by Oneida Research Services, Whitesboro, NY, and are within 0.4% unless otherwise stated. The X-ray crystallographic structure determination on **2** was performed by Oneida Research Services.

5-Aza-2,2,8,8-tetramethylnonane-3,7-dione (1) was prepared by the established literature procedure.[2a]

1-Chloro-3,7-di-*tert*-butyl-5-aza-2,8-dioxa-1-stannabicyclo[3.3.0]octa-2,4,6-triene (2). In a typical reaction **2** is prepared under nitrogen by addition of **1** (14.6 g, 68.4 mmol) in 60 mL of CH_2Cl_2 via a syringe to a solution of 17 g of $SnCl_4$ (68.4 mmol) in 150 mL of CH_2Cl_2. After the addition of **1** is complete, triethylamine (20 g, 0.2 mol) in 40 mL of CH_2Cl_2 is added dropwise. The orange/brown mixture is stirred for about 16 h, and then the solvent is removed in vacuo. The solid residue of extracted with hot benzene. The benzene is removed in vacuo, and the product is recrystallized from CH_3CN: yield 18 g (72%); mp 240 °C; ^1H NMR (CD_2Cl_2) δ 1.27 (s, *t*-Bu, 18 H), 7.79 (s, NCH, 2 H, tin satellites, $^3J_{Sn-H}$ = 20.4 Hz (119-117 not resolved)); $^{13}C\{^1H\}$ NMR (CD_2Cl_2) δ 27.5 (s, CH_3), 40.9 (s, CCH_3), 120.1 (s, CN, tin satellites, $^2J_{Sn-C}$ = 17.5 Hz (119-117 not resolved)), 202.2 (s, CO); $^{119}Sn\{^1H\}$ NMR (CD_2Cl_2) δ -378.1; $^{15}N\{^1H\}$ NMR (CD_2Cl_2) δ -63.2 (s, tin satellites, $^1J_{Sn-N}$ 560 Hz (119-117 not resolved)); solid state ^{13}C NMR δ 29, 41, 120, 201; MS EI (70 ev), *m/z* 365.02. Anal. ($C_{12}H_{20}ClNO_2Sn$): C, H, N.

1,1,1-Trichloro-3,7-di-*tert*-butyl-5-aza-2,8-dioxa-1-stannabicyclo-[3.3.0]octa-2,4,6-triene (4). In a typical reaction **4** is prepared under nitrogen by addition of a solution of 0.45 g (3.4 mmol) of SO_2Cl_2 to the suspension of 1.0 g (2.8 mmol) of **2** in toluene at 0 °C. The color of the solution changes from reddish/brown to yellow, and slowly all of **2** dissolves. The product begins to precipitate shortly after the addition of the SO_2Cl_2 is started. The product is collected by filtration, and the mother liquor is cooled to give a second crop. The crude product is recrystallized from toluene to yield 980 mg (73%) of pure **4** as a toluene solvate. A sample gave the following data: mp 251.5-252 °C (dec); ^1H NMR (CD_2Cl_2) δ 1.37 (s, *t*-Bu, 18 H), 7.66 (s, NCH, 2 H, tin satellites, $^3J_{Sn-H}$ 129.0/135.0 Hz ($^{117}Sn/^{119}Sn$); $^{13}C\{^1H\}$ NMR δ (CD_2Cl_2) 27.0 (s, CH_3), 41.8 (s, CCH_3), 114.6 (s, CN, tin satellites, $^1J_{Sn-C}$ = 90 Hz (119-117 not resolved)), 202.8 (s, CO); $^{119}Sn\{^1H\}$ NMR (CD_2Cl_2) δ -511.0; $^{15}N\{^1H\}$ NMR (CD_2Cl_2) δ -79.6. Anal. Calcd for ($C_{12}H_{20}NO_2Cl_3Sn\cdot{}^1/_2(C_6H_5CH_3)$): C, 38.12; H, 4.92; N, 2.84. Found: C, 38.67; H, 5.03; N, 2.91.

Acknowledgement is made to H. A. Craig for his excellent technical assistance.

Registry No. 1, 88686-46-8; **4**, 112070-04-9.

Supplementary Material Available: A complete description of the X-ray crystallographic structure determination of **2**, including experimental procedures, tables of data, and an ORTEP drawing (11 pages). Ordering information is given on any current masthead page.

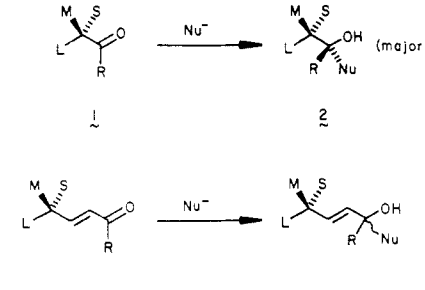
Molecular Recognition during 1,2-Addition of Chiral Vinyl Organometallics to Chiral β,γ-Unsaturated Ketones. Case Studies of Three 7,7-Disubstituted 2-Norbornenones[1]

Leo A. Paquette,* Keith S. Learn, Jeffrey L. Romine, and Ho-Shen Lin

Contribution from Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210. *Received July 27, 1987*

Abstract: The level of double diastereoselection attainable upon 1,2-addition of several chiral vinylorganocerium reagents to 7,7-disubstituted 5-norbornen-2-ones has been assessed. The effect of functional group variation at C-7 and bulk solvent influences have also been studied. The extent of diastereoselection has been found to vary with the degree and stereochemistry of pendant alkyl substitution or annulation of the cyclopentenyl nucleophiles at positions 4 and 5. When the purified alcohols so produced are subjected to anionic oxy-Cope rearrangement, polycyclic compounds are produced that carry a multitude of stereogenic centers installed in a predictable way. The methodology therefore constitutes a short and enormously powerful synthetic tool. Mechanistic considerations of these reactions are discussed in light of existing theory and available experimental facts.

Because of the central role played by carbon-carbon bond-forming reactions in organic synthesis, considerable attention has been focused over the years on the stereochemical course of nucleophilic addition to a carbonyl group. The particular diastereoselectivity encountered in those examples where the carbonyl functionality is specifically positioned adjacent to a chiral center has been rationalized in the context of Cram's rule.[2,3] That the pathway followed usually takes place in the sense **1** → **2** has attracted many others, most notably Cornforth,[4] Karabatsos,[5] Felkin,[6] Anh,[7] Houk,[8] and Fraser,[9] to offer comment on whether the reaction course is indeed governed by steric factors or whether electronic control is responsible.



1 **2**

3 **4**

Immense effort has also been expended on assessing the stereoselectivity of alkylation reactions involving chiral metal enolates,[10] the diastereoselectivity of aldol reactions involving enolates and aldehydes or ketones with prochiral faces in both components,[11] and the level of stereocontrol attainable with flanking

(1) Part 5. Part 4: Paquette, L. A.; Learn, K. S.; Romine, J. L. *Tetrahedron*, in press. Part 3: Paquette, L. A.; Learn, K. S.; Romine, J. L. *Synth. Commun.*, in press.
(2) Cram, D. J.; Abd Elhafez, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828.
(3) Eliel, E. L. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1983; Vol. 2, p 125.
(4) Cornforth, J. W.; Cornforth, R. H.; Mathew, K. K. *J. Chem. Soc.* **1959**, 112.
(5) Karabatsos, G. J. *J. Am. Chem. Soc.* **1967**, *89*, 1367.
(6) (a) Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199. (b) Cherest, M.; Felkin, H. *Ibid.* **1968**, 2205.
(7) Anh, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61.
(8) (a) Paddon-Row, M. N.; Rondan, N. G.; Houk, N. K. *J. Am. Chem. Soc.* **1982**, *104*, 7162. (b) Houk, K. N.; Paddon-Row, M. N.; Rondan, N. G.; Wu, Y.-D.; Brown, F. K.; Spellmeyer, D. C.; Metz, J. T.; Li, Y.; Loncharich, R. J. *Science (Washington, D.C.)* **1986**, *231*, 1108. (c) Wu, Y.-D.; Houk, K. N. *J. Am. Chem. Soc.* **1987**, *109*, 908.
(9) Fraser, R. R.; Stanciulescu, M. *J. Am. Chem. Soc.* **1987**, *109*, 1580.
(10) Evans, D. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1984; Vol. 3, p 1.
(11) (a) Heathcock, C. H. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1984; Vol. 3, p 111. (b) Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.

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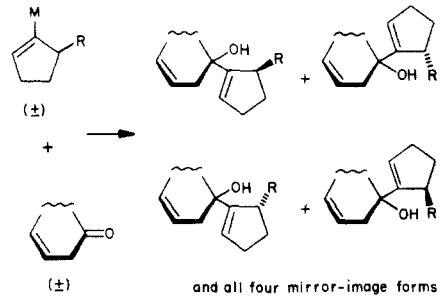
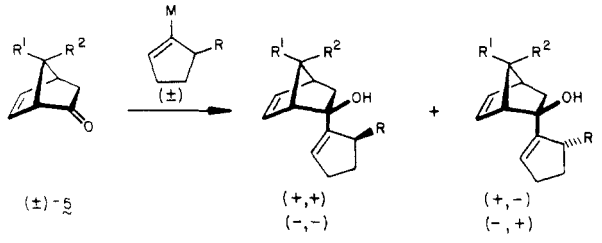
Scheme I



Scheme II



oxazoline[12] and hydrazone functionalities[13] as chiral auxiliaries. Studies involving asymmetric synthesis via addition of chiral nucleophiles to carbonyl centers have also been immensely fruitful.[14]

Much less well understood is the extent to which stereochemistry can be controlled, both in a relative and absolute sense, when the carbonyl group is only remotely perturbed. For example, in their search for a vinylogous version of Cram-like stereocontrol, Fleming and co-workers found that nucleophilic attack on ketones and aldehydes conjugated to a chiral center as in **3** proceeds with a low or negligible diastereoselectivity.[15,16]

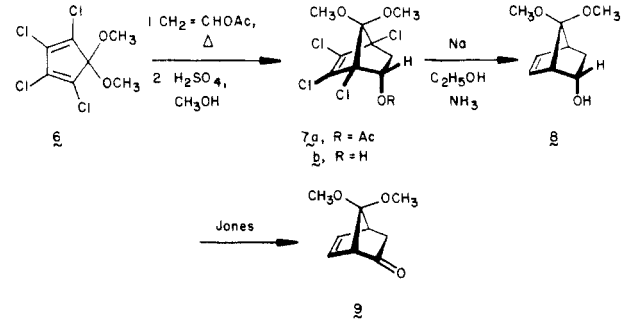
The reactions of chiral vinylmetal reagents with chiral β,γ-unsaturated ketones are of considerable interest in the context of stereocontrolled applications of the oxy-Cope rearrangement for natural products synthesis.[17] However, this 1,2-addition necessarily generates yet another stereogenic center and consequently gives rise at a minimum to *eight* diastereomeric products (Scheme I). Therefore, unless π-face stereoselectivity in this process is brought under strict control, resolution of *both* reactive components (double asymmetric synthesis)[11] would still not give rise to a single optically active product. Thus, it was not surprising to find that no example of this important transformation had been documented where both reaction partners are chiral.

In spite of this seemingly discouraging prognosis, there remained the intriguing possibility that molecular recognition during this condensation reaction might actually be high if properly dealt with. Two criteria appeared to be particularly desirable to implement at the outset: (1) that nucleophilic capture of the carbonyl be relegated exclusively to one prochiral surface by suitable steric control and (2) that the β,γ-unsaturation site be conformationally fixed in order that formulation of a transition-state model might be reasonably accomplished following analysis of the initial observations.

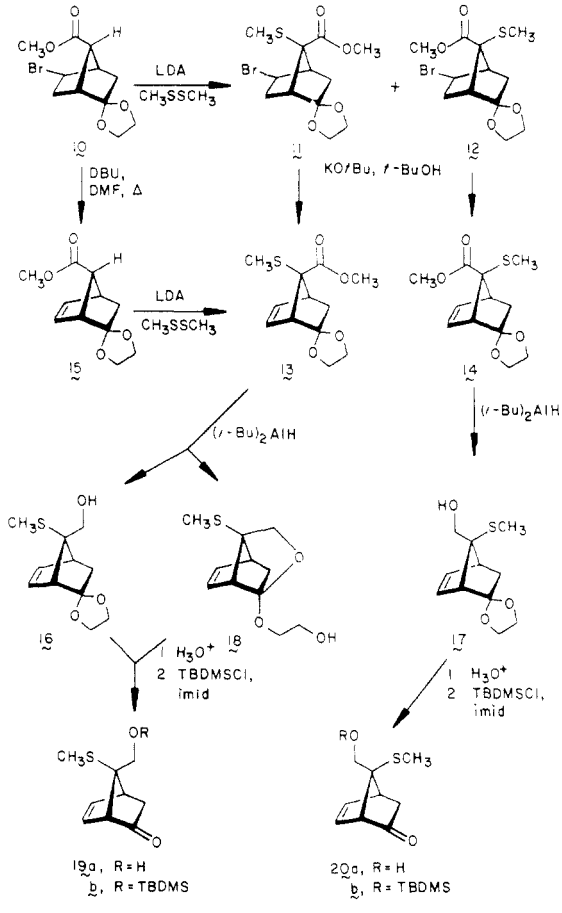
As a consequence, we have chosen to probe the levels of diastereoselectivity attainable upon condensation of various 1-cyclopentenylmetal reagents with 7,7-disubstituted 2-norbornenones (Scheme II). By precluding attack from the exo direction, only *four* diastereomeric alcohols can result. Consequently, the capacity for evaluating selective recognition patterns between the two racemic components can now be dealt with in reasonable fashion. Furthermore, if appreciable levels of diastereoselectivity are noted, then use of either reagent in homochiral form would result in kinetic resolution.

Herein, we examine the factors influencing diastereoselective addition to three racemic ketones of general formula **5** and establish that mutual kinetic resolution can indeed be impressively high. The major sense of alignment in each of these examples has been established by a combination of X-ray crystallography and high-field ^{1}H NMR analysis. Finally, the efficacy of chirality transfer during the subsequent oxy-Cope rearrangement of many of the resulting alcohols will be documented.[18]

Scheme III



Scheme IV



Results

Synthesis of the 7,7-Disubstituted Norbornenones. The dimethoxy derivative **9** was best prepared by the route originally reported by Jung (Scheme III).[19] Thus, Diels–Alder condensation

(12) Lutomski, K. A.; Meyers, A. I. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1984; Vol. 3, p 213.
(13) Enders, D. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1984; Vol. 3, p 275.
(14) Soladié, G. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1983; Vol. 2, p 157.
(15) Fleming, I.; Kuhne, H.; Takaki, K. *J. Chem. Soc., Perkin Trans. 1* **1986**, 725.
(16) Consult also: Lutz, R. E.; Gillespie, J. S. *J. Am. Chem. Soc.* **1950**, *72*, 200, 344.
(17) Paquette, L. A. *Pure Appl. Chem.*, in press.
(18) For a preliminary communication, see: Paquette, L. A.; Learn, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 7873.
(19) Jung, M. E.; Hudspeth, J. P. *J. Am. Chem. Soc.* **1977**, *99*, 5508. We thank Professor Jung for providing us with experimental details of his earlier effort.

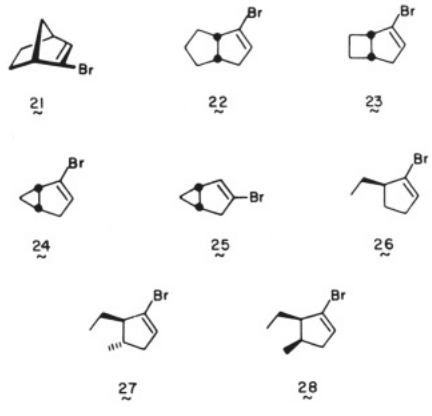
of dimethoxytetrachlorocyclopentadiene **6** with vinyl acetate at the reflux temperature furnished **7a**, which was subsequently hydrolyzed to **7b**. Following reductive dechlorination of this intermediate to give **8**, oxidation was effected and **9** emerged.

Access to reagents **19** and **20** was gained starting from the previously described *exo*-2-bromo-5,5-(ethylenedioxy)bicyclo-[2.2.1]heptane-*syn*-7-carboxylic acid methyl ester (**10**).[20] Sulfenylation[21] of the ester enolate anion of **10** with methyl disulfide resulted in conversion to a 4:1 mixture of α-methylthio esters **11** and **12** (Scheme IV).[22] Direct dehydrobromination of **11/12** employing potassium *tert*-butoxide in *tert*-butyl alcohol provided **13** and **14** as a difficultly separable pair of esters. The feasibility of arriving expediently at pure **13** by effecting introduction of the double bond first[23] was demonstrated concurrently. Once the bromine substituent is eliminated, as in **15**, sulfenylation proceeds stereospecifically to introduce the functional group anti to the ketal moiety exclusively. However, the yield of **15** is only modest, and attempts to employ potassium *tert*-butoxide caused transesterification.

For these reasons, it proved more advantageous for preparative purposes to proceed via **11/12** and **13/14**. This is because diols **19a** and **20b**, obtained by sequential Dibal reduction and deketalization of the norbornenyl ester mixture, could be chromatographically separated on a large scale without difficulty. Although the necessary stereochemical distinction between these epimers was achieved by independent conversion of isomerically pure **13** to **19a**, the lability of **16** to acid provided additional confirmation of our assignments. Transketalization within **16** to give **18** occurs simply on standing in $CDCl_3$ solution. This isomerization can, of course, also materialize during processing of the Dibal reaction mixture (**17** is inert in both sets of conditions). However, since both **16** and **18** undergo hydrolysis to give **19a**, separation of the epimeric alcohols was routinely deferred to this stage.

Independent conversion of **19a** and **20a** to their respective *tert*-butyldimethylsilyl ethers was achieved in conventional fashion.[24]

Preparation of the Vinyl Bromides. For reasons of consistency, attention was paid herein only to cyclopentenyl-derived organometallic species. Two routes to 2-bromonorbornene (**21**) were explored. Shapiro degradation[25,26] of 2-norbornanone[27] tosylhydrazone in tetramethylethylenediamine (TMEDA) solution[26] at −78 → 0 °C followed by addition of cyanogen bromide did give rise to **21**, albeit only in 11% yield. Greater success was realized when norbornylene was irradiated in the presence of dibromotetrachloroethane,[28] and the resulting dibromide mixture was heated with potassium *tert*-butoxide in *tert*-butyl alcohol. This methodology, which affords **21** in 29% overall yield and lends itself more easily to scale-up, is at present considered the method of choice.



Bromides **22–26** were prepared in isomerically pure condition by generation of the corresponding vinyl anions via the Shapiro protocol. The starting ketones *cis*-bicyclo[3.3.0]octan-2-one,[29] *cis*-bicyclo[3.2.0]heptan-2-one,[30] *cis*-bicyclo[3.1.0]hexan-2-one[31] *cis*-bicyclo[3.1.0]hexan-3-one,[32] and 2-ethylcyclopentanone[33] were

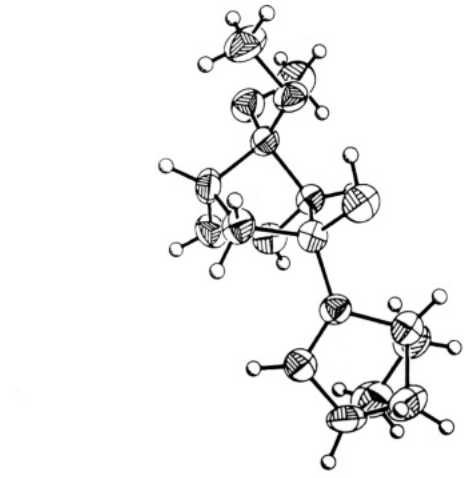
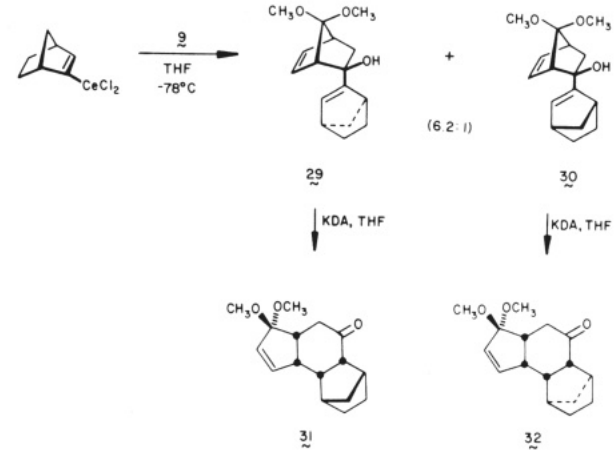


Figure 1. Computer-generated perspective view of the final X-ray model of **29** (courtesy of N. D. Jones, J. K. Swartzendruber, and J. B. Deeter, Eli Lilly Co.)

Scheme V



(20) Grieco, P. A.; Pogonowski, C. S.; Burke, S. D.; Nishizawa, M.; Miyashita, M.; Masaki, Y.; Wang, C.-L. J.; Majetich, G. *J. Am. Chem. Soc.* **1977**, *99*, 4111.

(21) Trost, B. M.; Tamaru, Y. *J. Am. Chem. Soc.* **1977**, *99*, 3101.

(22) Paquette, L. A.; Romine, J.; Barth, W.; Hsu, L.-Y. *Tetrahedron Lett.* **1985**, 576.

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(25) Shapiro, R. H. *Org. React.* (*N.Y.*) **1975**, *23*, 405.

(26) (a) Taylor, R. T.; Degenhardt, C. R.; Melega, W. P.; Paquette, L. A. *Tetrahedron Lett.* **1977**, 159. (b) Chan, T. H.; Baldassarre, A.; Massuda, D. *Synthesis* **1976**, 801. (c) Chamberlin, A. R.; Stemke, J. E.; Bond, F. T. *J. Org. Chem.* **1978**, *43*, 147. (d) Paquette, L. A.; Fristad, W. E.; Dime, D. S.; Bailey, T. R. *Ibid.* **1980**, *45*, 3017. (e) The original vinyl anions were not utilized directly because the presence of TMEDA and other reaction byproducts did not allow for clean and efficient conversion to the dichlorocerium reagent.

(27) The (1*R*) and (1*S*) forms of this ketone are also readily available: (a) Irwin, A. J.; Jones, J. B. *J. Am. Chem. Soc.* **1976**, *98*, 8476. (b) Seiichi, T.; Iwata, H.; Ogasawara, K. *Heterocycles* **1978**, *9*, 845. (c) Lightner, D. A.; Flores, M. J.; Crist, B. V.; Gawronski, J. K. *J. Org. Chem.* **1980**, *45*, 3518. (d) Nakazaki, M.; Chikamatsu, H.; Naemura, K.; Asao, M. *Ibid.* **1980**, *45*, 4432.

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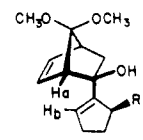
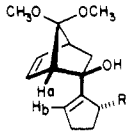
(31) Dauben, W. G.; Berezin, G. H. *J. Am. Chem. Soc.* **1963**, *85*, 468. A ready synthesis of the (+)-(1*R*,5*R*) enantiomer has been described: Lightner, D. A.; Jackman, D. E. *Tetrahedron Lett.* **1975**, 3051.

(32) (a) Bevan, J. W.; Legon, A. C.; Ljunggren, S. O.; Mjoberg, P. J. *J. Am. Chem. Soc.* **1978**, *100*, 8161. (b) Winstein, S.; Friedrich, E. C.; Baker, R.; Lin, Y. I. *Tetrahedron* **1966**, Suppl. 8, Part II, 621.

Table I. Diastereoselectivity Ratios for the Addition of Vinylcerium Reagents to **9** and Key ^{1}H NMR Chemical Shift Data (300 MHz, C_6D_6 Solution)





			MAJOR		MINOR	
vinyl bromide	isol yield,[a]	diaster ratio[b]	H_a	H_b	H_a	H_b
21	73	6.2:1 (86%)	3.52	5.51	3.10	5.57
22	92	16:1 (94%)	3.63	5.13	3.20	5.36
23	76	10.4:1 (91%)	3.80	5.37	3.38	5.38
24	86	2.1:1 (68%)	2.97	4.91	2.84	5.15
25		2.3:1 (70%)	3.23	5.49	2.95	5.62
26	90	10.4:1 (91%)	3.14	5.25	2.83	5.39
27	99	4.2:1 (81%)	2.88	5.20	2.85	5.30
28	83	12:1 (92%)	2.97	5.31	2.80	5.39

[a] Based on recovered **9**. [b] Values gleaned from two or more experiments.

acquired by literature methods or minor modifications thereof. In situ condensation of the derived anionic intermediates with cyanogen bromide furnished the targeted bromides in yields ranging from 7% for the sensitive **24** to 42% for **23**. Although the efficiencies of these reactions are at best modest, the syntheses are direct and convenient.[34]

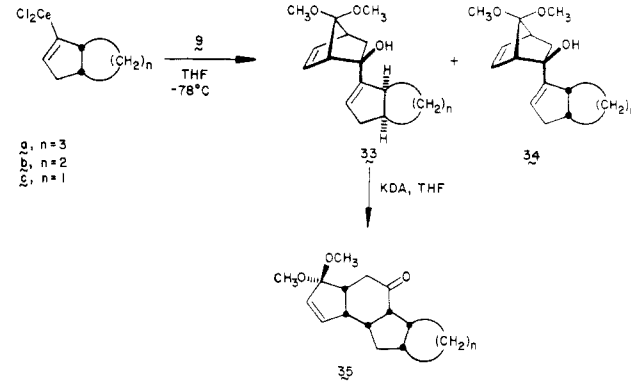
Substrates **27** and **28** were elaborated according to a predescribed route[35] that was modified as described in the Experimental Section to achieve brevity.

Condensation Reactions Involving Dimethoxy Derivative 9. When initial efforts to couple **9** with various vinyllithium reagents proved unpromising because of excessive enolization, recourse was made instead to dichlorocerium reagents because of their reputed capability to shun enolization even with substrates particularly renowned for this property.[36] Consequently, the standardized procedure came to involve halogen–metal exchange with *tert*-butyllithium in tetrahydrofuran at −78 °C, transfer of the vinyllithium reagent via cannula to a cold (−78 °C) slurry of anhydrous cerium trichloride in the same solvent, and ultimately dropwise addition of **9** to this rapidly stirred mixture.

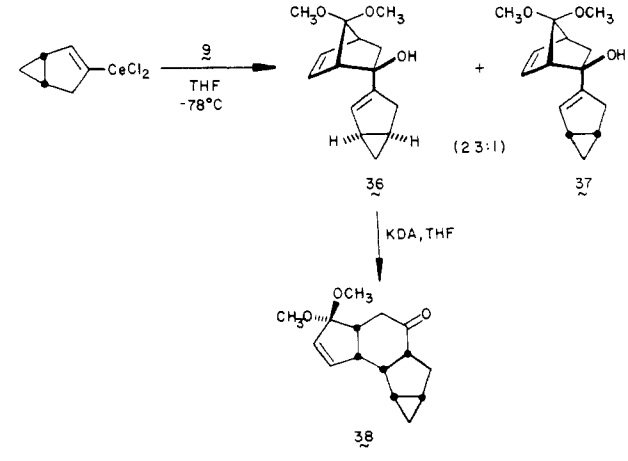
2-Bromonorbornene (**21**) responds well to the predescribed metalation and adds to **9** to give in good yield a 6.2:1 mixture (HPLC analysis) of **29** and **30** (Scheme V). These diastereomeric alcohols were chromatographically separated, and the major constituent was unequivocally identified as **29** by X-ray crystallographic analysis (Figure 1). In benzene-d_6 solution, two proton resonances in each isomer happen to be particularly diagnostic of the structural differences. Subsequent to unfold was recognition that the chemical shifts of the proximal bridgehead (H_a) and cyclopentenyl olefinic (H_b) protons exhibit an ordering pattern that correlates strictly with the relative configuration of the cyclopentenyl R substituent (Table I). This systemization presumably materializes because common conformational features are consistently adopted by all members within each series.

Independent anionic oxy-Cope rearrangement[37] of **29** and **30** gave rise to **31** and **32**, respectively. From this simple series of experiments is seen to emerge methodology capable of controlled simultaneous introduction of multiple stereogenic centers (in these examples, a total of six), some of which (e.g., the methano bridge of the norbornyl unit) reside at sites remote from chemically modifiable functionality.

Scheme VI



Scheme VII



While the level of diastereoselectivity encountered with **21** is modest (86%), the ease of separation of **29** and **30** infuses considerable synthetic utility into the scheme. Moreover, substantively improved discrimination is possible as witnessed by the conversion of **22** to coupled products **33a** and **34a** in a 16:1 ratio (Scheme VI). As before, these alcohols were easily separated, identified by appropriate spectral comparison with **29** and **30** (Table I), and, in the case of the major diastereomer, caused to undergo [3.3] sigmatropic rearrangement to give **35a**.

Particularly informative at the mechanistic level was the behavior of the triad of organocerium reagents derived from bromides **22–24**. Although the diastereoselectivity observed for the bicyclo[3.2.0]heptenyl example was still very respectable (**33b**:**34b** = 10.4:1), the extent was nevertheless diminished relative to the

(33) This ketone was prepared by heating 1-pyrrolidinocyclopentene with ethyl iodide. Its acquisition in optically active condition has been reported: Kergomard, A.; Renard, M. F.; Veschambre, H. *Tetrahedron Lett.* **1978**, 5197.

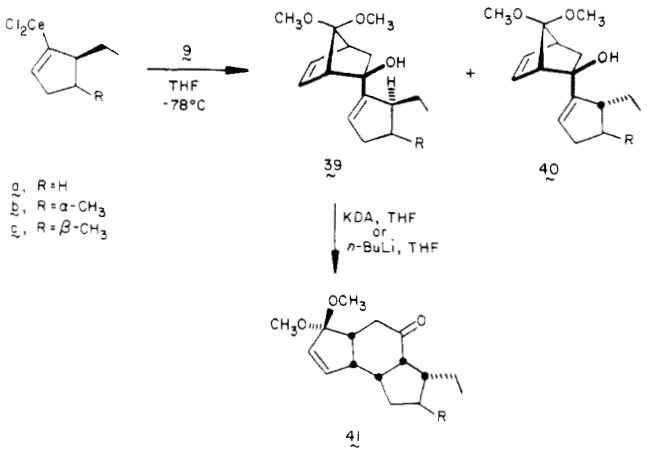
(34) For an alternative route to vinyllithium reagents, consult: Wulff, W. D.; Peterson, G. A.; Bauta, W. E.; Chan, K.-S.; Faron, K. L.; Gilbertson, S. R.; Kaesler, R. W.; Yang, D. C.; Murray, C. K. *J. Org. Chem.* **1986**, *51*, 277.

(35) Barth, W.; Paquette, L. A. *J. Org. Chem.* **1985**, *50*, 2438.

(36) (a) Imamoto, T.; Sugiura, Y.; Takiyama, N. *Tetrahedron Lett.* **1984**, 4233. (b) Imamoto, T.; Sugiura, Y. *J. Organometal. Chem.* **1985**, *285*, C21. (c) Imamoto, T.; Takiyama, N.; Nakamura, K. *Tetrahedron Lett.* **1985**, 4763.

(37) (a) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* **1975**, *97*, 4765. (b) Evans, D. A.; Baillargeon, D. J.; Nelson, J. V. *Ibid.* **1978**, *100*, 2242.

Scheme VIII



Scheme IX

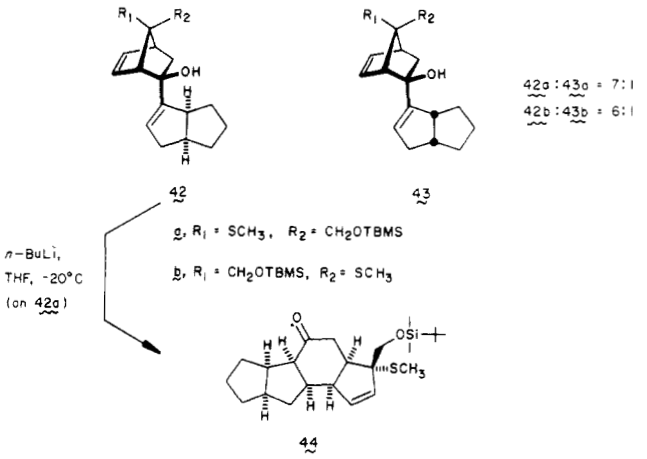


Table II. Solvent Effect Study Involving **9** and the Dichlorocerium Reagent of **22** (−78 °C)

solvent	yield,[a] %	**33a**:**34a**[b]	solvent	yield,[a] %	**33a**:**34a**[b]
THF	92	16.0:1	$PhCH_3$	96	11.8:1
Et_2O	100	13.9:1	THF–HMPA	92	6.8:1
DME[c]	68	11.6:1	(2 equiv)		

[a] Based on recovered **9**. [b] Values gleaned from duplicate experiments. [c] $CeCl_3$ not very soluble in this solvent.

bicyclo[3.3.0]octenyl homologue. Furthermore, a strikingly precipitous falloff in intermolecular discrimination was seen when the adjoining ring became cyclopropanoid as in **24** (**33c**:**34c** = 2.1:1). Thus, in the latter instance the energy gap between the pair of diastereomeric transition states has become significantly reduced. The important interdependence between nonbonded steric interaction and product distribution will be discussed in the sequel. Interestingly, the variant of positioning the three-membered ring as in **25** induces no further alteration of the product distribution. Alcohols **36** and **37** are formed in a 2.3:1 ratio (Scheme VII).

The effect of nucleophile structure on product distribution was also examined with less rigid substituents on the cyclopentenyl ring. An important reference point was the α-ethyl derivative **26**, whose cerium derivative added to **9** with very good discrimination (10.4:1) in favor of **39a** (Scheme VIII). Clearly, a 5-ethyl group is capable by itself of inducing rather disparate rates of 1,2-addition among the enantiomeric reaction partners. It was useful to learn that placement of a methyl group at C-4 in a trans relationship to the ethyl substituent more than halves the diastereoselectivity (**39b**:**40b** = 4.2:1). Importantly, a cis ethyl/methyl relationship as in **28** restores the strong preference (12:1) for formation of diastereomer **39**. Although **39c** could not be obtained in a form suitable for study by X-ray methods, crystallographic analysis of a transformation product confirmed the stereochemical assignment.[38] This additional proof of structure reflects very favorably as well on our ^1H NMR correlation (Table I).

The effect of solvent variation on diastereoselectivity was studied in some considerable detail with **22** as substrate (see Table II). The data show that this particular cerium reagent enters into more selective capture of **9** in ether solvents, with the order of efficacy being tetrahydrofuran > ether > 1,2-dimethoxyethane (DME). Diminished diastereoselectivity is realized in toluene solution, although the product distribution was no worse than in DME. A substantive increase in solvent polarity such as that involved in addition of HMPA to the tetrahydrofuran medium resulted in a diminished capacity for intermolecular recognition. This may well reflect changes brought on because of enhanced coordination of the lanthanide to the solvent environment (see below).

Another variable that can potentially influence product distribution is the metal counterion. To examine this point, the lithium derivative of **22** was added to **9**. Alcohols **33a** and **34a**, now isolated in only 39% yield because of competing enolization of the carbonyl reagent, were formed as a 12:1 mixture. The difference relative to cerium is consequently not great in this instance. Several attempts to add the corresponding vinylpotassium,[39] Grignard,[40] and manganous chloride[41] derivatives of **22** afforded only trace amounts of addition product(s) and were consequently not amenable to analysis.

Comparative Diastereoselectivity Studies Involving 19b and 20b. In view of the preceding developments, the remainder of this study was carried out in tetrahyrofuran solution at −78 °C. Supplantation of the 7,7-dimethoxy substituents in **9** by other functionality was considered advisable for at least three important reasons: (a) translocation to greater distances from the reaction center of those sites (e.g., the divalent sulfur atom) having some latent potential for complexation to the lanthanide, (b) the recognized inability of the ether oxygen in β-(*tert*-butyldimethylsilyl)oxy aldehydes to coordinate to Lewis acids,[42] and (c) positioning of somewhat larger groups at C-7 to induce small, though likely significant, perturbation of norbornenone structural geometry. At issue, of course, was the manner in which these factors might impact diastereoselectivity. An analysis of the response of the epimeric ketones **19a** and **20b** was therefore undertaken, with particular attention given to the dichlorocerium reagents derived from bromides **22**, **27**, and **28**. These reagents exhibited substantial discrimination toward **9**.

In line with expectation, the new series of 1,2-additions continued to operate with respectable diastereoselection; however, the trend in the relative capacities of the cerium reagents did not parallel that encountered earlier with **9**. The data contained in Scheme IX are exemplary. The results of the studies involving **22** and both methylthio-substituted norbornenones reveal that alcohols of type **42** continue to be favored over the isomeric counterparts **43**; however, the kinetic fractionation has now dropped to 6:1 and 7:1 from its loftier status (16:1). The assignment of relative stereochemistry to these readily separated reaction products was based on analogy with the previous examples and comparison with ^1H NMR spectra.

The conversion of **42a** to **44** upon exposure to *n*-butyllithium in tetrahydrofuran at −20 °C further illustrates the potential for obtaining polycyclic materials having well-defined clusters of stereogenic centers as often required in natural products total synthesis applications.

When trans-substituted vinyl bromide **27** became the reaction partner, a significant improvement in the diastereoselectivity ratio was noted upon chromatographic analysis (and separation) of

(38) Paquette, L. A.; Romine, J.; Lin, H.-S. *Tetrahedron Lett.* **1987**, 31.

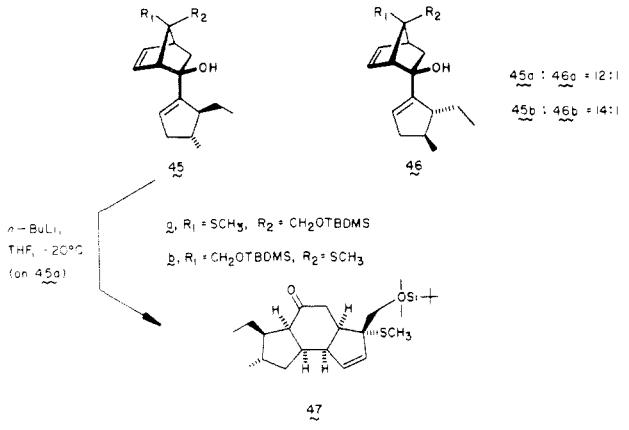
(39) The method of transmetalation with potassium *tert*-butoxide was employed.

(40) Jones, P. R.; Goller, E. J.; Kauffman, W. J. *J. Org. Chem.* **1969**, *34*, 3566.

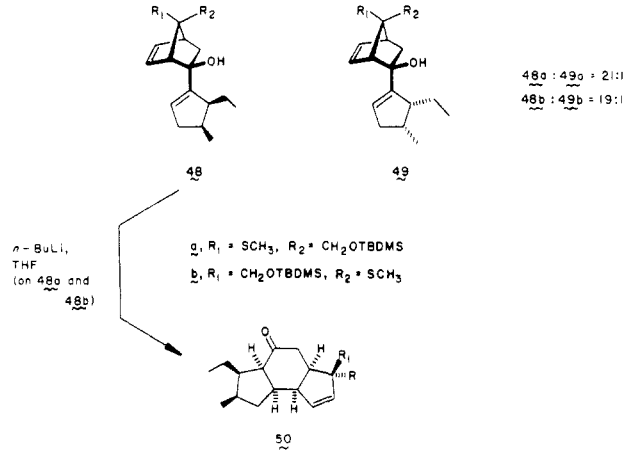
(41) Friour, G.; Alexakis, A.; Cahiez, G.; Normant, J. *Tetrahedron* **1984**, *40*, 683 and pertinent references cited therein.

(42) Keck, G. E.; Castellino, S. *Tetrahedron Lett.* **1987**, 281.

Scheme X



Scheme XI



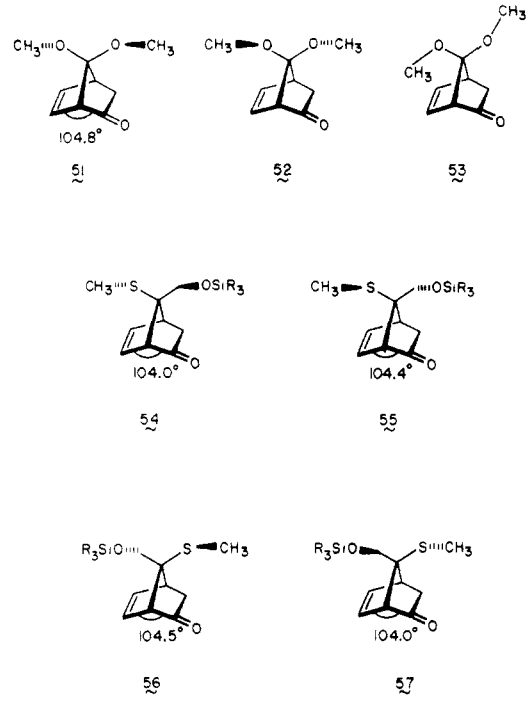
alcohols **45** and **46** (Scheme X). Although the level of intermolecular recognition was presently somewhat larger for **20b** (14:1) than for **19b** (12:1; contrast Scheme IX), this small difference can be accounted for by experimental error. However, it should be recalled that the condensation of **27** with **9** gave results that were considerably less dramatic (4:1).

Once again, one of the major diastereomeric alcohols (**45a**) was subjected to anionic oxy-Cope rearrangement. As before, the lithium alkoxide was observed to isomerize quite readily at −20 °C. This example delivered ketone **47**.

The most striking demonstration of the double diastereoselection phenomenon was exhibited by the cerium reagent derived from *cis*-cyclopentenyl bromide **28**. Condensation with **19b** and **20b** resulted, respectively, in 21:1 and 19:1 distributions of **48** and **49** (Scheme XI). The availability of **48a** and **48b** in quantity prompted us to examine the relative ease of their [3.3] sigmatropic isomerization to **50a,b**. The features of the oxy-Cope rearrangement that ensued upon exposure of **48a** to *n*-butyllithium in tetrahydrofuran at −20 °C were virtually the same as those previously studied, e.g., **42a** → **44** and **45a** → **47**. Most significantly, product formation was complete within 4 h. For **48b**, on the other hand, a temperature of 0 °C was necessary to realize a comparable reaction half-life. Although this rate difference is not overwhelmingly striking, it does illustrate the principle that small structural differences in this series can make a sensitive impact on intrinsic chemical reactivity.

Transition-State Model. A second purpose of this work was to gain insight into the characteristics of vinyl organometallic additions to 5-norbornen-2-ones. Optimistically, the level of detail in the resultant mechanistic model should provide reliable predictability for examples yet to be tested. As a basis for discussion, we excerpt first the structural features of the cyclopentenylcerium reagents examined and contrast their response toward **9**, **19b**, and **20b** relative to other, more conformationally mobile β,γ-unsaturated ketones.[1,43]

The data show than an alkyl fragment located at C-5 in the nucleophile exerts considerable impact on diastereoselectivity. This phenomenon, which is manifested because of proximity to the attacking center, is not completely overriding however. Steric contributions of comparable magnitude are brought into play by similar substitution at C-4. The emergence of the latter transition-state interactions seems to be dependent upon two reinforcing effects. The first is the demand by simple pendant alkyl groups to be projected quasi-equatorially from the unsaturated five-membered ring. When positions 4 and 5 are annulated, the overall size of the fused ring holds a direct link to the diastereoselectivity ratio of the condensation.

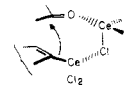


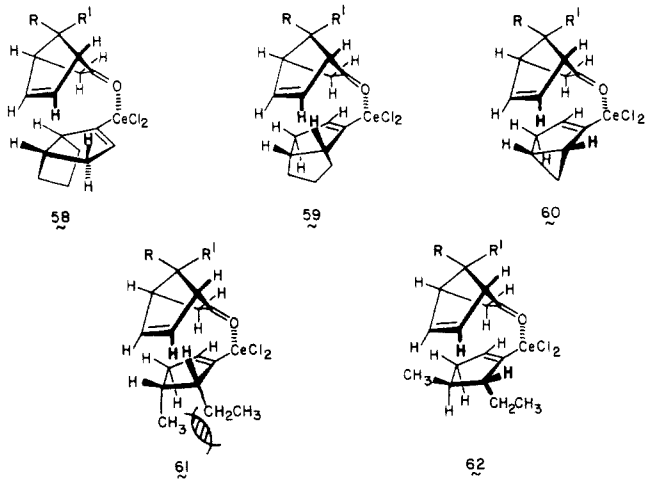
Particularly revealing in this connection is the triad of nucleophiles derived from vinyl bromides **22–24**, for which a striking falloff in diastereoselectivity is progressively observed. If one makes recourse to the Bürgi–Dunitz trajectory model[44] for carbonyl additions, with resultant stacking as in **58–62**,[45] then it appears that steric discrimination arises chiefly because of nonbonded interaction between the *proximal* ring juncture hydrogen of $RCeCl_2$ and the *proximal* vinyl proton of the particular norbornenone. On this basis, **59** (the progenitor of **34** and **53**) can be easily seen to be sterically disfavored relative to the diastereomeric combination **58** that leads to **33** and **52**. Reduction of the adjoining ring size through cyclobutane to cyclopropane induces major dihedral angle alterations such that the steric compression present in **59** is now appreciably dissipated in **60** as the direct result of the outward C–H splaying enforced by the three-membered ring. In kinetic terms, this means that transition-state **60** should compete quite well alongside its diastereomeric

(43) Paquette, L. A.; DeRussy, D. T.; Cottrell, C. E., the following paper in this issue.

(44) The dihedral angle of attack is assumed to be ca. 105° on the basis of crystal statics: (a) Bürgi, H. B.; Dunitz, J. D.; Shefter, E. *J. Am. Chem. Soc.* **1973**, *95*, 5065. (b) Bürgi, H. B.; Dunitz, J. D. *Acc. Chem. Res.* **1983**, *16*, 153 and pertinent references cited therein.

(45) Without question, structures **58–62** are oversimplified representations of the probable Ce···O coordination mode. It is not our intention to imply that the intermolecular attractive force is the result of interaction between the lanthanide cation and the carbonyl π bond. More probably, a first cerium atom coordinates with an oxygen nonbonded electron pair, thereby providing the opportunity for nucleophilic attack by subsequent involvement of a second cerium atom in a six-membered ring of the type

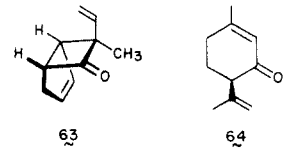




counterpart (similar to **58**) for bonding to the norbornenone. At the experimental level, diastereoselection is significantly lowered when **24** is involved.

In the case of **28**, a return to very good stereoselectivity is seen because nonbonded transition-state interactions are operative on an order comparable with those discussed for **22** (see **61**). On the other hand, the trans arrangement present in **27** causes the methyl and ethyl substituents to demand quasi-equatorial status and to induce the outward splaying of the pivotal H-5 as shown in **62**.

In allied investigations,[1,43] it has been determined that the capacity of ketones such as **63** and **64** for intermolecular recognition involving the same group of nucleophiles is considerably less good. The lower levels of diastereoselectivity in these examples likely stem from the dynamic conformational characteristics of the β,γ-unsaturated center. Thus, major advantages can accrue to more rigid structural frameworks where steric effects can gain greater relative importance as the nucleophile approaches.



Despite the attractiveness and practicability[38] of the preceding working hypothesis, certain major questions remain. The methoxyl oxygens at C-7, when present, do not appear to play a significant coordinative role, since other functionality at C-7 delivers roughly comparable results. The differences in the trends that have surfaced may be due to small norbornenone framework distortions. However, solvation and the coordinative role of the metal to the carbonyl center perhaps need to be given more accented consideration. Also, one-electron-transfer processes cannot be entirely dismissed. Stereoelectronic effects may also play a greater role than heretofore discussed.

Notwithstanding, the mechanistic analysis outlined here can be valuable in the prediction of preferred diastereoselection. Moreover, when linked to subsequent anionic oxy-Cope chemistry, the methodology provides a convenient method for setting the relative (and absolute if desired) stereochemistry of multiple stereogenic centers within intricate carbocyclic frameworks.

Experimental Section

7,7-Dimethoxybicyclo[2.2.1]hept-5-en-2-one (9).[19] 5,5-Dimethoxytetrachlorocyclopentadiene (24.2 g, 91.7 mmol) was dissolved in 180 mL of vinyl acetate, and the mixture was heated at the reflux temperature for 4.5 days. The volatiles were removed in vacuo at room temperature, and the residue was crystallized from methanol to give 29.2 g (91%) of **7a**: mp 83.5–84.0 °C (lit.[19] mp 81–82 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.48 (dd, J = 7.8, 2.5 Hz, 1 H), 3.59 (s, 3 H), 3.55 (s, 3 H), 2.80 (dd, J = 12.7, 7.8 Hz, 1 H), 2.05 (s, 3 H), 1.72 (dd, J = 12.7, 2.5 Hz, 1 H).

Dry potassium carbonate (0.33 g, 2.39 mmol) was added to a stirred solution of **7a** (8.35 g, 23.9 mmol) in 160 mL of dry methanol, and the mixture was stirred at room temperature for 15 min. The excess methanol was removed in vacuo at room temperature, and the residual oil was taken up in ether and washed with brine. The ethereal layer was dried, filtered, and evaporated. The residue was filtered through a small plug of silica gel (ether as eluent) to give 7.96 g (108% unpurified) of **7b** as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.60 (dd, J = 7.7, 2.4 Hz, 1 H), 3.56 (s, 3 H), 3.54 (s, 3 H), 2.65 (dd, J = 12.4, 7.7 Hz, 1 H), 2.18 (br s, 1 H), 1.75 (dd, J = 12.4, 2.4 Hz, 1 H).

A solution of the crude **7b** (7.96 g) and dry ethanol (4.21 mL, 71.7 mmol) in 45 mL of anhydrous ether was added dropwise to a vigorously stirred solution of sodium (5.50 g, 239 mmol) in 250 mL of dry ammonia at −78 °C under argon. A brilliant blue-green chemiluminescence was emitted during the addition. Following completion of this step, the reaction mixture was stirred at −78 °C for 5 min and treated in turn with isoprene, ether (200 mL), and saturated ammonium chloride solution (50 mL). The ammonia was allowed to evaporate and the usual ethereal extraction sequence followed. There was isolated 3.20 g (85%) of oily **8**.

Dry pyridine (22.9 mL, 0.283 mol) was added to a mechanically stirred suspension of dry chromium trioxide (14.2 g, 0.142 mol) in 400 mL of dry, cold (0 °C) dichloromethane under argon. The resulting mixture was allowed to warm to room temperature and stirred for 20 min. The solution was decanted from the residue, which was washed with ether (3 × 200 mL). The combined organic phases were filtered through a short silica gel column (ether as eluent) and concentrated in vacuo at room temperature. The pyridine was removed by distillation, bp 32–35 °C (28 Torr). Flash column chromatography of the residue on silica gel (elution with 11% ethyl acetate in petroleum ether) afforded 2.29 g (61% overall) of **9** as a colorless oil: bp 103–103.5 °C (7 Torr); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.55 (ddd, J = 6.0, 3.3, 0.7 Hz, 1 H), 6.02–5.97 (m, 1 H), 3.23 (s, 3 H), 3.21 (s, 3 H), 3.28–3.14 (m, 2 H), 2.28 (ddd, J = 16.3, 3.5, 0.7 Hz, 1 H), 1.90 (d, J = 16.3 Hz, 1 H).

Direct Sulfenylation of 10. Lithium diisopropylamide was prepared by reaction of diisopropylamine (5.3 mL, 37.8 mmol) dissolved in 200 mL of cold (0 °C), dry tetrahydrofuran with an equimolar amount of *n*-butyllithium in hexanes. The solution was stirred at 0 °C for 30 min, cooled to −78 °C, and treated dropwise with a solution of **10** (10.0 g, 34.4 mmol) in 50 mL of anhydrous tetrahydrofuran. Following completion of the addition, the reaction mixture was stirred for 45 min, treated with methyl disulfide (3.4 mL, 37.8 mmol), and stirred for an additional 45 min prior to warming to room temperature. Water (50 mL) was introduced, and the product was extracted into ether (3 × 100 mL). The combined organic layers were washed with brine (3 × 50 mL), dried, and concentrated to leave a white solid. Recrystallization from absolute ethanol gave 9.5 g (82%) of a mixture of **11** and **12** (ratio of 4:1) as white crystals, mp 80–89 °C. Repeated recrystallization of this material from absolute ethanol afforded pure **11** as a colorless crystalline solid: mp 89–90 °C; IR (KBr, cm^{-1}) 2950, 1720, 1440, 1330, 1270, 1100, 720; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.02 (dd, J = 5.5, 8.0 Hz, 1 H), 4.0–3.8 (m, 4 H), 3.74 (s, 3 H), 2.89 (dd, J = 4.6, 1.7 Hz, 1 H), 2.68–2.62 (m, 2 H), 2.54 (br s, 1 H), 2.26 (dd, J = 4.6, 14.3 Hz, 1 H), 2.18 (s, 3 H), 1.60 (d, J = 14.3 Hz, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$, ppm) 170.20, 142.71, 113.18, 64.63, 64.36, 53.07, 51.29, 49.33, 46.98, 44.02, 34.45, 13.79; MS, m/z (M^+) calcd 336.0030, obsd 336.0053. Anal. Calcd for $C_{12}H_{17}BrO_4S$: C, 42.74; H, 5.08. Found: C, 42.90; H, 5.13.

Methyl 5,5-(Ethylenedioxy)-7-(methylthio)-2-norbornene-7-carboxylate (13). A solution of lithium diisopropylamide in dry tetrahydrofuran (100 mL), prepared from 18.9 mmol of diisopropylamine and *n*-butyllithium in hexanes, was stirred at 0 °C for 30 min, cooled to −78 °C, and treated dropwise with a solution of **15** (3.61 g, 17.2 mmol) in 10 mL of anhydrous tetrahydrofuran during 45 min. Methyl disulfide (1.7 mL, 18.9 mmol) was added, stirring was maintained for 45 min, and the reaction mixture was allowed to warm to room temperature. Workup in the predescribed manner furnished 4.27 g (97%) of pure **13** as a colorless oil: IR (neat, cm^{-1}) 2900, 1740, 1430, 1250, 1100, 730; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.33 (m, 1 H), 6.13 (m, 1 H), 4.0–3.75 (m, 4 H), 3.75 (s, 3 H), 3.14 (br s, 1 H), 2.87 (br s, 1 H), 2.26 (dd, J = 3.6, 13.9 Hz, 1 H), 2.03 (s, 3 H), 1.68 (d, J = 13.0 Hz, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$, ppm) 138.17, 131.50, 116.47, 73.66, 64.36 (2 C), 54.74, 51.78, 47.20, 38.39, 14.28 (carbonyl not observed); MS, m/z (M^+ − SCH_3) calcd 209.0813, obsd 209.0823.

Dehydrobromination of 11/12. A solution of the epimeric methylthio esters (10.0 g, 29.7 mmol) in 25 mL of *tert*-butyl alcohol was added to potassium *tert*-butoxide (from 11.5 g (0.3 mol) of potassium metal) in 300 mL of the same solvent. After a reflux period of 24 h, the reaction mixture was cooled to room temperature, quenched with water (25 mL), and extracted with chloroform (3 × 100 mL). The combined organic phases were washed with brine (2 × 50 mL), dried, and concentrated to give 6.23 g (82%) of an oily mixture of **13** and **14**. ^{1}H NMR analysis showed the major constituent to be **13**.

Reduction of 13/14. A magnetically stirred solution of **13/14** (40.96 g, 0.16 mol) in dry benzene (400 mL) was cooled to 0 °C under nitrogen and treated dropwise with diisobutylaluminum hydride (480 mL of 1 M in hexanes). The reaction mixture was stirred for 1 h, quenched with 400 mL of cold 1 N hydrochloric acid, and stirred at room temperature for 40 min longer to dissolve the aluminum salts. The organic phase was separated, and the aqueous layer was extracted with ether (3 × 400 mL). The combined organic solutions were washed with saturated sodium bicarbonate solution (2 × 100 mL) and brine (2 × 100 mL) prior to drying. Filtration and concentration gave 32.14 g (88%) of the epimeric alcohols **16** and **17**.

Comparable treatment of pure **13** afforded the single isomer **16** as a colorless oil: IR (neat, cm^{-1}) 3500, 2990, 2920, 2890, 1480, 1440, 1400, 1320, 1230, 1210, 1120, 1050, 950, 900; ^1H NMR (300 MHz, $CDCl_3$) δ 6.28 (dd, J = 5.86, 2.89 Hz, 1 H), 6.12 (dd, J = 5.70, 3.32 Hz, 1 H), 3.98–3.72 (m, 6 H), 2.78 (br s, 1 H), 2.64–2.59 (m, 2 H), 2.12 (dd, J = 13.0, 3.54 Hz, 1 H), 1.88 (s, 3 H), 1.56 (d, J = 13.15 Hz, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$, ppm) 138.33, 133.80, 116.85, 78.20, 64.80, 63.98, 62.07, 55.07, 47.03, 38.94, 12.81; MS, m/z (M^+) calcd 228.0820, obsd 228.0816.

Transketalization of 16. A sample of pure **16** in $CDCl_3$ was allowed to stand at room temperature for 24 h. During this time, complete conversion to **18**, a colorless oil, occurred: IR (neat, cm^{-1}) 3400, 2900, 1750, 1420, 1100; ^1H NMR (300 MHz, $CDCl_3$) δ 6.29 (m, 1 H), 6.18 (m, 1 H), 4.1–3.7 (m, 7 H), 2.8 (br s, 1 H), 2.70 (br s, 1 H), 2.65 (dd, J = 12.0, 3.0 Hz, 1 H), 2.0 (s, 3 H), 1.6 (d, J = 12.6 Hz, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$, ppm) 141.12, 126.47, 111.33, 75.30, 67.97 (2 C), 62.01, 54.30, 49.23, 38.34, 12.59; MS, m/z ($M^+ - SCH_3$) calcd 181.0865, obsd 181.0870.

Deketalization of 16/17. A magnetically stirred solution of **16/17** (5.37 g, 23.5 mmol) in 15 mL of water and 60 mL of acetone containing 45 mg of *p*-toluenesulfonic acid was heated at reflux for 30 h. After cooling to room temperature, the acetone was removed on a rotary evaporator, and the residual aqueous mixture was neutralized with saturated sodium bicarbonate solution. The product was extracted into dichloromethane (3 × 150 mL) and washed with water (2 × 30 mL) and brine (2 × 50 mL) prior to drying. Concentration in vacuo gave the epimeric keto alcohols **19a** and **20a** (4.53 g, 100%) as a colorless oil. Separation of these epimers was effected by MPLC on silica gel (elution with 45% ethyl acetate in petroleum ether).

For **19a**: IR (neat, cm^{-1}) 3400, 2930, 1750, 1140, 1080; ^1H NMR (300 MHz, $CDCl_3$) δ 6.66 (dd, J = 5.63, 2.87 Hz, 1 H), 6.03 (m, 1 H), 3.68 and 3.65 (AB, J = 12.5 Hz, 2 H), 3.11 (br s, 1 H), 2.96 (br s, 1 H), 2.26 (dd, J = 17.0, 3.4 Hz, 1 H), 2.00 (d, J = 7.0 Hz, 1 H), 1.95 (s, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$, ppm) 144.69, 127.96, 75.45, 61.72, 61.01, 46.00, 34.95, 12.46 (carbonyl C not observed); MS, m/z ($M^+ - SCH_3$) calcd 137.0603, obsd 137.0609.

For **20a**: IR (neat, cm^{-1}) 3450, 2950, 1750, 1070, 730; ^1H NMR (300 MHz, $CDCl_3$) δ 6.61 (dd, J = 5.6, 2.9 Hz, 1 H), 6.04 (m, 1 H), 3.86 and 3.74 (AB, J = 11.8 Hz, 2 H), 3.07 (br s, 1 H), 3.01 (br s, 1 H), 2.66 (dd, J = 16.5, 3.4 Hz, 1 H), 2.44 (br s, 1 H), 2.00 (s, 3 H), 1.91 (d, J = 16.5 Hz, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$, ppm) 210.24, 143.30, 131.28, 75.45, 63.82, 59.35, 57.31, 40.83, 33.03; MS, m/z ($M^+ - H_2O$) calcd 166.0452, obsd 166.0427.

Silylation of 19a/20a. A solution of **19a/20a** (4.53 g, 23.5 mmol) in dry dimethylformamide (40 mL) was blanketed with nitrogen and treated with imidazole (6.40 g, 94.0 mmol) and *tert*-butyldimethylchlorosilane (5.56 g, 36.9 mmol). The reaction mixture was stirred at room temperature for 3 h, cooled to 0 °C, and quenched by addition of 50% saturated sodium bicarbonate solution (100 mL). Following extraction with ether (3 × 150 mL), the combined organic layers were washed with water (2 × 50 mL) and brine (2 × 50 mL), dried, and concentrated. The resulting silyl ethers **19b/20b** (6.53 g, 89%) were separated by MPLC on silica gel (elution with 8% ethyl acetate in petroleum ether).

For **19b**: IR (neat, cm^{-1}) 2955, 2930, 2890, 2857, 1750, 1260, 1145, 1120, 1090, 1040, 840, 770, 715; ^1H NMR (300 MHz, $CDCl_3$) δ 6.60 (dd, J = 5.7, 2.8 Hz, 1 H), 6.02 (m, 1 H), 3.88 and 3.81 (AB, J = 11.6 Hz, 2 H), 3.13 (br s, 1 H), 2.90 (br s, 1 H), 2.27 (dd, J = 16.7, 3.3 Hz, 1 H), 2.01 (s, 3 H), 1.97 (d, J = 16.7 Hz, 1 H), 0.86 (s, 9 H), 0.04 (s, 3 H), 0.02 (d, 3 H); ^{13}C NMR (200 MHz, $CDCl_3$, ppm) 210.94, 144.57, 128.47, 76.15, 65.68, 61.39, 46.83, 35.21, 25.82 (3 C), 18.21, 13.81, −5.55, −5.68; MS, m/z ($M^+ - SCH_3$) calcd 251.1467, obsd 251.1496. Anal. Calcd for $C_{15}H_{26}O_2SSi$: C, 60.33; H, 8.78. Found: C, 60.50; H, 8.88.

For **20b**: IR (neat, cm^{-1}) 2960, 2930, 2890, 2860, 1750, 1465, 1250, 1100, 1075, 840, 770, 720; ^1H NMR (300 MHz, $CDCl_3$) δ 6.57 (dd, J = 5.6, 3.0 Hz, 1 H), 6.0 (m, 1 H), 3.98 and 3.95 (AB, J = 10.3 Hz, 2 H), 3.0 (br s, 1 H), 2.95 (br s, 1 H), 2.64 (dd, J = 16.3, 3.3 Hz, 1 H), 2.11 (s, 3 H), 1.86 (d, J = 16.3 Hz, 1 H), 0.86 (s, 9 H), 0.01 (s, 6 H); ^{13}C NMR (20 MHz, $CDCl_3$, ppm) 210.56, 143.23, 128.53, 73.34, 64.90, 61.59, 44.85, 35.27, 25.82 (3 C), 18.21, 12.72, −5.49; MS, m/z (M^+) calcd 298.1423, obsd. 298.1425. Anal. Calcd for $C_{15}H_{26}O_2SSi$: C, 60.33; H, 8.78. Found: C, 60.47; H, 8.80.

2-Bromobicyclo[2.2.1]hept-2-ene (21). Norbornylene (29.19 g, 0.31 mol), dibromotetrachloroethane (51 g, 0.16 mol), and carbon tetrachloride (120 mL) were stirred mechanically and irradiated under argon with a GE 275-W sunlamp for 6 h. The carbon tetrachloride, excess norbornylene, and resulting tetrachloroethylene were removed under reduced pressure. The remaining dibromotetrachloroethane was separated from product by filtration through a plug of silica gel (carbon tetrachloride as eluant). Concentration of the eluate afforded a red oil that was combined with potassium *tert*-butoxide (22 g, 0.18 mol) in dry *tert*-butyl alcohol (150 mL) and heated at the reflux temperature under argon for 12 h. Concentration afforded a dark paste that was dissolved in water and extracted with petroleum ether. The combined organic layers were washed with water and brine before drying. Concentration followed by distillation of the dark oil at 70–85 °C (16 Torr) afforded a lighter oil, which was not totally homogeneous. Spinning band distillation of this material permitted separation of 7.93 g (29%) of pure **21**: bp 65–66 °C (15 Torr); ^1H NMR (300 MHz, $CDCl_3$) δ 6.02 (d, J = 2 Hz, 1 H), 2.89 (m, 2 H), 1.70–1.65 (m, 2 H), 1.62–1.54 (m, 1 H), 1.22–1.15 (m, 1 H), 1.15–1.09 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 134.83, 125.55, 50.55, 48.13, 43.96, 25.95, 24.43.

Vinyl Bromide Formation by the Shapiro Method. A. 2-Bromobicyclo[3.3.0]oct-2-ene (22). The tosylhydrazone of *cis*-bicyclo[3.3.0]-octan-2-one (mp 158–160 °C; 20.35 g, 70 mmol) dissolved in 150 mL of freshly distilled TMEDA was added dropwise during 20 min to a cold (−78 °C) mechanically stirred solution of *n*-butyllithium in hexanes (278 mmol). The reaction mixture was stirred at −78 °C for 30 min an subsequently allowed to warm to room temperature. After 3 h when nitrogen evolution had ceased, the vinyl anion solution was recooled to −78 °C, and cyanogen bromide (29.7 g, 278 mmol) dissolved in 19 mL of anhydrous tetrahydrofuran was added dropwise over 30 min. Stirring was continued for an additional 30 min before saturated sodium carbonate solution was introduced. The product was extracted into petroleum ether and the combined organic phases were washed successively with water, 5% hydrochloric acid, saturated sodium bicarbonate solution, and brine prior to drying. Concentration left a brown oil, distillation of which afforded 5.03 g (38%) of **22** as a colorless oil, bp 90–92 °C (16 Torr). VPC analysis (165 °C, 6 ft × 0.25 in. 15% SE-30) indicated the material to be homogeneous: ^1H NMR (300 MHz, $CDCl_3$) δ 5.70 (m, 1 H), 3.19 (m, 1 H), 2.75 (m, 1 H), 2.60 (m, 1 H), 1.95 (m, 1 H), 1.85–1.35 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 129.80, 125.15, 55.47, 40.41, 39.81, 35.96, 30.86, 24.84; MS, m/z (M^+) calcd 186.0044, obsd 186.0068.

B. 2-Bromobicyclo[3.2.0]hept-2-ene (23). Treatment of 18.22 g (65.5 mmol) of bicyclo[3.2.0]heptan-2-one tosylhydrazone (mp 155–156 °C) in the predescribed manner afforded 4.76 g (42%) of **23** as a colorless oil after spinning band distillation: bp 65 °C (16 Torr); ^1H NMR (300 MHz, $CDCl_3$) δ 5.86 (s, 1 H), 3.24 (m, 1 H), 2.94 (m, 1 H), 2.53 (m, 1 H), 2.37–2.14 (m, 2 H), 2.07 (dt, J = 3, 17 Hz, 1 H), 1.86 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 130.67, 125.81, 50.92, 40.12, 36.43, 26.75, 26.28; MS, m/z (M^+) calcd 171.9887, obsd 171.9893.

C. 2-Bromobicyclo[3.1.0]hex-2-ene (24). In identical fashion, 18.05 g (68.2 mmol) of bicyclo[3.1.0]hexan-2-one tosylhydrazone (mp 110–115 °C dec) furnished 870 mg (7%) of **24** as a colorless oil following purification by chromatography on silica gel (elution with petroleum ether): ^1H NMR (300 MHz, $CDCl_3$) δ 5.42 (d, J = 1 Hz, 1 H), 2.58 (ddd, J = 2, 7, 17 Hz, 1 H), 2.28 (dt, J = 3, 17 Hz, 1 H), 1.96 (m, 1 H), 1.66 (m, 1 H), 0.94 (dt, J = 4, 8 Hz, 1 H), 0.18 (dd, J = 4, 7 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 126.27, 124.47, 35.58, 28.65, 16.55, 16.08; MS, m/z (M^+) calcd 157.9731, obsd 157.9710.

D. 3-Bromobicyclo[3.1.0]hex-2-ene (25). Treatment of 21.35 g (80.8 mmol) of bicyclo[3.1.0]hexan-3-one tosylhydrazone according to the general procedure afforded 1.8 g (14%) of **25** as a colorless oil after silica gel chromatography (elution with petroleum ether): ^1H NMR (300 MHz, C_6D_6) δ 5.83 (dd, J = 2, 4 Hz, 1 H), 2.61 (ddd, J = 2, 7, 16 Hz, 1 H), 2.30 (d, J = 17 Hz, 1 H), 1.35 (m, 1 H), 1.10 (m, 1 H), 0.48 (ddd, J = 4, 7, 12 Hz, 1 H), −0.11 (dd, J = 4, 7 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 134.93, 118.45, 43.00, 23.31, 16.46, 15.49; MS, m/z (M^+) calcd 157.9731, obsd 157.9705.

E. 1-Bromo-5-ethylcyclopentene (26). From stepwise reaction of 23.73 g (84.6 mmol) of 2-ethylcyclopentanone tosylhydrazone (mp 113–116 °C) with *n*-butyllithium and cyanogen bromide as described above was isolated 4.3 g (29%) of **26** as a colorless oil: bp 60 °C (16 Torr); ^1H NMR (300 MHz, $CDCl_3$) δ 5.85 (dd, J = 2, 5 Hz, 1 H), 2.65 (m, 1 H), 2.27 (m, 2 H), 1.75 (m, 1 H), 1.63 (dq, J = 2, 4 Hz, 1 H), 1.30 (m, 1 H), 0.89 (t, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 130.70, 126.54, 50.59, 31.08, 27.87, 26.14, 10.56; MS, m/z (M^+) calcd 174.0044, obsd 174.0024.

F. *trans*-1-Bromo-5-ethyl-4-methylcyclopentene (27). Reaction of the tosylhydrazone of *trans*-2-ethyl-3-methylcyclopentanone (mp 102–104 °C) (7.3 g, 24.8 mmol) in the predescribed manner gave a dark oil that was filtered through neutral alumina (elution with petroleum ether) and distilled to give 1.22 g (26%) of **27** as a colorless liquid, bp 70–85 °C (25 Torr). The spectral properties of this material were identical with those previously reported.[35]

G. *cis*-1-Bromo-5-ethyl-4-methylcyclopentene (28). In identical fashion, the tosylhydrazone of *cis*-2-ethyl-3-methylcyclopentanone (mp 100–102 °C) (12.0 g, 41 mmol) was transformed into **28** (3.58 g, 46%). This colorless liquid exhibited IR and ^{1}H NMR spectra identical with those previously reported.[35]

Condensation of Dichlorocerium Reagents with 9. A. From 1-Bromonorbornene. Cerium(III) chloride heptahydrate (913 mg, 2.45 mmol) was dried in vacuo at 140 °C according to the procedure of Imamoto.[36c] The anhydrous white solid was allowed to cool, and dry tetrahydrofuran (8 mL) was added. The slurry was stirred for 2 h, during which time a cold (−78 °C) solution of vinyl bromide **21** (398 mg, 2.30 mmol) in 8 mL of dry tetrahydrofuran was added dropwise to *tert*-butyllithium (5.06 mmol). After being stirred for 30 min at −78 °C, this solution was transferred via cannula to the $CeCl_3$ slurry now also at −78 °C. The resulting orange reaction mixture was stirred for 30 min and treated dropwise during 10 min with a solution of **9** (336 mg, 2.0 mmol) in 5 mL of the same solvent. Saturated ammonium chloride solution was introduced 2 h later, and the products were extracted into ether. The combined organic extracts were washed successively with cold 5% hydrochloric acid, saturated sodium bicarbonate solution, and brine. Drying and concentration gave a residue that was directly subjected to MPLC purification on silica gel (elution with petroleum ether–ethyl acetate, 6:1). There was isolated 216 mg (41%) of a mixture of **29** and **30** along with 149 mg (44%) of recovered **9**. HPLC analysis of the diastereomeric alcohol mixture revealed the **29**/**30** ratio to be 6.2:1. The alcohols were separated by HPLC.

For **29**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.87 (dd, J = 1, 3 Hz, 1 H), 5.57 (dd, J = 1, 3 Hz, 1 H), 5.51 (d, J = 3 Hz, 1 H), 4.57 (s, 1 H), 3.52 (br s, 1 H), 2.92 (s, 3 H), 2.87 (s, 3 H), 2.76 (br s, 1 H), 2.70 (m, 1 H), 2.60 (m, 1 H), 1.79 (dd, J = 4, 12 Hz, 1 H), 1.64 (d, J = 13 Hz, 1 H), 1.64–1.55 (m, 3 H), 1.17 (m, 1 H), 1.07 (d, J = 8 Hz, 1 H), 1.04–0.95 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 151.79, 135.05, 131.86, 130.51, 121.19, 78.71, 54.37, 52.33, 49.58, 49.13, 45.17, 42.81, 42.23, 38.97, 25.62, 25.54; MS, m/z ($M^+ - CH_3OH$) calcd 230.1307, obsd 230.1305.

For **30**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.89 (m, 1 H), 5.71 (m, 1 H), 5.57 (d, J = 4 Hz, 1 H), 4.34 (s, 1 H), 3.10 (m, 1 H), 2.96 (s, 3 H), 2.87 (s, 3 H), 2.84 (m, 1 H), 2.78 (m, 1 H), 2.64 (m, 1 H), 1.79 (m, 2 H), 1.69 (m, 2 H), 1.40 (m, 1 H), 1.23 (m, 2 H), 1.10 (d, J = 8 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 151.70, 135.18, 131.66, 130.39, 120.68, 79.35, 53.92, 52.39, 49.58, 49.26, 45.55, 43.64, 42.36, 37.89, 25.82, 25.30; MS, m/z ($M^+ - CH_3OH$) calcd 230.1307, obsd 230.1266. Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 72.99; H, 8.51.

B. From 2-Bromobicyclo[3.3.0]oct-2-ene. Treatment of **22** (478 mg, 2.50 mmol) in identical fashion afforded after MPLC (silica gel, elution with petroleum ether–ethyl acetate, 3:1) 277 mg (50%) of a mixture of **33a** and **34a**, together with 154 mg (46%) of recovered **9**. HPLC analysis indicated the **33a**/**34a** ratio to be 16:1 and provided the pure diastereomers.

For **33a**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.90 (m, 1 H), 5.76 (m, 1 H), 5.13 (m, 1 H), 4.44 (s, 1 H), 3.63 (m, 1 H), 2.94 (s, 3 H), 2.90 (s, 3 H), 2.87 (m, 1 H), 2.60 (m, 2 H), 2.55 (m, 1 H), 1.98 (m, 1 H), 1.94–1.73 (m, 5 H), 1.60 (m, 1 H), 1.50 (m, 1 H), 1.28 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 150.28, 135.24, 131.88, 126.48, 121.36, 79.22, 55.41, 52.00, 51.88, 49.01, 45.53, 41.84, 41.48, 40.51, 36.03, 32.74, 26.76; MS, m/z ($M^+ - CH_3OH$) calcd 244.1463, obsd 244.1420.

For **34a**: ^{1}H NMR (300 MHz, C_6D_6) δ 6.01 (m, 1 H), 5.88 (m, 1 H), 5.36 (m, 1 H), 4.51 (s, 1 H), 3.20 (m, 1 H), 3.06 (s, 3 H), 2.99 (s, 3 H), 2.96 (m, 1 H), 2.82 (m, 1 H), 2.76 (m, 1 H), 2.68 (m, 1 H), 2.62 (m, 1 H), 2.17–2.06 (m, 2 H), 2.03 (d, J = 13 Hz, 1 H), 1.90 (dd, J = 4, 13 Hz, 1 H), 1.88 (m, 1 H), 1.68 (m, 1 H), 1.49 (m, 1 H), 1.45 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 148.18, 135.90, 131.26, 126.59, 120.50, 80.04, 54.35, 52.40, 52.09, 49.50, 45.95, 42.46, 40.76, 39.82, 35.71, 33.71, 26.87; MS, m/z (M^+) calcd 244.1463, obsd 244.1444.

C. From 2-Bromobicyclo[3.2.0]hept-2-ene (23). In an identical manner, 433 mg (2.50 mmol) of **23** was condensed with **9** to furnish after MPLC (silica gel, elution with petroleum ether–ethyl acetate, 3:1) a mixture of **33b**/**34b** (197 mg, 38%) along with unreacted **9** (168 mg, 50%). HPLC (silica gel, elution with petroleum ether–ethyl acetate, 4:1) provided the pure diastereomers and indicated the **33b**/**34b** ratio to be 10.4:1.

For **33b**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.95 (ddd, J = 1, 3, 6 Hz, 1 H), 6.84 (ddd, J = 1, 4, 9 Hz, 1 H), 5.37 (br s, 1 H), 4.42 (br s, 1 H), 3.80 (m, 1 H), 2.93 (s, 3 H), 2.89 (s, 3 H), 2.84 (m, 2 H), 2.67 (m, 1 H), 2.54 (m, 1 H), 2.42 (m, 1 H), 2.18–2.06 (m, 3 H), 1.85–1.68 (m, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 150.63, 135.44, 131.77, 127.19, 121.38, 79.15, 55.86, 52.04, 49.02, 46.90, 45.64, 41.01, 40.64, 36.76, 27.65, 27.39; MS, m/z ($M^+ - CH_3OH$) calcd 230.1307, obsd 230.1310. Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 72.71; H, 8.44.

For **34b**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.89 (dq, J = 3, 7 Hz, 1 H), 5.68 (dd, J = 3, 6 Hz, 1 H), 5.38 (br s, 1 H), 4.35 (br s, 1 H), 3.38 (m, 1 H), 2.93 (s, 3 H), 2.89 (m, 1 H), 2.88 (s, 3 H), 2.76 (m, 1 H), 2.75–2.46 (m, 4 H), 2.28–2.10 (m, 2 H), 1.91 (d, J = 13 Hz, 1 H), 1.72 (dd, J = 4, 13 Hz, 1 H), 1.35 (m, 1 H); MS, m/z ($M^+ - CH_3OH$) calcd 230.1307, obsd 230.1271.

D. 2-Bromobicyclo[3.1.0]hex-2-ene (24). A sample of 85% pure **24** (159 mg, 1.25 mmol) was caused to react with **9** in the manner described above. Chromatography of the reaction mixture on silica gel (elution with petroleum ether–ethyl acetate, 3:1) afforded 106 mg (43%) of a mixture of **33c** and **34c** along with 88 mg (50%) of recovered **9**. HPLC analysis and purification (silica gel, petroleum ether–ethyl acetate, 4:1) indicated the **33c**/**34c** ratio to be 2.1:1 and provided the pure alcohols.

For **33c**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.87 (m, 1 H), 5.76 (m, 1 H), 4.91 (br s, 1 H), 4.53 (s, 1 H), 2.96 (m, 1 H), 2.94 (s, 3 H), 2.90 (s, 3 H), 2.65 (m, 1 H), 2.52 (ddd, J = 2, 6, 17 Hz, 1 H), 2.43 (m, 1 H), 2.26 (m, 1 H), 1.76 (m, 2 H), 1.49 (m, 1 H), 0.74 (dt, J = 4, 8 Hz, 1 H), −0.16 (dd, J = 3, 4 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 152.40, 135.60, 131.72, 122.02, 121.39, 78.99, 54.84, 52.09, 49.04, 45.69, 39.01, 35.80, 23.97, 16.10, 15.50; MS, m/z ($M^+ - CH_3OH$) calcd 216.1150, obsd 216.1148.

For **34c**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.88 (m, 2 H), 5.15 (br s, 1 H), 4.50 (m, 1 H), 2.95 (s, 3 H), 2.90 (s, 3 H), 2.84 (br s, 1 H), 2.66 (m, 1 H), 2.47 (dd, J = 5, 12 Hz, 1 H), 2.30 (m, 1 H), 1.92 (m, 1 H), 1.83 (s, 1 H), 1.45 (m, 1 H), 1.34 (m, 1 H), 0.83 (m, 1 H), 0.09 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 153.10, 135.02, 131.93, 121.99, 121.10, 79.30, 55.09, 52.11, 49.11, 45.87, 39.83, 35.73, 25.23, 16.78, 15.96; MS, m/z ($M^+ - CH_3OH$) calcd 216.1150, obsd 216.1129.

E. 3-Bromobicyclo[3.1.0]hex-2-ene (25). In identical fashion, 395 mg (2.50 mmol) of **25** afforded after MPLC on silica gel (elution with petroleum ether–ethyl acetate, 3:1) 118 mg (24%) of a mixture of **36** and **37**. No **9** was recovered in this instance, since in situ sodium borohydride reduction was utilized to facilitate chromatographic separation. HPLC analysis and purification (silica gel, petroleum ether–ethyl acetate, 4:1) indicated the **36**/**37** ratio to be 2.3:1.

For **36**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.84 (m, 1 H), 5.56 (m, 1 H), 4.59 (d, J = 2 Hz, 1 H), 4.43 (s, 1 H), 3.23 (dd, J = 7, 17 Hz, 1 H), 2.91 (s, 3 H), 2.85 (s, 3 H), 2.59 (m, 2 H), 2.43 (d, J = 7 Hz, 1 H), 1.75–1.64 (m, 3 H), 1.46 (m, 1 H), 0.69 (dt, J = 4, 8 Hz, 1 H), −0.12 (dd, J = 4, 7 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 134.36, 130.45, 128.62, 127.33, 78.48, 53.82, 51.05, 47.99, 44.93, 38.60, 35.61, 22.19, 15.50, 14.05 (one C not observed); MS, m/z ($M^+ - CH_3OH$) calcd 216.1150, obsd 216.1155.

For **37**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.90 (m, 1 H), 5.75 (m, 1 H), 5.62 (m, 1 H), 4.35 (s, 1 H), 2.95 (m, 1 H), 2.90 (s, 3 H), 2.84 (s, 3 H), 2.71 (m, 1 H), 2.57 (m, 2 H), 1.68 (m, 3 H), 1.46 (m, 1 H), 0.70 (m, 1 H), 0.21 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 135.85, 131.21, 130.00, 129.30, 78.75, 54.29, 52.06, 48.99, 45.94, 39.83, 36.11, 23.30, 17.01, 15.65 (one C not observed); MS, m/z ($M^+ - CH_3OH$) calcd 216.1150, obsd 216.1153.

F. 1-Bromo-5-ethylcyclopentene (26). Analogous treatment of **26** (438 mg, 2.50 mmol) afforded after silica gel chromatography (elution with petroleum ether–ethyl acetate, 3:1) 322 mg (61%) of a mixture of **39a** and **40a** along with 108 mg (32%) of recovered **9**. HPLC analysis and separation (silica gel, elution with the same solvent systems) indicated the ratio to be 10.4:1.

For **39a**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.94 (ddd, J = 1, 3, 6 Hz, 1 H), 5.83 (dd, J = 3, 6 Hz, 1 H), 5.25 (m, 1 H), 4.45 (d, J = 8 Hz, 1 H), 3.14 (m, 1 H), 2.94 (s, 3 H), 2.89 (s, 3 H), 2.88 (m, 1 H), 2.66 (br s, 1 H), 2.39–1.99 (m, 4 H), 1.87 (dd, J = 4, 13 Hz, 1 H), 1.80 (d, J = 13 Hz, 1 H), 1.59 (m, 1 H), 1.36 (m, 1 H), 1.10 (t, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 151.57, 135.16, 131.93, 121.37, 116.89, 79.23, 55.39, 51.98, 49.00, 47.77, 45.48, 42.26, 31.36, 29.79, 27.40, 12.38; MS, m/z ($M^+ - CH_3OH$) calcd 232.1463, obsd 232.1495. Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.36; H, 9.26.

For **40a**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.93 (m, 1 H), 5.79 (m, 1 H), 5.39 (br s, 1 H), 4.38 (br s, 1 H), 2.94 (s, 3 H), 2.89 (s, 3 H), 2.83 (m, 1 H), 2.66 (m, 2 H), 2.40–1.41 (m, 1 H), 1.10 (t, J = 7 Hz, 3 H); MS, m/z ($M^+ - CH_3OH$) calcd 232.1463, obsd 232.1487.

G. *trans*-1-Bromo-5-ethyl-4-methylcyclopentene (27). Following treatment of a 2.50-mmol sample of **27** as described above, a dark oil was obtained that was subjected to MPLC (silica gel, elution with petroleum ether–ethyl acetate, 3:1). There was isolated 237 mg (43%) of a mixture of **39b** and **40b** along with 192 mg (57%) of unreacted **9**. HPLC (silica

gel, petroleum ether–ethyl acetate, 4:1) showed **39b** and **40b** to be present in a 4.2:1 ratio. The pure alcohols exhibited the following spectral features.

For **39b**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.91 (m, 1 H), 5.83 (m, 1 H), 5.20 (br s, 1 H), 4.41 (br s, 1 H), 2.94 (s, 3 H), 2.89 (s, 3 H), 2.88 (m, 1 H), 2.69 (m, 1 H), 2.62 (m, 1 H), 2.56 (m, 1 H), 2.03 (m, 2 H), 1.87–1.72 (m, 3 H), 1.43 (m, 1 H), 1.03 (m, 6 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 150.34, 135.13, 131.95, 125.92, 121.38, 79.04, 55.94, 55.65, 51.99, 49.00, 44.52, 42.24, 40.11, 36.64, 26.73, 23.25, 12.03; MS, m/z ($M^+ - CH_3OH$) calcd 246.1620, obsd 246.1622.

For **40b**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.92 (m, 1 H), 5.87 (m, 1 H), 5.30 (m, 1 H), 4.38 (m, 1 H), 2.94 (s, 3 H), 2.88 (s, 3 H), 2.85 (br s, 2 H), 2.64 (m, 2 H), 2.24 (m, 2 H), 2.08 (m, 1 H), 1.93 (d, J = 13 Hz, 1 H), 1.76 (m, 2 H), 1.13 (t, J = 7 Hz, 3 H), 0.98 (d, J = 7 Hz, 3 H); MS, m/z ($M^+ - CH_3OH$) calcd 246.1620, obsd 246.1632.

H. *cis*-1-Bromo-5-ethyl-4-methylcyclopentene (28). A 1.90-g (10.0 mmol) sample of **28** was transformed into its dichlorocerium reagent and added to **9** in the predescribed manner. MPLC on silica gel of the crude reaction mixture (elution with 12% ethyl acetate in petroleum ether) afforded the pure diastereomeric alcohols **39c** and **40c** (ratio 12:1) as colorless solids (combined yield 85.5%) and 7% unreacted **9**.

For **39c**: mp 58.5–59.0 °C (from petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.16–6.08 (m, 1 H), 5.92–5.84 (m, 1 H), 5.36–5.30 (m, 1 H), 4.38 (s, 1 H), 3.33 (s, 3 H), 3.20 (s, 3 H), 2.94–2.90 (m, 1 H), 2.89–2.84 (m, 1 H), 2.67–2.55 (m, 1 H), 2.95–2.25 (m, 2 H), 1.95–1.75 (m, 4 H), 1.55–1.34 (m, 1 H), 0.91 (d, J = 6.8 Hz, 3 H), 0.89 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 150.67, 135.24, 131.79, 126.96, 121.37, 79.46, 55.23, 52.00, 50.37, 49.04, 45.52, 41.91, 39.94, 36.36, 21.34, 15.60, 12.74; MS, m/z (M^+) calcd 246.1620, obsd 246.1630. Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41. Found: C, 73.49; H, 9.60.

For **40c**: mp 41.2–42.0 °C (from petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.13–6.07 (m, 1 H), 5.89 (dd, J = 5.8, 3.4 Hz, 1 H), 5.44 (br s, 1 H), 4.37 (s, 1 H), 3.33 (s, 3 H), 3.21 (s, 3 H), 2.95–2.90 (m, 1 H), 2.90–2.80 (m, 1 H), 2.80–2.15 (series of m, 3 H), 1.96 (d, J = 12.8 Hz, 1 H), 1.81 (dd, J = 12.8, 3.6 Hz, 1 H), 1.95–1.54 (series of m, 3 H), 1.00 (d, J = 6.8 Hz, 3 H), 0.89 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 149.24, 135.46, 131.41, 127.66, 120.60, 79.89, 53.81, 52.26, 50.05, 49.42, 45.44, 39.86, 39.09, 37.60, 21.36, 15.03, 12.15; MS, m/z (M^+) calcd 246.1620, obsd 246.1626. Anal. Calcd for $C_{17}H_{26}O_3$: C, 73.34; H, 9.41. Found: C, 73.42; H, 9.51.

Anionic Oxy-Cope Rearrangement of the Adducts to 9. A. Ketone 31. To diisopropylamine (0.07 mL, 0.48 mmol) and potassium *tert*-butoxide (48 mg, 0.43 mmol) in 5 mL of dry tetrahydrofuran at −78 °C was added dropwise 0.42 mmol of *n*-butyllithium in hexane solution. The yellow solution was stirred at −78 °C for 30 min before **29** (105 mg, 0.4 mmol) dissolved in dry tetrahydrofuran (3 mL) was introduced dropwise over several minutes. The reaction mixture was stirred at −78 °C for 15 min, allowed to warm to room temperature, and kept there for 2 h before being quenched with saturated brine. The product was extracted into ether, and the combined ethereal layers were washed with brine, dried, and evaporated. MPLC on Florisil (elution with petroleum ether–ethyl acetate, 3:1) gave 80 mg (76%) of **31** as a faint yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.12 (dd, J = 2, 6 Hz, 1 H), 5.81 (dd, J = 3, 6 Hz, 1 H), 3.33 (m, 1 H), 3.22 (s, 3 H), 3.16 (s, 3 H), 2.7–2.4 (m, 5 H), 2.31 (dd, J = 5, 14 Hz, 1 H), 2.12 (d, J = 14 Hz, 1 H), 2.01 (d, J = 22 Hz, 1 H), 1.60–1.20 (m, 4 H), 1.14 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 216.74, 139.21, 127.61, 113.55, 50.02, 49.87, 47.21, 46.47, 43.02, 41.32, 41.19, 41.07, 40.54, 40.09, 25.60, 23.30; MS, m/z (M^+) calcd 262.1569, obsd 262.1557.

B. Ketone 32. Reaction of **30** (26.2 mg, 0.1 mmol) in an identical manner afforded after chromatography (silica gel, elution with petroleum ether–ethyl acetate, 5:1) 18.5 mg (71%) of **32**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.95 (dd, J = 1, 6 Hz, 1 H), 5.74 (dd, J = 3, 6 Hz, 1 H), 3.20 (m, 1 H), 3.10 (s, 3 H), 3.09 (s, 3 H), 2.79 (m, 1 H), 2.55 (br s, 1 H), 2.45–2.08 (series of m, 5 H), 1.55–1.40 (m, 2 H), 1.25–0.95 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 213.29, 136.88, 130.91, 113.20, 55.38, 49.91, 49.68, 46.87, 45.37, 42.52, 40.72, 36.68, 36.38, 36.12, 29.98, 28.59; MS, m/z (M^+) calcd 262.1569, obsd 262.1555.

C. Ketone 35a. A 175-mg (0.70 mmol) sample of a 16:1 mixture of **33a**/**34a** was processed in an entirely analogous fashion. Chromatography of the crude product mixture on Florisil (elution with petroleum ether–ethyl acetate, 4:1) furnished 149 mg (85%) of **35a**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.83 (dd, J = 2, 6 Hz, 1 H), 5.58 (dd, J = 3, 6 Hz, 1 H), 3.08 (s, 3 H), 2.96 (dd, J = 5, 11 Hz, 1 H), 2.91 (s, 3 H), 2.63 (m, 2 H), 2.48 (m, 2 H), 2.36 (ddd, J = 1, 8, 14 Hz, 1 H), 2.20 (m, 1 H), 2.02 (m, 1 H), 1.70–1.15 (series of m, 8 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 213.56, 137.67, 130.23, 112.26, 53.06, 49.39, 49.03, 48.19, 45.54, 44.28, 44.11, 43.37, 40.14, 36.85, 32.83, 29.33, 27.60; MS, m/z (M^+) calcd 276.1725, obsd 276.1737.

D. Ketone 35b. A 10.4:1 mixture of **33b**/**34b** (156 mg, 0.60 mmol) was isomerized in identical fashion. Florisil chromatography (elution with petroleum ether–ethyl acetate, 4:1) gave 106 mg (68%) of **35b**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.86 (dd, J 2, 6 Hz, 1 h), 5.60 (dd, J = 3, 6 Hz, 1 H), 3.15 (m, 1 H), 3.09 (s, 3 H), 2.95 (m, 1 H), 2.94 (s, 3 H), 2.71 (m, 1 H), 2.60–2.45 (m, 3 H), 2.32 (m, 1 H), 2.10–1.80 (m, 4 H), 1.69–1.60 (m, 2 H), 1.37 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 212.68, 137.69, 130.30, 112.43, 53.46, 49.44, 49.15, 46.51, 44.29, 42.98, 42.92, 40.90, 39.36, 37.09, 24.53, 22.53; MS, m/z (M^+) calcd 262.1569, obsd 262.1572.

E. Ketone 35c. In identical fashion, isomerization of a mixture (2.1:1) of **33c**/**34c** (28 mg, 0.11 mmol) afforded after Florisil chromatography (elution with petroleum ether–ethyl acetate, 2:1) 11 mg (40%) of **35c**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.75 (dd, J = 2, 6 Hz, 1 H), 5.54 (dd, J = 2, 6 Hz, 1 H), 3.01 (s, 3 H), 2.90 (s, 3 H), 2.78–2.27 (series of m, 6 H), 1.70 (m, 1 H), 1.60–1.30 (m, 2 H), 1.10 (m, 1 H), 0.43 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 211.70, 137.10, 130.42, 112.63, 51.21, 49.42, 49.21, 47.28, 45.20, 43.32, 40.62, 32.41, 23.25, 19.37, 15.07; MS, m/z (M^+) calcd 248.1412, obsd 248.1443.

F. Ketone 41a. Submission of a 10.4:1 mixture of **39a**/**40a** (100 mg, 0.38 mmol) to analogous treatment gave rise to 154 mg (89%) of **41a** after purification by chromatography on Florisil (elution with petroleum ether–ethyl acetate, 3:1): ^{1}H NMR (300 MHz, C_6D_6) δ 5.86 (dd, J = 2, 6 Hz, 1 H), 5.58 (dd, J = 3, 6 Hz, 1 H), 3.07 (s, 3 H), 2.92 (s, 3 H), 2.71 (m, 2 H), 2.46 (m, 1 H), 2.23 (m, 2 H), 2.15 (m, 1 H), 1.80–1.50 (m, 4 H), 1.39 (m, 1 H), 1.30–1.07 (series of m, 2 H), 0.95 (t, J = 7 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 213.43, 137.77, 130.75, 112.41, 54.45, 49.31, 48.89, 47.64, 44.81, 44.46, 42.79, 42.06, 30.14, 25.42, 25.08, 13.54; MS, m/z (M^+) calcd 264.1725, obsd 264.1716.

G. Ketone 41b. Comparable anionic oxy-Cope rearrangement of a 4.2:1 mixture of **39b**/**40b** (141 mg, 0.41 mmol) yielded after Florisil chromatography (elution with petroleum ether–ethyl acetate, 4:1) 100 mg (71%) of **41b**: ^{1}H NMR (300 MHz, C_6D_6) δ 5.90 (m, 1 H), 5.58 (m, 1 H), 3.08 (s, 3 H), 2.91 (s, 3 H), 2.82 (t, J = 12 Hz, 1 H), 2.69 (m, 1 H), 2.58–2.35 (m, 3 H), 2.06 (m, 2 H), 1.60 (m, 1 H), 1.48–1.25 (m, 3 H), 1.19 (t, J = 6 Hz, 3 H), 1.03 (m, 1 H), 0.81 (d, J = 6 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 213.99, 137.76, 130.72, 112.49, 55.41, 54.22, 49.31, 48.86, 44.78, 44.26, 41.95, 40.75, 37.47, 34.84, 23.36, 20.46, 13.61; MS, m/z (M^+) calcd 278.1882, obsd 278.1893.

H. Ketone 41c. To a cold (−20 °C), magnetically stirred solution of **39c** (73 mg, 0.263 mmol), dry TMEDA (0.5 mL), and triphenylmethane (1 mg) in dry tetrahydrofuran (5 mL) under argon was added dropwise 0.23 mL of *n*-butyllithium (1.55 M in hexanes, 0.355 mmol) to cause a pink color to develop. This mixture was allowed to warm to room temperature where it was stirred for 11 h prior to being quenched with 0.5 mL of water. The tetrahydrofuran was evaporated in vacuo, and the product was extracted into ether. MPLC purification (neutral alumina, elution with 7.5% ethyl acetate in petroleum ether) gave 46.1 mg (63%) of **41c**: IR (neat, cm^{-1}) 2958, 2940, 2900, 2870, 1702, 1145, 1082, 1043, 1000, 935; ^{1}H NMR (300 MHz, C_6D_6) δ 5.87 (dd, J = 5.9, 1.9 Hz, 1 H), 5.61 (d, J = 5.9 Hz, 1 H), 3.09 (dd, J = 14.8, 10.7 Hz, 1 H), 3.07 (s, 3 H), 2.92 (s, 3 H), 2.85–2.74 (m, 1 H), 2.56–2.43 (m, 1 H), 2.37 (dd, J = 14.8, 7.9 Hz, 1 H), 2.20 (t, J = 6.6 Hz, 1 H), 2.02–1.65 (m, 5 H), 1.45–1.25 (m, 2 H), 1.11 (t, J = 6.9 Hz, 3 H), 0.81 (d, J = 7.2 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 213.06, 137.56, 130.38, 112.70, 52.39, 50.64, 49.44, 48.99, 43.88, 43.85, 41.48, 40.16, 36.36, 34.19, 20.94, 19.28, 14.25; MS, m/z (M^+) calcd 278.1882, obsd 278.1881.

Condensation of Dichlorocerium Reagents with 19b and 20b. In a two-necked 25-mL round-bottomed flask fitted with a rubber septum was placed cerium trichloride heptahydrate (350 mg, 0.94 mmol). The solid was heated at 140 °C and 0.3 Torr for 2.5 h with intermittent shaking. After being cooled, the flask was flushed with nitrogen, dry tetrahydrofuran (6 mL) was introduced, and stirring was effected for 2.5 h. Freshly distilled vinyl bromide (0.87 mmol) was placed in a 15-mL round-bottomed flask, dissolved in dry tetrahydrofuran (6 mL), cooled to −78 °C, and treated slowly with *tert*-butyllithium (1.87 mmol) during 20 min. The $CeCl_3$ solution was cooled to −78 °C, and the organolithium reagent was transferred via cannula.

The yellow solution was stirred for 30 min, and the ketone (200 mg, 0.67 mmol) dissolved in the same solvent (10 mL) was slowly added over 15 min. After 2 h, the reaction mixture was quenched with saturated ammonium chloride solution (15 mL) and then brine (15 mL). The product was extracted into ether (3 × 50 mL), and the combined organic phases were washed with brine (2 × 50 mL), dried, and concentrated. The residual oil was purified by MPLC on silica gel (elution with 8% ethyl acetate in petroleum ether).

For **42a**/**43a**: 40% yield with 46% recovery of **19b**.

42a: mp 64–64.5 °C; IR (neat, cm^{-1}) 3460, 2945, 2925, 2860, 1470, 1460, 1445, 1260, 1130, 1095, 1080, 1060, 845, 780, 710; ^{1}H NMR (300

MHz, $CDCl_3$) δ 6.1 (dd, J = 5.8, 3.0 Hz, 1 H), 5.92 (dd, J = 5.6, 3.2 Hz, 1 H), 5.24 (s, 1 H), 4.30 and 4.18 (AB, J = 11.2 Hz, 2 H), 3.37 (br s, 1 H), 3.16 (br s, 1 H), 2.90 (s, 1 H), 2.84 (s, 1 H), 2.71–2.52 (m, 2 H), 2.16 (dd, J = 13.1, 3.4 Hz, 1 H), 2.03 (s, 3 H), 2.0–1.93 (m, 1 H), 1.85–1.62 (m, 2 H), 1.60–1.41 (m, 3 H), 1.34–1.20 (m, 2 H), 0.93 (s, 9 H), 0.13 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 151.36, 136.25, 135.21, 126.22, 79.75, 75.99, 66.72, 59.58, 51.72, 47.59, 41.09, 40.30, 39.96, 35.49, 32.06, 26.32, 25.92 (3 C), 18.28, 14.66, -5.22, -5.41; MS, mz ($M^+ - SCH_3$) calcd 359.2407, obsd 359.2361.

43a: IR (neat, cm^{-1}) 3450, 2950, 2930, 2860, 1470, 1460, 1445, 1255, 1120, 1080, 1050, 835, 780, 710; ^1H NMR (300 MHz, C_6D_6) δ 5.99–5.96 (m, 1 H), 5.93–5.90 (m, 1 H), 5.13 (s, 1 H), 4.36 and 4.18 (AB, J = 11.0 Hz, 2 H), 2.94 (s, 1 H), 2.86 (br s, 1 H), 2.66 (s, 1 H), 2.63 (s, 1 H), 2.59–2.39 (m, 2 H), 2.05–1.22 (series of m, 9 H), 1.89 (s, 3 H), 1.04 (s, 9 H), 0.19 (s, 3 H), 0.15 (s, 3 H); MS, m/z ($M^+ - SCH_3$) calcd 359.2407, obsd 359.2480.

For **42b**/**43b**: 46.5% yield with 44% recovery of **20b**.

42b: IR (neat, cm^{-1}) 3420, 2960, 2940, 2870, 1470, 1460, 1450, 1390, 1260, 1120, 1100, 1070, 845, 780, 720; ^1H NMR (300 MHz, C_6D_6) δ 5.87–5.84 (m, 1 H), 5.76 (dd, J = 5.8, 3.2 Hz, 1 H), 5.45 (s, 1 H), 5.27 (s, 1 H), 4.03 and 3.88 (AB, J = 10.1 Hz, 2 H), 3.65 (br s, 1 H), 2.94 (s, 1 H), 2.76–2.66 (m, 3 H), 2.50 (dd, J = 13.3, 3.5 Hz, 1 H), 2.14–1.12 (series of m, 8 H), 1.98 (s, 3 H), 1.07 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H); MS, m/z ($M^+ - H_2O$) calcd 388.2256, obsd 388.2225.

43b: IR (neat, cm^{-1}) 3420, 2960, 2940, 2860, 1470, 1460, 1450, 1390, 1255, 1125, 1100, 1060, 840, 780, 720; ^1H NMR (300 MHz, C_6D_6) δ 5.83–5.80 (m, 1 H), 5.67 (dd, J = 5.7, 3.1 Hz, 1 H), 5.30 (s, 1 H), 5.26 (s, 1 H), 3.93 and 3.80 (AB, J = 10.2 Hz, 2 H), 3.08 (br s, 1 H), 2.82 (s, 1 H), 2.72–2.71 (m, 1 H), 2.67 (s, 1 H), 2.58–2.49 (m, 2 H), 2.35 (dd, J = 13.0, 3.3 Hz, 1 H), 2.10 (d, J = 12.9 Hz, 1 H), 2.04–1.93 (m, 2 H), 1.88 (s, 3 H), 1.83–1.75 (m, 2 H), 1.59–1.55 (m, 1 H), 1.43–1.41 (m, 1 H), 0.97 (s, 9 H), 0.46 (s, 3 H), 0.33 (s, 3 H); MS, m/z ($M^+ - C_4H_9$) calcd 349.1657, obsd 349.1678.

For **45a**/**46a**: 35.2% yield with 50% recovery of **19b**.

45a: mp 66.0–66.5 °C; IR (KBr, cm^{-1}) 3400, 2955, 2925, 2880, 2855, 1470, 1460, 1370, 1360, 1270, 1255, 1195, 1130, 1095, 1080, 845, 780, 720; ^1H NMR (300 MHz, C_6D_6) δ 5.92–5.87 (m, 2 H), 5.07 (s, 1 H), 4.40 and 4.20 (AB, J = 11.0 Hz, 2 H), 2.90 (s, 1 H), 2.66 (s, 1 H), 2.56 (s, 1 H), 2.48–2.40 (m, 1 H), 2.23–2.21 (m, 1 H), 2.13 (dd, J = 13, 3.4 Hz, 1 H), 1.92 (s, 3 H), 1.78–1.58 (m, 3 H), 1.29–1.19 (m, 2 H), 1.04 (s, 9 H), 0.96 (d, J = 6.9 Hz, 3 H), 0.90 (t, J = 7.4 Hz, 3 H), 0.19 (s, 3 H), 0.16 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 152.43, 136.65, 134.65, 125.14, 79.91, 76.42, 67.19, 60.23, 56.69, 47.83, 40.34, 40.02, 36.54, 26.90, 26.19 (3 C), 23.15, 18.63, 14.91, 12.02, -5.00, -5.15; MS, m/z (M^+) calcd 390.2413, obsd 390.2391.

46a: IR (neat, cm^{-1}) 3440, 2960, 2940, 2870, 1460, 1380, 1265, 1125, 1090, 1055, 845, 780, 715; ^1H NMR (300 MHz, C_6D_6) δ 5.75 (m, 1 H), 5.15 (m, 1 H), 5.85 (s, 1 H), 5.15 (s, 1 H), 3.89 and 3.75 (AB, J = 11.0 Hz, 2 H), 2.96 (s, 1 H), 2.85 (s, 1 H), 2.72–2.64 (m, 2 H), 2.40 (dd, J = 12.7, 3.4 Hz, 1 H), 2.10–1.91 (m, 3 H), 1.87 (s, 3 H), 1.33–1.22 (m, 2 H), 0.94 (s, 9 H), 0.90 (t, J = 7.9 Hz, 3 H), 0.83 (d, J = 7.0 Hz, 3 H), 0.04 (s, 3 H), 0.01 (s, 3 H); MS, m/z (M^+) calcd 390.2413, obsd 390.2449.

For **45b**/**46b**: 33% yield with 46.5% recovery of **20b**.

45b: IR (neat, cm^{-1}) 3420, 2950, 2930, 2860, 1470, 1460, 1385, 1255, 1120, 1100, 1065, 840, 780, 720; ^1H NMR (300 MHz, C_6D_6) δ 5.77 (dd, J = 5.7, 3.3 Hz, 1 H), 5.63 (dd, J = 5.7, 3.1 Hz, 1 H), 5.31 (s, 1 H), 5.21 (s, 1 H), 3.92 and 3.18 (AB J = 10.2 Hz, 2 H), 2.84–2.82 (m, 1 H), 2.63–2.54 (m, 3 H), 2.39 (dd, J = 13.2, 3.4 Hz, 1 H), 2.05–1.98 (m, 2 H), 1.93 (d, J = 13.2 Hz, 1 H), 1.87 (s, 3 H), 1.49–1.37 (m, 2 H), 1.06 (d, J = 6.9 Hz, 3 H), 1.03 (t, J = 7.3 Hz, 3 H), 0.96 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 150.61, 135.80, 133.34, 125.67, 81.33, 74.56, 67.41, 57.57, 56.34, 47.35, 42.50, 40.12, 36.64, 26.70, 26.13 (3 C), 23.24, 18.53, 12.53, 12.05, -5.22 (2 C); MS, m/z ($M^+ - SCH_3$ and H_2O) calcd 343.2457, obsd 343.2474.

46b: IR (neat, cm^{-1}) 3420, 2960, 2930, 2860, 1470, 1460, 1380, 1255, 1120, 1095, 840, 775, 715; ^1H NMR (300 MHz, C_6D_6) δ 5.76–5.73 (m, 1 H), 5.63 (dd, J = 5.8, 3.0 Hz, 1 H), 5.40 (s, 1 H), 5.26 (s, 1 H), 3.92 and 3.78 (AB, J = 10.2 Hz, 2 H), 2.78 (s, 1 H), 2.65 (s, 1 H), 2.50 (br s, 1 H), 2.35–2.21 (m, 3 H), 2.10–1.97 (m, 4 H), 1.85 (s, 3 H), 1.15 (t, J = 7.3 Hz, 3 H), 1.08 (d, J = 6.9 Hz, 3 H), 0.96 (s, 9 H), 0.35 (s, 3 H), 0.21 (s, 3 H); MS, m/z (M^+) calcd 408.2519, obsd 408.2506.

For **48a**/**49a**: 55.7% yield with 30.7% recovery of **19b**.

48a: IR (neat, cm^{-1}) 3440, 2960, 2925, 2860, 1470, 1460, 1255, 1120, 1090, 1070, 1050, 840, 775, 710; ^1H NMR (300 MHz, C_6D_6) δ 5.93 (dd, J = 8.6, 5.6 Hz, 1 H), 5.88 (dd, J = 5.7, 2.7 Hz, 1 H), 5.19 (s, 1 H), 4.35 and 4.20 (AB, J = 11.0 Hz, 2 H), 2.91 (s, 1 H), 2.73 (s, 1 H), 2.65 (s, 1 H), 2.58–2.54 (m, 1 H), 2.29–2.20 (m, 2 H), 2.11 (dd, J = 13.0, 3.4 Hz, 1 H), 1.90 (s, 3 H), 1.87–1.76 (m, 1 H), 1.79 (d, J = 12.7 Hz, 1 H), 1.47–1.40 (m, 2 H), 1.03 (s, 9 H), 0.90 (t, J = 7.4 Hz, 3 H), 0.87 (d, J = 7.0 Hz, 3 H), 0.18 (s, 3 H), 0.15 (s, 3 H); ^{13}C NMR (75 MHz C_6D_6, ppm) 152.60, 136.48, 134.86, 126.14, 80.28, 76.35, 67.25, 59.89, 50.86, 47.82, 40.56, 39.72, 36.11, 26.16 (3 C), 21.31, 18.59, 15.46, 14.84, 12.77, -5.01, -5.18; MS, m/z ($M^+ - SCH_3$) calcd 361.2563, obsd 361.2588.

49a: IR (neat, cm^{-1}) 3460, 2960, 2945, 2860, 1470, 1460, 1380, 1360, 1260, 1120, 1090, 1050, 840, 780, 710; ^1H NMR (300 MHz, C_6D_6) δ 5.94–5.87 (m, 2 H), 5.31 (s, 1 H), 4.31 and 4.18 (AB, J = 11.1 Hz, 2 H), 2.94 (s, 1 H), 2.80 (s, 1 H), 2.64 (s, 1 H), 2.35 (br s, 1 H), 2.25–1.91 (series of m, 4 H), 1.88 (s, 3 H), 1.87–1.66 (m, 3 H), 1.02 (s, 9 H), 0.97 (d, J = 6.9 Hz, 3 H), 0.96 (t, J = 7.5 Hz, 3 H), 0.18 (s, 3 H), 0.13 (s, 3 H); MS, m/z ($M^+ - SCH_3$) calcd 361.2563, obsd 361.2524.

For **48b**/**49b**: 54% yield with 19% recovery of **20b**.

48b: IR (neat, cm^{-1}) 3410, 2955, 2930, 2880, 2860, 1470, 1460, 1385, 1255, 1120, 1100, 1070, 840, 780, 720; ^1H NMR (300 MHz, C_6D_6) δ 5.91 (dd, J = 5.7, 3.4 Hz, 1 H), 5.75 (dd, J = 5.7, 3.1 Hz, 1 H), 5.40 (s, 2 H), 4.03 and 3.88 (AB, J = 10.2 Hz, 2 H), 3.02–2.99 (m, 1 H), 2.95 (s, 1 H), 2.75 (s, 1 H), 2.52–2.44 (m, 3 H), 2.27–2.21 (m, 1 H), 2.09–2.05 (m, 1 H), 1.98 (s, 3 H), 1.75–1.66 (m, 2 H), 1.15 (t, J = 7.4 Hz, 3 H), 1.07 (s, 9 H), 1.05 (d, J = 4.1 Hz, 3 H), 0.14 (s, 3 H), 0.13 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 150.89, 135.54, 133.55, 126.52, 81.83, 74.51, 67.40, 57.15, 50.86, 47.31, 42.27, 39.86, 36.14, 26.13 (3 C), 21.33, 18.53, 15.61, 12.88, 12.54, -5.21 (2 C); MS, m/z ($M^+ - CH_3SH$) calcd 360.2484, obsd 360.2480.

49b: IR (neat, cm^{-1}) 3420, 3060, 2960, 2930, 2860, 1470, 1460, 1390, 1255, 1120, 1090, 840, 780, 720; ^1H NMR (300 MHz, C_6D_6) δ 5.75 (dd, J = 5.7, 3.2 Hz, 1 H), 5.64 (dd, J = 5.6, 3.0 Hz, 1 H), 5.39 (s, 1 H), 5.24 (s, 1 H), 3.92 and 3.78 (AB, J = 10.2 Hz, 2 H), 2.79–2.78 (m, 1 H), 2.65 (s, 1 H), 2.49 (br s, 1 H), 2.35–2.21 (m, 3 H), 2.10–2.00 (m, 4 H), 1.86 (s, 3 H), 1.14 (t, J = 7.4 Hz, 3 H), 1.08 (d, J = 6.9 Hz, 3 H), 0.96 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); MS, m/z (M^+) calcd 408.2518, obsd 408.2491.

Anionic Oxy-Cope Rearrangement of the Adducts to 19b and 20b. A. Ketone 44. A solution of **42a** (50 mg, 0.123 mmol) and triphenylmethane (1 mg) in anhydrous tetrahydrofuran (1.5 mL) was blanketed with nitrogen and cooled to -20 °C. TMEDA (0.5 mL) was added, and the reaction mixture was titrated with n-butyllithium until a pink color persisted. Stirring was maintained at -20 °C for 4 h prior to quenching with water. The product was extracted into ether, and the combined ether layers were washed with brine, dried, and evaporated. The residual oil was purified by MPLC on silica gel (elution with 6% ethyl acetate in petroleum ether) to give 42.2 mg (84%) of **44**, a colorless oil; IR (neat, cm^{-1}) 2940, 2920, 2860, 1740, 1700, 1470, 1460, 1370, 1360, 1240, 1100, 1050, 910, 840, 780, 740; ^1H NMR (300 MHz, $CDCl_3$) δ 5.82 (dd, J = 5.7, 2.1 Hz, 1 H), 5.49 (dd, J = 5.7, 2.6 Hz, 1 H), 3.82 and 3.78 (AB, J = 1.07 Hz, 2 H), 3.25–3.20 (m, 1 H), 2.97 (t, J = 13.3 Hz, 1 H), 2.82–2.73 (m, 2 H), 2.69–2.59 (m, 2 H), 2.48–2.38 (m, 2 H), 1.96 (s, 3 H), 1.59 (s, 1 H), 1.52–1.46 (m, 3 H), 1.46–1.25 (m, 4 H), 0.88 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 215.76, 134.55, 131.92, 66.13, 65.44, 52.67, 47.87, 46.54, 44.89, 44.82, 43.61, 39.93, 38.49, 32.26, 28.87, 26.95, 25.90 (3 C), 18.37, 11.66, -5.41, -5.53; MS, m/z ($M^+ - SCH_3$) calcd 359.2406, obsd 359.2406.

B. Ketone 47. Comparable anionic oxy-Cope rearrangement of **45a** (94.7 mg, 0.23 mmol) afforded after MPLC 64.2 mg (68%) of **47** as a colorless oil: IR (CH_2Cl_2, cm^{-1}) 2940, 2920, 2850, 2840, 1700, 1410, 1085, 1070, 830; ^1H NMR (300 MHz, $CDCl_3$) δ 5.77 (dd, J = 5.7, 2.1 Hz, 1 H), 5.51 (dd, J = 5.7, 2.5 Hz, 1 H), 3.81 and 3.79 (AB, J = 10.7 Hz, 2 H), 3.24–3.20 (m, 1 H), 2.78–2.60 (m, 3 H), 2.45–2.41 (m, 1 H), 2.19–2.15 (m, 1 H), 1.96 (s, 3 H), 1.58–1.34 (m, 6 H), 1.03 (t, J = 7.1 Hz, 3 H), 0.96 (d, J = 6.1 Hz, 3 H), 0.88 (s, 9 H), 0.05 (s, 6 H); MS, m/z ($M^+ - SCH_3$) calcd 361.2563, obsd 361.2538.

C. Ketone 50a. Anionic oxy-Cope rearrangement of **48a** (513 mg, 1.3 mmol) at -20 °C as before afforded 350 mg (68%) of **50a** as a colorless solid: mp 83–83.5 °C; IR (neat, cm^{-1}) 2950, 2920, 2850, 1700, 1460, 1375, 1360, 1250, 1220, 1090, 1005, 840, 780; ^1H NMR (300 MHz, $CDCl_3$) δ 5.83 (dd, J = 5.7, 1.9 Hz, 1 H), 5.55 (dd, J = 5.7, 2.8 Hz, 1 H), 3.81 (s, 2 H), 3.37 (t, J = 8.2 Hz, 1 H), 2.92 (t, J = 13.6 Hz, 1 H), 2.77–2.68 (m, 1 H), 2.59–2.51 (m, 1 H), 2.46–2.34 (m, 2 H), 2.20–1.96 (m, 3 H), 1.99 (s, 3 H), 1.68–1.57 (m, 1 H), 1.39–1.27 (m, 2 H), 0.98 (t, J = 7.2 Hz, 3 H), 0.88 (s, 9 H), 0.77 (d, J = 6.6 Hz, 3 H), 0.06 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 212.21, 134.55, 132.13, 66.19, 65.40, 51.68, 50.65, 47.22, 45.37, 40.35, 40.20, 38.10, 34.24, 26.09 (3 C), 20.74, 19.27, 18.51, 14.28, 11.99, -5.35 (2 C); MS, m/z ($M^+ - SCH_3$) calcd 361.2563. obsd 361.2599.

D. Ketone 50b. The anionic oxy-Cope rearrangement of **48b** (93.7 mg, 0.23 mmol) was performed analogously, although at 0 °C to achieve a comparable rate. MPLC on silica gel afforded 71.6 mg (76.4%) of **50b** after chromatographic purification: IR (neat, cm^{-1}) 2920, 2900, 2830, 1680, 1400, 1390, 1365, 1240, 1080, 990, 920, 820, 760; ^1H NMR (300 MHz, C_6D_6) δ 5.55 (dd, J = 5.7, 2.0 Hz, 1 H), 5.51 (dd, J = 5.7, 1.9

Hz, 1 H), 3.61 and 3.56 (AB, J = 10.0 Hz, 2 H), 3.25 (t, J = 12.3 Hz, 1 H), 3.01-2.98 (m, 1 H), 2.78-2.68 (m, 1 H), 2.51 (dd, J = 14.2, 7.2 Hz, 1 H), 2.27 (t, J = 6.9 Hz, 1 H), 2.04-1.98 (m, 2 H), 1.91-1.78 (m, 3 H), 1.76 (s, 3 H), 1.67-1.61 (m, 1 H), 1.43-1.38 (m, 1 H), 1.12 (t, J = 7.1 Hz, 3 H), 0.94 (s, 9 H), 0.86 (d, J = 7.1 Hz, 3 H), 0.01 (s, 6 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 213.17, 134.88, 132.75, 69.46, 66.51, 52.86, 50.83, 46.26, 42.99, 41.96, 41.71, 37.25, 34.51, 26.04 (3 C), 21.00, 19.24, 18.47, 14.22, 12.45, -5.25, -5.32; MS, m/z ($M^+ - SCH_3$) calcd 361.2562, obsd 361.2561.

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Kinetic Resolution during Condensation of Chiral (Racemic) Cyclopentenyllithiums with (*R*)-(-)-Isopiperitenone. A Short Route to Optically Active Annulated Germacranolides

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Abstract: (*R*)-(-)-Isopiperitenone (**1**) has been reacted with a selection of chiral, racemic cyclopentenyllithium reagents in different stoichiometric proportions. The working principle is developed that a 3:1 ratio of RLi to **1** is most serviceable for simultaneously maximizing the level of kinetic resolution and yield of 1,2-addend. The product distributions in this step, which are characterized by low diastereoselectivity ratios, correlate well with the balance of steric impedance offered by **1** to the attacking nucleophile in the two competing transition states. Oxyanionic Cope rearrangement of these alcohols is distinguished by a very high level of stereocontrol resulting from adoption of a single chairlike transition state in every example. Assignment of absolute stereochemistry in each instance is thereby made with relative ease. The overall scope and promise of this methodology is commented upon.

Stereochemical analysis of the 1,2-addition of a chiral vinyl organometallic reagent to a chiral β,γ-unsaturated ketone reveals that a minimum of *eight* diastereomeric products can result unless π-face selectivity is brought under strict control.[2] When this is accomplished, usually by the simple tactic of steric blockade of one prochiral surface in the electrophile, the capacity for generating diastereomeric alcohols is halved. Furthermore, as shown in the preceding paper,[2] appreciable levels of diastereoselectivity are also capable of operating when the enone is conformationally rigid, such that one racemic product often dominates substantially over the second.

The earlier study was carried out with nonresolved reaction partners. Under these circumstances, 1:1 stoichiometry can be employed because *double diastereoselection* operates. Thus, if the situation happens to be one where the (*R*)-vinyllithium reacts preferentially with the (*S*) enantiomer of the ketone, the (*S*)-(*R*) condensation must proceed concomitantly and be governed by the identical second-order rate constant. The (*R*)-(*R*) and (*S*)-(*S*) processes are likewise defined by a different, but mutually identical k.[3] Whatever the actual specific detail, the two enantiomers of both reagents are consumed with equal rapidity.

In contrast, if either reagent is utilized in optically pure condition and significant levels of diastereomeric recognition are operative, the rates at which the (*R*) and (*S*) forms of the racemic coreactant are depleted from the reaction mixture will differ. Once one enantiomer is consumed to an appreciable level, the diastereomeric excess in product alcohol will necessarily begin to drop rapidly as the second enantiomer enters into covalent bonding. Under these circumstances, 1:1 stoichiometry is clearly ill-advised. From the preparative viewpoint, the most desirable facet of this chemistry is to realize the maximum yield of optically active product. The question arises as to what stoichiometry will routinely achieve this end result.

The focal point of the present study is (*R*)-(-)-isopiperitenone (**1**), which itself is readily available by oxidation of (*S*)-(-)-limonene.[4] Because of its conformationally mobile isopropenyl substituent, **1** represents a somewhat less than ideal substrate.[5] However, its availability in large quantity and Still's earlier successful deployment of **1** in an oxy-Cope strategem[6] suggested that this optically active ketone would otherwise serve our purposes well. The feasibility of kinetic resolution and the rapid construction of chiral, nonracemic annulated germacranolides combine to justify the outline of the conceptual scheme.

Results

Condensation Reactions. At the outset, two batches of **1** were prepared, and the individual lots exhibited $[\alpha]_D$ values in chloroform of -41.8° and -44.8°. Since the maximum rotation reported for (+)-isopiperitenone in this solvent happens to be +48.7°,[7] our samples were considered to possess 71.6 and 83.8% ee, respectively. The vinyl bromides have previously been described, with the exception of **6**. Shapiro degradation of the tosylhydrazone of 2-isopropylcyclopentanone[8] and quenching of the resulting vinyl anion with 1,2-dibromotetrafluoroethane[9,10] allowed ready access to this reagent. In the generalized procedure,

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