Stereoselectivity of Cyclization of Substituted 5-Hexen-1-yllithiums: Regiospecific and Highly Stereoselective Insertion of an Unactivated Alkene into a C–Li Bond

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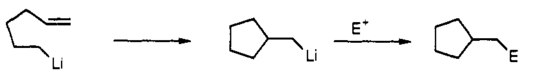
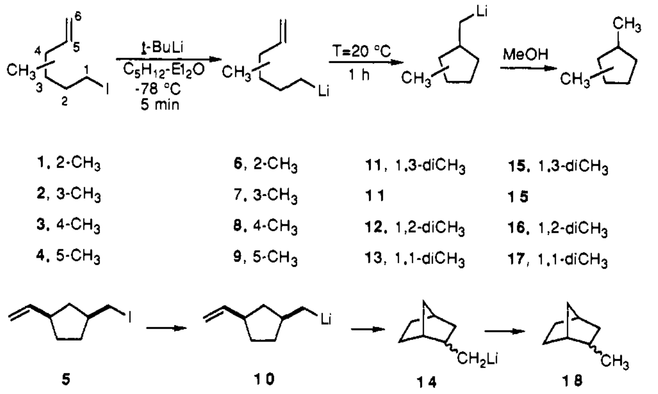
Abstract: Substituted 5-hexen-1-yllithiums, **6–10**, which were prepared in solutions of n-C_5H_{12}–Et_2O (3:2 by vol) by low-temperature lithium–iodine exchange between t-BuLi and the appropriate iodide, undergo clean, 5-exo-trig cyclization upon warming to give substituted (cyclopentyl)methyllithiums, **11–14**, in good yield and with a high degree of stereocontrol. In each case, the major product is the same isomer as that observed in studies of the isomerization of analogously substituted 5-hexen-1-yl radicals, but the organolithium cyclizations are invariably much more stereoselective than radical-mediated processes. Lewis base additives such as THF, TMEDA, and PMDTA serve to increase the rate of cyclization of the substituted 5-hexen-1-yllithiums, but such additives do not reduce the high stereoselectivity of the process. The observed regioselectivities and stereoselectivities of the intramolecular addition of a C–Li bond to an unactivated alkene suggest that the closure of the anion proceeds via a transition state that resembles a chair cyclohexane in which substituents preferentially occupy pseudoequatorial positions. Ab initio molecular orbital calculations at the 3-21G level, which support this transition-state structure (chair-like geometry with a C(1)–C(5) distance of 2.18 Å), suggest that the ground-state structure of 5-hexen-1-yllithium is essentially that of a cyclohexane chair [C(1)–C(5) distance of 3.35 Å] in which the lithium atom is coordinated with the C(5)–C(6) π-bond (Li–C(5) distance of 2.41 Å and Li–C(6) distance of 2.38 Å). The stabilizing interaction of the lithium atom with the π-system of the remote alkene moiety appears to be an important component of the cyclization since it serves to establish a chair-like geometry prior to the activation step leading to (cyclopentylmethyl)lithium. Calculation of the difference in energy between an axially substituted transition state and one bearing an equatorial substituent gave product ratios that were in very good agreement with experimental observations. The activated complex was also modeled via molecular mechanics calculations with modified MM2 parameters, and the results of these analyses were found to be in good accord with both the ab initio results and the experimentally observed selectivities. The preference of a substituent for the pseudoequatorial position in the chair-like transition state is, to a reasonable approximation, given by the conformational energy of the substituent in the cyclohexane system, and the stereoselectivity of cyclizations of substituted 5-hexen-1-yllithiums may be anticipated by recourse to such values.

The potential synthetic utility of intramolecular insertion of an unactivated alkene into a carbon–lithium bond to give cyclopentylmethyl-containing products has recently attracted the attention of a number of research groups.[2-7]



Interest in this organometallic route to cyclic structures derives from three features of the methodology: (1) the precursor organolithium may be easily generated from any of a number of substrates by a variety of methods including lithium–halogen interchange,[2,3,8-11] lithium–tin exchange,[5] Shapiro degradation of tosylhydrazones,[4] electrochemical reduction of a carbon–halogen bond,[6] or carbon–carbon bond cleavages;[7] (2) the cyclization is a facile, clean, and high yield process;[2-10] and most importantly (3) the initially formed cyclic organometallic may be easily trapped by reaction with suitable electrophiles to give good yields of functionalized product.[3,4,9,10]

Scheme I



Despite the current interest in this organometallic counterpart to more widely studied radical-based strategies for the construction of cyclic systems,[12-14] there is a dearth of information on the stereochemistry of the process. Herein we report the results of a coordinated experimental and theoretical study of the cyclization of substituted 5-hexen-1-yllithiums. As shown below, this anionic route to substituted five-membered rings is totally regiospecific

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(1) (a) University of Connecticut. (b) Yale University.

(2) Bailey, W. F.; Patricia, J. J.; DelGobbo, V. C.; Jarret, R. M.; Okarma, P. J. *J. Org. Chem.* **1985**, *50*, 1999.

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(14) (a) Beckwith, A. L. J.; Easton, C. J.; Serelis, A. K. *J. Chem. Soc., Chem. Commun.* **1980**, 482. (b) Beckwith, A. L. J.; Lawrence, T.; Serelis, A. K. *J. Chem. Soc., Chem. Commun.* **1980**, 484.

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and much more stereoselective than radical-mediated processes. As will be demonstrated below, the high degree of stereocontrol that characterizes the cyclization is a consequence of an energetically favorable coordination of the lithium atom of the substrate with the remote π-bond leading to a cyclohexane chair-like geometry for the 5-hexen-1-yllithium in which a substituent preferentially occupies a psuedoequatorial position.

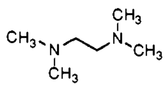
Results and Discussion

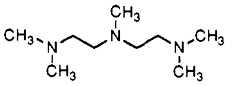
Olefinic alkyllithiums (**6**–**10**) were cleanly generated at −78 °C, as illustrated in Scheme I, by addition of 2.0–2.2 molar equiv of *tert*-butyllithium (*t*-BuLi) in pentane to a 0.1 M solution of the appropriate olefinic alkyl iodide (**1**–**5**) in *n*-pentane–diethyl ether (3:2 by volume) following our general protocol for lithium–iodine exchange.[11] A small, accurately weighed quantity of a pure hydrocarbon (typically *n*-heptane) was added to each iodide solution prior to the generation of **6**–**10** to facilitate quantitation of reaction products by gas chromatographic (GC) analysis. At the outset it is well to note explicitly that while organolithiums are often (as in Scheme I) depicted as monomers for the sake of pictorial clarity, they are known to exist as aggregates whose degree of association is affected by such factors as solvent, concentration, and temperature.[15]

The olefinic alkyllithiums, which are indefinitely stable in solution at −78 °C, cleanly isomerize to substituted (cyclopentyl)methyllithiums (**11**–**14**) upon warming to room temperature under an atmosphere of argon.[2] Thus, cyclizations were effected by simply allowing solutions of **6**–**10** to stand at room temperature for 1 h prior to the addition of dry, deoxygenated methanol (Scheme I). Analysis of the resulting solutions, as detailed in the Experimental Section, by capillary GC revealed that the reaction mixtures contained only internal standard, cyclic hydrocarbon (**15**–**18**), and a small quantity of uncyclized alkene generated as a byproduct of the initial lithium–iodine exchange.[3,8–11] The results of these experiments are presented in Table I. It might be noted that the cyclization of **3** (Table I, entry 9) has been reported previously.[3]

In view of the fact that lithiophilic Lewis bases have been found to facilitate the isomerization of 5-hexen-1-yllithiums,[3,4,8–10] it was of interest to assess the effect of such additives on the stereochemical course of the cyclizations. To this end, a separate series of experiments were conducted in which THF, or *N,N,N′,N′*-tetramethylethylenediamine (TMEDA), or *N,N,N′,N″,N″*-pentamethyldiethylenetriamine (PMDTA) were added at −78 °C to 0.1 M solutions of preformed **6**–**10** prior to warming of the organolithium solution to room temperature. The Lewis bases, whose structures are shown below, were added in the following amounts: THF, a volume equal to that of the diethyl ether used in the interchange; TMEDA, 2.0 equiv; PMDTA, 2.0 equiv. The results of these experiments are also summarized in Table I.

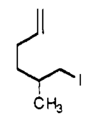
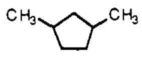
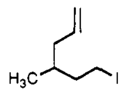
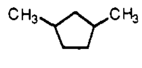
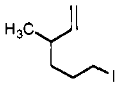
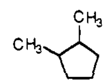
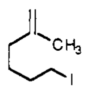
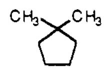
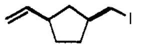
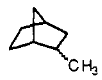

THF


TMEDA


PMDTA

Cursory inspection of the data summarized in Table I reveals that the insertion of an unactivated alkene into the C–Li bond of a 5-hexen-1-yllithium is a clean and totally regiospecific 5-exo-trig process that leads to a substituted (cyclopentyl)methyllithium, **11**–**14**, as the exclusive product of the reaction. In all instances for which data are available,[12–14] the major isomer produced upon cyclization of **6**–**10** (Table I; entries 1–12) is the same as that generated in the kinetically controlled isomerization of an analogously substituted 5-hexen-1-yl radical (Table II). Most significantly, *the cyclization of substituted 5-hexen-1-yllithiums,* **6**–**10**, *is much more stereoselective than the corresponding radical-mediated isomerizations* (cf. the data in Table II). Moreover, the high stereoselectivities are not compromised by the presence of Lewis bases such as THF, TMEDA, or PMDTA. These additives, which have been known for some time to facilitate the normally sluggish intermolecular addition of RLi to an alkene,[16] serve to increase the yield of cyclic product in those instances wherein a quaternary center is generated, such as in the transformation of **9** → **13** (Table I; entries 13–16), or when the product organolithium is somewhat strained, such as in the cyclization of **10** → **14** (Table I; entries 17–20). It should be noted that no attempt has been made in this study to maximize either the yields or the selectivities of the cyclization reactions for which

Table I. Stereoselectivity of Cyclization of Substituted 5-Hexen-1-yllithiums

entry	iodide	additive[a]	product	yield, %[b]	trans/cis[c]
1	 1	none	 15	83	10.7
2		THF		93	6.9
3		TMEDA		84	6.4
4		PMDTA		73	23.0
5	 2	none	 15	98	0.10
6		THF		87	0.11
7		TMEDA		97	0.10
8		PMDTA		88	0.06
9	 3	none	 16	79	11.7
10		THF		78	18.5
11		TMEDA		87	11.0
12		PMDTA		81	34.0
		32			
13	 4	none	 17	10	-
14		THF		70	-
15		TMEDA		77	-
16		PMDTA		45	-
17	 5	none	 18	26	24.5[d]
18		THF		85	47.8[d]
19		TMEDA		91	49.3[d]
20		PMDTA		77	27.5[d]

[a] The additive (2.1–2.2 equiv) was added at −78 °C to a solution of the 5-hexen-1-yllithium, generated at −78 °C by lithium–iodine exchange between the iodide and *t*-BuLi; the mixture was stirred for 5 min at −78 °C and then allowed to warm and stand at ambient temperature for 1 h before the addition of excess MeOH. [b] Yields of cyclized products were determined by capillary GC with internal standards and correction for detector response. [c] Ratio of cis and trans isomers of cyclized product. [d] Ratio of *endo*/*exo*-2-methylbicyclo[2.2.1]heptanes, **18**.

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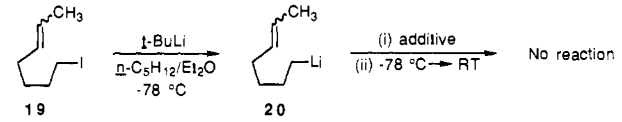
(15) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon: New York, 1974.

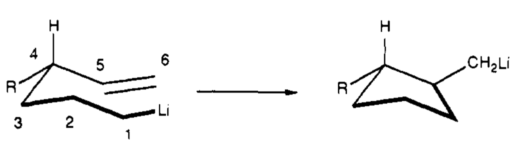
(16) Klumpp, G. W. *Recl. Trav. Chim. Pays-Bas* **1986**, *105*, 1.

data are presented in Table I. Indeed, while such optimization of reaction conditions was not the objective of this investigation, ongoing kinetic studies of the cyclization of 5-hexen-1-yllithiums in the presence of various Lewis base additives suggest that it should prove possible to conduct the reactions at temperatures well below ambient.

As noted elsewhere,[3,5] the isomerization of 5-hexen-1-yllithiums to (cyclopentyl)methyllithiums seems to be confined to situations in which the terminal alkene carbon is either unsubstituted or bears a substituent that is able to stabilize the alkyllithium generated in the cyclization.[17] Thus, for example, 5-hepten-1-yllithium, **20**, which is prepared from the corresponding iodide (**19**; *Z*/*E* = 78:22) as shown below, does not cyclize to the five-membered ring upon standing for 1 h at ambient temperature in the presence of TMEDA or PMDTA. Significantly, the relative proportions of (*Z*)- and (*E*)-20 (*Z*/*E* ≈ 80:20) do not change appreciably during the course of these experiments. This observation is clearly inconsistent with a scenario involving ring closure of **20** followed by rapid ring opening since such a process would lead to at least partial equilibration of the open-chain olefinic alkyllithiums. Indeed, there is no evidence that the intramolecular insertion of an alkene into the C–Li bond of a 5-hexen-1-yllithium is operationally reversible: the ratio of isomeric products found in the present study (Table I) do not reflect the thermodynamic stabilities of the carbocycles, and evidence has recently been adduced that demonstrates the essentially irreversible nature of these cyclizations.[18] Thus, the experimental data summarized in Table I reflect the regio- and stereoselectivities of a cyclization process that is kinetically controlled.



The regiospecific and highly stereoselective nature of the intramolecular insertion of the π-bond into the C–Li bond of a substituted 5-hexen-1-yllithium is easily rationalized by recourse to a transition-state model for the cyclization that resembles a cyclohexane chair. Indeed, just such a model has been proposed to explain the modest selectivities observed in isomerizations of analogously substituted 5-hexen-1-yl radicals.[19] In terms of such a model, illustrated below for the case of a 4-substituted 5-hexen-1-yllithium, stereocontrol is attributed to steric interactions in the transition state for the reaction that favor a geometry in which a substituent preferentially occupies a pseudoequatorial position in the cyclohexane chair-like transition state. Thus, for the case illustrated below, one would predict predominant formation of the trans isomer as observed for the cyclization of 4-methyl-5-hexen-1-yllithium (**8** → **12**; Table I, entries 9–12).



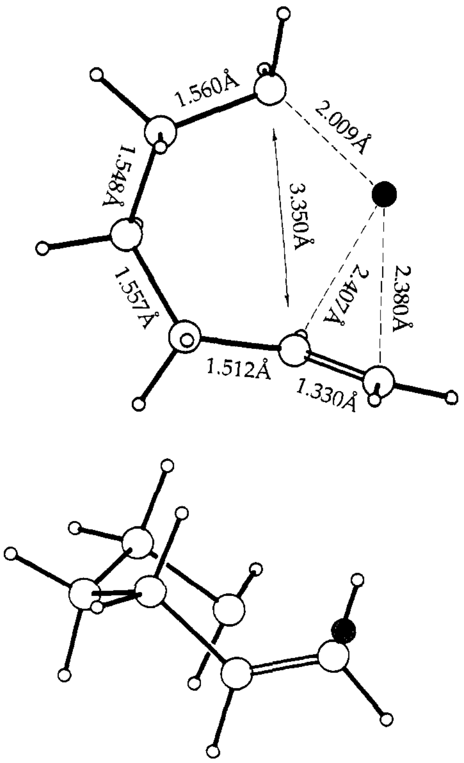


Figure 1. Calculated (3-21G) ground-state geometry of 5-hexen-1-yllithium.

While this rationalization has a certain heuristic value for qualitative prediction of the predominant stereoisomer produced upon cyclization of simple monosubstituted 5-hexen-1-yllithiums, the quantitative aspects of the process are not addressed by the model. In particular, it is not at all clear, a priori, why the intramolecular addition of a C–Li bond to an unactivated alkene should be significantly more regioselective and stereoselective than the closure of the analogous radical. In an effort to probe the factors responsible for the high degree of stereoselection observed in the cyclization of 5-hexen-1-yllithiums, we have carried out a series of ab initio molecular orbital calculations dealing with the course of the reaction.

To this end, the distance between the carbanionic center [C(1)] and the inner carbon of the double bond [C(5)] was taken as the reaction coordinate. Initially, this distance was fixed at 3.00 Å, and a geometry optimization was performed for several different relative orientations of the remaining atoms with the 3-21G basis set.[20] The lowest energy structure thus obtained did indeed correspond to the expected chair-cyclohexane geometry. When the geometrical constraint was removed and the geometry optimization was repeated, the calculated energy decreased by 1.4 kcal/mol, and the C(1)–C(5) distance increased to 3.35 Å giving the geometry displayed in Figure 1. Most significantly, this lowest energy structure, whose geometry closely resembles that of a cyclohexane chair, is an *intermediate*. The intermediate derives its stability from the fact that the lithium atom at C(1) is coordinated with the carbon–carbon π-bond: the Li–C(5)–C(6) array resembles an isosceles triangle having a *Li*–C(5) distance of 2.38 Å and a Li–C(6) distance of 2.41 Å (Figure 1). Recent theoretical studies by Houk and co-workers reveal that such an interaction is also an important component of the intermolecular addition of both LiH and CH_3Li to ethylene.[21] In this connection, it is of interest to note that a Li–alkene interaction of this sort was suggested some time ago by Oliver and co-workers on the basis of their pioneering studies of the cyclization reactions of various organometallic compounds.[22] In the present case, co-

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(17) The presence of a strongly electron-withdrawing group at the terminal alkene carbon of a 5-hexen-1-yllithium activates the olefinic unit toward nucleophilic attack and a Michael-type ring closure ensues, see: Cooke, M. P., Jr.; Widener, R. K. *J. Org. Chem.* **1987**, *52*, 1381 and references therein. We have recently found that attachment of a phenyl substituent or a trimethylsilyl group at C(6) also serves to facilitate cyclization. Thus, both 6-phenyl-5-hexen-1-yllithium and 6-trimethylsilyl-5-hexen-1-yllithium undergo rapid 5-exo-trig cyclization at temperatures well below ambient to give a (cyclopentyl)methyllithium that may be trapped with any of a variety of electrophiles to deliver functionalized products in high yield. It might be noted in this connection that the extent of cyclization of the organolithium derived from 7-iodo-2-methyl-2-heptene was incorrectly tabulated in ref 3: Table I, entry 6 should have read 1.6% rather than the 5.6% previously reported as the yield of isopropylcyclopentane generated upon standing at room temperature for 3 h. We thank the reviewer of the present manuscript for calling this error to our attention.

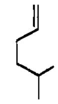
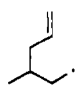
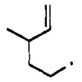
(18) Bailey, W. F.; Khanolkar, A. D. *Tetrahedron Lett.* **1990**, *31*, 5993.

(19) (a) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron Lett.* **1985**, *26*, 373. (b) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959.

(20) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

(21) Houk, K. N.; Rondan, N. G.; Schleyer, P. v. R.; Kaufmann, E.; Clark, T. *J. Am. Chem. Soc.* **1985**, *107*, 2821.

Table II. Stereoselectivities of Cyclization of 5-Hexen-1-yl Radicals[a]

radical	trans/cis
	1.78
	0.40
	4.76

[a] Data are for radical cyclizations conducted at 80 °C and are taken from ref 14. Essentially the same selectivities are observed[31] at 25 °C.

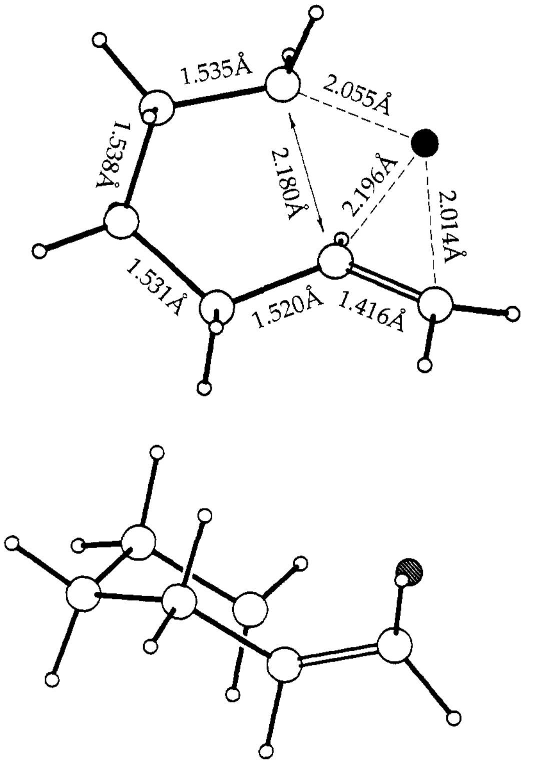


Figure 2. 3-21G chair-like transition-state structure for the closure of 5-hexen-1-yllithium to (cyclopentyl)methyllithium.

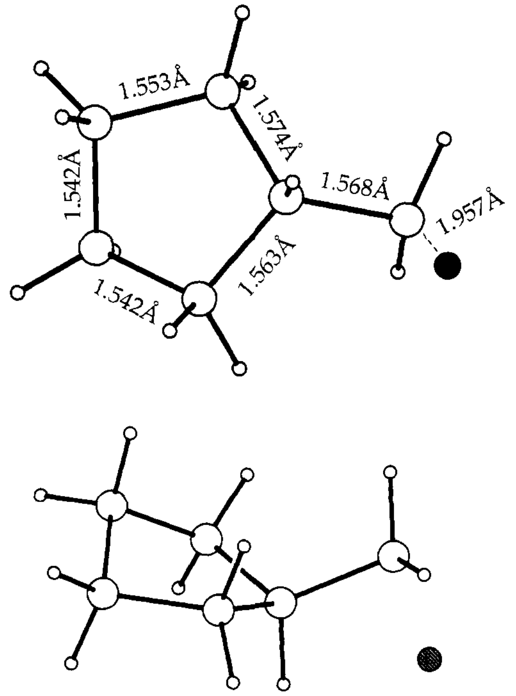


Figure 3. Calculated structure of (cyclopentyl)methyllithium.

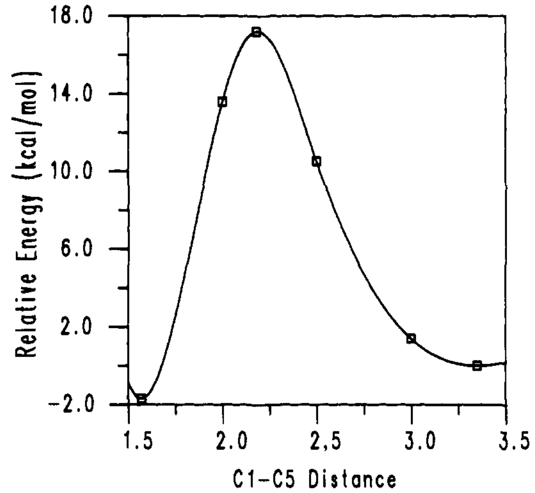


Figure 4. 3-21G energies as a function of the C(1)–C(5) distance for the ring closure of 5-hexen-1-yllithium to (cyclopentyl)methyllithium.

Table III. Calculated (3-21G) Energy as a Function of the C(1)–C(5) Distance for the Ring Closure of 5-Hexen-1-yllithium

distance	energy[a] (hartrees)	E_{rel} (kcal/mol)
linear	−239.64916	11.5
3.35 Å	−239.66755	0.0
3.0 Å	−239.66534	1.4
2.5 Å	−239.65084	10.5
2.18 Å (TS)	−239.64009	17.2
2.0 Å	−239.64588	13.6
1.57 Å	−239.67030	−1.7

[a] 1 hartree = 627.5 kcal/mol.

ordination of the Li atom at C(1) with the C(5)–C(6) π-bond serves to establish the geometry of the system prior to the activation step leading to product. An indication of the favorable energetics attendant to this intramolecular association of the Li atom with the double bond may be gleaned from the fact that linear 5-hexen-1-yllithium, in which such an interaction does not contribute to stability, is calculated to be some 11.5 kcal/mol less stable than the intermediate. It might also be noted that the difference in energy between the linear and complexed structures of 5-hexen-1-yllithium (11.5 kcal/mol) is close to the calculated interaction energy of monomeric CH_3Li with ethylene (12.1 kcal/mol) and monomeric LiH with ethylene (12.9 kcal/mol) when computed with the same basis set.[21]

In an effort to locate the transition-state geometry for the ring closure, geometry optimization was carried out for reaction coordinate distances of 2.5 and 2.0 Å as well as for the final product, (cyclopentyl)methyllithium. The 2.0-Å structure appeared to be near the transition state, and, starting from this structure, geometry optimization was carried out leading to a transition state structure having a C(1)–C(5) distance of 2.18 Å and lying 17.2 kcal/mol above the intermediate. The optimized transition-state geometry is shown in Figure 2. The product organolithium, whose optimized structure is illustrated in Figure 3, was computed to be 1.7 kcal/mol more stable than the intermediate (and, thus, some 13.2 kcal/mol more stable than a linear 5-hexen-1-yllithium). Relevant calculated energies are listed in Table III and displayed as a function of the reaction coordinate [the C(1)–C(5) distance] in Figure 4.

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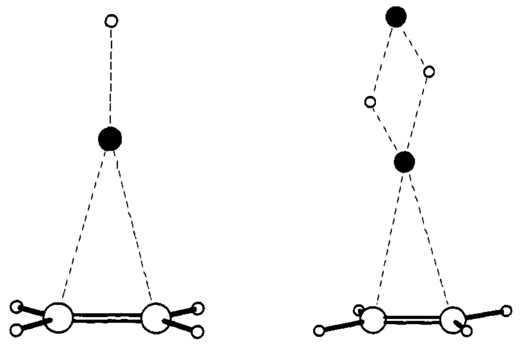
Table IV. Energies of Lithium Hydride and Its Ethylene Complexes, 6-311+G*



compd	energy (hartrees)	E_{rel} (kcal/mol)
LiH	-7.98545	0.0
Li_2H_2	-16.04404	-45.5
C_2H_4	-78.04872	
$LiHC_2H_4$	-86.04799	-8.7
$Li_2H_2C_2H_4$	-94.10478	-7.5

The calculations described above are, of course, for a monomeric 5-hexen-1-yllithium in the gas phase. In solution the organometallic will be solvated, and, depending on the solvent, it will most probably be aggregated to various extents.[15] In view of these limitations, it is encouraging (and perhaps somewhat surprising) that the calculated activation energy for closure of the coordinated 5-hexen-1-yllithium (17.2 kcal/mol) is in reasonably good agreement with the experimentally determined enthalpy of activation (ΔH^{*} = 11.8 ± 0.5 kcal/mol)[2] for the process in *n*-pentane–diethyl ether (3:2 by volume) solvent.

In addition to solvation and intermolecular aggregation, another factor which may affect the calculated energies is the potential problem of basis set superposition error.[23] Thus, if too small basis set is employed for calculations and two centers are brought near each other, an atom may use the basis functions of the proximate center to improve its charge distribution. The net result of such superposition error is that the calculated energies will suggest a greater stabilization than is appropriate for the actual system. This problem may be minimized by using a sufficiently flexible basis set for the calculations so that an atom need not "borrow" from the functions of a nearby center. In an effort to evaluate the significance of basis set superposition error on the calculated energies of 5-hexen-1-yllithium and to explore the possible effects of aggregation on the calculated energies, we have modeled the system by studying the dimerization of lithium hydride and the interaction of lithium hydride and its dimer with ethylene using the 6-311+G* basis set.[24] This flexible basis set, which is triple-ζ for all valence electrons, includes both diffuse functions and polarization functions on all atoms except hydrogen.

The use of the LiH–ethylene system as a model for the behavior of 5-hexen-1-yllithium was necessitated by the fact that it is not readily practical to examine an aggregate of the organometallic at the 6-311+G* level. Nevertheless, the choice of LiH as a mimic of the hexenyllithium seems reasonable since the interactions of the lithium atom are essentially all coulombic.[25] The results of calculations on lithium hydride, its dimer, lithium hydride coordinated to ethylene, and the dimer coordinated to ethylene are presented in Table IV.

Examination of the 6-311+G* calculations reveals that the dimerization of lithium hydride is energetically very favorable: the dimer is some 45.5 kcal/mol more stable than the monomer. The coordination of monomeric lithium hydride with ethylene was found to be favored by 8.7 kcal/mol, a somewhat smaller value than that previously reported (12.9 kcal/mol) for this interaction with the 3-21G basis set.[21] Most significantly, the interaction of dimeric LiH with ethylene had a similar interaction energy, 7.4 kcal/mol (Table IV). It therefore appears that dimer formation and, by extension, aggregation should not have a large effect on the energetically favorable coordination of lithium with a double bond.

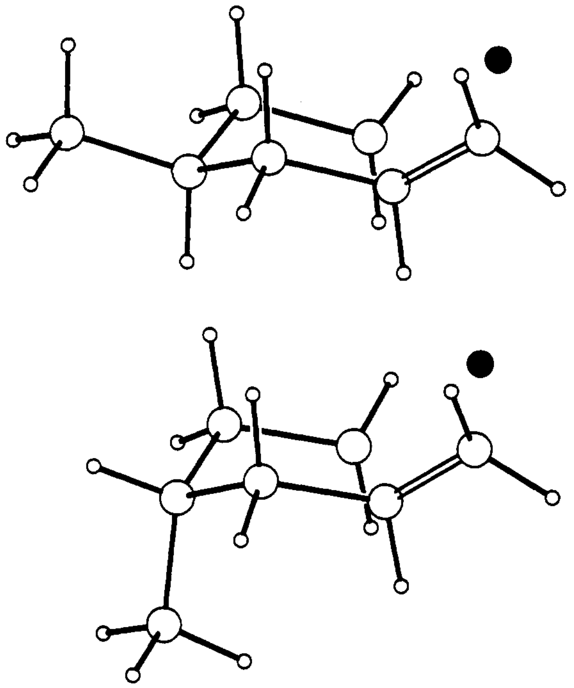


Figure 5. Calculated (3-21G) geometries and energies for the axial and equatorial conformers of 3-methyl-5-hexen-1-yllithium (7).

This encouraging result led us to examine the stereoselectivity of the cyclization of substituted 5-hexen-1-yllithiums by calculation of the difference in energy between a transition state having an axial substituent and one bearing an equatorial substituent. To this end, a methyl group was placed at C(3) on the 5-hexen-1-yllithium (giving **7**, Scheme I) and geometry optimization was performed with the 3-21G basis set with the distance between the reacting centers [C(1)–C(5)] set at the 2.18-Å value found to represent the transition state for closure of the parent organolithium. All other structural parameters were allowed to vary. The calculated geometries and their energies are shown in Figure 5. The axially substituted transition state for closure of **7** to **11** was found to lie higher in energy (calculated energy, −278.459 07 H) than the equatorially substituted case (calculated energy, −278.461 33 H) by approximately 1.4 kcal/mol. Thus, the transition state for closure of **7** to *cis*-**11** is calculated to be 1.4 kcal/mol more stable than that leading to *trans*-**11**. This difference in energy of activation for the competitive modes of ring closure is equivalent to a ratio of rates for the formation of *cis*-**11**/*trans*-**11** of approximately 11:1 at +20 °C, a value in excellent agreement with the experimentally observed selectivity of the reaction (Table I, entries 5–8). In the same manner, the difference in energy of activation for cyclization of 2-methyl-5-hexen-1-yllithium (**6**) to *trans*-**11** and *cis*-**11** was evaluated. The transition state having an axial methyl (calculated energy, −278.460 43 H) was now found to be ~0.63 kcal/mol higher in energy than the equatorially substituted geometry (calculated energy, −278.461 43 H). The ratio of products predicted by this analysis (*trans*-**11**/*cis*-**11** = ~3:1 at +20 °C) is somewhat less than the selectivity observed in the cyclization of **6** (Table I, entries 1–4). This discrepancy between calculated and experimentally observed stereoselection may well be a reflection of the fact that, although the 2-methyl substituent in **6** is relatively close to the reactive center and thus might be expected to alter the geometry of the transition state for the closure of **6** relative to that of the unsubstituted case, the calculation was predicated on the assumption of a fixed C(1)–C(5) distance in the transition state for both processes. While it is possible in principle to locate the energies

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Table V. Results of Modified MM2 Molecular Mechanics Calculations for the Transition State for the Ring Closure of Substituted 5-Hexen-1-yllithiums

substituent	SE equatorial	SE axial	ΔSE
2-methyl (**6**)	15.86	16.55	0.69
3-methyl (**7**)	15.18	16.41	1.23
3-phenyl	13.00	15.15	2.15
3-*tert*-butyl	21.90	26.39	4.49

and geometries of fully optimized transition states for the cyclization of substituted 5-hexen-1-yllithiums, such calculations are rather time-intensive. For this reason, we have attempted to model the activated complex leading to cyclization of substituted systems with molecular mechanics.

The MM2 parameter set[26] was modified to include a three-coordinate lithium with "bonds" to the three carbons of the substrate [C(1), C(5), and C(6)] of 2.0 Å and having a relatively low stretching force constant of 1 mdyne/Å. The C–Li bond length was taken as 2.0 Å and the C–Li–C angle was taken as 60° in accord with the ab initio calculations described above, and a relatively weak force constant of 0.1 mdyne/rad was assigned. A molecular mechanics calculation with these parameters gave a transition-state geometry for cyclization of 5-hexen-1-yllithium that was in close accord with the ab initio result: the C(1)–C(5) distance was calculated to have a length of 2.4 Å, in reasonable agreement with the 2.18-Å value obtained with the 3-21G basis set.

The results of molecular mechanics calculations for 2-methyl- (**6**) and 3-methyl-5-hexen-1-yllithium (**7**) are presented in Table V. The calculated minimum-energy transition-state structures for the axial and equatorial geometries of **7** are virtually identical with those illustrated in Figure 5. Comparison of these results with those derived from the ab initio calculations reveal that (1) the molecular mechanics approach provides transition-state geometries that are quite similar to the 3-21G structures (Figure 5) and (2) the MM2 energy differences are virtually identical with the ab initio results described above. In view of the success of the MM2 calculations for methyl-substituted 5-hexen-1-yllithiums, we extended the analysis to calculation of the relative energies for cyclization of 3-phenyl- and 3-*tert*-butyl-5-hexen-1-yllithium. The results of these modified MM2 calculations, which are presented in Table V, suggest (albeit not unexpectedly) that the presence of substituents more sterically demanding than methyl should greatly *increase* the stereoselection of the cyclization process. Indeed, the modified MM2 calculations suggest that the selectivity of cyclizations of substituted 5-hexen-1-yllithiums may be anticipated, at least qualitatively, by recourse to the conformational energy of a given substituent in the cyclohexane system.

The picture which emerges from both the ab initio calculations and the molecular mechanics analyses is compelling in its simplicity: the highly stereoselective and totally regiospecific intramolecular insertion of the alkene moiety into the C–Li bond of a substituted 5-hexen-1-yllithium is a consequence of the energetically favorable coordination of the Li atom with the π-system leading to a rigidly constrained transition state for the cyclization. Moreover, this scenario serves to explain the experimentally observed product distributions (Table I) on a semiquantitative level. There is, however, a rather dramatic and initially unexpected feature of the reaction that is not addressed by the computational results.

As noted above, the high stereoselectivities of the cyclization reactions are not adversely affected by the presence of Lewis base additives such as THF, TMEDA, and PMDTA (Table I) which facilitate the reaction. Indeed, the addition of the tridentate ligand PMDTA serves, in most instances, to significantly increase the selectivity of the process (Table I, entries 4, 8, and 12). Ironically, this ligand was selected at the inception of this study with the expectation that use of such a strongly coordinating tridentate molecule would result in a decrease in the stereoselection since PMDTA could use all three of its basic sites to saturate the coordination sphere of the Li atom at the expense of the intramolecular Li–alkene interaction. In light of the results noted above and in Table I, it would appear that nature did not share our naive view. Be that as it may, association of the lithium atom of the organometallic and a basic site on the addend will be in dynamic competition with intramolecular coordination to the π-bond. In view of the fact that lithium–ligand bond dissociation within an aggregate is a rather rapid process,[27] it is reasonable to suppose that displacement of a basic ligand atom and coordination of the C(5)–C(6) alkene moiety preceeds ring closure via the chair-like transition state described above. Moreover, this rationale is consistent with the observation that Lewis bases accelerate the cyclization of 5-hexen-1-yllithiums.[3,4,8-10] The residual lithium–Lewis base coordination that persists in the transition state should serve to increase the rate of the cyclization by helping to lengthen the C(1)–Li bond during the activation step. The 3-21G calculations indicate that the C(1)–Li distance increases from ~2.01 Å in the intermediate to ~2.06 Å at the transition state (compare Figures 1 and 2). Indeed, just such a rationale has been advanced by Klumpp to account for the ability of Lewis bases to facilitate the intermolecular addition of an organolithium to an alkene.[16] Thus, the observation that addition of a Lewis base often improves the selectivity of the cyclization of a substituted 5-hexen-1-yllithium (Table I) may simply be a consequence of the fact that such reactions occur at a lower temperature than those conducted in the absence of the additive. The results of ongoing kinetic studies should provide more quantitative information on this aspect of the cyclization.

Conclusions

The cyclization of 5-hexen-1-yllithiums provides a useful, and often superior, alternative to radical-mediated methods for the construction of cyclopentylmethyl-containing systems. The requisite organolithium, which is easily prepared in essentially quantitative yield by low-temperature lithium–iodine exchange,[11] is stable at −78 °C in a solution of *n*-pentane–diethyl ether.[2] On warming, the olefinic alkyllithium undergoes a clean and totally regiospecific 5-exo-trig cyclization to give a (cyclopentyl)methyllithium that may be trapped by reaction with an electrophile to deliver functionalized product in high yield. In addition to these attractive features of the methodology, the results presented above (Table I) demonstrate that cyclization of substituted 5-hexen-1-yllithiums is a much more stereoselective process than radical-mediated isomerization of analogous substrates. In each case for which data are available, the major isomer produced upon ring closure of a 5-hexen-1-yllithium is the same as that generated by cyclization of the analogous radical (Table II), but the former process invariably displays a higher degree of stereocontrol than the latter. Moreover, the high stereoselectivities characteristic of the anionic cyclization are not adversely affected by the addition of Lewis bases which have been found to facilitate the reaction.

Ab initio molecular orbital calculations reveal that the high stereoselectivity and total regiospecificity of the isomerization of substituted 5-hexen-1-yllithiums derives from energetically favorable coordination of the Li atom with the C(5)–C(6) π-bond leading to a rigid transition state resembling a cyclohexane chair (Figure 2) in which a substituent preferentially occupies a pseudoequatorial position (Figure 5). This transition-state geometry, which is apparently preserved in the presence of various Lewis base additives, may be modeled with modified MM2 parameters. As a consequence of the rigid chair-like transition state for the conversion of a 5-hexen-1-yllithium to a substituted (cyclopentyl)methyllithium, the stereochemical outcome of the cyclization may be anticipated, to a reasonable approximation, by reference to the conformational energy of a substituent in the

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cyclohexane system. In short, the stereocontrol provided by the rigid transition state for cyclization of a 5-hexen-1-yllithium, coupled with the ease with which such organolithiums may be prepared, suggests that this anionic route to five-membered rings will find wide utility in organic synthesis.

Experimental Section

General Procedures. Proton and carbon-13 magnetic resonance spectra were recorded on an IBM AF-270 NMR, and shifts were referenced with respect to internal Me_4Si. A Perkin-Elmer Series 1600 FTIR instrument was used to record infrared spectra. Bulb-to-bulb distillations were carried out by using a Kugelrohr distillation apparatus, and distillation temperatures recorded with this apparatus refer to the temperature of the air bath. All boiling points are uncorrected. Analytical gas-liquid chromatography (GC) was accomplished with Hewlett-Packard Model 5880A or 5890 chromatographs equipped with flame-ionization detectors and one of the following fused-silica capillary columns: (A) 25-m × 0.20-mm cross-linked methyl silicone (0.33-μm film thickness) or (B) 25-m × 0.25-mm methyl phenyl (20%) silicone (0.50-μm film thickness). Area ratios were determined with a Hewlett-Packard Model 3396A recording integrator, and, unless otherwise noted, all yields determined by GC analysis were corrected for detector response under the condition of the analysis with accurately weighed samples of pure product and hydrocarbon standard. Preparative GC was accomplished on a Varian Aerograph A-90P instrument fitted with one of the following 0.25-in. aluminum columns: (A) 9-ft, 15% SE-30 on Chromosorb W (NAW) (80/100 mesh) or (B) 10-ft, 15% FFAP on Chromosorb W (NAW) (80/100 mesh). GC-MS was performed on a Hewlett-Packard 5870B GC/MSD system with Chemstation software operating at 70 eV and fitted with a 12.5-m × 0.20-mm cross-linked dimethyl silicone fused-silica capillary column. High-resolution mass spectra were obtained on an AEI MS-902 instrument at 70 eV. Microanalyses were performed by Desert Analytics, Tuscon, AZ.

All reactions involving alkyllithiums were performed in flame-dried glassware with standard syringe/cannula techniques[28] under an atmosphere of dry, oxygen-free argon that had been passed through a column containing an activated BASF R3-11 copper catalyst. Diethyl ether and tetrahydrofuran were freshly distilled from dark purple solutions of sodium/benzophenone. *N,N,N',N'*-Tetramethylethylenediamine (TMEDA) and *N,N,N',N'',N''*-pentamethyldiethylenetriamine (PMDTA) were purified by distillation under nitrogen from calcium hydride: TMEDA, bp 120–122 °C; and PMDTA, bp 85–86 °C (12 mm). Dry, unsaturate-free *n*-pentane was obtained by repeated washings of commercial *n*-pentane with concentrated sulfuric acid until the acid layer remained clear, followed by washing with water and saturated aqueous sodium bicarbonate, drying over $MgSO_4$ and distillation of the purified pentane under nitrogen from lithium aluminum hydride. Methylene chloride was dried by distillation from calcium hydride. Acetone (Baker, analytical grade) was dried over calcium sulfate and distilled. Sodium iodide was dried at 100 °C (ca. 5 mm) for 8–10 h in a vacuum oven. The concentrations of solutions of *tert*-butyllithium in *n*-pentane (Aldrich) were determined by titration with *sec*-butyl alcohol in xylene with 1,10-phenanthroline as indicator.[29] All reagents used for the preparation and quench of organolithiums that had not been freshly distilled under argon (starting halides, internal standard, and MeOH) were rendered essentially oxygen free before use by bubbling dry, deoxygenated argon gas through the neat liquid for at least 5 min before use: failure to follow this rather stringent protocol was found to result in consumption of organolithiums through rapid reaction with adventitious oxygen. Thin-layer chromatography (TLC) was performed on E. Merck precoated (0.2-mm) silica gel 60 F_{254} plates. Visualization was accomplished by spraying with 10% ethanolic phosphomolybdic acid and heating. Flash chromatography[30] was carried out on Merck 70-230 mesh silica gel.

Literature procedures incorporating some minor modifications were followed for the preparation of 2-methyl-1-hexene,[31] 4-methyl-1-hexene,[31] 5-methyl-1-hexene,[31] *cis*-1,3-dimethylcyclopentane,[31] *endo*/*exo*-2-methylbicyclo[2.2.1]heptane,[32] 2-methyl-1,5-hexadiene,[33] *cis*- and *trans*-5-hepten-1-ol,[34] 3-methyl-5-hexen-1-ol,[31] 4-methyl-5-hexen-1-ol,[35,36] 6-iodo-3-methyl-1-hexene[37] (**3**), 5-methyl-5-hexen-1-ol,[38] 2-methyl-5-hexen-1-ol,[39] methyl *cis*-3-formylcyclopentanecarboxylate,[40,41] and methyl *cis*-3-ethenylcyclopentanecarboxylate.[43] The following hydrocarbons were obtained from commercial sources: *cis*-1,3-dimethylcyclopentane, *cis*-1,2-dimethylcyclopentane, *trans*-1,2-dimethylcyclopentane, *cis*/*trans*-1,3-dimethylcyclopentane, and 3-methyl-1-hexene from Wiley Organics, *cis*-2-heptene from Lancaster Synthesis, Ltd., and *trans*-2-heptene and citronellene from Fluka Chemical Corp.

6-Iodo-2-methyl-1-hexene (4). The mesylate of 5-methyl-5-hexen-1-ol, prepared from 1.99 g (17.4 mmol) of the alcohol by the method of Crossland and Servis,[37] was added to a solution of 5.22 g (34.8 mmol) of dry sodium iodide in 53 mL of dry acetone. The solution was stirred overnight and then heated under gentle reflux for 1 h. The precipitate was filtered and washed thoroughly with fresh acetone, and the combined filtrate and washings were concentrated under reduced pressure. The residue was taken up in pentane and washed successively with 10% aqueous sodium thiosulfate, water, and brine. The organic layer was dried ($MgSO_4$) and solvent removed to obtain the product. Kugelrohr distillation gave 2.45 g (63% from the alcohol) of 6-iodo-2-methyl-1-hexene: bp 90–95 °C (20 mm); IR (neat) 3200, 1690, 1240, 930 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.58 (m, 2 H), 1.75 (s, 3 H), 1.88 (m, 2 H), 2.05 (t, J = 7.50 Hz, 2 H), 3.21 (t, J = 6.90 Hz, 2 H), 4.71 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 6.86 (C(6)), 22.22 (CH_3), 28.31 (C(4)), 32.97 (C(3)), 36.56 (C(5)), 110.34 (C(2)), 145.06 (C(1)); mass spectroscopic weight calcd for $C_7H_{13}I$ 224.0068, found 224.0064.

6-Iodo-4-methyl-1-hexene (2). Following the general procedure of Crossland and Servis,[37] 4.88 g (63.7 mmol) of 3-methyl-5-hexen-1-ol[31] was converted into its mesylate. The crude mesylate was added to a solution of 13.4 g (89.7 mmol) of anhydrous sodium iodide in 150 mL of dry acetone, and the mixture was stirred for 13 h at room temperature under an argon atmosphere. Inorganic salts were removed by filtration and washed thoroughly with fresh acetone, and the combined filtrate and washings were concentrated at reduced pressure. The residue was partitioned between water and pentane, the aqueous layer was extracted with pentane, and the combined pentane extracts were washed successively with 10% aqueous sodium thiosulfate and water. The organic layer was dried ($MgSO_4$), solvent was removed by rotary evaporation, and the residue was distilled to give 6.72 g (70%) of the title alcohol: bp (Kugelrohr) 75–80 °C (10 mm); IR (neat) 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (d, J = 6.4 Hz, 3 H), 1.70 (m, 2 H), 1.93 (m, 2 H), 2.10 (m, 1 H), 3.20 (m, 2 H), 4.95–5.04 (m, 2 H), 5.80 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 4.82 (C(6)), 18.46 (CH_3)), 33.63 (C(4)), 40.18 (C(3)), 40.47 (C(5)), 116.25 (C(1)), 136.41 (C(2)); mass spectroscopic molecular weight calcd for $C_7H_{13}I$ 224.0068, found 224.0064. Anal. Calcd for $C_7H_{13}I$: C, 37.53; H, 5.85. Found: C, 37.79; H, 6.00.

6-Iodo-5-methyl-1-hexene (1). The mesylate of 2-methyl-5-hexen-1-ol was prepared from 2.28 g (20.0 mmol) of the alcohol by the method of Crossland and Servis.[37] The crude mesylate was added to a solution of 6.00 g (40.0 mmol) of anhydrous sodium iodide in 60.0 mL of dry acetone, and the mixture was heated overnight at gentle reflux under an atmosphere of nitrogen. The mixture was cooled, inorganic salts were removed by filtration, and the precipitate was washed thoroughly with acetone. The combined filtrate and washings were concentrated by rotary evaporation, the residue was taken up in pentane and washed successively with water, 10% aqueous sodium thiosulfate, and brine. The organic extract was dried ($MgSO_4$), concentrated, and distilled to give 2.48 g (55% from the alcohol) of the iodide: bp 88–90 °C (24 mm); IR (neat) 3190, 3030, 1690, 1240, 960, and 780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00 (d, J = 6.39 Hz, 3 H), 1.21–1.58 (m, 3 H), 2.08 (m, 2 H), 3.17 (A portion of ABX, J_{AB} = 9.52 Hz, J_{AX} = 4.37 Hz, 1 H), 3.23 (B portion of ABX, J_{AB} = 9.52 Hz, J_{BX} = 3.23 Hz, 1 H), 5.00 (m, 2 H), 5.79 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 17.46 (C(6)), 20.42 (CH_3), 31.03 (C(3)),

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33.97 (C(4)), 35.52 (C(5)), 114.77 (C(1)), 138.16 (C(2)). Anal. Calcd for $C_7H_{13}I$: C, 37.52; H, 5.85. Found: C, 38.00, H, 6.07. The analysis is somewhat outside the usual limits, but all of the data are only consistent with the assigned structure.

***cis*-3-(Ethenylcyclopentyl)methanol.** A solution of 2.43 g (15.8 mmol) of methyl *cis*-3-ethenylcyclopentanecarboxylate in 5 mL of dry diethyl ether was added dropwise to a suspension of 600 mg (15.8 mmol) of lithium aluminum hydride in 50 mL of dry diethyl ether, and the resulting suspension was stirred for 15 min at room temperature. The mixture was hydrolyzed by sequential, dropwise addition of 0.60 mL of water, 0.60 mL of 15% aqueous sodium hydroxide, and 1.80 mL of water. The mixture was filtered, the precipitate was washed with fresh ether, and the combined filtrate and washings were concentrated to give an oil which was purified by flash chromatography on silica gel (10% EtOAc in hexanes as eluent) to afford 1.82 g (92%) of the pure alcohol: R_f 0.12 (10% EtOAc–hexanes); IR (neat) 3342, 3072, 1637, 1044, 908 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00–2.29 (complex pattern, 8 H), 2.54 (br s, 1 H), 3.54 (d, $J = 6.83$ Hz, 2 H), 5.00 (m, 2 H), 5.83 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 28.02 (C(5)), 31.69 (C(2)), 36.36 (C(4)), 41.82 (C(1)), 44.36 (C(3)), 67.23 (CH_2OH), 112.45 ($=CH_2$), 142.87 ($=CH$); mass spectroscopic molecular weight calcd for C_8H_{12} ($M^+ - H_2O$) 108.0939, found 108.0939.

***cis*-1-Ethenyl-3-(iodomethyl)cyclopentane (5).** The mesylate of *cis*-3-(ethenylcyclopentyl)methanol, prepared from 3.91 g (31.0 mmol) of the alcohol by the procedure of Crossland and Servis,[37] was added to a solution of 9.30 g (62.0 mmol) of dry sodium iodide in 93.0 mL of anhydrous acetone, and the mixture was stirred overnight at gentle reflux under an atmosphere of nitrogen. The reaction mixture was then cooled, filtered, and concentrated by rotary evaporation. The residue was taken up in pentane and washed successively with 10% aqueous sodium thiosulfate, water, and brine. After drying ($MgSO_4$), solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexanes as eluent) to afford 4.60 g (65%) of the title iodide: R_f 0.47 (hexanes); IR (neat) 3072, 1637, 1420, 908, and 497 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.00–2.17 (complex m, 6 H), 2.30 (m, 1 H), 2.79 (m, 1 H), 3.2 (d, $J = 6.90$ Hz, 2 H), 4.92 (m, 2 H), 5.83 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 13.90 (CH_2I), 31.79 (C(4)), 32.24 (C(2)), 40.81 (C(5)), 42.43 (C(3)), 44.58 (C(1)), 112.77 ($=CH_2$), 142.54 ($=CH$). Anal. Calcd for $C_8H_{13}I$: C, 40.70; H, 5.55. Found: C, 40.27; H, 5.48.

***cis*-1-Ethenyl-3-methylcyclopentane.** The crude mesylate, prepared[37] from 1.00 g (7.90 mmol) of an 80:20 mixture of cis and trans isomers of 3-(ethenylcyclopentyl)methanol, was dissolved in 7.9 mL of dry THF and reduced by the method of Holder and Matturo[32] with 16.6 mL of a 1.0 M solution of lithium triethylborohydride in THF to give 790 mg (90%) of the hydrocarbons. An analytical sample of the cis isomer was prepared by preparative GLC on column A at 60 °C: ^1H NMR ($CDCl_3$) δ 1.00 (d, $J = 6.22$ Hz, 3 H), 1.13–2.17 (m, 7 H), 2.58 (m, 1 H), 5.00 (m, 2 H), 5.83 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.91 (CH_3), 31.91 (C(5)), 33.67 (C(3)), 34.56 (C(4)), 42.34 (C(2)), 44.74 (C(1)), 111.69 ($=CH_2$), 143.90 ($=CH$); mass spectroscopic molecular weight calcd for C_8H_{14} 110.1096, found 110.1093.

***cis*- and *trans*-7-Iodo-2-heptene (19).** The mesylate of 5-hepten-1-ol, prepared from 2.70 g (23.7 mmol) of the alcohol by the general method of Crossland and Servis,[37] was added to a solution of 7.20 g (48.0 mmol) of dry sodium iodide in 80 mL of dry acetone, and the mixture was stirred overnight at room temperature under an atmosphere of dry nitrogen. The reaction mixture was filtered and concentrated by rotary evaporation. The residue was taken up in pentane and washed successively with water, 10% aqueous sodium thiosulfate, water, and brine. After drying ($MgSO_4$), solvent was removed by rotary evaporation to give an oil that was distilled to afford 3.58 g (67% from the alcohol) of the title iodides as a mixture of isomers: cis/trans = 78/22 as adjudged by GC analysis; bp (Kugelrohr) 95–100 °C (10–11 mm); IR (neat) 3007, 2932, 1455, 1211, 1165, 966, and 724 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25–1.49 (m, 2 H), 1.55–1.71 (m, 3 H), 1.77–1.89 (m, 2 H), 1.96–2.11 (m, 2 H), 3.18 (t, $J = 7.04$ Hz, H(1) trans isomer), 3.19 (t, $J = 7.03$ Hz, H(1) cis isomer), 5.37–5.46 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 6.84 (C(7)), 12.72 (C(1)-cis), 17.85 (C(1)-trans), 25.66 (C(4)-cis), 30.28 (C(4)-trans), 30.33 (C(5)-cis), 31.37 (C(5)-trans), 32.94 (C(6)-cis), 33.02 (C(6)-trans), 124.39 (C(2)-cis), 125.38 (C(2)-trans), 129.72 (C(3)-cis), 130.52 (C(2)-trans). An analytical sample of the mixture of isomers was prepared by preparative GC on a 9-ft, 15% SE-30 on Chromosorb W (NAW, 80/100 mesh) column at 120 °C. Anal. Calcd for $C_7H_{13}I$: C, 37.52; H, 5.85. Found: C, 37.50; H, 5.94.

General Procedure for the Generation and Cyclization of 5-Hexen-1-yllithiums. A 0.1 M solution of the olefinic alkyl iodide (typically 0.25–0.50 mmol) containing an accurately weighed quantity of the hydrocarbon internal standard (typically 0.25–0.50 mmol of *n*-heptane) in *n*-pentane–diethyl ether (3:2 by volume) was cooled to −78 °C (acetone/dry ice) under an atmosphere of dry, oxygen-free argon and, with stirring, 2.2 molar equiv of *t*-BuLi in *n*-pentane was added via syringe over a 5-min period. The mixture was stirred at −78 °C for an additional 5 min before treatment in one of the following ways. (A) **Quench at −78 °C.** Dry, deoxygenated methanol (ca. 1 mL) was added at −78 °C to the stirred reaction mixture, and the cooling bath was removed. **(B) Cyclization at Elevated Temperature.** The cooling bath was removed, and the solution was allowed to warm to room temperature and then allowed to stand at room temperature under the blanket of argon for 1 h before addition of 1.0 mL of dry, deoxygenated methanol. **(C) Cyclization in the Presence of Additives.** The organolithium solution was maintained at −78 °C under a blanket of argon, and the additive (2.2 molar equiv of the polyamines TMEDA and PMDTA or a volume of dry THF equal to the volume of diethyl ether used in the interchange reaction) was added via syringe. The addition of polyamine or THF was generally accompanied by the formation of a white-to-light yellow precipitate and a change in the color of the solution from clear to pale yellow. The mixture was stirred for 5 min at −78 °C, the cooling bath was removed, and the reaction mixture was allowed to warm to room temperature and stand at room temperature for 1 h prior to the addition of 1.0 mL of dry, deoxygenated methanol. The reaction mixture was washed with water, dried ($MgSO_4$), and analyzed by GC with column A (40 °C isothermal) except in the case of the cyclization of the organolithium derived from 6-iodo-3-methyl-1-hexene when column B (with temperature programming; 40 °C for 1 min, 5 °C/min to 60 °C) was used to effect separation of the isomeric hydrocarbons. Reaction products were identified by comparing their GC retention times and mass spectra with those of authentic samples.

Calculations. The calculations were carried out with GAUSSIAN-88[44] and standard basis sets.

Acknowledgment. This work was supported by the Connecticut Department of Higher Education under Grant 90-630.