(relative intensity) that were superimposable on that of the naturally occurring compound.[2]

Preparation of (6*Z*,9*Z*,11*E*)-15,15-Bis(ethylthio)-13(*S*)-[(*tert*-butyldiphenylsilyl)oxy]pentadecatriene (6). The ylide was prepared in a manner similar to that used for the synthesis of (6*Z*,9*Z*)-heneicosadiene (3) with the exception that 3.5 equiv of the cuprate reagent and 3 equiv of vinyltriphenylphosphonium bromide were used. Aldehyde 5 was added to the ylide at −50 °C and the reaction brought to −20 °C over 1.5 h followed by stirring at room temperature for 3 h. The mixture was diluted with ether (70 mL), quenched with aqueous saturated NH_4Cl (40 mL), and filtered over Celite and the aqueous layer extracted with ether (2 × 70 mL). The combined ether extracts were washed with brine (3 × 30 mL) and dried over $MgSO_4$, and the solvent was removed under reduced pressure. Purification by column chromatography (1% ethyl acetate in petroleum ether) gave a mixture of triene 6 and a compound in which two acetylene units had been incorporated in 74% yield (52% and 22% yields, respectively): ^1H NMR ($CDCl_3$) δ 0.89 (m, 9 H), 1.05 (s, 9 H), 1.12–1.38 (m, 6 H), 2.0 (m, 2 H, CH_2CH=), 2.48 (m, 2 H, CH_2CHOSi), 2.72 (m, 2 H, =$CHCH_2CH$=), 3.78 (dd, 1 H, J_1 = J_2 = 7 Hz, $CH(SEt)_2$), 4.5 (m, 1 H, $CHOSi$), 5.19–5.44 (m, 3 H, CH=$CHCH_2CH$=), 5.56 (dd, 1 H, J ≐ 14.7 Hz, J = 7.7 Hz, CH=$CHCHOSi$), 5.80 (dd, 1 H, J_1 = J_2 = 10.7 Hz, =$CHCH$=CHCHOSi), 6.10 (dd, 1 H, J_1 = 14.7 Hz, J_2 = 10.7 Hz, CH=CHCHOSi), 7.25–7.68 (m, 10 H); LRMS (70 eV) *m/z* (relative intensity) 523 ($M^+ - t$-Bu, 9), 457 ($M^+ - C_9H_{15}$, 83), 199 ($HOSiPH_2$, 72), 135 ($CH(SEt)_2$, 100).

Preparation of 1-Phenyl-1,4-nonadiene (11). To a solution of (*Z*)-1-iodo-1-hexene (140 mg, 0.67 mmol) in dry THF (10 mL), under a nitrogen atmosphere at −78 °C, was added 1.6 M *tert*-butyllithium (0.83 mL, 1.34 mmol) dropwise. After 15 min, CuI (64 mg, 0.335 mmol) was added, the reaction mixture stirred at −40 °C for 1 h followed by the addition of vinyltriphenylphosphonium bromide (124 mg, 0.335 mmol) and HMPA (0.15 mL), and stirring continued at −40 °C for 18 h. Benzaldehyde (18 mg, 0.17 mmol) was introduced and the solution stirred at room temperature for 2 h. The mixture was diluted with hexanes (50 mL), quenched with aqueous saturated NH_4Cl (40 mL), and filtered over Celite and the aqueous layer extracted with hexanes (2 × 50 mL). The combined hexanes extracts were washed with saturated NH_4Cl (2 × 30 mL) and brine (2 × 30 mL) and dried over $MgSO_4$, and the solvent was removed under reduced pressure. Purification by flash chromatography (hexanes/ether = 100/1) gave 1-phenyl-1,4-nonadiene as a mixture of its *Z*/*E* isomers (87/13) in 50% yield. No traces of 10 or 12 could be detected by GC/MS. (1*Z*,4*Z*)-1-Phenylnonadiene: ^1H NMR ($CDCl_3$) δ 0.88 (m, 3 H, CH_3), 1.32 (m, 4 H), 2.0–2.1 (m, 2 H, C(6) H), 2.95–3.1 (m, 2 H, C(3) H), 5.43 (m, 2 H, C(4) H, C(5) H), 5.66 (ABX, 1 H, J_{AB} = 11.8 Hz, J_{AX} = 7.4 Hz, C(2) H), 6.43 (ABX, 1 H, J_{AB} = 11.8 Hz, J_{BX} = 1 Hz, C(1) H), 7.29 (s, 5 H); LRMS (70 eV) *m/z* (relative intensity) 200 (M^+, 12), 143 ($M^+ - C_4H_9$, 46), 129 ($M^+ - C_5H_{11}$, 87), 91 ($C_7H_7^+$, 100), 90 ($C_7H_6^+$, 70). (1*E*,4*Z*)-1-Phenylnonadiene: ^1H NMR ($CDCl_3$) δ 0.88 (m, 3 H, CH_3), 1.32 (m, 4 H), 2–2.1 (m, 2 H, C(6) H), 2.9–3.1 (m, 2 H, C(3) H), 5.4 (m, 2 H, C(4) H, C(5) H), 6.25 (ABX, 1 H, J_{AB} = 16 Hz, J_{AX} = 6 Hz, C(2) H), 6.5 (ABX, 1 H, J_{BA} = 16 Hz, J_{BX} = 1 Hz, C(1) H), 7.3 (s, 5 H); LRMS (70 eV) *m/z* (relative intensity) 200 (M^+, 27), 143 ($M^+ - C_4H_9$, 30), 129 ($M^+ - C_5H_{11}$, 72), 91 ($C_7H_7^+$, 69), 90 ($C_7H_6^+$, 100).

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada, Merck Frosst Canada, and the Ministry of Education, Province of Quebec, for financial support, Zhi Y. Wang for providing materials and carrying out the coupling reaction involving the HETE precursor, and Drs. Orval Mamer, Medical Mass Spectrometry Unit, McGill University, and John Finkenbine for mass spectra.

Cyclization of Polyenes. 46.[1] Synthesis of (±)-Asperdiol, an Anticancer Cembrenoid[2]

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On the basis of retrosynthetic perspective (Scheme I), the asperdiol skeleton (I = 24) and its geometrical isomer (II = 25) were constructed from *cis*- and *trans*-isopropenyl alcohols 3a and 3b. I (24) was converted into (±)-asperdiol 1 by the sequential reactions of bromo etherification to 33 followed by epoxidation and then reductive regeneration of the double bond.

Asperdiol (1) was discovered by Weinheimer and his co-workers in 1977 from Caribbean gorgonians of the *Eunicea* genus with the aid of in vitro P-388 lymphocytic leukemia (PS) and KB (cytotoxicity) bioassay.[3] Its structure including absolute configuration was revealed unequivocally as a highly oxygenated cembrenoid by X-ray crystallographic analysis.

The antitumor activity coupled with its conspicuous structural feature has elicited considerable interest in synthetic approaches to this novel macrocylcic natural product.[4]

In connection with our longstanding interest in the synthetic study of cembrenoids,[5] we focused our synthetic attention on asperdiol (1). We delineate here the details of our work starting from isopropenyl alcohols **3a** and **3b**, readily available from our common cembrenoid intermediate chloro ketone **2**.[6] The purpose of our synthetic study

(1) (a) Part 45. Fujiwara, S.; Takeda, K.; Uyehara, T.; Kato, T. *Chem. Lett.* **1986**, 1763. (b) Part 44. Yamaguchi, Y.; Uyehara, T.; Kato, T. *Tetrahedron Lett.* **1985**, *26*, 343.

(2) Preliminary communication: Aoki, M.; Tooyama, Y.; Uyehara, T.; Kato, T. *Tetrahedron Lett.* **1983**, *22*, 2267.

(3) Weinheimer, A. J.; Matson,J.; van der Helm, D.; Poling, M. *Tetrahedron Lett.* **1977**, 1295.

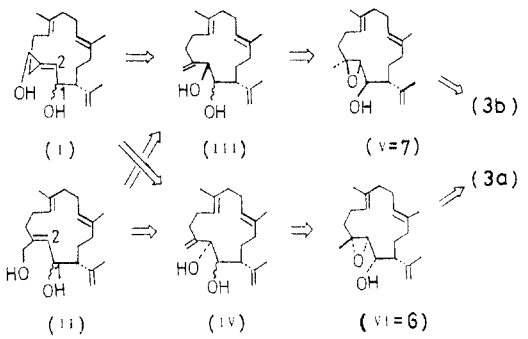
(4) (a) Still, W. C.; Mobilio, D. *J. Org. Chem.* **1983**, *48*, 4786. (b) Marshall, J. A.; Cleary, D. G. *J. Org. Chem.* **1986**, *51*, 859. (c) A recent reference on the cembrenoids: Dauben, W. G.; Saugier, R. K.; Fleischhauser, I. *J. Org. Chem.* **1985**, *50*, 3767.

(5) Kato, T. In *Synthesis of Macrocyclic Terpenoids by Cyclization*; Kagaku No Ryoiki, Zokan, No. 128; Nankodo: Tokyo, 1980; p 119.

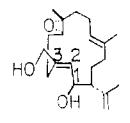
(6) Kato, T.; Kobayashi, T.; Kitahara, Y. *Tetrahedron Lett.* **1975**, 3299.

0022-3263/87/1952-1803$01.50/0

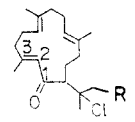
Scheme I



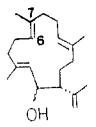
consists of not only construction of asperdiol itself but also evaluation of the conformational properties of macrocyclic cembrenoid intermediates.



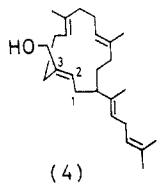
(1)



(2) R = H
(5) R = $CH_2CH{=}CMe_2$



(3a) cis OH
(3b) trans OH



(4)

The synthetic problems associated with the conversion of alcohols **3a** and **3b** to asperdiol are twofold: (1) selective functionalization of the 3-methyl to a hydroxymethyl with concomitant inversion of geometry of the 2,3-double bond and (2) selective epoxidation of only one (C_6–C_7) of the four double bonds in the molecule. The importance of the regioselective oxidation of the 3-methyl stems also from the occurrence of ceriferol (**4**), a sesterterpene related structurally to asperdiol. Ceriferol contains the same basic cembrene skeleton, to which a dimethylallyl group is appended. If selective oxidation of the C_3-methyl to the hydroxymethyl group in **3a** and **3b** could be achieved, the procedure might be applicable for the synthesis of ceriferol[7] from the homologous chloro ketone **5**.[8]

From the retrosynthetic perspective (Scheme I), we envisioned that the hydroxymethyl group at C-3 with the proper double bond geometry is constructed by the rearrangement of diol III or IV. The allyl alcohols **3a** and **3b** were viewed as attractive starting materials since the 2,3-double bond is easily distinguishable from the remaining three double bonds by selective epoxidation. The resultant epoxy alcohols V or VI might be convertible into the diols III or IV. Since no information was available on the exact conformation of the diols, prediction of the geometry of the newly formed 2,3-double bond in the key rearrangement reaction (III or IV to I or II) is not straightforward. It seemed, therefore, desirable to prepare

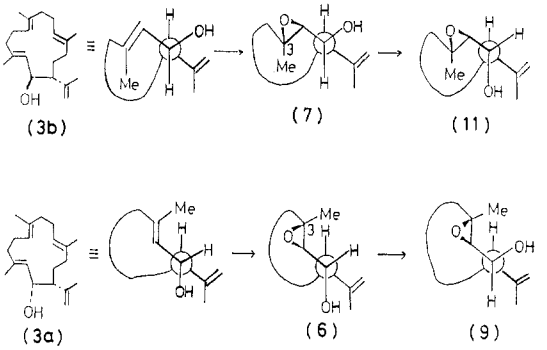


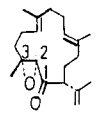
Figure 1.

the isomeric diols III and IV and examine independently their preferred mode of rearrangement.

Selective epoxidation of the 2,3-double bond of each alcohol **3a** and **3b** took place efficiently through careful addition of *tert*-butyl hydroperoxide (*t*-BuO_2H) in the presence of vanadyl acetylacetonate, affording the corresponding epoxides **6** (VI) and **7** (V). The regioselective opening of the epoxide ring was next pursued to obtain the diols III and IV efficiently. For this purpose, we planned to adopt the Sharpless conditions using tetraisopropyl orthotitanate ($Ti(OPr\text{-}i)_4$), which is reported to eliminate the proton from the substituent syn to the hydroxyl group regiospecifically by the formation of a metal epoxy alcohol complex.[9] By an X-ray crystallographic analysis and detailed ^1H NMR measurements, the isopropenyl alcohols **3a** and **3b** have been found to have the partial conformation shown in Figure 1.[10] Assuming that the conformation remains unchanged by the introduction of the epoxide ring, the C_1-hydroxyl group is positioned anti to the C_3-methyl in **6** (VI) and **7** (V) as shown in the figure. In order to eliminate the proton from the C_3-methyl group regiospecifically, the configuration of the C_1-hydroxyl group in **6** and **7** should be changed. The alcohol **6** was converted to the ketone **8** by Collins ($CrO_3{\cdot}Py_2$) oxidation. Reduction of the ketone with hydride reagents proceeded with unexpectedly high stereoselectivity: Reaction with sodium borohydride in the presence of cerous chloride ($CeCl_3$) at room temperature[11] or lithium aluminum hydride in ether at −20 °C afforded a mixture of **9** and **6** in a 98:2 ratio, while the former alcohol **9** was formed exclusively by the action of lithium aluminum tri-*tert*-butoxyhydride [$LiAlH(OBu\text{-}t)_3$] at room temperature. Similarly, the alcohol **7** was transformed to the isomeric alcohol **11** via the intermediate ketone **10** in virtually quantitative yield by the same treatment. The high stereoselectivity of the carbonyl reduction may be due to the fact that the stable three-dimensional arrangement of the ketones **8** and **10** appears to be a rigid tub in which the C_3-methyl is positioned close to the upper face of the carbonyl group. For this reason, hydride addition to this functional group is directed to the least hindered face, that being the one opposite to the C_3-methyl group. The partial conformation near the hydroxyl group in these four epoxy alcohols, shown in Figure 1, is consistent with the following evidence.

In the ^1H NMR spectra, **9** and **11** display the C_3-methyl signal at 1.42 and 1.47 ppm, whereas the equivalent resonances in **6** and **7** are more shielded, appearing at 1.30 and

(7) (a) Structure: Pawlak, J. K.; Tempesta, M. S.; Iwashita, T.; Nakanishi, K.; Naya, Y. *Chem. Lett.* **1983**, 1069. (b) Our preliminary communication on the synthesis of ceriferol: Fujiwara, S.; Aoki, M.; Uyehara, T.; Kato, T. *Tetrahedron Lett.* **1984**, *28*, 3003.
(8) Kato, T.; Suzuki, M.; Nakajima, Y.; Shimizu, K.; Kitahara, Y. *Chem. Lett.* **1977**, 705.
(9) Morgans, D. J., Jr.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 462.
(10) Kato, T.; Kabuto, C.; Kim, K. H.; Takayanagi, H.; Uyehara, T.; Kitahara, Y. *Chem. Lett.* **1977**, 827.
(11) Rucker, G.; Horster, H.; Gajewski, W. *Synth. Commun.* **1980**, *10*, 623.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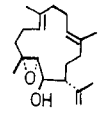
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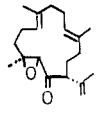
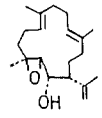

(10)

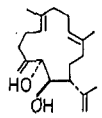

(11)

1.33 ppm, respectively. This difference suggests proximity of the C_3-methyl to the C_1-hydroxyl group in the former two alcohols **9** and **11**. These assignments were also supported by a lanthanide-induced chemical shift (LIS value) experiment with $Eu(fod)_3$, in which a ca. 10 ppm shift was observed in the former two alcohols whereas the latter two **6** and **7** exhibited a LIS of ca. 6 ppm. This evidence served to estimate the partial conformation of these four epoxy alcohols, indicating that **9** and **11** are suitable candidates to obtain III and IV (retrosynthesis scheme) by Ti(OPr-*i*)$_4$-mediated ring opening since the C_3-methyl is oriented syn to the C_1-hydroxyl group in these alcohols.

With these considerations in mind, we attempted elimination of the foregoing epoxy alcohols with Ti(OPr-*i*)$_4$. Although the alcohols **9** and **11** were recovered unchanged at room temperature, the reaction proceeded efficiently at 80 °C, leading to the exclusive formation of the respective diols, **12** from **9** (93% yield) and **13** from **11** (60% yield) as the sole isolable products. As expected, these results can be rationalized by assuming coordination of the epoxy alcohol to the metal center in a bidentate manner. The low yield of **13** is due to its instability toward silica gel during isolation.

In contrast to the clean transformation of **9** and **11**, exposure of **6** under the same conditions gave a mixture of diols **14**, **15**, and **16** in 45%, 17%, and 6% yields while epoxy alcohol **7** was converted to **17** in 89% yield. The epoxy alcohols **7** and **18** (dihydro derivative of **6**) gave similar results by the action of pyridinium hydrochloride (Py·HCl) in pyridine at 80 °C, that is, **18** gave a mixture of **19**, **20**, and **21** in 37%, 19%, and 9% yield while **7** was transformed into **17** in 79% yield by the same treatment. These results imply that in the case of **6** and **7**, Ti(OPr-*i*)$_4$, like Py·HCl, acts merely as an acid to the epoxide ring without the formation of a coordination complex. The geometry of the newly formed trisubstituted double bonds in **15**, **16**, and **17** was deduced from the chemical shifts of the ^{13}C NMR spectra in which the C_3-methyl groups appear at higher field in **15** (10.33 ppm) and **17** (11.44 ppm) as compared with **16** (18.14 ppm).

In order to achieve the rearrangement of diols **12** and **13**, the C_2-hydroxyl group should be selectively activated. After several experiments, it was found that such activation could be achieved through exposure of diols **12** and **13** to methanesulfonyl chloride at −20 °C, resulting in exclusive mesylation of the C_2-hydroxyl group to afford the mesylates **22** and **23** in virtually quantitative yield. The mesylate **22** was subjected to the action of K_2CO_3 in aqueous dioxane to give the rearranged diol **24** in 22% yield after purification by silica gel column chromatography. Upon treatment of **23** under the same conditions, the isomeric diol **25** was obtained in 54% yield. The rearrangement took place stereoselectively; none of the geometrical isomer was formed in each reaction. The disappointing yield in the rearrangement reaction is attributable to the formation of the unstable epoxy derivative **26** from **22**.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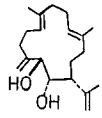
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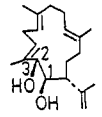
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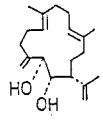
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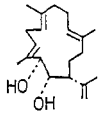
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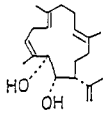
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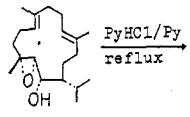
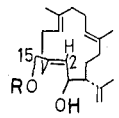
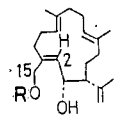
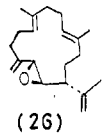


(18) (19) (20) (21)


(24) R=H
(29) R=COPh


(25) R=H
(30) R=COPh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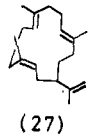

(27)

The geometry of the newly formed double bond was assigned from the ^1H NMR spectra of each compound. A 7% NOE was observed between the C_2-H and the C_{15}-Hs in **24** whereas no NOE was detected between these protons in the isomeric diol **25**. The following chemical transformation incidentally served to establish the assigned stereochemistry. The rearranged diol **24** was converted to the known hydrocarbon **27** by sequential acetylation to the diacetate followed by reductive removal of the acetoxyl group with Li in ethylamine. The hydrocarbon thus obtained was identical with (3*Z*)-cembrene A (**27**) isolated by Meinwald from the frontal gland secretion of a termite soldier (*Cubitermes umbratus* Williams)[12] and independently synthesized by Kodama and Ito.[13]

It appeared evident that by simply protecting the C_1-hydroxyl group of **22** we might effectively suppress the unwelcome epoxy ring formation and thereby direct the course of the reaction to the desired rearranged product. For this purpose, the mesylate was treated with trimethylsilyl chloride in the presence of catalytic amounts of (dimethylamino)pyridine (DMAP), yielding the protected mesylate **28**. The resulting trimethylsilyl ether **28** was exposed to benzoic acid in the presence of 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) and catalytic amounts of sodium iodide in DMF at 70 °C.[14] Allylic rearrangement took place smoothly to afford hydroxy benzoate **29** as the sole isolable product in 55% yield. At higher temperature (120 °C), the reaction generated **29** in low yield and contaminated with the corresponding 3*Z* isomer **30**, the yields being 40% and 17%, respectively.

The stereoselectivity in the rearrangement of the mesylates **22** and **23** might be related to the stable intrinsic conformation of each compound. While only crystallographic analysis can establish the exact conformation, the following observations may suggest plausible conformations around the C_{14}–C_1–C_2–C_3 bond as shown in Figure 2. The C_1–C_2 and C_3–C_4 bonds are trans and cis disposed with

(12) Wiemer, D. F.; Meinwald, J. *J. Org. Chem.* **1979**, *44*, 3950.
(13) Shimada, K.; Kodama, M.; Ito, S. *Tetrahedron Lett.* **1981**, *22*, 4275.
(14) Still, W. C.; Collum, D. B.; McDonald, J. H., III *J. Am. Chem. Soc.* **1980**, *102*, 2117.

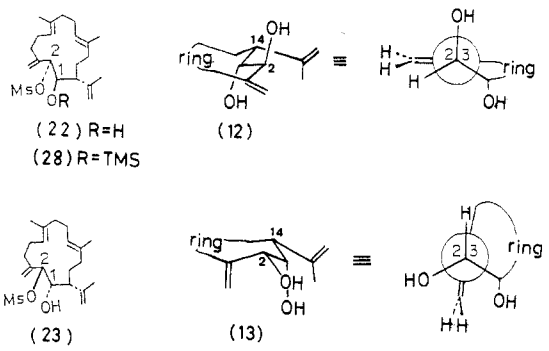
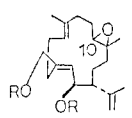


Figure 2.

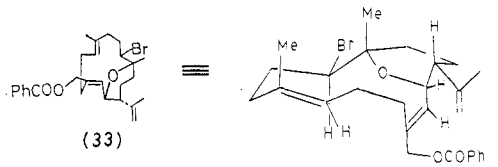
respect to the C_2–C_3 axis in **22** and **23**, respectively. Rearrangement may occur with retention of these arrangements under the moderate reaction conditions.

Since the chemical shift of the C_2-proton of mesylates **22** and **23** overlapped with the signals of the olefinic protons, ^{1}H NMR analysis could not be achieved. The following study was carried out with the original diols **12** and **13**. The similarity of the coupling patterns of the diols with the corresponding mesylates indicates that the conformations of the diols are unaffected by the mesylation reaction. The exocyclic methylene protons in **12** appear as a singlet at 5.10 ppm, showing a 7% NOE with the C_2-H and indicating the close location of these protons. In addition, one of the exocyclic methylene protons in **13** appears at relatively lower field (5.26 ppm) as compared with the other proton (5.08 ppm) owing to the deshielding effect of the hydroxyl group. Neither of the exocyclic methylene protons shows a detectable NOE with the C_2-H. Also notable is our observation that the chemical properties of the two mesylates **22** and **23** are considerably different: The former is unstable and prone to afford epoxide **26** on contact with silica gel while the other (**23**) is fairly stable and left intact after exposure to DBU. This differing chemical behavior can be explained in terms of conformational differences in which the two hydroxyl groups have trans-diaxial and cis-diequatorial orientations in **22** and **23**, respectively. All the evidence described so far is consistent with the partial conformation of the diols shown in Figure 2.

The final stage of the asperdiol synthesis is the regio- and stereoselective introduction of the epoxide ring to the C_6–C_7 double bond. According to the molecular shape of asperdiol disclosed by an X-ray crystallographic analysis, the environment near the C_6–C_7 epoxide moiety is less hindered as compared with that of the remaining three double bonds. It seems, therefore, not unreasonable to attempt direct epoxidation of **29** provided it would have the same conformation as asperdiol. On the basis of this assumption, the cis diol **24** was first converted to the dibenzoate so as to render the 2,3 and isopropenyl double bonds more resistant to epoxidation. The dibenzoate (**24**, PhCO instead of H) was subjected to the action of *m*-chloroperoxybenzoic acid (MCPBA) at −20 °C, resulting in the formation of one major product accompanied by trace amounts of three other products. It turned out that the epoxy diol **32**, derived by hydrolysis of the major product **31**, was not asperdiol or its β-epoxy isomer. The



(31) R = COPh
(32) R = H



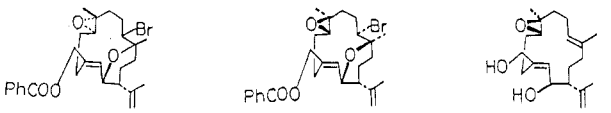
(33)

Figure 3.

^{1}H NMR spectrum demonstrated clearly that the epoxidation occurred mainly at the C_{10}–C_{11} double bond, although further study is needed to delineate the stereochemistry of the epoxide ring.

Since direct epoxidation was not satisfactory, the reactive C_{10}–C_{11} double bond was protected by utilizing the known propensity of the C_1-hydroxyl group to selectively attack the C_{10}-position.[15] Upon treatment with 2,4,4,6-tetrabromocyclohexadienone (TBCO), **29** underwent bromo etherification leading to the formation of **33** in 55% yield.

By assuming that bulky substituents such as bromine, isopropenyl, and benzoxymethylene groups assume the least hindered positions, bromo ether **33** is constrained to the relative orientation shown in Figure 3, which was supported by detailed inspection of the coupling patterns in the ^{1}H NMR spectrum. As can be seen from the plausible conformation of the bromo ether, the 2,3-double bond is blocked by the isopropenyl group and the ring carbons, whereas the α (outside) face of the C_6–C_7 double bond is less hindered than the β (inside) face. Thus, the conformation can accommodate approach of the oxidizing agent from the α side preferentially, thereby leading to the asperdiol stereochemistry. In fact, the bromo ether **33** gave, upon treatment with MCPBA at −20 °C, a 3:1 mixture, separable by conventional column chromatography, of two epoxides **34** and **35** in 83% yield. These compounds



(34) (35) (36)

were provisionally assigned as the α- and β-epoxides of the C_6–C_7 double bond. Subsequent experiments allowed the assignment of the individual epoxides. Each epoxide was treated with an excess of zinc dust in refluxing ethanol to regenerate the C_{10}–C_{11} double bond.[16] Hydrolysis of each reduction product afforded the α-epoxide **1** and its β-isomer **36** cleanly. The former exhibited identical ^{13}C and ^{1}H NMR spectra with those reported for asperdiol.[17] Soon after completion of our total synthesis of asperdiol, two groups reported successful syntheses by different routes.[4a,b]

It should be emphasized that the present study demonstrates that cembrenoid intermediates, as described in the present paper, have fixed stable conformations rather than flexible ones at ambient temperature.

Experimental Section

Epoxy Alcohol 6. To a mixture of *cis*-isopropenyl alcohol **3a** (810 mg, 2.81 mmol) and $VO(acac)_2$ (8 mg) in 50 mL of benzene was added dropwise 70% *t*-BuO_2H (0.44 mL, 3.09 mmol) at 5 °C.

(15) (a) Kato, T.; Yen, C. C.; Uyehara, T.; Kitahara, Y. *Chem. Lett.* **1977**, 565. (b) Yamaguchi, Y.; Uyehara, T.; Kato, T. *Tetrahedron Lett.* **1985**, *26*, 343 and references cited therein.
(16) Kato, T.; Suzuki, M.; Takahashi, M.; Kitahara, Y. *Chem. Lett.* **1977**, 456.
(17) Weinheimer, A. J.; Martin, G. E.; Matson, J. A. *Tetrahedron Lett.* **1979**, 2195.

The reaction mixture was stirred at room temperature for 3 h and washed with aqueous $Na_2S_2O_3$ and then brine. The combined organics were dried (Na_2SO_4) and concentrated in vacuo. Careful silica gel chromatography eluting with a hexane–AcOEt (10:1 and then 4:1) solution gave the recovered alcohol **3a** (25 mg), epoxy alcohol **6** (651 mg, 76%), and diepoxide (97 mg, 11%). **Epoxy alcohol 6**: colorless oil; IR (CCl_4) 3200–3500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.08 (m, 2 H), 4.81 (m, 1 H), 4.71 (br s, 1 H), 3.51 (d, J = 8.8 Hz, 1 H), 2.86 (d, J = 8.8 Hz, 1 H), 2.35 (t, J = 6.8 Hz, 1 H), 1.77 (br, s, 3 H), 1.63 (br s, 3 H), 1.60 (br s, 3 H), 1.30 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 147.3 (s), 135.6 (s), 133.5 (s), 124.6 (d), 122.6 (d), 111.9 (t), 72.4 (d), 66.6 (d), 62.2 (s), 45.9 (d), 39.2 (t), 38.3 (t), 34.5 (t), 24.4 (t), 23.8 (t), 22.1 (t), 20.4 (q), 17.4 (q), 17.4 (q), 16.3 (q); MS, m/e (relative intensity) 304 (24, M^+), 137 (51), 136 (52), 135 (93), 121 (100), 109 (61), 108 (64), 107 (96), 95 (85); exact mass calcd 304.2394, found 304.2405.

Epoxy Alcohol 7. A mixture of *trans*-isopropenyl alcohol **3b** (2.03 g, 7.05 mmol), $VO(acac)_2$ (20 mg), and 70% t-BuO_2H (1 mL) in 200 mL of benzene was stirred at room temperature overnight. An additional 70% of t-BuO_2H (0.2 mL) was added and the solution was stirred at 80 °C for 30 min. The organics were washed with aqueous $Na_2S_2O_3$, followed by brine, and then dried (Na_2SO_4). The volatile materials were evaporated in vacuo and the residue was passed through a silica gel column with a hexane–AcOEt (10:1 and then 4:1) solution as eluent to give the recovered alcohol 3b (200 mg), epoxy alcohol **7** (1.47 g, 69%), and diepoxide (350 mg, 16%). **Epoxy alcohol 7**: colorless oil; IR (CCl_4) 3200–3600 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.2 (m, 2 H), 5.02 (m, 1 H), 4.88 (br d, J = 1.8 Hz, 1 H), 3.41 (t, J = 8.2 Hz, 1 H), 2.86 (d, J = 8.2 Hz, 1 H), 2.33 (dt, J = 8.0, 6.0 Hz, 1 H), 1.74 (dd, J = 1.5, 0.8 Hz, 3 H), 1.61 (s, 6 H), 1.33 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.4 (s), 134.4 (s), 134.2 (s), 126.0 (d), 124.2 (d), 115.4 (t), 69.8 (d), 65.9 (d), 62.2 (s), 49.2 (d), 39.5 (t), 36.6 (t), 34.6 (t), 27.3 (t), 23.8 (t), 22.3 (t), 19.2 (q), 19.0 (q), 17.3 (q), 15.7 (q); MS, m/e (relative intensity) 304 (28, M^+), 147 (56), 136 (65), 135 (100), 134 (53), 123 (62), 109 (51), 95 (79); exact mass calcd 304.2394; found 304.2390.

Epoxy Alcohol 9. Epoxy alcohol **6** (6.54 g, 21.5 mmol) in 10 mL of CH_2Cl_2 was poured into a stirred mixture of CrO_3·Py_2 (39.3 g, 152 mmol) in CH_2Cl_2 (530 mL) at room temperature. The stirring was continued for 8 min and then AcOEt (300 mL) was added. The resulting precipitate was filtered and the solvent of the filtrate was removed in vacuo to give the crude epoxy ketone **8** (6.55 g). The epoxy ketone **8** (6.55 g) in anhydrous ether (10 mL) was added dropwise to a stirred suspension of $LiAlH(OBu\text{-}t)_3$ (10.9 g, 43.0 mmol) in anhydrous ether (500 mL) at room temperature. After the mixture was left stirring for 5 h, aqueous NH_4Cl was added, followed by anhydrous $MgSO_4$. The organics were evaporated in vacuo. The resulting residue was passed through a silica gel column eluted with hexane–AcOEt (7:1) to give the isomeric epoxy alcohol **9** (5.96 g, 91%): colorless oil; IR ($CHCl_3$) 3550 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.08–5.26 (m, 2 H), 5.02 (m, 1 H), 4.87 (br d, J = 2 Hz, 1 H), 3.42 (dd, J = 6.6, 9.8 Hz, 1 H), 2.95 (d, J = 6.6 Hz, 1 H), 2.29 (dt, J = 9.8, 2.2 Hz, 1 H), 1.70 (s, 3 H), 1.62 (s, 3 H), 1.59 (s, 3 H), 1.42 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.6 (s), 134.0 (s), 133.3 (s), 125.9 (d), 122.0 (d), 116.3 (t), 70.1 (d), 62.9 (d), 61.3 (s), 53.3 (d), 38.9 (t), 34.9 (t), 33.6 (t), 24.5 (t), 24.3 (t), 24.0 (t), 19.5 (q), 18.8 (q), 18.0 (q), 14.9 (q); MS, m/e (relative intensity) 304 (5, M^+), 121 (66), 109 (68), 107 (87), 95 (65), 93 (65), 81 (100); exact mass calcd 304.2394, found 304.2375.

Epoxy Alcohol 11. Epoxy alcohol **7** (186 mg, 0.61 mmol) in CH_2Cl_2 (2 mL) was added to a stirred mixture of CrO_3·Py_2 (1.26 g, 4.89 mmol) in 10 mL of CH_2Cl_2 and the mixture was stirred for 10 min. AcOEt (10 mL) was added and the resulting precipitate was filtered. The solvent of the filtrate was removed in vacuo to give crude epoxy ketone **10** (190 mg). To the stirred ether (5 mL) solution of the crude epoxy ketone **10** (190 mg) was added $LiAlH(OBu\text{-}t)_3$ (320 mg) at room temperature, and the stirring was continued for 3 h. The reaction mixture was quenched with aqueous NH_4Cl and dried ($MgSO_4$). The combined organics were evaporated and the resulting residue was passed through a silica gel column eluted with haxane–AcOEt (7:1) to give the epoxy alcohol **11** (176 mg, 95%): colorless oil; IR (CCl_4) 3300–3650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.15 (t, J = 6 Hz, 1 H), 5.12 (t, J = 6 Hz, 1 H), 4.89 (m, 1 H), 4.86 (br s, 1 H), 3.91 (q, J = 4.5 Hz, 1 H), 2.86 (d, J = 5.1 Hz, 1 H), 2.43 (dt, J = 3.7, 6.5 Hz, 1 H), 1.81 (d, J = 4.8 Hz, 1 H), 1.78 (dd, J = 1.2, 0.8 Hz, 3 H), 1.63 (br d, J = 0.8 Hz, 3 H), 1.61 (br d, J = 0.8 Hz, 3 H), 1.47 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 147.2 (s), 135.4 (s), 134.7 (s), 125.1 (d), 124.7 (d), 112.4 (t), 71.6 (d), 65.8 (d), 61.8 (s), 47.6 (d), 39.4 (t), 38.2 (t), 35.9 (t), 24.6 (t), 23.7 (t), 23.7 (t), 20.5 (q), 17.7 (q), 17.0 (q), 15.7 (q); MS, m/e (relative intensity) 304 (28, M^+), 134 (67), 81 (100).

Diol 12. A mixture of epoxy alcohol **9** (404 mg, 1.33 mmol) and $Ti(OPr\text{-}i)_4$ (0.56 mL, 1.86 mmol) in toluene (40 mL) was stirred at 90 °C overnight under a nitrogen atmosphere. After cooling to room temperature, 10% H_2SO_4 (20 mL) was added, and the mixture was stirred vigorously for 90 min. The organic layer was washed with aqueous $NaHCO_3$, followed by brine, and then dried (Na_2SO_4). The combined organics were concentrated in vacuo. Silica gel column chromatography with hexane–AcOEt (7:1) gave the diol **12** (382 mg, 95%): colorless needles, mp 79–80 °C; IR ($CHCl_3$) 3570 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.10 (br s, 2 H), 4.9–5.1 (m, 2 H), 4.96 (d, J = 1.2 Hz, 1 H), 4.87 (d, J = 2.4 Hz, 1 H), 4.19 (d, J = 4 Hz, 1 H), 3.76 (dd, J = 4.3, 9.6 Hz, 1 H), 2.86 (m, 1 H), 1.71 (dd, J = 1.0, 1.4 Hz, 3 H), 1.68 (s, 3 H), 1.50 (s, 3 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 146.2 (s), 145.2 (s), 133.4 (s), 133.0 (s), 125.9 (d), 125.5 (d), 116.6 (t), 113.0 (t), 77.5 (d), 73.1 (d), 46.7 (d), 39.6 (t), 35.3 (t), 29.4 (t), 25.1 (t), 24.6 (t), 23.6 (t), 18.3 (q), 16.6 (q), 16.1 (q); MS, m/e (relative intensity) 304 (40, M^+), 163 (53), 157 (59), 156 (70), 147 (68), 139 (58), 136 (54), 135 (100), 124 (54), 121 (99), 107 (99), 94 (53), 82 (59). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 78.88; H, 10.80.

Diol 13. Epoxy alcohol **11** (1.02 g, 3.34 mmol) in toluene (13 mL) was treated with $Ti(OPr\text{-}i)_4$ (1.29 mL, 6.47 mmol) at 90 °C by using the same procedure employed for the preparation of diol **12**. The crude reaction mixture was purified by silica gel chromatography with benzene–AcOEt (10:1) as eluent to give the diol **13** (637 mg, 62%): colorless needles, mp 103–104 °C; IR ($CHCl_3$) 3560 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.26 (br s, 1 H), 5.18 (t, J = 7 Hz, 1 H), 5.08 (br s, 1 H), 4.96 (quint, J = 1.6 Hz, 1 H), 4.89 (dd, J = 5.5, 8.5 Hz, 1 H), 4.72 (br s, 1 H), 4.25 (br d, J = 4 Hz, 1 H), 3.82 (quint, J = 3.5 Hz, 1 H), 1.71 (s, 3 H), 1.66 (s, 3 H), 1.54 (s, 3 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 145.5 (s), 144.9 (s), 133.8 (s), 133.8 (s), 125.8 (d), 124.3 (d), 114.0 (t), 111.6 (t), 76.1 (d), 73.4 (d), 44.8 (d), 39.4 (t), 35.6 (t), 30.6 (t), 25.1 (t), 23.5 (t), 23.2 (t), 20.3 (q), 16.2 (q), 15.8 (q); MS, m/e (relative intensity) 304 (5, M^+), 131 (42), 109 (47), 107 (48), 95 (58), 93 (47), 81 (100). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 78.78; H, 10.66.

Diol 17. Epoxy alcohol **7** (202 mg, 0.66 mmol) in toluene (7 mL) was treated similarly with $Ti(OPr\text{-}i)_4$ (0.28 mL, 0.93 mmol). The resultant reaction mixture was passed through a silica gel column eluted with benzene–AcOEt (10:1) to give the diol **17** (180 mg, 89%): colorless needles, mp 111–112 °C; IR (CCl_4) 3200–3650 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 5.5 (br t, J = 8.3 Hz, 1 H), 4.7–5.1 (m, 2 H), 4.93 (br s, 1 H), 4.72 (d, J = 2.4 Hz, 1 H), 3.82 (d, J = 9.5 Hz, 1 H), 3.45 (dd, J = 3.0, 9.5 Hz, 1 H), 1.77 (m, 3 H), 1.63 (s, 6 H), 1.55 (s, 3 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 144.8 (s), 133.6 (s), 133.4 (s), 133.2 (s), 128.3 (d), 126.0 (d), 122.0 (d), 115.5 (t), 79.7 (d), 75.7 (d), 44.6 (d), 39.0 (t), 36.3 (t), 28.4 (t), 26.8 (t), 24.8 (t), 21.5 (q), 15.6 (q), 15.4 (q), 11.4 (q); MS, m/e (relative intensity) 304 (4, M^+), 221 (55), 109 (59), 107 (57), 95 (80), 84 (66), 81 (100), 67 (70). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 78.72; H, 10.53.

A mixture of epoxy alcohol **7** (100 mg) and pyridine hydrochloride (140 mg) in pyridine (5 mL) was refluxed for 3 h, poured into ice water, and then extracted with ether. The ether solution was washed with aqueous HCl and brine and dried (Na_2SO_4). The volatile materials were removed in vacuo and the residue was passed through a silica gel column to give diol **17** (79 mg).

Diols 14, 15, and 16. A mixture of epoxy alcohol **6** (1.52 g, 5.0 mmol) and $Ti(OPr\text{-}i)_4$ (2.09 mL, 7.0 mmol) in 150 mL of toluene was stirred at 80 °C overnight and treated with 10% H_2SO_4 (75 mL) under the same conditions as for epoxy alcohol **9**. The resultant reaction mixture was submitted to flash silica gel column chromatography with hexane–AcOEt (4:1) as eluent to give diols **14** (0.68 g, 45%), **15** (0.26 g, 17%), and **16** (0.09 g, 6%). **Diol 14**: colorless needles, mp 130–131 °C; IR ($CHCl_3$) 3200–3650 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.13 (br s, 1 H), 5.04 (t, J = 1.7 Hz, 1 H), 5.0 (m, 1 H), 4.94 (t, J = 1 Hz, 1 H),

4.8 (m, 1 H), 4.81 (t, J = 0.8 Hz, 1 H), 4.13 (d, J = 8.7 Hz, 1 H), 3.69 (dd, J = 1.6, 8.7 Hz, 1 H), 1.81 (s, 3 H), 1.67 (s, 3 H), 1.47 (t, J = 1.2 Hz, 3 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 146.2 (s), 144.8 (s), 133.7 (s), 133.5 (s), 126.8 (d), 124.5 (d), 113.8 (t), 112.0 (t), 80.2 (d), 75.0 (d), 43.3 (d), 39.5 (t), 36.0 (t), 28.2 (t), 25.4 (t), 23.4 (t), 23.0 (q), 20.1 (t), 16.4 (q), 16.2 (q); MS, m/e (relative intensity) 304 (18, M^+), 234 (85), 163 (51), 151 (51), 147 (64), 139 (58), 136 (68), 135 (67), 121 (100), 107 (68). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 78.95; 10.65. **Diol 15**: colorless needles, mp 108–109 °C; IR (CCl_4) 3400 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 5.24 (dd, J = 6, 9.9 Hz, 1 H), 4.7–5.0 (m, 2 H), 4.87 (br s, 1 H), 4.68 (br s, 1 H), 3.90 (d, J = 9.5 Hz, 1 H), 3.54 (d, J = 9.5 Hz, 1 H), 2.84 (s, 2 H), 2.5–3.0 (m, 2 H), 1.76 (s, 3 H), 1.65 (br s, 3 H), 1.51 (s, 3 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 147.4 (s), 134.8 (s), 133.1 (s), 132.4 (s), 128.4 (d), 125.6 (d), 122.2 (d), 111.8 (t), 79.9 (d), 75.2 (d), 43.9 (d), 38.8 (t), 36.2 (t), 26.8 (t), 25.8 (t), 21.5 (q), 21.1 (t), 15.9 (q), 15.8 (q), 10.3 (q); MS, m/e (relative intensity) 304 (4, M^+), 109 (62), 107 (55), 93 (47), 81 (100). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 78.67; H, 10.58. **Diol 16**: colorless viscous oil; IR ($CHCl_3$) 3200–3650 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 5.53 (ddq, J = 11.1, 5.9, 1.5 Hz, 1 H), 4.7–4.9 (m, 2 H), 4.9 (m, 1 H), 4.74 (br s, 1 H), 4.38 (d, J = 8.6 Hz, 1 H), 3.64 (bd, J = 8.6 Hz, 1 H), 3.0 (m, 1 H), 1.76 (m, 3 H), 1.71 (m, 3 H), 1.54 (s, 6 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 146.0 (s), 135.6 (s), 133.6 (s), 132.7 (s), 130.2 (d), 125.1 (d), 124.0 (d), 112.7 (t), 73.7 (d), 71.0 (d), 46.7 (d), 38.8 (t), 37.0 (t), 26.7 (t), 24.7 (t), 24.4 (t), 21.1 (q), 18.1 (q), 15.7 (q), 15.7 (q); MS, m/e (relative intensity) 304 (17, M^+), 147 (40), 137 (65), 121 (63), 109 (100), 108 (52), 107 (68), 95 (93), 84 (69), 69 (68).

Diols 19, 20, and 21. A mixture of epoxy alcohol **18** (371 mg, 1.21 mmol) and pyridine hydrochloride (1.4 g, 12 mmol) in anhydrous pyridine (35 mL) was refluxed for 6 h. The reaction mixture was poured into ice water and extracted with ether. The extracts were pased through a silica gel column hexane–AcOEt (5:1) as eluent to give **19** (136.6 mg, 37%), **20** (72 mg, 19%), **21** (35 mg, 9%), and recovered epoxy alcohol **18** (29 mg, 8%). **Diol 19**: mp, 124–125 °C; IR (KBr) 3350, 1035, 895 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ 4.8–5.2 (m, 2 H), 5.12 (br s, 1 H), 4.93 (m, 1 H), 4.04 (d, J = 8 Hz, 1 H), 3.95 (d, J = 8 Hz, 1 H), 1.66 (s, 3 H), 1.50 (s, 3 H), 1.00 (d, J = 7 Hz, 3 H), 0.96 (d, J = 7 Hz, 3 H); MS, m/e 306 (M^+). Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.36; H, 11.19. **Diol 20**: mp 113–114 °C; IR (KBr) 3380, 1035 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ 4.7–5.4 (m, 3 H), 3.85 (d, J = 10 Hz, 1 H), 3.75 (d, J = 10 Hz, 1 H), 2.8 (m, 2 H), 1.67 s, 3 H) 1.64 (s, 3 H), 1.53 (s, 3 H), 0.96 (d, J = 7 Hz, 6 H); MS, m/e 306 (M^+). Anal. Calcd for $C_{20}H_{34}O_2$: C, 78.38; H, 11.18. Found: C, 78.61; H, 11.38. **Diol 21**: viscous oil; IR (film) 3400, 1010 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ 5.4–5.8 (m, 1 H), 4.7–5.2 (m, 2 H), 4.39 (d, J = 9 Hz, 1 H), 3.85 (br d, J = 9 Hz, 1 H), 2.7 (m, 2 H), 1.75 (s, 3 H), 1.54 (s, 6 H), 0.96 (d, J = 7 Hz, 6 H); MS, m/e 306 (M^+).

Rearrangement of Allyl Alcohol 12. To a CH_2Cl_2 (3 mL) solution of allyl alcohol **12** (32 mg, 0.11 mmol) was added Et_3N (29.3 μL, 0.21 mmol) and MsCl (12.3 μL, 0.16 mmol) at −78 °C. The temperature of the mixture was raised gradually to −20 °C, water was added, and the mixture was extracted with ether. The combined organics were washed with brine and dried (Na_2SO_4). Evaporation of the solvent afforded crude mesylate **22** (33 mg). This sample was dissolved in 5 mL of 67% aqueous dioxane and K_2CO_3 (1 g) was added. After being stirred at room temperature overnight, the mixture was poured into water and extracted with ether. The combined organics were washed with brine and dried (Na_2SO_4). The residue obtained by evaporation of the solvent under reduced pressure was passed through a silica gel column eluted with hexane–AcOEt to give diol **24** (7 mg, 22%) and epoxide **26** (5 mg, 17%). **Diol 24**: colorless prisms, mp 98–99 °C; IR (CCl_4) 3400 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 5.49 (d, J = 8.6 Hz, 1 H), 4.8–5.2 (m, 2 H), 4.93 (br s, 1 H), 4.72 (br s, 1 H), 4.34 (dd, J = 3.8, 8.6 Hz, 1 H), 4.04 (br s, 2 H), 1.79 (s, 3 H), 1.62 (s, 3 H), 1.56 (s, 3 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 145.6 (s), 139.0 (s), 133.9 (s), 133.5 (s), 129.7 (d), 125.5 (d), 124.4 (d), 113.6 (t), 69.4 (d), 65.5 (t), 49.3 (d), 40.3 (t), 36.0 (t), 28.1 (t × 2), 24.5 (t × 2), 23.0 (q), 15.7 (q), 15.3 (q); MS, m/e (relative intensity) 304 (3, M^+), 136 (47), 119 (100), 109 (45). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 79.03; H, 10.80. **Epoxide 26**: colorless oil; IR (CCl_4) 1644 cm^{-1}; ^{1}H NMR (90 MHz, CCl_4) δ 4.6–5.0 (m, 6 H), 2.84 (m, 1 H), 2.60 (dd, J = 2.1, 3.2 Hz, 1 H), 1.69 (s, 3 H), 1.55 (s, 6 H); MS, m/e (relative intensity) 286 (15, M^+), 175 (53), 159 (94), 148 (71), 147 (84), 133 (100), 122 (66), 121 (66), 119 (66), 109 (66), 108 (64), 105 (57), 95 (70), 93 (76), 81 (70).

Rearrangement of Trimethylsilyl Mesylate 28. To a cooled CH_2Cl_2 (50 mL) solution of allyl alcohol **12** (1.60 g, 5.24 mmol) were added Et_3N (1.1 mL, 7.86 mmol) and MsCl (0.49 mL, 6.29 mmol) at −90 °C. The temperature of the reaction mixture was gradually raised to −10 °C. Et_3N (4.38 mL, 31.4 mmol) and Me_3SiCl (3.31 mL, 26.2 mmol) were added to the mixture at −10 °C. After being stirred at 10 °C overnight, the mixture was poured into water and extracted with ether. The combined ether solution was washed with brine and dried (Na_2SO_4). Evaporation of the volatile materials under reduced pressure gave trimethylsilyl mesylate **28** (2.44 g). A DMF (25 mL) solution of the crude mesylate **28** (2.44 g) was added to a mixture of benzoic acid (1.29 g, 10.5 mmol), DBU (1.57 mL, 10.5 mmol), and NaI (5 mg) in DMF (25 mL), and the mixture was stirred at 70 °C for 2 days. After being cooled to room temperature, the mixture was poured into water (200 mL) and extracted with ether. The combined organics were successively washed with aqueous $Na_2S_2O_3$ and brine and dried (Na_2SO_4). The residue obtained by evaporation of the organics was passed through a silica gel column eluted with hexane–AcOEt (20:1 and then 4:1) solution to give hydroxy benzoate **29** (1.17 g, 54%). **Hydroxy benzoate 29**: colorless oil; IR (CCl_4) 3500, 1720 cm^{-1}; ^{1}H NMR (90 MHz, CCl_4) δ 7.8–8.0 (m, 2 H), 7.2–7.6 (m, 3 H), 5.60 (d, J = 9.0 Hz, 1 H), 5.0 (br m, 2 H), 4.78 (br s, 1 H), 4.64 (s, 1 H), 4.84 (d, J = 12.9 Hz, 1 H), 4.58 (d, J = 12.9 Hz, 1 H), 4.30 (dd, J = 3.6, 9.0 Hz, 1 H), 1.76 (s, 3 H), 1.63 (s, 3 H), 1.56 (s, 3 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 166.3 (s), 145.3 (s), 134.2 (s), 133.9 (s), 133.4 (s), 133.2 (d), 132.9 (d), 130.2 (s), 129.6 (d), 129.6 (d), 128.3 (d), 128.3 (d), 125.7 (d), 124.2 (d), 113.8 (t), 69.5 (d), 67.4 (t), 49.2 (d), 40.2 (t), 36.0 (t), 28.7 (t), 27.9 (t), 24.6 (t), 24.6 (t), 23.2 (q), 15.7 (q), 15.4 (q); MS, m/e (relative intensity) 408 (19, M^+), 286 (63), 204 (58), 161 (56), 149 (54), 137 (60), 136 (100), 123 (69), 122 (53), 109 (58). **Hydroxy benzoate 30**: colorless prisms; mp 80–81 °C; IR ($CHCl_3$) 3550, 1710 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.9–8.1 (m, 2 H), 7.2–7.7 (m, 3 H), 5.30 (d, J = 9.6 Hz, 1 H), 5.01 (br s, 3 H), 5.00 (d, J = 12.3 Hz, 1 H), 4.86 (br s, 1 H), 4.76 (d, J = 12.3 Hz, 1 H), 4.30 (t, J = 9.6 Hz, 1 H), 1.73 (s, 3 H), 1.63 (s, 3 H), 1.60 (s, 3 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 166.5 (s), 144.5 (s), 136.2 (s), 134.3 (s), 133.9 (s), 133.0 (d), 131.7 (d), 130.1 (s), 129.6 (d), 129.6 (d), 128.3 (d), 128.3 (d), 126.1 (d), 122.2 (d), 116.4 (t), 67.9 (d), 63.2 (t), 53.1 (d), 39.3 (t), 33.7 (t), 33.4 (t), 27.2 (t), 24.1 (t), 23.5 (t), 18.7 (q), 18.0 (q), 15.5 (q); MS, m/e (relative intensity) 408 (10, M^+), 136 (100), 122 (72), 105 (54). Anal. Calcd for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.07; H, 8.94.

***dl*-(3*Z*)-Cembrene A (27).** A mixture of diol **24** (30 mg, 0.099 mmol), Ac_2O (100 mg, 0.98 mmol), and trace amounts of DMAP in pyridine (1 mL) was stirred at room temperature overnight. The volatile materials were removed in vacuo. The residue was passed through a short silica gel column eluted with hexane–AcOEt (20:1) to give diacetate **24** (CH_3CO instead of H) (30 mg). To an ethylamine (5 mL) solution of the diacetate (30 mg, 0.077 mmol) was added Li (8 mg, 1.2 mmol) at −78 °C with stirring. When the reaction mixture became blue, it was quenched with NH_4Cl. Ethylamine was evaporated in vacuo and the residue was stirred with ether. The ether solution was successively washed with aqueous NH_4Cl and then brine and dried (Na_2SO_4). The ether was evaporated and the residue was passed through a silica gel column eluted with hexane to give hydrocarbon **27** (17 mg, 81%) (*dl*-(3*Z*)-cembrene A): colorless oil; IR (CCl_4) 1650 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.9–5.3 (m, 3 H), 4.72 (m, 1 H), 4.63 (br d, J = 2.2 Hz, 1 H), 1.65 (m, 9 H), 1.55 (br s, 3 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 148.5 (s), 134.3 (s), 133.0 (s), 133.0 (s), 125.2 (d), 124.9 (d), 124.9 (d), 111.0 (t), 45.4 (d), 40.2 (t), 36.0 (t), 31.1 (t), 30.6 (t), 29.6 (t), 24.6 (t), 24.6 (t), 22.5 (q), 18.6 (q), 15.6 (q), 15.5 (q); MS(EI), m/e (relative intensity) 272 (64, M^+), 121 (85), 107 (100), 93 (73), 68 (94).

Epoxidation of Dibenzoate (24, PhCO instead of H). A mixture of hydroxy benzoate **29** (212 mg, 0.52 mmol), benzoic anhydride (0.5 mL), and catalytic amounts of DMAP in Et_3N (1.5 mL) was kept at room temperature for 4 h. The mixture was diluted with ether and the ether solution was washed with brine and dried (Na_2SO_4). The volatile organics were removed in vacuo

and the residue was passed through a short silica gel column eluted with hexane–AcOEt (30:1) to isolate the dibenzoate (261 mg, 98%). To a CH_2Cl_2 (10 mL) solution of the dibenzoate (252 mg, 0.49 mmol) containing $NaHCO_3$ (58 mg, 0.69 mmol) was added MCPBA (102 mg, 0.59 mmol) in CH_2Cl_2 (1.5 mL) at −20 °C, and the reaction mixture was kept for 40 min at the same temperature. The mixture was poured into aqueous $NaHCO_3$ solution and extracted with ether. The combined organics were washed with brine and dried (Na_2SO_4). The residue obtained by evaporation of the volatile materials was passed through a silica gel column eluted with hexane–AcOEt (7:1 and then 2:1) solution to obtain the starting dibenzoate (31 mg) and a mixture of monoepoxides (194 mg, 75%) and diepoxides (29 mg, 11%). The mixture of monoepoxides with the ratio of 1:22:5:2 was submitted to HPLC separation (Lichrosorb SI 100 with hexane–ether, 10:1) to isolate the major epoxy dibenzoate **31**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 5.74 (t, J = 9 Hz, 1 H), 5.50 (d, J = 9 Hz, 1 H), 5.18 (br t, J = 6.6 Hz, 1 H), 4.88 (d, J = 13.5 Hz, 1 H), 4.82 (br s, 2 H), 4.68 (d, J = 13.5 Hz, 1 H), 1.72 (s, 3 H), 1.68 (s, 3 H), 1.24 (s, 3 H) (signals due to aromatics are omitted); MS, m/e (relative intensity) 528 (4, M^+), 285 (52), 284 (100), 256 (63), 215 (35), 173 (33).

A mixture of epoxy dibenzoate **31** (16 mg) and 0.5 N NaOH (0.1 mL) in dioxane (2 mL) was refluxed for 2 days, and the reaction mixture was diluted with ether. The organics were washed with brine and dried (Na_2SO_4). Evaporation of the volatile materials and silica gel column chromatography (hexane–AcOEt, 1:1) of the resulting residue gave epoxy diol **32** (9 mg): ^{1}H NMR (90 MHz, $CDCl_3$) δ 5.36 (d, J = 9 Hz, 1 H), 4.9–5.1 (br s, 1 H), 4.97 (m, 1 H), 4.86 (br s, 1 H), 4.21 (t, J = 9 Hz, 1 H), 4.08 (br s, 2 H), 1.75 (br s, 3 H), 1.64 (s, 3 H), 1.20 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 144.6 (s), 141.7 (s), 133.8 (s), 128.2 (d), 125.3 (d), 115.8 (t), 68.4 (d), 65.8 (t), 62.8 (d), 61.2 (s), 54.3 (d), 38.5 (t), 37.3 (t), 27.3 (t), 27.0 (t), 24.6 (t), 24.4 (t), 18.3 (q), 16.4 (q), 15.0 (q); MS, m/e (relative intensity) 320 (2, M^+), 109 (55), 107 (61), 95 (52), 93 (83), 81 (100), 79 (60), 69 (87), 67 (80).

Bromo Ether 33. To a CH_2Cl_2 (230 mL) solution of hydroxy benzoate **29** (94 mg, 0.23 mmol) was added 2,4,4,6-tetrabromocyclohexadienone (TBCO) (104 mg, 0.25 mmol), and the mixture was stirred at room temperature overnight. The reaction mixture was successively washed with 2 N NaOH, aqueous NH_4Cl, and then brine and dried (Na_2SO_4). The solvent was evaporated. The residue was passed through a silica gel column eluted with a hexane–AcOEt (60:1 and then 4:1) solution to give bromo ether **33** (62 mg, 55%) and an unidentified allyl bromide (26 mg, 23%). **Bromo ether 33**: colorless prisms, mp 71–72° C; IR (CCl_4) 1720 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.8–8.0 (m, 2 H), 7.2–7.5 (m, 3 H), 5.83 (d, J = 9.7 Hz, 1 H), 5.39 (br d, J = 9 Hz, 1 H), 5.05 (m, 1 H), 4.94 (m, 1 H), 4.91 (dd, J = 1.0, 12.7 Hz, 1 H), 4.71 (dd, J = 1.0, 12.7 Hz, 1 H), 4.51 (dd, J = 4.4, 9.7 Hz, 1 H), 4.41 (d, J = 9.4 Hz, 1 H), 1.75 (s, 3 H), 1.71 (s, 3 H), 1.30 (s, 3 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.3 (s), 143.9 (s), 134.4 (s), 134.0 (s), 133.0 (d), 130.4 (s), 129.7 (d), 129.7 (d), 129.3 (d), 128.4 (d), 128.4 (d), 122.0 (d), 113.7 (t), 76.8 (s), 69.0 (d), 68.4 (t), 57.4 (d), 44.1 (d), 33.7 (t), 31.6 (t), 30.2 (t), 28.3 (t), 24.8 (t), 23.7 (t), 22.8 (q), 21.3 (q), 19.2 (q); MS(EI), m/e (relative intensity) 332 (70), 330 (64), 135 (64), 134 (61), 105 (100). Anal. Calcd for $C_{27}H_{35}O_3Br$: C, 66.53; H, 7.24. Found: C, 66.53; H, 7.61. **Unidendified allyl alcohol**: colorless oil; IR (CCl_4) 3550, 1720 cm^{-1}; ^{1}H NMR (90 MHz, CCl_4) δ 7.8–8.1 (m, 2 H), 7.2–7.6 (m, 3 H), 5.42 (d, J = 9 Hz, 1 H), 4.5–5.1 (m, 7 H), 4.29 (dd, J = 5.1, 9 Hz, 1 H), 4.11 (t, J = 9.3 Hz, 1 H), 1.76 (s, 3 H), 1.66 (s, 3 H); MS(EI), m/e (relative intensity) 488, 486 (7, M^+), 77 (100).

Epoxy Bromo Ethers 34 and 35. To a CH_2Cl_2 (7 mL) solution of bromo ether **33** (137 mg, 0.28 mmol) were added $NaHCO_3$ (31 mg, 0.37 mmol) and MCPBA (54 mg, 0.31 mmol) at −20 °C with stirring. The stirring was continued for 48 h at −20 °C. The reaction mixture was diluted with ether, washed successively with aqueous $Na_2S_2O_3$, aqueous $NaHCO_3$, and brine, and then dried (Na_2SO_4). The combined organics were concentrated in vacuo. Silica gel column chromatography of the residue gave recovered material **33** (24 mg, 18%) and a mixture of mono epoxides **34** and **35**. The mixture was separated by high pressure liquid chromatography (Lichrosorb SI 100) with hexane–ether (8:1) to give **34** (68 mg) and **35** (24 mg). **34**: colorless oil; IR ($CHCl_3$) 1720 cm^{-1}; ^{1}H NMR (90 MHz, CCl_4) δ 7.8–8.1 (m, 2 H), 7.2–7.6 (m, 3 H), 5.70 (br d, J = 9.9 Hz, 1 H), 4.93 (dd, J = 1.2, 13.5 Hz, 1 H), 4.85 (m, 1 H), 4.80 (m, 1 H), 4.62 (dd, J = 1.2, 13.5 Hz, 1 H), 4.41 (dd, J = 4.4, 9.9 Hz, 1 H), 4.15 (d, J = 9.8 Hz, 1 H), 2.82 (dd, J = 2.1, 9.4 Hz, 1 H), 1.74 (s, 3 H), 1.35 (s, 3 H), 1.23 (s, 3 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 144.2 (s), 135.2 (s), 133.0 (d), 130.1 (s), 129.6 (d), 129.6 (d), 128.5 (d), 128.3 (d), 128.3 (d), 114.0 (t), 77.4 (s), 67.4 (t), 67.4 (d), 60.5 (s), 58.7 (d), 58.4 (d), 44.6 (d), 33.5 (t), 30.9 (t), 29.1 (t), 25.1 (t), 24.9 (t), 22.9 (q), 22.6 (t), 20.8 (q), 20.4 (q). **35**: colorless plates, mp 156–157 °C; IR ($CHCl_3$) 1720 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.9–8.1 (m, 2 H), 7.2–7.6 (m, 3 H), 5.76 (br d, J = 8.7 Hz, 1 H), 4.97 (br s, 1 H), 4.89 (m, 1 H), 4.76 (d, J = 12 Hz, 1 H), 4.71 (d, J = 12 Hz, 1 H), 4.4–4.6 (m, 2 H), 3.03 (t, J = 6.4 Hz, 1 H), 1.75 (d, J = 0.9 Hz, 3 H), 1.26 (s, 6 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 166.2 (s), 143.8 (s), 134.3 (s), 133.1 (d), 130.1 (s), 129.6 (d), 129.6 (d), 129.6 (d), 128.4 (d), 128.4 (d), 113.8 (t), 77.3 (s), 68.7 (d), 68.2 (t), 63.5 (s), 61.0 (d), 56.9 (d), 44.4 (d), 33.8 (t), 30.1 (t), 29.8 (t), 26.4 (t), 24.2 (t), 23.6 (q), 22.7 (t), 21.0 (q), 18.1 (q); MS(EI), m/e (relative intensity) 504, 502, 301 (47), 175 (84), 147 (65), 136 (100), 135 (65), 121 (74).

***dl*-Asperdiol (1).** Zn dust (0.38 g, 5.76 mmol) was suspended in 2 N HCl and irradiated by ultrasound under an argon atmosphere for 5 min. The 2 N HCl was removed by decantation and the Zn dust was washed successively with degassed water and then degassed acetone. After drying completely under reduced pressure, the Zn dust was suspended in degassed EtOH (2 mL), to which epoxy bromide **34** (58 mg, 0.12 mmol) in EtOH (2 mL) and water (0.1 mL) was added. The mixture was refluxed for 1 h with stirring and cooled to room temperature. The Zn dust was filtered and the combined organics were concentrated in vacuo. The residue was dissolved in MeOH (2 mL). Water (0.5 mL) and 2 N KOH–MeOH (0.5 mL) were added to the solution and the mixture was kept at 50 °C for 2 h with stirring. The reaction mixture was poured into water and extracted with ether. The combined organics were successively washed with 2 N HCl, aqueous $NaHCO_3$, and then brine and dried (Na_2SO_4). The solvents were removed in vacuo and the residue was passed through a silica gel column eluted with hexane–AcOEt (1:1) to give epoxy diol (*dl*-asperdiol) **1** (34 mg, 93%): colorless needles, mp 119–120 °C; IR ($CHCl_3$) 3200–3700 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 5.42 (d, J = 7.5 Hz, 1 H), 5.11 (br t, J = 5.7 Hz, 1 H), 4.91 (m, 1 H), 4.73 (br s, 1 H), 4.47 (dd, J = 5.3, 7.5 Hz, 1 H), 4.03 (s, 2 H), 2.68 (dd, J = 3.9, 5.7 Hz, 1 H), 1.77 (m, 3 H), 1.63 (s, 3 H), 1.18 (s, 3 H); ^{13}C NMR (23 Hz, $CDCl_3$) δ 145.8 (s), 139.4 (s), 135.4 (s), 128.6 (d), 124.6 (d), 113.6 (t), 68.4 (d), 65.5 (t), 64.9 (d), 60.4 (s), 50.5 (d), 37.5 (t), 36.1 (t), 28.1 (t), 26.6 (t), 25.8 (t), 24.0 (t), 22.3 (q), 16.6 (q), 15.8 (q); MS(EI), m/e (relative intensity) 320 (3, M^+), 177 (52), 152 (100), 148 (77), 108 (54), 95 (90). Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.96; H, 10.20.

***dl*-6,7-Epiasperdiol (36).** Zn dust (300 mg), activated by ultrasound as described in the previous experiment, was suspended in EtOH (5 mL) containing 0.1 mL of water. To this suspension was added epoxy bromo ether **35** (18 mg, 0.036 mmol) dissolved in 1 mL of ether. The mixture was refluxed for 1 h and cooled to room temperature and the Zn dust was filtered. The combined organics were concentrated in vacuo. To the residue were added MeOH (2 mL), water (0.5 mL), and 2 N KOH–MeOH (0.5 mL). The mixture was warmed at 50 °C for 2 h, poured into water, and extracted with ether. The combined organics were successively washed with 2 N HCl, aqueous $NaHCO_3$, and then brine and dried (Na_2SO_4). The organics were concentrated and the residue was passed through a silica gel column with hexane–AcOEt (2:3) to give epiasperdiol **36** (11.5 mg, 100%): colorless prisms, mp 88–89 °C; IR ($CHCl_3$) 3200–3700 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 5.57 (d, J = 9.3 Hz, 1 H), 5.16 (br t, J = 7.5 Hz, 1 H), 4.93 (m, 1 H), 4.73 (br s, 1 H), 4.47 (dd, J = 3.8, 9.3 Hz, 1 H), 4.18 (d, J = 14 Hz, 1 H), 4.02 (d, J = 14 Hz, 1 H), 2.62 (dd, J = 4.8, 6.2 Hz, 1 H), 1.80 (br s, 3 H), 1.60 (s, 3 H), 1.13 (s, 3 H); ^{13}C NMR (23 MHz, $CDCl_3$) δ 145.9 (s), 138.6 (s), 134.9 (s), 130.0 (d), 124.7 (d), 113.7 (t), 67.4 (d), 66.1 (t), 62.2 (d), 60.9 (s), 49.1 (d), 38.6 (t), 36.0 (t), 28.1 (t), 25.1 (t), 24.6 (t), 24.0 (t), 23.0 (q), 17.1 (q), 15.4 (q); MS(EI), m/e (relative intensity) 320 (7, M^+), 170 (44), 150 (77), 139 (100), 135 (90), 124 (41), 121 (44), 107 (64). Anal. Calcd for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06. Found: C, 74.96; H, 10.12.

Registry No. (±)-**1**, 86853-19-2; (±)-**3a**, 59664-63-0; (±)-**3b**, 59686-17-8; (±)-**6**, 86838-67-7; (±)-**7**, 86853-14-7; (±)-**8**, 107099-08-1; (±)-**9**, 86853-12-5; (±)-**10**, 107171-90-4; (±)-**11**, 86853-15-8; (±)-**12**,

107171-91-5; (±)-13, 86900-19-8; (±)-14, 86853-16-9; (±)15, 107171-92-6; (±)-16, 107171-93-7; (±)-17, 107171-94-8; (±)-18, 107171-95-9; (±)-19, 107099-09-2; (±)-20, 107099-10-5; (±)-21, 107171-96-0; (±)-22, 86838-70-2; (±)-24, 86838-71-3; (±)-26, 107099-11-6; (±)-27, 73246-00-1; (±)-28, 86848-71-7; (±)-29, 86838-72-4; (±)-29 (dibenzoate), 107099-15-0; (±)-30, 107171-97-1; 31, 107114-68-1; 32, 107099-12-7; (±)-33, 107099-13-8; (±)-34, 107099-14-9; (±)-35, 107171-98-2; (±)-36, 107171-99-3.

Reactions of Azines. 12. Preparation and Reactions of Triphenyl[2-((phenyl(methoxycarbonyl)methylene)hydrazono)propyl]-phosphonium Bromide

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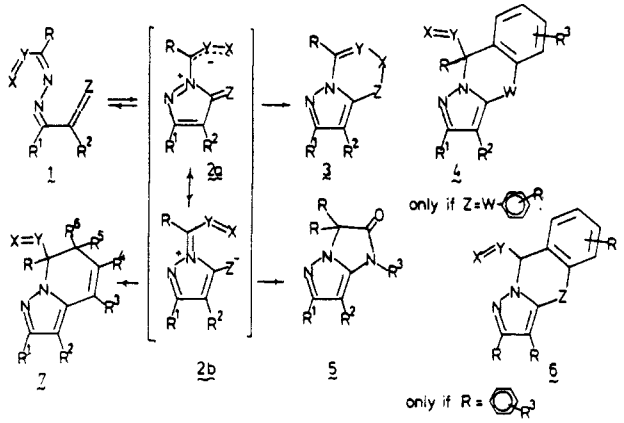
Preparation of triphenyl[2-((phenyl(methoxycarbonyl)methylene)hydrazono)propyl]phosphonium bromide (**13**), triphenyl[1-methyl-2-((phenyl(methoxycarbonyl)methylene)hydrazono)propyl]phosphonium iodide (**15**), and their corresponding ylides **14** and **16** was accomplished. The reaction of **14** with diphenylketene gave 2-methyl-4,9-diphenyl-9-(methoxycarbonyl)-4,9-dihydropyrazolo[1,5-*b*]isoquinoline (**19**/**20**). The reaction of **16** with phenyl isocyanate gave 6,7-dimethyl-3-methoxy-1,3-diphenyl-1*H*-imidazo[1,2-*b*]pyrazol-2(3*H*)-one (**27b**), 2,3-dimethyl-9-(methoxycarbonyl)-9-phenyl-4,9-dihydropyrazolo[5,1-*b*]quinazoline (**30**), and 2,3-dimethyl-9-phenylpyrazolo[5,1-*b*]quinazoline (**31**). Phenylacetoxyketene, on reacting with triphenyl[2-((diphenylmethylene)hydrazono)propyl]phosphorane (**35**), gave 2-methyl-4,9-diphenylpyrazolo[1,5-*b*]isoquinoline (**40**). Carbon disulfide with ylide **16** gave the 2,3-dimethyl-9-(methoxycarbonyl)-9*H*-pyrazolo[5,1-*b*][1,3]benzothiazine (**45**) and desaurine **42** as well as the *trans*-5,10-bis(methoxycarbonyl)-5,10-diphenyldipyrazolo[1,5-*a*:1′,5′-*e*][1,5]diaza-[3,6]dithiocine (**46**). Confirmation of the structures **31**, **42**, and **46** was obtained by crystallographic analyses.

Previously it has been shown that cumulated azines **1** are excellent synthons for a variety of fused pyrazolo heterocycles (**3**–**7**).



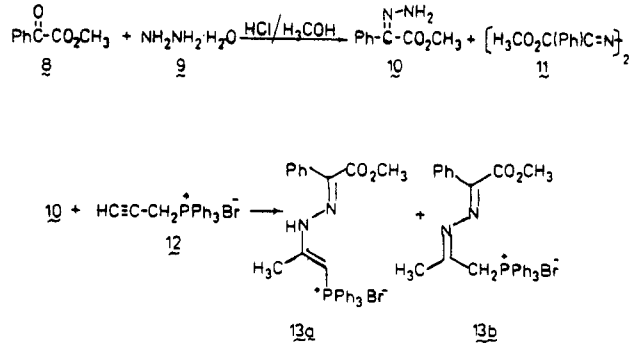
The species produced in high yields from readily available starting materials have been pyrazolo[5,1-*c*]-1,4-oxazines **3** (Y = CR^3, X = O, Z = CR_2^4),[1,2] 4,5-dihydropyrazolo-[1,5-*b*]isoquinolines **4** (W = CR_2^4) or **6** (Z = CR_2^4),[1-3] 2,3-dihydro-1*H*-imidazo[1,2-*b*]pyrazol-2-ones **5**,[4] 4,9-dihydropyrazolo[5,1-*b*]quinazolines **4** (W = NH) or **6** (Z = NR^4),[4] 4,5-dihydropyrazolo[1,5-*a*]pyridines **3** (Y = CR^3, X = CR^4R^5, Z = CR^6R^7),[5] and 6,7-dihydropyrazolo[1,5-*a*]-pyridines **7**.[5]

The resonance hybrids **2a** ↔ **2b** are the logical intermediates for all of the species (**3**–**7**) reported to date in this reaction series. In the previous work we have never isolated any products attributable to the dimerization of the intermediates **2**. In this paper we report the isolation of a product that is the direct result of such a dimerization.

We also report the preparation of the azine phosphoranes **13** and **16** and their conversion via cumulated azines of type **1** into fused pyrazolo heterocycles similar to those shown by formulas **3**–**7**.

Results and Discussion

On repeating the preparation of methyl α-hydrazonophenylacetate (**10**) from benzoylformate **8** and hydrazine hydrate **9**, described by Neunhoeffer et al.,[6] we obtained the azine **11** as well as the reported **10** in 42% and 17% yields, respectively. Slightly altered reaction conditions, given in the Experimental Section, gave us yields of 17% and 53% of **11** and **10**, respectively. The phosphonium salt **13** was produced (75%) by allowing the hydrazone **10**



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