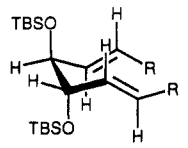
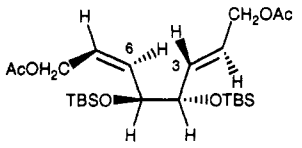
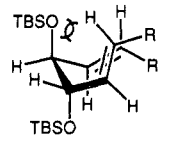
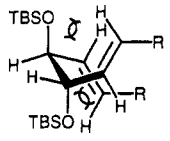
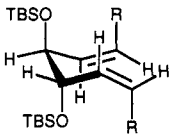
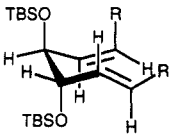

A


3b(C)

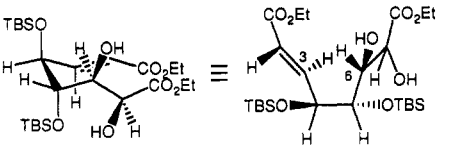

A'


A"


B


C

the initial introduction of the 2,3-dihydroxyl functionality. We tested this point by an NOE experiment. A strong NOE (5%) was again observed for the C-3 proton of **8a** when the C-6 proton was irradiated. Thus conformational assignment of **8a** as **8a**(A) is justified. This is obviously crucial for high discrimination by osmium tetraoxide in the second oxidation leading to **11a**, and this situation has proven also to be the case for both **9** and **10**.


8a(A)

All facts obtained in this work are consistent with the proposal that osmylation of bis-allylic dienes **1**, **2**, or **3** proceeds by way of conformers A, B, or C, respectively. Stereoelectronic π-facial bias imposed by the allylic TBSO group (Kishi's model)[1d] seems to be insufficient to explain the dramatic change in diastereoselection from **4**–**7** to **1a** (Scheme I), although this model does predict the diastereomeric outcome of each reaction. The exceptionally high % de observed for **1**, **2**, and **3** are not satisfactorily accounted for by other proposed models.[1i,n,12]

Acknowledgment. We thank to The SC-NMR Laboratory of Okayama University for the high-field (500-MHz) NMR experiments. We deeply appreciate the financial support by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, and Culture, Japan.

Supplementary Material Available: Representative syntheses, physical data (^{1}H NMR, ^{13}C NMR, IR, $[\alpha]_D$, and elemental analyses), and NMR spectra (20 pages). Ordering information is given on any current masthead page.

(12) (a) Houk, K. N.; Paddon-Row, M. N.; Randan, N. G.; Wu, Y.-D.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Loncharich, R. J. *Science* **1986**, *231*, 1108. (b) Houk, K. N.; Duh, H.-Y.; Wu, Y.-D.; Moses, S. R. *J. Am. Chem. Soc.* **1986**, *108*, 2754.

Preparation of Bicyclo[5.3.0]decan-1-ols from the Tandem Anionic Oxy-Cope Rearrangement/Allylsilane Cyclization of 1,2-Divinylcyclohexanols

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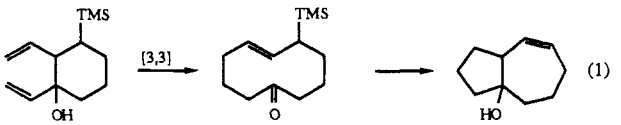
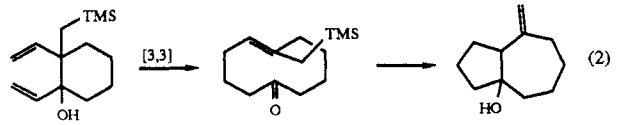
Summary: Intramolecular cyclization of the allylsilanes produced from anionic oxy-Cope rearrangement of 1,2-divinylcyclohexanols led to hydroazulenols with the cis ring fusion.

A number of natural products of biological interest, such as the tumor-promoting phorbol esters[1] and the neurotoxic grayanotoxins,[2] contain as part of their structure, a hydroazulene with a bridgehead hydroxyl group. We envisioned a two-step process for converting appropriately substituted cyclohexanols into hydroazulenols, which is illustrated in eqs 1 and 2. Anionic oxy-Cope rearrangement of divinylcyclohexanols **1a–b** is well precedented[3] and leads to the cyclodecenones **2a–b**. As a consequence of the rearrangement, an allylsilane is generated in **2a–b**, which, if capable of intramolecular cyclization[4] with the ketone,


(1)

1a **2a** **3a**


(2)

1b **2b** **3b**

leads to the bicyclo[5.3.0]decan-1-ols **3a–b**. We report herein our preliminary investigation into this synthetic methodology.[5]

The 1,2-divinylcyclohexanols **1a–b** were prepared as shown in Scheme I. Silyl enol ether **4**[6] was converted into

(1) For a lead reference on phorbol esters and structurally related compounds, see: Wender, P. A.; Lee, H. Y.; Wilhelm, R. S.; Williams, P. D. *J. Am. Chem. Soc.* **1989**, *111*, 8954-7.

(2) Codding, P. W. *J. Am. Chem. Soc.* **1984**, *106*, 7905-9.

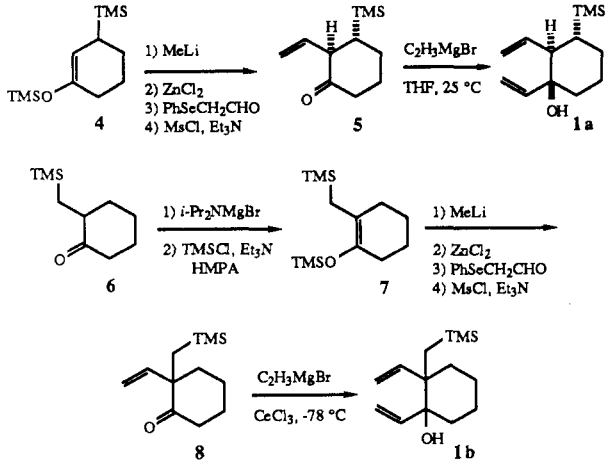
(3) (a) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4186-7. (b) Still, W. C. *J. Am. Chem. Soc.* **1979**, *101*, 2493-5. (c) Clive, D. L. J.; Russell, C. G.; Suri, S. C. *J. Org. Chem.* **1982**, *47*, 1632-41.

(4) For a recent review on intramolecular allylsilane cyclizations, see: Schinzer, D. *Synthesis* **1988**, 263-73.

(5) An alternative approach to hydroazulenes involving anionic oxy-Cope rearrangement of divinylcyclohexanols followed by intramolecular alkylation of the intermediate enolate has recently been described. For examples, see: (a) Sworin, M.; Lin, K.-C. *J. Am. Chem. Soc.* **1989**, *111*, 1815-25. (b) Paquette, L. A.; Reagan, J.; Schreiber, S. L.; Teleha, C. A. *J. Am. Chem. Soc.* **1989**, *111*, 2331-2. (c) Paquette, L. A.; Shi, Y.-J. *J. Org. Chem.* **1989**, *54*, 5205-7.

0022-3263/90/1955-5426$02.50/0

Scheme I

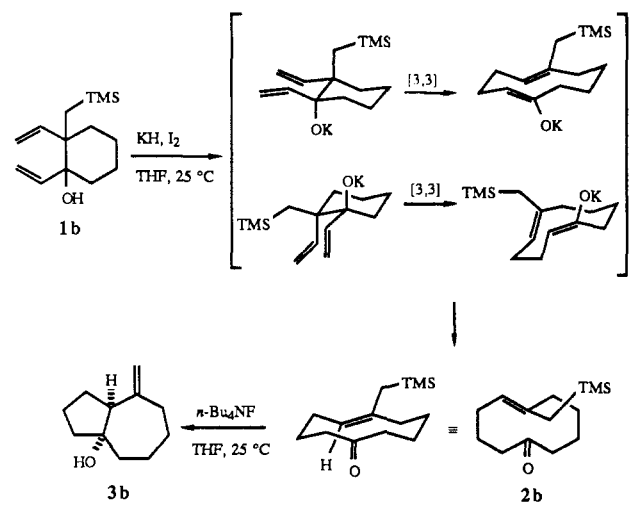


its zinc enolate (1.05 equiv of MeLi, 0 °C → room temperature, 2 h; 1.3 equiv of $ZnCl_2$) and condensed with the vinyl cation equivalent (phenylseleno)acetaldehyde.[3c,7] Elimination of the intermediate aldol product (3 equiv of MsCl, 5 equiv of Et_3N, CH_2Cl_2, 0 °C) gave ketone **5** in 77% overall yield from **4**. The diequatorial relationship between the TMS and vinyl appendages was evident from the ^1H NMR spectrum of cyclohexanone **5**. The coupling constant between the hydrogens on C-2 and C-3 was 11.5 Hz, which is indicative of a diaxial relationship between these two hydrogens. Addition of CH_2=CHMgBr (3 equiv, −40 °C → room temperature, 85%) to the equatorial face of the ketone gave divinylcyclohexanol **1a** as the major diastereomer (≥15:1) as judged from its ^{13}C NMR and ^1H NMR spectra.

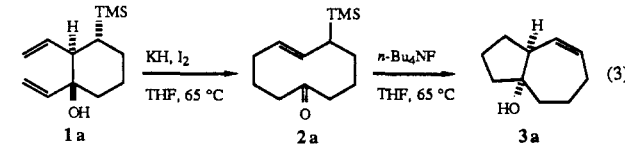
Divinylcyclohexanol **1b** was prepared from cyclohexanone **6**.[8] This ketone was converted into the silyl enol ether **7** by the method of Krafft and Holton[9] (1.3 equiv of *i*-Pr_2NMgBr, ether, room temperature, 12 h; 3 equiv of TMSCl, 1 equiv of Et_3N, 5 equiv of HMPA, room temperature, 1.5 h, 95%). The same sequence used to convert **4** into **5** was used to convert silyl enol ether **7** into cyclohexanone **8** (68% yield). Direct addition of CH_2=CHMgBr to this neopentyl ketone resulted in low yields (≤50%), but addition of $CeCl_3$[10] to the reaction mixture (1.5 equiv of CH_2=CHMgBr, 1.5 equiv of $CeCl_3$, −78 °C, 1 h, 88%) led to smooth addition to give **1b** as a 1.9:1 mixture of diastereomers.

Anionic oxy-Cope rearrangement of this mixture of **1b** (3 equiv of KH, 0.15 equiv of I_2,[11] THF, room temperature, 4 h, 93%) led, as expected,[3c] to a single cyclodecenone **2b** in which the alkene is trans with respect to the ring (Scheme II). Each diastereomeric divinylcyclohexanol **1b** rearranges to a distinct dienolate that differs from the other dienolate only in the geometry of the enolate double bond, but this stereochemical difference is lost upon protonation of the enolate. Exposure of allylsilane **2b** to fluoride (3 equiv of *n*-Bu_4NF, THF, room temperature 12 h, 90%) resulted in the desired cyclization to give exclusively the cis fused hydroazulenol **3b**. The proof of this stereochemical assignment will be discussed later and is presumably the result of cyclization from the lowest energy CC[12] conformation.

Scheme II

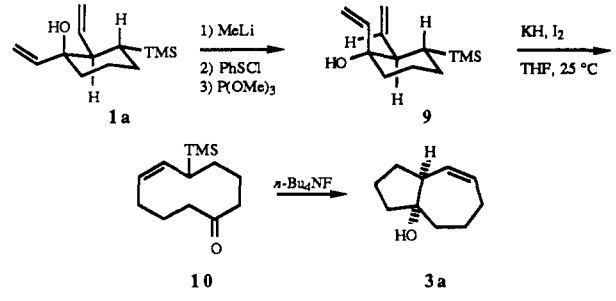


Anionic oxy-Cope rearrangement of divinylcyclohexanol **1a** (5 equiv of KH, 0.4 equiv of I_2,[11] THF, 65 °C, 2.5 h, 81%) also proceeded smoothly to provide cyclodecenone **2a** (eq 3) with the trans double bond (J_{alkene} = 14.6 Hz).



Allylsilane **2a** proved less reactive than **2b**, but it too underwent the desired cyclization upon heating in the presence of fluoride (2 equiv of *n*-Bu_4NF, THF, 65 °C, 5 h, 91%) to give a single hydroazulenol **3a**, which also proved to have the cis ring fusion.

From divinylcyclohexanol **1a** it was also possible to prepare *cis*-cyclodecenone **10** to determine what affect the olefinic geometry might have on the stereochemistry of the fluoride-induced allylsilane condensation (eq 4). Epimerization of the carbinol carbon of **1a** was effected by conversion of **1a** to the allylic sulfoxide from [2,3]-sigmatropic rearrangement of its sulfenate ester[13] (1.6 equiv of MeLi, THF, −40 °C; 2 equiv of PhSCl, −65 °C → room temperature). Treatment of the sulfoxide with a thiophile (4 equiv of $P(OMe)_3$, MeOH, reflux, 6 h, 85%) led to a separable diastereomeric mixture of **9** and **1a** (1.2:1). Anionic oxy-Cope rearrangement of divinylcyclohexanol



(6) Silyl enol ether **4** was prepared using a modification of the method of Still; see the supplementary material for details. Still, W. C. *J. Org. Chem.* **1976**, *41*, 3063–4.

(7) Kowalski, C. J.; Dung, J.-S. *J. Am. Chem. Soc.* **1980**, *102*, 7950–1.

(8) (a) Hudrlik, P. F.; Hudrlik, A. M., Nagendrappa, G.; Yimenu, T.; Zellers, E. T.; Chin, F. *J. Am. Chem. Soc.* **1980**, *102*, 6894–6. (b) Fleming, I.; Goldhill, J. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1493–8.

(9) Krafft, M. E.; Holton, R. A. *Tetrahedron Lett.* **1983**, *24*, 1345–8.

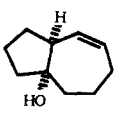
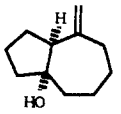
(10) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, Y. *J. Am. Chem. Soc.* **1989**, *111*, 4392–8.

(11) Macdonald, T. L.; Natalie, K. J., Jr.; Prasad, G.; Sawyer, J. S. *J. Org. Chem.* **1986**, *51*, 1124–6. The addition of approximately 10% molar equivalent of I_2 to the KH increased the yield from 10 to 30%.

(12) For an explanation of this nomenclature, see: Sutherland, J. K. *Tetrahedron* **1974**, *30*, 1651–60.

(13) Evans, D. A.; Andrews, G. C. *Acc. Chem. Res.* **1974**, *7*, 147–55.

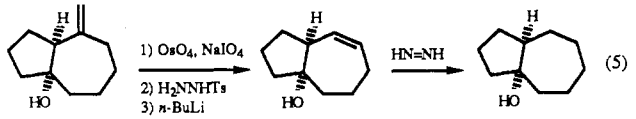
Table I. Chemical Shifts of the Bridgehead Allylic Hydrogens of 3a-b in $CDCl_3$ and Pyridine-d_5

	 3a	 3b
δ (pyridine-d_5)	2.95	2.87
δ ($CDCl_3$)	2.63	2.53
$\Delta\delta$	0.32	0.34

9 (4 equiv of KH, 0.4 equiv of I_2,[11] THF, 65 °C, 1.5 h, 75%) led to *cis*-cyclodecenone **10** (J_{alkene} = 10.7 Hz). Fluoride treatment of **10** (2 equiv of *n*-Bu_4NF, THF, 65 °C, 3.5 h, 95%) led to the same hydroazulenol **3a** previously obtained from the *trans*-cyclodecenone **2b**.

The cis stereochemistry of the ring fusion in bicyclo[5.3.0]decan-1-ols **3a-b** was ascertained both from spectroscopic data and by chemical transformations. In cyclic systems, it is known that the ^1H NMR chemical shifts of a hydrogen that is vicinal and syn to a hydroxyl group is deshielded and shifted downfield in pyridine-d_5 relative to the chemical shift of that same hydrogen in $CDCl_3$.[14] Such a deshielding for the allylic bridgehead hydrogen of **3a-b** would be observed for the cis ring fusion, but not for the trans ring fusion, since the deshielding is a through-space effect from the complexation of the pyridine with the hydroxyl group. A comparison of the ^1H NMR spectra taken in $CDCl_3$ and in pyridine-d_5 for **3a-b** revealed a greater than δ 0.3 shift for the bridgehead allylic hydrogen, which is consistent with a cis, but not a trans ring fusion for **3a-b**.

The cis stereochemistry of the ring fusion was further demonstrated by the conversion of **3b** into **3a**, and the reduction of **3a** into the known, fully saturated hydroazulenol **11** (eq 5). Oxidative cleavage of the alkene (0.01



(5)

3b **3a** **11**

equiv of OsO_4, 2.5 equiv of $NaIO_4$, 3:1 dioxane/H_2O, 0 °C → room temperature, 2 h, 88%) led to the corresponding ketone,[15] which was further subjected to the Shapiro reaction (1.1 equiv of H_2NNHTs, <0.01 equiv of *p*-TsOH, MeOH, room temperature 1 h; excess *n*-BuLi, -75 °C → -15 °C, 20 h, 25%) to give hydroazulenol **3a** that was identical by ^{13}C NMR spectroscopy with **3a** prepared from allylsilane cyclization of **2a**. **3a** itself could be reduced with diimide (3 equiv of $KO_2CN{=}NCO_2K$, 6 equiv of HOAc, 12 equiv of pyridine, MeOH, room temperature, 1 h, 95%) to the hydroazulenol **11**. Both the cis and trans ring fusion isomers of bicyclo[5.3.0]decan-1-ol are known compounds,[16] and the ^{13}C NMR spectrum of **11** was identical with that published for the cis isomer.

In conclusion, we have successfully demonstrated that our two-step methodology efficiently converts 1,2-divinylcyclohexanols into bicyclo[5.3.0]decan-1-ols. This methodology leads to one-carbon ring expansion of the cyclohexane nucleus with concomitant cyclopentane annulation. For the substrates so far examined, the use of fluoride-induced allylsilane cyclization results in formation of only the cis ring fusion in the hydroazulenols. The ease of preparation of the divinylcyclohexanols allows for both the synthesis of additional cyclodecenones and the study of their cyclization to hydroazulenols. Such studies are in progress, and will be reported in due course.

Acknowledgment. We thank the Robert A. Welch Foundation, the National Institutes of Health, and the Donors of the Petroleum Research Fund, administered by the American Chemical Society, for their generous support for this research. Exact mass spectral data were obtained at the Michigan State University Mass Spectroscopy Facility, which is supported, in part, by a grant (DRR-00480) from the Biotechnology Research Branch, Division of Research Resources, National Institutes of Health. We also thank Dr. Whe-Narn Chou for obtaining the NMR spectroscopic data.

Supplementary Material Available: Complete spectroscopic data (IR, ^1H and ^{13}C NMR, and MS) for all compounds, HRMS on key intermediates, and complete experimental details plus NMR spectra (63 pages). Ordering information is given on any current masthead page.

(14) Demarco, P. V.; Farkas, E.; Doddrell, D.; Mylari, B. L.; Wenkert, E. *J. Am. Chem. Soc.* **1968**, *90*, 5480-6.

(15) This β-hydroxy ketone has been previously prepared, but no ^{13}C NMR data has been reported. The coupling constant observed in the ^1H NMR spectrum for the bridgehead hydrogen alpha to the ketone (t, J = 8 Hz) is the same as that reported by Warner, Jacobson, et al. for the isomer with the cis ring fusion. Warner, P. M.; Lu, S.-L.; Myers, E.; DeHaven, P. W.; Jacobson, R. A. *J. Am. Chem. Soc.* **1977**, *99*, 5102-18. See also: House, H. O.; Lee, J. H. C.; VanDerveer, D.; Wissinger, J. E. *J. Org. Chem.* **1983**, *48*, 5285-8.

(16) (a) Crandall, J. K.; Magaha, H. S.; Henderson, M. A.; Widener, R. K.; Tharp, G. A. *J. Org. Chem.* **1982**, *47*, 5372-80. (b) Molander, G. A.; Etter, J. B. *J. Org. Chem.* **1986**, *51*, 1778-86.

1,4-Addition of Optically Active Transferable Ligands from Organocuprates. Generation and Reaction of Homochiral α-Alkoxyorganocuprates

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Summary: Homochiral higher order cyano α-alkoxyorganocuprate addition to ynoates and enones occurs with 0-97% retention of configuration; results that imply multiple reaction pathways may be operative in 1,4-addition reactions of these species.

Organocuprate reagents are now commonplace in synthetic organic chemistry as a method for the regioselective

