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

Acknowledgment. This work was assisted financially by Grant GM-28468 from the National Institutes of Health. We also thank the Eli Lilly crystallographic analysis team for their invaluable contributions.

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

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

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

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

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

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

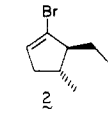
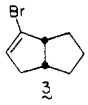
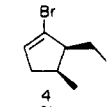
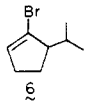
Results

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

(1) Campus Chemical Instrument Center.
(2) (a) Paquette, L. A.; Learn, K. S.; Romine, J. L.; Lin, H.-S., preceding paper in this issue. (b) Paquette, L. A.; Learn, K. S. *J. Am. Chem. Soc.* **1986**, *108*, 7873.
(3) Paquette, L. A. *Pure Appl. Chem.*, in press.
(4) (a) Schenck, G. O.; Gollnick, K.; Buchwald, G.; Schroeter, S.; Ohloff, G. *Justus Liebigs Ann. Chem.* **1964**, *674*, 93. (b) Schenck, G. O.; Neumuller, O.-A.; Ohloff, G.; Schroeter, S. *Ibid.* **1965**, *687*, 26. (c) Dauben, W. G.; Lorber, M.; Fullerton, D. S. *J. Org. Chem.* **1969**, *34*, 3587. (d) See also: Sully B. D. *Chem. Ind. (London)* **1964**, 263.
(5) (a) Paquette, L. A.; Learn, K. S.; Romine, J. L. *Synth. Commun.* **1987**, *17*, 369. (b) Paquette, L. A.; Learn, K. S.; Romine, J. L. *Tetrahedron*, in press.
(6) Still, W. C. *J. Am. Chem. Soc.* **1977**, *99*, 4186.
(7) Erman, W. F.; Gibson, T. W. *Tetrahedron* **1969**, *25*, 2493.
(8) Ijima, A.; Takahashi, K. *Chem. Pharm. Bull.* **1973**, *21*, 215.
(9) (a) Habata, Y.; Akabori, S.; Sato, M. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3540. (b) Paquette, L. A.; Pierre, F.; Cottrell, C. E. *J. Am. Chem. Soc.* **1987**, *109*, 5731.
(10) (a) Chan, T. H.; Baldassare, A.; Massuda, D. *Synthesis* **1976**, 801. (b) Taylor, R. T.; Degenhardt, C. R.; Melega, W. P.; Paquette, L. A. *Tetrahedron Lett.* **1977**, 159. (c) Chamberlin, A. R.; Stemke, J. E.; Bond, F. T. *J. Org. Chem.* **1978**, *43*, 147. (d) The original vinyl anions were not utilized directly, because the presence of TMEDA and other reaction byproducts did not allow for clean and efficient conversion to the organometallic reagent.

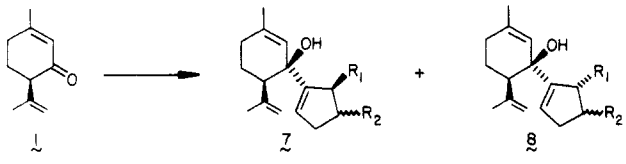
0002-7863/88/1510-0890$01.50/0

Table I. 1,2-Addition of Vinyl Organometallics to (*R*)-(−)-Isopiperitinone (**1**)[a]

vinyl bromide	vinyl bromide:ketone	7:8[b]	yield,[c]
 **2**	1.25:1	1.9:1	67
	1.25:1[d]	2.2:1	45–51
	3.0:1	3.1:1	73–81
	6.0:1	4.0:1	73–92
 **3**	1.25:1	2.6:1	59–72
	1.25:1[d]	1.5:1	67
	3.0:1	4.0:1	77
	6.0:1	3.8:1	74–92
 **4**	1.25:1	2.0:1	61–69
	3.0:1	2.8:1	88–91
	6.0:1	2.7:1	79–89
 **5**	1.2:1[e]	2.2:1	67–71[f]
	3.0:1[e]	2.7:1	24–34[f]
	6.0:1[e]	2.4:1	34–36[f]
 **6**	1.25:1[e]	2.0:1	45–79
	3.0:1[e]	4.0:1	74–76
	6.0:1[e]	4.3:1	53–72

[a] The quality of the ketone used was 71.6% ee, except where noted to be otherwise. [b] Averaged over all of the runs performed; the variability was ±0.2 of the value given. [c] Yields pertain to quantities of isolated products obtained following chromatography. As concerns the products derived from **5**, the low yields reflect a particular sensitivity to silica gel. [d] Anhydrous cerium trichloride (1.375 equiv) added. [e] Starting from samples of **1** possessing 83.8% ee. [f] These yields have been corrected to account for the coproduction of *tert*-butylated alcohol resulting from capture by **1** of unreacted *tert*-butyllithium.

the cyclopentenyl bromide was exposed to 2 equiv of *tert*-butyllithium in tetrahydrofuran at −78 °C,[11] and **1** was subsequently introduced dropwise to effect the 1,2-addition. Product mixtures were analyzed chromatographically. Special care was taken during this phase of the work as well as during preparative-scale separation of the diastereomeric alcohols because of their recognized sensitivity to certain adsorbents.

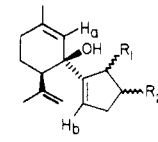


1 **7** **8**

Table I provides a summary of the reactions examined, the great majority of which were carried out in duplicate or triplicate. In all cases, only two diastereomers were seen. This is the direct result of π-face selectivity associated with the capture of **1** by nucleophiles of reasonable size. The ^{1}H NMR data compiled in Table II provide evidence that the alcohols can easily be assigned to one series or the other solely on this basis. Thus, H_a in the major product is shielded relative to its counterpart in the minor series. This particular vinylic proton is readily identified by means of its coupling to the adjoining sp^2-bound methyl group. Since the olefinic protons of the isopropenyl group most often appear as a singlet, the identification of H_b was also simplified. Characteristically, the latter proton signal was very diagnostic, appearing significantly more downfield in **7** than in **8**. The special sensitivity of the H_a and H_b absorptions is believed to be associated with the particular relative conformation adopted by the cyclopentenyl ring, which in turn is directly linked to the specific stereochemical orientation of the groups at its C-4 (and C-5) sites. That the absolute configurational assignments shown in **7** and **8** are indeed correct was subsequently established by X-ray crystallographic analysis of oxy-Cope rearrangement products, as will be discussed later.

(11) Tetrahydrofuran has been shown to be the solvent of choice in an earlier study[2] and was employed uniquely in the present investigation.

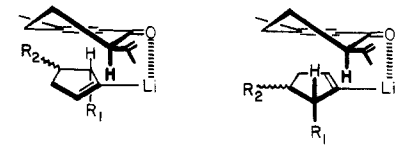
Table II. Select ^{1}H NMR Chemical Shift Data for **7a–e** and **8a–e** (300 MHz, C_6D_6 Solution)



vinyl bromide	diastereomer	chemical shift, δ H_a	chemical shift, δ H_b
2	**7a**	5.35	5.82
	8a	5.49–5.50	5.39
3	**7b**	5.35–5.36	5.69–5.71
	8b	5.47	5.30–5.31
4	**7c**	5.37	5.90–5.91
	8c	5.46–5.47	5.51
5	**7d**	5.49–5.50	5.83
	8d	5.49–5.51	5.56
6	**7e**	5.40–5.41	5.97–5.98
	8e	5.53	5.45

Quite striking were the observations that the expectedly low diastereomeric ratios that materialize when the vinyl bromide/ketone ratio is almost equal (1.25:1) approach an upper limit roughly defined by a 3.0:1 ratio of reagents. Although improvement was seen in the case of **2** when a sixfold amount of the vinyl bromide was utilized, this phenomenon proved not to be general. From the practical point of view, it would therefore be wasteful of vinyl bromide and *tert*-butyllithium to surpass the 3.0:1 ratio, particularly on a preparative scale. The two experiments performed in the presence of added cerium trichloride[12] gave results that proved not to be dramatically different, in line with precedent.[2] Since lowered yields were often attained under these circumstances, probably as the result of the reduced nucleophilicity of organocerium reagents, this aspect of the investigation was not further pursued.

The response of (−)-**1** to the lithium reagents derived from **2–6** follows a general pattern. The isopropenyl substituent is adequately bulky to guarantee its predominant equatorial disposition in **1**. In line with a great deal of precedent[13] and the successful qualitative theory developed by Cieplak,[14,15] a pronounced preference for axial approach of the nucleophile would be in evidence. Superpositioning of the Bürgi–Dunitz model for the directionality of nucleophilic capture by the carbonyl group[16] gives rise to transition-state structural possibilities such as **9** and **10**[17] for ultimate arrival at **7** and **8**, respectively. The principal difference



9 **10**

between the bonding pathways to **1** and to 7,7-disubstituted norbornen-2-ones is the greater coercion the latter structural type places on the mutual alignment of the reaction partners in the

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

(13) Review: Wigfield, D. C. *Tetrahedron* **1979**, *35*, 449.

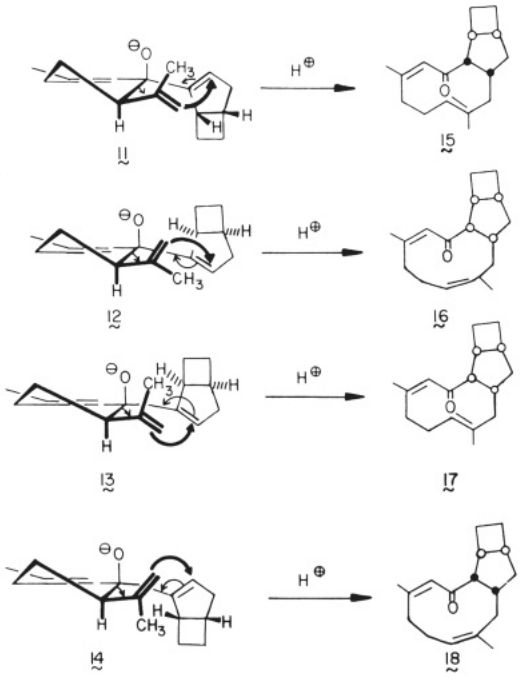
(14) (a) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540. (b) Cheung, C. K.; Tseng, L. T.; Lin, M.-H.; Srivastava, S.; le Noble, W. J. *J. Am. Soc.* **1986**, *108*, 159.

(15) For a contrasting viewpoint, consult: Lodge, E. P.; Heathcock, C. H. *J. Am. Chem. Soc.* **1987**, *109*, 2819, 3353.

(16) (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.

(17) As noted in the preceding paper (see ref 45), representations such as **9** and **10** are oversimplified versions of the probable interactions involving the Li cation. The actual transition states are very likely characterized by higher levels of aggregation as indicated. In the absence of specific information regarding such details, the streamlined representations offer simplicity while retaining suitable predictive power.

Scheme I



available transition states. Although diastereoselectivity is consequently lower for **1**, sufficient steric discrimination is operational to permit the favored production of **7** in the systems examined. Since alcohols **7** and **8** can readily be separated, kinetic resolution can be routinely achieved.

Stereochemical Options for the Oxy-Cope Rearrangement of 7 and 8. The second line of mechanistic inquiry delved into during this investigation relates to the anionic oxy-Cope rearrangement of alcohols **7** and **8**. The number of stereogenic centers in these substrates allows considerable insight to be gained into the preferred conformational characteristics of this [3.3] sigmatropic shift. The four options for **7d** are illustrated in Scheme I. Compounds **8**, of course, have available the same number and type of diastereomeric reaction trajectories (Scheme II).

Should the six-electron reorganizations in question be intramolecular as fully expected,[18] the configuration about the asymmetric carbon atoms and the double-bond geometry happen not to be independent variables. The only optional phenomenon is the chair or boat nature of the cyclic transition state. However, the highly ordered characteristics of whichever geometry is ultimately adopted in the activated complex provide the final piece of stereochemical information needed to elucidate the entire course of events.

Structures **11** and **12** represent the two possible chairlike transition states available to **7d**. In **11**, the orientation of the isopropenyl group is such that the incipient medium-ring double bond is required to be trans. Moreover, carbon–carbon bond formation occurs on the convex face of the bicyclo[3.2.0]heptene unit, the result being a cis,anti,cis arrangement of the four contiguous chiral centers in **15**. The geometrical and stereochemical outcomes that would materialize if **12** were involved would be in large part reversed. The new double bond within the ten-membered ring would possess cis geometry, and the bicycloheptane subunit would now carry an all-cis arrangement as shown in **16**. In related fashion, the boatlike alternatives **13** and **14** lead directly to isomers **17** and **18**, respectively.

The mechanistic analysis was expected to be unequivocal, since all four product possibilities (**15**–**18**) have different structures.

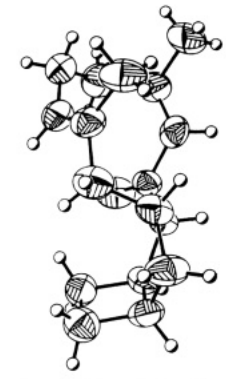


Figure 1. ORTEP drawing of **20** as derived from X-ray crystallographic analysis (courtesy of N. D. Jones, J. D. Swartzendruber, and J. B. Deeter, Eli Lilly Co.).

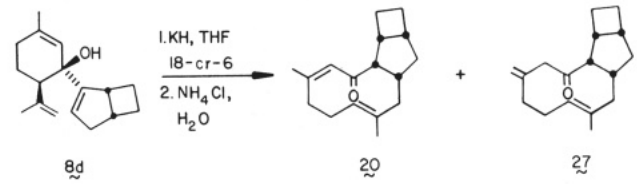
Table III. Crystallographic Data for Germacranolides **20** and **32**

	20	**32**
formula	$C_{17}H_{24}O$	$C_{18}H_{26}O$
FW	244.38	258.41
space group	$P2_12_12_1$	$P2_12_12_1$
a, Å	10.446 (2)	11.714 (2)
b, Å	12.918 (2)	19.965 (3)
c, Å	21.170 (4)	6.563 (1)
α, deg	90.00 (0)	90.00 (0)
β, deg	90.00 (0)	90.00 (0)
γ, deg	90.00 (0)	90.00 (0)
V, Å^3	2857	1534
Z	8	4
ρ_{calcd}, g/cm^3	1.136	1.118
final R	0.095	0.0659

If first principles of conformation theory are applied to this problem, one could surmise that **13** and **14** might not be as energetically accessible as the chair alternatives because of the added energy costs generally associated with boatlike arrangements.[19,20] Steric considerations also suggest that conventional concertedness would be less readily accommodated in **12** and **13**, where bonding to the more congested concave surface of the bicyclo[3.2.0]heptene double bond[21] is mandated. On a purely a priori basis, therefore, **11** can be targeted as the potentially least energy-demanding transition state for anionic oxy-Cope rearrangement within **7d**.

It should be clear that, whatever the ultimate eventuality, chirality transfer should be complete in all four examples. Stated differently, no loss of optical purity should be incurred while proceeding to **15**–**18**, all of which are drawn in proper absolute configuration. Consequently, the coupling of an initial kinetic resolution with a concerted [3.3] sigmatropic rearrangement is seen to be hardly rivaled in its capacity for constructing relatively complex molecules having multiple chiral centers.

Chirality Transfer via Oxyanionic [3.3] Sigmatropy. The generalized reaction conditions adopted for the isomerization of **7** and **8** involved refluxing anhydrous tetrahydrofuran as solvent and iodine-pretreated potassium hydride[22] as the base. Treatment of **8d** in this fashion with 18-crown-6 present as catalyst[22] resulted in the complete consumption of alcohol within 30 min. The cooled



(18) (a) Rozeboom, M. D.; Kiplinger, J. P.; Bartmess, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 1025. (b) Steigerwald, M. L.; Goddard, W. A., III; Evans, D. A. *Ibid.* **1979**, *101*, 1994. (c) Evans, D. A.; Baillargeon, D. L. *Tetrahedron Lett.* **1978**, 3315, 3319. (d) Epiotis, N. D. *J. Am. Chem. Soc.* **1973**, *95*, 1101, 1200, 1206, 1214. (e) Carpenter, B. K. *Tetrahedron* **1978**, *34*, 1877. (f) Ahlgren, G. *Tetrahedron Lett.* **1979**, 915. (g) Bach, P. D.; Coddens, B. A., private communication.

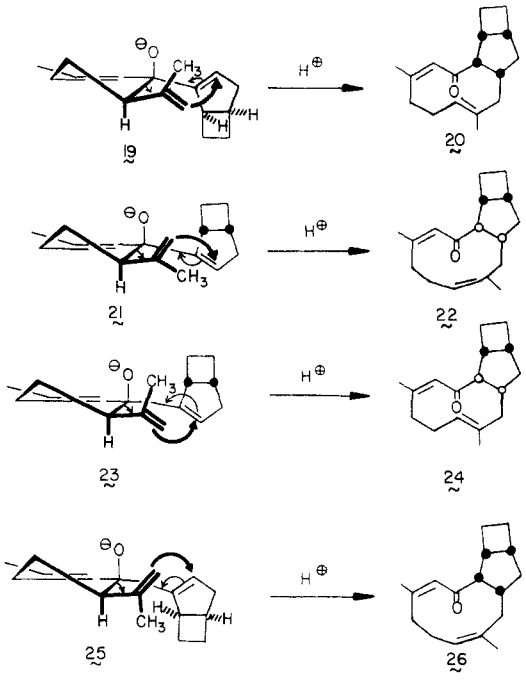
(19) Doering, W. v. E.; Roth, W. R. *Tetrahedron* **1962**, *18*, 67.

(20) Hill, R. K. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: New York, 1984; Vol. III, Chapter 8.

(21) Paquette, L. A. *Top. Curr. Chem.* **1979**, *79*, 41; **1984**, *119*, 1.

(22) Macdonald, T. L.; Natalie, K. J., Jr.; Prasad, G.; Sawyer, J. S. *J. Org. Chem.* **1986**, *51*, 1124.

Scheme II



reaction mixture was then treated with saturated ammonium chloride solution and subjected to chromatographic purification. Two ketones were isolated in yields of 43 and 31%, respectively. The major product, $[\alpha]^{23}_D$ −77.8°, exhibits intense infrared absorptions at 1667 and 1623 cm^{-1}. NMR spectroscopy at 300 MHz showed its two methyl signals to resonate at δ 1.52 and 1.32; the pair of vinylic protons appear at δ 5.71 and 5.10. Although these features are fully consistent with the presence of a germacranolide ring, recourse was made to X-ray crystallography for the purpose of establishing the actual stereochemistry of the molecule. As seen in Table III and Figure 1, the three-dimensional characteristics of this crystalline solid unquestionably define it to be **20**.

The second ketone possesses but one vinylic methyl group (δ 1.44), the chemical shift of which indicates it to be that which is positioned transannular to the ketone functionality. The appearance of three vinylic protons suggested that the double bond in the proximity of the carbonyl group had experienced deconjugation as in **27**. Evidently, the alkaline conditions serve to promote a modicum of deprotonation away from the original site of enolate anion formation, with ultimate installation of the β,-γ-double bond.

It remained to establish that **20** and **27** were otherise of identical stereochemistry. Possible equilibration was not feasible because of the relative ease with which **20** was destroyed when resubjected to alkaline conditions. The greater conformational flexibility of **27** was evident upon inspection of its 500-MHz ^{1}H NMR spectrum recorded at ambient temperature. Following an increase in the probe temperature to 373 K (Figure 2), all of the signals had sharpened considerably to the point where COSY (Figure 3) and NOE studies could be performed conventionally. Once the individual proton assignments were finalized, the assignment of stereochemistry was accomplished readily by selected nuclear Overhauser measurement (Table IV). Importantly, double irradiation of the methyl protons D resulted in integral enhancements of the absorptions due to protons B and G. These phenomena confirm the trans stereochemistry of the adjoining intraring double bond as well as the β-configuration of H_G. Next, independent excitation of H_E induced a 10.9% response in the integral of the H_C absorption. This pair of protons can be proximal only when the double bond they flank is of trans geometry. Finally, irradiation of H_J generated responses from H_G and H_I in addition to H_D (Table IV). The cis-β relationship among all of the stereogenic protons within the bicyclo[3.2.0]heptane subunit was thereby established.

Comparable isomerization of **7d** with potassium hydride gave

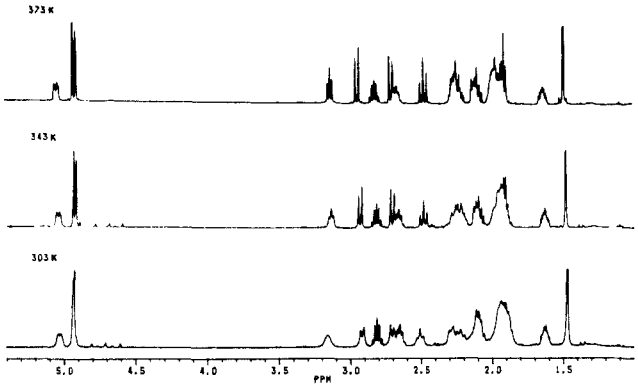


Figure 2. Variable-temperature ^{1}H NMR behavior of **27** (500 MHz, C_6D_5Cl solution).

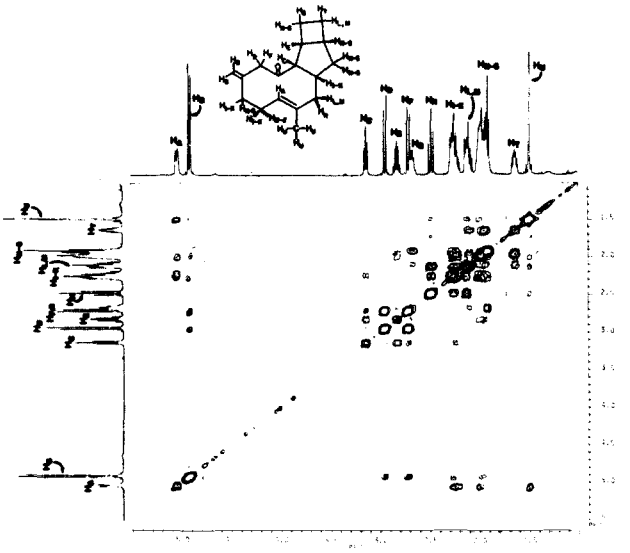
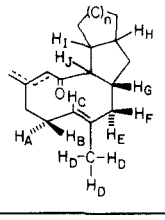


Figure 3. 2-D COSY spectrum of **27** (500 MHz, C_6D_5Cl, 373 K).

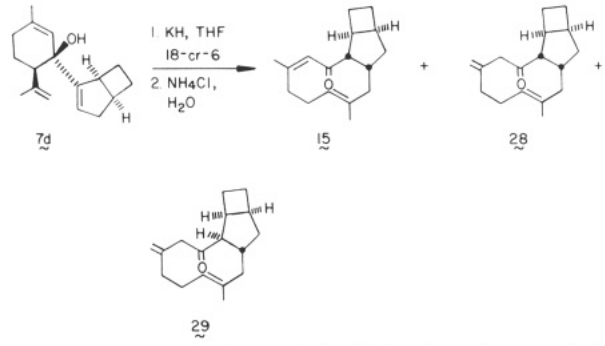
Table IV. Selected Nuclear Overhauser Effects (500 MHz, C_6D_6 Solution Except Where Noted)



proton irrad	ketone	enhancement, %
D	**15**[a]	B (4.1); G (5.3)
	28[a]	B (4.2); F/G (7.8);[d] J (3.8)
	29[a]	B/F (7.1);[d] G (4.8)
	27[b]	B/G (8.6);[d] J (5.0)
	31[c]	B/G (7.1);[d] F (5.3); J (4.2)
E	**15**	C (7.0)
	28	C (3.1)
	29	C (2.0)
	27	C (10.9)
	31	C (2.3)
I	**29**	J (3.5)
J	**27**	D (4.5), G (5.2), I (9.4)
	31	D (1.9), G (2.8), I (7.8)

[a] Recorded at regular probe temperature. [b] Recorded at 100 °C in C_6D_5Cl. [c] Recorded at 70 °C. [d] Overlapping absorptions.

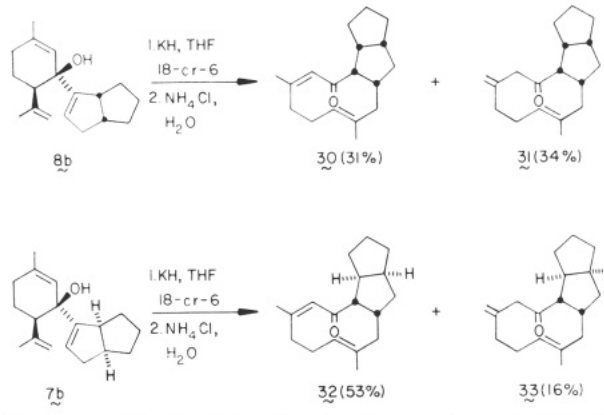
rise to three chromatographically separable isomeric ketones isolated in yields of 24, 39, and 19%. The first of these was identified as (+)-**15** on the strength of COSY (Figure 4) and NOE experiments (Table IV). Elevated temperatures were not required in this instance. The presence of a trans double bond in the



southern sector was clearly revealed as before by an intense H_C–H_E interaction. The proximity of H_D to H_G, indicated by a 5.3% enhancement, rule **17** out of consideration.

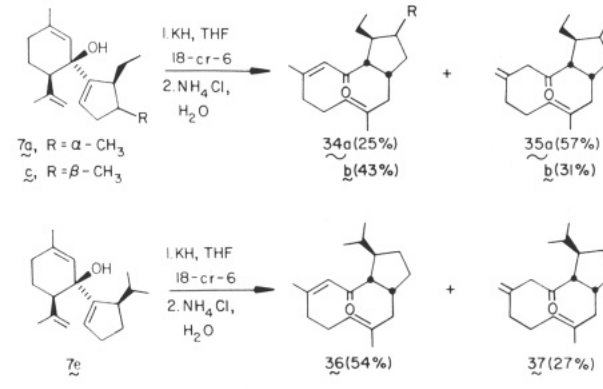
The structural assignments to **28** and **29** were unequivocally realized with equal rigor (Table IV). Ketone **29** served to indicate that protonation at the ring juncture site α to the carbonyl group can materialize from both possible directions.

The response of **8b** and **7b** to anionic oxy-Cope rearrangement was entirely similar, two ketones being isolated from each of these reactions. The COSY and NOE studies performed on **31** and



33 were consistent only for the stereoisomer shown (Table IV). No additonal special assumptions are necessary to permit **30** and **31** to be formulated as shown. Nevertheless, confirmatory evidence was sought in the form of an X-ray crystallographic analysis of **32** (Table III). The ORTEP diagram presented in Figure 5 is seen to corroborate nicely the underlying mechanistic premise.

The oxy-Cope stereoselectivities of potassium alkoxides **7a**, **7c**, and **7e** were also investigated. In each instance, the wholesale similarity of the 300-MHz ^{1}H NMR spectra of the pairs of ketonic products to those recorded for **15**, **28**, **32**, and **33** was striking. These examples were considered not to have intrinsic reason for transversing a different rearrangement transition-state trajectory (see Scheme II) than the somewhat more structurally demanding **7b** and **7d**. Consequently, the absolute stereochemistries given to **34**–**37** have been formulated in a manner consistent with the prior findings.



Conclusion. The general course of chirality transfer by oxyanionic Cope rearrangement of alcohols **7** and **8** justifies further utilization of this process in stereocontrolled synthetic processes. The evidence is consistent with exclusive adaptation of that chairlike transition state which features incipient bonding the face of the π bond in the original vinyl anion that generates a transoid medium-ring double bond. Stated differently, we see that stereochemical control is excellent and that **15** (Scheme I) and **20** (Scheme II) eventuate because the particular electronic reorganization depicted by **11** and **19** is strictly followed. Although the enormous advantage associated with the absence of stereorandomness are to some extent dissipated by proton transfer within the first-formed enolate anion, the ease with which the product ketones can be separated restores this utilitarian feature. This double migration is not often encountered when smaller ring sizes are involved and is consequently not a persistent factor.

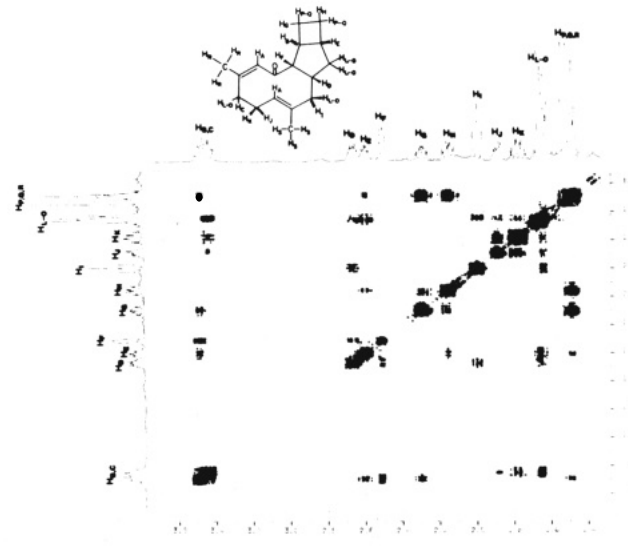


Figure 4. 2-D COSY spectrum of **15** in the δ 3.6–1.4 region (500 MHz, C_6D_6).

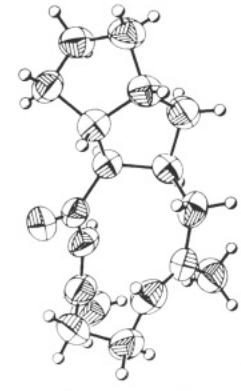


Figure 5. ORTEP drawing of **32** as derived from X-ray crystallographic analysis (courtesy of N. D. Jones, J. D. Swartzenruber, and J. B. Deeter, Eli Lilly Co.).

Noteworthily, all products shown are of relatively high optical purity and possess the absolute configurations illustrated. Therefore, the two-step process leading from (−)-isopiperitenone (**1**) to these germacranolides extends the earlier findings of others who observed preferred adoption of chair transition states for [3.3] sigmatropic rearrangements wherever this is feasibile.[19,20] The implementation of a kinetic resolution step prior to the oxy-Cope process as described herein considerably extends the serviceability of this important reaction.

Experimental Section

1-Bromo-5-isopropylcyclopentene (6). 2-Isopropylcyclopentanone[8] (20.0 g, 1.59 mmol) was dissolved in methanol (60 mL) and treated in one portion with tosylhydrazide (29.61 g, 159 mmol). The reaction mixture was stirred at room temperature for 3 days, at which time the solvent was evaporated. The resulting solid was collected by filtration, washed thoroughly with petroleum ether, and dried overnight under high vacuum. There was obtained 43.72 g (94%) of the tosylhydrazone as a

white powder: mp 129.5–130 °C (from hexane–ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 (d, J = 8.3 Hz, 2 H), 7.38 (s, 1 H), 7.28 (d, J = 8.1 Hz, 2 H), 2.41 (s, 3 H), 2.41–2.25 (m, 2 H), 2.06–1.92 (m, 2 H), 1.89–1.73 (m, 2 H), 1.64–1.33 (m, 2 H), 0.86 (d, J = 6.9 Hz, 3 H), 0.58 (d, J = 6.8 Hz, 3 H).

The tosylhydrazone (25.0 g, 85 mmol) was dissolved in 250 mL of dry tetramethylethylenediamine, cooled to −60 °C, and treated during 1 h while being magnetically stirred with 340 mmol of *n*-butyllithium in hexanes (4 equiv). The reaction mixture was stirred at −60 °C for 1.5 h and allowed to warm to room temperature. Upon cessation of nitrogen evolution (ca. 2 h), the deep red solution was recooled to −78 °C, and 1,2-dibromotetrafluoroethane (88.3 g, 340 mmol) was introduced via a syringe pump at the rate of 3 mL/min. Warming to −10 °C was allowed to occur during 2 h. After the mixture was recooled to −78 °C, water (500 mL) was added, and stirring was maintained for another 1 h. The mixture was poured into brine (1 L), the phases were separated, and the aqueous phase was extracted with petroleum ether (3 × 500 mL). The combined organic layers were washed successively with 5% hydrochloric acid (3 × 250 mL), saturated sodium bicarbonate solution (3 × 250 mL), and brine (3 × 250 mL) before drying and solvent evaporation. The crude product was filtered through neutral alumina (elution with petroleum ether) and distilled to give 6.89 g (43%) of **6** as a colorless liquid: bp 68–69 °C (7 Torr); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (dd, J = 2.3, 2.2 Hz, 1 H), 2.76–2.72 (m, 1 H), 2.28–2.21 (m, 2 H), 2.16–2.06 (m, 1 H), 1.97–1.85 (m, 1 H), 1.80–1.69 (m, 1 H), 0.94 (d, J = 7.0 Hz, 3 H), 0.75 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 131.16, 125.85, 54.97, 31.46, 28.50, 22.39, 20.79, 15.28; MS, m/z (M^+) calcd 188.0200, obsd 188.0205.

General Procedure for Vinyllithium Additions to 1. In an oven-dried round-bottomed flask flushed with nitrogen were placed the vinyl bromide and 10 mL of anhydrous tetrahydrofuran. The magnetically stirred solution was cooled to −78 °C, treated dropwise with 2 equiv of *tert*-butyllithium, and allowed to stir for an additional 30 min. At this point, a solution of **1** in tetrahydrofuran (2 mL) was introduced via syringe during 10 min, and reaction was allowed to proceed for 2.5 h before the addition of saturated ammonium chloride solution (5 mL) and warming to room temperature. The reaction mixture was partitioned between brine and ether, and the aqueous layer was extracted with ether (3 × 50 mL). The combined organic phases were washed with brine (3 × 50 mL) prior to drying and solvent evaporation. Gravity column chromatography on silica gel (elution with 10% ethyl acetate in petroleum ether) was used to separate unreacted **1** from **7** and **8**. Finally, MPLC on silica gel (elution with 3% ethyl acetate or 6% ether in petroleum ether) was employed to separate the diastereomeric alcohols.

A. *trans*-1-Bromo-5-ethyl-4-methylcyclopentene (2). From 378 mg (2.0 mmol) of **2** and 50 mg (0.333 mmol) of **1** were isolated 61 mg (70%) of **7a** and 19 mg (22%) of **8a**.

For **7a**: colorless oil; $[\alpha]^{23}_D$ −8.1° (c 5.9, $CHCl_3$); IR (neat, cm^{-1}) 3536, 3486, 2956, 2926, 2870, 1446, 1377; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.66–5.65 (m, 1 H), 5.27 (t, J = 1.3 Hz, 1 H), 4.93–4.92 (m, 1 H) 4.83–4.82 (m, 1 H), 2.54 (ddt, J = 16.6, 8.3, 2.3 Hz, 1 H), 2.41 (dd, J = 12.2, 3.1 Hz, 1 H), 2.25–2.21 (m, 1 H), 2.09–2.03 (m, 1 H), 2.00–1.53 (series of m, 6 H), 1.80 (d, J = 0.7 Hz, 3 H), 1.67 (d, J = 0.7 Hz, 3 H), 1.21–1.11 (m, 1 H), 1.01–0.81 (m, 1 H), 1.00 (d, J = 7.0 Hz, 3 H), 0.84 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 151.28, 147.45, 134.94, 129.81, 124.89, 113.33, 72.71, 55.72, 48.76, 39.54, 37.74, 30.91, 26.62, 25.02, 23.42, 23.36, 23.32, 11.70; MS, m/z (M^+) calcd 260.2140, obsd 260.2130. Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 82.72; H, 10.80.

For **8a**: colorless oil; $[\alpha]^{23}_D$ −39.4° (c 4.3, $CDCl_3$); IR (neat, cm^{-1}) 3548, 3488, 2958, 2920, 2876, 1449, 1376, 1076; ^{1}H NMR (300 MHz, C_6D_6) δ 5.49 (d, J = 1.3 Hz, 1 H), 5.35 (s, 1 H), 4.91–4.90 (m, 2 H), 2.60 (ddt, J = 16.4, 7.8, 2.2 Hz, 1 H), 2.38–2.30 (m, 2 H), 2.08–1.93 (m, 2 H), 1.87–1.66 (m, 3 H), 1.84 (d, J = 0.8 Hz, 3 H), 1.6 (s, 1 H), 1.57–1.25 (m, 2 H), 1.52 (d, J = 0.7 Hz, 3 H), 1.05–0.88 (m, 1 H), 1.04 (d, J = 7.0 Hz, 3 H), 0.98 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 152.10, 147.22, 134.74, 129.72, 124.54, 113.43, 72.96, 56.67, 52.14, 39.77, 37.27, 30.28, 27.30, 24.98, 24.06, 23.37, 23.28, 12.29; MZ, m/z (M^+) calcd 260.2140, obsd 260.2165.

B. *cis*-2-Bromobicyclo[3.3.0]oct-2-ene (3). From 374 mg (2.0 mmol) of **3** and 50 mg (0.333 mmol) of **1** were isolated 61 mg (71%) of **7b** and 18 mg (21%) of **8b**.

For **7b**: colorless oil, $[\alpha]^{24}_D$ +40.1° (c 3.07, $CHCl_3$); IR (neat, cm^{-1}) 3542, 3482, 2920, 2860, 1446, 1376, 1087, 904, 890, 760; ^{1}H NMR (300 MHz, C_6D_6) δ 5.71 (t, J = 1.7 Hz, 1 H), 5.36 (s, 1 H), 4.94–4.92 (m, 1 H), 4.89 (s, 1 H), 3.10–3.08 (m, 1 H), 2.69–2.66 (m, 1 H), 2.59–2.52 (m, 1 H), 2.44–2.39 (m, 1 H), 2.03–1.26 (series of m, 12 H), 1.80 (d, J = 0.6 Hz, 3 H), 1.52 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6 ppm) 152.09, 147.62, 135.44, 129.05, 124.74, 113.12, 72.80, 51.85, 48.61, 42.58, 39.81, 35.53, 32.85, 31.10, 27.31, 24.88, 24.06, 23.40; MS, m/z (M^+) calcd 258.1984, obsd 258.1990. Anal. Calcd for $C_{18}H_{26}O$: C, 83.67; H, 10.14. Found: C, 83.44; H, 10.09.

For **8b**: colorless oil; $[\alpha]^{26}_D$ −30.7° (c 3.55, $CHCl_3$); IR (neat, cm^{-1}) 3452, 2932, 2861, 1448, 1377, 892; ^{1}H NMR (300 MHz, C_6D_6) δ 5.47 (s, 1 H), 5.31 (d, J = 1.2 Hz, 1 H), 4.93 (s, 1 H), 4.90 (s, 1 H), 3.17–3.14 (m, 1 H), 2.74–2.51 (m, 2 H), 2.26–2.22 (m, 1 H), 2.05–1.26 (series of m, 12 H), 1.84 (s, 3 H), 1.54 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 153.43, 147.67, 135.06, 129.89, 124.54, 113.09, 73.82, 52.88, 52.36, 42.31, 40.25, 35.53, 33.87, 30.73, 26.93, 25.10, 24.21, 23.39; MS, m/z (M^+) calcd 258.1984, obsd 258.1954.

C. *cis*-1-Bromo-5-ethyl-4-methylcyclopentene (4). From 236 mg (1.25 mmol) of 4 and 150 mg (1.0 mmol) of **1** were isolated 116 mg (45%) of **7c** and 64 mg (25%) of **8c**.

For **7c**: colorless oil; $[\alpha]^{22}_D$ +23.6° (c 3.92, $CHCl_3$); IR (neat, cm^{-1}) 3500, 2910, 2880, 2835, 1463, 1447, 1380, 1075, 970; ^{1}H NMR (300 MHz, C_6D_6) δ 5.91 (d, J = 1.5 Hz, 1 H), 5.37 (d, J = 1.1 Hz, 1 H), 4.92 (s, 1 H), 4.85 (s, 1 H), 2.53–2.51 (m, 1 H), 2.46–2.22 (m, 3 H), 1.98–1.83 (m, 2 H), 1.79 (s, 3 H), 1.79–1.73 (m, 2 H), 1.67–1.55 (m, 2 H), 1.51 (s, 3 H), 1.51–1.38 (m, 2 H), 0.97 (d, J = 6.9 Hz, 3 H), 0.90 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 151.85, 147.50, 135.50, 128.55, 125.83, 113.10, 72.52, 49.81, 48.39, 39.29, 37.26, 30.96, 24.86, 23.98, 23.40, 21.41, 15.30, 12.35; MS, m/z (M^+) calcd 260.2140, obsd 260.2136. Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: 82.94; H, 10.78.

For **8c**: colorless oil; $[\alpha]^{22}_D$ −5.0° (c 3.33, $CHCl_3$); IR (neat, cm^{-1}) 3500, 2965, 2920, 2880, 2830; ^{1}H NMR (300 MHz, C_6D_6) δ 5.51 (s, 1 H), 5.46 (q, J = 1.3 Hz, 1 H), 4.91 (d, J = 1.2 Hz, 1 H), 4.88 (s, 1 H), 2.62–2.61 (m, 1 H), 2.43 (heptet, J = 7.3 Hz, 1 H), 2.31–2.22 (m, 2 H), 1.98 (ddt, J = 15.5, 7.6, 2.0 Hz, 1 H), 1.87 (s, 3 H), 1.84–1.69 (m, 4 H), 1.53 (s, 3 H), 1.51–1.45 (m, 2 H), 1.12 (s, 1 H), 1.02 (d, J = 7.1 Hz, 3 H), 0.97 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6 ppm) 154.11, 147.65, 135.55, 129.24, 125.20, 113.04, 73.14, 52.92, 50.20, 39.71, 37.50, 30.64, 24.90, 23.75, 23.39, 21.66, 15.57, 12.87; MS, m/z (M^+) calcd 260.2140, obsd 260.2137.

D. *cis*-2-Bromobicyclo[3.2.0]hept-2-ene (5). From 173 mg (1.0 mmol) of **5** and 124 mg (0.83 mmol) of **1** were obtained 73 mg (36%) of **7d** and 38 mg (19%) of **8d**.

For **7d**: colorless oil; $[\alpha]^{22}_D$ +9.1° (c 7.5, C_6H_{12}); IR (neat, cm^{-1}) 3550, 3482, 2972, 2944, 2916, 2856; ^{1}H NMR (300 MHz, C_6D_6) δ 5.83 (s, 1 H), 5.50–5.49 (m, 1 H), 4.93–4.91 (m, 1 H), 4.87 (s, 1 H), 3.30–3.22 (m, 1 H), 2.88–2.84 (m, 1 H), 2.53–2.45 (m, 1 H), 1.77 (s, 3 H), 2.36–1.73 (series of m, 9 H), 1.69 (s, 1 H), 1.51 (s, 3 H), 1.51–1.46 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6 ppm) 152.70, 147.59, 135.25, 129.10, 125.90, 113.07, 72.95, 48.89, 46.73, 40.10, 37.44, 31.07, 27.75, 27.70, 24.85, 24.05, 23.35; MS, m/z (M^+) 244.1827, obsd 244.1816. Anal. Calcd for $C_{27}H_{24}O$: C, 83.55; H, 9.90. Found: C, 83.32; H, 9.89.

For **8d**: colorless oil; $[\alpha]^{22}_D$ −6.6° (c 3.5, C_6H_{12}); IR (neat, cm^{-1}) 3544, 3486, 2966, 2928, 2906, 2838; ^{1}H NMR (300 MHz, C_6D_6) δ 5.56 (s, 1 H), 5.51–5.49 (m, 1 H), 4.93 (s, 1 H), 4.93 (s, 1 H), 3.40–3.37 (m, 1 H), 2.87–2.81 (m, 1 H), 2.56–2.34 (m, 2 H), 2.27–2.09 (m, 4 H), 1.83 (t, J = 1.1 Hz, 3 H), 1.90–1.74 (m, 4 H), 1.53 (d, J = 0.9 Hz, 3 H), 1.60–1.46 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 153.90, 135.38, 129.88, 125.58, 113.09, 72.28, 52.30, 47.45, 40.59, 37.00, 30.58, 28.48, 27.69, 25.00, 24.14, 23.37 (one C not observed).

E. 1-Bromo-5-isopropylcyclopentene (6). From 378 mg (2.0 mmol) of **6** and 100 mg (0.67 mmol) of **1** were isolated 100 mg (58%) of **7e** and 31 mg (18%) of **8e**.

For **7e**: colorless oil; $[\alpha]^{22}_D$ +19.0° (c 10.6, $CHCl_3$); IR (neat, cm^{-1}) 3547, 3477, 2967, 2939, 2913, 1449; ^{1}H NMR (300 MHz, C_6D_6) δ 5.98–5.97 (m, 1 H), 5.41–5.40 (m, 1 H), 4.93–4.90 (m, 2 H), 2.82–2.78 (m, 1 H), 2.46 (dd, J = 12.1, 2.5 Hz, 1 H), 2.24–2.05 (m, 3 H), 1.81 (s, 3 H), 1.96–1.71 (m, 5 H), 1.63 (s, 1 H), 1.50 (d, J = 0.7 Hz, 3 H), 1.53–1.45 (m, 1 H), 0.95 (d, J = 6.9 Hz, 3 H), 0.81 (d, J = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 151.82, 147.49, 135.32, 128.92, 127.35, 113.21, 72.60, 52.40, 48.22, 31.81, 30.92, 29.40, 24.94, 24.58, 23.96, 23.33, 22.81, 15.83; MS, m/z (M^+) calcd 260.2140, obsd 260.2142. Anal. Calcd for $C_{18}H_{28}O$: C, 83.02; H, 10.84. Found: C, 82.95; H, 10.83.

For **8e**: colorless oil; $[\alpha]^{22}_D$ +5.5° (c 10.2, $CHCl_3$; IR (neat, cm^{-1}) 3540, 3468, 2958, 2948, 2870, 2856, 1468, 1448; ^{1}H NMR (300 MHz, C_6D_6) δ 5.53 (s, 1 H), 5.45 (s, 1 H), 4.90 (s, 1 H), 4.88 (s, 1 H), 2.88–2.86 (m, 1 H), 2.57 (ddq, J = 6.9, 6.9, 2.6 Hz, 1 H), 2.34–2.12 (m, 3 H), 1.83 (d, J = 0.5 Hz, 3 H), 1.83–1.69 (m, 5 H), 1.54 (s, 3 H), 1.54–1.42 (m, 2 H), 1.01 (d, J = 6.9 Hz, 3 H), 0.90 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (20 MHz, C_6D_6, ppm) 153.36, 147.68, 134.65, 129.72, 112.99, 73.31, 53.84, 53.02, 32.53, 30.61, 30.23, 25.03, 24.56, 23.98, 23.30, 22.56, 16.20 (one peak obscured by solvent); MS, m/z (M^+) calcd 260.2140, obsd 260.2143.

Cerium Trichloride as Additive. General Procedure. Cerium(III) chloride heptahydrate (1.02 g, 2.75 mmol) was dried by heating at 140

°C for 2 h under high vacuum. After the salt was cooled to room temperature, anhydrous tetrahydrofuran (8 mL) was slowly added, and the resultant slurry was stirred for 2 h and cooled to −78 °C. Concomitantly, the vinyl bromide (2.50 mmol) in dry tetrahydrofuran (5 mL) was being treated with 5.0 mmol of *tert*-butyllithium in hexanes at −78 °C as described above. After 30 min, the organolithium reagent was transferred via syringe to the cerium chloride slurry. The reaction mixture was stirred at −78 °C for 0.5 h, treated with **1** over a 10-min period, stirred at −78 °C for 2.5 h, and processed in a manner identical with that outlined above.

General Procedure for the Anionic Oxy-Cope Rearrangements. Potassium hydride (ca. 5 equiv) as a 25% mineral oil suspension was washed with molecular sieve dried pentane (3 × 1 mL) and suspended in anhydrous tetrahydrofuran (1.5 mL). The slurry was treated with a solution of iodine in tetrahydrofuran until an orange color persisted for ca. 5 min. A solution of 18-crown-6 (5 equiv) and the alcohol (1 equiv) in the same solvent (0.5 mL) was added, and hydrogen evolution was seen. The magnetically stirred reaction mixture was heated at reflux, and the progress of the rearrangement was monitored by TLC. After the alcohol was completely consumed, the reaction mixture was cooled to −78 °C and treated with 1.5 mL of saturated ammonium chloride solution before being poured into a mixture of petroleum ether (5 mL) and saturated ammonium chloride solution (5 mL). The organic phase was washed with brine prior to drying and solvent evaporation. The product ketones were separated by MPLC on silica gel (elution with 1–3% ethyl acetate in petroleum ether).

A. Rearrangement of 7a. From 121 mg of 7a were isolated 30 mg (25%) of **34a** and 69 mg (57%) of **35a** after a 1-h reaction period.

For **34a**: low-melting white solid; $[\alpha]^{22}_D$ +67.1° (*c* 8.4, $CHCl_3$); IR (neat, cm^{-1}) 2970, 2930, 1675, 1620, 1455, 1377, 1365, 1345, 1315, 1267, 1235, 1217, 1195, 1171, 1145, 1135, 1095, 1077, 1041, 1026, 982, 950, 885, 855, 835; ^1H NMR (300 MHz, C_6D_6) δ 5.75 (s, 1 H), 5.08–5.04 (m, 1 H), 3,53–3.25 (m, 1 H), 2.59–0.80 (series of m, 13 H), 1.53 (d, *J* = 1.3 Hz, 3 H), 1.30 (s, 3 H), 1.01 (d, *J* = 6.7 Hz, 3 H), 0.88 (d, *J* = 7.5 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 203.07, 148.21, 135.15, 129.94, 129.63, 61.19, 48.11, 47.28, 43.31, 41.20, 37.86, 30.90, 27.47, 25.69, 25.19, 20.67, 15.25, 11.65; MS, *m/z* (M^+) calcd 260.2140, obsd. 260.2154.

For **35a**: ^1H NMR (300 MHz, C_6D_6) δ 5.13–5.10 (m, 1 H), 4.93 (s, 1 H), 4.89 (s, 1 H), 3.07 (d, *J* = 12.7 Hz, 1 H), 2.78 (d, *J* = 13.2 Hz, 1 H), 2.70–2.68 (m, 1 H), 2.44–2.40 (m, 1 H), 2.20–0.72 (series of m, 12 H), 1.46 (s, 3 H), 1.28 (d, *J* = 7.2 Hz, 3 H); 0.79 (t, *J* = 7.3 Hz, 3 H); MS, *m/z* (M^+) calcd 260.2140, obsd 260.2156.

B. Rearrangement of 7b. From 113 mg of **7b** were isolated 60 mg (53%) of **32** and 18 mg (16%) of **33** after a 1-h reaction period.

For **32**: white crystals; mp 88–89 °C (from ethanol); $[\alpha]^{25}_D$ +63.0° (*c* 3.3, $CHCl_3$); IR (KBr, cm^{-1}) 2940, 2864, 1666, 1626, 1445, 1386, 1268, 1173, 1099, 849, 759; ^1H NMR (300 MHz, C_6D_6) δ 5.73 (s, 1 H), 4.96 (dd, *J* = 11.3, 5.0 Hz, 1 H), 3.50 (td, *J* = 12.4, 4.1 Hz, 1 H), 3.31 (q, *J* = 9.5 Hz, 1 H), 2.56–2.40 (m, 2 H), 2.29–1.22 (series of m, 14 H), 1.52 (d, *J* = 1.1 Hz, 3 H), 1.28 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 202.11, 146.45, 137.12, 129.33, 127.18, 64.61, 45.15, 44.36, 42.85, 41.14, 40.41, 33.73, 33.27, 30.777, 27.01, 25.29, 25.06; 15.89; MS, *m/z* (M^+) calcd 258.1983, obsd 258.1972.

For **33**: colorless oil; ^1H NMR too broad for assignment at room temperature (compare Figure 2); MS, *m/z* (m^+) calcd 258.1983, obsd 258.2000.

C. Rearrangement of 7c. From 115 mg of **7c** were isolated 50 mg (43%) of **34b** and 36 mg (31%) of **35b** after a 45-min reaction period.

For **34b**: colorless oil; $[\alpha]^{23}_D$ +111.1° (*c* 2.98, $CHCl_3$); IR (neat, cm^{-1}) 2960, 2956, 2872, 1677, 1621, 1455; ^1H NMR (300 MHz, C_6D_6) δ 5.72–5.02 (m, 1 H), 3.50–3.41 (m, 1 H), 2.68–2.54 (m, 2 H), 1.52 (d, *J* = 1.3 Hz, 3 H), 1.29 (d, *J* = 0.5 Hz, 3 H), 2.36–0.99 (series of m, 12 H), 0.90 (t, *J* = 7.3 Hz, 3 H), 0.78 (d, *J* = 7.1 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 203.24, 148.22, 134.95, 130.30, 129.85, 59.68, 46.49, 44.37, 43.27, 41.08, 33.65, 30.94, 27.54, 25.71, 23.17, 15.53, 15.26, 13.11; MS, *m/z* (M^+) calcd 260.2140, obsd 260.2138.

For **35b**: colorless oil; ^1H NMR (300 MHz, C_6D_6) δ 5.18–4.93 (m, 3 H), 3.15–0.73 (series of m, 22 H), 1.45 (s, 3 H); MS, *m/z* (M^+) calcd 260.2140, obsd 260.2139.

D. Rearrangement of 7d. From 105 mg of **7d** were isolated 25 mg (24%) of **15**, 41 mg (39%) of **28**, and 20 mg (19%) of **29** after a 30-min reaction period.

For **15**: colorless crystals; mp 78–78.5 °C (from ethanol); $[\alpha]^{23}_D$ +60.2° (*c* 0.6, $CHCl_3$); IR ($CHCl_3$, cm^{-1}) 3008, 2981, 2942, 1669, 1622, 1455; ^1H NMR (300 MHz, C_6D_6) δ 5.80 (s, 1 H), 4.89 (dd, *J* = 10.3, 5.3 Hz, 1 H), 3.53–3.39 (m, 2 H), 2.71–2.49 (m, 3 H), 1.54 (d, *J* = 1.2 HZ, 3 H), 1.28 (s, 3 H), 2.45–1.24 (series of m, 11 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 201.58, 146.52, 136.72, 129.38, 127.53, 66.00, 46.85, 44.90, 43.95, 37.33, 36.44, 30.81, 27.08, 26.75, 25.62, 25.38, 15.87; MS, *m/z* (M^+) calcd 244.1827, obsd 244.1833.

For **28**: colorless crystals; mp 78–79 °C (from ethanol); ^1H NMR (300 MHz, C_6D_6) δ 5.07 (d, *J* = 10.4 Hz, 1 H), 4.83 (s, 1 H), 4.80 (s, 1 H), 3.02–2.67 (m, 5 H), 1.54 (s, 3 H), 2.47–1.33 (series of m, 13 H); MS, *m/z* (M^+) calcd 244.1827, obsd 244.1887.

For **29**: colorless crystals; mp 109–110 °C (from ethanol); ^1H NMR (300 MHz, C_6D_6) δ 5.08 (dd, *J* = 10.0, 3.5 Hz, 1 H), 4.98 (s, 1 H), 4.93 (s, 1 H), 3.24–3.09 (m, 1 H), 2.90 (d, *J* = 14.0 Hz, 1 H), 2.71–2.56 (m, 3 H), 1.60 (s, 3 H), 2.36–1.37 (series of m, 12 H), 1.16–1.05 (m, 1 H); MS, *m/z* (M^+) calcd 244.1828, obsd 244.1827.

E. Rearrangement of 7e. From 265 mg of **7e** were isolated 143 mg (54%) of **36** and 72 mg (27%) of **37** after a 45-min reaction period.

For **36**: colorless oil; $[\alpha]^{23}_D$ +72.6° (*c* 0.92, $CHCl_3$); IR (neat, cm^{-1}) 3066, 2948, 2872, 1676, 1630, 1453; ^1H NMR (300 MHz, C_6D_6) δ 5.75 (s, 1 H), 5.00 (dd, *J* = 11.4, 4.8 Hz, 1 H), 3.55–3.45 (m, 1 H), 2.79–2.69 (m, 1 H), 2.63–2.53 (m, 1 H), 2.33–2.24 (m, 2 H), 1.84–1.80 (m, 1 H), 1.76–1.62 (m, 6 H), 1.53 (d, *J* = 1.3 Hz, 3 H), 1.30 (s, 3 H), 1.31–1.27 (m, 2 H), 0.91 (d, *J* = 6.9 Hz, 3 H), 0.81 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (20 MHz, C_6D_6, ppm) 202.42, 147.95, 135.44, 129.57, 128.87, 59.98, 45.25, 43.61 (2 C, 34.74, 31.26, 30.96, 27.39, 26.08, 25.56, 22.02, 18.77, 15.44; MS, *m/z* (M^+) calcd 260.2140, obsd 260.2147.

For **37**: colorless oil; ^1H NMR (300 MHz, C_6D_6) δ 5.74–4.91 (m, 3 H), 1.49 (s, 3 H), 3.15–0.84 (series of m, 16 H), 0.79 (d, *J* = 6.8 Hz, 3 H), 0.75 (d, *J* = 6.7 Hz, 3 H); MS, *m/z* (M^+) calcd 260.2140, obsd 260.2147.

F. Rearrangement of 8b. From 89 mg of **8b** were isolated 28 mg (31%) of **30** and 30 mg (34%) of **31** after a 3-h reaction period.

For **30**: colorless crystals; mp 91.5–92 °C (from ethanol); $[\alpha]^{23}_D$ −52.5° (*c* 0.4, $CHCl_3$); IR ($CHCl_3$, cm^{-1}) 3114, 3047, 2972, 1671, 1626, 1456; ^1H NMR (300 MHz, C_6D_6) δ 5.74 (s, 1 H), 5.02 (dd, *J* = 10.8, 4.9 Hz, 1 H), 3.40 (td, *J* = 12.3, 4.1 Hz, 1 H), 2.66–2.51 (m, 3 H), 2.48–2.40 (m, 1 H), 1.85 (s, 3 H), 1.82 (d, *J* = 1.4 Hz, 3 H), 2.33–1.11 (series of m, 13 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 202.73, 145.82, 137.74, 130.17, 127.16, 59.37, 46.98, 46.49, 44.08, 43.36, 40.61, 34.69, 32.29, 30.64, 28.05, 26.94, 25.29, 15.85; MS, *m/z* (M^+) calcd 258.1983, obsd 258.2014.

For **31**: colorless crystals; mp 68–69 °C (from ethanol); ^1H NMR (300 MHz, C_6D_6) δ 5.07 (d, *J* = 11.2 Hz, 1 H), 4.89 (s, 1 H), 4.85 (s, 1 H), 3.20 (t, *J* = 7.9 Hz, 1 H), 2.97 (d, *J* = 11.5 Hz, 1 H), 2.76 (d, *J* = 11.4 Hz, 1 H), 2.54–2.35 (m, 2 H), 2.25–2.06 (m, 4 H), 1.44 (s, 3 H), 1.99–1.23 (series of 11 H); MS, *m/z* (M^+) calcd 258.1983, obsd 258.1968.

G. Rearrangement of 8d. From 105 mg of **8d** were isolated 45 mg (43%) of **20** and 33 mg (31%) of **27** after a 30-min reaction period.

For **20**: colorless crystals; mp 110–111 °C (from ethanol); $[\alpha]^{23}_D$ −77.8° (*c* 0.36, $CHCl_3$); IR ($CHCl_3$, cm^{-1}) 3008, 2968, 2940, 2858, 1667, 1623, 1455; ^1H NMR (300 MHz, C_6D_6) δ 5.71 (s, 1 H), 5.10 (dd, *J* = 11.0, 5.2 Hz, 1 H), 3.49–3.39 (m, 1 H), 3.08–2.97 (m, 2 H), 2.74–2.55 (m, 4 H), 2.35–2.21 (m, 2 H), 1.52 (d, *J* = 1.3 Hz, 3 H), 2.08–1.32 (series of m, 7 H), 1.32 (s, 3 H); ^{13}C NMR (75 MHz, C_6D_6, ppm) 202.59, 146.34, 137.94, 129.88, 127.10, 60.52, 46.97, 44.64, 41.95, 41.18, 37.50, 30.70, 26.99, 26.60, 25.16, 23.59, 15.82; MS, *m/z* (M^+) calcd 244.1827, obsd 244.1823.

For **27**: ^1H NMR (300 MHz, C_6D_6) δ 5.13 (d, *J* = 11.3 Hz, 1 H), 4.84 (d, *J* = 5.3 Hz, 2 H), 3.08 (m, 1 H), 2.85–2.59 (m, 5 H), 2.59–1.44 (series of m, 12 H), 1.44 (s, 3 H); MS, *m/z* (M^+) calcd 244.1827, obsd 244.1830.

Acknowledgment. This work was assisted financially by Grant GM-28468 from the National Institutes of Health. Thanks are also extended to the Eli Lilly crystallographic team for their invaluable contributions.

Supplementary Material Available: Tables of atomic coordinates, bond lengths, bond angles, anisotropic temperature factors, hydrogen coordinates, and nonbonded distances for **20** and **32** (16 pages). Ordering information is given on any current masthead page.