

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

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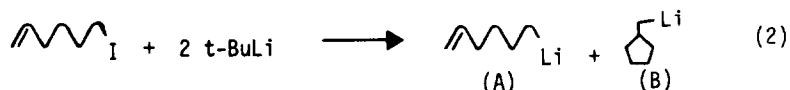
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Abstract: The reaction of *t*-BuLi with cyclizable 1° and 2° alkyl halide radical probes at low temperature produced stable cyclized and uncyclized organolithium products as well as cyclized hydrocarbons which clearly indicate the presence of radical intermediates during the course of these reactions.

For many years, the exchange of halogen and lithium atoms in the reaction of an organic halide with an organolithium compound has been known as metal-halogen exchange (eq. 1).¹⁻⁵



Russell suggested that such reactions proceed by single electron transfer⁶ (SET), although, there are several references in the literature that suggest that the reaction pathway is heterolytic in nature.⁷ Among 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 cumene⁸; (b) formation of the trityl radical from trityl chloride⁹; (c) nuclear polarization in the olefin products¹⁰ or in the alkyl halide¹¹; and (d) the formation of the expected coupling and disproportionation products of R and R'.⁸⁻¹¹ In 1984 Bailey reported that 6-iodo-1-hexene, when treated with *t*-BuLi at -23°C, undergoes intramolecular cyclization (eq. 2), which seemed to indicate that



metal-halogen exchange proceeds by SET.¹² However, more recently, he reported¹³ that 5-hexenylithium (A) cyclizes to (B) at -23°C. Thus indicating that cyclize product (B) could have been formed from (A) after the reaction of 6-iodo-1-hexene with *t*-BuLi was complete. Recently Newcomb has also challenged Bailey's results and the SET nature of metal-halogen exchange. He concludes that, "the major pathway for cyclization of the 6-halo-1-hexenes is now known to be the anion route".¹⁴ However, based on the results reported herein involving the reaction of *t*-BuLi with three different alkyl halide radical probes, including 6-iodo-1-hexene, we conclude that metal-halogen exchange does indeed involve the intermediate formation of radicals.

Prior to Bailey's latest report, we had found that the reaction of *t*-BuLi with 6-bromo- and 6-iodo-1-hexene in pentane-Et₂O at -23°, and even -78°C, produced both uncyclized (A) and



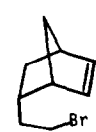



cyclized (B) organolithium product. However, the product ratio (A:B) changed on standing even at -78°C . On the other hand, when we carried out this reaction by addition of the reagents at -130°C , we found that the reaction was complete in 5 minutes and, the ratio of A:B (81:19) did not change over a four hour period. The cyclized product therefore does not arise from the cyclization of the hexenyllithium after it is formed.

In order to explore the mechanism of metal-halogen exchange further, we allowed two additional cyclizable alkyl halide radical probes¹⁵ to react with t-BuLi in pentane/ether at -78°C . In the table are presented data for the reactions of endo-5-(2'-bromoethyl)-2-norbornene (1) and 6-bromo-1-heptene (5). When a 0.1 M solution of (1) was allowed to react with a 0.2 M solution of t-BuLi in pentane/ether (4:1 ratio)¹⁶ at -78°C , followed by quenching with D_2O after 30 min. and the products analyzed by GLC, we obtained an 82% yield of (2) and a 15.3% yield of (3), which contained 61% d_1 and 60% d_1 respectively (exp 2). The ratio of (2) to (3) remained constant over a period of 24 hrs (exps. 1-3), indicating that cyclized product (3) is formed during, not after the reaction is over.¹⁷ In an attempt to make the organolithium compound (2) more carbanionic in order to increase its chances of carbanion cyclization to product (3), we treated the reaction mixture with TMEDA, HMPA and 18-crown-6 at -78°C after the reaction was over (exps. 4-6). We observed that organolithium compounds (2) and (3) were indeed made more carbanionic since more ether cleavage products (hydrocarbon) were formed; however, no additional cyclization was observed. The results of exp. 2 show also that 39% of (2) and 40% of (3) is straight-chain and cyclized hydrocarbons, respectively, produced before hydrolysis. The hydrocarbon formation is probably the result of a radical precursor (radical abstraction of hydrogen from solvent or RLi since carbanion cleavage is too slow at -78°C to account for such a high degree of hydrocarbon formation after 10 min of reaction). All of the above data are consistent with the formation and cyclization of a radical intermediate.

Furthermore, when 6-bromo-1-heptene (5) was treated with t-BuLi in pentane/ether (3:2 ratio) at -78°C , 1-heptene (6) and 1,2-dimethylcyclopentane (7) were obtained (on reaction with D_2O) in 63.2% and 37% yield, respectively. The ratio of cis to trans-1,2-dimethylcyclopentane (7) was 3.9 (exp. 7). Recently, Garst et al¹⁸ 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 predominately the trans isomer, whereas the cis/trans ratio observed here (3.9) is what is to be expected and what has been observed earlier for radical cyclization.¹⁹ The product ratio (6:7) remained constant up to 24 hrs and also was constant after adding lithium complexing agents (HMPA, TMEDA, 18-crown-6) (exps. 8- 11).

All of the above data suggest the following mechanism (Scheme I): t-BuLi transfers an electron to the alkyl halide 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 t-BuLi to give the straight-chain compound (D) which on reaction with D_2O gives (2). (C) can also abstract hydrogen from solvent to form (2) or cyclize to give radical (E). Radical (E) can then further abstract hydrogen from solvent to give (3) or react with t-BuLi to give (F).

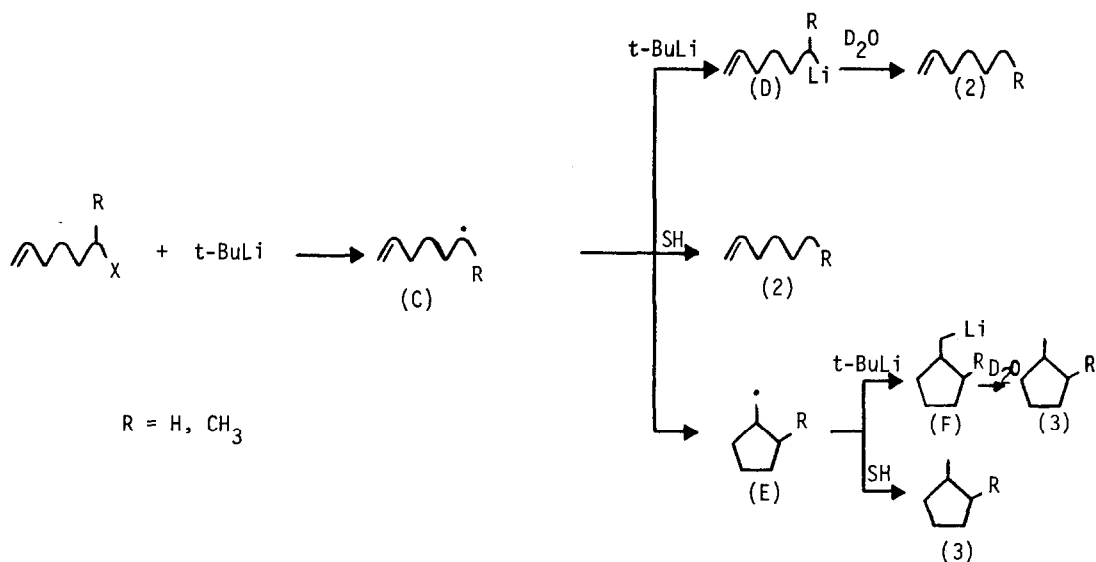
Table. Reactions of 1° and 2° Alkyl Bromides with *t*-BuLi at -78 °C^a

Exps	RBr	Time	Additive	% Yield of Hydrocarbon formed on reaction with D ₂ O ^b		Ratio
				Straight Chain	Cyclized	
						
				(2)	(3)	(2:3)
1		10	none	75.9 (61.8% d ₁)	13.2 (55.1% d ₁)	5.7
2	(1)	180	"	82.0 (60.8% d ₁)	15.3 (59.9% d ₁)	5.4
3		1140	"	83.0 (60.8% d ₁)	15.0 (62.6% d ₁)	5.5
4		240	2 TMEDA ^c	82.1 (60.8% d ₁)	16.2 (52.6% d ₁)	5.1
5		240	4 HMPA ^c	82.0 (56.8% d ₁)	15.0 (30.7% d ₁)	5.5
6		240	2(18-Crown-6) ^c	81.5 (51.9% d ₁)	16.7 (32.4% d ₁)	4.9
						
				(6)	(7)	(6:7)
7		10	none	63.2	37.0(3.9) ^d	1.7
8	(5)	1140	none	62.7	35.4 (4.0)	1.8
9		240	2 TMEDA ^c	61.1	37.5 (4.1)	1.6
10		240	4 HMPA ^c	64.0	33.5 (4.1)	1.9
11		240	2(18-Crown-6) ^c	63.8	34.2 (4.0)	1.9

^aReactions conducted using 0.1 M initial concentration of organic halides. ^bPercent yield of hydrocarbon determined by gas chromatography using a 30 m capillary column of DB.1 at 70° - 150° for 2 and 3 and at 30°/6 min to 250° for 6 and 7 with a flame ionization detector calibrated with 1,5-cyclooctadiene and *n*-octane as the internal standards. ^cAdditives were added at -78°C after the reaction was complete. ^d Cis/trans ratio of 1,2-dimethylcyclopentane.

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Scheme I



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