Oxygen-Directed Carbocyclizations of 2,3-Epoxy Alcohols: Stereoselective Construction of Polyfunctionalized Seven-Membered Rings by 7-*Endo-Tet* Ring Closures

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The stereocontrolled construction of cycloheptanoid ring systems, relevant to sesquiterpenes and diterpenes of biological activity, is described. A new and highly efficient cyclization methodology provides stereocontrolled routes to polyfunctionalized and hydroxylated cycloheptanoid (and cyclohexanoid) rings. An alkyne or alkene terminus is shown to cyclize onto a 2,3-epoxy alcohol unit to give a cycloheptanoid ring incorporating syn-1,2-dihydroxylated functionality. Unusually, these carbocyclizations take place at the less substituted epoxide carbon atom of 2,3-epoxy alcohols, to the effective exclusion of alternative modes of cyclization. Chelation control is invoked to account for the highly efficient 7-*endo-tet* processes. Those processes occur at the expense of the normally *more favored 6-exo-tet* cyclizations. The little used Lewis acids $SnBr_4$ and $Sn(OTf)_2$ are shown to be effective in promoting acetylenic epoxy alcohol cyclizations. The effect of the relative configuration of the epoxy alcohol unit upon the outcome of the cyclization was studied.

Cyclizations involving epoxides have a venerable chemical and biogenetic history.[1] Epoxide cyclizations leading to cycloheptanoid rings[2] are rare[3] and represent a desirable goal, in view of the importance of naturally occurring systems containing a seven-membered ring,[4] and the enhancement of biological activity by strategic positioning of hydroxy groups and the carbocyclic array.[5] Polyhydroxylated natural products that contain *syn*-1,2-dihydroxy groups both attached to a central seven-membered cycloheptanoid ring and one residing at the junction of a 5,7-fused ring system[6] include the antitumorogenic ortho ester, gnididin,[6a] the irritant esters of ingenol,[6b] and the cardiotoxic diterpenoid grayanotoxin.[6c] The stereocontrolled placement of contiguous oxygenated functionality is important for biological activity, especially in the context of protein kinase C activation by diacylglycerols and a variety of tumor promoters including phorbol esters and 3-*O*-acyl derivatives of ingenol (Figure 1).[4e,7]

Cyclization of epoxy alcohols possessing an acetylenic terminator is essentially unexplored.[8] Recently, epoxy alcohols have been used to assemble fused cycloheptanoid systems,[2] but the scope was not extended beyond the use of aromatic π-nucleophiles. Regiochemical control during

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(1) (a) Goldsmith, D. J. *J. Am. Chem. Soc.* **1962**, *84*, 3913. (b) Sutherland, J. K. *Chem. Soc. Rev.* **1980**, *9*, 265. (c) Sutherland, J. K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, pp 341−377. (d) van Tamelen, E. E. *Acc. Chem. Res.* **1968**, *1*, 111. (e) For examples of acetylenic epoxy ketones that undergo cyclization to give five- and six-membered rings, see: Johnson, W. S.; Gravestock, M. B.; Parry, R. J.; Myers, R. F.; Bryson, T. A.; Miles, D. H. *J. Am. Chem. Soc.* **1971**, *93*, 4330. Mellor, M.; Santos, A.; Scovell, E. G.; Sutherland, J. K. *J. Chem. Soc., Chem. Commun.* **1978**, 528. Amupitan, J. A.; Scovell, E. G.; Sutherland, J. K. *J. Chem. Soc., Perkin Trans. 1* **1983**, 755. (f) For synthetic methodologies for the construction of polycarbocyclic systems, see: Ho, T.-L., Ed. *Carbocyclic Construction in Terpene Synthesis*; VCH: Deerfield Beach, 1988. Heathcock, C. H. in *The Total Synthesis of Natural Products*; ApSimon, J., Eds.; Wiley: New York, 1973; Vol. 2, pp 197−558.

(2) For an epoxy alcohol cyclization requiring a ketone adjacent to the epoxide group and involving an arene π-nucleophile, see: (a) Marson, C. M.; Benzies, D. W. M.; Hobson, A. D.; Adams, H.; Bailey, N. A. *J. Chem. Soc., Chem. Commun.* **1990**, 1516. (b) Marson, C. M.; Benzies, D. W. M.; Hobson, A. D. *Tetrahedron* **1991**, *47*, 5491.

(3) For examples of nonepoxide cyclizations to cycloheptanoid rings that involve an alkyne but during which a stereogenic center is destroyed, see: Lansbury, P. T.; Serelis, A. K. *Tetrahedron Lett.* **1978**, 1909. Mehta, G.; Krishnamurthy, N. *Synth. Commun.* **1988**, *18*, 1267. For an isolated example of an allylsilane terminus attacking the quaternary carbon atom of an epoxide, resulting in a seven-membered ring, though with destruction of a stereogenic center, see: Wang, D.; Chan, T.-H. *J. Chem. Soc., Chem. Commun.* **1984**, 1273. For cyclizations of unsaturated epoxides and unsaturated epoxy acetates to five- or six-membered rings but which lack chemoselectivity or regioselectivity, see: Procter, G.; Russell, A. T.; Murphy, P. J.; Tan, T. S.; Mather, A. N. *Tetrahedron* **1988**, *44*, 3953.

(4) (a) Gijsen, H. J. M.; Wijnberg, J. B. P. A.; Stork, G. A.; de Groot, A.; de Waard, M. A.; van Nistelrooy, J. G. M. *Tetrahedron* **1992**, *48*, 2465. (b) Shook, C. A.; Romberger, M. L.; Jung, S.-H.; Xiao, M.; Sherbine, J. P.; Zhang, B.; Lin, F.-T.; Cohen, T. *J. Am. Chem. Soc.* **1993**, *115*, 10754. (c) Chakraborty, R.; Basu, M. K.; Ranu, B. C. *Tetrahedron* **1992**, *48*, 8849. (d) Snider, B. B.; Yang, K. *J. Org. Chem.* **1990**, *55*, 4392. (e) Wender, P. A.; Keenan, R. M.; Lee, H. Y. *J. Am. Chem. Soc.* **1987**, *109*, 4390. (f) Jacobi, P. A.; Selnick, H. G. *J. Org. Chem.* **1990**, *55*, 202.

(5) (a) Hartwell, J. L. *Adv. Pharmacol. Chemother.* **1969**, *7*, 117. (b) Fujita, E.; Nagao, Y. *Bioorg. Chem.* **1977**, *6*, 287. (c) For a review of antitumor diterpenoids bearing hydroxyl groups, see: Rahman, A., Ed. *Studies in Natural Product Chemistry*, Elsevier: New York, 1988−1990; Vols. 1−6. Fraga, B. M. *Nat. Prod. Rep.* **1988**, *5*, 497−521.

(6) (a) Evans, F. J.; Taylor, S. E. *Fortschr. Chem. Org. Naturst.* **1983**, *44*, 1. (b) Paquette, L. A.; Ross, R. J.; Springer, J. P. *J. Am. Chem. Soc.* **1988**, *110*, 6192. (c) Burke, J. W.; Doskotch, R. W.; Ni, C.-Z.; Clardy, J. *J. Am. Chem. Soc.* **1989**, *111*, 5831.

(7) Wang, S.; Milne, G. W. A.; Nicklaus, M. C.; Marquez, V. E.; Lee, J.; Blumberg, P. M. *J. Med. Chem.* **1994**, *37*, 1326.

(8) One allenylcyclohexanediol has been prepared: Morgans, D. J., Jr. Sharpless, K. B.; Traynor, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 462. For rearrangement of an epoxide and subsequent intramolecular ene reaction to give a methylenecyclohexanol, see: Murase, N.; Maruoka, K.; Oii, T.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 707.

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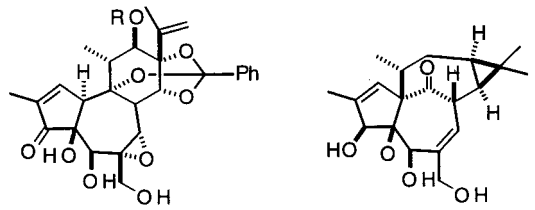
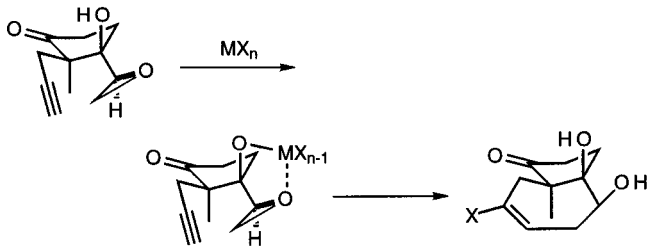


Figure 1.

Scheme 1

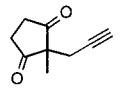
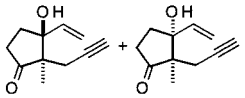
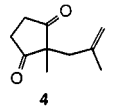
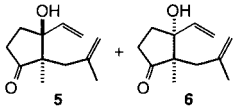
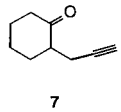
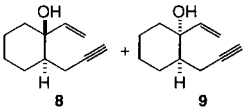


the cyclization of 2,3-epoxy alcohols enabled 7-*endo* attack to be preferred over 6-*exo* cyclization, thereby affording oxepanes.[9] Such participation of two oxygen atoms in a five-atom assembly with the Lewis acid (borontrifluoride etherate) also suggested that seven-membered carbocycles could be efficiently accessed by a cyclization that resulted in a similar five-atom array (as in the oxygen atoms of a *vic*-diol when bonded to a metal atom). Accordingly, we wished to investigate whether epoxide cyclizations could be enhanced in terms of chemoselectivity, yield, and stereoselectivity by the presence of an hydroxy group adjacent to the epoxide. We have discovered that such epoxy alcohols indeed possess unique advantages in cyclizations and *herein report (a) the first examples of alkyne−epoxy alcohol cyclizations that lead to seven-membered carbocyclic rings* (Scheme 1)[10] and (b) the first comprehensive study that demarcates *the influence of bidentate chelation control during cyclizations of 2,3-epoxy alcohols*.

A variety of allylic alcohols were prepared (Table 1), some involving α-alkylation of ketones,[11] followed by addition of vinylmagnesium bromide. The corresponding epoxy alcohols **10**−**18** (Table 2) were then prepared by epoxidation of the allylic alcohols, which in the cases of cyclopentanol derivatives **2**, **3**, **5**, and **6** gave notable stereoselectivities; only the respective epoxides **10**, **11**, **12**, and **13** were isolated, resulting from syn-stereoselective[12] epoxidations.[13] Epoxidation of the cyclohexanols with *tert*-butyl hydroperoxide (TBHP) (1.5 equiv, catalytic $VO(acac)_2$, benzene, 18 h reflux) were much less stereoselective than for the cyclopentanols; **8** afforded a 3:2 mixture (67%) of the epimers **15** and **16**, and **9** (conditions as above) gave a 3:2 mixture (64%) of the epimers **17** and **18**. In the latter case, the epimers were separated by column chromatography. Scheme 2 presents a rationalization, based upon minimization of $A^{1,3}$ interactions, of the preference for *syn*-epoxy alcohols derived from the TBHP−$VO(acac)_2$ system. The *anti*-epoxy alcohol **14** was prepared from **3** using *m*-CPBA, taking advantage of the different requirements[13] in delivery of the oxygen atom compared with the former system.

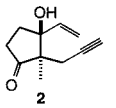
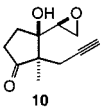
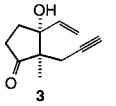
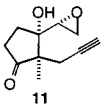
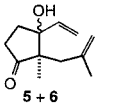
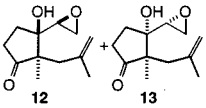
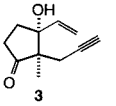
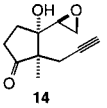
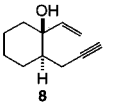
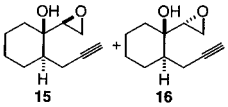
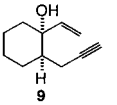
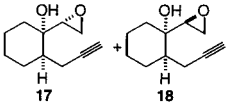
The epoxy alcohols were reacted with Lewis acids (Table 3). Spectral data of all products are consistent

Table 1. Preparation of Allylic Alcohols Using Vinylmagnesium Bromide

Entry	Ketone	Allylic alcohol[a]	Yield (%) (*trans*:*cis*)
1	 **1**	 **2** (*trans*) **3** (*cis*)	88 (1:1)
2	 **4**	 **5** **6**	40 (3:1)
3	 **7**	 **8** **9**	61 (2:1)

[a] Racemic modifications were used throughout this work, and only relative configurations are depicted.

Table 2. Epoxidation of Allylic Alcohols

Entry	Allylic alcohol	Reagent	Epoxy alcohol(s)	Yield (%)
1	 **2**	TBHP $VO(acac)_2$	 **10**	79
2	 **3**	TBHP $VO(acac)_2$	 **11**	80
3	 **5 + 6**	TBHP $VO(acac)_2$	 **12** **13**	39
4	 **3**	*m*-CPBA	 **14**	61
5	 **8**	TBHP $VO(acac)_2$	 **15** **16**	67
6	 **9**	TBHP $VO(acac)_2$	 **17** **18**	64

(9) Molander, G. A.; Andrews, S. W. *J. Org. Chem.* **1989**, *54*, 3114.

(10) For a preliminary account see: Marson, C. M.; Khan, A.; McGregor, J.; Grinter, T. J. *Tetrahedron Lett.* **1995**, *36*, 7145.

(11) (a) Schick, H.; Schwarz, H.; Finger, A.; Schwarz, S. *Tetrahedron* **1982**, *38*, 1279. (b) Jackman, L. M.; Lange, B. C. *Tetrahedron* **1977**, *33*, 2737.

(12) For convenience, *trans* (or cis) is used to describe the same substituents, whether for allylic alcohols or the corresponding epoxy alcohols, that are *trans* (or cis) in the cyclized bicyclic products. Similarly, *syn* (or anti) epoxy alcohols correspond in relative configuration to the 1,2-dihydroxy groups that are *syn* (or anti) in the cyclized products. Thus, *trans*,*syn*-diol **19** is obtained from *trans*,*syn*-epoxy alcohol **10**. Structures depicted refer to racemic modifications.

(13) Nonselective epoxidations of 1-vinylcycloalkan-1-ols have been reported, but to our knowledge, the present examples are the first report of π-face selectivity in the epoxidation of 1-vinylcyclopentan-1-ols. That can be interpreted in terms of minimization of 1,2- and especially 1,3-eclipsing interactions. An O−C−C═C dihedral angle of approximately 50° has been assumed; see: Chong, A. O.; Sharpless, K. B. *J. Org. Chem.* **1977**, *42*, 1587.

Scheme 2

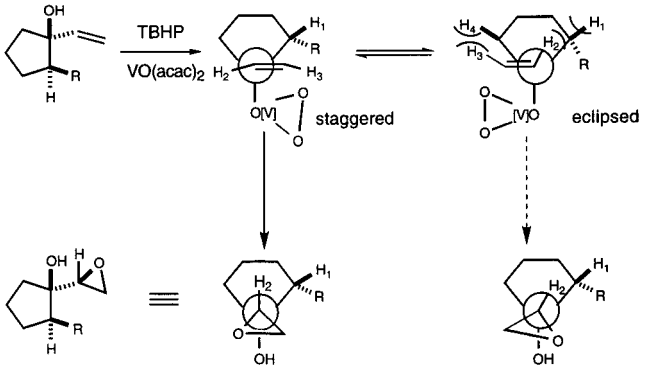
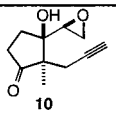
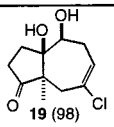
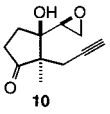
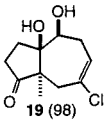
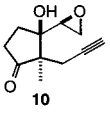
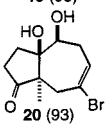
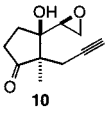
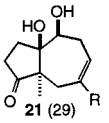
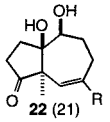
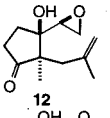
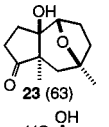
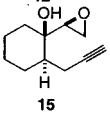
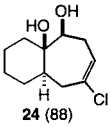
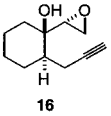
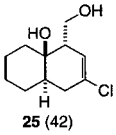
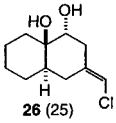
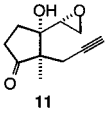
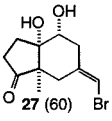
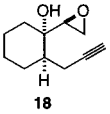
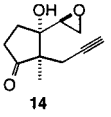
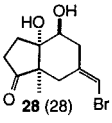


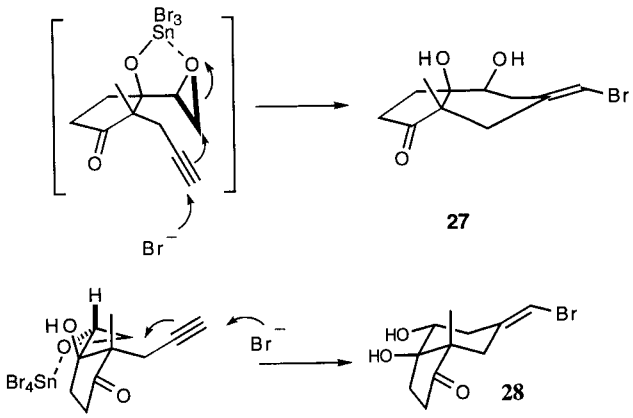
Table 3. Cyclization of Epoxy Alcohols

Entry	Epoxy alcohol	Reagent and conditions	Product (s) (%)	
1	 **10**	$TiCl_4$ CH_2Cl_2 -78°C	 **19** (98)	
2	 **10**	$SnBr_4$ CH_2Cl_2 -78 °C	 **19** (98)	
3	 **10**	$SnBr_4$ CH_2Br_2 -78 °C-20 °C	 **20** (93)	
4	 **10**	$Sn(OTf)_2$ toluene 20 °C	 **21** (29)	 **22** (21)
5[a]	 **12**	$SnBr_4$ CH_2Cl_2 -78 °C	 **23** (63)	
6[b]	 **15**	$TiCl_4$ CH_2Cl_2 -78 °C	 **24** (88)	
7[b]	 **16**	$TiCl_4$ CH_2Cl_2 -78 °C	 **25** (42)	 **26** (25)
8	 **11**	$SnBr_4$ CH_2Br_2 -78 °C-20 °C	 **27** (60)	
9	 **18**	$TiCl_4$ CH_2Cl_2 -78 °C	No cyclized products detected	
10	 **14**	$SnBr_4$ CH_2Br_2 -78 °C-20 °C	 **28** (28)	

[a] A 2:1 mixture of **12**:**13** was used. No cyclization products derived from **13** were isolated. [b] A 3:2 mixture of **15**:**16** was used.

with the structures assigned. Additionally, single-crystal X-ray determinations of **10** and **28** were carried out.[14] The constitution and relative configuration of **20** was confirmed by an X-ray determination performed on the

Scheme 3



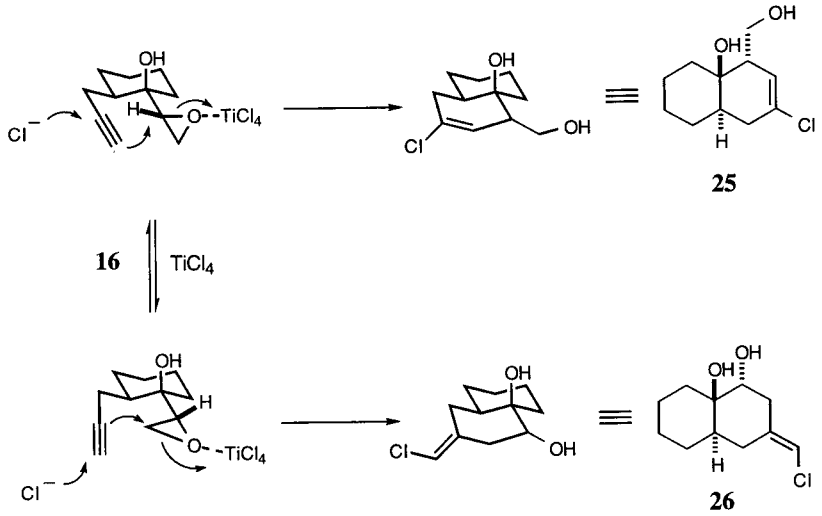
cyclic sulfites obtained by reacting **20** with $SOCl_2$ (CCl_4, reflux, 95%).[15] Entries 1−5 show that 7-*endo-tet* cyclizations of such epoxy alcohols take place *in preference* to attack at the more substituted carbon atom of the epoxide despite the latter being an *exo* mode of ring opening and generally favored.[16] Such processes can be explained in terms of a chelation-controlled mode of cyclization (Scheme 1).

The marked contrast in the modes of cyclization of the two epimers **15** and **16** to give, respectively, diol **24** (bidentate chelation-controlled) and both diols **25** and **26** (nonbidentate chelation) is notable, as is the isolation of single regioisomers of exocyclic vinyl halides (Table 3, entries 7, 8, and 10). Whereas complex mixtures have resulted from the treatment of unsaturated epoxy alcohols with a variety of Lewis acids,[9] **12** was found to cyclize satisfactorily to a carbocycle formed by efficient internal trapping. This tandem cyclization has potential in natural product chemistry; a key step in Wender's total synthesis of phorbol[4e] involved the cleavage of an ether bridge spanning a cycloheptane ring, with the location and stereochemistry as in the closely related 5,7-fused system **23**. When a mixture of **12** and its diastereoisomer **13** was treated with $SnBr_4$, no products were detected that derived from epoxide **13**, which is believed to undergo fragmentation. An X-ray structure determination[14] confirmed the relative configuration of **28** and, hence, that of the epoxide **14**, prepared by epoxidation of **3** with *m*-CPBA (1.5 equiv, $CHCl_3$, 20 °C, 16 h).

Attempts to detect intermediates did not succeed. However, the presence of a cationic species (or at least the development of incipient positive charge at the internal site of the alkyne) is probable, in view of the cyclization of **10** with intermolecular trapping by an arene. The ability of *solvent* to be efficiently trapped in these 7-*endo* cyclizations is shown in entry 2 (Table 3), in which the carbon−chlorine bond in dichloromethane is evidently sufficiently weak, and also accessible, to act as the source of nucleophilic trapping of the presumed incipient carbocation. Such donation of a halogen atom from CH_2X_2 as the solvent has been observed during the quenching of highly electrophilic intermediates generated from acetyl hypofluorite and a pyridine ring.[17] In con-

(14) Adams, H.; Bailey, N. A.; Khan, A.; Marson, C. M. *Acta Crystallogr. C*, in preparation.
(15) Hursthouse, M. B.; Khan, A.; Marson, C. M. *Acta Crystallogr. C*, in preparation.
(16) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.
(17) Hebel, D.; Rozen, S. *J. Org. Chem.* **1991**, *56*, 6298.

Scheme 4



trast, the cases of the 6-*endo* cyclizations leading to an *exo*-halomethylene unit (Table 3, entries 7, 8, and 10) the situation may be quite different; the stabilization of a terminally unsubstituted vinylic carbocation would be much less than the cation arising from the 7-*endo* cyclizations. For the 6-*exo* cyclizations, a trans addition of SnX_4 across the alkyne bond, prior to epoxide cleavage and cyclization, was not able to be excluded (or confirmed). Again, while not the only feasible explanation, the formation of **23** is also consistent with a carbocationic species, sufficiently long-lived (tertiary) to be internally trapped by a nucleophilic oxygen atom.

Reaction of **10** with $Sn(OTf)_2$ (1.5 equiv) in toluene (addition at 0 °C and then stirring at 20 °C for 18 h) afforded a 4:3 mixture (50%) of isomeric enediols **21** and **22** (R = *p*-C_6H_4·CH_3). The formation of **22** has not been investigated but might involve direct acid-catalyzed migration of the double bond in **21**. This is consistent with **21** being the kinetic product and **22** the thermodynamically favored isomer. At −78 °C, cyclizations lead to analogues of **21** (entries 1, 2, 3, and 6 in Table 3), but at 20 °C a substantial quantity of the more thermodynamically stable isomer **22** is formed, in the case of entry 4. MM2 calculations indicate a preference of **22** (R = Br) over **20** (= **21** where R is bromo) of somewhat more than 3 kcal mol^{-1}, principally attributable to the substantial 1,3-diaxial interactions for isomer **21** of groups at the ring junction with hydrogen atoms on the seven-membered ring.

Treatment of *cis,anti*-epoxy alcohol **14** with tin(IV) bromide gave the bicyclo[4.3.0]nonane **28** with an exocyclic alkene (Scheme 3). For **28**, the hydrogen atom attached to the carbon atom bearing the secondary alcohol showed values of J = 6, 12 Hz, whereas for **27** the corresponding hydrogen atom resonated as a triplet, J = 5 Hz, consistent with the expected dihedral angles for the fused cyclohexane ring in which the secondary hydroxyl group adopts the axial position, thus benefitting from presumed hydrogen bonding involving the adjacent angular hydroxyl group. If bidentate chelation of **14** were to occur it would lead to a geometry in which the alkyne cannot become antiperiplanar to the epoxide C−O bond, so that chelation cannot lead to cyclization. Consequently, in the absence of such factors, a six-membered ring is formed, being of lower entropic demand than seven-membered ring formation. However, cyclization can occur through a monochelated conformer, as depicted in Scheme 3. The low yield (28%) indicates side reactions (possibly semipinacol rearrangement or fragmentation of **14** or epoxide cleavage by bromide ion).

In contrast to **14**, the epimeric *cis,syn*-epoxide **11** gave a satisfactory yield (60%) of the epimeric bicyclo[4.3.0]nonane **27**. Models show that the internal alkyne site can present in a collinear alignment to the terminus of the epoxide group when that epoxide forms part of a bidentate-chelated complex (depicted in Scheme 3, with arbitrary tin ligands). The cis disposition of the epoxide and alkyne substituents does not permit the proximity of the *termini* of the epoxide and alkyne moieties (with or without chelation), and seven-membered ring formation was not detected.

Cyclization of Six-Membered Ring Epoxy Alcohols. The *trans,syn*-epoxide **15** undergoes cyclization to give the desired bicyclo[5.4.0]decane ring system **24**. As for the five-membered case **10**, bidentate chelation with the Lewis acid locks the epoxide conformation so as to favor seven-membered ring formation. On the other hand, cyclization of the *trans,anti*-epoxide **16** (Scheme 4) gave a mixture of unsaturated decalindiols in which the alkene unit is endocyclic in **25** but exocyclic in isomer **26**. Bidentate chelation with $TiCl_4$ would place the CH_2 of the epoxide group remote from the alkyne chain, and it would also preclude collinear orbital alignment of the alkyne moiety (either terminus) with the departing C−O bond. Therefore, cyclization can occur only through monochelation to give the six-membered ring products; the formation of both **25** and **26** shows that both termini of the alkyne can participate in cyclization. Only the *E* configuration was observed in products of the type **26**−**28**, a fact consistent with requirements for collinear orbital alignments.

Treatment of the *cis,syn*-epoxides **17** and *cis,anti*-epoxides **18** with titanium(IV) chloride gave no cyclization products in either case. From each epoxide, two compounds were isolated that were difficult to purify, but the ^1H NMR spectrum indicated that the products may be the result of semipinacol rearrangements, as has been observed for other epoxy alcohols that are tertiary substituted at C-1 and lack the possibility of cyclization.[18]

In conclusion, carbocyclizations of *trans,syn*-2,3-epoxy alcohols usually take place at the *less* substituted epoxide carbon atom of 2,3-epoxy alcohols, to the effective exclusion of alternative modes of cyclization. Bidentate chelation control is invoked to account for the highly efficient 7-*endo*-*tet* processes. Cyclizations can afford unsaturated carbocyclic rings with multiple functionality including hydroxylic groups and contiguous stereogenic centers. The highly functionalized fused ring systems can be assembled in only three steps. A terminal alkene can act as a π-nucleophile that is converted by cyclization with concomitant halide trapping into an exocyclic halomethylene group of exclusively *(E)*-selectivity, useful for further synthetic transformation. The cyclizations are notable for suppressing competing reactions, particularly semipinacol rearrangements,[18] or the ring-opening of the epoxide by halide derived from the Lewis acid.

Experimental Section

General Methods. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded at 250 and 68.8 MHz, respectively, using tetramethylsilane as the internal reference. Flasks were flame-dried before use. Thin-layer chromatography was carried out on 0.2 mm plastic backed plates with a layer of silica gel 60 F_{254} and cerium(IV) sulfate spray for visualization. Column chromatography was carried out using silica gel C60-H (40−60 mesh) under gravity. Petroleum ether (40−60 fraction) and ethyl acetate were distilled prior to use. Evaporation refers to the removal of solvent under reduced pressure.

2-Methyl-2-propynylcyclopentane-1,3-dione (**1**),[11a] *N*-cyclohexylidenecyclohexylamine,[19] and 2-(2-propynyl)cyclohexanone (**7**)[20] were prepared according to literature procedures.

3-Ethenyl-3-hydroxy-2-methyl-2-propynylcyclopentan-1-ones (2) and (3). To a solution of **1** (3.0 g, 20.0 mmol) in THF (150 mL) at −78 °C was added vinylmagnesium bromide (60 mL, 59.9 mmol, 1.0 M solution in THF). The mixture was stirred at 20 °C for 4 h and poured onto ammonium chloride solution (60 mL) and the aqueous layer extracted with ether. The combined organic extracts were dried ($MgSO_4$), the solvent was evaporated, and the residue was purified by column chromatography (20% ethyl acetate in petroleum ether) to give two diastereoisomers: **2** as a colorless oil (1.78 g, 47%) [^{1}H NMR ($CDCl_3$) δ 6.26 (1H, dd, J = 18.1, 11.9 Hz), 5.36 (1H, dd, J = 18.1, 0.6 Hz), 5.25 (1H, dd, J = 11.9, 0.6 Hz), 2.60−1.75 (8H, m), 1.05 (3H, s); ^{13}C NMR ($CDCl_3$) δ 219.7 (s), 139.35 (d), 115.4 (t), 82.0 (s), 71.2 (d), 54.6 (s), 35.8 (s), 33.05 (t), 31.7 (t), 19.9 (t), 18.8 (q); *m/z* (EI) 178 (M^+, 25), 163 (20), 108 (90), 55 (100); HRMS for $C_{11}H_{14}O_2$ calcd *m/e* 178.0994, found 178.0999] and **3** as a colorless oil (1.58 g, 41%): IR (thin film) 3400, 3290, 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.00 (1H, dd, J = 17.5, 11.0 Hz), 5.40 (1H, dd, J = 17.5, 1.0 Hz), 5.28 (1H, dd, J = 11.0, 1.0 Hz), 2.70−1.80 (8H, m), 1.14 (3H, s); ^{13}C NMR ($CDCl_3$) δ 218.2 (s), 138.8 (d), 115.1 (t), 81.4 (s), 71.5 (d), 55.1 (s), 39.0 (s), 33.8 (t), 32.1 (t), 23.8 (t), 15.3 (q); *m/z* (EI) 178 (M^+, 25), 163 (20), 108 (90), 55 (100); HRMS calcd for $C_{11}H_{14}O_2$ *m/z* 178.0994, found 178.0999.

2-Methyl-2-(2-methylallyl)cyclopentane-1,3-dione (4). To a solution of sodium hydroxide (1.78 g, 46 mmol) in water (100 mL) was added 2-methylcyclopentane-1,3-dione (5.0 g, 46 mmol). Once the dione had dissolved, 1-chloro-2-methyl-2-propene (4.85 g, 54 mmol) and potassium iodide (3.70 g, 20 mmol) were added, and the mixture was heated to 60 °C for 2 h. The mixture was then cooled to 20 °C and extracted with dichloromethane, and the combined organic extracts were washed with saturated aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated. The residue was distilled to give **4** as a colorless oil (3.65 g, 48%): bp 90 °C/0.5 mmHg; IR (thin film) 1770, 1730, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.64 (2H, dt, J = 6.2, 1.0 Hz), 2.77 (4H, ddd, J = 6.0, 3.0, 1.0 Hz), 2.42 (2H, s), 1.63 (3H, s), 1.12 (3H, s); ^{13}C NMR ($CDCl_3$) δ 218.5 (s), 140.7 (s), 114.9 (t), 56.8 (s), 43.7 (t), 35.5 (t), 23.9 (q), 20.5 (q); *m/z* (EI) 166 (M^+, 35), 138 (40), 55 (100); HRMS calcd for $C_{10}H_{14}O_2$ *m/z* 166.0994, found 166.0987. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.96; H, 8.58.

***trans*- and *cis*-3-Ethenyl-3-hydroxy-2-methyl-2-(2-methylallyl)cyclopentanones (5) and (6).** To a solution of **4** (3.5 g, 21 mmol) in THF (100 mL) at −78 °C was added vinylmagnesium bromide (63 mL, 63 mmol, 1.0 M solution in THF). The mixture was stirred at 20 °C for 3 h and poured into saturated aqueous ammonium chloride and the aqueous layer extracted with ether. The combined organic extracts were dried ($MgSO_4$) and evaporated, and the residue was purified by column chromatography (3:7 ethyl acetate/petroleum ether) to give a 3:1 mixture of **5** and **6** as a pale yellow oil (1.6 g, 40%): IR (thin film) 3400, 1720, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.08 (1H, dd, J = 18.0, 12.0 Hz), 5.47 (2H, ddd, J = 18.0, 12.0, 1.0 Hz), 4.70 (2H, m), 1.91−2.34 (6H, m), 1.73 (3H, s), 0.94 (3H, s); ^{13}C NMR ($CDCl_3$) δ 219.6 (s), 145.5 (s), 139.4 (d), 115.5 (t), 113.0 (t), 83.3 (s), 56.8 (s), 39.7 (t), 34.3 (t), 33.7 (t), 24.8 (q), 22.2 (q); *m/z* (EI) 194 (M^+, 25), 166 (25), 55 (100); HRMS calcd for $C_{12}H_{18}O_2$ *m/e* 194.1307, found 194.1298.

***trans*- and *cis*-1-Ethenyl-2-(2-propynyl)cyclohexanols (8) and (9).** To **7** (1.31 g, 9.62 mmol) in dry THF (26 mL) at −78 °C was added vinylmagnesium bromide in THF (14.4 mL, 14.4 mmol, 1 M) dropwise, an orange precipitate forming. The mixture was stirred at 20 °C for 16 h. The clear orange solution was poured into saturated ammonium chloride, the layers were separated, and the aqueous layer was extracted with ether. The combined organic extracts were dried ($MgSO_4$) and evaporated to give a 2:1 mixture of **8** and **9** as shown by ^{1}H NMR spectrometry. Column chromatography (3:97 ethyl acetate/petroleum ether) gave **8** as a colorless oil (0.63 g, 41%) [IR (thin film) 3300, 2160, cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.82 (1H, dd, J = 18.0, 1.0 Hz), 5.28 (1H, dd, J = 18.0, 1.0 Hz), 5.10 (1H, dd, J = 11.0, 1.0 Hz), 2.40−1.10 (13H, m); ^{13}C NMR ($CDCl_3$) δ 145.1 (d), 112.4 (t), 84.0 (s), 74.3 (s), 69.7 (d), 43.15 (d), 39.0 (t), 26.4 (t), 25.7 (t), 21.2 (t), 19.7 (t), (terminal alkyne carbon signal not observed); *m/z* (EI) 164 (M^+, 10), 91 (100); HRMS for $C_{11}H_{16}O$ calcd *m/e* 164.1201, found 164.1205] and **9** as a colorless oil (0.31 g, 20%): IR (thin film) 3300, 2160 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.80 (1H, dd, J = 17.5, 10.0 Hz), 5.23 (1H, dd, J = 18.0, 1.0 Hz), 5.10 (1H, dd, J = 10.0, 1.0 Hz), 2.50−1.15 (13H, m); ^{13}C NMR ($CDCl_3$) δ 145.0 (d), 112.5 (t), 76.3 (s), 74.0 (s), 69.7 (d), 43.2 (d), 39.0 (t), 26.7 (t), 25.6 (t), 21.2 (t), 20.4 (t); *m/z* (EI) 164 (M^+, 10), 91 (100); HRMS calcd for $C_{11}H_{16}O$ *m/e* 164.1201, found 164.1204.

3-Oxiranyl-3-hydroxy-2-methyl-2-propynylcyclopentan-1-ones (10) and (14). A stirred solution of *m*-CPBA (0.95 g, 5.48 mmol) in chloroform (40 mL) at 0 °C was treated over 15 min with a solution of **2** and **3** (0.65 g, 3.65 mmol; 1:1) in chloroform (30 mL). The mixture was stirred at 20 °C for 18 h and then washed with aqueous 10% sodium hydrogen carbonate and dried ($MgSO_4$). The residue was purified by column chromatography (3:7 ethyl acetate/petroleum ether) to give **10** as white microprisms (0.21 g, 30%) [mp 152−154 °C; IR (KBr disk) 3450, 3360, 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.1 (1H, dt, J = 3.0, 1.0 Hz), 2.70 (2H, m), 1.70−2.40 (8H, m), 1.00 (3H, s); ^{13}C NMR ($CDCl_3$) δ 218.1 (s), 79.9 (s), 71.7 (t), 54.4 (s), 53.8 (d), 44.8 (t), 34.0 (s), 33.9 (t), 31.8 (t), 23.3 (t), 18.4 (q); *m/z* (EI) 194 (M^+, 45), 91 (55), 55 (100). Anal. Calcd for $C_{11}H_{14}O_3$: C, 67.99; H, 7.42. Found: C, 67.75; H, 7.41] and **14** as a colorless oil (0.20 g, 28%): IR (thin film) 3450, 3360, 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.14 (1H, dd, J = 5.6, 1.3 Hz), 2.90 (1H, dd, J = 5.6, 3.0 Hz), 2.80 (1H, dd, J = 6.9, 5.6 Hz), 2.60−1.80 (8H, m), 1.10 (3H, s); ^{13}C NMR ($CDCl_3$) δ 218.0 (s), 79.9 (s), 71.7 (d), 54.4 (s), 53.8 (d), 44.1 (t), 34.0 (s), 33.9 (t), 31.8 (t), 23.3 (t), 15.9 (q); *m/z* (EI) 194 (M^+, 45), 91 (55), 55 (100); HRMS calcd for $C_{11}H_{14}O_3$ *m/z* 194.0943, found 194.0942.

(18) (a) Marson, C. M.; Walker, A. J.; Pickering, J.; Hobson, A. D.; Wrigglesworth, R.; Edge, S. J. *J. Org. Chem.* **1993**, *58*, 5944. (b) Maruoka, K.; Hasegawa, M.; Yamamoto, H.; Suzuki, K.; Shimazaki, M.; Tsuchihashi, G. *J. Am. Chem. Soc.* **1986**, *108*, 3827.

(19) Richer, J.-C.; Perelman, D. *Can. J. Chem.* **1970**, *48*, 570.

(20) Kuehne, M. E. *Synthesis* **1970**, 510.

***trans,syn*-3-Oxiranyl-3-hydroxy-2-methyl-2-propynylcyclopentan-1-one (10).** To a stirred solution of **2** (0.15 g, 0.84 mmol) in benzene (38 mL) was added a catalytic amount of vanadyl acetylacetonate followed by dropwise addition of aqueous TBHP (0.16 mL, 1.26 mmol, 70%). The mixture was then heated at reflux for 18 h, cooled to 20 °C, and poured into saturated aqueous sodium sulfite (40 mL). The aqueous layer was extracted with ether, and the combined organic extracts were dried ($MgSO_4$) and evaporated to give the single diastereoisomer **10** (0.13 g, 79%) as white microprisms: mp 152−154 °C; IR (KBr disk) 3450, 3360, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.1 (1H, dt, J = 3.0, 1.0 Hz), 2.70 (2H, m), 1.70−2.40 (8H, m), 1.00 (3H, s); *m/z* (EI) 194 (M^+, 45), 163 (30), 55 (100).

***cis,syn*-3-Oxiranyl-3-hydroxy-2-methyl-2-propynylcyclopentan-1-one (11)**. To a stirred solution of **3** (50 mg, 0.28 mmol) in benzene (13 mL) was added a catalytic amount of vanadyl acetylacetonate followed by dropwise addition of aqueous TBHP (0.052 mL, 0.42 mmol, 70%). The mixture was heated at reflux for 18 h and then worked up as described for **10** to give a residue that was purified by column chromatography (3:7 ethyl acetate/petroleum ether) to give **11** as white microprisms (43 mg, 80): mp 88−90 °C; IR (KBr disk) 3450, 3360, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.16 (1H, dd, J = 5.0, 1.3 Hz), 2.95 (1H, dd, J = 5.0, 1.3 Hz), 2.80 (1H, dd, J = 5.0, 1.3 Hz), 2.63−2.25 (5H, m), 2.15−1.95 (3H, m), 1.10 (3H, s); ^{13}C NMR ($CDCl_3$) δ 218.1 (s), 79.9 (s), 71.7 (d), 54.4 (s), 53.8 (d), 44.1 (t), 34.0 (s), 33.9 (t), 31.7 (t), 23.3 (t), 15.8 (q); *m/z* (EI) 194 (M^+, 45), 163 (30), 55 (100); HRMS calcd for $C_{11}H_{14}O_3$ *m/z* 194.0943, found 194.0942. Anal. Calcd for $C_{11}H_{14}O_3$: C, 67.99; H, 7.22. Found: C, 67.75; H, 7.27.

3-Oxiranyl-3-hydroxy-2-methyl-2-(2-methyl-2-propenyl)cyclopentan-1-ones (12) and (13). A solution of **5** and **6** (0.60 g, 3.09 mmol; 3:1) in benzene (80 mL) was treated with a catalytic amount of vanadyl acetylacetonoate, followed by aqueous *tert*-butyl hydroperoxide (0.56 g, 4.32 mmol, 70%). The mixture was heated at reflux for 3 h and then worked up as described for **10** to give a residue that was purified by column chromatography (3:7 ethyl acetate/petroleum ether) to give a 2:1 mixture of **12** and **13** as a colorless oil (0.25 g, 39%): IR (thin film) 3500, 3060, 1730, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.56 (2H, m), 2.73 (1H, t, J = 3.0 Hz), 2.52 (2H, dd, J = 6.0, 3.0 Hz), 1.77−2.30 (6H, m), 1.57 (3H, s), 0.81 (3H, s); ^{13}C NMR ($CDCl_3$) δ 220.3 (s), 143.3 (s), 115.5 (t), 79.8 (s), 57.0 (s), 55.8 (d), 44.1 (t), 39.1 (t), 33.5 (t), 29.9 (t), 24.6 (q), 20.0 (q); *m/z* (EI) 210 (20, M^+), 119 (40), 55 (100); HRMS calcd for $C_{12}H_{18}O_3$ *m/z* 210.1256, found 210.1265.

***trans*-1-Oxiranyl-2-(2-propynyl)cyclohexanols (15) and (16).** To a stirred solution of **8** (0.27 g, 1.64 mmol) in benzene (50 mL) was added a catalytic amount of vanadyl acetylacetonate followed by aqueous *tert*-butyl hydroperoxide (0.31 mL, 2.47 mmol, 70%). The mixture was heated at reflux for 18 h, allowed to cool to 20 °C, and then worked up as described for **10** to give an orange oil that was purified by column chromatography (1:9 ethyl acetate/petroleum ether) to give a 3:2 mixture of **15** and **16** as a white solid (0.20 g, 67): mp 42−44 °C; IR (thin film) 3500, 3300, 2160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.95−1.15 (16H, m); ^{13}C NMR ($CDCl_3$) δ 83.9 (s), 74.9 (s), 69.75 (d), 57.6 (d), 42.1 (t), 41.9 (d), 36.7 (t), 27.0 (t), 25.5 (t), 20.8 (t), 19.8 (t); *m/z* (EI) 180 (M^+, 10), 91 (100), 55 (80); HRMS calcd for $C_{11}H_{16}O_2$ *m/z* 180.1150, found 180.1154.

***cis*-1-Oxiranyl-2-(2-propynyl)cyclohexanols (17) and (18).** To a stirred solution of **9** (0.10 g, 0.61 mmol) in benzene (27 mL) was added a catalytic amount of vanadyl acetylacetonate followed by aqueous *tert*-butyl hydroperoxide (0.12 mL, 0.91 mmol, 70%). The mixture was heated at reflux for 18 h, allowed to cool to 20 °C, and then worked up as described for **10** to give an orange oil that was purified by column chromatography (1:9 ethyl acetate/petroleum ether) to give a 3:2 mixture **17** and **18** (70 mg, 64%). **17** (higher R_f): colorless oil; IR (thin film) 3500, 3300, 2160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.00−2.70 (3H, m), 2.50−1.10 (13H, m); ^{13}C NMR ($CDCl_3$) δ 76.0 (s), 73.2 (s), 69.5 (d), 57.6 (d), 44.9 (t), 42.1 (d), 36.75 (t), 27.25 (t), 25.45 (t), 20.39 (t), 20.42 (t); *m/z* (EI) 180 (M^+, 10), 91 (100), 55 (80). **18** (lower R_f): colorless oil; IR (thin film) 3500, 3300, 2160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.00−2.75 (3H, m), 2.50−1.20 (13H, m); ^{13}C NMR ($CDCl_3$) δ 76.0 (s), 73.25 (s), 69.5 (d), 57.6 (d), 44.9 (t), 42.1 (d), 36.8 (t), 27.25 (t), 25.45 (t), 20.6 (t), 20.4 (t); *m/z* (EI) 180 (M^+, 10), 91 (100), 55 (80); HRMS calcd for $C_{11}H_{16}O_2$ *m/z* 180.1150, found 180.1152.

(3aα,4α,8aβ)-(±)-7-Chloro-3,3a,4,5,8,8a-hexahydro-3a,4-dihydroxy-8a-methyl-1-(2*H*)-azulenone (19). Method 1. To a solution of **10** (10 mg, 0.052 mmol) in dichloromethane (30 mL) at −78 °C was added titanium tetrachloride (0.011 mL, 0.103 mmol), dropwise. The reaction was complete after 10 min, and the mixture was quenched by pouring onto ice (10 g). The aqueous layer was extracted with dichloromethane, and the organic layers were combined, washed with brine and water, dried ($MgSO_4$), and evaporated to give pure **19** (9.8 mg, 98%) as white microprisms: mp 210−212 °C; IR (KBr disk) 3440, 3000, 1740, 1650 cm^{-1}; ^1H NMR (CD_3OD) δ 5.85 (1H, dt, J = 12.0, 3.0 Hz), 3.72 (1H, dd, J = 12.0, 6.0 Hz), 3.05 (1H, dt, J = 18.0, 3.0 Hz), 2.62 (1H, m), 1.96−2.32 (5H, m), 1.31 (1H, s), 1.03 (3H, s); ^{13}C NMR (CD_3OD) δ 220.8 (s), 134.8 (s), 124.4 (d), 83.5 (s), 70.8 (d), 55.2 (s), 37.5 (t), 32.7 (t), 32.1 (t), 30.8 (t), 17.5 (q); *m/z* (%), (EI) 230 (15, M^+), 212 (20), 194 (20), 177 (100); HRMS calcd for $C_{11}H_{15}ClO_2$ ($M^+ - H_2O$) *m/z* 212.0604, found 212.0595.

Method 2. To a solution of **10** (10 mg, 0.052 mmol) in dichloromethane (30 mL) at −78 °C was added tin tetrabromide (0.05 g, 0.103 mmol) in portions. After 1 h, the mixture was worked up as described in method 1 above to give pure **19** (9.8 mg, 98%).

(3aα,4α,8aβ)-(±)-7-Bromo-3,3a,4,5,8,8a-hexahydro-3a,4-dihydroxy-8-methyl-1-(2*H*)-azulenone (20). To a solution of **10** (0.06 g, 0.31 mmol) in dibromomethane (40 mL) at −78 °C was added tin tetrabromide (0.28 g, 0.62 mmol) in portions. The mixture was stirred at 20 °C for 15 min and then worked up as described for **19** to give **20** as white microprisms (56 mg, 93): mp 197−198 °C; IR (KBr disk) 3440, 1740, 1640 cm^{-1}; ^1H NMR (CD_3OD) δ 6.10 (1H, dt, J = 12.0, 3.0 Hz), 3.60 (1H, dd, J = 12.0, 6.0 Hz), 3.20 (1H, dt, J = 18.0, 3.0 Hz), 2.60 (1H, m), 2.00−2.40 (8H, m), 1.10 (3H, s); ^{13}C NMR (CD_3OD): δ 212.3 (s), 129.1 (d), 124.6 (s), 83.6 (s), 70.6 (d), 55.8 (s), 39.8 (t), 33.6 (t), 32.7 (t), 30.8 (t), 17.4 (q); *m/z* (EI) 276 (M^+, ^{81}Br, 30), 256 (30), 212 (35), 177 (100); HRMS calcd for $C_{11}H_{15}O_3{}^{81}Br$ *m/z* 276.0185, found 276.0188.

(3aα,4α,8aβ)-(±)-3,3a,4,5,8,8a-Hexahydro-3a,4-dihydroxy-8a-methyl-7-(4-methylphenyl)-1-(2*H*)-azulenone (21) and Its Isomer (22). To a solution of **10** (0.10 g, 0.51 mmol) in toluene (30 mL), at 0 °C, was added tin(II) trifluoromethanesulfonate (0.32 g, 0.77 mmol) in portions. The mixture was stirred at 20 °C for 18 h and then poured onto ice (10 g). Workup as for **19** gave a residue that was purified by column chromatography (38:62 ethyl acetate/petroleum ether) to give a 4:3 mixture of **21** and **22** (73.5 mg, 50%) as a white solid: mp 147−151 °C; IR (KBr disk) 3415, 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.80−6.90 (4H, m), δ 5.90 and 5.62 (1H, m), 4.05 (dd, J = 11.5, 3.5 Hz) and 4.00 (dd, J = 11.5, 3.0 Hz) 1H, 3.15−1.90 (8H, m), 1.05 (3H, s), 1.00 (3H, s); ^{13}C NMR ($CDCl_3$) δ 218.5 (s), 218.3 (s), 146.1 (s), 143.6 (s), 142.3 (s), 136.6 (s), 134.7 (s), 130.1 (d), 128.9 (d), 127.7 (d), 126.65 (d), 124.0 (d), 122.1 (d), 83.0 (s), 82.9 (s), 70.7 (d), 53.9 (s), 53.7 (s), 32.2 (t), 32.1 (t), 31.8 (t), 31.7 (t), 30.6 (t), 29.6 (t), 21.0 (q), 20.2 (q), 17.6 (q), 17.3 (q); *m/z* (EI) 286 (M^+, 100), 268 (23), 250 (25); HRMS calcd for $C_{18}H_{22}O_3$ *m/z* 286.1566, found 286.1569.

Reaction of 3-Oxiranyl-3-hydroxy-2-methyl-2-(2-methyl-2-propenyl)cyclopentan-1-ones (12) and (13) with Tin(IV) Bromide. To a solution of **12** and **13** (0.12 g, 5.71 mmol, 2:1) in dichloromethane (50 mL) at −78 °C was added tin tetrabromide (0.50 g, 1.14 mmol), dropwise. After 45 min, the mixture was poured onto ice (10 g) then worked up as described for **19** to give a residue which was purified by column chromatography (1:1 ethyl acetate/petroleum ether) to give the single diastereoisomer **23** as prisms (50 mg, 63), mp 75−77 °C (petroleum ether); IR (KBr disk) 3500, 1730 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.51 (1H, t, J = 3.0 Hz), 1.52−2.41 (11H, m), 1.23 (3H, s), 1.01 (3H, s); ^{13}C NMR ($CDCl_3$) δ 221.2 (s), 92.2 (s), 81.5 (s), 67.0 (d), 58.4 (s), 45.8 (t), 33.5 (t), 32.2 (t), 26.7 (t),

26.4 (q), 25.6 (t), 15.0 (q); *m/z* (EI) 210 (15, M^+), 167 (65), 137 (30), 125 (90), 109 (80), 97 (40), 81 (40), 69 (40), 55 (100); HRMS calcd for $C_{12}H_{18}O_3$ *m/z* 210.1256, found 210.1248. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.56; H, 8.63. Found: C, 68.31; H, 8.66.

Reaction of 1-Oxiranyl-1-hydroxy-2-(2-propynyl)cyclohexanes (15) and (16) with Titanium(IV) Chloride. To a stirred solution of **15** and **16** (0.17 g, 0.94 mmol, 3:2) in dichloromethane (27 mL) at −78 °C was added titanium(IV) chloride (0.25 mL, 2.22 mmol) dropwise via a syringe. When the addition was complete, the mixture was stirred at −78 °C for 20 min. The dark solution was then poured onto ice (10 g) and stirred until the ice had melted. The mixture was worked up as described for **19** to give a residue that was purified by column chromatography (1:4 ethyl acetate/petroleum ether) to give diol **24** as a white prisms (71 mg, 88%) [mp 109−110 °C; ^{1}H NMR ($CDCl_3$) δ 5.68 (1H, m), 3.25 (1H, m), 3.01 (1H, m), 2.70 (1H, m), 2.20−1.80 (4H, m), 1.75−1.05 (9H, m); ^{13}C NMR ($CDCl_3$) δ 137.9 (s), 122.0 (d), 74.85 (s), 74.6 (d), 42.9 (d), 39.3 (t), 36.2 (t), 31.0 (t), 30.1 (t), 25.9 (t), 21.0 (t); *m/z* (EI) 216 (M^+, 35), 198 (11), 180 (42), 98 (100); HRMS calcd for $C_{11}H_{17}O_2Cl$ *m/e* 216.0917, found 216.0924], diol **25** as a white solid (50 mg, 42) [mp 122−123 °C; IR (KBr disk) 3400 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.18 (1H, m), 3.60 (2H, d, J = 6.3 Hz), 2.25−2.05 (3H, m), 1.80−1.73 (1H, m), 1.70−1.10 (10H, m); ^{13}C NMR ($CDCl_3$) δ 133.4 (s), 123.1 (d), 70.2 (s), 63.0 (t), 51.8 (d), 38.0 (d), 36.7 (t), 35.0 (t), 28.5 (t), 25.3 (t), 21.4 (t); *m/z* (EI) 216 (M^+, 25), 198 (20), 163 (100); HRMS calcd for $C_{11}H_{17}O_2Cl$ *m/z* 216.0917, found 216.0922], and diol **26** as an orange oil (30 mg, 25%): ^{1}H NMR ($CDCl_3$) δ 5.75 (1H, s), 3.25 (1H, t, J = 9.0 Hz), 2.45 (1H, dd, J = 12.5, 4.7 Hz), 2.30 (2H, d, J = 7.8 Hz), 2.10−1.00 (12H, m); ^{13}C NMR ($CDCl_3$) δ 138.0 (s), 110.1 (d), 75.9 (d), 72.0 (s), 41.8 (d), 37.8 (t), 34.6 (t), 29.8 (t), 27.9 (t), 25.8 (t), 21.2 (t); *m/z* (EI) 216 (M^+, 29), 198 (100), 180 (64), 163 (98); HRMS calcd for $C_{11}H_{17}O_2Cl$ *m/z* 216.0919, found 216.0922.

(3aα,4a,7aα)-(±)-6-*(E)*-(Bromomethylene)-2,3,3a,4,5,6,-7,7a-octahydro-3a,4-dihydroxy-7a-methyl-1-indanone (27). To a solution of **11** (60 mg, 0.31 mmol) in dibromomethane (6 mL) at −78 °C was added tin tetrabromide (0.27 g, 0.62 mmol) in portions. The mixture was then stirred at 20 °C for 30 min and then poured onto ice (3 g). Workup as described for **19** gave an orange-red oil, which was purified by column chromatography (1:1 ethyl acetate/petroleum ether) to give **27** as a colorless oil (50 mg, 60%): ^{1}H NMR ($CDCl_3$) δ 6.06 (1H, s), 4.17 (1H, t, J = 5.0 Hz), 2.75 (1H, s, OH), 2.60−2.10 (8H, m), 1.95−1.80 (1H, m), 1.07 (3H, s); ^{13}C NMR ($CDCl_3$) δ 217.95 (s), 135.75 (s), 103.8 (d), 79.55 (s), 72.15 (d), 54.8 (s), 39.05 (t), 35.3 (t), 33.75 (t), 29.0 (t), 16.0 (q); *m/z* (EI) 274 (M^+,^{79}Br, 6), 256 (13), 84 (100); HRMS calcd for $C_{11}H_{15}O_3{}^{81}Br$ *m/z* 276.0184, found 276.0188.

(3aα,4b,7aα)-(±)-6-(*E*)-(Bromomethylene)-2,3,3a,4,5,6,7,-7a-octahydro-3a,4-dihydroxy-7a-methyl-1-indanone (28). To a solution of **14** (0.25 g, 1.29 mmol) in dibromomethane (17 mL) at −78 °C was added tin tetrabromide (1.13 g, 2.58 mmol) in portions. The mixture was then stirred at 20 °C for 30 min and poured onto ice (5 g). Workup as described for **19** gave an amber oil that was purified by column chromatography (1:1 ethyl acetate/petroleum ether) to give **28** as a white prisms (97 mg, 28): mp 173−174 °C; ^{1}H NMR ($CDCl_3$) δ 6.14 (1H, t, J = 1.3 Hz), 3.75 (1H, dd, J = 12.0, 6.0 Hz), 2.65−2.52 (2H, m), 2.50−1.80 (3H, m), 1.78−1.30 (3H, m), 1.82 (1H, s, OH), 1.75 (1H, s, OH), 0.98 (3H, s); *m/z* (EI) 274 (M^+, ^{79}Br, 18), 256 (14), 177 (100); HRMS calcd for $C_{11}H_{15}O_3{}^{81}Br$ *m/z* 276.0184, found 276.0184.

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