrahydroisoquinoline ($pK_a = 6.4$): Vedejs, E.; Lee, N.; Sakata, S. T. *J. Am. Chem. Soc.* **1994**, *116*, 2175 and Ott, H.; Hardtmann, G. E.; Denzer, M.; Frey, A. J.; Gogerty, J. H.; Leslie, G. H.; Trapold, J. H. *J. Med. Chem.* **1968**, *11*, 777. When portion of the 27:4:2:1 mixture was stirred overnight in NaOMe and MeOH at rt, the GLC ratio changed to 85:6:5:1.

(7) Energy calculations were carried out using HyperChem (version 3.0) at the MM+ level. The following values were found for the four diastereomers 1*R**,2*S**,5*S** (**15**); 1*R**,2*S**,5*R**; 1*R**,2*R**,5*R**; 1*R**,2*R**,5*S**, respectively: 28.3, 32.6, 33.8, 35.3 kcal/mol.

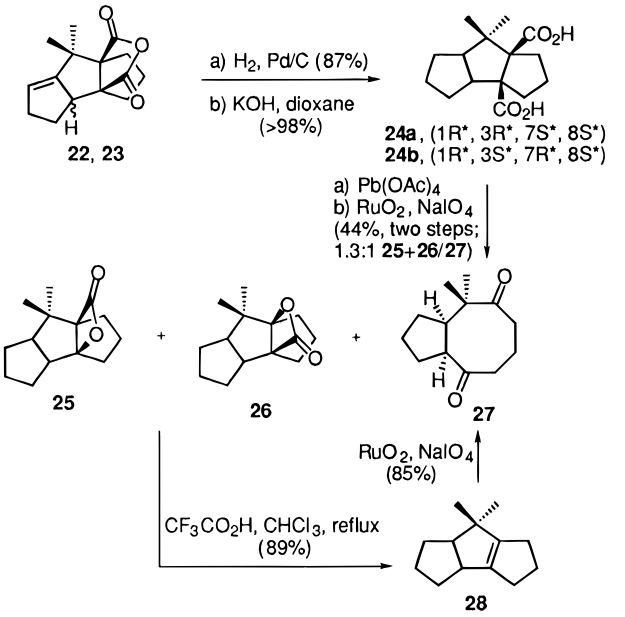
(8) Little, R. D.; Bukhari, A.; Venegas, M. G. *Tetrahedron Lett.* **1979**, *20*, 305.

(9) Grieco, P. A.; Nishizawa, M.; Marinovic, N.; Ehmann, W. J. *J. Am. Chem. Soc.* **1976**, *98*, 7102. Also, see ref 26.

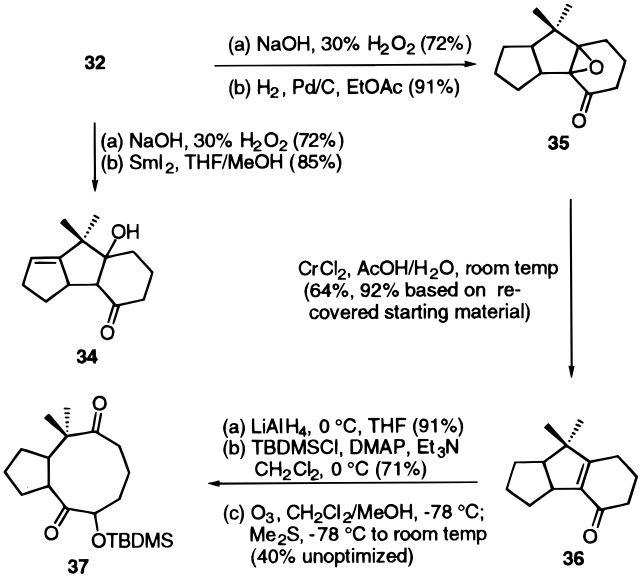
(10) (a) Pak, C. S.; Kim, S. K.; Lee, H. K. *Tetrahedron Lett.* **1991**, *32*, 6011. (b) Pak, C. S.; Kim, S. K. *J. Org. Chem.* **1990**, *55*, 1954. (c) de Mayo, P. *Acc. Chem. Res.* **1971**, *4*, 41. (d) Hikino, H.; de Mayo, *J. Am. Chem. Soc.* **1964**, *86*, 3582. (e) Hill, J. H. M.; Reid, S. T. *J. Chem. Soc., Chem. Commun.* **1983**, 501. (f) Umehara, M.; Honnami, H.; Hishida, S.; Kawata, T.; Ohba, S.; Zen, S. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 562.

(11) (a) Ginsburg, D. *Tetrahedron*, **1983**, *39*, 2095. (b) Little, R. D.; Muller, G. W. *J. Am. Chem. Soc.* **1979**, *101*, 7129. (c) Little, R. D.; Muller, G. W.; Venegas, M. G.; Carroll, G. L.; Bukhari, A.; Patton, L.; Stone, K. *Tetrahedron* **1981**, *37*, 4371. (d) Little, R. D.; Higby, R. G.; Moeller, K. D. *J. Org. Chem.* **1983**, *48*, 3139.

Scheme 2. Formation of the Bicyclo[6.3.0] Framework

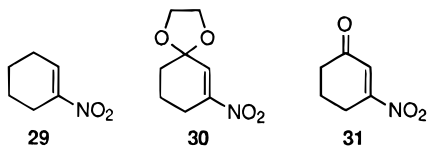


Scheme 3. Formation of the Bicyclo[7.3.0] Framework

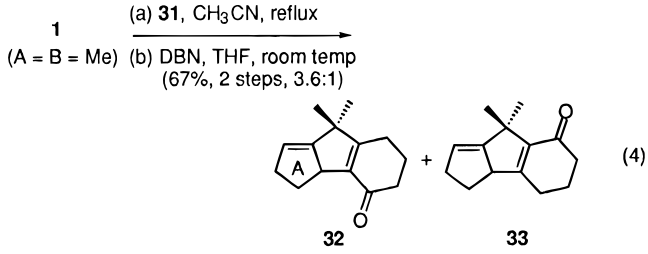


alkene **28** in good yield using trifluoroacetic acid; subsequent treatment with ruthenium dioxide/sodium periodate afforded an 85% yield of the desired bicyclo[6.3.0] adduct **27**.[13] We portray a cis-ring junction stereochemistry in **27** based on two factors: only a single isomer is obtained, and given the 7−8 kcal/mol energy difference between cis and trans-fused bicyclo[3.3.0]octane, it is likely that hydrogenation of **22**/**23** affords a cis-fused adduct. Once that fusion is determined, subsequent transformations leave it unmodified.

Bicyclo[7.3.0] Framework. We first elected to examine the utility of 1-nitrocyclohexene (**29**) and related nitroalkenes **30** and **31** as diylophiles. The idea simply called for cycloaddition, elimination, and oxidative cleavage of the resulting C−C π bond. 1-Nitrocyclohexene (**29**) proved to be a satisfactory, but not an ideal trapping agent, since it afforded a mixture of regioisomeric cycloadducts and diyl dimers (62% combined, 1:1.4 cycloadduct/dimers). Ketal **30** was less useful, delivering only a 21% yield of cycloadducts mixed with dimers (19%). We suspect that the steric interaction between the ketal unit in **30** and the *gem*-methyl group of the diyl **2** (A = B = CH_3) might at least be partially responsible for the diminished yield in this instance.[8,14]



Given the electron deficient character of 3-nitrocyclohexenone (**31**), we anticipated that it would serve admirably as a diylophile. It did. We used the adducts to explore two approaches to the desired ring system. In one, the initially formed β-nitro ketone tricycles were reduced in an effort to generate an amine that was to serve as a substrate for a retro-Mannich reaction.[15] Unfortunately, we encountered a number of difficulties and elected to abandon this route. Instead, we chose to follow a two-step protocol calling for cycloaddition and β-elimination of the nitro group in the manner portrayed by eq 4. This afforded a 67% yield of a 3.6:1 mixture of regioisomers **32** and **33**. The identity of each was readily established using shift reagent and NOE experiments.



(4)

The major regioisomer **32** was converted to the β-hydroxy ketone **34** in the manner shown in Scheme 3. However, all attempts to effect a retroaldol reaction failed.[10,16] In a successful alternative, we elected to remove the A-ring π bond, clearly a potentially valuable site for functionalization in future work, and oxidatively cleave the remaining carbon-carbon double bond. The enone was first masked as an epoxy ketone, and the double bond was then reduced to afford compound **35**.

(12) (a) Sheldon, R. A.; Kochi, J. K. *Org. React.* **1972**, *19*, 279−421. (b) Cimarusti, C. M.; Wolinsky, J. *J. Am. Chem. Soc.* **1968**, *90*, 113−20.

(13) By comparing the conversion of **28** to **27** and the two-step conversion of **24** to **25**, **26**, and **27**, it is clear that the low yield in the latter process is associated with the lead acetate step. See also, ref 12a. 1,2-Dibromocyclopentene was used as a diylophile in an effort to obtain a higher yield of **28** and reduce the number of steps required for its synthesis. It was thought that interception of diyl **2** by this cycloalkene, followed by hydrogenation would lead to the vicinal dibromo equivalent of **24**. Reduction, using Zn or NaI promised to afford **28**. Unfortunately, using conditions similar to those portrayed in eq 3, cycloaddition did not occur. Instead, dimers of diyl **2** were produced in >95% yield.

(14) (a) Little, R. D.; Bode, H.; Stone, K. J.; Wallquist, O.; Dannecker, R. *J. Org. Chem.* **1985**, *50*, 2400. (b) Siemionko, R.; Shaw, A.; O'Connell, G.; Little, R. D.; Carpenter, B. K.; Shen, L.; Berson, J. A. *Tetrahedron Lett.* **1978**, 3542.

(15) (a) Booker-Milburn, K. I.; Cowell J. K.; Harris, L. J. *Tetrahedron Lett.* **1994**, *35*, 3883. (b) Hünig, S.; Buysch, H.; Hoch, H.; Lendle, W. *Chem. Ber.* **1967**, *100*, 3996. (c) Hünig, S.; Buysch, H. *Chem. Ber.* **1967**, *100*, 4010, 4017.

(16) Use of *t*-BuOK in MeOH at rt, or aqueous KOH in dioxane (rt to reflux) led to facile formation of enone **32**. Use of $(Me_3Si)_2NK$ in PhMe at rt did not form enone **32**, but lead to destruction of material.

Re-establishment of the enone was achieved using chromium(II) chloride (**35** → **36**),[17] thereby setting the stage for a selective 1,2-hydride addition and silylation.

Ozonolytic cleavage of the π bond led to the nine-membered ring and the desired bicyclo[7.3.0] framework **37**.[18]

Concluding Remarks. The intermolecular diyl trapping reaction provided a rapid entry to several bicyclic ring systems of the [*n*.3.0] type and exceptionally simple access to the linearly fused [5.5.4] ring systems. The latter serve as a convenient source of the bicyclo[5.3.0]-decane skeleton which is associated with many natural products. Of the diylophiles studied, the electron deficient systems **6**, **7**, and **21** proved most reactive, while the push-pull (**9**, **10**, **19**, and **20**) and electron rich (**8**) alkenes were unreactive. The low regio- and stereoselectivity associated with the intermolecular cycloaddition will undoubtedly be obviated by using the *intra*molecular variation of the diyl trapping reaction; work to test this notion is underway.

Experimental Section

General. All solvents were purified and dried following standard procedures, with the exception of MeCN; it was used directly after degassing with N_2 for 30 min prior to use. The term "concentrated" refers to the use of a rotary evaporator, and "concentrated *in vacuo*" to the use of a rotary evaporator followed by a vacuum pump at 0.25 torr. Temperatures refer to the theoretical bath temperatures rather than measured values. Melting points are uncorrected. Me_4Si was used as the internal reference for ^{1}H NMR, and $CDCl_3$ for ^{13}C NMR spectroscopy. Peak assignments were made by extensive use of ^{1}H decoupling, COSY, HETCOR, and NOE experiments. The terms *R** and *S** denote relative rather than absolute stereochemistry. The cycloalkenes are either commercially available (**8**, **19**, **21**, **29**, and 1,2-dibromo-1-cyclopentene) from Aldrich or have been previously prepared and reported in the literature (**6**, **7**, **9**, **10**, **20**, **30**, and **31**).[19−25]

(1*R,7*R**,8*S**)- and (1*R**,7*S**,8*S**)-1,8-Dicyano-2,2-dimethyltricyclo[6.2.0.0^{3,7}]dec-3(4)-ene (13 and 14).** A solution of dimethyl diazene **1** (402 mg, 2.95 mmol) and 1,2-dicyanocyclobutene (**7**) (920 mg, 8.85 mmol) in CH_3CN (5.3 mL) was refluxed for 3 h. The reaction mixture was concentrated, leaving a 1.3:1 mixture of cis-syn **13**:cis-anti **14** diastereomers, as evidenced by ^{1}H NMR spectroscopy. This mixture was chromatographed using a 5 × 30 cm column packed with silica gel, eluting with 1:1 pentane:CH_2Cl_2 to give a mixture of **13** and **14** (686 mg, 89%). R_f = 0.38 (**13** and **14**, 30% Et_2O in pentane, *p*-anisaldehyde). The mixture was passed through a 5 × 24 cm column packed with silica gel and eluted with 10−20% Et_2O in pentane to afford cis-syn **13** (287 mg), cis-anti **14** (188 mg), and a fraction containing mixed isomers.

For the cis-syn isomer **13**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.57 (apparent q, J = 2 Hz, 1H, vinyl), 3.72−3.64 (m, 1H, allylic methine), 2.73−2.59 (m, 2H, allylic CH_2), 2.59−2.49 (m, 1H, C_9-H or C_{10}-H), 2.31 (dt, J = 4, 12 Hz, 1H, C_9-H or C_{10}-H), 2.20−2.08 (m, 2H, one homoallylic CH_2, C_9-H or C_{10}-H), 2.06−1.96 (m, 1H, C_9-H or C_{10}-H), 1.79−1.68 (m, 1H, homoallylic CH_2), 1.28 (s, 3H, CH_3), 1.15 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 153.6 (vinyl), 122.9 (vinyl *C*H), 121.1 (*C*N), 118.6 (*C*N), 56.9 (both R_3CCN), 54.1 (allylic methine), 42.4 (R_2CMe_2), 36.1 (allylic CH_2), 25.1, 25.0 (CH_3), 24.4, 21.2, 18.3 (CH_3); FTIR (KBr) 2233 (CN), 2227 (CN), 1653 (C=C) cm^{-1}; exact mass [HRMS (EI)] calcd for $C_{14}H_{16}N_2$: 212.1313. Found: 212.1289. Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.20. Found: C, 79.35; H, 7.67; N, 13.15. Mp 104−105.5 °C.

For the cis-anti isomer **14**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.48 (apparent q, J = 3 Hz, 1H, vinyl), 3.62−3.54 (m, 1H, allylic methine), 2.81−2.73 (m, 1H), 2.70-2.60 (m, 3H), 2.46−2.39 (m, 1H), 2.29−2.21 (m, 1H), 2.16−2.10 (m, 1H), 2.05−1.94 (m, 1H), 1.37 (s, 3H, CH_3), 1.21 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9 (vinyl), 122.1 (vinyl *C*H), 119.7 (*C*N), 117.9 (*C*N), 60.9, 56.9, 47.3, 40.8, 36.7, 29.3, 28.5, 27.8, 26.9, 24.2; FTIR (KBr) 2229 (CN), 1657 (C=C); exact mass [HRMS (EI)] calcd for $C_{14}H_{16}N_2$: 212.1313. Found: 212.1340. Anal. Calcd for $C_{14}H_{16}N_2$: C, 79.21; H, 7.60; N, 13.20. Found: C, 79.14; H, 7.61; N, 13.07. Mp 104−105.5 °C.

(1*R,7*R**,8*S**)- and (1*R**,7*S**,8*S**)-1,8-Dicarbomethoxy-2,2-dimethyltricyclo[6.2.0.0^{3,7}]dec-3(4)-ene (11 and 12).** 1,2-Dicarbomethoxycyclobutene (**6**, 1.31 g, 7.69 mmol) and dimethyl diazene **1** (211 mg, 1.55 mmol) were heated to 75 °C for 80 min. The reaction mixture was concentrated and eluted through a 5 × 16 cm column packed with silica gel using 20% Et_2O in pet ether to give **11** and **12** (400 mg, 94%) in a 4.5:1 ratio as indicated by GLC (Hewlett-Packard model 5890 gas chromatograph equipped with a 30-m 5% phenylmethylpolysiloxane capillary column with the following temperature program: T_1 = 60 °C, τ_1 = 1 min; ramp 10 °C/min; T_2 = 300 °C, τ_2 = 30 min). R_f = 0.35 (20% Et_2O in pet ether, *p*-anisaldehyde).

For the cis-syn isomer **11:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.38 (m, 1H, vinyl), 3.84 (m, 1H, allylic methine), 3.73 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 2.64−2.50 (m, 2H), 2.48−2.38 (m, 1H), 2.10−2.02 (m, 1H), 1.99−1.86 (m, 2H), 1.82−1.71 (m, 1H), 1.68−1.57 (m, 1H), 1.18 (s, 3H, CH_3), 1.11 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$, APT assignment) δ 175.7 (*C*=O), 173.8 (*C*=O), 158.1 (vinyl), 118.3 (vinyl *C*H), 67.6 (C_1 or C_8), 54.8 (C_1 or C_8), 52.8 (dn), 51.9 (dn), 51.4 (dn), 41.6 (R_2CMe_2), 35.9 (allylic CH_2), 24.6 (CH_3), 24.5, 23.9, 19.7 (CH_3), 18.7; FTIR (NaCl solution cell/$CDCl_3$) 1723 (C=O), 1609 (C=C), 1288 (C−O) cm^{-1}; exact mass [HRMS (EI)] calcd for $C_{14}H_{18}O_4$ ($M^+ - C_2H_4$): 250.1205. Found: 250.1220.

For the cis-anti isomer **12**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.28 (dd, J = 4, 2 Hz, 1H, vinyl), 3.69 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.60−3.53 (m, 1H, allylic methine), 2.61−2.47 (m, 3H, both allylic CH_2, C_9-H or C_{10}-H), 2.43 (ddd, J = 8, 10, 10 Hz, 1H, C_9-H or C_{10}-H), 2.03−1.93 (m, 2H, one homoallylic CH_2 and C_9-H or C_{10}-H), 1.79 (ddd, J = 2, 8, 10 Hz, 1H, C_9-H or C_{10}-H), 1.50−1.39 (m, 1H, homoallylic CH_2), 1.23 (s, 3H, CH_3), 1.18 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) (APT assignment) δ 174.7 (*C*=O), 173.7 (*C*=O), 162.4 (vinyl), 117.9 (vinyl *C*H), 72.9, 58.8 (dn), 55.5, 51.2 (dn), 50.9 (dn), 40.9, 36.3, 27.7, 27.1 (CH_3), 26.1, 25.8, 24.4 (CH_3); FTIR (NaCl solution cell/$CDCl_3$) 1731 (C=O), 1658 (C=C), 1286 (C−O) cm^{-1}; exact mass [HRMS (EI)] calcd for $C_{16}H_{22}O_4$: 278.1518. Found: 278.1512.

Conversion of Dinitrile Adducts 13 and 14 to Diesters 11 and 12. A solution of cis-syn dinitrile **13** (53 mg, 0.25 mmol) and NaOH (181 mg, 4.5 mmol) in H_2O (0.3 mL), ethylene glycol (0.2 mL), and MeOH (1.6 mL) was heated from 60 to 105 °C over 6 h and maintained at 105 °C for 48 h. Water was added as needed to maintain a fixed volume. After 48 h, the reaction mixture was cooled to rt, and MeI (0.5 mL, 7.70 mmol) in DMF (2 mL) was added. After an additional 24 h, saturated aqueous $NaHCO_3$ (20 mL) was added, and the solution was extracted with CH_2Cl_2 (6 × 10 mL), concentrated, and chromatographed to give pure cis-syn diester **11** (24 mg, 37%).

A solution of cis-anti dinitrile **14** (100 mg, 0.47 mmol) was also converted to pure cis-anti diester **12** (18 mg, 13%) in the manner just described.

(1*R,2*S**,5*S**)-2,5-Dicarbomethoxy-6,6-dimethylbicyclo-[5.3.0]dec-7(8)-ene (15).** A mixture of diesters **11** and **12** (215

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mg, 0.773 mmol) in THF (4 mL) was added to a −78 °C solution of Li (10 mg, 1.4 mmol) in $NH_{3(l)}$ (20 mL) under Ar. The blue color immediately faded, and more Li (5 mg, 0.71 mmol) was added. After 8 min, saturated aqueous NH_4Cl (3 mL) was added over a few seconds. After 20 min at −78 °C, the reaction mixture was warmed to evaporate the NH_3. The resulting solution was cooled to 0 °C, and saturated aqueous $NaHCO_3$ (10 mL) and CH_2Cl_2 (15 mL) were added. The organic layer was removed, and the aqueous layer was extracted with CH_2Cl_2 (7 × 6 mL). The combined organics were passed through a plug of silica gel to give a 27:4:2:1 diastereomeric mixture of bicyclo[5.3.0] diesters (157 mg, 72%) as indicated by GCMS. A portion of the mixture (4 mg) was stirred overnight in NaOMe (10 mg) and MeOH (1 mL) at rt; the GLC ratio changed to 85:6:5:1. A portion of the major diastereomer **15** was isolated (35 mg) by eluting the 27:4:2:1 mixture through a 3 × 18 cm column packed with silica gel using 0−15% Et_2O in pentane. An NOE experiment was performed on a degassed (freeze thaw) sample (6 mg) dissolved $CDCl_3$ (1 mL).

For major isomer **15**: R_f = 0.26 (15% Et_2O in pentane, *p*-anisaldehyde); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.60 (dd, J = 2, 3 Hz, 1H, vinyl), 3.68 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 2.86 (dd, J = 8, 10.5 Hz, 1H, allylic methine), 2.53 (d, J = 9.5 Hz, 1H, C_5-H), 2.41−2.27 (m, 2H, C_2-H and allylic CH_2), 2.10 (ddd, J = 3, 8.5, 16 Hz, 1H, allylic CH_2), 2.00 (dddd, J = 2, 6.5, 7.5, 13.5 Hz, 1H, C_3-H), 1.96−1.85 (m, 2H, homoallylic H and C_4-H), 1.63−1.51 (m, 2H, homoallylic H and C_3-H), 1.43 (dddd J = 1.5, 9.5, 11.5, 14 Hz, 1H, C_4-H), 1.18 (s, 3H, CH_3), 1.09 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 176.7 (*C*=O), 175.6 (*C*=O), 155.1 (vinyl), 125.0 (vinyl *C*H), 54.7 (C_5), 51.6 (OCH_3), 51.3 (OCH_3), 50.4 (C_2), 45.4 (allylic methine), 38.9 (R_2CMe_2), 33.2, 33.1, 30.8 (CH_3), 29.1, 26.2, (C_4), 22.7 (CH_3); FTIR (neat/NaCl) 1733 (C=O), 1623 (C=C), 1154 (C−O) cm^{-1}; exact mass [HRMS (CI)] calcd for $C_{16}H_{25}O_4$ [M + H]: 281.1753. Found: 281.1748.

(1*R,7*R**,8*S**)- and (1*R**,7*S**,8*S**)-2,2-Dimethyltricyclo[6.3.0.0^{3,7}]undec-3(4)-ene-1,8-dicarboxylic Acid Anhydride (23 and 22).** Dimethyl diazene **1** (423 mg, 3.11 mmol) in MeCN (4 mL) was added portionwise over 3 h (∼0.3 mL/15−20 min) to a solution of cyclopent-1-ene-1,2-dicarboxylic acid anhydride (**21**, 343 mg, 2.48 mmol) in MeCN (3 mL) heated to reflux. After an additional 90 min, the reaction mixture was cooled to rt and concentrated *in vacuo* to give a 5:1 ratio of diastereomeric adducts **22** and **23**, respectively, as evidenced by ^{1}H NMR spectroscopy. This mixture was purified on a 4 × 20 cm column packed with silica gel. Eluting with 3% EtOAc in pentane afforded a mixture of diastereomers (584 mg, 96%). R_f = 0.61 (40% Et_2O in pentane, *p*-anisaldehyde). A portion of this material was separated using a 3 × 36 cm column packed with silica gel and eluting with 2.5% EtOAc in pentane, to give isolated cis-anti **22** and cis-syn **23** materials. Their slight R_f differences (TLC) could only be seen after five elutions with 0.5% EtOAc in pentane.

For the cis-anti isomer **22**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.37 (m, 1H, vinyl), 3.29−3.22 (m, 1H, allylic methine), 2.57−2.42 (m, 2H), 2.41−2.35 (m, 1H), 2.18 (dddd, J = 21.5, 8.5, 8.5, 2.5 Hz, 1H), 2.14−2.01 (m, 3H), 1.95 (dddd, J =13.5, 8, 8, 8 Hz, 1H), 1.83−1.65 (m, 2H), 1.30 (s, 3H, CH_3), 1.16 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.2 (*C*=O), 174.7 (*C*=O), 158.1 (vinyl), 119.6 (vinyl *C*H), 74.1 (C_1 or C_8), 66.3 (C_1 or C_8), 55.9 (allylic methine), 40.9 (R_2CMe_2), 38.3, 35.5, 31.9, 29.1, 26.4 (CH_3), 26.3, 23.9 (CH_3); FTIR (neat/NaCl) 1831 (C=O, shoulder at 1876), 1776 (C=O), 1215 (C−O) cm^{-1}; exact mass [HRMS (EI)] calcd for $C_{15}H_{18}O_3$: 246.1256. Found: 246.1251.

For the cis-syn isomer **23**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.37 (m, 1H, vinyl), 3.63−3.56 (m, 1H, allylic methine), 2.64−2.56 (m, 1H), 2.56−2.48 (m, 1H), 2.24−2.09 (m, 3H), 1.89−1.75 (m, 2H), 1.72 (ddd, J = 13, 13, 6.5 Hz, 1H), 1.51 (ddd, J = 13.5, 13.5, 6 Hz, 1H), 1.44−1.32 (m, 1H), 1.26 (s, 3H, CH_3), 1.19 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 177.3 (*C*=O), 174.8 (*C*=O), 155.3 (vinyl), 120.7 (vinyl *C*H), 73.4 (C_1 or C_8), 61.4 (C_1 or C_8), 51.6 (allylic methine), 40.9 (R_2CMe_2), 35.8, 34.2, 32.9, 25.6, 25.2 (CH_3), 24.8, 21.0 (CH_3); FTIR (neat/NaCl) 1851 and1830 (C=O), 1775 (C=O), 1667 (C=C), 1219 (C−O) cm^{-1}; exact mass [HRMS (EI)] calcd for $C_{15}H_{18}O_3$: 246.1256. Found: 246.1256.

(1*R,3*R**,7*S**,8*S**)- and (1*R**,3*S**,7*R**,8*S**)-2,2-Dimethyltricyclo[6.3.0.0^{3,7}]undecane-1,8-dicarboxylic Acid Anhydride (dihydro 22 and 23).** A balloon filled with hydrogen was inserted through a serum cap into a round bottom flask charged with a diastereomeric mixture of cycloadducts **22** and **23** (365 mg, 1.48 mmol) and 10% Pd/C (200 mg) in EtOAc (35 mL) at rt. After stirring for 5 h, the solution was passed through a pad of Celite/silica and concentrated *in vacuo* to give a mixture of cycloadducts dihydro **22** and **23** (320 mg, 87%). R_f = 0.92 (40% Et_2O in pentane, cerric molybdate).

For the major product, dihydro **22**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.58−2.46 (m, 2H), 2.20−2.13 (m, 1H), 2.03−1.91 (m, 3H), 1.87−1.77 (m, 2H), 1.77−1.61 (m, 3H), 1.59−1.42 (m, 3H), 1.10 (s, 3H, CH_3), 1.05 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.8 (*C*=O), 175.7 (*C*=O), 73.8, 65.8, 59.0 (methine), 54.4 (methine), 44.9, 42.2, 33.8, 28.8, 27.3, 26.6 (CH_3), 25.8, 25.2, 22.8 (CH_3); FTIR (neat/NaCl) 1851 (C=O), 1775 (C=O), 1219 (C−O) cm^{-1}; exact mass [HRMS (CI CH_4/trace NH_3)] calcd for $C_{15}H_{21}O_3$ [M + H]: 249.1491. Found: 249.1491.

For the minor product, dihydro **23**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.05−2.99 (m, 1H), 2.37−2.25 (m, 2H), 2.20−2.11 (m, 1H), 2.06−1.90 (m, 3H), 1.87−1.77 (m, 2H), 1.75−1.58 (m, 3H), 1.54−1.38 (m, 2H), 1.18 (s, 3H, CH_3), 1.17 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.4 (*C*=O), 175.9 (*C*=O), 73.2, 66.7, 63.6 (methine), 47.6 (methine), 42.8, 35.7, 35.6, 29.7 (CH_3), 28.9, 26.9, 26.6, 26.4, 21.8 (CH_3); FTIR (neat/NaCl) 1854 (C=O), 1829 (C=O), 1774 (C=O, 1728 shoulder peak), 1211 (C−O) cm^{-1}; exact mass [HRMS (CI CH_4/trace NH_3)] calcd for $C_{15}H_{21}O_3$ [M + H]$^+$: 249.1491. Found: 249.1481.

(1*R,3*R**,7*S**,8*S**)- and (1*R**,3*S**,7*R**,8*S**)-2,2-Dimethyltricyclo[6.3.0.0^{3,7}]undecane-1,8-dicarboxylic Acid (24a and 24b).** A mixture of dihydro **22** and **23** (320 mg, 1.29 mmol) and 10 M KOH (2 mL, 20 mmol) in dioxane (3 mL) was stirred for 18 h at rt. The solution was cooled to 0 °C, and 1 M HCl (24 mL, 24 mmol) was added. This mixture was extracted with CH_2Cl_2 (5 × 20 mL), dried over $MgSO_4$, and concentrated *in vacuo* to afford diacids **24a** and **24b** (410 mg, 120%, possibly due to a hydrated complex).

For the major isomer, (1*R**,3*R**,7*S**,8*S**)-**24a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.38 (bs, 2H, both CO_2H's), 2.60 (ddd, J = 13, 9, 9 Hz, 1H), 2.37 (ddd, J = 10, 9, 6 Hz, 1H), 2.33−2.24 (m, 2H), 2.14−2.07 (m, 1H), 2.07−1.99 (m, 1H), 1.90−1.78 (m, 3H), 1.78−1.70 (m, 1H), 1.70−1.59 (m, 2H), 1.59−1.45 (m, 2H), 1.21 (s, 3H, CH_3), 1.12 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 183.1 (*C*=O), 182.4 (*C*=O), 71.1, 66.1, 56.1, 54.5, 45.6, 41.3, 36.7, 30.5, 27.5, 27.1, 24.6, 23.7, 22.3; FTIR (neat/NaCl) 3550−2350 (OH), 1702 (C=O), 1692 (C=O), 1284 (C−O) cm^{-1}; exact mass [HRMS (FAB)] calcd for $C_{15}H_{23}O_4$ [M + H]$^+$: 267.1596. Found: 267.1607.

For the minor isomer, (1*R**,3*S**,7*R**,8*S**)-**24b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.49 (bs, 2H, both CO_2H's), 3.40 (ddd, J = 12, 7.5, 7.5 Hz, 1H), 2.70 (ddd, J = 11.5, 7.5, 7.5 Hz, 1H), 2.48 (ddd, J = 15, 13, 7.5 Hz, 1H), 2.10 (ddd, J = 14, 10, 8.5 Hz, 1H), 2.06−1.93 (m, 2H), 1.89 (ddd, J = 15, 9, 1.5 Hz, 1H), 1.81−1.68 (m, 3H), 1.66−1.57 (m, 1H), 1.57−1.44 (m, 3H), 0.99 (s, 3H, CH_3), 0.98 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 185.3 (*C*=O), 183.7 (*C*=O), 76.2, 66.7, 55.8, 48.2, 45.6, 34.4, 30.4, 29.6, 29.2, 29.0, 27.9, 23.8, 23.6; FTIR (neat/NaCl) 3500−2350 (OH), 1693 (C=O), 1272 (C−O) cm^{-1}; exact mass [HRMS (FAB)] calcd for $C_{15}H_{23}O_4$ [M + H]: 267.1596. Found: 267.1590.

(1*R,8*S**)-7,7-Dimethyl-2,6-dioxobicyclo[6.3.0]undecane (27), (1*R**,3*R**,7*S**,8*S**)-2,2-Dimethyltricyclo[6.3.0.0^{3,7}]undecane-1,8-carbolactone (25) and (1*R**,2*R**,6*S**,8*S**)-7,7-Dimethyltricyclo[6.3.0.0^{2,6}]undecane-1,8-carbolactone (26).** Lead tetraacetate[12] (1.30 g, 2.93 mmol) was added to the diacids **24a** and **24b** (343 mg, 1.29 mmol) in pyridine (4.5 mL, dried over 3 Å sieves and purged with O_2 for 45 min prior to use). The reaction mixture was heated to 66 °C for 10 min. After cooling to 0 °C, 2 M HNO_3 (115 mL) was added, and the solution was extracted with Et_2O (4 × 100 mL). The combined organics were extracted with saturated aqueous $NaHCO_3$ (3 × 150 mL) and brine (1 × 200 mL), dried over $MgSO_4$, and concentrated to give a solid (235 mg) which was used without further purification. Ruthenium

dioxide hydrate[26] (15 mg) and $NaIO_4$ (800 mg, 3.74 mmol) were added to the solid (235 mg) and dissolved in CCl_4 (5 mL), MeCN (5 mL), and H_2O (5 mL) at rt. After 40 min, brine (30 mL) was added, and the solution was extracted with CH_2Cl_2 (6 × 15 mL). The combined organics were passed through a silica gel plug, concentrated, and run through a 3 × 16 cm column packed with silica gel, eluting with 5−40% Et_2O in pentane to give *β*-lactones **25** and **26** (93 mg, 31%, 1.5:1 ratio by 200 MHz ^{1}H NMR) and cyclooctanedione **27** (58 mg, 21%).

For *β*-lactone mixture **25** and **26**: R_f = 0.58 (40% Et_2O in pentane, *p*-anisaldehyde); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 2.66−2.42 (m, 3H), 2.28−1.28 (m, 25H), 1.18 (s, 3H, CH_3, major isomer), 1.17 (s, 3H, CH_3, minor isomer), 1.08 (s, 3H, CH_3, major isomer), 1.01 (s, 3H, CH_3, minor isomer); ^{13}C NMR (50 MHz, $CDCl_3$, some carbons have identical shifts) *δ* 175.2 (*C*═O), 175.0 (*C*═O other isomer), 105.8 (R_3*C*OR′), 101.4 (R_3*C*OR′ other isomer), 79.2, 67.4, 66.9, 53.4, 45.9, 45.4, 41.0, 38.5, 33.9, 32.0, 29.4, 29.2, 28.8, 28.0, 27.8, 27.2, 25.3, 24.8, 24.5, 21.1, 20.1; FTIR (neat/NaCl) 1811 (C═O), 1110 (C−O) cm^{-1}; exact mass [HRMS (CI/NH_3)] calcd for $C_{14}H_{21}O_2$ [M + H]$^+$: 221.1542. Found: 221.1540.

For cyclooctanedione **27**: R_f = 0.15 (40% Et_2O in pentane, *p*-anisaldehyde); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 3.05 (ddd, *J* = 9.5, 9.5, 8 Hz, 1H, C_1-H), 2.92 (ddd, *J* = 13, 8.5, 4.5 Hz, 1H, C_3-H or C_5-H), 2.85 (ddd *J* = 8, 8, 5 Hz, 1H, C_8-H), 2.59 (ddd, *J* = 13.5, 9.0, 4.5 Hz, 1H, C_3-H or C_5-H), 2.40 (ddd, *J* = 12, 7.5, 4.5 Hz, 1H, C_3-H or C_5-H), 2.33 (ddd, *J* = 12, 7, 5 Hz, 1H, C_3-H or C_5-H), 2.21−2.06 (m, 2H, CH_2 at C_4), 2.00−1.88 (m, 2H, C_{11}-H and C_9-H), 1.88−1.78 (m, 2H, C_{10}-H and C_9-H), 1.68−1.54 (m, 2H, C_9-H and C_{10}-H), 1.12 (s, 3H, CH_3), 1.00 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 216.1 (*C*═O), 213.4 (*C*═O), 56.6 (C_1), 50.6 (R_2CMe_2), 47.7 (C_8), 43.1 (C_3 or C_5), 37.1 (C_3 or C_5), 27.2, 27.0, 26.8, 24.2 (C_4), 22.7, 19.2 (*C*H$_3$); FTIR (solid/KBr) 3367 (C═O overtone), 1694 (C═O) cm^{-1}; exact mass [HRMS (EI)] calcd for $C_{13}H_{20}O_2$: 208.1463. Found: 208.1469. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68; O, 15.36. Found: C, 74.70; H, 9.87; O, 15.55. Mp 85−86.5 °C.

Alternate Method To Open Purified (3*R, 7*S**)-2,2-Dimethyltricyclo[6.3.0.0^{3,7}]undec-1(8)-ene (28) to Cyclooctanedione 27.** Ruthenium dioxide hydrate[26] (15 mg) and $NaIO_4$ (181 mg, 0.84 mmol) were added to alkene **28** (53 mg, 0.30 mmol) in CCl_4 (2.5 mL), MeCN (2.5 mL), and H_2O (2.5 mL) at rt. After 30 min, aqueous NaCl (15 mL) was added, and the solution was extracted with CH_2Cl_2 (5 × 15 mL). The combined organics were concentrated and passed through a 2 × 24 cm column packed with silica gel using 40% Et_2O in pentane to afford cyclooctanedione **27** (53 mg, 85%).

(3*R,7*S**)-2,2-Dimethyltricyclo[6.3.0.0^{3,7}]undec-1(8)-ene (28).** A mixture of *β*-lactones **25** and **26** (83 mg, 0.38 mmol) in $CHCl_3$ (2.5 mL) and CF_3CO_2H (0.75 mL) was heated at reflux for 24 h. The reaction mixture was cooled, and saturated aqueous $NaHCO_3$ (10 mL) and Et_2O (15 mL) were added. The aqueous layer was removed, and the organic layer was extracted with saturated aqueous $NaHCO_3$ (1 × 10 mL) and brine (1 × 10 mL), concentrated, and purified by passing through a 1 × 24 cm column packed with silica gel, eluting with pentane to give alkene **28** (59 mg, 89%). R_f = 0.76, 40% Et_2O in pentane, *p*-anisaldehyde); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 3.02−2.92 (m, 1H), 2.54 (apparent q, *J* = 7 Hz, 1H), 2.21−2.09 (m, 3H), 2.08−1.97 (m, 3H), 1.61−1.33 (m, 6H), 1.01 (s, 3H, CH_3), 0.95 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 152.2 (vinyl), 144.6 (vinyl), 60.1, 45.1, 42.0, 29.9, 29.5, 29.3, 27.9, 27.5, 25.7, 22.3; FTIR (neat/NaCl) 2946 (sp^3 CH), 2895 (sp^3 CH) cm^{-1}; exact mass [HRMS (EI)] calcd for $C_{13}H_{20}$: 176.1565. Found: 176.1559.

8,8-Dimethyl-3-oxotricyclo[7.3.0.0^{2,7}]dodeca-2(7),9(10)-diene (32) and 2,2-Dimethyl-4-oxotricyclo[7.3.0.0^{3,8}]dodeca-1(12),3(8)-diene (33). A solution of dimethyl diazene **1** (203 mg, 1.49 mmol) and 3-nitro-2-cyclopenten-1-one (**31**, 408 mg, 2.89 mmol) dissolved in MeCN (5 mL) was heated to reflux for 2 h. The reaction was concentrated and passed through a silica gel plug to give an oil (274 mg). 1,5-Diazabicyclo[4.3.0]-non-5-ene (DBN, 205 mg, 1.65 mmol) was added to the oil dissolved in THF (4 mL) at rt. The reaction mixture immediately turned bright yellow; the color quickly faded (3 s), and a solid formed. After 3 h, the reaction mixture was concentrated and passed through a 3 × 15 cm column packed with silica gel to afford a 3.6:1 ratio (^{1}H NMR) of **32** and **33** . This mixture was passed through a 4 × 20 cm column packed with silica gel and eluted with 3% acetone in pentane to give **32** (114 mg, 38%), **33** (39 mg, 13%), and a mixed fraction of **32** and **33** (48 mg, 16%). R_f = 0.36, 0.49 (**32** and **33**, 10% acetone in pentane, UV active).

For **32**: ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 5.53−5.43 (m, 1H, vinyl), 3.78−3.68 (m, 1H, allylic methine), 2.57−2.49 (m, 1H, allylic C_{11}-H), 2.49−2.43 (m, 1H, homoallylic C_{12}-H), 2.40−2.30 (m, 3H), 2.30−2.24 (m, 2H), 2.06−1.98 (m, 2H), 1.51−1.42 (m, 1H, homoallylic C_{12}-H), 1.24 (s, 3H, CH_3), 1.12 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 197.8 (*C*═O), 173.5 (vinyl C_7), 157.9 (vinyl), 138.3 (vinyl C_2), 118.9 (vinyl *C*H), 50.8 (allylic methine), 44.6 (R_2CMe_2), 37.9, 34.7, 32.9 (homoallylic C_{12}), 24.0 (*C*H$_3$), 23.4, 22.9 (*C*H$_3$), 22.3; FTIR (neat/NaCl) 1666 (C═O), 1602 (C═C) cm^{-1}; exact mass [HRMS (EI)] calcd for $C_{14}H_{18}O_1$: 202.1358. Found: 202.1353.

For **33**: ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 5.45−5.41 (m, 1H, vinyl), 3.76−3.69 (m, 1H, allylic methine), 2.60−2.50 (m, 1H, allylic C_{11}-H), 2.47−2.25 (m, 5H), 2.25−2.18 (m, 1H, homoallylic C_{10}-H), 2.08−1.98 (m, 1H), 1.98−1.90 (m, 1H), 1.57−1.47 (m, 1H, homoallylic C_{10}-H), 1.42 (s, 3H, CH_3), 1.20 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 197.4 (*C*═O), 165.3 (vinyl C_8), 158.7 (vinyl), 144.9 (vinyl C_3),118.1 (vinyl *C*H), 56.3 (allylic methine), 42.4 (R_2CMe_2), 38.8, 34.6, 30.6 (homoallylic C_{10}), 24.9, 24.5 (CH$_3$), 24.4 (CH$_3$), 23.1; FTIR (neat/NaCl) 1662 (C═O), 1597 (C═C) cm^{-1}; exact mass [HRMS (EI)] calcd for $C_{14}H_{18}O_1$: 202.1358. Found: 202.1354.

NOE and Eu(fod)$_3$ Experiments: Compounds 32 and 33. Separate samples of **32** (10 mg) and **33** (10 mg) were each dissolved in $CDCl_3$ (1 mL) and degassed (freeze thaw) prior to use. Using a 500 MHz ^{1}H NMR spectrometer, a small NOE (2.1%) was noticed at the C_6 protons in **32** when the gem dimethyls were irradiated. There was no NOE observed in **33**.

Samples of **32** (15 mg) and **33** (15 mg) were each dissolved in $CDCl_3$ (1 mL). Eu(fod)$_3$ (600 mg, 8 equiv) was dissolved in $CDCl_3$ (2 mL). Increments of the Eu(fod)$_3$ solution were added to each sample, and the proton spectrum was obtained after each increment. Initially, 250 *μ*L of Eu(fod)$_3$ solution was added to **32**, and the gem dimethyl signals originally at 1.13 and 1.25 ppm moved to 3.12 and 3.21 ppm. Similarly, 250 *μ*L of Eu(fod)$_3$ solution was added to **33**, and the gem dimethyl signals originally at 1.20 and 1.42 ppm moved to 6.26 and 7.47 ppm. These results indicate that the carbonyl is nearer the gem dimethyl unit in **33** than in **32**. These results are consistent with the structure assignments made from the NOE experiments.

2,7-Epoxy-8,8-dimethyl-3-oxotricyclo[7.3.0.0^{2,7}]dodec-9(10)-ene. Sodium hydroxide (25 mg, 0.63 mmol in 0.1 mL of H_2O, 6 M) was added to a solution of cycloadduct **32** (250 mg, 1.24 mmol) in MeOH (1.3 mL) and H_2O_2 (0.4 mL of 30% aqueous H_2O_2, 3.88 mmol) at 10 °C. After 4 h, brine (10 mL) was added and the solution was extracted with CH_2Cl_2 (7 × 15 mL). The combined organics were concentrated and passed through a 3 × 18 cm column packed with silica gel; eluting with 15% Et_2O in pentane afforded *α*,*β*-epoxy ketone (194 mg, 72%). R_f = 0.29 (15% Et_2O in pentane, *p*-anisaldehyde); ^{1}H NMR (200 MHz, $CDCl_3$) *δ* 5.47−5.40 (m, 1H, vinyl), 3.46−3.28 (m, 1H, allylic methine), 2.66−1.60 (m, 10 H), 1.22 (s, 3H, CH_3), 1.07 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 206.3 (*C*═O), 153.7 (vinyl), 121.9 (vinyl *C*H), 78.9 (epoxy C_7), 67.1 (epoxy C_2), 47.4 (allylic methine), 41.1, 36.4, 35.8, 27.3, 22.6 (*C*H$_3$), 20.0 (*C*H$_3$), 19.8, 19.3; FTIR (neat/NaCl) 1705 (C═O), 1646 (C═C) cm^{-1}; exact mass [HRMS (EI)] calcd for $C_{14}H_{18}O_2$: 218.1307. Found: 218.1303.

7-Hydroxy-8,8-dimethyl-3-oxotricyclo[7.3.0.0^{2,7}]dodec-9(10)-ene. The epoxy ketone whose preparation is described above (52 mg, 0.24 mmol) in THF/MeOH (2 mL/0.4 mL) was

(26) Mehta, G.; Murthy A. N. *J. Org. Chem.* **1987**, *52*, 2875.

added to a solution of SmI_2[27] (5 mL of a 0.1 M solution in THF, 0.5 mmol) cooled to −90 °C. After 10 min, TLC indicated the presence of starting material, so additional SmI_2 (3 mL of 0.1 M soln) was added. After another 10 min, a phosphate buffer (pH 8, 0.7 g of $Na_2HPO_4 \cdot 7H_2O$, 3.4 mmol, and 0.02 g of $NaH_2PO_4 \cdot 1H_2O$, 0.14 mmol, in 25 mL of H_2O) was added. The solution was warmed to rt and extracted with Et_2O (7 × 15 mL). The combined organics were dried over Na_2SO_4, concentrated, and passed through a 2 × 28 cm column packed with silica gel; elution with 30% Et_2O in pentane afforded a mixture of *β*-hydroxy ketone **34** (21 mg, 40%, 44% based on recovered starting material), α,*β*-unsaturated ketone **32** (18 mg, 38%, 41% based on recovered starting material), and starting material (4 mg).

For hydroxy ketone **34**: $R_f = 0.06$ (30% Et_2O in pentane, *p*-anisaldehyde); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 5.52−5.43 (m, 1H, vinyl), 3.49−3.32 (m, 1H, allylic methine), 2.50−2.48 (m, 1H, allylic CH_2), 2.48−2.37 (m, 3H, one allylic CH_2 plus two unassigned protons), 2.31 (d, $J = 8$ Hz, methine at C_2), 2.30−2.20 (m, 1H, homoallylic CH_2), 2.20−2.10 (m, 1H), 1.97−1.86 (m, 1H), 1.86−1.70 (m, 1H), 1.52−1.35 (m, 1H, homoallylic CH_2), 1.08 (s, 3H, CH_3), 0.93 (s, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) *δ* 212.5 (*C*═O), 158.6 (vinyl), 119.9 (vinyl *C*H), 89.6 (R_3COH), 65.7 (methine at C_2), 47.3 (allylic methine), 44.7 (R_2CMe_2), 38.7, 35.2 (allylic CH_2), 34.1 (homoallylic CH_2), 30.0, 22.8 (CH_3), 22.2 (CH_3), 20.9; FTIR (neat/NaCl) 3456 (sharp, OH), 1695 (C═O), 1097 (C−O) cm^{-1}; exact mass [HRMS (EI)] calcd for $C_{14}H_{20}O_2$: 220.1463. Found: 220.1454.

(1*R,9*S**)-2,7-Epoxy-8,8-dimethyl-3-oxotricyclo[7.3.0.0^{2,7}]-dodecane (35).** A balloon filled with hydrogen was inserted through a serum cap attached to a round bottom flask charged with epoxy ketone (92 mg, 0.42 mmol) and 10% Pd/C (128 mg) in ethyl acetate (10 mL) at rt. This mixture was stirred for 4 h, passed through a pad of Celite, and concentrated to give dihydro epoxy ketone **35** (84 mg, 91%). $R_f = 0.48$ (30% Et_2O in pentane, same R_f as starting material but stains much lighter, *p*-anisaldehyde); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 2.88−2.77 (m, 1H), 2.47 (dt, $J = 18$, 5 Hz, 1H), 2.08−1.84 (m, 6H), 1.81−1.73 (m, 1H), 1.70−1.55 (m, 2H), 1.54-1.44 (m, 1H), 1.44−1.22 (m, 2H), 1.10 (s, 3H, CH_3), 1.03 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 206.6 (*C*═O), 81.1 (epoxy C_7), 72.5 (epoxy C_2), 54.6 (methine), 42.0, 39.7 (methine), 36.4, 30.1, 28.3, 27.5 (CH_3), 27.0, 21.1, 19.3, 18.9 (CH_3); FTIR (neat/NaCl) 1703 (C═O) cm^{-1}; exact mass [HRMS (CI/NH_3)] calcd for $C_{14}H_{21}O_2$ $[M + H]^+$: 221.1542. Found: 221.1534.

(1*R,9*S**)-8,8-Dimethyl-3-oxotricyclo[7.3.0.0^{2,7}]dodec-2(7)-ene (36).** A solution of $CrCl_2$[17] (78 mg, 0.63 mmol) dissolved in H_2O (1.25 mL) was added to epoxy ketone **35** (42 mg, 0.19 mmol) in glacial acetic acid (1 mL) at 0 °C. After 3 h at rt, there was still starting material (TLC), so more $CrCl_2$ (78 mg, 0.63 mmol) dissolved in H_2O (1.25 mL) was added. After an additional 2 h, H_2O (10 mL) was added, and the solution was extracted with CH_2Cl_2 (7 × 15 mL). The combined organics were concentrated and passed through a 2 × 18 cm column packed with silica gel. Elution with 12% Et_2O in pentane gave enone **36** (24 mg, 64%, 92% based on recovered starting material) and starting material **35** (14 mg).

For enone **36**: $R_f = 0.32$ (30% Et_2O in pentane, UV active); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 3.37−3.25 (m, 1H), 2.48−2.15 (m, 5H), 2.02−1.90 (m, 3H), 1.68−1.31 (m, 5H), 1.08 (s, 3H, CH_3), 1.08 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 198.9 (*C*═O), 170.6 (vinyl C_7), 137.9 (vinyl C_2), 53.5 (methine), 48.2, 45.4 (methine), 38.3, 31.0, 29.6 (CH_3), 29.1, 26.8, 23.7, 22.7, 21.2 (CH_3); FTIR (neat/NaCl) 1666 (C═O), 1627 (C═C) cm^{-1}; LRMS (EI) *m*/*z* 204 (M^+), 189 ($M^+ - CH_3$); exact mass [HRMS (EI)] calcd for $C_{14}H_{20}O$: 204.1514. Found: 204.1508.

(1*R,9*S**)-3-(*tert*-Butyldimethylsiloxy)-8,8-dimethyltricyclo[7.3.0.0^{2,7}]dodec-2(7)ene.** Enone **36** (23 mg, 0.11 mmol) in THF (2 mL) was added to a solution of $LiAlH_4$ (24 mg, 0.63 mmol) in THF (1.7 mL) at 0 °C . After 30 min, H_2O (24 *μ*L, over 5 min), 15% aqueous NaOH (24 *μ*L, over 5 min), and H_2O (72 *μ*L) were added sequentially. After 90 min at rt, the reaction mixture was passed through a silica gel plug with Et_2O and concentrated to afford 21 mg (91%) of allylic alcohol which was carried on immediately. Triethylamine (0.2 mL, 1.43 mmol) was added to a solution of allylic alcohol (21 mg, 0.10 mmol), *t*-BuMe_2SiCl (37 mg, 0.25 mmol), and *N*,*N*-(dimethylamino)pyridine (DMAP, 24 mg, 0.20 mmol) in CH_2Cl_2 (2 mL). After 12 h at rt, TLC indicated the presence starting material. Additional *t*-BuMe_2SiCl (38 mg, 0.25 mmol) and Et_3N (0.08 mL, 0.58 mmol) were added. After 7 h, Et_2O (50 mL) was added, and the solution was extracted with 10% aqueous HCl (2 × 25 mL). The combined aqueous layers were extracted with Et_2O (5 × 25 mL). The organics were extracted with saturated aqueous $NaHCO_3$ (1 × 50 mL) and brine (1 × 50 mL), concentrated, and passed through a 3 × 25 cm column packed with silica gel; elution with pentane afforded protected allylic alcohol (23 mg, 71%). $R_f = 0.93$ (30% Et_2O in pentane, *p*-anisaldehyde); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 4.21−4.13 (m, 1H, $R_2CHOSiR_3$), 3.28−3.15 (m, 1H, allylic methine), 2.23−2.13 (m, 1H, homoallylic methine), 1.91−1.80 (m, 1H), 1.80−1.62 (m, 4H), 1.62−1.31 m, 7H), 0.99 (s, 3H, CH_3), 0.91 (s, 3H, CH_3), 0.88 (s, 9H, $OSiR_2C(CH_3)_3$), 0.07 (s, 3H, OR_2SiCH_3), 0.06 (s, 3H, OR_2SiCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 143.3 (vinyl), 136.9 (vinyl), 65.0 ($R_2CHOSiR'_3$), 53.7 (methine), 47.2 (methine), 46.5, 33.4, 29.8, 29.6 (CH_3), 29.1, 26.8, 25.9 ($OSiR_2C(CH_3)_3$), 21.8 (CH_3), 21.6, 19.7, 18.1, −4.0 ($OSiR_2CH_3$), −4.7 ($OSiR_2CH_3$); FTIR (neat/NaCl) 1068 (C−$OSiR_3$) cm^{-1}; LRMS (EI) *m*/*z* 320 (M^+), 305 ($[M - CH_3]^+$), 263 ($[M - C(CH_3)_3]^+$); exact mass [HRMS (EI)] calcd for $C_{20}H_{36}OSi$: 320.2535. Found: 320.2540.

(1*R,8*S**)-3-(*tert*-Butyldimethylsiloxy)-7,7-dimethyl-2,6-dioxobicyclo[7.3.0]dodecane (37).** Ozone[18] was bubbled through a solution of protected allylic alcohol (18.5 mg, 0.058 mmol) in CH_2Cl_2 (7.5 mL) and MeOH (2.5 mL) for 8 min at −78 °C. Then, N_2 was bubbled through the solution for 20 min at −78 °C to remove excess O_3. Dimethyl sulfide (0.2 mL, 2.7 mmol) was added. After 1 h at −78 °C and 2 h at rt, the reaction mixture was passed through a plug of silica, concentrated, and passed through a 2 × 22 cm column packed with silica gel. Elution with 10% Et_2O in pentane afforded cyclononaanedione **37** (8 mg, 40%). $R_f = 0.53$ (30% Et_2O in pentane, phosphomolybdic acid, difficult to visualize); ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 3.98 (dd, $J = 2$, 8 Hz, 1H, $R_2CHOTBDMS$), 3.69−3.58 (m, 1H, methine C_1), 2.90−2.76 (m, 1H), 2.65 (q, $J = 8$ Hz, 1H), 2.29 (dt, $J = 17$, 5 Hz, 1H), 2.10−2.01 (m, 1H), 1.95−1.76 (m, 7H), 1.75−1.67 (m, 1H), 1.53-1.41 (m, 1H), 1.13 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 0.93 (s, 9H, $OSiR_2C(CH_3)_3$), 0.08 (s, 3H, $OSiR_2CH_3$), 0.03 (s, 3H, $OSiR_2CH_3$); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 217.6 (*C*═O), 215.6 (*C*═O), 78.6 ($R_2CHOSiR'_3$), 50.5, 49.7 (methine), 47.2 (methine), 34.2, 32.2, 31.7, 28.2 (CH_3), 28.0, 25.7 ($OR_2SiC(CH_3)_3$), 24.8, 18.7 (CH_3), 18.5, 18.1, −4.9 (OR_2SiCH_3), −5.3 (OR_2SiCH_3); FTIR (neat/NaCl) 1707 (C═O), 1119 (C−O−SiR_3) cm^{-1}; LRMS (EI) *m*/*z* 352 (M^+), 337 ($[M - CH_3]^+$), 295 ($[M - C(CH_3)_3]^+$); exact mass [HRMS (EI)] calcd for $C_{20}H_{36}O_3Si$: 352.2434. Found: 352.2426.

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Supporting Information Available: Spectral data for compounds **11**−**16**, **22**, **23**, dihydro-**22** and -**23**, **24a**,**b**, **25**−**28**, **32**−**37**, epoxy ketone derived from **33**, alkene precursor of **37** (123 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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