# Articles

## Model for Diastereomer Differentiation during 1,2-Addition of Chiral (Racemic) Cyclopentenyl Organometallics to [4.2.0] Bicyclic Enones Carrying Exocyclic $\beta,\gamma$-Double Bonds

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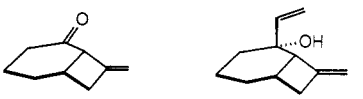
The level of diastereoselection operative during 1,2-addition of several chiral 1-cyclopentenyl dichlorocerate reagents to five differently substituted *cis*-8-methylenebicyclo[4.2.0]octan-2-ones has been evaluated. The extent of intermolecular recognition reaches a maximum in the case of **8**, which displays quite good selectivity for formation of alcohols in which the proximal cyclopentene substituent is $\alpha$-oriented. Ketones **4** and **5** also display a partiality for "$\alpha$-alcohol" formation, although to a more attenuated level. In contrast, parent ketone **1** is $\beta$-selective, and **3** exhibits a mixed product distribution depending upon the substitution pattern in the nucleophile. The structural assignments to the many alcohols were arrived at by a combination of two techniques. Anionic oxy-Cope rearrangement of these oils gave crystalline ketones, the stereochemistries of which were established by X-ray crystallography in four examples. This information then made apparent a diagnostic $^1$H NMR correlation involving the individual cyclopentenyl olefinic and allylic cyclobutyl protons when the alcohols were dissolved in benzene-$d_6$. The data allow for a transition-state model to be formulated that is consistent with the greater diastereomeric discriminatory power of substituents positioned in the vicinity of the four-membered ring. From the synthetic viewpoint, the method constitutes a short and enormously powerful means for crafting macroring ketones having several well-defined stereogenic centers.

The onset of molecular recognition during 1,2-addition of chiral vinyl organometallics to chiral $\beta,\gamma$-unsaturated ketones holds considerable interest[2] in the context of stereoselective alicyclic[3] and heterocyclic synthesis.[4] When nucleophilic attack at the carbonyl center is relegated to one prochiral surface (usually because of its particular steric environment), stereochemical relationships are developed that can be effectively deployed for setting less readily accessible stereogenic centers simply by subjecting the alcohol to oxyanionic Cope rearrangement.[5] One objective of our research in this area, required to support applications in natural product synthesis, has been to develop a detailed appreciation of the control elements at play during nucleophilic capture by the carbonyl $\pi$ bond. To the extent that the developing diastereomeric relationships can be anticipated on an a priori basis, the latent synthetic potential of this two-step process can be implemented with increasing predictability.

From among the numerous chiral $\beta,\gamma$-unsaturated ketone series worthy of consideration, *cis*-8-methylenebicyclo[4.2.0]octan-2-ones appeared to be well suited to our objectives. First of all, **1** and its congeners are readily accessible and share in common a structural definition that




**1** **2**

encourages kinetically more rapid nucleophilic capture from that direction anti to the methylenecyclobutane subunit. Second, the configurational stabilities of these ketones qualify them as substrates suitable for the evaluation of selective recognition patterns. Finally, Schreiber and co-workers have shown that stereochemical information present in simple vinylmagnesium bromide adducts such as **2** can be transmitted predictably via cyclic transition states to cyclodecenones possessing a cyclobutene bridgehead double bond.[6]

### Results

**The Ketonic Substrates.** In our selection of analogues of **1** for study, we were guided by the Bürgi–Dunitz model for the directionality of nucleophilic capture by the carbonyl group[7] and by Houk's more recent theoretical evaluation of this subject.[8] Thus, it seemed of greatest relevance to position one or more alkyl groups above and behind the carbonyl carbon in order to maximize the potential for useful diastereoselective interaction with the incoming nucleophile.

To this end, ketones **1**, **3**–**5**, and **8** became the focal points of the present study. The first of these is well-

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(4) (a) Oplinger, J. A.; Paquette, L. A. *Tetrahedron Lett.* **1987**, *28*, 5441. (b) Paquette, L. A.; Oplinger, J. A. *Tetrahedron* **1989**, *45*, 107.

(5) (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.

(6) (a) Schreiber, S. L.; Santini, C. *Tetrahedron Lett.* **1981**, *22*, 4651. (b) Schreiber, S. L.; Santini, C. *J. Am. Chem. Soc.* **1984**, *106*, 4038. (c) Schreiber, S. L.; Hawley, R. C. *Tetrahedron Lett.* **1985**, *26*, 5971.

(7) (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.

(8) Houk, K. N.; Wu, Y. In *Stereochemistry of Organic and Bioorganic Transformations*; Bartmann, W., Sharpless, K. B., Eds.; VCH Publishers: New York, 1987; pp 247–260.

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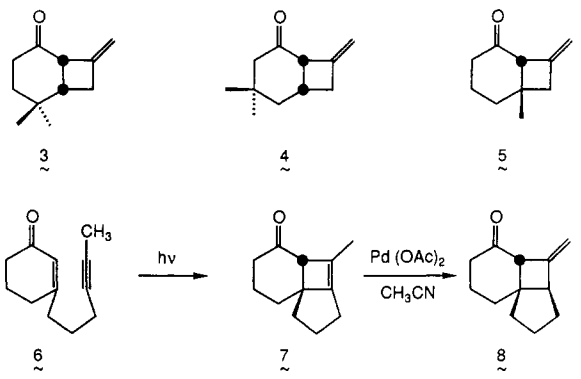
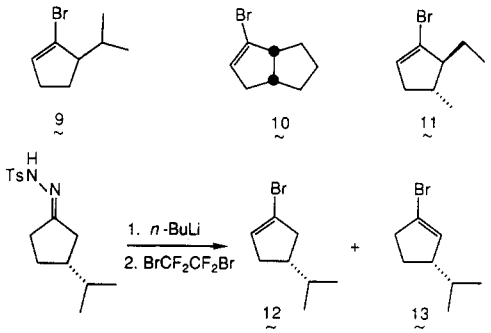



known, having been reported by Corey et al. as early as 1964.[9] Compounds **3–5** were synthesized analogously by photocycloaddition of allene to the appropriately substituted 2-cyclohexenone. The tricyclic system **8** was produced by the route recently described by Wang and Paquette.[10] Subsequent to the intramolecular [2 + 2] photocycloaddition of **6**, cyclobutene **7** was exposed to palladium(II) acetate in order to isomerize its double bond to the less strained exocyclic site.

**Preparation of the 1-Cyclopentenyl Nucleophiles.** The series of cyclopentenyl bromides **9–12** was utilized to probe the level of diastereoselective discrimination realizable with the predescribed ketones. In **9**, an isopropyl




group flanks the nucleophilic seat of reaction. Bromides **10** and **11** were selected because of their 4,5-disubstituted nature, **11** possessing a trans arrangement of its alkyl groups and **10** being cis annulated. The 4-isopropyl-substituted example **12** was available in optically active condition, thus allowing as well for possible kinetic resolution.[3f]

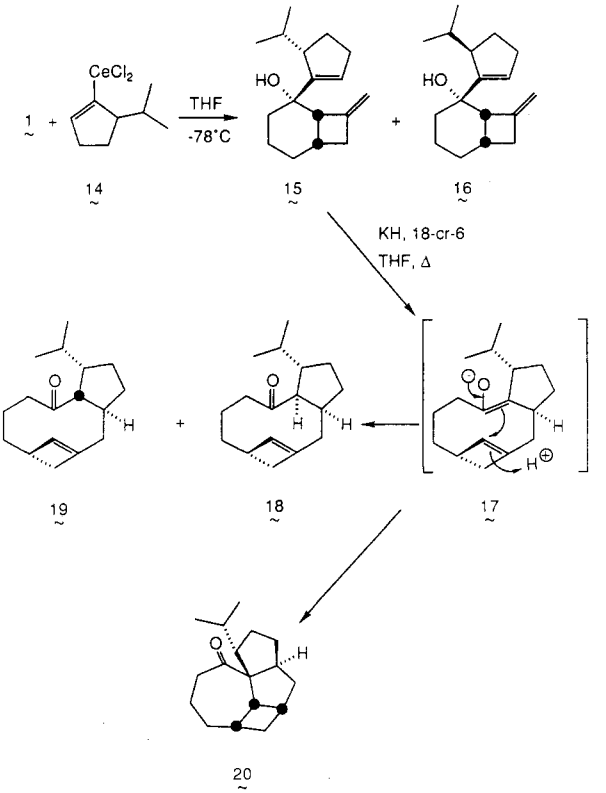
The first three vinyl bromides have been described previously.[3] When the tosylhydrazone of (*R*)-(+)-3-isopropylcyclopentanone[11] was subjected to the Shapiro reaction[12] and the resulting anions were quenched with 1,2-dibromo-1,1,2,2-tetrafluoroethane,[13] **12** and **13** were produced in a 97:3 ratio. Although two $\alpha$-methylene sites are available for deprotonation during this degradation, excellent regioselectivity is achieved presumably as the direct result of steric hindrance provided by the pendant alkyl substituent.

When probe experiments involving 1-lithio-5-isopropylcyclopentene and **1** gave relatively low yields of alcohol products because of excessive competing enolization, recourse was made instead to the dichlorocerium reagent, prepared in situ by reaction of the RLi species with anhydrous cerium trichloride.[14] For reasons of consistency and in order to maximize conversion to the alcohols, attention was paid thereafter only to the use of vinyl dichlorocerium reagents.

**Condensation Reactions Involving 1.** In each of the experiments described below, special care was taken to use freshly distilled tetrahydrofuran solvent, to drive off water from $CeCl_3 \cdot 7H_2O$ under high vacuum in a consistent fashion (140–150 °C, 0.1 Torr, 2 h), to reproduce reaction time and temperature, and to quench the reaction mixtures identically on every occasion. Details of the generalized procedure are given in the Experimental Section.

Parent compound **1** was reacted with two of the designated organocerium reagents. Studies at a comparable level were performed on the other ketones; however, **10** was coupled with all five ketones in order to effect a calibration. Table I summarizes all of the available data.

The condensation of **1** with **14** gave, as expected, a mixture of the two diastereomeric alcohols **15** and **16**.




HPLC analysis of three runs showed **16** to dominate over **15** by a factor of 2.5:1. Although pure samples of these oily alcohols could readily be obtained by medium-pressure chromatography, assignment of relative stereochemistry in these initial examples was nontrivial. Attempts to distinguish between them by $^1H$ NMR techniques were not satisfying because of the lack of information concerning the preferred conformations of the diastereomers. Similarly, it was not feasible to make reliable deductions on the basis of $^{13}C$ NMR data.

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(10) Wang, T.-Z.; Paquette, L. A. *J. Org. Chem.* **1986**, *51*, 5232.
(11) (a) Naves, Y. R. *Bull. Soc. Chim. Fr.* **1958**, 1372. (b) Huckel, W.; Bross, R. *Justus Liebigs Ann. Chem.* **1963**, *644*, 1.
(12) (a) Shapiro, R. H. *Org. React. (N.Y.)* **1975**, *23*, 405. (b) Taylor, R. T.; Degenhardt, C. R.; Melega, W. P.; Paquette, L. A. *Tetrahedron Lett.* **1977**, 159. (c) Chan, T. H.; Baldassarre, A.; Massuda, D. *Synthesis* **1976**, 801. (d) Chamberlin, A. R.; Stemke, J. E.; Bond, F. T. *J. Org. Chem.* **1978**, *43*, 147. (e) Paquette, L. A.; Fristad, W. E.; Dime, D. S.; Bailey, T. R. *Ibid.* **1980**, *45*, 3017. (f) Barth, W.; Paquette, L. A. *Ibid.* **1985**, *50*, 2438.
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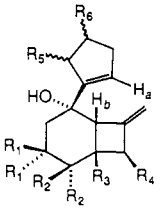
(14) (a) Imamoto, T.; Sugiura, Y.; Takiyama, N. *Tetrahedron Lett.* **1984**, *25*, 4233. (b) Imamoto, T.; Sugiura, Y. *J. Organomet. Chem.* **1985**, *285*, C21. (c) Imamoto, T.; Takiyama, N.; Nakamura, K. *Tetrahedron Lett.* **1985**, *26*, 4763.

**Table I. Diastereoselectivity Ratios**[a]

| $RCeCl_2$ | 1 | 3 | 4 | 5 | 8 |
|---|---|---|---|---|---|
| 14 | **15/16**<br>1:2.7 (65, 76)<br>1:2.4 (62, 76)<br>1:2.5 (68, 79)<br>av 1:2.5 | **28/29**<br>2.1:1 (60, 74)<br>1.5:1 (69, 89)<br>1.6:1 (65, 92)<br>av 1.7:1 | **43a/44a**<br>1.1:1 (40, 85)<br>1.2:1 (69, 87)<br>av 1.1:1 | **45/46**<br>5.4:1 (83)[b]<br>6.2:1 (85)[b]<br>av 5.8:1 | **51a/52a**<br>10.7:1 (77, 86)<br>9.5:1 (56, 85)<br>9.1:1 (77, 81)<br>av 9.8:1 |
| 23 | **24/25**<br>1:1.4 (59, 77)<br>1:1.35 (54, 75)<br>av 1:1.4 | **33/34**<br>1:1.6 (67, 98)<br>1.1.5 (67, 91)<br>av 1:1.6 | α-rich | | **55/56**<br>6.6:1 (68, 81)<br>6.6:1 (76, 89)<br>av 6.6:1 |
| 37 | β-rich | **38/39**<br>1:2.3 (77, 81)[b]<br>1:2.3 (83, 87)[b]<br>av 1:2.3 | | **47/48**<br>3.1:1 (79)<br>3.1:1 (87)<br>av 3.1:1 | |
| 42 | | | **43b/44b**<br>1.03:1 (46, 79)<br>1.1:1 (41, 86)<br>av 1.1:1 | | **51b/52b**<br>1.2:1 (22, 78)[b]<br>1.2:1 (18, 76)[b]<br>av 1.2:1 |

[a] The first number in parentheses is the isolated yield. The second, where given, is the yield based on recovered starting material. All ratios were determined by analytical HPLC except where indicated. [b] Ratio determined by 300- or 500-MHz $^1H$ NMR spectroscopy.

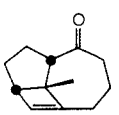
**Table II. Select $^1H$ NMR Chemical Shift Data for the Alcohols (300 MHz, $C_6D_6$ Solution)**




| diastereomer | series | chemical shift, δ $H_a$ | chemical shift, δ $H_b$ | diastereomer | series | chemical shift, δ $H_a$ | chemical shift, δ $H_b$ |
|---|---|---|---|---|---|---|---|
| **15** | α | 5.58–5.56 | 3.28–3.25 | **43b** | α | 5.51 | 3.28–3.08[a] |
| **16** | β | 5.45 | 3.14–3.10 | **44b** | β | | |
| **24** | α | 5.33 | 3.22–3.20 | **45** | α | 5.64–5.62 | 2.95–2.94 |
| **25** | β | 5.30 | 3.18–3.06 | **46** | β | 5.51 | 2.88–2.82 |
| **28** | α | 5.73 | 3.26–3.24 | **47** | α | 5.48 | 2.92 |
| **29** | β | 5.51 | 3.01–2.99 | **48** | β | 5.36 | 2.86 |
| **33** | α | 5.48–5.47 | 3.27–3.25 | **51a** | α | 5.60–5.58 | 2.90 |
| **34** | β | 5.37–5.36 | 3.11–3.02 | **52a** | β | 5.56–5.54 | 2.86–2.80 |
| **38** | α | 5.54 | 3.28–3.22 | **51b** | α | 5.52–5.51 | 4.88–4.87[a] |
| **39** | β | 5.34 | 3.04–3.01 | **52b** | β | | |
| **43a** | α | 5.69 | 3.32–3.27 | **55** | α | 5.40 | 3.27–3.08 |
| **44a** | β | 5.44 | 3.19–3.13 | **56** | β | 5.40 | 3.16–3.11 |

[a] Inseparable mixtures.

Consequently, **15** was subjected to anionic oxy-Cope rearrangement. With potassium hydride as the base, a mixture of **18** (77%) and **19** (8%) was realized. Since pure **18** proved to be nicely crystalline, its structure was confirmed unequivocally by X-ray methods (see below). A rather unanticipated result occurred when **15** was heated instead with potassium hexamethyldisilazide in tetrahydrofuran. Under these circumstances, **18** was again obtained (67%); however, the companion product now proved to be a saturated tetracyclic ketone. This compound has been tentatively identified as **20**, chiefly on the strength of its spectral similarities to **21** and **22**, ketones that have been isolated in an independent study.[15] The



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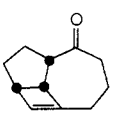

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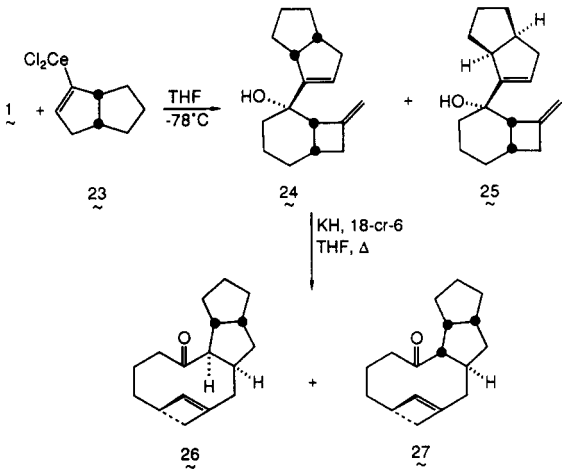
interdependency of base and tetracyclic product formation is not understood at present. On the other hand, the **18**:**19** ratio rests instead on the direction of protonation of intermediate anion **17**. Indeed, this product distribution can be altered simply by introducing modifications in the workup procedure (e.g., inverse quench).

The results obtained with **23** compare closely to those realized in the condensation involving **14**, since the so-called "β-stereoisomeric alcohol" still predominates (**24**:**25** = 1:1.4). These diastereomeric products were purified chromatographically, and **24** was transformed by potassium hydride promoted anionic Cope rearrangement into **26** (74%) and **27** (14%). At this point, we came to recognize that two proton resonances in each alcohol pair appeared to be diagnostic of the structural differences separating the two series, particularly when the spectra

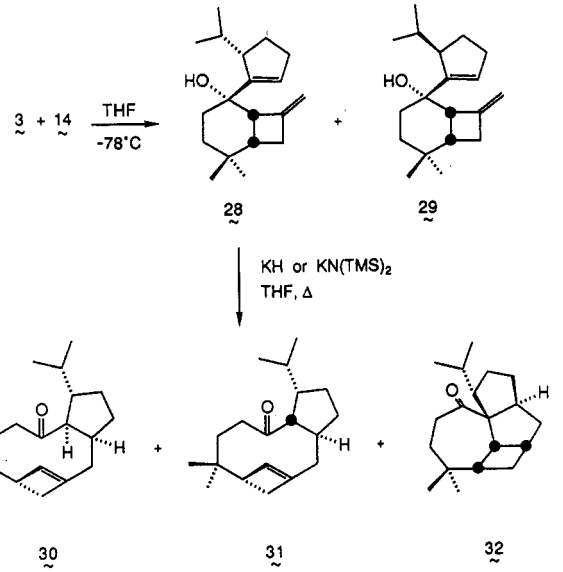
(15) Paquette, L. A.; Reagan, J.; Schreiber, S. L.; Teleha, C. A. *J. Am. Chem. Soc.* **1989**, *111*, 2331.




23 24 25 26 27

are recorded in benzene-$d_6$ solution. As matters will unfold in the sequel, an ordering pattern that correlates nicely with the relative configuration of the *proximal* cyclopentenyl substituent is seen to manifest itself. The compilation in Table II concisely reveals that the chemical shifts of the cyclopentenyl olefinic proton ($H_a$) when $R_5$ is $\alpha$-oriented experience a greater level of deshielding than when $H_5$ is situated $\beta$. Since magnetic anisotropy in the same direction is displaced by the allylic cyclobutyl proton $H_b$, the combination constitutes an entirely reliable tool for establishing stereochemistry in this series. Several additional crystallographic studies were performed subsequently in order to solidify the correlation. This overall systemization is workable presumably because all members within each series adopt conformational features that are mutually consistent.

**Coupling of 3 with Dichlorocerates 14, 23, and 37.** It was particularly striking to find that combining **3** with **14** gives rise to a diastereoselectivity preference for **28** over **29** (1.7:1). Thus, the pattern set by **1** is not followed when



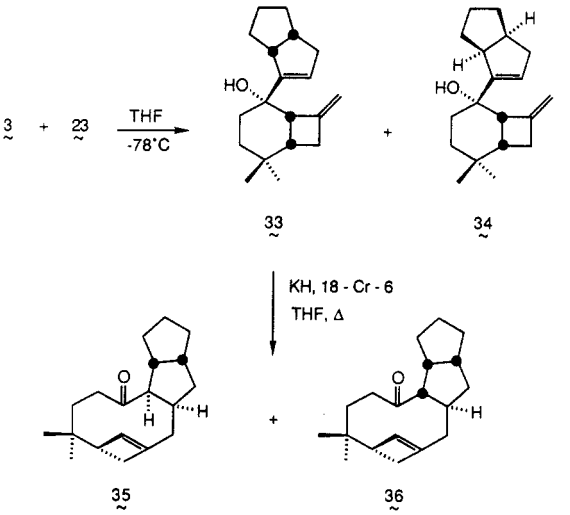

28 29 30 31 32

two geminal methyl groups are strategically positioned in the ketone. As before, these alcohols were easily purified, identified by appropriate spectral comparison (Table II), and in the case of major diastereomer **28**, caused to undergo [3,3] sigmatropic rearrangement.

In this instance, the influence of reaction conditions on the oxy-Cope product distribution was briefly examined. When potassium hexamethyldisilazide was employed, tetracyclic ketone **32** was formed predominantly (39%), alongside **30** (34%) and a trace of **31**. Remarkably, the use of potassium hydride resulted in a precipitous decrease in the amount of **32** formed (now only 3%). The proportionate increases in **30** and **31** were substantial, the more so with **30** (79% isolated).

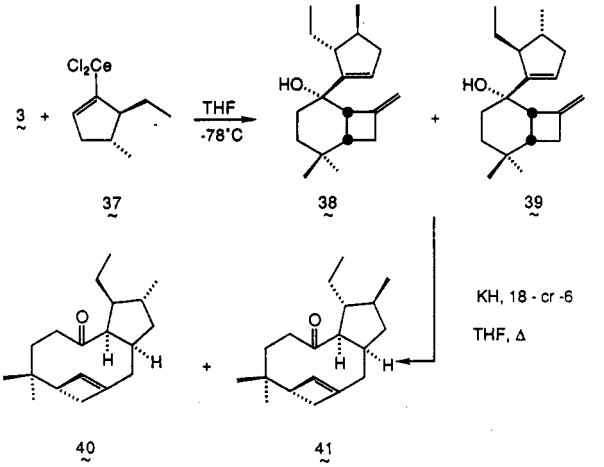
An additional accurate point of stereochemical reference was acquired by three-dimensional crystal structure analysis of **30** as discussed later.

The reaction of **3** with **23** was next examined. Relevantly, the distribution of resultant alcohols **33** and **34** (ratio 1:1.6) was seen to compare very closely to that determined earlier for **24** and **25**. These compounds were defined stereochemically by making recourse to their diagnostic $^1$H NMR signals (Table II). Stereochemical assignment to **35**, the major [3,3] sigmatropic partner of **34**, was addressed by X-ray analysis.




33 34 35 36

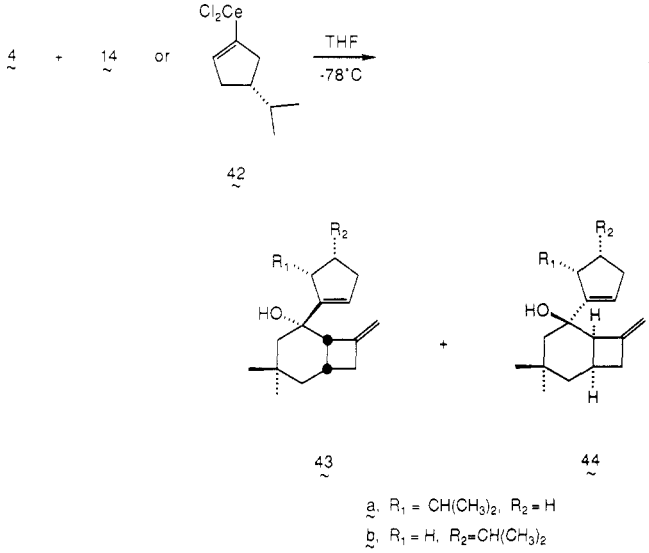
On the basis of this limited number of condensations, a crossover in preferred diastereoselectivity (relative to **1**) was seen to be operating during nucleophilic attack by **14**, but not by **23**. Consequently, it was considered desirable to evaluate the discriminatory capacity of **37**. Under the standard conditions, this reaction provided **38** and **39** as an inseparable 1:2.3 mixture, as determined by direct $^1$H NMR spectroscopic analysis (Table II). Thus, the trend established by **23** is mirrored in the response of **3** to nucleophilic attack by **37**.




37 38 39 40 41

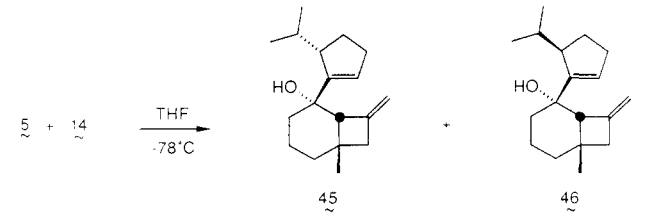
From a practical point of view, the **38**/**39** mixture could be rearranged directly to **40** and **41**. In turn, these crystalline diastereomers proved capable of ready chromatographic separation. Their stereochemical assignments rest on the premise that the major product of this efficient isomerization, viz., **40**, originates from the alcohol present in the greatest amount, i.e., **39**.

**Modifications in Diastereoselection Resulting from Alternative Placement of the *gem*-Dimethyl Group.** Why does placement of a *gem*-dimethyl array as in **3** cause formation of "β-stereoisomeric alcohols" (e.g., **34** and **39**) to be intrinsically favored except when the cyclopentenyl substituent is 5-isopropyl (**28** is preferred to **29**)? To explore this question, we investigated the diastereoselective response of **4**, a simple positional isomer of **3**. Rather strikingly, the product distributions determined for reaction of **4** with **14** and with **42** deviated only minimally from purely statistical! In either series, the proportion of the diastereomeric pair was only 1.1:1. Assignment of configuration to **43a** and **44a** could be derived from the previously established $^1$H NMR chemical shift correlations (Table II).



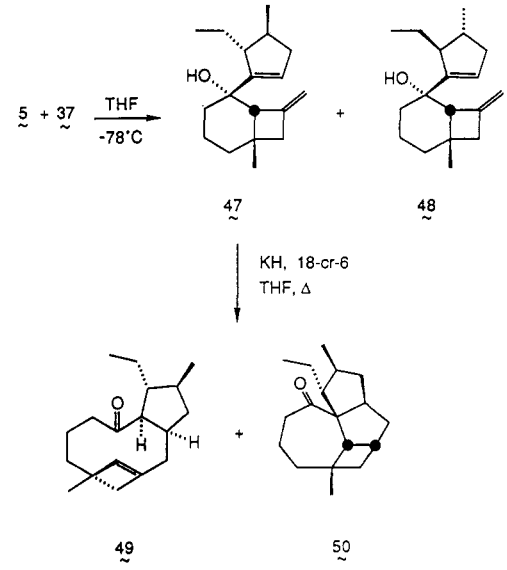

Although some vestige of preferred α-orientation of the pendant isopropyl group (as in **1**) remains, the decrease in intermolecular recognition during C–C bond formation can be taken as an indicator that appropriate steric biases do not surface in **4** because of increased distance from the trajectory of approach. Alternatively, of course, a fortuitous cancellation of effects might be involved. Clarification of this dichotomy would be realized by repositioning of the β-methyl substituent as in **5** and perhaps more dramatically by annulation as in **8**. To the extent that reasonably ordered transition states are involved and diastereoselectivity is controlled because of a penchant for nucleophilic attack from that direction above the site of ring fusion, then **5** and **8** would be expected to recognize diastereomeric differences to a magnified degree. Experimental support for this conclusion follows.

**The Consequences of Angular Methylation.** The addition of **14** to **5** was studied initially. Since the **45**:**46**




ratio was 5.8:1, it is clear that relocation of the methyl group as in **5** has a beneficial effect on that transition state involving coupling with α-orientation of the isopropyl side chain. In **45**, $H_a$ appears at δ 5.64–5.62 and $H_b$ materializes in the δ 2.95–2.94 range ($C_6D_6$ solution). Both signals appear downfield of those in **46** (δ 5.51 and 2.88–2.82, respectively) and reflect the fact by analogy that **45** belongs to the α-series (Table II).

In the condensation of **5** with dichlorocerate **37**, the pair of alcohols **47** and **48** were formed as a 3.1:1 mixture. The



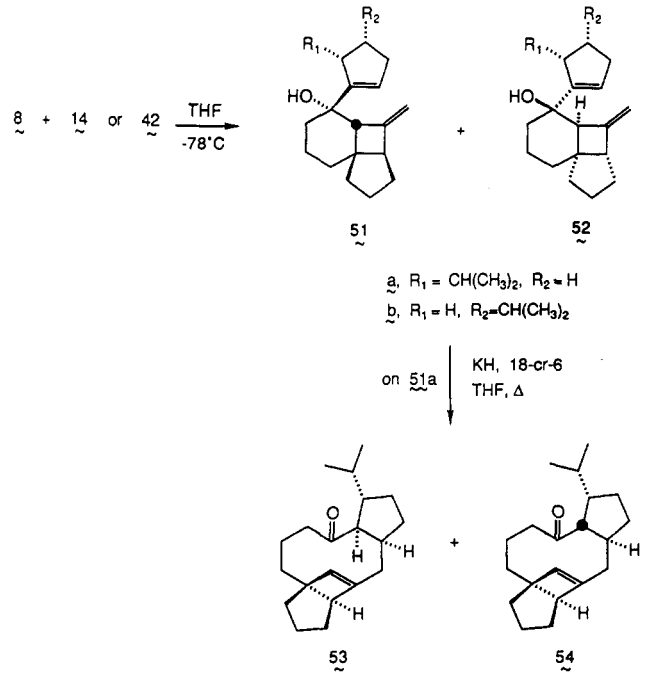

conclusion that the α-stereoisomeric product was again dominant was arrived at on the basis of comparative $^1$H NMR data (Table II). While attack by **37** proceeds preferentially with the same double diastereoselectivity as **14**, the controlling impact on the 5-isopropyl group is seen to be roughly twice as great as that provided by the *trans*-5-ethyl-4-methyl combination. The conformational mobility of isopropyl presumably generates an average substituent steric volume that provides **14** with increased steric bulk in the vicinity of its chiral center. To all appearances, a group as small as methyl positioned at C4 in the cyclopentenyl reagent finds little opportunity to steer the approaching nucleophile to minimize steric strain on one or the other π surface.

Heating **47** with potassium hydride in tetrahydrofuran afforded ketone **49** as expected (61%). However, the intermediate enolate anion in this instance also displays a reasonable penchant for cyclization to **50** (14% isolated).

**Trimethylene Bridge Directed Diastereoselection.** The special structural feature provided by **8** is its added trimethylene chain that effectively brackets one sector of the molecule. Since our experiments involving **5** gave reason to believe that **8** might well be capable of good diastereoselective discrimination, the decision was made to use this latent potential for the purpose of gaining more rigorous insight into the relative effectiveness of diastereocontrol by C4 and C5 substituents within the cyclopentenyl nucleophile. Accordingly, condensations involving **14** and **42** were initially compared.

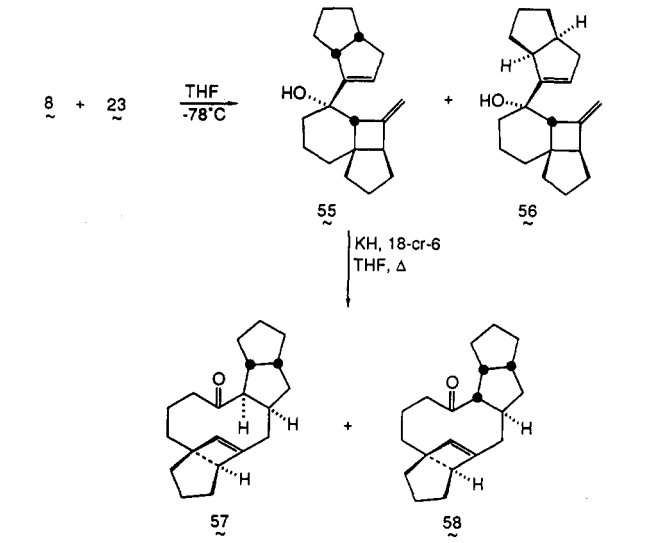
The effect of this change in location of the isopropyl side chain was remarkable. As revealed in Table I, the relative amounts of **51a** and **52a** averaged 9.8:1, this margin constituting the maximum selectivity realized in this study. On the other hand, the ratio in the **b** series was only 1.2:1. While the α- or β-stereoisomeric nature of the preferred diastereomer could not be defined precisely by $^1$H NMR (Table II), this issue is not of major consequence. What is clear is that the remote 4-isopropyl group cannot compete as effectively as that located more proximal to the nucleophilic site.

The structural assignments to **51a** and **52a** are based on $^1$H NMR spectroscopic data (Table II). In addition, **51a** was subjected to anionic oxy-Cope rearrangement, and




X-ray crystallography was used to establish the stereochemistry of **53**.[16]

Respectable diastereoselection returned in the reaction of **8** with **23**. The α-stereoisomeric alcohol, viz., **55**, was again the major diastereomer (ratio 6.6:1), and this product responded well to base-induced [3,3] sigmatropy, giving **57** (79%) and **58** (10%).




The foregoing results are nicely accommodated by the product ratios described earlier and allow an intuitively reasonable transition-state model to be deduced for the trajectory of nucleophilic attack at the carbonyl group of *cis*-8-methylenebicyclo[4.2.0]octan-2-ones (see Discussion).

**Summary of X-ray Crystallographic Studies.** Knowledge of the conformations adopted by molecules with internal strain has attracted considerable interest for many years. In the present instance, several bridgehead cyclobutenes were prepared by oxyanionic Cope rearrangement of oily alcohol precursors and advantage was taken of their crystallinity for achieving stereochemical definition by crystallography. These sigmatropic processes

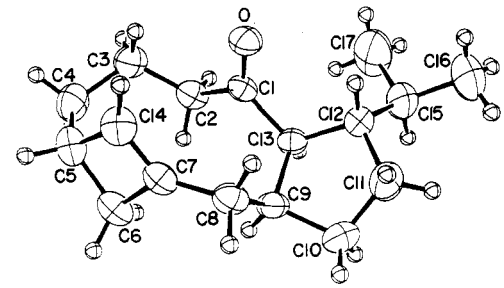


**Figure 1.** ORTEP drawing of **18** showing the numbering scheme. The non-hydrogen atoms are represented by 50% probability thermal ellipsoids. The hydrogen atoms are drawn with an artificial radius.

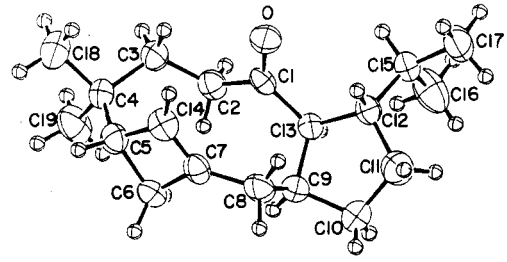


**Figure 2.** ORTEP diagram of **30**. See caption to Figure 1.

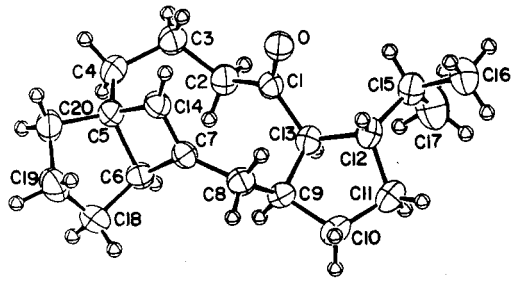


**Figure 3.** ORTEP diagram of **53**. See caption to Figure 1.

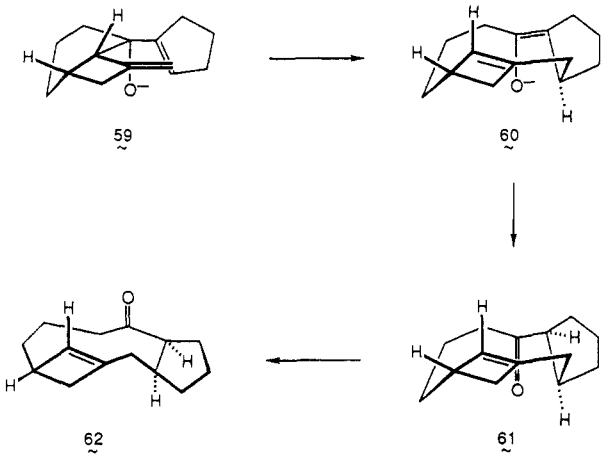
result in the dismantling of a methylenecyclobutane unit with migration of the double bond to a site internal to the four-membered ring. Configurational information is necessarily transferred and new stereogenic centers are formed during this electronic reorganization. Therefore, it is necessary to be informed as to whether a boat or chair transition state is adopted.[17,18]

Steric factors present in the bicyclo[4.2.0]octanones examined here combine with the relative bulk of the cyclopentenylcerium reagents to direct nucleophilic attack exclusively to the β face. Careful analysis of the spatial arrangement of the double bond in the resulting alcohols reveals that [3,3] sigmatropy can be implemented only if the chair conformation depicted by **59** is reached. The boat alternative does not bring the olefinic termini into adequate proximity. With matters thus unequivocally defined, passage via **59** to enolate anion **60** is followed (most often) by kinetically controlled protonation from the molecular exterior to give **61**. This conformation of the ketonic product is not thermodynamically favored, however, and facile realignment occurs to give the more extended arrangement **62**, which all four compounds examined crystallographically adopt.

The ORTEP diagrams of **18**, **30**, and **53** (Figures 1–3) nicely illustrate the trend. The crystallographic details for these ketones are compiled in Table III. Cyclobutene **35**

(16) The assignments in the **b** series are tenuous and could be reversed. However, in light of the near identical extent to which **51b** and **52b** are formed, precise stereochemical analysis was not pursued further.

(17) Hill, R. K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. III, Chapter 8.
(18) Ziegler, F. E. *Chem. Rev.* **1988**, *88*, 1423.



59 60 62 61

was obtained as twinned crystals. An initial analysis of the diffraction data for **35** indicated that all four molecules in the asymmetric unit adopt the same global geometry (the isotropic refinement converged at $R = 0.21$).

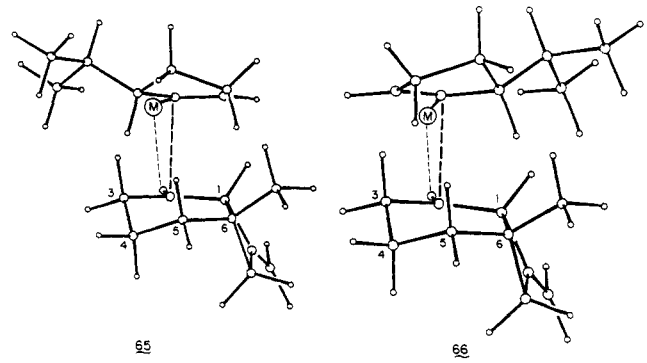
The geometric variations among the three experimentally determined structures are small, especially in light of the incremental peripheral substitution that materializes in progressing from **18** to **30** and ultimately to **53**. The syn relationship of the carbonyl oxygen and cyclobutene double bond has at least two significant consequences: (i) the transannular gap between the two functional groups is modestly compressed; transannular interaction is indeed apparent by infrared spectroscopy ($\nu_{CO}$ 1690–1705 $cm^{-1}$); (ii) in those isomers where the substituted cyclopentane is cis fused to the macroring, the five-membered cycle is projected diequatorially.

To facilitate a comparison of the geometries of the three ketones, the core atoms common to all three structures are numbered identically as shown in the figures. The atoms peripheral to the core are numbered arbitrarily. Table IV contains a list of bond lengths, while Table V is a compilation of bond angles for this series.

## Discussion

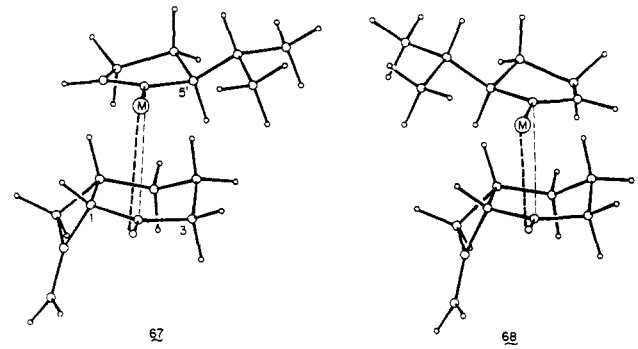
The structural requirements within the 8-methylenebicyclo[4.2.0]octan-2-one most conductive to good diastereoselectivity are best met by 6-methyl substitution as in **5** and especially five-membered-ring annulation across C6 and C7 as in **8**. Intramolecular recognition is highest when the cyclopentenyl nucleophile carries an isopropyl group at C5. The foregoing results reveal further that ketones **3–5**, and **8** all prefer to enter into covalent bonding with **14** along that reaction trajectory that finds isopropyl to be $\alpha$-oriented in the product (Table I). The reverse is true for **1**, which actually gives evidence of responding uniformly to cyclopentenyl nucleophiles in the opposite stereochemical sense. Thus, the preference in this instance is to deliver the "$\beta$-alcohol" predominantly. Particularly unique is the crossover in diastereoselectivity displayed by **3** when progressing from reaction with **14** ($\alpha$-rich) to condensation with **23** and **27** ($\beta$-rich).

As a basis for rationalizing these interesting differentiation patterns, recourse has been made to energy minimization of the conformers of **1** and **3–5** through use of Still's MODEL program (version KS 2.92).[19] Each of these ketones was found to adopt three conformations of closely comparable steric energy as summarized in Table VI.



65 66

**Figure 4.** Diastereomeric transition state models for the addition of **14** to **5** (shown) and **4** (delete C6 methyl and add a pair of methyl groups at C4). The intermolecular distance has been arbitrarily selected.

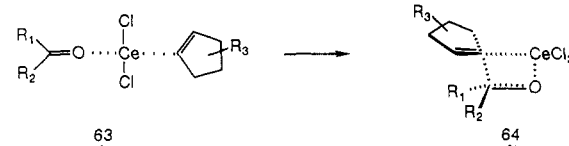


67 68

**Figure 5.** Diastereomeric transition state models for the capture of **14** by **1**. The intermolecular distance has been arbitrarily selected.

Since the interconversions involved are of the simple chair $\rightleftarrows$ half-chair $\rightleftarrows$ chair type, the relative activation energies for passage from one spatial arrangement to the other can be assumed to be lower than any $\Delta H^{\ddagger}$ associated with attack by one of the dichlorocerium reagents.[8] Consequently, our model combines this information with overall qualitative minimization of *intermolecular* steric interaction to define the preferred matched diastereomer relationship. Also, the cerium species is depicted as monomeric, although this is not likely to be so.

As usual for organometallic reactions, a complex of type **63** with the cerium coordinated to oxygen likely materializes first.[20] This event is followed by formation of a



63 64

four-centered transition state (**64**) whose energy is similar to that of the reactants. During the progression from **63** to **64**, the inherent ability of the particular ketone molecule to exercise its preference for engaging the *R* or *S* form of the chiral nucleophile develops rapidly and impacts on the $\Delta H^{\ddagger}$'s of the two competing reactions.

The particular transition-state conformation adopted by the cyclohexanone ring in **4** and **5** is believed to be as shown in **65** and **66** (Figure 4). An important geometry-determining feature is the lessening of nonbonded steric interference to the proximal C4 substituent (a methyl

(19) (a) Still, W. C.; MacPherson, L. J.; Harada, T.; Rheingold, A. *Tetrahedron* **1984**, *40*, 2275. (b) Still, W. C.; Galynker, I. *Ibid.* **1981**, *37*, 3981.

(20) (a) Houk, K. N.; Rondan, N. G.; Schleyer, P. von R.; Kaufmann, E.; Clark, T. *J. Am. Chem. Soc.* **1985**, *107*, 2821. (b) Kaufmann, E.; Schleyer, P. von R.; Houk, K. N.; Wu, Y.-D. *Ibid.* **1985**, *107*, 5560.

**Table III. Crystallographic Data for Cyclobutene Bridgehead Olefins 18, 30, and 53[a]**

| | 18 | 30 | 53 |
|---|---|---|---|
| formula | $C_{17}H_{26}O$ | $C_{19}H_{30}O$ | $C_{20}H_{30}O$ |
| fw, amu | 246.40 | 274.45 | 286.46 |
| space group | $P2_1/a$ | $P2_1/a$ | $P2_1$ |
| $a$, Å | 14.267 (2) | 10.824 (2) | 5.811 (1) |
| $b$, Å | 5.6418 (6) | 13.354 (1) | 17.310 (2) |
| $c$, Å | 19.088 (2) | 11.445 (1) | 8.731 (1) |
| $\beta$, deg | 107.54 (1) | 92.42 (1) | 107.70 (1) |
| V, Å$^3$ | 1465 | 1653 | 837 |
| $Z$ | 4 | 4 | 2 |
| $\rho_{calcd}$, g/cm$^3$ | 1.12 | 1.10 | 1.14 |
| cryst dimens, mm | 0.33 × 0.44 × 0.49 | 0.08 × 0.25 × 0.46 | 0.19 × 0.38 × 0.46 |
| linear abs coeff, cm$^{-1}$ | 0.72 | 0.70 | 0.72 |
| $2\theta$ limits | $3° \le 2\theta \le 55°$ | $4° \le 2\theta \le 55°$ | $4° \le 2\theta \le 55°$ |
| scan speed, deg/min in $\omega$ | 12 (with up to 8 rescans) | 6 (with up to 5 rescans) | 6 (with up to 5 rescans) |
| bkgd time/scan time | 0.5 | 0.5 | 0.5 |
| scan range, deg in $\omega$ | 1.16 + 0.35(tan $\theta$) | 1.10 + 0.35(tan $\theta$) | 1.10 + 0.35(tan $\theta$) |
| data collected | $+h,+k,\pm l$ | $+h,+k,\pm l$ | $+h,+k,\pm l$ |
| unique data | 3731 | 3993 | 2016 |
| unique data with $F_o^2 > 3\sigma(F_o^2)$ | 1655 | 1332 | 1509 |
| final no. of variables | 163 | 181 | 190 |
| $R(F)$[b] | 0.048 | 0.048 | 0.040 |
| $R_w(F)$[c] | 0.054 | 0.052 | 0.047 |
| error in observn of unit wt, e | 1.71 | 1.49 | 1.66 |

[a] Determined at 22 °C with Mo K$\alpha$ radiation and graphite monochromator. [b] $R(F) = \sum||F_o| - |F_c||/\sum|F_o|$. [c] $R_w(F) = [\sum w[|F_o| - |F_c|]^2/\sum w|F_o|^2]^{1/2}$, with $w = 1/\sigma^2(F_o)$.

**Table IV. Bond Distances (Å) for 18, 30, and 53**

| | | 18 | 30 | 53 |
|---|---|---|---|---|
| | | A. Common Bonds | | |
| O | C1 | 1.208 (3) | 1.211 (4) | 1.209 (3) |
| C1 | C2 | 1.512 (3) | 1.520 (4) | 1.521 (4) |
| C1 | C13 | 1.517 (3) | 1.500 (4) | 1.511 (4) |
| C2 | C3 | 1.531 (3) | 1.526 (5) | 1.533 (4) |
| C3 | C4 | 1.526 (4) | 1.537 (5) | 1.534 (4) |
| C4 | C5 | 1.523 (4) | 1.538 (5) | 1.530 (4) |
| C5 | C14 | 1.508 (4) | 1.507 (5) | 1.507 (4) |
| C5 | C6 | 1.563 (4) | 1.548 (5) | 1.570 (4) |
| C6 | C7 | 1.512 (4) | 1.507 (4) | 1.512 (4) |
| C7 | C14 | 1.324 (3) | 1.319 (5) | 1.324 (4) |
| C7 | C8 | 1.485 (3) | 1.484 (5) | 1.487 (4) |
| C8 | C9 | 1.528 (3) | 1.527 (5) | 1.533 (4) |
| C9 | C10 | 1.522 (3) | 1.522 (5) | 1.549 (4) |
| C9 | C13 | 1.554 (3) | 1.548 (5) | 1.562 (4) |
| C10 | C11 | 1.508 (4) | 1.486 (5) | 1.514 (5) |
| C11 | C12 | 1.540 (4) | 1.532 (5) | 1.533 (4) |
| C12 | C13 | 1.542 (3) | 1.529 (4) | 1.533 (4) |
| | | B. Other Bonds | | |
| C12 | C15 | 1.520 (4) | 1.527 (5) | 1.530 (4) |
| C15 | C17 | 1.507 (4) | 1.527 (5) | 1.510 (5) |
| C15 | C16 | 1.526 (5) | 1.519 (5) | 1.520 (5) |
| C4 | C18 | | 1.540 (6) | |
| C4 | C19 | | 1.525 (5) | |
| C5 | C20 | | | 1.524 (4) |
| C6 | C18 | | | 1.525 (4) |
| C18 | C19 | | | 1.518 (5) |
| C19 | C20 | | | 1.530 (5) |

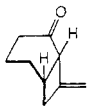
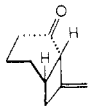
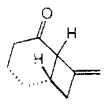
**Table V. Bond Angles (deg) for 18, 30, and 53**

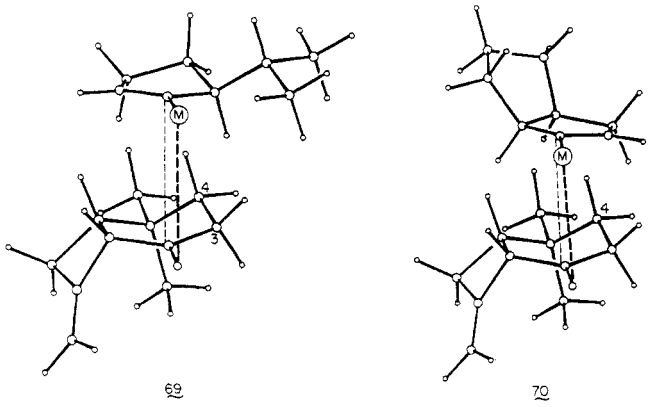
| | 18 | 30 | 53 |
|---|---|---|---|
| | A. Common Bond Angles | | |
| O–C1–C2 | 121.4 (2) | 120.1 (3) | 121.9 (3) |
| O–C1–C13 | 121.4 (2) | 122.0 (3) | 121.4 (3) |
| C2–C1–C13 | 117.1 (2) | 117.6 (3) | 116.5 (2) |
| C1–C2–C3 | 116.1 (2) | 115.4 (3) | 115.8 (3) |
| C4–C3–C2 | 117.0 (2) | 120.6 (3) | 117.2 (2) |
| C5–C4–C3 | 116.6 (2) | 114.0 (3) | 116.5 (2) |
| C14–C5–C4 | 115.7 (2) | 117.1 (3) | 115.0 (2) |
| C14–C5–C6 | 84.9 (2) | 85.2 (2) | 84.8 (2) |
| C4–C5–C6 | 116.5 (2) | 118.8 (3) | 117.8 (2) |
| C7–C6–C5 | 85.9 (2) | 86.0 (3) | 85.6 (2) |
| C14–C7–C8 | 135.9 (2) | 136.4 (3) | 135.2 (3) |
| C14–C7–C6 | 93.7 (2) | 93.8 (3) | 93.9 (2) |
| C8–C7–C6 | 130.1 (2) | 129.4 (3) | 130.8 (2) |
| C7–C8–C9 | 111.0 (2) | 111.8 (3) | 112.0 (2) |
| C10–C9–C8 | 112.5 (2) | 112.9 (3) | 111.0 (3) |
| C10–C9–C13 | 101.6 (2) | 101.4 (3) | 103.7 (2) |
| C8–C9–C13 | 114.6 (2) | 114.1 (3) | 115.2 (2) |
| C11–C10–C9 | 104.8 (2) | 107.3 (3) | 107.3 (2) |
| C10–C11–C12 | 106.0 (2) | 107.4 (3) | 104.4 (2) |
| C15–C12–C11 | 113.5 (2) | 116.2 (3) | 116.3 (2) |
| C15–C12–C13 | 112.9 (2) | 114.2 (3) | 116.2 (2) |
| C11–C12–C13 | 105.1 (2) | 105.1 (3) | 101.3 (2) |
| C1–C13–C12 | 114.2 (2) | 114.5 (3) | 115.0 (2) |
| C1–C13–C9 | 114.8 (2) | 116.0 (3) | 115.4 (2) |
| C12–C13–C9 | 106.4 (2) | 105.5 (3) | 104.3 (2) |
| C7–C14–C5 | 95.1 (2) | 94.7 (3) | 95.3 (2) |
| | B. Angles Not in Common | | |
| C17–C15–C12 | 113.2 (2) | 111.6 (3) | 114.0 (3) |
| C17–C15–C16 | 109.4 (3) | 109.8 (3) | 110.6 (3) |
| C12–C15–C16 | 111.8 (3) | 113.7 (3) | 110.7 (3) |
| C19–C4–C3 | | 110.9 (3) | |
| C19–C4–C5 | | 109.2 (3) | |
| C3–C4–C18 | | 106.3 (3) | |
| C5–C4–C18 | | 107.2 (3) | |
| C18–C4–C19 | | 109.1 (3) | |
| C14–C5–C20 | | | 116.7 (2) |
| C20–C5–C4 | | | 113.9 (2) |
| C20–C5–C6 | | | 105.1 (2) |
| C7–C6—C18 | | | 115.6 (2) |
| C18–C6–C5 | | | 105.8 (2) |
| C19–C18–C6 | | | 105.6 (3) |
| C18–C19–C20 | | | 103.1 (3) |
| C5–C20–C19 | | | 104.4 (2) |

group in the case of **4**) by the complexed organometallic. Notwithstanding this low-energy structural adjustment, the global volume of space demanded by the cyclopentenyl nucleophile in that region bracketed by C4 to C6 is easily seen to be better accommodated within **65** rather than **66**. Since a reasonable angle of attack is consequently better served by the first of these transition structures, ultimate passage to the relevant $\alpha$ alcohol is kinetically favored.

The concern of methyl steric contributions does not apply to **1**. In **67** and **68** (Figure 5), the discriminatory steric impact gives evidence of being related to the relative spatial orientation of the allylic C-5′ methine hydrogen of the cyclopentenyl nucleophile. Because the C1–H bond in **1** is splayed outwardly to a greater degree than is the C3–H bond (see Figure 4), this ketone has greater intrinsic capability for accomodating the more space filling C5′ of the incoming cyclopentenyl species above the cyclo-

**Table VI. Calculated Conformational Steric Energies for the 8-Methylenebicyclo[4.2.0]octan-2-ones**

| conformer | | steric energy, kcal mol$^{-1}$ | | | |
|---|---|---|---|---|---|
| | | 1 | 3 | 4 | 5 |
|  | half-chair | 37.22 | 40.45 | 40.77 | 37.64 |
|  | chair | 37.35 | 40.09 | 40.77 | 38.08 |
|  | chair | 37.43 | 42.06 | 39.18 | 38.32 |



69 70

**Figure 6.** The preferred transition state combinations for condensation of **3** with **14** and **23**. The differing diastereoselectivity is to be particularly noted. The intermolecular distance has been arbitrarily selected.

butanone ring as in **68**. Thus, **1** differs from **5** in that the canting of the $\alpha$-carbonyl C–H bonds exerts the major influence on the relative activation energies. This intermolecular recognition is not as large as the effects present in **5**, with the result that diastereoselectivity biases are less substantive.

Where **3** is concerned, a unique predisposition is observed for giving rise preferably to either $\alpha$ or $\beta$ alcohol, depending on the particular structure of the cerium reagent. In actuality, this crossover is controlled simply by whether the cyclopentenyl reagent carries a substituent at C4 or not. It is, of course, imperative that the methyl groups in **3** be positioned away from the trajectory of nucleophilic attack. For this reason, the chair conformation shown in **69** and **70** is adopted (Figure 6). Beyond that, the attack by **14** is better accommodated sterically by those nonbonded energy differences shown in **67** (for **1**) due to the particular location of its 5$\beta$-methyl group. However, when the cyclopentenyl species is 4-substituted, formation of $\beta$ product is now facilitated because of greater compression against itself along the $\alpha$ reaction channel. Transition-state models **69** and **70** are the kinetically preferred combinations.

The key features of the analysis just presented should prove serviceable in the prediction of preferred diastereoselection in yet untested related examples. The conformational profiles of the competing transition states are such that substitution of the ketone along its cyclobutane sector is more controlling than elsewhere in the cyclohexanone ring. Also, because of the mandated stacking of the electrophile–nucleophile pair as in **64**, maximum steric contributions arise when the cyclopentenyl ring is substituted at C5. However, groups positioned elsewhere can affect the stereochemical outcome, especially if the bicyclooctanone also carries substituents at C3 to C6.

Finally, when the diastereoselection demonstrated in this study is linked to a subsequent anionic oxy-Cope transformation, the two-step methodology is seen to serve as a convenient protocol for setting relative (and absolute if desired) stereochemistry at multiple stereogenic centers within relatively intricate carbocyclic frameworks.

## Experimental Section

**5,5-Dimethyl-8-methylenebicyclo[4.2.0]octan-2-one (3).** The photolysis apparatus previously described by Cargill[21] was flushed with nitrogen and filled with a solution of 4,4-dimethylcyclohex-2-en-1-one[22] (13.86 g, 112 mmol) in 2500 mL of pentane. After cooling of this solution to −78 °C, allene (83 g, 18.5 equiv) that had been condensed into a cold flask was added. With continued nitrogen ebullition, the reaction mixture was irradiated with a modified (outer globe removed) 1000-W GE street lamp for 15 h and then allowed to warm slowly to room temperature. After solvent evaporation under reduced pressure, the residue was subjected to HPLC purifications (silica gel, elution with 5% ethyl acetate in petroleum ether). There were obtained 3.74 g (20%) of **3**, bp 75–76 °C at 0.5 Torr, and 3.88 g (28%) of unreacted starting material. The analytical sample was obtained by preparative gas chromatography as a colorless liquid: IR (neat, cm$^{-1}$) 2955, 2929, 2872, 1700, 1666, 1469, 1463; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.95–4.92 (m, 1 H), 4.88–4.86 (m, 1 H), 3.57–3.54 (m, 1 H), 2.80–2.70 (m, 1 H), 2.67–2.58 (m, 1 H), 2.49–2.25 (m, 3 H), 2.04 (dddd, $J$ = 13.9, 7.2, 6.8, 6.7 Hz, 1 H), 1.46 (ddt, $J$ = 14.0, 6.8, 2.2 Hz, 1 H), 0.95 (s, 3 H), 0.91 (s, 3 H); $^{13}$C NMR (80 MHz, $CDCl_3$) (ppm) 210.04, 142.82, 109.03, 54.23, 41.12, 35.24, 31.77, 30.91, 30.30, 26.08, 25.84; MS $m/z$ (M$^+$) calcd 164.1202, obsd 164.1224.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.15; H, 9.76.

**4,4-Dimethyl-8-methylenebicyclo[4.2.0]octan-2-one (4).** A solution of 5,5-dimethylcyclohex-2-en-1-one (14.00 g, 113 mmol)[23] and allene (89 g, 20 equiv) in 2500 mL of pentane was irradiated in the predescribed manner for 5 h. HPLC (silica gel, elution with 5% ethyl acetate in petroleum ether) followed by distillation gave 8.33 g (45%) of **4** as a colorless liquid: bp 72–74 °C at 0.5 Torr; IR (neat, cm$^{-1}$) 2958, 2919, 2870, 2844, 1704, 1669, 1466, 1455; $^1$H NMR (300 MHz, $CDCl_3$) $\delta$ 4.87–4.83 (m, 2 H), 3.55–3.53 (m, 1 H), 2.97–2.92 (m, 1 H), 2.71–2.65 (m, 1 H), 2.23–2.15 (m, 2 H), 2.04 (ddd, $J$ = 16.3, 2.7, 1.3 Hz, 1 H), 1.86 (ddd, $J$ = 13.6, 7.5, 2.6 Hz, 1 H), 1.45 (dd, $J$ = 13.7, 10.4 Hz, 1 H), 1.01 (s, 3 H), 0.84 (s, 3 H); $^{13}$C NMR (80 MHz, $CDCl_3$) (ppm) 209.53, 145.10, 107.51, 52.64, 52.02, 41.53, 37.37, 33.75, 30.98, 28.84, 25.22; MS $m/z$ (M$^+$) calcd 164.1201, obsd 164.1227.

Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.11; H, 9.85.

**Prototypical Organocerium Addition to the Ketones.** In an oven-dried 25-mL flask flushed with nitrogen was placed **9** (454 mg, 2.40 mmol) and 10 mL of anhydrous tetrahydrofuran. This solution was cooled to −78 °C, treated dropwise with *tert*-butyllithium (2.82 mL of 1.7 M, 4.8 mmol) in pentane, and stirred for 30 min. Previously, cerium trichloride heptahydrate (1.12 g, 3.00 mmol) was dried by heating at 140–150 °C and 0.1 Torr for 2 h, slurried overnight in 8 mL of anhydrous tetrahydrofuran, and cooled to −78 °C. The vinyllithium reagent was transferred via cannula to this slurry, which was in turn stirred magnetically for 1 h. A solution of **1**[9] (272 mg, 2.00 mmol) in 2 mL of tetrahydrofuran was added slowly over 10 min, and stirring was continued at −78 °C for an additional 2.5 h before 5 mL of saturated ammonium chloride solution was introduced. The mixture was partitioned between ether and brine, and the aqueous phase was extracted three times with ether. The combined organic layers

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(22) Flaugh, M. E.; Crowell, T. A.; Farlow, D. S. *J. Org. Chem.* **1980**, *45*, 5400.
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were washed with brine, dried, and evaporated. MPLC of the residue on silica gel (elution with 1% ether in petroleum ether) furnished 94 mg (19%) of **15** and 243 mg (49%) of **16**, both as colorless oils. Flushing the column with 20% ether in petroleum ether returned 31 mg (11%) of unreacted **1**. The overall yield based on recovered **1** was therefore 79%. The average **15**:**16** ratio determined by HPLC on unpurified mixtures was 1:2.5.

For **15**: IR (neat, $cm^{-1}$) 3565, 3490, 2940, 2873, 1672, 1468; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.58–5.56 (m, 1 H), 5.18 (q, $J$ = 2.3 Hz, 1 H), 4.92 (q, $J$ = 2.1 Hz, 1 H), 3.28–3.25 (m, 1 H), 2.72–2.68 (m, 1 H), 2.58 (ddt, $J$ = 13.6, 7.6, 2.3 Hz, 1 H), 2.42 (dqq, $J$ = 6.8, 6.8, 2.8 Hz, 1 H), 2.27–2.05 (m, 4 H), 1.89–1.55 (m, 6 H), 1.46–1.33 (m, 2 H), 1.22–1.08 (m, 1 H), 0.94 (d, $J$ = 6.9 Hz, 3 H), 0.79 (d, $J$ = 6.7 Hz, 3 H); $^{13}C$ NMR (20 MHz, $C_6D_6$) (ppm) 151.09, 150.08, 127.78, 107.20, 72.24, 51.46, 50.82, 37.96, 32.56, 32.04, 30.52, 30.13, 27.02, 24.30, 22.44, 20.00, 15.94; MS $m/z$ ($M^+$) calcd 246.1983, obsd 246.1957.

Anal. Calcd for $C_{17}H_{26}O$: C, 82.87; H, 10.64. Found: C, 82.48; H, 10.65.

For **16**: IR (neat, $cm^{-1}$) 3564, 3468, 2957, 2928, 2868, 1669, 1467, 1454; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.45 (d, $J$ = 0.9 Hz, 1 H), 5.16–5.14 (m, 1 H), 4.90–4.89 (m, 1 H), 3.14–3.10 (m, 1 H), 2.86–2.83 (m, 1 H), 2.59–2.51 (m, 1 H), 2.34–2.11 (m, 5 H), 1.90–1.26 (m, 9 H), 0.95 (d, $J$ = 7.0 Hz, 3 H), 0.76 (d, $J$ = 6.8 Hz, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 152.85, 149.81, 126.23, 107.42, 72.43, 52.29, 51.91, 37.70, 34.20, 32.55, 30.57, 30.14, 26.49, 24.14, 22.51, 19.30, 15.67; MS $m/z$ ($M^+$) calcd 246.1983, obsd 246.2015.

**Addition of 23 to 1.** The dichlorocerium reagent was prepared from 468 mg (2.50 mmol) of **10**, 5.00 mmol of *tert*-butyllithium, and 1.02 g (2.75 mmol) of cerium trichloride heptahydrate as described above and reacted with **1** (272 mg, 2.00 mmol). Following MPLC (silica gel, elution with 2% ether in petroleum ether), there were isolated 116 mg (24%) of as a colorless oil and 170 mg (35%) of **25** as a white solid, mp 53.0–53.5 °C (from hexane). In addition, 49 mg (18%) of **1** was recovered; overall yield 77%; the average HPLC ratio was determined to be 1:1.4.

For **24**: IR (neat, $cm^{-1}$) 3562, 3472, 3052, 2932, 2862, 1673, 1448; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.33 (d, $J$ = 1.3 Hz, 1 H), 5.21–5.19 (m, 1 H), 4.93–4.91 (m, 1 H), 3.22–3.20 (m, 1 H), 2.99–2.96 (m, 1 H), 2.62–2.42 (m, 3 H), 2.27–2.14 (m, 2 H), 1.98–1.12 (series of m, 14 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 152.22, 149.95, 124.92, 107.17, 72.22, 50.91, 50.80, 42.34, 39.84, 37.90, 35.41, 33.94, 32.97, 30.51, 27.13, 26.95, 19.70; MS $m/z$ ($M^+$) calcd 224.1827, obsd 244.1837.

For **25**: IR ($CDCl_3$, $cm^{-1}$) 3596, 3561, 3059, 2971, 2871, 1671, 1452; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.30 (dd, $J$ = 3.7, 2.2 Hz, 1 H), 5.18 (dd, $J$ = 4.6, 2.5 Hz, 1 H), 4.92 (q, $J$ = 2.1 Hz, 1 H), 3.18–3.06 (m, 2 H), 2.67–2.44 (m, 3 H), 2.32–2.20 (m, 2 H), 1.98–1.22 (m, 14 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 153.11, 149.80, 124.25, 107.47, 72.10, 51.48, 51.02, 42.50, 40.05, 37.70, 35.20, 33.86, 33.68, 30.36, 27.28, 26.58, 19.38; MS $m/z$ ($M^+$) calcd 244.1827, obsd 244.1838.

Anal. Calcd for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.52; H, 9.93.

**Addition of 14 to 3.** From 393 mg (2.08 mmol) of **9**, 4.15 mmol of *tert*-butyllithium, 554 mg (2.25 mmol) of anhydrous cerium trichloride, and 284 mg (1.73 mmol) of **3**, there were obtained after MPLC (silica gel, 2% ether in petroleum ether) 184 mg (39%) of **28**, 144 mg (30%) of **29**, and 56 mg (20%) of unreacted **3**; overall yield 89%; the average HPLC ratio of **28**:**29** was determined to be 1.7:1.

For **28**: colorless oil; IR (neat, $cm^{-1}$) 3572, 3072, 3055, 2955, 2895, 2870, 1668, 1469; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.73 (s, 1 H), 4.89 (s, 1 H), 4.82 (s, 1 H), 3.26–3.24 (m, 1 H), 2.80–2.74 (m, 2 H), 2.31–2.04 (m, 6 H), 1.92–1.71 (m, 4 H), 1.55–1.50 (m, 1 H), 1.08–1.04 (m, 1 H), 0.93 (d, $J$ = 7.9 Hz, 3 H), 0.84 (s, 3 H), 0.82 (s, 3 H), 0.77 (d, $J$ = 7.8 Hz, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 153.79, 148.61, 127.14, 107.04, 70.77, 51.58, 49.88, 40.97, 35.73, 32.83, 32.10, 30.44, 30.24, 28.86, 28.60, 27.28, 24.60, 22.44, 15.72; MS $m/z$ ($M^+$) calcd 274.2297, obsd 274.2320.

Anal. Calcd for $C_{19}H_{30}O$: C, 83.15; H, 11.12. Found: C, 83.12; H, 11.03.

For **29**: colorless oil; IR (neat, $cm^{-1}$) 3570, 3074, 2957, 2895, 2871, 2855, 1668, 1469, 1453; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.51 (q, $J$ = 1.3 Hz, 1 H), 5.50–4.87 (m, 2 H), 3.01–2.99 (m, 1 H), 2.84–2.75 (m, 2 H), 2.32–2.03 (m, 6 H), 2.00–1.63 (m, 5 H), 1.08–1.01 (m, 1 H), 0.95 (d, $J$ = 6.9 Hz, 3 H), 0.86 (s, 3 H), 0.82 (s, 3 H), 0.79 (d, $J$ = 6.8 Hz, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 154.30, 148.18, 125.48, 106.60, 70.85, 52.35, 51.91, 41.33, 35.81, 33.12, 32.35, 30.21, 30.13, 28.80, 28.54, 27.28, 24.59, 22.38, 15.52; MS $m/z$ ($M^+$) calcd 274.2297, obsd 274.2316.

**Addition of 23 to 3.** A combination of 351 mg (1.88 mmol) of **10**, 3.75 mmol of *tert*-butyllithium, 770 mg (2.1 mmol) of cerium trichloride heptahydrate, and ketone **3** (246 mg, 1.5 mmol) gave after MPLC (silica gel, 2% ether in petroleum ether) 108 mg (26%) of **33**, 166 mg (41%) of **34**, and 77 mg (31%) of unreacted **3**. The overall yield was 98%; the average **33**:**34** ratio determined by HPLC on unpurified mixtures was 1:1.6.

For **33**: colorless oil; IR (neat, $cm^{-1}$) 3572, 3071, 3052, 2943, 2862, 1667, 1450; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.48–5.47 (m, 1 H), 4.88 (s, 1 H), 4.80 (q, $J$ = 1.4 Hz, 1 H), 3.16–3.13 (m, 1 H), 3.01–2.99 (m, 1 H), 2.80 (tq, $J$ = 11.1, 2.7 Hz, 1 H), 2.69–2.57 (m, 1 H), 2.54–2.44 (m, 1 H), 2.35–2.25 (m, 1 H), 2.20–1.00 (series of m, 13 H), 0.86 (s, 3 H), 0.83 (s, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 154.59, 148.46, 124.10, 106.85, 70.82, 51.20, 50.00, 42.73, 41.01, 39.75, 35.68, 35.36, 34.12, 32.81, 30.35, 28.87, 28.52, 27.30, 27.20; MS $m/z$ ($M^+$) calcd 272.2140, obsd 272.2123.

For **34**: colorless oil; IR (neat, $cm^{-1}$) 3572, 3462, 3072, 3050, 2951, 2863, 1666, 1451; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.37–5.36 (m, 1 H), 4.91–4.90 (m, 1 H), 4.87–4.85 (m, 1 H), 3.27–3.02 (m, 2 H), 2.87–2.76 (m, 1 H), 2.70–2.60 (m, 1 H), 2.50 (ddq, $J$ = 16.7, 9.7, 1.0 Hz, 1 H), 2.34–2.25 (m, 1 H), 2.17–1.53 (m, 9 H), 1.49–1.34 (m, 1 H), 1.31–1.21 (m, 1 H), 1.13–1.02 (m, 2 H), 0.85 (s, 3 H), 0.82 (s, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 154.61, 148.23, 123.13, 106.94, 70.48, 51.62, 51.14, 42.81, 41.25, 39.83, 35.77, 35.19, 34.22, 32.49, 30.13, 28.86, 28.43, 27.30 (2 C); MS $m/z$ ($M^+$) calcd 272.2140, obsd 272.2118.

Anal. Calcd for $C_{19}H_{28}O$: C, 83.77; H, 10.36. Found: C, 83.68; H, 10.39.

**Addition of 37 to 3.** In line with the predescribed procedure, 340 mg (1.80 mmol) of **11** was transformed into **37** with 3.6 mmol of *tert*-butyllithium and 730 mg (1.95 mmol) of cerium trichloride heptahydrate. Following the addition of **3** (246 mg, 1.5 mmol) and the usual workup, there were isolated 341 mg (83%) of an inseparable mixture of **38** and **39** as a colorless oil and 11 mg (4%) of unreacted **3**. HPLC analysis showed the average ratio of alcohols to be 1:2.3, respectively. For the **38**/**39** mixture: IR (neat, $cm^{-1}$) 3576, 3479, 3075, 2956, 2926, 2872, 1670, 1455; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.54 (t, $J$ = 2.2 Hz, 0.3 H), 5.34 (t, $J$ = 2.1 Hz, 0.7 Hz), 4.91–4.88 (m, 1.4 H), 4.81–4.80 (m, 0.6 H), 3.29–3.22 (m, 0.3 H), 3.04–3.01 (m, 0.7 H), 2.83–2.74 (m, 1 H), 2.56–2.47 (m, 1 H), 2.33–1.29 (series of m, 11 H), 1.08–0.82 (series of m, 13 H); MS $m/z$ ($M^+$) calcd 274.2297, obsd 274.2281.

**Addition of 14 to 4.** Ketone **4** (328 mg, 2.00 mmol) was treated with **14** prepared as described above from 454 mg (2.40 mmol) of **9**, 4.8 mmol of *tert*-butyllithium, and 970 mg (2.6 mmol) of cerium trichloride heptahydrate. The crude product was purified by MPLC on silica gel (elution with 1% ether in petroleum ether) to give 378 mg (69%) of a mixture of **43a** and **44a** and 61 mg (18%) of unreacted **4**. The overall yield was therefore 87%; HPLC analysis showed the average **43a**:**44a** ratio to be 1.1:1. Pure samples of the alcohols were obtained by means of analytical HPLC.

For **43a**: IR (neat, $cm^{-1}$) 3562, 3052, 2975, 2872, 2857, 1673, 1466; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.69 (s, 1 H), 4.89–4.85 (m, 2 H), 3.32–3.27 (m, 1 H), 2.81–2.71 (m, 2 H), 2.44–2.36 (m, 2 H), 2.35–2.24 (m, 3 H), 2.21–1.86 (m, 3 H), 1.79–1.72 (m, 2 H), 1.35 (dd, $J$ = 12.6, 6.6 Hz, 1 H), 1.20 (s, 3 H), 1.11 (dd, $J$ = 14.1, 2.3 Hz, 1 H), 0.95 (d, $J$ = 6.9 Hz, 3 H), 0.86 (s, 3 H), 0.79 (d, $J$ = 6.8 Hz, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 152.98, 150.69, 127.24, 109.01, 73.40, 51.68, 49.09, 46.47, 39.40, 37.47, 34.15, 31.91, 31.26, 30.20, 29.97, 27.35, 24.54, 22.44, 15.78; MS $m/z$ ($M^+$) calcd 274.2297, obsd 274.2318.

For **44a**: IR (neat, $cm^{-1}$) 3567, 3072, 3042, 2932, 2892, 2875, 1664, 1469; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.44 (s, 1 H), 4.88–4.85 (m, 2 H), 3.19–3.13 (m, 1 H), 2.81–2.68 (m, 1 H), 2.73 (ddt, $J$ = 15.7, 8.8, 2.5 Hz, 1 H), 2.42–2.25 (m, 2 H), 2.22–2.11 (m, 3 H), 2.04–1.88 (m, 3 H), 1.78–1.70 (m, 2 H), 1.35 (dd, $J$ = 12.7, 6.7 Hz, 1 H), 1.20 (dd, $J$ = 14.1, 2.0 Hz, 1 H), 1.19 (s, 3 H), 0.97 (d, $J$ = 6.8 Hz, 3 H), 0.88 (s, 3 H), 0.82 (d, $J$ = 6.9 Hz, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 154.21, 150.35, 125.83, 108.94, 73.77, 52.13, 51.98, 48.31, 39.43, 37.47, 34.12, 32.59, 31.52, 30.26, 30.14, 27.65,

24.63, 22.44, 15.70; MS $m/z$ ($M^+$) calcd 274.2297, obsd 274.2305.

Anal. Calcd for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 83.06; H, 10.91.

**(*R*)-(+)-1-Bromo-4-isopropylcyclopentene (12).** (*R*)-(+)-3-Isopropylcyclopentanone (5.36 g, 42.6 mmol) was dissolved in methanol (40 mL) and treated with *p*-toluenesulfonohydrazide (7.93 g, 42.6 mmol). After 20–30 min, the product precipitated. An additional 30 mL of methanol was added, and the slurry was stirred for 12 h before the solvent was evaporated. The product was washed with hexane and dried in vacuo. There was isolated 10.12 g (81%) of tosylhydrazone as a colorless solid: mp 155–157 °C dec (from methanol); IR ($CDCl_3$, $cm^{-1}$) 3296, 3221, 2961, 2936, 2879, 1716, 1600; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.85 (d, $J$ = 1.7 Hz, 1 H), 7.82 (d, $J$ = 1.7 Hz, 1 H), 7.50–7.47 (m, 1 H), 7.31–7.28 (m, 2 H), 2.60–2.26 (m, 2 H), 2.42 (s, 3 H), 2.17–1.90 (m, 2 H), 1.79–1.54 (m, 1 H), 1.46–1.21 (m, 2 H), 0.97–0.86 (m, 7 H); MS $m/z$ ($M^+$) calcd 294.1402, obsd 294.1392; $[\alpha]_D^{21}$ +46.9° (*c* 1.11, methanol).

Anal. Calcd for $C_{15}H_{22}N_2O_2S$: C, 61.19; H, 7.53. Found: C, 61.40; H, 7.59.

An oven-dried 500-mL three-necked flask fitted with a mechanical stirrer and low-temperature thermometer was flushed with argon and charged with *N,N,N',N'*-tetramethylethylenediamine (100 mL) and *n*-butyllithium (137 mmol). After this solution was cooled to −78 °C, the tosylhydrazone (10.09 g, 34.4 mmol) was introduced in small portions, stirred for 1 h, and warmed to room temperature until nitrogen evolution ceased (1.5 h). The resulting dark red reaction mixture was treated at −78 °C during 10 min with 1,1,2,2-tetrafluoro-1,2-dibromoethane (16.2 mL, 35.6 g, 137 mmol), stirred for 1 h, and the aqueous phase was extracted with petroleum ether (3 × 150 mL). The combined organic layers were washed with water (3 × 500 mL), 10% hydrochloric acid (3 × 75 mL), saturated sodium bicarbonate solution (3 × 75 mL), and brine (3 × 75 mL) prior to drying. The solution was filtered through a bed of neutral alumina and evaporated. Distillation of the residue afforded 1.43 g (22%) of a colorless liquid, bp 64–65 °C at 6 Torr, capillary GC analysis of which showed it to consist of 97% **12** and 3% **13**.

For **12**: $[\alpha]_D^{24}$ +16.4° (*c* 1.10, methanol); $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 5.80–5.78 (m, 1 H), 2.65–2.55 (m, 1 H), 2.44–2.30 (m, 2 H), 2.21–1.97 (m, 2 H), 1.60–1.51 (m, 1 H), 0.88 (d, $J$ = 6.6 Hz, 3 H), 0.87 (d, $J$ = 6.6 Hz, 3 H); MS $m/z$ ($M^+$) calcd 188.0200, obsd 188.0224.

Anal. Calcd for $C_8H_{13}Br$: C, 50.81; H, 6.93. Found: C, 51.13; H, 6.98.

**Addition of 42 to 4.** The general procedure was adapted (except for addition of ketone in one portion at −98 °C) to 189 mg (1.00 mmol) of (+)-**12**, 2.00 mmol of *tert*-butyllithium, 410 mg (1.1 mmol) of cerium trichloride heptahydrate, and 492 mg (3.0 mmol) of **4**. MPLC purification (silica gel, elution with 1% ether in petroleum ether) gave 126 mg (46%) of **43b** and **44b** as a colorless oily inseparable mixture and 383 mg of recovered **4**, for an overall yield of 79%. HPLC analysis showed the average **43b**:**44b** ratio to be 1.1:1. For the mixture: IR (neat, $cm^{-1}$) 3570, 3076, 3060, 2957, 2926, 2876, 1675, 1470; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.51 (s, 1 H), 4.88–4.82 (m, 2 H), 3.29–3.08 (m, 1 H), 2.80–2.71 (m, 1 H), 2.44–2.16 (m, 4 H), 2.09–1.88 (m, 5 H), 1.77–1.72 (m, 1 H), 1.49–1.34 (m, 2 H), 1.18–1.06 (m, 4 H), 0.88–0.84 (m, 9 H); MS $m/z$ ($M^+$) calcd 274.2297, obsd 274.2273.

**Addition of 14 to 5.** Reaction of **9** (227 mg, 1.20 mmol) with 2.40 mmol of *tert*-butyllithium, 480 mg (1.3 mmol) of cerium trichloride heptahydrate, and 150 mg (1.0 mmol) of **5** afforded after MPLC on silica gel (elution with 2% ether in petroleum ether) 221 mg (85%) of **45** and **46** as an inseparable mixture of diastereomers in an average 5.8:1 ratio: IR (neat, $cm^{-1}$) 3608, 3565, 3485, 3054, 2969, 2955, 1667, 1468; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.64–5.51 (m, 1 H), 5.22–5.18 (m, 1 H), 4.96–4.94 (m, 1 H), 2.95–2.72 (m, 2 H), 2.44–1.91 (m, 5 H), 1.91–1.54 (m, 6 H), 1.43–1.11 (m, 3 H), 1.06–0.94 (m, 6 H), 0.81–0.78 (m, 3 H); MS $m/z$ ($M^+$) calcd 260.2140, obsd 260.2141.

**Addition of 37 to 5.** From 454 mg (2.40 mmol) of **11**, 4.8 mmol of *tert*-butyllithium, 970 mg (2.60 mmol) of cerium trichloride heptahydrate, and 300 mg (2.0 mmol) of **5**, there were isolated, following MPLC (silica gel, 1% ether in petroleum ether), 107 mg (20%) of **48** and 345 mg (67%) of **47**, both as colorless oils. The average analytical HPLC ratio was 3.1:1.

For **47**: IR (neat, $cm^{-1}$) 3567, 3477, 3059, 2932, 2865, 1669, 1454; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.48 (m, 1 H), 5.23 (q, $J$ = 2.3 Hz, 1 H), 4.96–4.94 (m, 1 H), 2.92 (d, $J$ = 2.2 Hz, 1 H), 2.48 (ddt, $J$ = 16.5, 7.5, 2.0 Hz, 1 H), 2.34 (dq, $J$ = 14.1, 2.2 Hz, 1 H), 2.22–2.16 (m, 2 H), 2.02–1.82 (m, 3 H), 1.74–1.54 (m, 4 H), 1.43–1.21 (m, 4 H), 1.04 (s, 3 H), 0.94 (d, $J$ = 7.0 Hz, 3 H), 0.90 (t, $J$ = 7.4 Hz, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 151.39, 148.08, 125.07, 107.99, 71.84, 56.39, 55.30, 44.25, 39.33, 36.98, 35.06, 33.12, 32.28, 28.46, 27.14, 23.09, 18.78, 11.83; MS $m/z$ ($M^+$) calcd 260.2140, obsd 260.2147.

Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 82.89; H, 10.90.

For **48**: IR (neat, $cm^{-1}$) 3567, 3474, 3074, 3033, 2924, 2869, 2809, 1667, 1455; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.37 (s, 1 H), 5.19 (q, $J$ = 2.4 Hz, 1 H), 4.94 (q, $J$ = 2.2 Hz, 1 H), 2.86 (d, $J$ = 2.2 Hz, 1 H), 2.50 (ddt, $J$ = 16.5, 7.6, 2.2 Hz, 1 H), 2.40 (dq, $J$ = 14.4, 2.4 Hz, 1 H), 2.28–2.26 (m, 1 H), 2.16 (dt, $J$ = 14.4, 2.0 Hz, 1 H), 2.01–1.56 (series of m, 8 H), 1.47–1.26 (m, 3 H), 1.06 (s, 3 H), 0.95 (d, $J$ = 7.0 Hz, 3 H), 0.91 (t, $J$ = 7.4 Hz, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 152.23, 147.93, 123.91, 108.64, 71.93, 57.36, 55.50, 43.71, 39.42, 37.00, 34.78, 33.75, 32.63, 28.48, 26.99, 23.01, 18.88, 11.93; MS $m/z$ ($M^+$) calcd 260.2140, obsd 260.2163.

**Addition of 14 to 8.** The dichlorocerium reagent was prepared as before with 454 mg (2.40 mmol) of **9**, 4.8 mmol of *tert*-butyllithium, and 970 mg (2.6 mmol) of cerium trichloride heptahydrate. Condensation with **8** and subsequent MPLC on silica gel (elution with 2% ether in petroleum ether) afforded 398 mg (70%) of **51a**, 43 mg (8%) of **52a**, and ultimately (elution with 20% ether in petroleum ether) 32 mg (9%) of unreacted **8**. The overall yield was therefore 86%, and the average **51a**:**52a** ratio was 9.8:1.

For **51a**: colorless oil; IR (neat, $cm^{-1}$) 3565, 3062, 2970, 2875, 2855, 1662, 1468; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.60–5.58 (m, 1 H), 4.96 (t, $J$ = 2.3 Hz, 1 H), 4.88 (t, $J$ = 2.2 Hz, 1 H), 2.90 (d, $J$ = 2.4 Hz, 1 H), 2.83–2.76 (m, 2 H), 2.50 (dddd, $J$ = 13.7, 6.8, 6.8, 2.8 Hz, 1 H), 2.21–2.12 (m, 2 H), 1.95–1.39 (m, 14 H), 1.15 (ddd, $J$ = 12.3, 12.3, 6.7 Hz, 1 H), 0.98 (d, $J$ = 7.0 Hz, 3 H), 0.86 (d, $J$ = 6.7 Hz, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 153.97, 151.55, 127.54, 108.88, 72.06, 54.70, 51.91, 51.84, 45.98, 41.06, 33.23, 32.06, 31.24, 30.28, 28.66, 25.54, 24.49, 22.45, 18.59, 15.91; MS $m/z$ ($M^+$) calcd 286.2297, obsd 286.2300.

Anal. Calcd for $C_{20}H_{30}O$: C, 83.86; H, 10.56. Found: C, 84.04; H, 10.74.

For **52a**: colorless oil; IR (neat, $cm^{-1}$) 3564, 3064, 2944, 2880, 2859, 1660, 1470; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.56–5.54 (m, 1 H), 5.03–5.02 (m, 1 H), 4.88–4.87 (m, 1 H), 2.86–2.80 (m, 3 H), 2.44–2.39 (m, 1 H), 2.22–2.15 (m, 2 H), 1.96–1.41 (series of m, 13 H), 1.27–1.03 (m, 2 H), 0.97 (d, $J$ = 6.8 Hz, 3 H), 0.84 (d, $J$ = 6.8 Hz, 3 H); $^{13}C$ NMR (75 MHz, $C_6D_6$) (ppm) 153.64, 152.24, 126.75, 108.93, 72.29, 55.40, 51.93, 51.45, 46.04, 41.32, 33.22, 32.79, 32.50, 30.23, 28.86, 25.56, 24.39, 22.53, 19.07, 15.79; MS $m/z$ ($M^+$) calcd 286.2297, obsd 286.2252.

**Addition of 42 to 8.** A combination of 189 mg (1.00 mmol) of (+)-**12**, 2.0 mmol of *tert*-butyllithium, 410 mg (1.1 mmol) of cerium trichloride heptahydrate, and 526 mg (3.00 mmol) of **8** performed at −98 °C as described earlier led, after MPLC (silica gel, 4% ether in petroleum ether), to the isolation of **51b** and **52b** as an inseparable diastereomeric mixture (62 mg, 22%) and to recovery of 448 mg of **8** (78% overall yield). The average **51b**:**52b** ratio was 1.2:1 (500-MHz $^1H$ NMR analysis): IR (neat, $cm^{-1}$) 3562, 3452, 3057, 2927, 2872, 2847, 1663, 1467; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.52–5.51 (m, 1 H), 5.50–4.95 (m, 1 H), 4.88–4.87 (m, 1 H), 2.84–2.82 (m, 1 H), 2.76–2.74 (m, 1 H), 2.51–2.30 (m, 2 H), 2.18–1.37 (series of m, 16 H), 1.24–1.10 (m, 1 H), 0.91–0.84 (m, 6 H); MS $m/z$ ($M^+$) calcd 286.2297, obsd 286.2286.

**Addition of 23 to 8.** Condensation of the dichlorocerate derived from **10** (468 mg, 2.50 mmol), 5.0 mmol of *tert*-butyllithium, and cerium trichloride heptahydrate (1.02 g, 2.75 mmol) with **8** (352 mg, 2.0 mmol) gave rise, after MPLC on silica gel (elution with 2% ether in petroleum ether), to 368 mg (65%) of **55** and 63 mg (11%) of **56** in addition to 46 mg (13%) of recovered **8** (20% ether in petroleum ether). The overall yield of 89% was accompanied by an average HPLC-derived **55**:**56** ratio of 6.6:1.

For **55**: colorless oil; IR (neat, $cm^{-1}$) 3562, 3477, 3056, 2912, 2877, 1660, 1466, 1448; $^1H$ NMR (300 MHz, $C_6D_6$) $\delta$ 5.40 (s, 1 H), 4.97 (s, 1 H), 4.88–4.87 (m, 1 H), 3.27–3.08 (m, 1 H), 2.85–2.80

(m, 2 H), 2.70–2.58 (m, 1 H), 2.53–2.44 (m, 1 H), 2.00–0.86 (series of m, 20 H); $^{13}$C NMR (63 Hz, $C_6D_6$) (ppm) 153.83, 152.62, 124.84, 108.70, 72.05, 54.52, 51.89, 51.30, 45.85, 42.42, 41.17, 39.82, 35.46, 33.80, 33.14, 31.62, 29.07, 27.01, 25.55, 18.47; MS $m/z$ ($M^+$) calcd 284.2121, obsd 284.2178.

Anal. Calcd for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.17; H, 9.96.

For **56**: colorless oil; IR (neat, cm$^{-1}$) 3559, 3532, 2944, 2869, 2854, 1657, 1452; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.40 (s, 1 H), 5.02 (t, $J$ = 2.1 Hz, 1 H), 4.89 (t, $J$ = 2.1 Hz, 1 H), 3.16–3.11 (m, 1 H), 2.85–2.82 (m, 2 H), 2.72–2.60 (m, 1 H), 2.55–2.46 (m, 1 H), 1.98–1.04 (series of m, 20 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 153.62, 152.84, 124.60, 108.97, 72.17, 54.89, 51.53, 51.09, 45.92, 42.54, 41.24, 40.01, 35.37, 33.72, 33.20, 32.12, 28.98, 27.10, 25.58, 18.93; MS $m/z$ ($M^+$) calcd 284.2141, obsd 284.2151.

**Prototypical Oxy-Cope Rearrangement Involving Potassium Hydride as Base. Isomerization of 15.** In an oven-dried 25-mL two-necked flask flushed with nitrogen was placed 0.132 mL of 25% KH in mineral oil (33 mg, 0.83 mmol). This reagent was washed three times with molecular sieve dried pentane and suspended in anhydrous tetrahydrofuran (2 mL). A solution of **15** (101 mg, 0.41 mmol) and 18-crown-6 (216 mg, 0.82 mmol) in 2 mL of tetrahydrofuran was added in one portion, and the reaction mixture was refluxed for 30 min, cooled to −78 °C, and treated with 1 mL of saturated ammonium chloride solution. The mixture was partitioned between petroleum ether and ammonium chloride solution, and the organic phase was washed with brine and dried. Solvent evaporation and MPLC purification (silica gel, elution with 2% ether in petroleum ether) gave 8 mg (8%) of **19** followed by 78 mg (77%) of **18**.

For **18**: colorless crystals, mp 49–50 °C (from ethanol); IR ($CDCl_3$, cm$^{-1}$) 3045, 2980, 2935, 2876, 1702, 1681, 1448; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.67 (d, $J$ = 1.6, 1 H), 2.78 (s, 1 H), 2.45–1.88 (series of m, 9 H), 1.77–1.53 (m, 6 H), 1.45–1.31 (m, 1 H), 1.29–1.24 (m, 1 H), 1.13–1.06 (m, 1 H), 0.79 (d, $J$ = 6.8 Hz, 3 H), 0.75 (d, $J$ = 6.7 Hz, 3 H); $^{13}$C NMR (20 MHz, $C_6D_6$) (ppm) 210.36, 146.28, 136.72, 55.95, 48.83, 44.89, 40.92, 38.38, 35.61, 34.69, 34.25, 31.61, 30.03, 28.26, 21.95, 19.52, 19.42; MS $m/z$ ($M^+$) calcd 246.1983, obsd 246.1993; X-ray analysis, see below.

For **19**: colorless crystals, mp 64–65 °C (from ethanol); IR (film, cm$^{-1}$) 2970, 2938, 2890, 2870, 2858, 2839, 1679, 1637; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.57 (s, 1 H), 2.87–2.84 (m, 1 H), 2.63–2.47 (m, 3 H), 2.28–2.11 (m, 4 H), 2.01 (d, $J$ = 12.5 Hz, 1 H), 1.75–147 (m, 9 H), 1.11–0.72 (m, 1 H), 0.82 (d, $J$ = 6.6 Hz, 3 H), 0.75 (d, $J$ = 6.4 Hz, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 217.41, 149.28, 133.04, 60.28, 54.16, 51.62, 45.82, 38.91, 37.86, 34.30, 33.33, 31.67, 29.87, 29.00, 23.57, 21.92, 20.82; MS $m/z$ ($M^+$) calcd 246.1984, obsd 246.2021.

**Prototypical Oxy-Cope Rearrangement Involving Potassium Hexamethyldisilazide as Base. Isomerization of 15.** In an oven-dried 25-mL two-necked flask flushed with nitrogen was placed 149 mg (0.606 mmol) of **15**, 192 mg (0.727 mmol) of 18-crown-6, and 5 mL of anhydrous tetrahydrofuran. Potassium hexamethyldisilazide (0.713 mL of a 1.02 M solution in tetrahydrofuran, 0.727 mmol) was added dropwise, and the reaction mixture was refluxed for 30 min and worked up as described above. MPLC purification (silica gel, elution with 2% ether in petroleum ether) afforded 13 mg (9%) of **20** followed by 100 mg (67%) of **18**.

For **20**: pale yellow oil; IR (neat, cm$^{-1}$) 2952, 2866, 1695, 1470, 1455; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 2.50 (t, $J$ = 6.3 Hz, 1 H), 2.37–2.31 (m, 2 H), 2.14–2.03 (m, 3 H), 1.78–1.08 (series of m, 14 H), 0.88 (d, $J$ = 6.8 Hz, 3 H), 0.84 (d, $J$ = 6.7 Hz, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) (ppm) 216.34, 55.93, 52.18, 47.34, 46.74, 40.80, 40.41, 40.09, 33.16, 31.88, 31.68, 30.04, 27.71, 27.23, 21.45, 19.15, 16.20; MS $m/z$ ($M^+$) calcd 246.1983, obsd 246.1971.

**Rearrangement of 24.** Heating 103 mg (0.422 mmol) of **24** with KH (34 mg, 0.844 mmol) and 18-crown-6 (223 mg, 0.844 mmol) in tetrahydrofuran (2 mL) for 1 h and MPLC (silica gel, elution with 2% ether in petroleum ether) gave 76 mg (74%) of **26** and 14 mg (14%) of **27**.

For **26**: colorless crystals, mp 85–85.5 °C (from ethanol); IR ($CDCl_3$, cm$^{-1}$) 2940, 2869, 1699, 1634, 1449; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.66–5.65 (m, 1 H), 3.38–3.28 (m, 1 H), 2.76 (m, 1 H), 2.55–2.30 (m, 4 H), 2.19–2.01 (m, 3 H), 1.76–0.93 (series of m, 14 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 207.70, 145.86, 136.19, 63.19, 42.20, 42.08, 41.38, 41.22, 40.76, 38.03, 37.83, 33.98, 33.70, 33.28, 28.11, 25.40, 19.83; MS $m/z$ ($M^+$) calcd 244.1827, obsd 244.1835.

Anal. Calcd for $C_{17}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.30; H, 9.91.

For **27**: colorless crystals, mp 74–75 °C (from ethanol); IR ($CDCl_3$, cm$^{-1}$) 3024, 2936, 2869, 1689, 1627, 1454; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.56 (s, 1 H), 2.90–2.79 (m, 2 H), 2.54–2.44 (m, 2 H), 2.40–2.26 (m, 5 H), 2.06 (dd, $J$ = 13.0, 6.0 Hz, 1 H), 1.96 (dd, $J$ = 15.5, 9.9 Hz, 1 H), 1.79–1.08 (series of m, 12 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 211.08, 150.31, 135.30, 61.84, 46.57, 46.10, 45.05, 44.34, 41.19, 39.04, 37.20, 35.17, 34.46, 29.65, 29.54, 27.82, 19.56; MS $m/z$ ($M^+$) calcd 244.1827, obsd 244.1847.

**Rearrangement of 28 with Potassium Hydride.** Heating 114 mg (0.416 mmol) of **28** with 33 mg (0.832 mmol) of KH and 220 mg (0.832 mmol) of 18-crown-6 in tetrahydrofuran (2 mL) for 3 h and MPLC purification (silica gel, 2% ether in petroleum ether) furnished 90 mg (79%) of **30**, 14 mg (13%) of **31**, and 3 mg (3%) of **32**.

For **30**: colorless crystals, mp 89.5–90 °C (from ethanol); IR ($CDCl_3$, cm$^{-1}$) 2959, 2935, 2874, 1706, 1686, 1469; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.75 (d, $J$ = 1.0 Hz, 1 H), 2.52–1.80 (series of m, 11 H), 1.71–1.63 (m, 2 H), 1.47–1.36 (m, 3 H), 1.13–1.08 (m, 1 H), 0.90 (s, 3 H), 0.89 (s, 3 H), 0.81 (d, $J$ = 6.8 Hz, 3 H), 0.78 (d, $J$ = 6.7 Hz, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 210.75, 147.81, 136.09, 55.07, 50.13, 49.96, 41.51, 41.16, 34.84, 34.54, 34.36, 33.30, 32.31, 31.89, 29.46, 28.97, 27.83, 22.03, 19.72; MS $m/z$ ($M^+$) calcd 274.2297, obsd 274.2310; X-ray analysis, see below.

For **31**: colorless crystals, mp 72.5–73 °C (from ethanol); IR (neat, cm$^{-1}$) 3048, 2928, 2863, 1686, 1634, 1469; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.81 (s, 1 H), 2.82 (ddd, $J$ = 15.4, 7.9, 1.5 Hz, 1 H), 2.69–2.55 (m, 3 H), 2.34–2.08 (m, 5 H), 1.89–1.58 (m, 6 H), 1.49–1.37 (m, 1 H), 1.10–0.84 (m, 1 H), 0.97 (s, 3 H), 0.92 (d, $J$ = 6.6 Hz, 3 H), 0.90 (s, 3 H), 0.85 (d, $J$ = 6.4 Hz, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 217.20, 149.76, 131.85, 60.38, 54.06, 51.93, 50.24, 42.24, 37.71, 35.16, 34.43, 34.34, 33.49, 32.21, 30.44, 29.02, 26.30, 23.62, 21.94; MS $m/z$ ($M^+$) calcd 274.2296, obsd 274.2290.

For **32**: colorless oil; IR (neat, cm$^{-1}$) 2930, 2868, 1702, 1468; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 2.46 (t, $J$ = 7.7 Hz, 1 H), 2.36 (t, $J$ = 8.9 Hz, 1 H), 2.15–2.02 (m, 3 H), 1.77 (t, $J$ = 6.1 Hz, 1 H), 1.72–1.05 (m, 12 H), 0.99 (s, 3 H), 0.91 (s, 3 H), 0.89 (d, $J$ = 6.8 Hz, 3 H), 0.86 (d, $J$ = 6.7 Hz, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 213.56, 55.58, 51.14, 47.37, 46.98, 42.80, 40.76, 40.33, 37.55, 32.83, 32.35, 32.25, 32.18, 31.91, 29.42, 28.37, 27.90, 21.63, 19.65; MS $m/z$ ($M^+$) calcd 274.2296, obsd 274.2280.

**Rearrangement of 33.** Heating 81 mg (0.298 mmol) of **33** with KH (29 mg, 0.60 mmol) and 18-crown-6 (158 mg, 0.596 mmol) in tetrahydrofuran (2 mL) for 1 h and subsequent MPLC on silica gel (elution with 2% ether in petroleum ether) afforded 55 mg (68%) of **35** and 19 mg (23%) of **36**.

For **35**: colorless solid, mp 84–85 °C (from ethanol); IR ($CDCl_3$, cm$^{-1}$) 3047, 2950, 2870, 1696, 1634, 1455; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.69 (s, 1 H), 3.35–3.24 (m, 1 H), 2.60–2.07 (series of m, 9 H), 1.71–1.04 (series of m, 11 H), 0.94 (s, 3 H), 0.92 (s, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 207.86, 147.01, 135.87, 62.89, 49.78, 42.42, 42.41, 41.56, 41.35, 37.26, 34.11, 33.89, 33.68, 33.41, 33.22, 32.69, 32.18, 27.17, 25.43; MS $m/z$ ($M^+$) calcd 272.2140, obsd 272.2146; for ORTEP diagram obtained by X-ray crystallographic analysis, see supplementary material.

For **36**: colorless solid, mp 96–97 °C (from ethanol); IR ($CDCl_3$, cm$^{-1}$) 2963, 2941, 2873, 1690; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.68 (s, 1 H), 2.91–2.80 (m, 1 H), 2.60–2.24 (m, 7 H), 2.05 (dd, $J$ = 12.8, 6.1 Hz, 1 H), 1.86–1.70 (m, 4 H), 1.61–1.47 (m, 2 H), 1.38–1.10 (m, 6 H), 0.90 (s, 3 H), 0.85 (s, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 210.91, 150.81, 134.15, 61.67, 50.42, 47.14, 46.03, 45.15, 41.22 (2 C), 37.09, 35.20, 35.04, 34.40, 33.04, 30.45, 29.46, 27.86, 27.00; MS $m/z$ ($M^+$) calcd 272.2140, obsd 272.2163.

**Rearrangement of 38/39. A. Regular Quench.** A 1:2.3 mixture of **38** and **39** (165 mg, 0.602 mmol) in tetrahydrofuran (3 mL) was refluxed for 2.5 h with KH (48 mg, 1.2 mmol) and 18-crown-6 (317 mg, 1.2 mmol) and worked up in the usual manner. MPLC purification (silica gel, 2% ether in petroleum ether) gave 55 mg (33%) of **40** and 37 mg (24%) of **41**. The normalized yields are 48% and 74%, respectively.

For **40**: colorless solid, mp 47–47.5 °C (from ethanol); IR (film, cm$^{-1}$) 3032, 2956, 2932, 2874, 1694, 1464; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.74 (s, 1 H), 2.81–2.73 (m, 2 H), 2.44–2.36 (m, 2 H), 2.27–2.11

(m, 3 H), 2.00–1.90 (m, 2 H), 1.74–1.18 (series of m, 8 H), 0.95 (d, $J$ = 6.6 Hz, 3 H), 0.88 (s, 3 H), 0.82 (s, 3 H), 0.79 (t, $J$ = 7.4 Hz, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 215.63, 149.46, 133.04, 66.69, 55.56, 50.39, 47.19, 41.63, 41.11, 39.08, 38.35, 34.90, 33.78, 32.78, 30.49, 26.66, 26.32, 20.28, 12.05; MS $m/z$ ($M^+$) calcd 274.2296, obsd 274.2313.

For **41**: colorless crystals, mp 48–49 °C (from ethanol); IR (film, cm$^{-1}$) 3044, 2959, 2949, 2877, 1705, 1634, 1455; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.73 (s, 1 H), 2.59 (t, $J$ = 10.5 Hz, 1 H), 2.42–2.08 (series of m, 7 H), 1.90–1.80 (m, 3 H), 1.55–1.12 (series of m, 6 H), 0.92 (d, $J$ = 6.4 Hz, 3 H), 0.89 (s, 3 H), 0.88 (s, 3 H), 0.77 (t, $J$ = 7.5 Hz, 3 H); $^{13}$C NMR (20 MHz, $C_6D_6$) (ppm) 211.28, 148.15, 136.23, 56.35, 52.72, 50.00, 43.65, 42.26, 39.63, 39.37, 35.04, 34.16, 33.21, 32.21, 28.83, 28.00, 25.25, 18.51, 11.72; MS $m/z$ ($M^+$) calcd 274.2296, obsd 274.2254.

Anal. Calcd for $C_{19}H_{30}O$: C, 83.15; H, 11.02. Found: C, 82.87; H, 10.97.

**B. Inverse Quench.** The same procedure was adopted with the exception that the reaction mixture was quenched by transfer via cannula into a flask containing cold (0 °C), saturated ammonium chloride solution. Beginning with 209 mg of the same **38**/**39** mixture, there was isolated 46 mg (22%) of **40** and 51 mg (24%) of **41**. The normalized yields are 32% and 81%.

**Rearrangement of 47.** Heating of **47** (182 mg, 0.700 mmol) with KH (56 mg, 1.40 mmol) and 18-crown-6 (370 mg, 1.40 mmol) in anhydrous tetrahydrofuran (2 mL) for 2.5 h and MPLC of the product mixture (silica gel, 1% ether in petroleum ether) gave rise to **49** (111 mg, 61%) followed by **50** (26 mg, 14%).

For **49**: colorless oil; IR (neat, cm$^{-1}$) 3018, 2915, 2840, 1692, 1634, 1456; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.59 (d, $J$ = 1.3 Hz, 1 H), 2.72–2.02 (series of m, 8 H), 1.79–1.60 (m, 5 H), 1.42–1.28 (m, 5 H), 1.10 (s, 3 H), 0.88 (d, $J$ = 6.2 Hz, 3 H), 0.76 (t, $J$ = 7.2 Hz, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$) (ppm) 217.95, 146.59, 137.63, 60.92, 53.36, 49.03, 45.24, 43.40, 43.27, 41.60, 38.41, 37.44, 36.87, 28.35, 22.75, 21.63, 18.86, 13.82; MS $m/z$ ($M^+$) calcd 260.2140, obsd 260.2119.

Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 82.97; H, 10.85.

For **50**: colorless oil; IR (neat, cm$^{-1}$) 2936, 2836, 1698, 1455; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 2.41–2.05 (m, 4 H), 1.87–1.64 (m, 3 H), 1.54–1.21 (m, 10 H), 1.17–0.87 (m, 1 H), 0.96 (d, $J$ = 6.6 Hz, 3 H), 0.91 (s, 3 H), 0.90 (t, $J$ = 7.4 Hz, 3 H), 0.86–0.74 (m, 1 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 213.28, 57.61, 52.33, 49.50, 45.93, 42.69, 42.22, 41.51, 39.25, 38.86, 38.55, 35.15, 27.56, 25.83, 20.49, 17.93, 11.67; MS $m/z$ ($M^+$) calcd 260.2140, obsd 260.2142.

**Rearrangement of 51a.** A 149-mg (0.521 mmol) sample of **51a** was heated in tetrahydrofuran (2 mL) with KH (42 mg, 1.04 mmol) and 18-crown-6 (275 mg, 1.04 mmol) for 1 h. MPLC purification (silica gel, 2% ether in petroleum ether) gave 98 mg (66%) of **53** and 43 mg (29%) of **54**.

For **53**: colorless solid, mp 95–96 °C (from ethanol); IR ($CDCl_3$, cm$^{-1}$) 3034, 2959, 2934, 2900, 2874, 2849, 1701, 1637, 1447; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.48 (t, $J$ = 2.2 Hz, 1 H), 2.59 (dd, $J$ = 7.7, 2.2 Hz, 1 H), 2.52–2.27 (m, 5 H), 2.13 (dd, $J$ = 13.6, 11.9 Hz, 1 H), 1.96–1.86 (m, 1 H), 1.75–1.08 (series of m, 14 H), 0.95–0.76 (m, 1 H), 0.82 (d, $J$ = 6.7 Hz, 3 H), 0.77 (d, $J$ = 6.7 Hz, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 209.79, 145.02, 135.81, 57.39, 55.22, 49.81, 47.38, 43.01, 40.40, 34.09, 33.87, 33.21, 32.77, 31.48, 27.67, 25.78, 23.72, 21.91, 20.31, 19.41; MS $m/z$ ($M^+$) calcd 286.2297, obsd 286.2297; X-ray analysis, see below.

For **54**: colorless solid, mp 73–74 °C (from ethanol); IR ($CDCl_3$, cm$^{-1}$) 3020, 2960, 2938, 2906, 2878, 2866, 1688, 1638; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.39 (s, 1 H), 2.65–2.52 (m, 4 H), 2.31–2.17 (m, 2 H), 2.04–1.99 (m, 1 H), 1.86–1.36 (series of m, 13 H), 1.19–1.06 (m, 1 H), 1.02–0.75 (m, 2 H), 0.82 (d, $J$ = 6.6 Hz, 3 H), 0.76 (d, $J$ = 6.4 Hz, 3 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 217.08, 148.89, 132.79, 60.13, 55.82, 53.96, 51.56, 46.66, 45.94, 35.54, 35.35, 34.98, 34.22, 33.31, 29.02, 25.49, 24.42, 23.63, 23.16, 21.90; MS $m/z$ ($M^+$) calcd 286.2297, obsd 286.2309.

**Rearrangement of 55.** Alcohol **55** (153 mg, 0.539 mmol) was heated at reflux in tetrahydrofuran (2 mL) with KH (54 mg, 1.35 mmol) and 18-crown-6 (357 mg, 1.35 mmol) for 1.5 h. The usual workup followed by MPLC (silica gel, elution with 2% ether in petroleum ether) led to the isolation of 121 mg (79%) of **57** and 16 mg (10%) of **58**.

For **57**: colorless solid, mp 112.5–113 °C (from ethanol); IR ($CDCl_3$, cm$^{-1}$) 3041, 2944, 2871, 2850, 1698, 1455; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.43 (t, $J$ = 2.0 Hz, 1 H), 3.36 (q, $J$ = 9.0 Hz, 1 H), 2.61–2.33 (m, 5 H), 2.11–2.02 (m, 2 H), 1.76–1.16 (series of m, 18 H), 0.94–0.84 (m, 1 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 207.55, 144.84, 135.39, 63.46, 54.92, 50.93, 42.17, 41.69, 41.37, 40.92, 39.74, 34.09, 33.70, 33.24, 31.78, 31.74, 25.83, 25.26, 23.56, 19.80; MS $m/z$ ($M^+$) calcd 284.2140, obsd 284.2153.

Anal. Calcd for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.30; H, 9.96.

For **58**: colorless solid, mp 79–79.5 °C (from ethanol); IR ($CDCl_3$, cm$^{-1}$) 2941, 2871, 1690, 1631, 1455; $^1$H NMR (300 MHz, $C_6D_6$) $\delta$ 5.36 (s, 1 H), 2.83–2.77 (m, 2 H), 2.56–2.32 (m, 5 H), 2.05–1.97 (m, 2 H), 1.78–1.11 (m, 17 H), 0.92–0.84 (m, 1 H); $^{13}$C NMR (75 MHz, $C_6D_6$) (ppm) 210.70, 149.82, 134.92, 61.89, 55.70, 49.36, 46.19, 45.97, 44.84, 44.02, 41.11, 35.27, 35.21, 34.98, 34.61, 29.66, 27.88, 25.77, 24.24, 21.37; MS $m/z$ ($M^+$) calcd 284.2140, obsd 284.2147.

**X-ray Crystallographic Analysis of 18.** The clear, colorless crystal of **18** used for data collection was obtained by cutting a large crystal down to a suitable size. Preliminary examination of the diffraction pattern on a Rigaku AFC5 diffractometer indicated a monoclinic crystal system with systematic absences: $h0l$, $h = 2n + 1$, and $0k0$, $k = 2n + 1$. The space group is uniquely determined as $P2_1/a$. The cell constants $a$ = 14.267 (2) Å, $b$ = 5.6418 (6) Å, $c$ = 19.088 (2) Å, and $\beta$ = 107.54 (1)° were based on a least-squares refinement of the setting angles for 24 reflections with $2\theta$ values in the range 29–30° and with Mo K$\alpha$ radiation.

Intensities were measured by the $\omega$–$2\theta$ scan method at ambient temperature. Six standard reflections were measured after every 150 reflections and indicated that a small amount of crystal decomposition had occurred during the course of data collection. Data reduction included Lorentz, polarization, and crystal-decay corrections. All calculations were done by using the TEXSAN package of crystallographic programs.[24]

The structure was solved by the direct-methods program MITHRIL.[25] All the non-hydrogen atoms were located on the electron density map. Full-matrix least-squares isotropic refinement of the model converged at an $R$ value of 0.136. After one cycle of anisotropic refinement, all of the hydrogen atoms, including the methyl group hydrogen atoms, were located on a difference electron density map. The hydrogen atoms were then included in the model as fixed contributions at their calculated positions with C–H = 0.98 Å and $B_H = 1.2B_{eq}$ (attached carbon atom). The methyl group hydrogen atoms were idealized to sp$^3$ geometry based on their positions in the difference electron density map. All least-squares refinements were based on $F$ (for all three structures reported here), so that the function minimized in least squares was $\sum w(|F_o| - |F_c|)^2$ where $w = 1/\sigma^2(F_o)$. The final refinement cycle for the 1655 intensities with $F_o^2 > 3\sigma(F_o^2)$ and the 163 variables (anisotropic non-hydrogen atoms and hydrogen atoms fixed) yielded agreement indices of $R$ = 0.048 and $R_w$ = 0.054. The final difference electron density map had maximum and minimum peak heights of 0.15 and −0.18 e/Å$^3$. Scattering factors were obtained from the usual sources.[26]

**X-ray Crystallographic Analysis of 30.** Crystals of **30** are clear, colorless rectangular plates. Examination of the diffraction pattern on a Rigaku AFC5 diffractometer indicated a monoclinic crystal system with systematic absences, $h0l$, $h = 2n + 1$, and $0k0$, $k = 2n + 1$, which uniquely define the space group as $P2_1/a$. At room temperature, the cell constants $a$ = 10.824 (2) Å, $b$ = 13.354 (1) Å, $c$ = 11.445 (1) Å, and $\beta$ = 92.42 (1)° are based on a least-squares refinement of the diffractometer setting angles for 25 reflections with $2\theta$ values between 20° and 30° and with Mo K$\alpha$ radiation.

Intensities were measured by the $\omega$–$2\theta$ scan method. Six standard reflections were measured after very 150 reflections and

(24) TEXSAN, TEXRAY Structure Analysis package, version 2.1, Molecular Structure Corporation, College Station, TX, 1987.

(25) Gilmore, C. J. *MITHRIL: A Computer Program for the Automatic Solution of Crystal Structures from X-ray Data*; University of Glasgow: Scotland, 1983.

(26) Scattering factors for C and O are from: *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, England, 1974; Vol. IV, p 71. The scattering factors for the hydrogen atom are from: Stewart, R. F.; Davidson, E. R.; Simpson, W. T. *J. Chem. Phys.* **1965**, *42*, 3175.

indicated that a small amount of crystal deterioration had occurred during the course of data collection. The intensities of this set of standards had decreased by an average value of 8.5% at the end of the data collection. Data reduction, including correction for crystal decay, and all further calculations were done with the TEXSAN package of crystallographic programs.[24]

The structure was solved with the direct-methods program MITHRIL,[25] where all of the non-hydrogen atoms were located on an electron density map. Most of the hydrogen atoms were located on a difference electron density map after the anisotropic stage had been reached. The hydrogen atoms were subsequently added to the model as fixed contributions at calculated positions with the assumptions C–H = 0.98 Å and $B_H = 1.2B_{eq}$ (attached carbon atom). The methyl hydrogen atoms were idealized to $sp^3$ geometry based on their locations in the difference electron density map. The final refinement cycle for the 1332 intensities with $F_o^2 > 3\sigma(F_o^2)$ and the 181 variables (anisotropic non-hydrogen atoms and hydrogen atoms fixed) gave agreement indices of $R = 0.048$ and $R_w = 0.052$. The final difference electron density map contained maximum and minimum peak heights of 0.16 and −0.19 e/Å$^3$. Scattering factors were obtained from the usual sources.[26]

**X-ray Crystallographic Analysis of 53.** Crystals of **53** are clear and colorless with a rodlike habit. Examination of the diffraction pattern on a Rigaku AFC5 diffractometer indicated a monoclinic crystal system with systematic absences $0k0$, $k = 2n + 1$. Since two molecules in the unit cell result in a reasonable calculated density, the space group is assumed to be $P2_1$. At room temperature, the cell constants $a = 5.811$ (1) Å, $b = 17.310$ (2) Å, $c = 8.731$ (1) Å, and $\beta = 107.70$ (1)° are based on a least-squares refinement of the diffractometer setting angles for 25 reflections with $2\theta$ values between 28° and 30° and with Mo K$\alpha$ radiation.

Intensities were measured by the $\omega$–$2\theta$ scan method. Six standard reflections were measured after every 150 reflections and indicated that the crystal was stable during the course of data collection. Data reduction and all additional calculations were done with the TEXSAN package of crystallographic programs.[24]

The structure was solved by the direct-methods program MITHRIL,[25] where all the non-hydrogen atoms appeared on an electron density map. The choice of enantiomer was made arbitrarily. Many of the hydrogen atoms were located on a difference electron density map after the anisotropic stage of refinement had been reached. All of the hydrogen atoms were subsequently added to the model as fixed contributions at calculated positions with the assumptions C–H = 0.98 Å and $B_H = 1.2B_{eq}$ (attached carbon atom). The methyl hydrogen atoms were idealized to $sp^3$ geometry based on their locations in the difference electron density map. A secondary extinction coefficient was refined in the final cycles of least squares; a value of 1.7 (1) × $10^{-5}$ was obtained for this parameter. The final refinement cycle for the 1509 intensities with $F_o^2 > 3\sigma(F_o^2)$ and the 190 variables (anisotropic non-hydrogen atoms and hydrogen atoms fixed) gave agreement indices of $R = 0.040$ and $R_w = 0.047$. The final difference electron density map contained maximum and minimum peak heights of 0.15 and −0.12 e/Å$^3$. Scattering factors were obtained from the usual sources.[26]

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**Supplementary Material Available:** Stereodrawings of the unit cells and tables of torsion angles, final positional parameters, and final thermal parameters as well as ORTEP drawings of the four molecules in the asymmetric unit of **35** (22 pages); tables of structure factors for **18**, **30**, and **53** (33 pages). Ordering information is given on any current masthead page.

# Comparative Analysis of Molecular-Recognition Levels Attained during Capture of Chiral Cyclopentenyl Organometallics by Conformationally Immobilized Ketonic Systems

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The diastereoselectivity of the reactions of the chiral organocerates **10**, **15**, **20**, and **22** with $\beta,\gamma$-unsaturated ketones **1** and **7** is described. The reactions involving the tricyclic substrate **7** exhibit excellent $\pi$-facial stereoselectivity (syn to the double bond) and are respectably diastereoselective when **10** (11:1) and **15** (8.1:1) are involved. In the case of the bicyclic **6**, there is continued preference for nucleophilic capture syn to the double bond; however, the absence of the cyclopropane ring is accompanied by a dropoff in molecular-recognition capability. Stereochemical assignments were made by NMR correlations and defined unequivocally in four cases by X-ray crystallographic analysis of the anionic oxy-Cope rearrangement products. The stereochemistries of these bridgehead unsaturated ketones reveal in addition that chair-like transition states are adopted during the sigmatropic reorganizations. The results clearly show that the particular substitution pattern in the vinyl organometallic is a significant variable in determining diastereoselectivity. Those interactions considered most important have been analyzed by MODEL calculations. Nonbonded interactions in the interstitial space following complexation of cerium to oxygen and adoption of a somewhat obtuse trajectory give evidence of exerting the greatest control.

Our understanding of the extent and direction of single or double diastereoselection[2] attainable during nucleophilic additions of chiral vinyl organometallics to $\beta,\gamma$-unsaturated ketones is currently founded on a limited number of case studies.[3] These have involved 7,7-disubstituted 5-norbornen-2-ones (1),[4] 7-methyl-7-vinylbicyclo[3.2.0]hept-2-

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