(94% yield) and its *Z* isomer **4a**[7] (96% yield), respectively, without isomerization of the olefin. In contrast to these results, the asymmetric *Z,E* ether **3c**[7] gave a mixture of **2**, **4b**, and **4a**[7] (9:41:50, total 95% yield) with high regioselectivity but with poor stereoselectivity[8] (Scheme II).

We then attempted the [2,3]-Wittig rearrangement of **7** for the synthesis of costunolide (**5**) (Scheme I). The bromo alcohol **8a** was prepared from easily available farnesyl acetate (**8b**) in three steps [(1) SeO_2/*t*-BuOOH, (2) CBr_4/PPh_3, (3) K_2CO_3/MeOH]. The macrocyclic ether **7** was synthesized from **8a** in 60% yield by using high dilution technique; a solution of **8a** (16.0 mmol) in dry benzene (100 mL) was added dropwise over 2 h to a suspension of NaH (30 mmol) and dicyclohexano-18-crown-6 (16.0 mmol) in benzene (200 mL) at 80 °C. The rearrangement of **7** in ether under the same condition described above gave a mixture of **6a**[9,10] and **9** in a 75:25 ratio (total isolated yield, 98%). None of diastereomer of **6a** could be detected by HPLC analysis.

The exclusive formation of the trans isomer **6a** can be understood by examining the possible transition states[11] for rearrangement of the allyllithiums A and B obtained upon lithiation of the comformers **7a** and **7b**[12] (Figure 2). The transition-state B developed from **7b** suffers from the 1,3-interaction between C(6–5) C–C bond and C(11)–Me and likewise the eclipsing 1,2-interaction between C(6–5) and C(7–8) C–C bonds. The transition-state A formed from **7a** does not experience these unfavorable interactions. Therefore, the rearrangement proceeds in such a way as to make two adjacent larger groups, C(6–5) and C(7–8) C–C bonds, becoming trans to each other in the five-membered cyclic transition states.

The isopropenyl moiety in **6a** was oxidized[14] with *sec*-BuLi/TMEDA/O_2[15] to give the diol **6b** in 60% yield. Moreover the diol **6b** was obtained directly from **7** with *sec*-BuLi in ether and then TMEDA/O_2 in 40% yield. The diol **6b** was converted to **5** with MnO_2 in ether at room temperature for 12 h. The synthetic (±)-costunolide (**5**) (mp 64–66 °C) was found by IR and ^1H NMR spectra and TLC analysis to be identical with a sample of natural product.[9]

This type of stereocontrol might have predictable value in organic synthesis. Development of this methodology combined with remote stereochemical control and cyanohydrin methodology[16] to the synthesis of natural products are in progress.[17]

Acknowledgment. We are grateful to Professor T. Nakai (Tokyo Institute of Technology) and Professor S. Ito (Tohoku University) for helpful discussions on the transition state of [2,3]-Wittig rearrangements. We also thank I. Miura (Otsuka Pharmaceutical Co.) and T. Nakata (The Institute of Physical and Chemical Research) for their help in the interpretation of the NMR spectra.

Registry No. (±)-**2**, 104423-38-3; **3a**, 104423-35-0; **3b**, 104423-36-1; **3c**, 104423-37-2; (±)-**4a**, 104486-18-2; (±)-**4b**, 104486-19-3; (±)-**5**, 104527-18-6; (±)-**6a**, 104423-07-6; (±)-**6b**, 104486-16-0; (±)-**6c**, 104423-08-7; (±)-**6c** (epoxide), 104423-42-9; **6c**-ol (isomer 1), 104438-53-1; **6c**-ol (isomer 2), 104423-43-0; **7**, 104423-09-8; **8a**, 104423-12-3; **8a** (acetate), 104423-44-1; **8b**, 4128-17-0; **8b**-ol, 93787-91-8; **9**, 104423-11-2; (±)-**10**, 104423-10-1; I, 629-09-4; II, 6089-04-9; IIIa, 104423-13-4; IIIb, 3516-38-9; IIIc, 104423-14-5; IV, 72312-54-0; V, 72312-58-4; VI, 104423-18-9; VIIa, 104423-15-6; VIIb, 104423-16-7; VIIIa, 72312-63-1; VIIIb, 104423-17-8; IX, 104423-19-0; IX (THP), 104423-45-2; X, 104423-20-3; X·XI (ester), 104423-40-7; XI, 104423-21-4; XII, 104423-22-5; XII-ol, 104423-41-8; XIII, 104423-23-6; XIII-ene, 104423-46-3; XIV, 104423-24-7; XIV (tosylate), 104423-47-4; XV, 104423-25-8; XV-diol (tosylate), 104423-48-5; XVI, 104423-26-9; (±)-XVII, 104423-27-0; (±)-XVII (acetate), 104423-28-1; XVII (ethoxyethylether), 104423-49-6; (±)-XVII (tetrahydro acetate), 104423-29-2; XVII (tetrahydro alcohol), 104423-30-5; XVII (tetrahydro tosylate), 104423-31-6; (±)-XVIII, 104423-32-7; (±)-XVIII-al, 104423-33-8; (±)-XIX, 104423-39-4; (±)-XX, 104486-17-1; (±)-XXI, 104486-20-6; XXII, 104423-34-9.

Supplementary Material Available: Preparation methods for **3a–c**, relative stereochemical determinations of **2** and **4a,b**, and NMR and IR spectra of **2**, **3a–c**, **4a,b**, **5**, **6a**, and **7** (27 pages). Ordering information is given on any current masthead page.

(7) Comparison of our results with those of acyclic systems[5b] regarding stereoselectivity is outlined as follows: (1) higher degree with the same sense in the case of *E,E*, (2) higher degree with the opposite sense in the case of *Z,Z*. Preparations of **3a–c**, and determinations of relative stereochemistry of **2** and **4a,b** are available in the supplementary material.

(8) [2,3]-Wittig rearrangement of the corresponding *Z,E* acyclic system has not been examined.

(9) The structure of **6a** was confirmed by ^1H NMR and ^{13}C NMR. Moreover the stereoselective Cope rearrangement of **6a** gave **10** as a single product (refluxing in benzene for 6 h). The observed coupling constant ($J_{H_aH_b} = J_{H_aH_c} = 9.4$ Hz) of **10** suggest the trans stereochemistry between C(6) and C(7) and the (4*E*,10*E*)-olefin geometry in **6a** (see ref 3h).

(10) Recently I. Kitagawa and H. Shibuya have synthesized the same compound by macrocyclization of the aldehyde allylic bromide promoted by Cr(II) and completed the synthesis of costunolide (14 steps from farnesyl acetate). We are indebted to Professor Kitagawa for providing NMR spectra of this compound and natural costunolide. Shibuya, H.; Ohashi, K.; Kawashima, K.; Hori, K.; Murakami, N.; Kitagawa, I. *Chem. Lett.* **1986**, 85.

(11) Three types envelope transition-state models for the acyclic [2,3]-Wittig rearrangement have been proposed: (a) Trost, B. M.; Hammen, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 962. (b) Still, W. C.; Mitra, A. *Ibid.* **1978**, *100*, 1928. See also ref 5c,d.

(12) Although the mechanism of the lithiation is not fully understood, the structure of the π orbital at C(7,11) and C(4,5) may play an important role in the lithiation at C(6). The transition state of this rearrangement would be very early (see ref 11b). Therefore, 32 conformers of the ground-state model **7** were created on the basis of the fact that all the sp^2 planes are perpendicular to the medium ring plane. The results of these MM2 calculations[13] indicated that conformers **7a** and **7b** had the shortest distance between C(6) and C(7) despite its lower energy.

(13) (a) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127; *QCPE 395*. (b) Jamie, C.; Osawa, E. *Tetrahedron* **1983**, *39*, 2769.

(14) Epoxidation and hydroboration of silylated compound **6c** using mCPBA and disiamylborane also proceeded at the most reactive C(1),-C(10) olefin. Oxidation of **6c** with SeO_2 or with *sec*-BuLi/TMEDA/O_2 gave the C(10)-hydroxymethyl derivative.

(15) (a) Crawford, R. J.; Erman, W. F.; Broaduss, C. D. *J. Am. Chem. Soc.* **1972**, *94*, 4298. (b) Suemune, H.; Iwasaki, G.; Ueno, K.; Sakai, K. *Chem. Pharm. Bull.* **1984**, *32*, 4632.

(16) Takahashi, T.; Nemoto, H.; Tsuji, J. *Tetrahedron Lett.* **1983**, *24*, 3485.

(17) Professor J. A. Marshall (Marshall, J. A.; Jensen, T. M.; DeHoff, B. S. *J. Org. Chem.*, accompanying paper in this issue) reports his successful independent new route to the carbon skeleton of cembranoid using [2,3]-Wittig rearrangement of 17-membered diallylic ether. We thank him for communicating his results to us in advance of publication.

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[2,3]Wittig Ring Contraction. A New Route to Cembranoid Natural Products

Summary: A new route to the cembranoid skeleton is described wherein a 17-membered propargyl allyl ether is subjected to [2,3]Wittig rearrangement to afford a 14-membered carbocyclic with substituents appropriate for elaboration to cembrane natural products.

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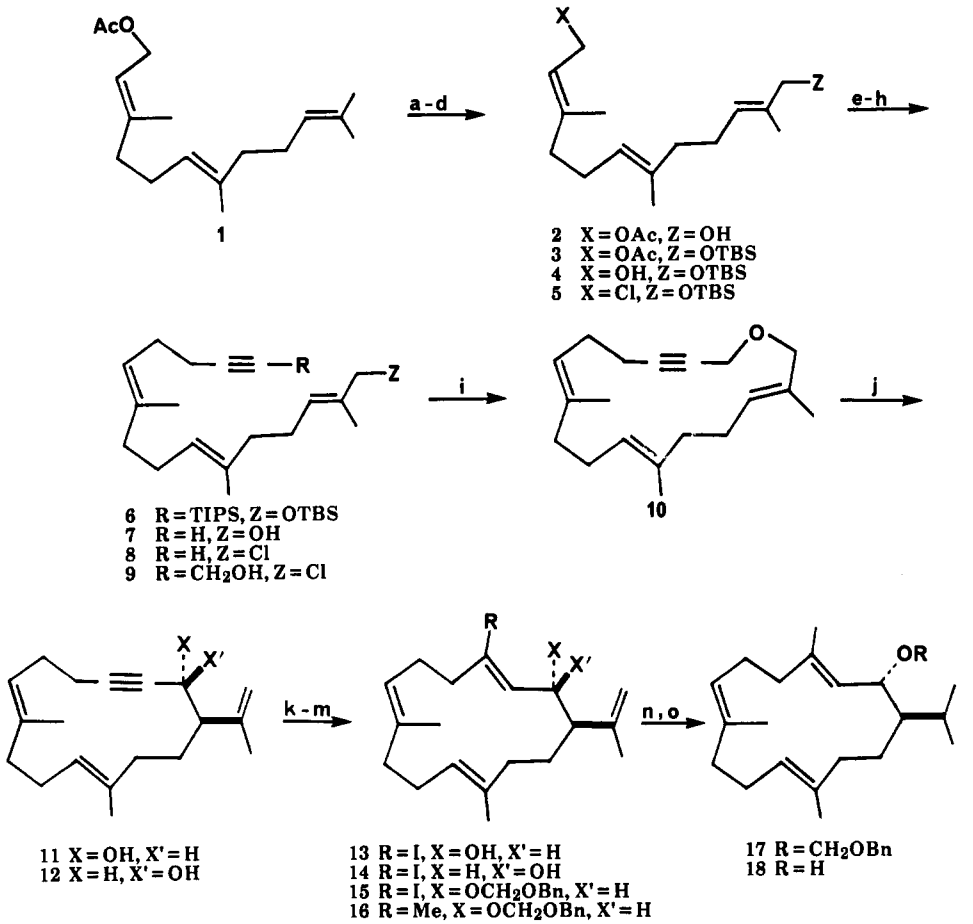
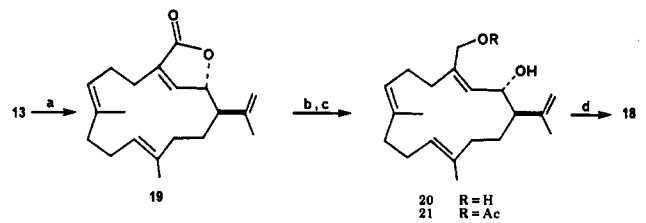
Scheme I[a]



[a] (a) SeO_2, *t*-BuOOH, CH_2Cl_2, 0 °C, 1 h; (b) *t*-$BuMe_2SiCl$, DMAP, Et_3N, CH_2Cl_2, room temperature, 1 h; (c) K_2CO_3, CH_3OH, 0 °C, 3 h; (d) LiCl, 2,6-lutidine, MsCl, DMF, 0 °C, 7 h; (e) (*i*-Pr)$_3$SiC≡CCH_2MgBr, CuI, THF, −78 to −20 °C, 3 h; (f) *n*-Bu_4NF, THF, room temperature, 3 h; (g) LiCl, 2,6-lutidine, MsCl, DMF, 0 °C, 7 h; (h) *n*-BuLi, $(CH_2O)_n$, THF, −78 °C to room temperature, 3 h; (i) EtMgBr, HMPA, THF, 0 °C to reflux, 0.02 M, 4.5 h; (j) *n*-BuLi, hexane–THF (10:1), −78 °C, 1 h, or *n*-BuLi, THF–HMPA (3:1), −78 °C, 1 h; (k) Red-Al, THF, room temperature, I_2, THF, −78 to 0 °C; (l) $BnOCH_2Cl$, *i*-Pr_2NEt, CH_2Cl_2; (m) *t*-BuLi, THF, $MeOSO_2F$, −78 to 0 °C; (n) H_2, $(Ph_3P)_3RhCl$, C_6H_6, EtOH; (o) Na, NH_3, THF.

Scheme II[a]



[a] (a) $(Ph_3P)_4Pd$, Bu_3SnH, CO, $PhCH_3$; (b) DIBAH, THF; (c) Ac_2O, Et_3N; (d) Li, NH_3, THF.

Sir: In the 25 years since their initial structure elucidation[1] the cembrane diterpenes have been increasingly recognized as a major class of natural products.[2,3] To date, synthetic efforts in this area have mainly focused on the simplest structural members of the family with heavy emphasis on macrocyclization methodology.[4] Successful routes have employed $Ni(CO)_4$-promoted coupling of allylic halides,[4a] alkylation of sulfur-stabilized carbanions,[4b] Friedel–Crafts acylation of alkenes,[4c] alkylation of protected cyano-

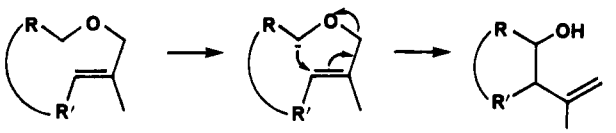


Figure 1. [2,3]Wittig ring contraction.

(1) Dauben, W. G.; Thiessen, W. E.; Resnick, P. R. *J. Am. Chem. Soc.* **1962**, *84*, 2015. Kobayashi, H.; Akiyoshi, S. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 1044.

(2) For a comprehensive review of cembranoid natural products isolated through 1977, see: Weinheimer, A. J.; Chang, C. W.; Matson, J. A. *Fortschr. Chem. Org. Naturst.* **1979**, *36*, 281.

(3) For a leading reference on recently isolated tobacco cembranoids, see: Wahlberg, I.; Forsblom, I.; Vogt, C.; Eklund, A. M.; Nishida, T.; Enzell, C. R.; Berg, J. E. *J. Org. Chem.* **1985**, *50*, 4527.

(4) (a) Dauben, W. G.; Beasley, G. H.; Broadhurst, M. D.; Muller, B.; Peppard, D. J.; Pesnelle, P.; Suter, C. *J. Am. Chem. Soc.* **1974**, *96*, 4723. Dauben, W. G.; Beasley, G. H.; Broadhurst, M. D.; Muller, B.; Peppard, D. J.; Pesnelle, P.; Suter, C. *J. Am. Chem. Soc.* **1975**, *97*, 4973. Crombie, L.; Kneen, G.; Pattenden, G. *J. Chem. Soc., Chem. Commun.* **1976**, 66. (b) Kodama, M.; Matsuki, Y.; Ito, S. *Tetrahedron Lett.* **1975**, 3065. Kodama, M.; Matsuki, Y.; Ito, S. *Tetrahedron Lett.* **1981**, *22*, 4275. Takayanagi, H.; Uyehara, T.; Kato, T. *J. Chem. Soc., Chem. Commun.* **1978**, 359. Dauben, W. G.; Saugier, R. K.; Fleishhauer, I. *J. Org. Chem.* **1985**, *50*, 3767. Marshall, J. A.; Cleary, D. G. *J. Org. Chem.* **1986**, *51*, 858. (c) Kato, T.; Kobayashi, T.; Kitahara, Y. *Tetrahedron Lett.* **1975**, 3299. Kato, T.; Suzuki, M.; Kobayashi, T.; Moore, B. P. *J. Org. Chem.* **1980**, *45*, 1126. Kitahara, Y.; Kato, T.; Kobayashi, T.; Moore, B. P. *Chem. Lett.* **1976**, 219. Kato, T.; Yen, C. C.; Kobayashi, T.; Kitahara, Y. *Chem. Lett.* **1976**, 1191. Kato, T.; Suzuki, M.; Takahashi, M.; Kitahara, Y. *Chem. Lett.* **1977**, 465. Kato, T.; Yen, C. C.; Uyehara, T.; Kitahara, Y. *Chem. Lett.* **1977**, 565. Kato, T.; Suzuki, M.; Nakazima, Y.; Shimizu, K.; Kitahara, Y. *Chem. Lett.* **1977**, 705. Aoki, M.; Tooyama, Y.; Uyehara, T.; Kato, T. *Tetrahedron Lett.* **1983**, *24*, 2267. (d) Takahashi, T.; Nemoto, H.; Tsuji, J. *Tetrahedron Lett.* **1983**, *24*, 3485. (e) Still, W. C.; Mobilio, D. *J. Org. Chem.* **1983**, *48*, 4785. (f) Tius, M. A.; Fauq, A. H. *J. Am. Chem. Soc.* **1986**, *108*, 1035. (g) Wender, P. A.; Holt, D. A. *J. Am. Chem. Soc.* **1985**, *107*, 7771.

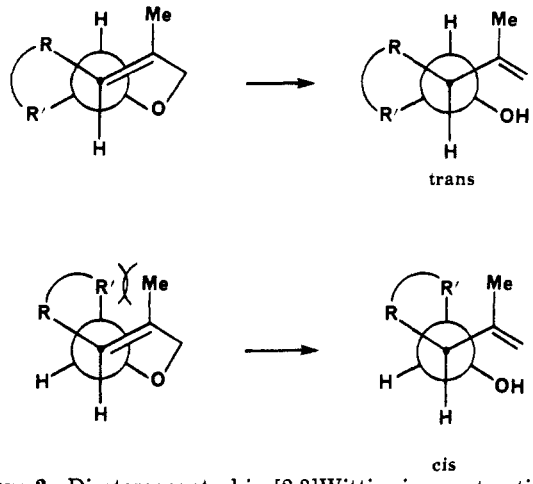


Figure 2. Diastereocontrol in [2,3]Wittig ring contractions.

hydrins,[4d] allylchromium–aldehyde addition,[4e] and Horner–Emmons–Wittig condensation[4f] as ring-closing reactions. In addition, an ingenious macroexpansion approach utilizing the oxy Cope rearrangement has recently been reported.[4g] All of these approaches except for the last use carbon–carbon bond-forming reactions for macrocyclization, an often difficult process. In an effort to circumvent problems encountered in attempted cyclizations of sulfone-stabilized carbanions,[5] we formulated the strategy depicted in Figure 1 whereby a macrocyclic allylic ether would be subjected to [2,3]Wittig rearrangement to construct the carbocyclic ring.[6,7,8] The proximity of the reacting centers enforced by the macrocyclic ring was expected to facilitate carbon–carbon bond formation in this novel ring contracting variant of the Wittig rearrangement. Furthermore, consideration of probable transition-state geometry suggested that a high degree of stereocontrol might be realized (Figure 2).[6]

The starting material for our initial exploration of this plan was prepared by selective allylic oxidation of *all-trans*-farnesyl acetate (**1**) with SeO_2–*t*-butyl hydroperoxide.[9] Conversion of the resultant hydroxy acetate **2** to the allylic chloride **5** was readily effected as shown in Scheme I. Addition of the TIPS-protected propargyl Grignard reagent to chloride **5** in the presence of CuI led to exclusive α,α-coupling to give trienyne **6**.[10] Fluoride-induced cleavage of the silyl-protecting groups gave the acetylene alcohol **7**. Treatment of the chloro derivative[11] **8** with *n*-BuLi at −78 °C followed by addition of paraformaldehyde afforded the chloro alcohol **9**. Cyclization to ether **10** was effected in 71% yield by addition of 1 equiv of EtMgBr to a dilute solution (0.02 M) of chloro alcohol **9** in HMPA–THF and stirring at reflux for 4 h.

Ether **10** underwent facile rearrangement upon treatment with *n*-BuLi in hexane–THF (10:1) at −20 °C to give a 4.5:1 mixture of alkynols **11** and **12** in 85% yield. Tentative stereochemical assignments were made through comparison of the chemical shift and coupling patterns of the carbinyl protons with those of epimukulol (**18**) and mukulol (carbinyl epimer of **18**).[12] Surprisingly, alkynol **12** was formed as the major stereoisomer (60% yield, >6:1) when the rearrangement was conducted in THF–HMPA.[13] On the basis of previous findings with acyclic[6a] and large ring[6b] systems, we expected the trans isomer to be favored in the hexane–THF solvent system (Figure 2).[13] This point was confirmed through conversion of **11** to epimukulol as shown in Scheme I.[12] The failure of vinylic iodide **13** to undergo direct coupling with methyl cuprate reagents[14] is noteworthy. The conversion was achieved less directly through metalation of the protected derivative **15** followed by methylation with methyl fluorosulfonate or dimethyl sulfate and deprotection.

An alternative route was also examined (Scheme II) whereby the vinyl iodide **13** was converted to the butenolide **19** via Pd-catalyzed carbonylation.[15] Reduction with DIBAH afforded the diol **20**, the 3*Z* isomer of desoxyasperdiol.[16] As expected, major differences were observed in the ^1H NMR spectra of **20** and authentic desoxyasperdiol. Monoacetylation of diol **20** was effected with acetic anhydride in Et_3N. Treatment of the mono acetate **21** with lithium in ammonia afforded epimukulol (**18**) directly. Reduction of the isopropenyl double bond is likely facilitated by the proximate alcohol grouping of **21** or the deacetylated intermediate.

The foregoing sequence illustrates a novel and practical route to the cembranoid skeleton. It should be noted that cyclization leading to the 17-membered ether **10** is facile and efficient, even without high dilution. The obvious entropic advantage of the cyclic Wittig rearrangement variant is reflected in the ease with which alkynol **11** is produced.[17] Finally, the concept is potentially applicable to other ring sizes[18] and other types of heterocyclic substrates in the context of a generalized heteroatom-directed macrocyclic ring contraction strategy for carbocyclic synthesis.

(5) Coghlan, M. J. Ph.D. Thesis, Northwestern University, 1984. Clark, J. D. Ph.D. Thesis, University of South Carolina, 1986.

(6) For recent work on the [2,3]Wittig rearrangement, see: (a) Mikami, K.; Azuma, K.; Nakai, T. *Tetrahedron* **1984**, *40*, 2303 and references therein. (b) Marshall, J. A.; Jenson, T. M. *J. Org. Chem.* **1984**, *49*, 1707. (c) Midland, M. M.; Kwon, Y. C. *Tetrahedron Lett.* **1985**, *26*, 5017 and references therein.

(7) For an analogous strategy employing the enolate Claisen rearrangement, see: Ableman, M. M.; Funk, R. L.; Munger, J. D., Jr. *J. Am. Chem. Soc.* **1982**, *104*, 4030. Brunner, R. K.; Borschberg, H. *J. Helv. Chim. Acta* **1983**, *66*, 2608. Ireland, R. E.; Varney, M. D. *J. Org. Chem.* **1986**, *51*, 635.

(8) Medium-ring carbocycles have been prepared by ring contraction of macrocyclic lactam sulfoxides via internal carbanion acylation. Ohtsuka, Y.; Oishi, T. *Tetrahedron Lett.* **1986**, *27*, 203. Ingenious ring-expansion routes to medium- and large-ring carbocyclics via [2,3]sulfonium ylide rearrangements have been developed by Vedejs and co-workers. Vedejs, E. *Acc. Chem. Res.* **1984**, *17*, 358.

(9) The procedure of Sharpless et al. was employed. Umbriet, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 5526. Marshall, J. A.; Andrews, R. C. *J. Org. Chem.* **1985**, *50*, 1602. *all-trans*-Farnesol is available from Aldrich Chemical Co., Milwaukee, WI.

(10) Corey, E. J.; Rücker, C. *Tetrahedron Lett.* **1982**, *23*, 719. The use of propargylmagnesium bromide proved less satisfactory owing to significant production of allenic byproduct. Corey, E. J.; Kirst, H. A. *Tetrahedron Lett.* **1968**, 5041. Ireland, R. E.; Dawson, M. J.; Lipinski, C. A. *Tetrahedron Lett.* **1970**, 2247.

(11) The procedure of Meyers and Collington was used. Collington, E. W.; Meyers, A. I. *J. Org. Chem.* **1971**, *36*, 3044.

(12) Kato, T.; Kobayashi, T.; Kugamai, T.; Kitahara, Y. *Synth. Commun.* **1976**, *6*, 365. Prasad, R. S.; Dev. S. *Tetrahedron* **1976**, *32*, 1437.

(13) The complete reversal in stereoselectivity with the THF–HMPA solvent system has not previously been observed in [2,3]Wittig rearrangements and is contrary to the proposed transition state for the concerted reaction (see Figure 2).

(14) Corey, E. J.; Katzenellenbogen, J. A.; Posner, G. H. *J. Am. Chem. Soc.* **1967**, *89*, 4245. Corey, E. J.; Posner, G. H. *J. Am. Chem. Soc.* **1968**, *90*, 5615.

(15) Cowell, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4193.

(16) Marshall, J. A.; Cleary, D. G. *J. Org. Chem.* **1986**, *51*, 858. Aoki, M.; Tooyama, Y.; Uyehara, T.; Kato, T. *Tetrahedron Lett.* **1983**, *24*, 2267.

(17) Typical reaction times of 6–8 h at −85 to 0 °C are employed for acyclic [2,3]rearrangements of propargyl allyl ethers.[6a] Rearrangement of ether **10** was complete in 1 h at −78 °C in which case a 3:1 mixture of **11** and **12** was formed. Higher temperatures appear to favor production of **11**.

(18) While the work described in this manuscript was being completed we learned of a conceptually related synthesis of 10-membered carbocycles via ring contraction of 13-membered diallylic ethers. Takahashi, T.; Nemato, H.; Kanda, Y.; Tsuji, J.; Fujise, Y. *J. Org. Chem.*, accompanying paper in this issue. We appreciate the cooperation of Professor Takahashi in coordinating publication of our independent results.

Acknowledgment. We are indebted to the National Institutes of Health for support through Research Grant GM 29775. Funds for the AM-300 NMR spectrometer used in this work were provided by the NSF through instrument Grant CHE-8411172. The kind cooperation of Professors Kato and Dev in supplying spectra of epimukulol is gratefully acknowledged.

Registry No. 1, 4128-17-0; 2, 93787-91-8; 3, 104465-85-2; 4, 104465-86-3; 5, 104465-87-4; 6, 104465-88-5; 7, 104465-89-6; 8, 104465-90-9; 9, 104465-91-0; 10, 104487-53-8; (±)-11, 104465-92-1; (±)-12, 104528-78-1; (±)-13, 104465-93-2; (±)-14, 104528-79-2; (±)-15, 104465-94-3; (±)-16, 104465-95-4; (±)-17, 104465-96-5; (±)-18, 59686-16-7; (±)-19, 104465-97-6; (±)-20, 104595-99-5; (±)-21, 92214-89-6; $(i\text{-Pr})_3SiC{\equiv}CCH_2Br$, 104465-98-7.

Supplementary Material Available: IR and ^1H NMR spectral data for 4, 5, 7–13, and 15–21 (4 pages). Ordering information is given on any current masthead page.

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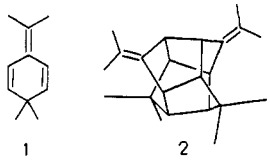
Crisscross Dimerization of 1-Isopropylidene-4,4-dimethyl-2,5-cyclohexadiene

Summary: Treatment of 1-isopropylidene-4,4-dimethyl-2,5-cyclohexadiene (1) with acid in the presence of trifluoroacetic anhydride and trifluoroacetic acid causes efficient formation of the dimer 3,10-bis(1-methylethylidene)-6,6,12,12-tetramethylpentacyclo-[6.3.1.$0^{2,7}$.$0^{4,11}$.$0^{5,9}$]dodecane (2), a structural transformation without precedent in the absence of transition metals.

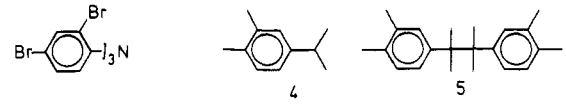
Sir: We report here that the substituted dendralene[1] 1-isopropylidene-4,4-dimethyl-2,5-cyclohexadiene[2] (1) can



1 2

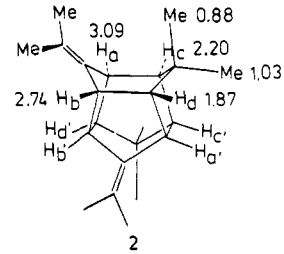
be efficiently converted to its crisscross dimer 2 in a single operation, in which four σ bonds form to generate four five-membered rings. We initially studied 1 to see if cation–radical-catalyzed oxygenation would occur, as it does with some methyl-substituted alkenes to give dioxetanes[3]. Cyclic voltammetry on 1 in 0.1 M $TBABF_4$ in CH_2Cl_2 with trifluoroacetic acid (TFA) and trifluoroacetic anhydride (TFAA) (20:1:1 by volume) diplayed a partially reversible wave at a potential of 1.3 V vs. SCE, so formation of 1^+ with the one-electron oxidant $3^+SbCl_6^-$ is exothermic by 8 kcal/mol. When 1 was treated with 3^+ in the 20:1:1 solvent, the green color of 3^+ was discharged rapidly even at low temperatures, and 1 was consumed, but no oxygenation occurred. The products observed were formed both in the presence and in the absence of oxygen, so reaction of oxygen with 1^+ is slower than the observed chemistry to be reported.

The nonpolymeric products observed from 1 upon treatment with 3^+ are the acid-catalyzed rearrangement product 3,4-dimethylcumene (4), the dehydro dimer octamethylbicumyl (5), and a nonaromatic cage dimer,



3 4 5

identified as 3,10-bis(1-methylethylidene)-6,6,12,12-tetramethylpentacyclo[6.3.1.$0^{2,7}$.$0^{4,11}$.$0^{5,9}$]dodecane (2). High resolution mass spectroscopy established the empirical formula of 2 as $C_{22}H_{32}$, yet it shows 11 carbons by ^{13}C NMR (δ 138.4, 115.4 [C_q, vinyl]; 39.3 [C_q]; 56.2, 55.6, 45.5, 45.3 [CH]; 31.0, 20.8, 20.09, 20.05 [CH_3]), so it must have a symmetry element despite the fact that both symmetry planes of the starting material 1 have been lost. Its ^1H NMR spectrum shows four methyl singlets, δ 1.61, 1.60 (assigned as $Me_2C[sp^2]$) and 1.03, 0.88 ($Me_2C[sp^3]$), and four non-first-order CH multiplets at 3.09 (H_a) and 2.74 (H_b) (assigned as allylic hydrogens) and 2.20 (H_c) and 1.87 (H_d) (assigned as nonallylic hydrogens). Both endocyclic vinyl groups of triene 1 are lost in going to the dimer, but the exocyclic $Me_2C{=}C$ unit appears to be intact. Both



2

the ^{13}C and ^1H NMR spectra are uniquely consistent with the crisscross dimeric structure shown for 2. We assign the upfield methyl group and the upfield allylic and nonallylic CH hydrogens (H_b and H_d, respectively) as those forced to lie in the shielding cone of the $Me_2C{=}C$ groups. The proton coupling constants, as well as the shielding cone argument, are only consistent with this assignment. The vicinal dihedral angles at the HCCH units which are about horizontal in the view shown are forced to be nearly 0°, while those held near vertical are about 30°, and must have a smaller J value. Decoupling experiments show that J_{ac} and J_{bd} are about 9 Hz, while $J_{ad'}$ is about 5.5 Hz, as expected from the Karplus $\cos^2\theta$ relationship. The non-first-order envelopes of H_a and H_d are nearly identical (largest absorption in the middle of the pattern), as are those of H_b and H_c (largest absorption displaced from the middle of the pattern), as is required by the diagonal relationships across the cage of 2. The H_a and H_d multiplets have an extra expressed coupling compared to the H_b and H_c multiplets; the 30° vicinal hydrogen to H_b is $H_{b'}$ and to H_c is $H_{c'}$. In addition, the nearly perfect W plan ^4J couplings J_{ab} and J_{cd} are about 3 Hz, clearly larger than the non-W plan ^4J couplings $J_{ac'}$ and $J_{bd'}$. A 2D-COSY experiment showed that the two ^5J couplings J_{bc} and $J_{bc'}$ are completely absent, which is remarkable in such a cage structure; even couplings between the vinyl and aliphatic methyl groups could be clearly detected in this experiment. We argue that the C_2 symmetry present in the dimer and the pattern of chemical shifts and couplings observed makes our NMR assignment as 2 secure. This material is very difficult to crystallize, and X-ray quality crystals have not been obtained, although 2 slowly formed a waxy solid upon standing.

The relative amounts of 2, 4, and 5 observed are extremely sensitive to the reaction conditions. Considerable

(1) Hopf, H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 948.
(2) 1 was synthesized by the Wittig reaction of 4,4-dimethyl-2,5-cyclohexadienone and isopropylidenetriphenylphosphorane.
(3) (a) Nelsen, S. F.; Kapp, D. L.; Teasley, M. F. *J. Org. Chem.* **1984**, *49*, 579. (b) Nelsen, S. F.; Teasley, M. F. *Ibid.* **1986**, *51*, 3221.

0022-3263/86/1951-4319$01.50/0