Pergamon

Tetrahedron Vol. 50, No. 20, pp. 5957-5970, 1994

0040-4020/94 $7.00+0.00

0040-4020(94)E0285-2

Anionic Cyclization of Olefinic Alkyllithiums: Ring Closure of Terminally Substituted 5-Hexenyllithiums.

William F. Bailey* and Kaustubh V. Gavaskar

Department of Chemistry, University of Connecticut, Storrs, CT 06269-3060

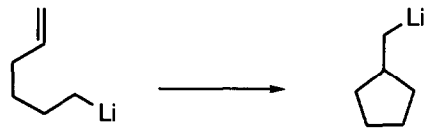
Abstract: A series of 5-hexenyllithiums having a phenyl, trimethylsilyl, or cyclopropyl substituent at the terminal [C(6)] alkene carbon have been prepared from the corresponding iodides by lithium–iodine exchange with *t*-butyllithium at –78 °C. Although 6-alkyl-substituted 5-hexenyllithiums do not isomerize to five-membered rings upon warming, terminally substituted 5-hexenyllithiums bearing a moderately activating phenyl or trimethylsilyl group cleanly undergo a totally regiospecific 5-*exo* cyclization at sub-ambient temperatures to afford five membered rings bearing a CHRLi moiety that may be trapped with an electrophile to deliver high yields of functionalized product. Cyclization of 6-cyclopropyl-5-hexenyllithium is accompanied by ring opening of the three-membered ring.

The anionic cyclization of olefinic,[1,2] diolefinic,[3] and acetylenic alkyllithiums[4] provides a regiospecific and highly stereoselective route to functionalized carbocycles. In particular, the 5-*exo*-*trig* isomerization of substituted 5-hexenyllithiums has been exploited to prepare a variety of functionalized cyclopentylmethyl-containing products. To date, these isomerizations have been confined to substrates in which the terminal alkene carbon of the 5-hexenyllithium is either unsubstituted[1-3] or bears a strongly electron-withdrawing group that activates the olefinic unit toward intramolecular nucleophilic attack.[5] Herein we report that the attachment of a moderately activating group such as phenyl, trimethylsilyl, or cyclopropyl to the terminal C(6) carbon of a 5-hexenyllithium serves to facilitate the cyclization.

BACKGROUND INFORMATION

The isomerization of 5-hexenyllithium (**1**) to (cyclopentyl)methyllithium (**2**) was first reported by Drozd and coworkers in the late 1960's.[6] These authors, who prepared the unsaturated organometallic from the corresponding bromide by treatment with lithium metal in diethyl ether, suggested that the cyclization of **1** to **2** was more rapid than the sluggish isomerization of the analogous Grignard reagent.[7] This observation was confirmed by Oliver and coworkers in a series of prescient reports dating from the mid-1970's.[8] In particular, it was noted that **1**, which

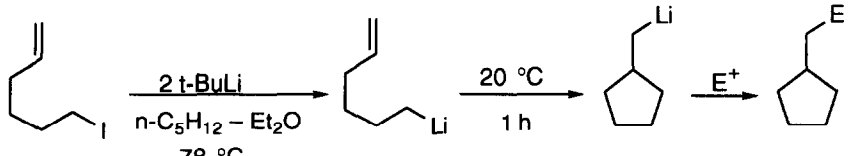
was prepared from di(5-hexenyl)mercury by transmetallation with lithium metal in diethyl ether, was converted to **2** upon standing for 1 h at 25 °C. Although quantitative kinetic data for the isomerization of **1** to **2** were not reported, it was suggested that the fairly rapid cyclization was the result of intramolecular coordination of the lithium atom at C(1) with the carbon-carbon π-bond in the ground-state of 5-hexenyllithium.[8]



1 **2**

With the exception of two notes by Wilson demonstrating that substituted 5-hexenyllithiums also cyclize upon warming,[9] the apparently regioselective ring closure of 5-hexenyllithiums was not put to immediate synthetic use. This somewhat surprising state of affairs was, in retrospect, most likely due to two factors; there was no efficient method available at the time for the generation of unsaturated alkyllithiums without the intervention of radical intermediates and there were no quantitative data demonstrating that the cyclization of **1** to **2** was more rapid than other reactions that would consume the reactive anions.

In the course of a mechanistic study of the lithium-halogen exchange reaction,[10] it was discovered that primary alkyllithiums such as 5-hexenyllithium could be prepared in virtually quantitative yield by low-temperature lithium-iodine exchange between a primary alkyl iodide and 2 equivalents of *tert*-butyllithium (*t*-BuLi) in a solvent system composed of *n*-pentane and diethyl ether (3:2 by volume).[11] Under these conditions the exchange most likely proceeds via rapid attack of *t*-BuLi on the iodine atom of the halide and there is no evidence of radical intermediates during the process.[10] Using this general protocol, 5-hexenyllithium (**1**) may be prepared in 95 - 98% yield from 6-iodo-1-hexene (**3**). When solutions of **1** are allowed to warm, a clean 5-exo ring closure to **2** ensues.[12] The isomerization of **1** to **2**, which is easily monitored by ^{1}H NMR,[12] is a first-order process, characterized by $\Delta H^{\ddagger}$ = 11.8 kcal/mol and $\Delta S^{\ddagger}$ = –30 eu, that is more rapid than proton abstraction from solvent. As suggested by these activation data, the rate of cyclization of 5-hexenyllithium is a strong function of temperature: **1** is indefinitely stable at –78 °C but it is rapidly converted to **2** upon warming to temperatures above 0 °C ($t_{1/2} \approx 23$ min at 0 °C and 5.5 min at +20 °C). In practice, simply allowing solutions of **1** to stand at room temperature for 1 h serves to generate **2** and addition of any of a variety of electrophiles delivers high yields of functionalized cyclopentylmethyl-containing products.[1]

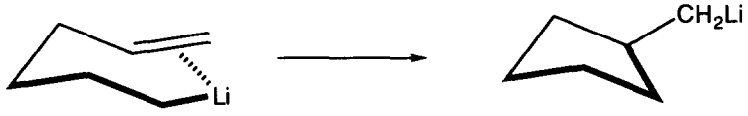


3 **1** **2**

The overall process (lithium-halogen exchange – cyclization – functionalization) is remarkably clean given the propensity of organolithiums to abstract a proton from ethereal solvents: virtually the only contaminant present in crude reaction mixtures is a small quantity of unfunctionalized open-chain alkene produced in the initial lithium-iodine exchange by proton abstraction from the cogenerated *t*-BuI.[1,11] It should be noted that the higher homolog, 6-heptenyllithium, has also been studied and it too cyclizes regioselectively to give (cyclohexyl)methyllithium,[1a] albeit more slowly and in lower yield than the facile 5-*exo* isomerization of **1**.[12]

While the lithium-iodine exchange provides a convenient route to unsaturated alkyllithiums such as **1**, these species may also be generated by other methods that do not involve the intermediate formation of unsaturated alkyl radicals which are, inter alia, prone to rapid cyclization. Thus, substituted 5-hexenyllithiums have been prepared by lithium-tin[13] or lithium-selenium exchange[14] and used for the construction of functionalized five-membered rings.[13,14]

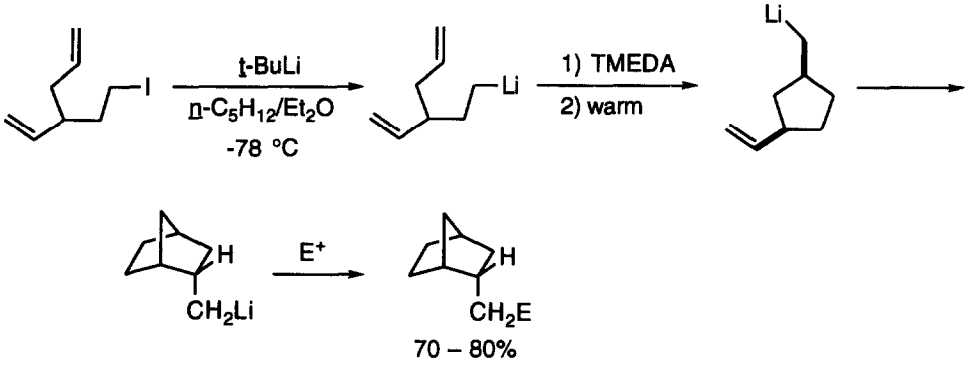
The regioselective 5-*exo* ring closure of substituted 5-hexenyllithiums has been found to proceed with a high degree of stereocontrol via a transition state that resembles a chair cyclohexane.[2] Moreover, in every case for which data are available, the anionic cyclization of a 5-hexenyllithium is much more stereoselective than the more rapid isomerization of an analogously substituted 5-hexen-1-yl radical.[15] Ab initio molecular orbital calculations indicate that the highly stereoselective and totally regiospecific ring closure of substituted 5-hexenyllithiums is, as suggested by Oliver,[8] a consequence of energetically favorable coordination of the Li atom at C(1) with the C(5) - C(6) π-bond giving a fairly rigid transition state, shown below, in which a substituent preferentially occupies a pseudoequatorial position on the chair-like structure.[2]



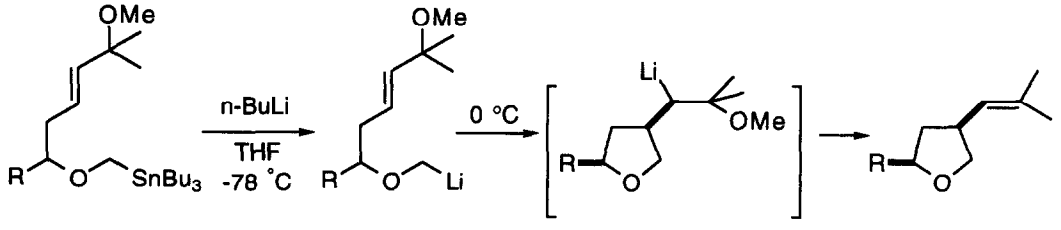
The cyclization of a 5-hexenyllithium to a (cyclopentyl)methyllithium is a thermodynamically favorable process since it generates a C–C σ-bond (bond energy ca. 88 kcal/mol) at the expense of a π-bond (bond energy ca. 60 kcal/mol). Nonetheless, the isomerization is often slow relative to side reactions that consume anions particularly in situations involving generation of a quaternary center or the formation of a strained ring system.[1,2] Fortunately, it has been found that such sluggish cyclizations may be facilitated by the addition of a lithiophilic Lewis base such as N, N, N', N'-tetramethylethylenediamine (TMEDA), THF, or the like. Moreover, the high stereoselectivities characteristic of the isomerization of substituted 5-hexenyllithiums are not compromised by the presence of such Lewis base additives.[2]

The predictable stereochemistry of the facile ring closure of substituted 5-hexenyllithiums, coupled with the ease with which the product organolithium may be functionalized, permits rational design of synthetic routes to rather complex polycyclic systems via sequential cyclizations of polyolefinic substrates.[3] Thus, for example, stereoisomerically pure *endo*-2-substituted bicyclo[2.2.1]hexanes may be prepared by functionalization of the bicyclic organolithium

generated by tandem cyclization of the diolefinic alkyllithium derived from 3-(2-iodoethyl)-1,5-hexadiene. This one-pot synthesis, illustrated below, provides pure *endo*-2-substituted norboranes in 70 - 80% isolated yield.[3c] Spirocyclic systems, trans-fused bicyclo[3.3.0]octanes, and [4.3.3]propellanes have been prepared by similar tandem-cyclization approaches.[3]

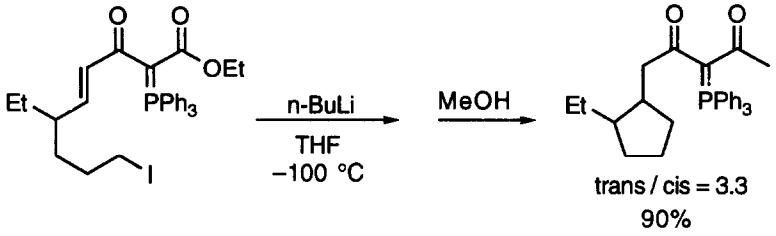


A major limitation of this anionic approach to carbocyclic products is the failure of 5-hexenyllithiums bearing a simple alkyl group at the terminal olefinic carbon to cyclize.[1,2,13] It would seem that the isomerization of a primary alkyllithium to an unstabilized secondary or tertiary species is energetically too costly even under forcing conditions.[2] This limitation may be circumvented by taking advantage of the facile loss of an alkoxide to drive the cyclization as illustrated below by Broka's elegant preparation of substituted tetrahydrofurans via intramolecular S_N' cyclization of an α-oxa-5-hexenyllithium generated by lithium-tin exchange.[13] Alternatively, the cyclization of acetylenic alkyllithiums may be employed to produce to cycloalkylidenes that can be reduced to give alkyl substituted carbocycles.[4] Nevertheless, neither of these strategies leads upon ring-closure to a reactive alkyllithium that can be functionalized or employed to mediate tandem cyclizations.



In contrast to the behavior of 5-hexenyllithium bearing alkyl groups at the C(6) position, the presence of a strongly electron-withdrawing substituent at the terminal carbon of an olefinic alkyllithium activates the olefinic unit toward nucleophilic addition and a very rapid intramolecular Michael addition ensues. Cooke has demonstrated that such intramolecular conjugate additions may be initiated by low-temperature lithium-iodine exchange to give high yields of 3-, 4-, 5-, and 6-membered rings.[5] The rapid exchange reaction is compatible with a variety of Michael acceptors including *tert*-butyl esters, hindered boryl groups, and the acyl ylide shown below. These

cyclizations, which occur within minutes at low temperature, are less stereoselective than are the slower isomerizations of unactivated olefinic alkyllithiums but they provide a convenient route to a variety of carbocyclic products that are not easily prepared by other routes.[5]



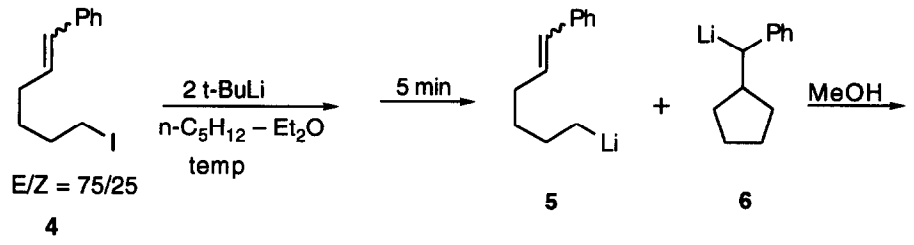
trans / cis = 3.3
90%

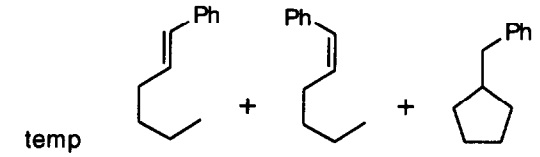
The ability to construct carbocycles via cyclization of olefinic alkyllithiums having a variety of substituents at the terminal alkene carbon would considerably extend the utility of the methodology. To this end, we have investigated the preparation and isomerization of 5-hexenyllithiums bearing moderately activating groups at the C(6) position. As shown below, 6-phenyl- and 6-trimethylsilyl-5-hexenyllithiums undergo regiospecific 5-*exo* cyclization to give high yields of readily functionalized organolithiums. Cyclization of 6-cyclopropyl-5-hexenyllithium is accompanied by ring opening of the three-membered ring.

RESULTS AND DISCUSSION

6-Phenyl-5-hexenyllithium. Treatment of an approximately 0.1 M solution of 6-iodo-1-phenyl-1-hexene (**4**; E/Z = 75/25) in dry *n*-pentane – diethyl ether (3:2 by volume) at –78 °C with 2.2 molar equiv of *t*-BuLi following our general protocol for lithium-iodine exchange[11] served to generate 6-phenyl-5-hexenyllithium (**5**). The reaction mixture was stirred at –78 °C for 5 min and then quenched with an excess of MeOH. GC analysis revealed that, in addition to the expected presence of E- and Z-1-phenyl-1-hexene, (cyclopentyl)phenylmethyllithium (**6**), assayed as benzylcyclopentane, had been formed in 75% yield (Scheme 1). In light of the unexpectedly rapid cyclization of **5** to **6**, the exchange was conducted at –130 °C (liquid nitrogen – pentane) in an effort to suppress the isomerization. Remarkably, even at this low temperature, the ring-closure of **5** proceeds to the extent of 14% in only 5 min! Clearly, the cyclization of **5** is much more rapid than the isomerization of the parent 5-hexenyllithium (**1**). Indeed, the conversion of **5** to **6** is evident visually by the rapid development of a beautiful red color characteristic of the α-phenyl alkyllithium product.[16] It is of some interest to note that E-**5** apparently isomerizes more quickly than the Z-isomer (Scheme 1).

Complete conversion of **5** to **6** may be achieved by allowing solutions to stand at low temperature but it was found more convenient for preparative scale cyclizations to simply remove the cooling bath and allow reaction mixtures to warm and sit at room temperature for 1 h. Solutions of **6** are stable for extended periods at room temperature and, as would be expected, addition of any of a variety of electrophiles provides functionalized product in good yield. The results of these experiments are summarized in Table 1.

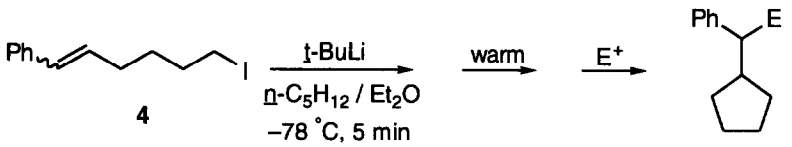




temp			
−130 °C	60%	26%	14%
−78 °C	3%	22%	75%

Scheme 1

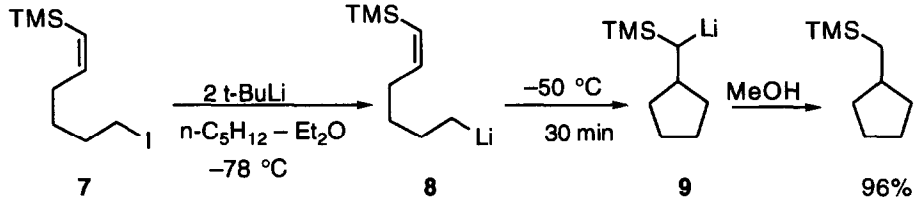
Table 1. Preparation of Substituted (Phenylmethyl)cyclopentanes.[a]



entry	E^+	E	yield,[b] %
1	CH_3OH	H	95
2	CH_3OD	D	87
3	CO_2	CO_2H	82
4	$(CH_3)_2NCHO$	CHO	81
5	$(CH_3)_2CO$	$(CH_3)_2C(OH)$	72
6	CH_3CHO	$CH_3CH(OH)$	73
7	$(CH_3)_3SiCl$	$Si(CH_3)_3$	84

[a] The olefinic alkyllithium was generated at -78 °C by addition of 2.2 molar equiv of t-BuLi to a 0.1 M solution of **4** in n-pentane-diethyl ether (3:2 by vol), the cooling bath was removed and the mixture was allowed to warm and stand at room temperature for 1h before the addition of an excess of the electrophile. [b] Isolated yields of chromatographically pure product.

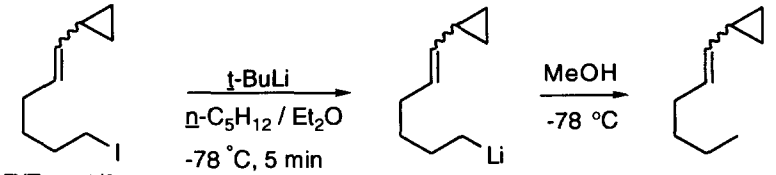
6-Trimethylsilyl-5-hexenyllithium. Isomerically pure Z-6-iodo-1-trimethylsilyl-1-hexene (**7**), used for the generation of Z-6-trimethylsilyl-5-hexenyllithium (**8**), was easily prepared in two steps by reduction of 6-bromo-1-trimethylsilyl-1-hexyne[17] with DIBALH followed by conversion to the iodide. Lithium-iodine exchange between **7** and 2.2 equiv of *t*-BuLi in *n*-pentane – diethyl ether (3:2 by vol) at –78 °C for 5 min followed by quench with MeOH gave a 96% yield of Z-1-trimethylsilyl-1-hexene and a small amount (ca. 3%) of (trimethylsilylmethyl)cyclopentane. Thus, the ring closure of **8** is somewhat slower than is the cyclization of 6-phenyl-5-hexenyllithium (**5**). Conversion of the TMS-substituted olefinic alkyllithium to [(trimethylsilyl)cyclopentyl]methyllithium (**9**) could be effected in virtually quantitative yield by allowing solutions of **8** to stand at –50 °C for 30 min.



7 **8** **9** 96%

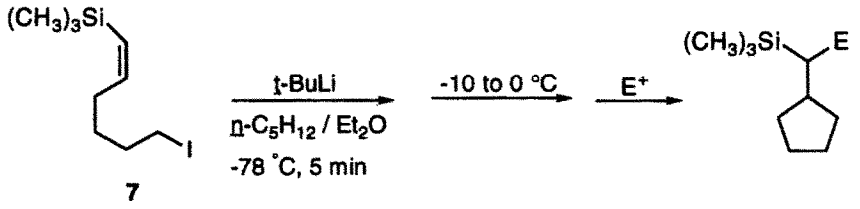
Substituted (trimethylsilylmethyl)cyclopentanes may be readily prepared by addition of an electrophile to solutions of **9**. It should be noted, however, that **9** is somewhat susceptible to unintentional quench by proton abstraction from solvent at temperatures near ambient. For this reason, preparative scale cyclizations leading to functionalized product are best conducted at temperatures below 0 °C. This is most conveniently accomplished by allowing solutions of **8**, generated from **7** at –78 °C via lithium-iodine exchange, to warm to –10 ° – 0 °C prior to the addition of an electrophile. As demonstrated by the results presented in Table 2, functionalized (trimethylsilylmethyl)cyclopentanes may be isolated in 70 – 85% yield. It should be noted that the precise conditions used to effect cyclization of **8** to **9** are not crucial: longer reaction times or temperatures higher than 0 °C lead to functionalized product in only slightly diminished yield.

6-Cyclopropyl-5-hexenyllithium. Wittig olefination of 2-hydroxytetrahydropyran with the ylide derived from (cyclopropylmethyl)triphenylphosphomium bromide[18] (KHMDS/THF) followed by conversion to the iodide gave 1-cyclopropyl-6-iodo-1-hexene (**10**; E/Z = 91/9). The corresponding alkyllithium, **11**, was cleanly generated by lithium-iodine exchange at –78 °C as demonstrated by the fact that quench of the reaction mixture with MeOH afforded an essentially quantitative yield (93% isolated) of 1-cyclopropyl-1-hexene (E/Z = 91/9).



E/Z = 91/9 **10** **11** 93%

Table 2. Preparation of Substituted (Trimethylsilylmethyl)cyclopentanes.[a]

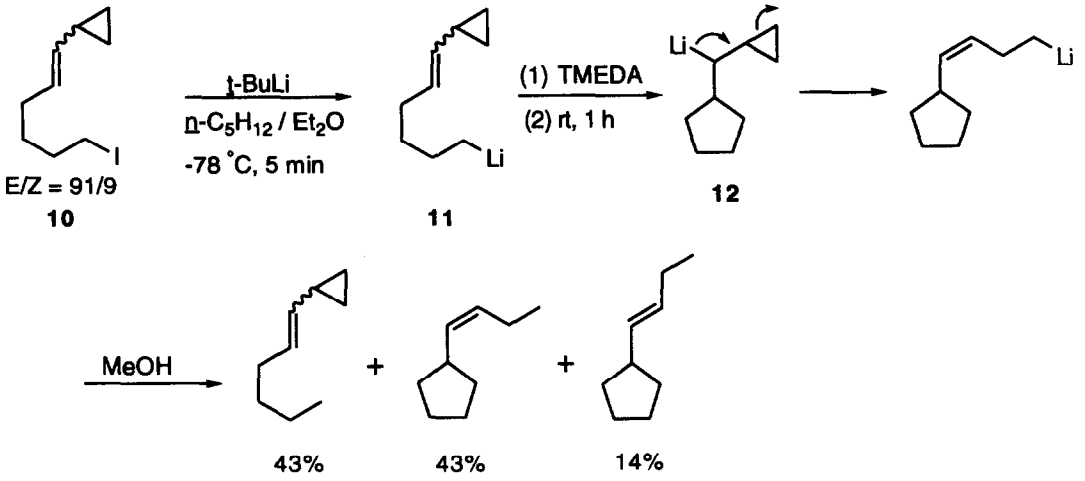


7

entry	E^+	E	yield,[b] %
1	CH_3OH	H	84
2	CH_3OD	D	83
3	CO_2	CO_2H	81
4	CH_2O	CH_2OH	78
5	$(CH_3)_2CO$	$(CH_3)_2C(OH)$	70
6	CH_3CHO	$CH_3CH(OH)$	72
7	$(CH_3)_3SiCl$	$Si(CH_3)_3$	78

[a] The olefinic alkyllithium was generated at -78 °C by addition of 2.2 molar equiv of t-BuLi to a 0.1 M solution of **7** in n-pentane-diethyl ether (3:2 by vol), the cooling bath was removed and the mixture was allowed to warm to −10 to 0 °C (~ 6 min) before the addition of an excess of the electrophile. [b] Isolated yields of chromatographically pure product.

The 6-cyclopropyl-5-hexenyllithium (**11**) is less activated toward ring closure than are the 6-phenyl (**5**) or 6-trimethylsilyl- (**8**) analogs. Allowing pentane – ether solutions of **11** to warm and stand at room temperature for extended periods of time prior to quench with MeOH does not lead to isomerization: indeed, the 1-cyclopropyl-1-hexene isolated from such reaction mixtures had the same isomeric composition (ie, E/Z ≈ 91/9) as the organolithium precursor. Cyclization of **11** may be effected, albeit in only 57% yield, by the addition of 2.2 equiv of TMEDA to the reaction mixture prior to warming at room temperature for 1 h. Under these conditions, as illustrated in Scheme 2, the isomerization of **11** produces, following quench with MeOH, a 3:1 mixture of Z- and E-1-butenylcyclopentane. It would seem that cyclization of **11** to **12** is driven by ring opening of the (cyclopropylmethyl)lithium moiety to give a *cis*-rich 4-cyclopentyl-3-butenyllithium. This rearrangement finds precedent in the observations made by Lansbury and coworkers regarding the facile ring opening of (cyclopropylmethyl)lithium to 3-butenyllithium.[19]



Scheme 2

The relatively large amount of 1-cyclopropyl-1-hexene detected in the experiment employing TMEDA (Scheme 2) was cause for initial concern since it is consistent with incomplete ring-closure of **11**. However, under the forcing conditions needed to effect isomerization of **11**, proton abstraction from solvent leading to quench of the organometallics is a serious problem. Indeed, there is no deuterium incorporation into any of the products upon addition of deoxygenated MeOD to reaction mixtures that had stood at room temperature for 1 h. Thus, it has not proved possible to functionalize the putative 4-cyclopentyl-3-butenyllithium intermediate presumably generated upon isomerization of **11**.

In summary, both 6-phenyl-5-hexenyllithium (**5**) and 6-trimethylsilyl-5-hexenyllithium (**8**) readily isomerize via a 5-*exo* cyclization at temperatures well below ambient. The ease with which such terminally substituted 5-hexenyllithiums undergo ring closure is undoubtedly a consequence of the ability of the substituents to stabilize the resulting organometallic. It remains to be seen whether such moderately activating substituents can be used to advantage in tandem cyclization strategies.

EXPERIMENTAL SECTION

Proton and carbon-13 NMR spectra were recorded on an IBM AF-270 spectrometer, and shifts are referenced with respect to internal Me_4Si. Other spectroscopic and chromatographic procedures, methods used for the purification of solvents and reagents, and precautions regarding the preparation and manipulation of organolithiums are described elsewhere.[2] The concentration of commercial solutions of *t*-BuLi in *n*-pentane (Aldrich) were determined immediately prior to use by titration with *sec*-butanol in xylene using 1,10-phenanthroline as indicator.[20]

E- and Z-6-Phenyl-5-hexen-1-ol. A solution of potassium hexamethyldisilazide (KHMDS) in dry THF was prepared under nitrogen by addition of 15.50 mL (73.64 mmol) of 1,1,3,3-hexamethyldisilazane to a stirred suspension of 2.940 g (73.50 mmol) of oil-free potassium

hydride in 45 mL of dry THF over a 20-min period at room temperature. The resulting mixture was stirred at room temperature until evolution of hydrogen gas ceased and it was then added dropwise to a cold (0-5 °C) suspension of 34.26 g (88.10 mmol) of benzyltriphenylphosphonium bromide in 230 mL of dry THF. The mixture was stirred at 0 °C for 10 min and then at room temperature for 1.5 h. The resulting red ylide solution was recooled to 0 °C and a solution of 3.000 g (29.41 mmol) of 2-hydroxytetrahydropyran[21] in 20 mL of dry THF was added over a 30-min period. The mixture was stirred at 0 °C for 30 min and at room temperature for 3 h and then partitioned between 50 mL of cold 10% aqueous HCl and 50 mL of diethyl ether. The organic layer was separated and the aqueous phase was extracted 50 mL of diethyl ether. The combined ethereal extracts were washed with two 50-mL portions of saturated aqueous sodium bicarbonate and two 50-mL portions of brine. The organic phase was dried ($MgSO_4$) and concentrated to give an oil which was purified by flash chromatography on silica gel (25% ethyl acetate - hexanes) to give 2.83 g (55%) of the known[22] title alcohol as a mixture of isomers: E/Z = 75/25 as determined by GC analysis; IR (neat) 3341, 3024, 2930, 2362, 1650, 1598, 1156, 1072, 965, and 740 cm^{-1}; ^1H NMR δ 7.33-7.16 (m, 5H), 6.42 (d, J_{cis} = 11.54 Hz, H(6) Z-isomer), 6.38 (d, J_{tr} = 15.79 Hz, H(6) E-isomer), 6.20 (d of t, J_{tr} = 15.79 Hz, ^3J = 6.73 Hz , H(5) E-isomer), 5.64 (d of t, J_{cis} = 11.54 Hz, ^3J = 7.23 Hz, H(5) Z-isomer), 3.62 (t, J = 6.20 Hz, H(1) E-isomer), 3.59 (t, J = 6.40 Hz, H(1) Z-isomer), 2.40-2.15 (m, 2H), 2.12 (br s, 1H, OH), 1.65-1.45 (m, 4H); ^{13}C NMR (two isomers; several of the resonances are common to both isomers) δ 137.65, 132.56, 130.49, 130.02, 128.99, 128.62, 128.36, 128.03, 126.74, 126.39, 125.82, 62.51, 32.61, 32.16, 32.09, 28.17, 25.98, 25.38.

E- and Z-6-Iodo-1-phenyl-1-hexene (4). The crude mesylate prepared from 1.50 g (8.52 mmol) of 6-phenyl-5-hexen-1-ol by the method of Crossland and Servis[23] was added to a solution of 2.59 g (17.2 mmol) of dry sodium iodide in 25 mL of dry acetone and the mixture was stirred overnight at room temperature under an atmosphere of nitrogen. The mixture was then filtered, the filtrate was concentrated and residue was extracted with 75 mL of pentane. The pentane extract was washed successively with two 50-mL portions of water, two 25-mL portions of 10% aqueous sodium thiosulfate and a 50-mL portion of brine. The organic phase was dried ($MgSO_4$) and concentrated to give an oil which was purified by flash chromatography on silica gel (hexanes) to afford 1.75 g (72%) of a mixture of E- and Z-isomers of the title iodide in a ratio (E/Z) of 75/25 as estimated by GC on a cross-linked methyl silicon gum column: R_f 0.16 (hexanes). The isomers were identified on the basis of the following spectroscopic data: IR (neat) 3024, 2927, 2357, 1598, 1493, 1072, 964, and 743 cm^{-1}; ^1H NMR δ 7.34-7.25 (m, 5H), ca 6.45 (singlet line of expected doublet, H(1) Z-isomer), 6.38 (d, J_{tr} = 16.00 Hz, H(1) E-isomer, 6.18 (d of t , J_{tr} = 16.00 Hz, ^3J = 6.70 Hz, H(2) E-isomer), 5.62 (d of t, J_{cis} = 11.54 Hz, ^3J = 7.22 Hz, H(2) Z-isomer), 3.19 (t, J = 6.97 Hz, H(6) E-isomer), 3.14 (t, J = 6.95 Hz, H(6) Z-isomer), 2.33 (m, H(3) Z-isomer), 2.22 (m, H(3) Z-isomer), 1.91-1.80 (m, 2H), 1.62-1.49 (m, 2H); ^{13}C NMR (two isomers; several of the resonances are common to both isomers) δ 137.54, 131.92, 130.40, 129.88, 129.43, 128.64, 128.43, 128.10, 126.90, 126.53, 125.90, 33.00, 32.90, 31.82, 30.60, 30.10, 27.36, 6.73; mass spectroscopic molecular weight calcd for $C_{12}H_{15}I$ 286.0219, found 286.0221.

Z-6-Bromo-1-trimethylsilyl-1-hexene. Following the general procedure described by Zweifel and On,[24] 12.10 mL of a 1.50 M solution of diisobutylaluminum hydride (18.15 mmol) in toluene was diluted with 50 mL of dry diethyl ether under nitrogen. The temperature of the solution was maintained at 20 -30 °C and 3.000 g (12.90 mmol) of 6-bromo-1-trimethylsilyl-1-hexyne[17] was added. The mixture was stirred for 15 min at room temperature and then at 40 °C for 6 h. The clear solution was then cautiously poured into 50 mL of vigorously stirred, cold 10% aqueous hydrochloric acid. The mixture was extracted with two 25-mL portions of diethyl ether and the combined organic layers were washed successively with two 25-mL portions of 10% aqueous hydrochloric acid, one 40-mL portion of saturated aqueous sodium bicarbonate and one 50-mL portion of brine. The organic phase was dried ($MgSO_4$) and concentrated to give an oil which was purified by flash chromatography on silica gel (20% ethyl acetate - hexanes) to give 2.340 g (77%) of the known[25] title compound: R_f 0.53 (25% ethyl acetate - hexanes); IR (neat) 2959, 1607, 1438,

1248, 837, 763, 691, and 472 cm^{-1}; ^1H NMR δ 6.26 (d of t, J_{cis} = 14.02 Hz, ^3J = 7.00 Hz, H(2)), 5.50 (d, J_{cis} = 14.02 Hz, H(1)), 3.40 (t, J = 6.79 Hz, H(6)), 2.18-2.10 (m, 2H), 1.92-1.81 (m, 2H), 1.57-1.46 (m, 2H), 0.09 (s, 9H); ^{13}C NMR δ 147.98, 129.78, 33.62, 32.48, 32.34, 28.16, 0.20.

Z-6-Iodo-1-trimethylsilyl-1-hexene (7). A solution of 2.34 g (9.96 mmol) of Z-6-bromo-1-trimethylsilyl-1-hexene and 2.98 g (19.87 mmol) of dry sodium iodide in 30 mL of dry acetone was stirred at room temperature for 18 h under a nitrogen atmosphere. The mixture was then filtered, the filtrate was concentrated at reduced pressure and the residue was extracted with 75 mL of pentane. The pentane extract was then washed successively with two 50-mL portions of water, two 25-mL portions of 10% aqueous sodium thiosulfate and one 50-mL portion of brine. The organic phase was dried ($MgSO_4$) and concentrated to give an oil which was purified by flash chromatography on silica gel (hexanes) to afford 2.47 g (88%) of the title iodide: R_f 0.39 (hexanes); IR (neat) 3854, 3649, 2958, 1608, 1426, 1248, 1165, 838, 763, and 690 cm^{-1}; ^1H NMR δ 6.25 (d of t, J_{cis} = 13.98 Hz, ^3J = 7.01 Hz, H(2)), 5.49 (d, J_{cis} = 13.98 Hz, H(1)), 3.18 (t, J = 7.01 Hz, H(6)), 2.18-2.09 (m, 2H), 1.89-1.78 (m, 2H), 1.53-1.42 (m, 2H), 0.09 (s, 9H); ^{13}C NMR δ 147.98, 129.76, 33.12, 32.30, 30.49, 6.71, 0.22. An analytical sample was prepared by preparative GC on a 9-ft, 15%-SE-30 on Chromosorb W (NAW, 80/100 mesh) column at 180 °C. Anal. Calcd for $C_9H_{19}ISi$: C, 38.30 ; H, 6.79. Found: C, 38.37 ; H, 6.74.

E- and Z-6-Cyclopropyl-5-hexen-1-ol. A solution of KHMDS in dry THF was prepared under nitrogen by addition of 4.90 mL (23.2 mmol) of 1,1,3,3-hexamethyldisilazane over a 20 min period to a stirred suspension of 0.922 g (23.0 mmol) of oil-free potassium hydride in 15 mL of dry THF at room temperature. The resulting suspension was stirred at room temperature until evolution of hydrogen gas ceased and was then added dropwise at 0 °C to 5 °C to a suspension of 9.20 g (23.2 mmol) of (cyclopropylmethyl)triphenylphosphonium bromide[18] in 50 mL of dry THF. The mixture was stirred at 0 °C for 10 min and then at room temperature for 1.5 h. To the resulting red suspension was added 2.36 g (23.2 mmol) of 2-hydroxytetrahydropyran in 20 mL of dry tetrahydrofuran over a 30-min period while maintaining the temperature at 0 °C to 5 °C. The mixture was stirred at 0 °C for 30 min and at room temperature for 3 h and then poured into 50-mL of cold 10% aqueous hydrochloric acid. The mixture was extracted with two 50-mL portions of diethyl ether, the ethereal extracts were washed with two 50-mL portions of saturated aqueous sodium bicarbonate and two 50-mL portions of brine. The organic phase was dried ($MgSO_4$) and concentrated to give an oil which was distilled under vacuum to give 1.97 g (61%) of a 91/9 mixture (E/Z) of of the title alcohols: bp 110-112 °C (10-12 mm); IR (neat) 3357, 3081, 3006, 2932, 1653, 1453, 1064, 938, 811, and 728 cm^{-1}; ^1H NMR δ 5.51-5.22 (m, 1H, H(6)), 5.04-4.67 (m, 1H, H(5)), 3.62 (t, J = 6.50 Hz, 2H, H(1)), 2.21-2.13 (m, 1H), 1.78 (OH), 1.64-1.27 (m, 6H), 0.72-0.58 (m, 2H), 0.30-0.24 (m, 2H); ^{13}C NMR δ (two isomers; several of the resonances are common to both isomers) 134.19 (C(6) E-isomer), 134.08 (C(6) Z-isomer), 127.72, 62.78, 32.30, 32.17, 32.12, 27.25, 25.90, 25.72, 9.53, 6.75, 6.29; mass spectroscopic molecular weight calcd for $C_9H_{16}O$ 140.1201, found 140.1200.

E- and Z-1-Cyclopropyl-6-iodo-1-hexene (10). The mesylate of 6-cyclopropyl-5-hexen-1-ol, prepared from 1.50 g (10.7 mmol) of the alcohol by the method of Crossland and Servis,[23] was added to a solution of 3.30 g (22.0 mmol) of sodium iodide in 40 mL of dry acetone and the mixture was stirred overnight at room temperature under an atmosphere of dry nitrogen. The mixture was then filtered, the filtrate was concentrated and residue was extracted with 75 mL of pentane. The pentane extract was washed successively with two 50-mL portions of water, two 25-mL portions of 10% aqueous thiosulfate, and a 50-mL portion of brine. The organic phase was dried ($MgSO_4$) and concentrated to give an oil which was purified by distillation to afford 2.04 g (76%) of an isomeric mixture of the title iodide in a ratio (E/Z) of 91/9: bp 125-130 °C (3-4 mm); IR (neat) 3078, 3004, 2930, 2855, 1651, 1450, 1213, 1172, 942, 809, 729, and 596 cm^{-1}; ^1H NMR δ 5.52-5.23 (m, 1H), 5.02-4.72 (m, 1H), 3.21 (t, J = 7.00 Hz, 2H), 2.24-2.15 (m, 1H), 1.03-1.77 (m, 2H), 1.60-1.45 (m, 4H), 0.76-0.59 (m, 2H), 0.34-0.22 (m, 2H); ^{13}C NMR (two isomers; several of the

resonances are common to both isomers) δ 134.56 (C(1) E-isomer), 134.45 (C(1) Z-isomer), 127.16, 33.01, 31.30, 30.52, 30.46, 26.39, 13.42, 9.55, 6.91, 6.82, 6.35; mass spectroscopic molecular weight calcd for $C_9H_{15}I$ 250.0220 , found 250.0219.

General Procedure for the Generation and Cyclization of Terminally Substituted 5-Hexenyllithiums. Olefinic alkyl iodides were deoxygenated immediately prior to use by bubbling dry, oxygen-free argon gas through the neat liquid for several min. An approximately 0.1 M solution of the iodide in anhydrous n-pentane – diethyl ether (3:2 by vol) was stirred and cooled to −78 °C (or lower) under argon, 2.0 – 2.2 molar equivalents of t-BuLi in pentane were added dropwise via syringe, and the mixture was stirred at −78 °C (or lower) for an additional 5 min. In the case of 6-cyclopropyl-5-hexenyllithium (**11**), 2.2 equiv of dry, deoxygenated TMEDA was added to the cold reaction mixture. The reaction mixtures were then allowed to stand under argon for a period of time at the appropriate temperature to effect the isomerization: specific conditions of time and temperature used to complete the cyclization of the various substrates are given in footnotes to Tables 1 and 2 and in Scheme 2. Functionalization of the resulting alkyllithiums was accomplished by addition of an excess (typically 2 equiv) of the appropriate electrophile that had been carefully purified immediately prior to use. The reaction mixtures were worked up in the usual manner[26] and products were purified by flash chromatography, short-path distillation or recrystallization as appropriate. The yields of the products given in Tables 1 and 2 refer to isolated, chromatographically homogeneous material. Benzylcyclopentane,[27] 2-cyclopentyl-2-phenylacetic acid,[28] and [(trimethylsilyl)methyl]cyclopentane[29] are know compounds whose physical and spectroscopic properties were fully in accord with those reported for these materials. The structures of the remaining derivatives prepared in this study were established on the basis of the data presented below (all products were liquids; product yields may be found in Tables 1 and 2 and Scheme 2).

2-Cyclopentyl-2-phenylacetaldehyde (Table 1, entry 4): ^{1}H NMR δ 9.66 (d, J = 3.04 Hz, 1H), 7.35-7.19 (m, 5H), 3.30 (d of d, J = 10.52 Hz, J = 3.04 Hz, 1H), 2.61-2.45 (m, 1H), 2.02-0.99 (complex m, 8H); ^{13}C NMR δ 200.90, 136.42, 129.25, 129.09, 127.60, 65.47, 40.48, 31.25 , 30.92, 25.41, 24.67; mass spectroscopic molecular weight calcd for $C_{13}H_{16}O$ 188.1201, found 188.1199.

1-Cyclopentyl-2-methyl-1-phenyl-2-propanol (Table 1, entry 5): ^{1}H NMR δ 7.17-7.06 (m, 5H), 2.36(d, J = 9.92 Hz, 1H), 2.27-2.13 (m, 1H), 1.97-1.88 (m, 1H), 1.59-1.17 (m, 7H), 1.14 (s, 3H), 1.01 (s, 3H), 0.86-0.73 (m, 1H); ^{13}C NMR δ 143.26, 129.52, 127.87, 126.19, 73.61, 62.83, 42.07, 33.71, 33.59, 29.87, 27.90, 25.71, 23.78; mass spectroscopic molecular weight calcd for $C_{15}H_{20}$ ($M^+ - H_2O$) 200.1565, found 200.1560.

1-Cyclopentyl-1-phenyl-2-propanol (Table 1, entry 6): ^{1}H NMR δ 7.44-7.03 (m, 5H), 4.08 (apparent pentet, 1H), 2.65-2.59 (m, 1H), 2.29-1.10 (m, 10H), 1.04 (d, J = 6.46 Hz, 3H); ^{13}C NMR (two diastereomers; several of the resonances are common to both diastereomers) δ 143.39, 129.70, 128.83, 127.93, 126.40, 125.20, 70.16, 69.71, 58.53, 41.81, 41.72, 32.44, 31.91, 31.51, 25.37, 24.99, 24.90, 24.37, 19.31; mass spectroscopic molecular weight calcd for $C_{14}H_{18}$ ($M^+ - H_2O$) 186.1409, found 186.1402.

1-Cyclopentyl-1-phenyl-1-trimethylsilylmethane (Table 1, entry 7): ^{1}H NMR δ 7.29-6.99 (m, 5H), 2.41-2.25 (m, 1H), 2.02-1.91 (m, 1H), 1.86 (d, J = 11.14 Hz, 1H), 1.80-1.33 (m, 5H), 1.30-1.13 (m, 1H), 1.02-0.92 (m, 1H), -0.03 (s, 9H); ^{13}C NMR δ 145.46, 128.07, 127.91, 124.18, 43.86, 42.62, 34.27, 33.32, 25.55, 24.13, -1.32; mass spectroscopic molecular weight calcd for $C_{15}H_{24}Si$ 232.1647, found 232.1649.

2-Cyclopentyl-2-(trimethylsilyl)acetic acid (Table 2, entry 3): ^{1}H NMR δ 2.23-2.10 (m, 1H), 1.99-1.75 (m, 2H), 1.85 (d, J = 10.76 Hz, 1H), 1.69-1.45 (m, 4H), 1.26-1.00 (m, 2H), 0.11

(s, 9H); ^{13}C NMR δ 182.50, 44.18, 39.29, 33.78, 32.22, 25.17, 24.22, –1.73; IR (neat) 3058 (broad), 2955, 2871, 1685, 1409, 1253, 1212, 847, and 694 cm^{-1}; mass spectroscopic molecular weight calcd for $C_9H_{17}O_2Si$ ($M^+ - CH_3$) 185.0998, found 185.0996.

2-Cyclopentyl-2-(trimethylsilyl)ethanol (Table 2, entry 4): ^1H NMR δ 3.88 (d of d, ^2J = 10.66 Hz, ^3J = 3.74 Hz, 1H), 3.78 (d of d, ^2J = 10.66 Hz, ^3J = 5.09 Hz, 1H), 2.4-1.4 (m, 7H), 1.3-1.1 (m, 2H), 1.23 (br s, 1H), 0.80-0.70 (m, 1H), 0.05 (s, 9H); ^{13}C NMR δ 63.84, 39.58, 35.70, 33.23, 32.16, 25.02, 24.51, –0.74; mass spectroscopic molecular weight calcd for $C_9H_{17}Si$ ($M^+ - CH_3$ and H_2O) 153.1100, found 153.1100.

1-Cyclopentyl-2-methyl-1-trimethylsilyl-2-propanol (Table 2, entry 5): ^1H NMR δ 2.09-1.95 (m, 1H), 1.83-1.31 (m, 9H), 1.31 (s, 1H), 1.28 (s, 3H), 1.26 (s, 3H), 0.89-0.84 (m, 9H); ^{13}C NMR δ 75.33, 44.89, 40.72, 34.58, 31.63, 31.39, 30.23, 26.03, 24.50, 2.82; mass spectroscopic molecular weight calcd for $C_{12}H_{24}Si$ ($M^+ - H_2O$) 196.1647, found 196.1647.

1-Cyclopentyl-1-trimethylsilyl-2-propanol (Table 2, entry 6): ^1H NMR δ 4.17-4.09 (m, 1H), 1.98-1.44 (m, 10H), 1.21 (d, J = 6.55 Hz) and 1.22 (d, J = 6.48 Hz, 3H), 0.94-0.86 (m, 1H), 0.09 (s, 9H); ^{13}C NMR (two diastereomers; several of the resonances are common to both diastereomers) δ 69.90, 69.49, 41.11, 40.83, 40.07, 39.49, 33.46, 33.32, 24.71, 24.56, 24.04, 22.86, 21.72, 0.83, 0.33; mass spectroscopic molecular weight calcd for $C_{10}H_{21}OSi$ ($M^+ - CH_3$) 185.1362, found 185.1365.

1-Cyclopentyl-1-[bis(trimethylsilyl)]methane (Table 2, entry 7): ^1H NMR δ 2.04-1.94 (m, 1H), 1.76-1.24 (m, 8H), 0.18 (d, J = 3.14 Hz, 1H), 0.05 (s, 18H); ^{13}C NMR δ 39.80, 34.59, 25.03, 19.06, 1.81; mass spectroscopic molecular weight calcd for $C_{11}H_{25}Si_2$ ($M^+ - CH_3$) 213.1495, found 213.1497.

Z-1-Butenylcyclopentane. A suspension of 6.780 g (60.54 mmol) of potassium *tert*-butoxide and 21.18 g (55.01 mmol) of propyltriphenylphosphonium bromide in 100 mL of dry diethyl ether was stirred for 1.5 h at room temperature. The mixture was then cooled to 0 °C and 4.900 g (50.00 mmol) of cyclopentanecarboxaldehyde in 50 mL of dry diethyl ether was added. The reaction mixture was stirred for 3 h at room temperature and then poured into 100 mL of water- ice mixture. The ether layer was separated and the aqueous layer was extracted with two 50-mL portions of diethyl ether. The combined ethereal extracts were washed with 100 mL of water, dried ($MgSO_4$) and concentrated to give an oil which was distilled to give 1.29 g (21%) of the title compound: bp 80-90 °C; ^1H NMR δ 5.91-5.21 (m, 2H), 2.77-2.62 (m, 1H), 2.11-2.01 (m, 2H), 1.80-1.52 (m, 6H), 1.27-1.16 (m, 2H), 0.96 (t, J = 7.53 Hz, 3H); ^{13}C NMR δ 134.76, 130.20, 38.10, 33.85, 25.38, 20.81, 14.68; mass spectroscopic molecular weight calcd for C_9H_{15} ($M^+ - 1$) 123.1174, found 123.1174. The major alkene isolated from the isomerization of 6-cyclopropyl-5-hexenyllithium (Scheme2) was identical in all respects to this authentic sample.

Acknowledgment. This work was supported by the Connecticut Department of Economic Development.

REFERENCES AND NOTES

1. (a) Bailey, W. F.; Nurmi, T. T.; Patricia, J. J.; Wang, W. *J. Am. Chem. Soc.* **1987**, *109*, 2442. (b) Chamberlin, A. R.; Bloom, S. H.; Cervini, L. A.; Fotsch, C. H. *J. Am. Chem. Soc.* **1988**, *110*, 4788 and references therein. (c) Bailey, W. F.; Khanolkar, A. D. *J. Org. Chem.* **1990**, *55*, 6058. (d) Bailey, W. F.; Khanolkar, A. D. *Tetrahedron* **1991**, *47*, 7727. (e) Bailey, W. F.; Khanolkar, A. D. *Organometallics* **1993**, *12*, 239.
2. Bailey, W. F.; Khanolkar, A. D.; Gavaskar, K.; Ovaska, T. V.; Rossi, K.; Thiel, Y.; Wiberg, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 5720.
3. (a) Bailey, W. F.; Rossi, K. *J. Am. Chem. Soc.* **1989**, *111*, 765. (b) Bailey, W. F.; Khanolkar, A. D. *Tetrahedron Lett.* **1990**, *31*, 5993. (c) Bailey, W. F.; Khanolkar, A. D.; Gavaskar, K. V. *J. Am. Chem. Soc.* **1992**, *114*, 8053.
4. Bailey, W. F.; Ovaska, T. V. *J. Am. Chem. Soc.* **1993**, *115*, 3080.
5. (a) Cooke, M. P., Jr. *J. Org. Chem.* **1984**, *49*, 1144. (b) Cooke, M. P., Jr.; Widener, R. K. *J. Org. Chem.* **1987**, *52*, 1381. (c) Cooke, M. P., Jr. *J. Org. Chem.* **1992**, *57*, 1495.
6. (a) Drozd, V. N.; Ustynyuk, Uy. A.; Tsel'eva, M. A.; Dmitriev, L. B. *J. Gen. Chem. USSR* **1968**, *38*, 2047; *Zh. Obsch. Khim.* **1968**, *38*, 2144. (b) Drozd, V. N.; Ustynyuk, Yu. A.; Tsel'eva, M. A.; Dmitriev, L. B. *J. Gen. Chem. USSR* **1969**, *39*, 1951; *Zh. Obsch. Khim.* **1969**, *39*, 1991.
7. (a) Richey, H. G., Jr.; Rothman, A. M. *Tetrahedron Lett.* **1968**, 1457. (b) Kossa, W. C., Jr.; Rees, T. C.; Richey, H. G., Jr. *Tetrahedron Lett.* **1971**, 3455. (c) Hill, E. A. *J. Organomet. Chem.* **1975**, *91*, 123.
8. (a) St. Denis, J.; Dolzine, T.; Oliver, J. P. *J. Am. Chem. Soc.* **1972**, *94*, 8260. (b) St. Denis, J.; Oliver, J. P.; Dolzine, T. W.; Smart, J. B. *J. Organomet. Chem.* **1974**, *71*, 315. (c) Dolzine, T. W.; Oliver, J. P. J. *Organomet. Chem.* **1974**, *78*, 165.
9. (a) Wilson, S. E. *Tetrahedron Lett.* **1975**, 4651. (b) Smith, M. J.; Wilson, S. E. *Tetrahedron Lett.* **1981**, *22*, 4615.
10. (a) Bailey, W. F.; Patricia, J. J.; Nurmi, T. T.; Wang, W. *Tetrahedron Lett.* **1986**, *27*, 1861. (b) Bailey, W. F.; Patricia, J. J.; Nurmi, T. T. *Tetrahedron Lett.* **1986**, *27*, 1865. (c) Bailey, W. F.; Patricia, J. J. *J. Organomet. Chem.* **1988**, *352*, 1.
11. Bailey, W. F.; Punzalan, E. R. *J. Org. Chem.* **1990**, *55*, 5404.
12. Bailey, W. F.; Patricia, J. J.; DelGobbo, V. C.; Jarret, R. M.; Okarma, P. J. *J. Org. Chem.* **1985**, *50*, 1999.
13. (a) Broka, C. A.; Lee, W. J.; Shen, T. *J. Org. Chem.* **1988**, *53*, 1338. (b) Broka, C. A.; Shen, T. *J. Am. Chem. Soc.* **1989**, *111*, 2981.
14. (a) Krief, A.; Barbeaux, P. *J. Chem. Soc., Chem. Commun.* **1987**, 1214. (b) Krief, A.; Barbeaux, P. *Synlett*, **1990**, 511. (c) Krief, A.; Barbeaux, P. *Tetrahedron Lett.* **1991**, 32, 417.
15. Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073.
16. Fraenkel, G.; Geckle, J. M. *J. Am. Chem. Soc.* **1980**, *102*, 2869 and references therein
17. Fujikura, S.; Inoue, M.; Utimoto, K.; Nozaki, H. *Tetrahedron Lett.* **1984**, *25*, 1999.
18. Schweizer, E. E.; Thompson, J. G.; Ulrich, T. A. *J. Org. Chem.* **1968**, *33*, 3082.
19. Lansbury, P. T.; Pattison, V. A.; Clement, W. A.; Sidler, J. D. *J. Am. Chem. Soc.* **1964**, *86*, 2248.
20. Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.
21. Kinney, R. J.; Jones, W. D.; Bergman, R. G. *J. Am. Chem. Soc.* **1978**, *100*, 7902.
22. (a) Cosseau, J.; Lamant, M. *Bull. Soc. Chim. Fr.* **1967**, 4702. (b) Marples, B. A.; Saint, C. G.; Traynor, J. R. *J. Chem. Soc., Perkin Trans. 1* **1986**, 567.
23. Crossland, R. K.; Servis, K. L. *J. Org. Chem.* **1970**, *35*, 3195.
24. Zweifel, G.; On, H. *Synthesis* **1980**, 803.
25. Trost, B. M.; Braslau, R. *J. Org. Chem.* **1988**, *53*, 532.
26. Wakefield, B. J. *Organolithium Methods*; Academic Press: New York, 1988.
27. Eliel, E. L.; McCoy, J. W.; Price, C. C. *J. Org. Chem.* **1958**, *22*, 1533.
28. Kolloff, H. G.; Hunter, J. H.; Woodruff, E. H.; Moffett, R. B. *J. Am. Chem. Soc.* **1948**, *70*, 3862.
29. Paquette, L. A.; Daniels, R. G. *J. Am. Chem. Soc.* **1981**, *103*, 2901.

(*Received* 30 *August* 1993)