

Single Electron Transfer in Metal-Halogen Exchange. The Reaction of Organolithium Compounds with Alkyl Halides

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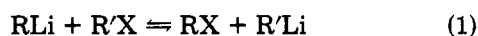
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Halogen-metal exchange has been studied by allowing *tert*-butyllithium to react with a series of alkyl halides containing a cyclizable radical probe in order to evaluate the occurrence of a radical intermediate in the reaction. It was found that radical intermediates, formed via a single-electron-transfer pathway, are involved in the reactions of *t*-BuLi with the radical probe, *endo*-5-(2-bromoethyl)-2-norbornene in pentane/Et₂O at -78 °C, since cyclized hydrocarbons were formed during the reaction. However, there was no evidence to support an electron-transfer pathway in reactions of the corresponding iodide and chloride with *t*-BuLi under the same conditions since only the straight-chain organolithium compound was formed. However, evidence indicative of a radical intermediate was obtained from reactions of the iodo compound with *t*-BuLi in pentane/Et₂O at higher temperatures (-45 °C and -23 °C) and in pure pentane at -78 °C and -23 °C in which stable cyclized hydrocarbon product was obtained. Lithium complexing agents such as TMEDA, HMPA, and 18-crown-6 were employed in these reactions in order to increase the carbanionic nature of the organolithium products. It was found that cyclization of the straight-chain organolithium compound to the corresponding cyclized organolithium compound in the presence of such complexing agents is relatively slow. On the other hand, the effectiveness of the complexing agents to increase carbanion character of the straight-chain organolithium compound was demonstrated by a significant lowering of the deuterium content of the straight-chain product due to ether cleavage by the straight-chain organolithium compound. Reactions of the 6-halo-1-heptenes with *t*-BuLi were also examined. It was shown that 6-bromo-1-heptene reacted with *t*-BuLi via a SET pathway in both pentane/Et₂O and pentane at -78 °C since cyclized product with a high *cis/trans* ratio was the major product in these reactions. On the other hand, the reaction of the corresponding iodide with *t*-BuLi in pentane/Et₂O at -78 °C produced a high yield of cyclized product with a low *cis/trans* ratio (1.7). The reaction of the alkyl iodide with *t*-BuLi in pure pentane produced the cyclized product with a *cis/trans* ratio (4.0) indicative of a radical intermediate. Lithium complexing agents were also added to these reaction mixtures, in which the product ratio remained constant although the deuterium concentration decreased. Hence, the presence of the cyclized products with a high *cis/trans* ratio in the presence of cation complexing agents is indicative of the formation of radical intermediates both in the presence and absence of such intermediates.

Introduction

The exchange of halogen and lithium atoms in the reaction of an organic halide with an organolithium compound is known as metal-halogen exchange (eq 1) and was



first reported simultaneously by Gilman¹ and Wittig.² The vast literature on this topic has been reviewed thoroughly.³⁻¹² Although metal-halogen exchange has been known to be an useful method for the preparation of organolithium compounds,⁹ its mechanism of reaction is still controversial with the possibility of both heterolytic and radical pathways in operation.

There are several studies of the mechanism of metal-halogen exchange reported in the literature^{4,6} with the most detailed studies focusing on aryl halide exchange with aryllithium compounds.^{13,14} In addition to the mechanism

suggested by studies of aryl halide-aryllithium exchange, additional mechanisms include concerted methathesis via a four-center transition state,^{4,6} reversible formation of an ate complex by nucleophilic attack of the organolithium compound on the halogen of the organic halide,¹⁵ and various single-electron-transfer (SET)-mediated processes.^{4,16-18}

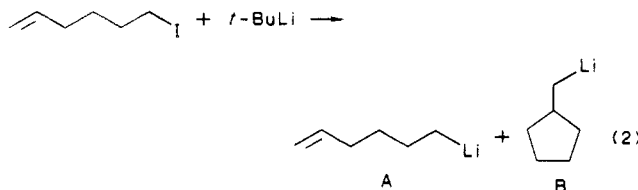
Although Russell¹⁸ suggested that reactions between ethyllithium and ethyl iodide proceed by single electron transfer, there are several references in the literature which indicate that the reaction pathway is heterolytic in nature.¹⁹⁻²⁴ Moreover, Letsinger²⁵ proposed an ionic mechanism for metal-halogen exchange based on the observation of partial retention of configuration in the reaction of *sec*-butyllithium with optically active 2-iodooctane at -70 °C. However, on raising the temperature to 0 °C, the activity of the product was lost. The retention of configuration in metal-halogen exchange also has been confirmed by the reaction of 1-bromotriptycene with *n*-butyllithium,²⁶

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and in the reaction of *cis*- and *trans*-cyclohexyllithium derivatives with methyl iodide and bromobenzene.²⁷ Thus, investigations have shown that the reactions studied take place with retention of configuration, which is evidence against the involvement of free radicals. On the other hand, the reactions of benzyl- and allyllithium compounds with alkyl halides proceed with complete inversion of configuration,^{19,28-30} suggesting a S_N2 pathway. Nevertheless, the interaction of *n*-butyllithium with *sec*-butyl bromide results in racemization.³¹ Therefore, from these considerations, the stereochemical results of metal-halogen exchange can involve racemization, inversion, or retention of configuration. In addition, the experimental observations supporting radical intermediates in the reaction of RLi with R'X are the following: (a) formation of 2,3-dimethyl-2,3-diphenylbutane when the reaction is carried out in the presence of cumene;³² (b) formation of the trityl radical from trityl chloride;³³ (c) nuclear polarization in the olefin products³⁴ or in the alkyl halide³⁵ and the formation of the expected coupling and disproportionation products of R and R'.³²⁻³⁵

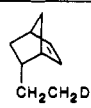
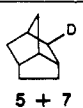
In 1984, Bailey and co-workers reported that 6-iodo-1-hexene when treated with *t*-BuLi at -23 °C, undergoes intramolecular cyclization, indicating that metal-halogen exchange proceeds by SET.³⁶ More recently, they reported^{37,38} that 5-hexenyllithium (A) cyclizes to B at -23 °C, thus cyclization may not be the result of a radical intermediate (eq 2). In addition Reich³⁹ and co-workers have recently reported evidence for an ate complex in reactions involving phenyllithium and iodobenzene.



Prior to Bailey's latest report, we found that the reaction of *t*-BuLi with 6-iodo-1-hexene in pentane/Et₂O at -23 °C, and even -78 °C, produced both uncyclized (A) and cyclized (B) organolithium product. However, the product ratio (A/B) changed on standing even at -78 °C. On the other hand, when we carried out this reaction by addition of the reagents at -130 °C, we found that the reaction was complete in 5 min and that the ratio of A/B (81/19) did not change over a 4-h period. However, Bailey has pointed out that our result showing cyclized product at -130 °C is due to incomplete hydrolysis with D₂O, and when the hydrolysis was carried out using C₂H₅OD, the results showed no cyclized product. Although hydrolysis of or-

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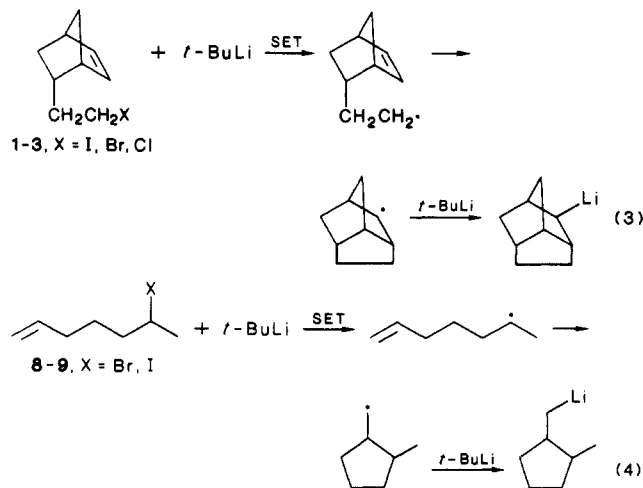
Table I. Reaction of *endo*-5-(2-Haloethyl)-2-norbornenes 1-3 with *t*-BuLi in Pentane/Et₂O (4:1) at -78 °C^a

expt	RX	time (min)	% yield (% d)	
			 4 + 6	 5 + 7
1	1 (X = I)	30	100.0 (100) ^b	0.0
2		1440	99.0 (95.0)	<0.1
3	2 (X = Br)	180	82.0 (60.8)	15.3 (59.9)
4		1440	83.0 (60.8)	15.0 (62.6)
5	3 (X = Cl)	1440	<0.1	<0.1 ^c

^a All reactions carried out were 0.2 M in *t*-BuLi and 0.1 M in halide and then quenched with D₂O. ^b Deuterium content was determined by GC-MS. ^c Recovered alkyl halide accounts for the material balance.

ganolithium compounds at -78 °C with D₂O has been standard practice, Bailey's results clearly show that hydrolysis is only complete on warming to -20 to 0 °C. We have repeated Bailey's recent findings with C₂H₅OD and indeed find that he is correct for the 6-halo-1-hexene system, namely, there is no cyclization at -130 °C and therefore no evidence of a radical intermediate in this system. However most of our report dealt with the reaction of 1° and 2° alkyl bromides. These cyclization results are valid since the same data was obtained by using either D₂O or C₂H₅OD in the hydrolysis step.⁴⁰

Since there seems to be some confusion concerning the mechanistic pathway describing the reaction of organolithium compounds with alkyl halides, the reactions of *tert*-butyllithium with two different alkyl halides were studied in detail. The methodology used to study the model systems involved (1) the use of cyclizable probes in the alkyl halide and (2) the use of complexation agents. With respect to the use of cyclizable probes (1), we have studied reactions of alkyl halides containing the 5-hexenyl group with *t*-BuLi. Thus, if a 5-hexenyl radical, or its derivative, is produced in such reactions, the occurrence of SET is confirmed by the observation of cyclic products (eq 3 and 4). With respect to (2), the presence of radical cyclization vs. carbanion cyclization can be studied by (a)



(40) We are indebted to Dr. Bailey for revealing his results to us prior to publication and alerting us as to the problem of hydrolyzing with D₂O at low temperatures.⁴¹

(41) Since this manuscript was completed, Bailey's results have been published. Bailey, W. F.; Patricia, J. J.; Nurmi, T. *Tetrahedron Lett.* **1986**, *27*, 1865. Bailey, W.; Patricia, J.; Nurmi, T.; Wang, W. *Tetrahedron Lett.* **1986**, *27*, 1861.

aging the reaction mixture to see if further cyclization takes place and then (b) adding some lithium complexation agents such as TMEDA, HMPA, or 18-crown-6 in order to enhance the carbanionic character of the resulting organolithium compound to see if this effect causes further cyclization. If the uncyclized product does not cyclize further on addition of the lithium complexation agents, it would be reasonable to conclude that the cyclized product observed was formed during not after the reaction was complete.

For the systems reported herein (compounds 1, 2, 8, and 9), it was shown that D_2O and C_2H_5OD hydrolysis produced the same results. Therefore, unlike the 5-hexenyl halide case reported by Bailey,³⁷ the organolithium product is insensitive to the compound used for hydrolysis.

Results and Discussion

When a solution of 0.2 M *t*-BuLi was allowed to react with 0.1 M *endo*-5-(2-iodoethyl)-2-norbornene (1) in pentane/ Et_2O (4:1 by volume)²⁴ at $-78^\circ C$ followed by careful quenching with D_2O and the product analyzed by GLC, *endo*-5-(2-deuterioethyl)-2-norbornene (6) was formed in quantitative yield (100%) (expt 1, Table I). The position of the deuterium atom of 6 represents the original location of the C–Li bond and the lack of deuterium incorporation (protio hydrocarbon (4)) simply implies that some hydrocarbon is formed during the reaction and before hydrolysis (Figure 1). In the tables, products 4 + 6 represent total uncyclized hydrocarbon formed (protio + deuterio). The lack of cyclized hydrocarbon products (4 + 6, protio + deuterio) could indicate that metal–halogen exchange of *t*-BuLi with 1 is best described as a heterolytic process or, if radical species are involved, then the second electron transfer from another *t*-BuLi molecule to the radical to form the carbanionic organolithium product must be substantially faster than cyclization of the probe. It is most important to note that the organolithium compound (precursor of 6) did not cyclize at $-78^\circ C$ for a period of 24 h, although we did observe some ether cleavage of the product (deuterium incorporation content decreased from 100% to 95%) (expt 2).

Table I provides additional data on the reactions of *t*-BuLi with *endo*-5-(2-haloethyl)-2-norbornenes 2 and 3 at $-78^\circ C$. It is interesting that when 2 ($X = Br$) was allowed to react with *t*-BuLi, a 15.3% yield of the cyclized products 5 + 7 was observed. This result indicates that a substantial amount of radical intermediate was formed during the reaction. The fact that the product ratio of (4 + 6):(5 + 7) did not change over a 24-h period (expt 3 and 4), indicates that 5 + 7 is formed during, not after the reaction is over. The results of expt 3 show that 39.2% of 4 and 40.1% of 5 is straight-chain and cyclized protio hydrocarbon, respectively, produced before hydrolysis. The hydrocarbon formation is probably the result of a radical precursor (radical abstraction of hydrogen from solvent or *t*-BuLi since carbanion cleavage is too slow at $-78^\circ C$ to account for such a high degree of hydrocarbon after 180 min of reaction). No reaction was observed on mixing *t*-BuLi with the corresponding chloride 3 (expt 5).

The data in expt 3 and 4 are consistent with the formation and cyclization of radical intermediates formed during the reaction. Although more detailed studies involving halogen–metal exchange will be described later, a reasonable suggestion for the mechanism involving radical intermediates is suggested in Figure 1. In this suggestion, *t*-BuLi transfers an electron to the alkyl bromide radical probe in the first step to form a radical anion–radical cation pair. The radical anion rapidly dissociates to radical C, which then can receive another electron from

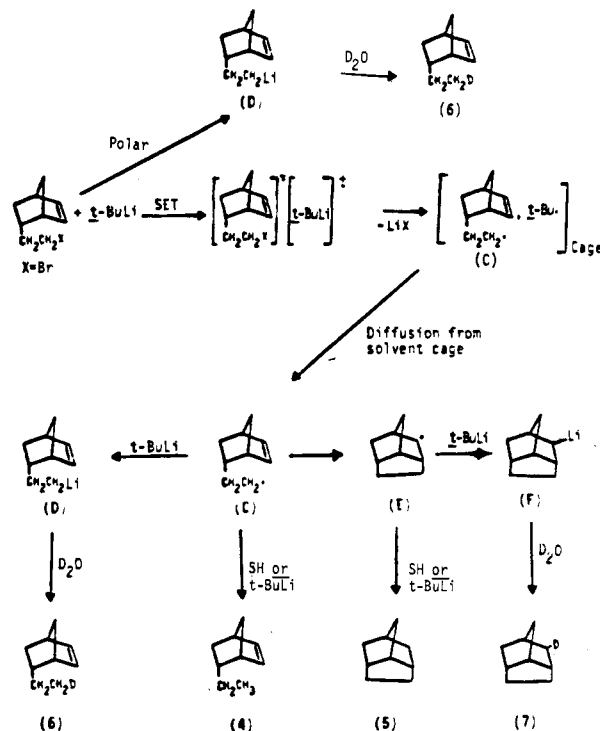
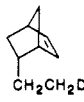
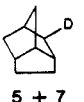


Figure 1. Suggested mechanistic scheme for the reaction of *endo*-5-(2-bromoethyl)-2-norbornene (2) with *tert*-butyllithium.

t-BuLi to give the straight-chain compound D, which on reaction with D_2O gives 6. Of course, D can also be formed by a heterolytic pathway in which a direct exchange between *t*-BuLi and the alkyl halide occurs. This latter possibility seems most probable when $X = I$. C can also abstract hydrogen from solvent (Et_2O) or *t*-BuLi to form 4 (there is no evidence of hydrogen abstraction from solvent at this time, however, there is evidence of hydrogen abstraction from *t*-BuLi as is shown latter in this text) or cyclize to give radical E. Radical E can then further abstract hydrogen from solvent or *t*-BuLi to give 5 or receive another electron from *t*-BuLi to give F, which on reaction with D_2O gives 7. It is possible that a substantial amount of the cyclized product F, which was formed in the reaction of *t*-BuLi with 2, could result from the reaction of D with *tert*-butyl bromide. However, when 1 equiv of *tert*-butyl bromide was added to the reaction mixture from expt 1, the ratio of products 6/7 remained constant. Thus, the formation of the stable cyclized product observed here is indicative of radical intermediates which were formed during the course of the reaction.

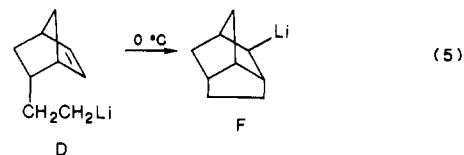
Since there was no evidence of a radical intermediate in the reaction of the iodo compound (1) with *t*-BuLi at $-78^\circ C$, this reaction was studied in more detail at higher temperatures. Table II shows the results of the reaction of 1 with *t*-BuLi at $-78^\circ C$, $-45^\circ C$, $-23^\circ C$, and $0^\circ C$, respectively, in pentane/ Et_2O . After 30 min at $-45^\circ C$, the reaction mixture was quenched with D_2O and analyzed by GLC. The cyclized products 5 + 7 were obtained in 3.3% yield. As expected, the product ratio (4 + 6):(5 + 7) did not change over a period of 1 h. Next, the iodo compound 1 was allowed to react with *t*-BuLi at $-23^\circ C$ (expt 5, Table II). The cyclized products 5 + 7 were formed in 5.5% yield, and, once again, the product ratio (4 + 6):(5 + 7) remained constant up to a 48-h period (expt 6) although some ether cleavage of the product took place (95.8 to 90.5% d_1). The observation of the cyclized products 5 + 7 and especially 5 and the constancy of the ratio of (4 + 6):(5 + 7) in the reactions of the iodo compound 1 with *t*-BuLi indicates that some radicals were formed in this

Table II. Effect of Temperature on the Reaction of *endo*-5-(2-Iodoethyl)-2-norbornene (1) with *t*-BuLi in Pentane/Et₂O (4:1)^a

expt	time (min)	temp (°C)	% yield (% d)	
			 4 + 6	 5 + 7
1	30	-78	100.0 (100) ^b	0.0
2	1440	-78	99.0 (95.0)	0.1
3	30	-45	95.0 (95.3)	3.3 (45.5)
4	60	-45	93.0 (95.6)	4.0 (44.7)
5	5	-23	90.0 (95.8)	5.5 (22.0)
6	2880	-23	92.5 (90.5)	5.2 (20.4)
7	2	0	96.0 (79.0)	5.0 (11.6)
8	10	0	90.0 (57.8)	11.0 (16.3)
9	35	0	72.0 (35.9)	30.0 (21.7)

^aAll reactions carried out were 0.2 M in *t*-BuLi and 0.1 M in halide and then quenched with D₂O. ^bDeuterium content was determined by GC-MS.

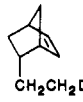
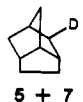
reaction. In addition, when the reaction of 1 with *t*-BuLi was performed at 0 °C, the cyclization of D to F was observed to take place after the reaction was over (expt 7-9).



Bailey³⁷ observed the cyclization of the 5-hexenyllithium compound (A) to its cyclic organolithium compound (B) from -23 °C to +20 °C as shown in eq 2. Therefore, the observation of the cyclized products 5 + 7 at this temperature cannot be considered exclusively as a radical cyclization but rather as a mixture of radical cyclization during the reaction and carbanion cyclization of the organolithium compound D to F (eq 5) after the reaction was complete.

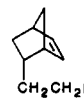
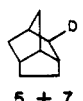
In an attempt to make the organolithium compound D more carbanionic in order to increase its chance of carbanion cyclization to produce F, the reaction mixtures from Tables I and II were treated with TMEDA, HMPA, and 18-crown-6, respectively, and the results are given in Table III. The data show that the organolithium compounds D and F were indeed made more carbanionic by these cation complexing agents since more ether cleavage products (4 and 5, protio hydrocarbon) were formed (expt

Table III. Effects of TMEDA, HMPA, and 18-Crown-6 in the Reaction of *endo*-5-(2-Haloethyl)-2-norbornenes 1 and 2 with *t*-BuLi in Pentane/Et₂O^{a,b}

expt	substrate	time (min)	temp (°C)	additive	% yield (% d)	
					 4 + 6	 5 + 7
1	1 (X = I)	30	-78	none	100.0 (100) ^f	0.0
2		60	-78	2 TMEDA ^c	98.0 (90.5)	0.0
3		570	-78	2 TMEDA	92.0 (84.3)	5.0 (5.2)
4		360	-78	4 HMPA ^d	99.0 (60.8)	0.1
5		30	-23	none	91.0 (95.5)	4.1 (23.4)
6		10	-23	2 TMEDA	92.4 (91.3)	4.5 (26.9)
7		150	-23	2 TMEDA	86.7 (87.0)	12.6 (19.6)
8		260	-23	4 HMPA	92.5 (90.6)	5.1 (5.6)
9		180	-23	2 18-crown-6 ^e	91.8 (67.5)	4.2 (6.4)
10	2 (X = Br)	180	-78	none	82.0 (60.8) ^f	15.3 (59.9)
11		240	-78	2 TMEDA ^c	82.1 (60.8)	16.2 (52.6)
12		315	-78	2 TMEDA	77.0 (60.3)	20.5 (50.9)
13		240	-78	4 HMPA ^d	82.0 (56.8)	15.0 (30.7)
14		240	-78	2 18-crown-6 ^e	81.5 (51.9)	16.7 (32.4)

^aAll reactions carried out were 0.2 M in *t*-BuLi and 0.1 M in halide and then quenched with D₂O. ^bTMEDA, HMPA, and 18-crown-6 solutions were added to the reaction mixture, respectively, after the reaction was complete. ^c2 equiv of TMEDA. ^d4 equiv of HMPA. ^e2 equiv of 18-crown-6. ^fDeuterium content was determined by GC-MS.

Table IV. Effects of Solvent and Temperature on the Reaction of *endo*-5-(2-Iodoethyl)-2-norbornene (1) with *t*-BuLi

expt	time (min)	temp (°C)	solvent	% yield (% d)	
				 4 + 6	 5 + 7
1	30	-78	pentane/ether ^a	100.0 (100) ^d	0.0
2	1440	-78	pentane/ether ^a	99.0 (95.0)	0.1
3	30	-78	pentane ^b	8.4 (67.3)	2.2 (10.0) ^{d,e}
4	880	-78	pentane ^b	60.0 (62.5)	7.0 (10.7) ^e
5	1440	-78	pentane ^b	88.0 (66.0)	10.0 (12.1)
6	2880	-78	pentane ^b	89.5 (65.4)	9.8 (11.4)
7	210	-23	pentane ^b	76.2 (83.0)	23.0 (34.4)
8	420	-23	pentane ^b	75.8 (83.4)	22.5 (37.6)
9	400	-23	pentane ^{b,c}	60.0 (17.9)	39.5 (64.8)

^aReactions carried out were 0.2 M in *t*-BuLi and 0.1 M in halide and then quenched with D₂O. ^bReactions carried out were 1.0 M in *t*-BuLi and 0.1 M in halide. ^c*t*-BuLi-*d*₉ was used then quenched with H₂O. ^dDeuterium content was determined by GC-MS. ^eRecovered alkyl halide accounts for the material balance in expt 3 and 4.

2-4, 6-9, and 11-14). However, no additional cyclization was observed in the presence of HMPA or 18-crown-6. On the other hand, TMEDA appeared to be a more powerful complexation agent toward lithium than HMPA or 18-crown-6, since we observed that D slowly cyclized to F (expt 1-3, 5-7, and 10-12). In addition when TMEDA was added to the reaction mixture of 1 with *t*-BuLi at -23 °C, the yield of 4 + 6 also decreased from 92.4% to 86.7% and the yield of 5 + 7 increased from 4.5% to 12.6%, respectively, in a period of 140 min as shown in expt 6 and 7 of Table III. On the other hand, the addition of HMPA and 18-crown-6 did not significantly affect the ratio of (4 + 6):(5 + 7) at -23 °C. The constancy of the ratio of (4 + 6):(5 + 7) in the presence of complexing agents that increase the carbanionic nature of the organolithium products is therefore supportive evidence of a radical intermediate that cyclizes before not after the organolithium products are formed. These studies show that the complexing agents indeed increase the carbanionic character of D and F, however, cyclization of D to F is relatively slow.

It is known that when Et₂O is added to *t*-BuLi in pentane, dissociation of the tetramer takes place and solvation of the cation by the Et₂O causes considerable carbanionic character of the *t*-Bu group.²⁴ Such activation increases the reactivity of the *t*-BuLi compound toward the alkyl iodide 1 yet gives no evidence of a radical intermediate (expt 1 of Table I). On the other hand, in a poorer coordinating solvent such as pure pentane, radicals might be observed in the reaction of 1 with *t*-BuLi even at -78 °C. This statement is based on the work of Kuivila⁴² who has shown that a decrease in cation coordinating ability of the solvent increases the extent of the SET pathway in competition with the S_N2 pathway in the reaction of Me₃SnNa with alkyl halides. Thus, 0.1 M *endo*-5-(2-iodoethyl)-2-norbornene (1) was allowed to react with excess *t*-BuLi (1.0 M) in pentane at -78 °C and the results are given in Table IV. As expected, the reaction of 1 with *t*-BuLi in pentane is much slower than that in pentane/ether and produced 10% yield of the cyclized product 5 + 7 (expt 5) after 48 h. A constant deuterium content of the products indicates that the ratio of (4 + 6):(5 + 7) is constant during the entirety of the reaction.

In order to observe more radical product, 1 was also allowed to react with excess *t*-BuLi at a higher temperature (-23 °C) in pentane. The yield of 5 + 7 was 23% and the yield of 4 + 6 was 76.2% and the product ratio (4 + 6):(5 + 7) and deuterium content remained constant during a 420-min period (expt 7-8, Table IV). The constancy of the product ratio over a long period of time indicates that the cyclization product was not formed after the reaction was over but rather as a result of radical cyclization during reaction. One might expect the deuterium incorporation of both the uncyclized and cyclized products to be 100% since hydrogen abstraction from solvent to form hydrocarbon is unlikely. However, it is possible that the intermediate radical abstracts hydrogen from *t*-BuLi (excess *t*-BuLi used) before the radical can obtain a second electron from *t*-BuLi to form the corresponding organolithium compounds D and F. For additional information on the formation of hydrocarbons 6 and 7 on reaction of 1 with *t*-BuLi in pure pentane, *t*-BuLi-*d*₉ was prepared and allowed to react with 1 at -23 °C in pentane. After quenching the product with H₂O, 39.5% yield of the cyclized product 5 + 7 was obtained (expt 9). Note that more cyclized product was formed in this reaction than with protio *t*-BuLi because the hydrogen abstraction from *t*-

BuLi by radicals is easier than the deuterium abstraction from *t*-BuLi-*d*₉ (isotope effect). Therefore radical intermediate C has a longer lifetime and a better chance to cyclize to give more E when allowed to react with *t*-BuLi-*d*₉ than with protio *t*-BuLi (expt 7 and 9). Experiment 7 shows that about 17% straight-chain and 65% cyclized hydrocarbons are a result of hydrogen abstraction from *t*-BuLi since the reaction of 1 with *t*-BuLi-*d*₉ (expt 9) also shows deuterium incorporation content in both products (17.9% *d*₁ in the straight chain and 64.8% *d*₁ in the cyclized hydrocarbon). It is important to note that the deuterium incorporation in both products 6 and 7 from expt 9 reflect exactly the amount of protio hydrocarbons 4 and 5 formed in expt 7. In addition, a 76.2% yield of 4 + 6 in expt 7 with 83.0% *d*₁ indicates that once radical C (Figure 1) has escaped from the solvent cage, it will more easily accept another electron from *t*-BuLi to form the stable primary carbanion D than to abstract hydrogen from *t*-BuLi. On the other hand, a 23.0% yield of 5 + 7 with a lower *d*₁ content than that of 4 + 6 (34.4% *d*₁, expt 7) shows that the radical E more readily abstracts hydrogen from *t*-BuLi to form 5 than to form the less stable secondary carbanion F (Figure 1).

Note that the *d*₁ content in both products 4 + 6 and 5 + 7 in expt 6 (65.4% *d*₁ in 4 + 6 and 11.4% *d*₁ in 5 + 7) are somewhat lower than that of expt 7 (83.0% *d*₁ in 4 + 6 and 34.4% *d*₁ in 5 + 7). This can be explained by assuming that either the straight-chain hydrocarbon is formed directly in the solvent cage (Figure 1) or the second electron-transfer step is slower than the hydrogen abstraction step at such a low temperature. Thus, at -78 °C less radical escapes from the solvent cage than at -23 °C; therefore more straight-chain hydrocarbon product 4 + 6 at -78 °C was observed than at -23 °C. Since the deuterium content of the products of expt 7 is greater than at the lower temperature in expt 6, it is clear that the reaction of C with *t*-BuLi to form D and the reaction of E with *t*-BuLi to form F is faster compared to the reduction of C and E by *t*-BuLi to form 4 and 5. In any event the observation of cyclized products 5 + 7 in the reactions of the alkyl iodide 1 with *t*-BuLi in pentane is indicative of radical intermediate formation, the mechanism of which is described in Figure 1.

In addition, it is well-known that the formation of 1,2-dimethylcyclopentane with a 2.2:1 *cis* to *trans* ratio at 65 °C or 4.0:1 *cis* to *trans* ratio at room temperature from 6-halo-1-heptenes is indicative of radical cyclization.⁴³⁻⁴⁵ Therefore, a 0.1 M solution of 6-bromo-1-heptene (8) was allowed to react with a 0.2 M solution of *t*-BuLi in pentane/Et₂O at -78 °C. *cis*- and *trans*-1,2-dimethylcyclopentane (11) with a *cis/trans* ratio of 5.8 and 1-heptene (10) were formed in 26.0% and 39.1% yield, respectively, along with about 30% of other hydrocarbons (diene, dimer, and coupling products) in less than 5 min (expt 1, Table V).⁴⁶ The observation of predominant *cis* cyclic product in this case is highly suggestive of the presence of a radical intermediate in the metal-halogen exchange. Recently, Garst and Hines⁴⁵ reported a *cis/trans* ratio of 0.32 in the reaction of 6-bromo-1-heptene with a sodium mirror and concluded that (2-methyl-5-hexenyl)sodium resembles a carbanion and cyclizes to give predominantly the *trans*

(42) Alnajjar, M. S.; Kuivila, H. G. *J. Am. Chem. Soc.* 1985, 107, 416.

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(44) Brace, N. O. *J. Org. Chem.* 1967, 32, 2711.

(45) (a) Garst, J. F.; Hines, J. B., Jr. *J. Am. Chem. Soc.* 1984, 106, 6443. (b) Garst, J. F.; Hines, J. B., Jr.; Bruhnke, J. D. *Tetrahedron Lett.* 1986, 27, 1963.

(46) The formation of these hydrocarbon byproducts will be discussed in detail by Professor W. F. Bailey.

Table V. Reaction of 6-Bromo-1-heptene (8) with *tert*-Butyllithium in Pentane/Ether at $-78\text{ }^{\circ}\text{C}^a$

expt	time (min)	additive	% yield (% d)		
			10	11	other ^e
1	5	none	39.1 (5.5) ^c	26.0 [5.8] ^b (t = 95.0) ^{c,d} (c = 94.5) ^{c,e}	30.0
2	180	none	40.0 (4.3) ^c	27.6 [5.7] (t = 98.0) (c = 93.5)	28.5
3	1440	none	41.1 (3.6) ^c	27.2 [5.7] (t = 99.2) (c = 94.5)	29.0
4	10	2 TMEDA ^f	35.6 (2.2) ^c	28.0 [6.2] ^b (t = 40.5) ^{c,d} (c = 93.0) ^{c,e}	30.0
5	240	2 TMEDA ^f	39.5 (0.7) ^c	28.5 [6.1] (t = 20.6) (c = 95.2)	31.5
6	240	2 18-crown-6 ^g	38.4 (4.1) ^c	27.6 [4.4] (t = 39.5) (c = 81.3)	30.0
7	240	4 HMPA ^f	37.2 (3.7) ^c	28.3 [5.3] (t = 29.3) (c = 65.3)	28.5

^aAll reactions carried out were 0.2 M in *t*-BuLi and 0.1 M in halide and then quenched with D₂O. ^bNumber in brackets indicates the *cis/trans* ratio of 1,2-dimethylcyclopentane. ^cDeuterium content was determined by GC-MS. ^dDeuterium content in the *trans*-1,2-dimethylcyclopentane. ^eDeuterium content in the *cis*-1,2-dimethylcyclopentane. ^f2 equiv of TMEDA, 4 equiv of HMPA, and 2 equiv of 18-crown-6 were added to the reaction mixture, respectively, after the reaction was complete. ^gDienes, dimer, and coupling products.

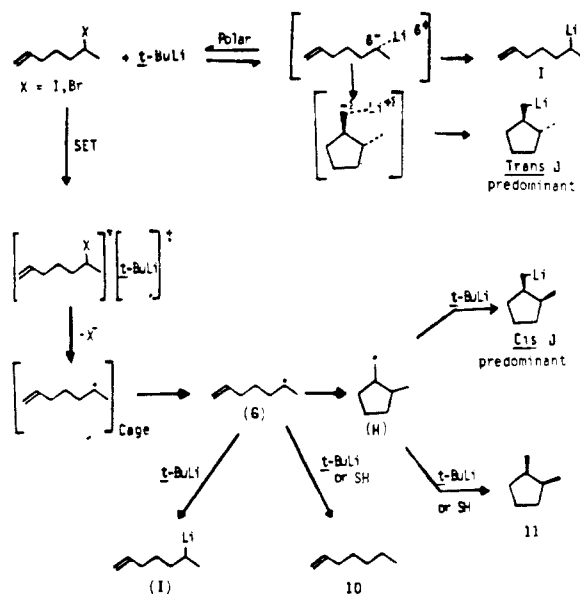
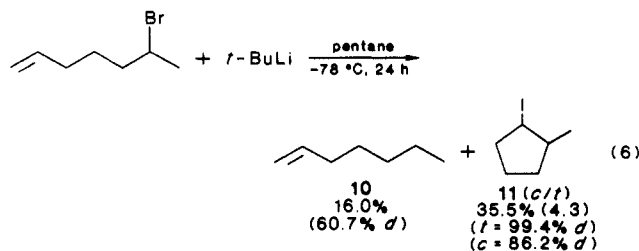


Figure 2. Proposed mechanistic scheme for the reaction of 6-halo-1-heptenes 8 and 9 with *tert*-butyllithium.

cyclic isomer, whereas the *cis/trans* ratio observed here (5.8) is similar to what has been observed earlier for radical cyclization at $-78\text{ }^{\circ}\text{C}$.⁴⁷ A reasonable suggestion for the mechanism involving radical intermediates in the reaction of 8 with *t*-BuLi is shown in Figure 2. Note that the results of expt 1 show that 94.5% of 10 and 5.0% of 11 are straight-chain and *trans* and *cis* cyclized protio hydrocarbon, respectively. The low deuterium content in 10

indicates the formation of a radical precursor because the secondary radical intermediate (G), once diffused from the solvent cage, will either rapidly abstract hydrogen from solvent (or *t*-BuLi) to give 10 or cyclize to give the corresponding cyclized primary radical (H). Since the primary carbanion is more easily formed than the secondary carbanion, the radical H then accepts another electron from *t*-BuLi to form the organolithium compound J more rapidly than H abstracts hydrogen from solvent (or *t*-BuLi). The low deuterium content of 10 and the high deuterium content in both *cis*- and *trans*-11 are therefore explained. In addition, when the reaction mixture was allowed to stand up to 24 h, the product ratio of 10:11 remained constant (expts 2-4, Table V), although some other cleavage of the straight-chain product slowly took place (5.5% to 3.6% *d*₁ in 10). Thus the hydrocarbon formation in this reaction is the result of a radical precursor since carbanion cleavage is too slow to explain such a high degree of protio hydrocarbon in 10 after 5 min of reaction.

In addition, 8 was allowed to react with excess *t*-BuLi in pure pentane at $-78\text{ }^{\circ}\text{C}$ and a similar result to that obtained in pentane/Et₂O was observed. The exception was that the deuterium content in the uncyclized product 10 increased from 5.5% *d*₁ to 60.7% *d*₁ (eq 6). One might

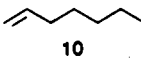



(47) Ashby, E. C.; DePriest, R. N.; Su, W. Y. *Organometallics* 1984, 3, 1718.

(48) W. F. Bailey also observed the same trend in the formation of *cis/trans* ratio of 1,2-dimethylcyclopentane in the reaction of 6-iodo-1-heptene with *t*-BuLi in pentane/Et₂O. Private communication from Bailey to E. C. Ashby.

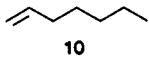

expect the deuterium content in 10 to be 100% since hydrogen abstraction from solvent to form hydrocarbon is less likely with pure pentane as the solvent. The deuterium content is a lot higher in pure pentane (60.7% *d*₁) than in pentane/ether (5% *d*₁) but not 100% because the

Table VI. Reaction of 6-Iodo-1-heptene (9) with *tert*-Butyllithium in Pentane/Ether at -78 °C^a

expt	time (min)	additive	% yield (% d)		
			 10	 11	other ^e
1	5	none	44.0 (16.0) ^c	11.3 [1.7] ^b (t = 96.0) ^{c,d} (c = 97.1) ^{c,e}	42.0
2	1440	none	43.2 (15.8)	11.4 [1.9] (t = 95.4) (c = 93.6)	45.0
3	240	4 HMPA ^f	40.5 (4.4)	12.7 [1.6] (t = 37.8) (c = 72.0)	40.0
4	240	2 TMEDA ^f	41.0 (1.2)	13.2 [1.5] (t = 20.5) (c = 90.0)	43.5
5	240	2 18-crown-6 ^f	44.5 (6.0)	12.2 [1.5] (t = 43.4) (c = 80.7)	41.0

^aAll reactions carried out were 0.2 M in *t*-BuLi and 0.1 M in halide and then quenched with D₂O. ^bNumber in brackets indicates the *cis/trans* ratio of 1,2-dimethylcyclopentane. ^cDeuterium content was determined by GC-MS. ^dDeuterium content in the *trans*-1,2-dimethylcyclopentane. ^eDeuterium content in the *cis*-1,2-dimethylcyclopentane. ^f2 equiv of TMEDA, 4 equiv of HMPA, and 2 equiv of 18-crown-6 were added to the reaction mixture, respectively, after the reaction was complete. ^gDienes, dimer, and coupling products.

Table VII. Effect of the Rate of Addition of *tert*-Butyllithium in the Reaction with 6-Iodo-1-heptene (9) in Pentane/Ether at -78 °C^a

expt	time of addition of <i>t</i> -BuLi	% yield (% d)		
		 10	 11	other ^f
1	at once (5 s)	38.8 (17.5) ^c	18.4 [0.05] ^b (t = 95.8) ^{c,d} (c = 96.7) ^{c,e}	40.0
2	3 min	37.8 (13.2)	37.5 [0.13] (t = 96.7) (c = 95.2)	27.0
3	25 min	44.0 (16.0)	11.3 [1.7] (t = 96.0) (c = 97.1)	42.0

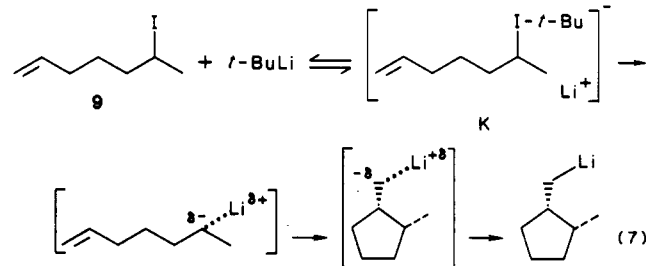
^aAll reactions carried out were 0.2 M in *t*-BuLi and 0.1 M in halide and then quenched with EtOD. ^bNumber in brackets indicates the *cis/trans* ratio of 1,2-dimethylcyclopentane. ^cDeuterium content was determined by GC-MS. ^dDeuterium content in the *trans*-1,2-dimethylcyclopentane. ^eDeuterium content in the *cis*-1,2-dimethylcyclopentane. ^fDienes, dimer, and coupling products.

radical can abstract hydrogen from *t*-BuLi. The deuterium content in both *trans*- and *cis*-11 was high (99.4%) and 86.2%, respectively), indicating that the primary radical H receives a second electron from *t*-BuLi to form the corresponding organolithium compound J more rapidly than it abstracts hydrogen from *t*-BuLi.

When lithium complexing agents such as HMPA, TMEDA, and 18-crown-6 (expt 5–8, Table V) were added to the reaction mixture of 8 and *t*-BuLi in pentane/ether at -78 °C, no additional cyclization was observed, only additional ether cleavage indicating enhanced carbanionic character imparted to 10 and 11 by the complexing agent. Interestingly, the data in expt 5–8 show that the straight-chain organolithium compound I and the *trans* organolithium compound J were indeed made more carbanionic by these cation complexing agents than the corresponding *cis* organolithium compound J since more ether cleavage products (hydrocarbon) were formed. These results can be explained by assuming that the *trans* organolithium compound J has less steric effect when the methyl group is *trans* to the CH₂Li than when it is *cis*; therefore, cation complexing agents will complex more

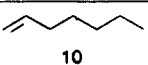

readily with the lithium cation of *trans* J than *cis* J. The presence of large amounts of 11 with a *cis/trans* ratio of 5.8, the high yield of protio hydrocarbon 10, and the lack of increased cyclization in the presence of cation complexing agents is supportive evidence of a radical intermediate in these reactions.

Next, when 6-iodo-1-heptene (9) was allowed to react with *t*-BuLi at -78 °C in pentane/Et₂O, the results were similar to the results obtained with the bromide except that the *cis/trans* ratio of 11 was 1.7 rather than 5.8 (expt 1, Table VI) as previously observed for the bromide. This result is not consistent with that expected for a radical intermediate in halogen-metal exchange reactions between a secondary alkyl iodide and *t*-BuLi in pentane/ether at -78 °C. Since Reich³⁹ and co-workers have recently reported evidence for an ate complex in the reaction of phenyllithium and iodobenzene, one also could assume that there is an ate complex intermediate (K) involved in the reaction of 6-iodo-1-heptene (9) with *t*-BuLi in pentane/ether at -78 °C (eq 7). This complex could then



rapidly dissociate to form the halogen-metal exchange product. The transition state leading to this product has carbanionic character leading to cyclization of the incipient carbanion to form predominantly the *trans* cyclic product. Therefore, a *cis/trans* ratio of 1.7 is consistent with either a carbanion cyclization⁴⁵ or a mechanism involving rapid attack of the *t*-BuLi on the iodide atom of the alkyl iodide followed by formation of an ate complex intermediate possessing carbanion character.^{15,39} When the reaction mixture was allowed to stand for up to 24 h, the product ratio of 10:11 remained constant (expt 2). Therefore, the straight-chain organolithium compound I, once formed, did not cyclize further to the cyclized organolithium compound J and when lithium complexing agents were used, no ad-

Table VIII. Effect of Mode of Addition of *tert*-Butyllithium in the Reaction of 6-Halo-1-heptenes in Pentane/Ether at $-78\text{ }^{\circ}\text{C}^a$

expt	X	mode of addition	% yield (% d)		
					other ^f
1	Br	normal	39.1 (5.5) ^c	26.0 [5.8] ^b (t = 95.0) ^{c,d} (c = 94.5) ^{c,e}	30.0
2	Br	inverse	36.5 (8.0)	24.2 [5.5] (t = 94.5) (c = 96.5)	28.0
3	I	normal	44.0 (16.0)	11.3 [1.7] (t = 96.0) (c = 97.1)	42.0
4	I	inverse	38.0 (10.5)	45.6 [0.03] (t = 98.0) (c = 95.0)	20.0

^aAll reactions carried out were 0.2 M in *t*-BuLi and 0.1 M in halide and then quenched with EtOD. ^bNumber in brackets indicates the cis/trans ratio of 1,2-dimethylcyclopentane. ^cDeuterium content was determined by GC-MS. ^dDeuterium content in the *trans*-1,2-dimethylcyclopentane. ^eDeuterium content in the *cis*-1,2-dimethylcyclopentane. ^fDienes, dimer, and coupling products.

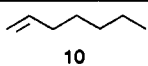

ditional cyclization was observed; only a decrease of d_1 content in **10** and **11** (expt 3–5, Table VI). It is interesting to note that the cis/trans ratio in the reaction of **9** with *t*-BuLi was found to be dependent on the rate of addition of *t*-BuLi to the alkyl halide. The results are given in Table VII. When *t*-BuLi was added to a solution of **9** all at once (in 5 s), the cis/trans ratio of 1,2-dimethylcyclopentane (**11**) is 0.05 (expt 1), on the other hand when *t*-BuLi was added to **9** at a slower rate (3 min and 25 min, respectively) the cis/trans ratio of **11** increased to 0.13 and 1.7, respectively (expt 2 and 3, Table VII). Moreover, when a 0.1 M solution of **9** was added to a solution of *t*-BuLi in pentane/ether at $-73\text{ }^{\circ}\text{C}$ (inverse addition), the cis/trans

ratio of **11** was 0.03 (expt 3, Table VIII). On the other hand, the cis/trans ratio of **11** in the reaction of **8** (X = Br) was independent of the mode of addition of *t*-BuLi (expt 1 and 2, Table VIII).

These results indicate that the amount of excess *t*-BuLi present in the reaction mixture plays a role in the cis/trans ratio of **11** in the reaction with 6-iodo-1-heptene. Thus, when more *t*-BuLi is present in the reaction mixture, it has more of a chance to react further with **9** to form the intermediate **K** which has carbanion character leading to cyclization to form the *trans* product. In the case where slow addition of *t*-BuLi to the alkyl iodide was performed (expt 3, Table VII), the cis/trans ratio of **11** was 1.7, which indicates that two mechanistic pathways (heterolytic and radical) are in competition in the reaction. Furthermore, when **9** was allowed to react with *t*-BuLi in pure pentane at $-78\text{ }^{\circ}\text{C}$, the results were similar to the results obtained with the corresponding bromide (eq 6) in which the cis/trans ratio of **11** was 4.0 and the yield of **11** was 37.4% as shown in expt 2 of Table IX. The observation of predominant *cis* cyclic product in this case is therefore highly suggestive of the presence of a radical intermediate in the reaction of **9** with *t*-BuLi in pure pentane. Once again, the product ratio of **10**:**11** was stable during a 24-h period (expt 3).

Finally, lithium complexing agents (TMEDA, HMPA, and 18-crown-6) were employed in order to observe the cyclization of **I** to **J**. The results are given in expt 4–7 of Table IX. The data show that no additional cyclized product was formed yet the straight-chain organolithium compound **I** and the cyclized organolithium compound **J** were indeed made more carbanionic by these complexing agents since more ether cleavage products (protio hydrocarbon) were formed. Thus, the observation of a high yield of cyclized product **11** with a high *cis* to *trans* ratio of **11** in the reactions of secondary alkyl iodide **9** with *t*-BuLi in pure pentane at $-78\text{ }^{\circ}\text{C}$ is indicative of a radical intermediate (mechanism described in Figure 2).

Table IX. Effects of Solvent and Additive on the Reaction of 6-Iodo-1-heptene (9**) with *t*-BuLi at $-78\text{ }^{\circ}\text{C}$**

expt	time (min)	solvent	additive	% yield (% d)		
						other ^h
1	5	pentane/ether ^a (4:1)	none	44.0 (16.0) ^d	11.3 [1.7] ^c (t = 96.0) ^{d,e} (c = 97.1) ^{d,f}	42.0
2	15	pentane ^b	none	18.0 (63.8)	37.4 [4.0] (t = 100) (c = 82.2)	40.0
3	1440	pentane ^b	none	16.1 (65.2)	34.7 [3.6] (t = 100.0) (c = 88.5)	41.5
4	30	pentane ^b	2 TMEDA ^g	19.2 (4.9)	32.4 [3.7] (t = 89.5) (c = 84.6)	40.0
5	240	pentane ^b	2 TMEDA ^g	17.1 (0.5)	33.7 [3.7] (t = 49.5) (c = 81.6)	42.0
6	240	pentane ^b	4 HMPA ^g	16.5 (16.8)	35.6 [3.7] (t = 40.5) (c = 81.4)	43.5
7	240	pentane ^b	2 18-crown-6 ^g	19.5 (24.8)	34.0 [3.3] (t = 17.1) (c = 87.3)	40.0

^aReaction carried out was 0.2 M in *t*-BuLi and 0.1 M in halide and then quenched with D₂O. ^bReaction carried out was 1.0 M in *t*-BuLi and 0.1 M in halide and then quenched with D₂O. ^cNumber in brackets indicates the cis/trans ratio of 1,2-dimethylcyclopentane. ^dDeuterium content was determined by GC-MS. ^eDeuterium content in the *trans*-1,2-dimethylcyclopentane. ^fDeuterium content in the *cis*-1,2-dimethylcyclopentane. ^g2 equiv of TMEDA, 4 equiv of HMPA, and 2 equiv of 18-crown-6 were added to the reaction mixture, respectively, after the reaction was complete. ^hDienes, dimer, and coupling products.

Table X. Reaction of *endo*-5-(2-Haloethyl)-2-norbornenes 1-3 with *t*-BuLi in Pentane/Et₂O (4:1) at -78 °C Hydrolyzed with D₂O and C₂H₅OD



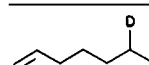
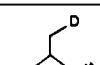
expt	X	H ⁺	additive	time (min)	% yield (% d)	
					 CH ₂ D	
1	Br	D ₂ O	none	180	82.0 (60.8)	15.3 (59.9)
2	Br	EtOD	none	180	80.2 (56.2)	16.5 (57.7)
3	Br	D ₂ O	TMEDA	315	77.0 (60.3)	20.5 (50.9)
4	Br	EtOD	TMEDA	300	78.0 (58.1)	20.5 (45.5)
5	I	D ₂ O	none	5	100.0 (100)	0.0
6	I	EtOD	none	5	98.5 (99.8)	0.0

Table XI. Reactions of 6-Bromo-1-heptene (8) with *t*-BuLi in Pentane/Et₂O (4:1) at Different Temperatures Hydrolyzed with D₂O or C₂H₅OD

expt	H ⁺	time (min)	temp (°C)	% yield (% d)	
					 [cis/trans]
1	D ₂ O	5	-78	39.1 (5.5)	26.0 [5.8] (t = 95.0) (c = 94.5)
2	EtOD	5	-78	41.5 (7.5)	27.5 [5.8] (t = 94.6) (c = 91.2)
3	D ₂ O	30	-23	38.0 (9.8)	32.7 [5.0] (t = 97.8) (c = 51.1)
4	EtOD	30	-23	39.5 (10.8)	30.5 [4.7] (t = 59.9) (c = 69.7)
5	D ₂ O	30	0	42.0 (9.5)	30.6 [5.6] (t = 18.5) (c = 55.2)
6	EtOD	30	0	40.5 (8.2)	30.0 [5.0] (t = 15.3) (c = 51.1)

Bailey³⁷ has shown that hydrolysis of 5-hexenyllithium at low temperature with D₂O and C₂H₅OD produces different results, a point on which we agree. For this reason we have hydrolyzed reaction mixtures from the reactions of *t*-BuLi with both 1 and 9 with both D₂O and C₂H₅OD and have shown that the results are the same (Tables X and XI). Therefore the results we report in this study for hydrolysis of reaction mixtures involving D₂O are valid. This is undoubtedly due to the fact that the organolithium compounds produced from 1 and 9 are much less likely to rearrange than the one produced from 5-hexenyl bromide or iodide.

Experimental Section

Materials. Olefin-free solvent-grade pentane (99% pure) was purchased from Aldrich and distilled over NaAlH₄ under nitrogen. Reagent-grade diethyl ether was obtained from Fisher and distilled under nitrogen from a deep purple solution of sodium benzophenone ketyl. Hexamethylphosphoramide (HMPA) from Aldrich was fractionally distilled from sodium at reduced pressure. Samples of 1,5-cyclooctadiene, *n*-octane, and 1-heptene from Aldrich were used as received. TMEDA (trimethylethylenediamine) was purchased from Aldrich and distilled from BaO₂ under

nitrogen. Deuterium oxide (D₂O) and ethanol-*d* (EtOD) were purchased from Aldrich and stored under nitrogen before use. *tert*-Butyllithium solution was obtained from Aldrich and used after standardization by the Eastham-Watson⁴⁹ method and acid-base titration.

Authentic samples of *cis*- and *trans*-1,2-dimethylcyclopentane (11) were obtained from Wiley Organic Co.

A sample of *endo*-5-ethyl-2-norbornene (4) (¹H NMR 0.50–0.60 ppm (1 H, m), 0.80–0.90 (3 H, d, *J* = 6 Hz), 1.0–1.40 (4 H, m), 1.65–1.90 (2 H, m), 5.80–6.20 (2 H, m); mass spectrum, M⁺ = 122) was obtained by preparative GLC of a hydrolyzed sample of the reaction mixture of *endo*-5-(2-iodoethyl)-2-norbornene (1) with LiAlH₄ in THF.

A sample of tricyclo[4.2.1.0^{3,9}]nonane (5) (¹H NMR 0.70 ppm (1 H, m), 0.87 (1 H, m), 1.15–1.90 (12 H, m); mp 99–100 °C (lit.⁵⁰ mp 98–99 °C); mass spectrum, M⁺ = 122) was obtained by preparative GLC of a hydrolyzed sample of the reaction mixture of 1 with *n*-Bu₃SnH catalyzed by AIBN.

General Procedures. All glassware and syringes were oven-dried at 150 °C for at least 2 h and cooled under a flow of purified nitrogen just prior to use. Transfer of reagents was performed by using syringes equipped with stainless steel needles. Reactions were carried out in round-bottomed flasks equipped with T-bore stopcocks attached to male 24/40 standard taper joints (allows nitrogen flush while reagents are being added or removed through the stopcock by syringe) and a Teflon-coated magnetic stirring bar.

Proton NMR spectra were recorded on either a Varian T-60A or Bruker WM-300 instrument with chemical shifts reported relative to Me₄Si. Mass spectral analyses were performed on a Varian MAT-112s spectrometer. IR spectra were recorded on a Perkin-Elmer 299 infrared spectrophotometer.

Quantitative gas-liquid chromatographic (GLC) analyses were conducted on either a Varian Model 3700 instrument coupled to a Varian CDS 111 electronic integrator using a DB 1 capillary column or a Hewlett-Packard Model 700 instrument using a 10 ft, 10% Na₂SO₄ on alumina column. GLC yields were determined by using internal standards and comparing peak areas which were corrected for response factors. Preparative GLC separations were performed on a F&M Model 720 instrument equipped with a thermal conductivity detector. For quantitative GLC analyses, a 30-m DB 1 capillary column was used to analyze *endo*-5-(2-iodoethyl)-2-norbornene (1), *endo*-5-(2-bromoethyl)-2-norbornene (2), *endo*-5-(2-chloroethyl)-2-norbornene (3), *endo*-5-ethyl-2-norbornene (4), tricyclo[4.2.1.0^{3,9}]nonane (5) with 1,5-cyclooctadiene as an internal standard with initial temperature at 70 °C to 250 °C using a programmed rate of 5° per min and 17 psi helium pressure. A 10-ft 10% Na₂SO₄ on alumina column was used to analyze 1-heptene (10), *cis*- and *trans*-1,2-dimethylcyclopentane (11), 1,6-heptadiene, and 1,5-heptadiene with *n*-

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heptane as an internal standard with the column temperature at 150 °C and 35 psi nitrogen pressure.

Preparations of *endo*-5-(2-Haloethyl)-2-norbornenes 1-3. By use of published procedures,⁵¹ 1 (X = I), 2 (X = Br), and 3 (X = Cl) were obtained. For X = I: bp 83-84 °C (2.5 mmHg); ¹H NMR 0.47-0.54 ppm (1 H, m), 1.0-2.20 (5 H, m), 2.65-2.95 (2 H, m), 3.28-3.60 (2 H, t, *J* = 7 Hz), 5.85-6.14 (2 H, m). For X = Br: bp 71-73 °C (2.5 mmHg); ¹H NMR 0.48-0.54 ppm (1 H, m), 1.0-2.28 (5 H, m), 2.65-2.90 (2 H, m), 3.08-3.40 (2 H, t, *J* = 7 Hz), 5.88-6.17 (2 H, m). For X = Cl: bp 86-87 °C (12 mmHg) (lit.⁵² bp 87-90 °C at 14 mmHg); ¹H NMR 0.45-0.51 ppm (1 H, m), 1.0-2.30 (5 H, m), 2.65-3.08 (2 H, m), 3.50-3.80 (2 H, t, *J* = 7 Hz), 5.85-6.12 (2 H, m).

Preparations of 6-Halo-1-heptenes 8 and 9. 8 (X = Br) and 9 (X = I) were prepared by a previously described method.⁵³

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General Procedure for the Reaction of *t*-BuLi with Alkyl Halides. A solution of 0.1 M of an appropriate halide in pentane/ether was cooled to -78 °C under a blanket of nitrogen or argon and 0.2 M of *t*-BuLi as a solution in pentane was added via syringe over a 5-min period. In cases where complexation reagents were employed (TMEDA, HMPA, 18-crown-6), the solutions of additive were precooled and added to the reaction mixture at -78 °C after the reaction was complete. At the chosen time, reaction mixtures were carefully quenched with D₂O (or EtOD), internal standard was added, and GLC analyzes were performed. Deuterium incorporation was evaluated by GC-MS.

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Selective Mono-N-alkylation of Aromatic Amines by Dialkyl Carbonate under Gas-Liquid Phase-Transfer Catalysis (GL-PTC) Conditions

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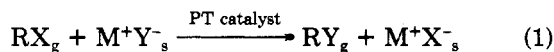
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The reaction between aromatic amines and dialkyl carbonates, carried out in gas phase under gas-liquid phase-transfer catalysis (GL-PTC) conditions, in a continuous-flow process, produces the mono-N-alkylation product and its carboxyalkyl derivative (selectivity > 99%). The catalyst is a polyethylene glycol in the presence of a base (K₂CO₃). The reaction produces CO₂ so it can be carried out indefinitely because the chemical nature of the catalytic bed, at steady conditions, does not change during the time. According to the mechanism discussed, this high selectivity might be due the following: (i) the reaction between the amine and dialkyl carbonate that produces only carboxymethylated compound (ArNHCOOR); (ii) the subsequent reaction of this intermediate with the dialkyl carbonate that exclusively produces N-alkylated products (ArNR₂COOR, from which ArNHR is selectively produced).

Introduction

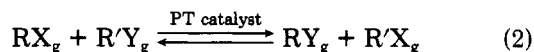
The development of new synthetic methods are of interest because more attention is turned to work safety and to use of reagents less dangerous from an industrial and environmental point of view; so new reactions and new synthetic methods often offer the opportunity to improve productive processes. An example is gas-liquid phase-transfer catalysis (GL-PTC).¹ This new synthetic method, with its theoretical basis in phase-transfer catalysis (PTC),² takes advantage of anionic activation of PTC in processes that are carried out in continuous flow and in gas-phase conditions.

It has been reported that GL-PTC can work in two different ways: (1) with a bed that consumes itself progressively during the reaction (eq 1; the gaseous reagent



RX flows on a solid bed composed of the salt M⁺Y⁻ and a PT catalyst; its transformation into RY then occurs. The

solid reagent M⁺Y⁻ is progressively consumed).^{1c} (2) with a bed that is not consumed during the reaction (eq 2: The



solid bed is composed of a solid supporting a PT catalyst. RX and R'Y can be, in this case, two alkyl halides; they undergo halogen exchange at the outlet of reactor).^{1d}

This second possibility is surely of greater interest because the reaction can be carried out for an indefinite time, making the bed effectively catalytic.

Dimethyl carbonate (DMC) is a well-known reagent which provides carboxymethylation with nucleophiles when the reaction is carried out in liquid phase.³ More-

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