

REACTIONS OF 1-HALO-5-HEXENES WITH ALKYL LITHIUMS. EVIDENCE FOR A PRONOUNCED HALOGEN EFFECT  
ON THE MECHANISM OF THE METAL-HALOGEN INTERCHANGE REACTION OF PRIMARY ALKYL HALIDES

William F. Bailey\*, Jeffrey J. Patricia and Timo T. Nurmi†

Department of Chemistry, University of Connecticut, Storrs, CT 06268

**Abstract:** Reaction of *t*-BuLi with 1-halo-5-hexenes and 1-halo-6-methyl-5-heptenes at -78°C has revealed that, whereas 1° alkyl iodides are cleanly converted to alkyl lithiums in a non-radical process, the corresponding 1° alkyl bromides undergo interchange at least partially via a radical-mediated, SET pathway.

The metathesis reaction between an organolithium and an organic halide is known as the metal-halogen interchange<sup>1,2</sup> (Eq. 1).<sup>3</sup> Early studies of the reaction, first reported in 1938 by the research groups of Wittig and Gilman,<sup>4</sup> demonstrated that it is a reversible process,<sup>5</sup> most readily accomplished with bromine and iodine containing halides,<sup>1</sup> leading to an equilibrium mixture favoring the more stable organolithium.<sup>1,5</sup>



The mechanism of this intriguing reaction has been the subject of debate for over four decades and several schemes have been proposed to account for the process. These include: (1) concerted exchange via a four-center transition state,<sup>1,2</sup> (2) reversible formation of an ate-complex by attack of RLi on the halogen atom of the organic halide<sup>7</sup> and, (3) various single-electron transfer (SET) mediated processes.<sup>2,6,8,9</sup> Unfortunately, the accumulated evidence from numerous studies is often in conflict and no consensus has emerged as to the mechanism of the metal-halogen interchange and its relationship (if any) to that of the Wurtz-coupling reaction.

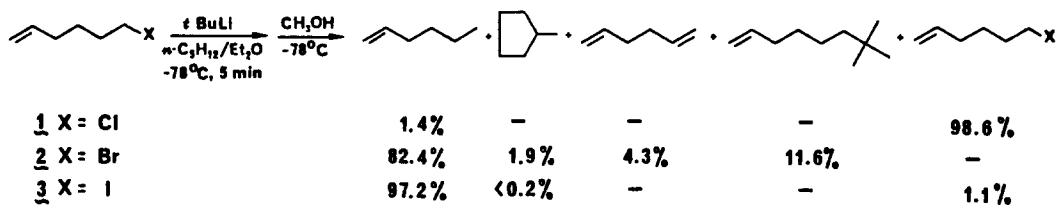
Our recent studies of the reactions of  $\alpha,\omega$ -dihaloalkanes with *t*-BuLi suggested that bromides and iodides may behave quite differently when treated with an alkyl lithium.<sup>6,10</sup> We have further explored the disparate behavior of alkyl bromides and iodides by investigation of the reactions of 5-halo-1-hexenes with *t*-BuLi at low temperature (-78°C). Herein we report evidence of a halogen effect on the mechanism of the metal-halogen interchange. As shown below, there is a SET component to the interchange between primary alkyl bromides and *t*-BuLi under conditions that provide no evidence for radical intermediates in reactions of the analogous primary alkyl iodides.<sup>11</sup>

Reactions were conducted at -78°C (dry-ice/acetone) by addition of 2 equiv *t*-BuLi in pure *n*-pentane to a 0.1 M solution of the substrate in *n*-pentane-diethyl ether (3:2 by vol) as previously described.<sup>11</sup> The reaction mixtures were stirred for 5 min at -78°C then quenched at -78°C with an excess of anhydrous methanol and analyzed.<sup>12</sup> A survey of the outcome of reactions

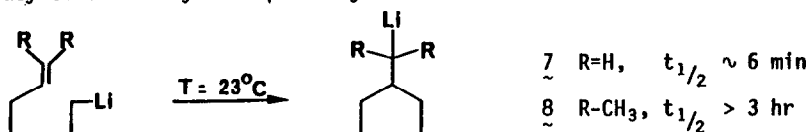
†On leave from the University of Turku, Turku, Finland.

of  $t$ -BuLi with 1-halo-5-hexenes (1-3) is given in *Scheme I*. The material balance for all reactions is in excess of 97% and the markedly distinct behavior of the substrates is apparent from examination of the products and yields. Thus, whereas the iodide (3) undergoes clean metal-halogen interchange in essentially quantitative yield, the analogous bromide (2) affords a mixture of hydrocarbons resulting from both interchange and coupling with  $t$ -BuLi. The low but non-negligible yield of methylcyclopentane produced from 2 is notable since it suggests the intermediacy of a 5-hexen-1-yl radical in the interchange reaction of the bromide. Due to the sluggish reaction of the chloride (1), no further experiments were performed with this substrate.

*Scheme I.*

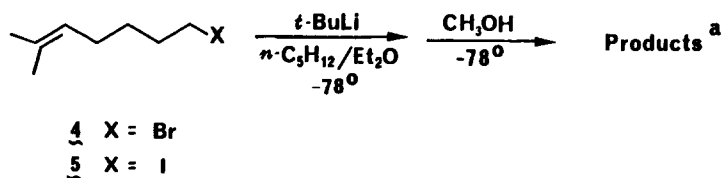


Clear evidence for the intermediacy of radicals in the metal-halogen interchange between primary alkyl bromides and  $t$ -BuLi was obtained from experiments employing 1-bromo-6-methyl-5-heptene (4) and 1-iodo-6-methyl-5-heptene (5). The benefits deriving from the use of such substrates in mechanistic studies of organometallic reactions is evident upon consideration of the relative tendency for cyclization of the radical and organolithium that may be generated from such molecules. Generation of a radical via SET to 4 and 5 would lead to rapid cyclization since the primary 6-methyl-5-hepten-1-yl radical (6) is known to isomerize to the cyclopentyl-containing tertiary radical with a rate constant approximately 2.5-times that for cyclization of the parent 5-hexen-1-yl radical.<sup>13</sup> In contrast to this rapid radical-mediated isomerization, the corresponding organo-lithium is much more resistant to cyclization than the parent 1-lithio-5-hexene.<sup>14</sup> Whereas 1-lithio-5-hexene (7) isomerizes completely in less than 1 hr at 23°C,<sup>13</sup> we have found that only ca. 3% of 8 (prepared from 5 by metal-halogen interchange with  $t$ -BuLi at -78°C)<sup>11</sup> undergoes rearrangement in the same time period. Consequently, observation of cyclized product from reactions involving 4 or 5 provides *prima facie* evidence for the intermediacy of a 6-methyl-5-hepten-1-yl radical.



When reactions of 4 or 5 with  $t$ -BuLi were conducted as described above, the results (*Table I*, entries 1 and 2) were analogous to those obtained from the 1-halo-5-hexenes. The essentially quantitative yield of 2-methyl-2-heptene from 5 is consistent with a non-radical pathway for interchange between  $t$ -BuLi and primary alkyl iodides.<sup>11</sup> The formation of isopropylcyclopentane from 4 implies, by contrast, that at least a portion of the primary bromide was reduced to a 6-methyl-5-heptene-1-yl radical (6) by SET from  $t$ -BuLi during the interchange.

Table I.



Entry	Halide	[ <i>t</i> -BuLi] <sup>c</sup> , M	Addition time, <sup>d</sup> min	Products, % Yield <sup>b</sup>					
						C <sub>9</sub> H <sub>14</sub> <sup>e</sup>			
1	<u>4</u>	2.5	5	78.6	4.0	~3.4	3.9	10	
2	<u>5</u>	2.5	5	>98					
3	<u>4</u>	0.025	124	47.7	15.4	~13.5	3.0	10	10
4	<u>5</u>	0.025	124	90.7	<0.3	<0.5			4

<sup>a</sup>Reactions conducted by dropwise addition of 2-3 equiv of *t*-BuLi to 0.1 M solutions of halide (typically 0.5 mmol). <sup>b</sup>Yields determined by GLC analysis<sup>12</sup> using cyclohexane as internal standard and correction for detector response. <sup>c</sup>Initial concentration of *t*-BuLi in *n*-pentane.

<sup>d</sup>Amount of time required for addition of *t*-BuLi. <sup>e</sup>Tentatively identified as isopropenylcyclopentane on the basis of its MS fragmentation; detector response assumed to be equal to that of the isomeric diene.

An additional test of these conclusions was provided by determination of the effect of variation in the initial concentration of *t*-BuLi on the ratio of 2-methyl-2-heptene/isopropylcyclopentane produced in reactions 4 and 5. The rationale for such experiments follows from the fact that unimolecular cyclization of any 6 that may be produced upon SET from *t*-BuLi is in competition with further reduction of 6 by *t*-BuLi to 1-lithio-5-methyl-5-heptene (8). Since the rate of this latter reduction depends on the concentration of the reducing agent (i.e., [*t*-BuLi]),<sup>3</sup> a decrease in [*t*-BuLi] should result in an increase in cyclized product at the expense of 2-methyl-2-heptene. Such a scenario (treated quantitatively by Garst and Barton in their elegant study of the reaction of 1-fluoro-5-hexene with alkali naphthalenes)<sup>15</sup> predicts that the 2-methyl-2-heptene/isopropylcyclopentane ratio should decrease with decreasing concentration of *t*-BuLi. This is precisely the trend observed for reaction of the primary bromide (*Table I*, compare entries 1 and 3): at high initial concentration of *t*-BuLi (2.5 M) the ratio of alkene to cyclized product is ~19.5 while at lower concentration (2.5 × 10<sup>-2</sup> M) the ratio decreases to ~3.1. As expected,<sup>11</sup> dilution of the *t*-BuLi has no effect on the clean metal-halogen interchange of the primary iodide (*Table I*, entries 2 and 4).

In conclusion, the results presented above indicate that alkyl bromides and iodides may behave quite differently, both with respect to the metal-halogen interchange as well as other competing reactions, when treated with an alkyllithium. There is no evidence for radical intermediates in the interchange reaction between a primary alkyl iodide and *t*-BuLi at low temperature<sup>11</sup> and the results are consistent with, albeit not supportive of, a mechanism involving rapid attack of the *t*-BuLi on the iodine atom of the iodide.<sup>7</sup> The metal-halogen interchange of 4 with low

concentrations of  $t$ -BuLi indicates that at least ca. 15% of the reaction involves radical intermediates. This result, which is consistent with the recent report of Newcomb's group on the reaction of 4-bromo-3,3-dimethyl-1-butene with  $t$ -BuLi<sup>9a</sup> and with the data of Ashby and co-workers on the metal-halogen interchange of primary alkenyl bromides,<sup>9b</sup> implies that at least a portion of the interchange proceeds via SET from the alkyllithium to the primary bromide.

The fact that primary bromides, rather than the more easily reduced iodides, undergo metal-halogen interchange at least partially by a radical-mediated process demonstrates that the reduction potential of a substrate is not always a valid predictor of the occurrence of SET in a given reaction. Although the reduction potentials of the substrates suggest that SET to the iodide would be more facile than to the bromide, the more easily reduced halide is apparently the one that is most susceptible to nucleophilic attack by the alkyllithium reagent.<sup>7</sup>

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#### References and Notes

- (a) Gilman, H.; Jones, R. G. *Org. React.* 1951, **6**, 339. (b) Jones, R. G.; Gilman, H. *Chem. Rev.* 1954, **54**, 835. (c) Schollkopf, U. in "Methoden der Organischen Chemie"; Georg Thieme: Stuttgart, 1970, Vol. 13/1.
- Wakefield, B. J. "The Chemistry of Organolithium Compounds"; Pergamon Press: New York, 1974.
- Although organolithiums are often (as here) represented as monomeric species, they are known to exist as aggregates whose degree of association may be affected by solvent, concentration and temperature (see ref. 2). For the sake of pictorial clarity, monomeric species will be used in mechanistic formulations.
- (a) Wittig, G.; Pockels, U.; Droge, H. *Chem. Ber.* 1938, **71**, 1903. (b) Gilman, H.; Jacoby, A. L. *J. Org. Chem.* 1938, **3**, 108.
- Applequist, D. E.; O'Brien, D. F. *J. Am. Chem. Soc.* 1963, **85**, 743.
- Bailey, W. F.; Gagnier, R. P.; Patricia, J. J. *J. Org. Chem.* 1984, **49**, 2098.
- (a) Wittig, G.; Schollkopf, U. *Tetrahedron* 1958, **3**, 91. (b) Reich, H. J.; Phillips, N. H.; Reich, I. L. *J. Am. Chem. Soc.* 1985, **107**, 4101.
- See ref. 6 and articles cited therein.
- (a) Newcomb, M.; Williams, W. G.; Crumpacker, E. L. *Tetrahedron Lett.* 1985, **26**, 1183. (b) Ashby, E. C.; Pham, T. N.; Park, B. *Tetrahedron Lett.* 1985, **26**, 4691.
- Bailey, W. F.; Gagnier, R. P. *Tetrahedron Lett.* 1982, **23**, 5123.
- Bailey, W. F.; Patricia, J. J.; Nurmi, T. T.; Wang, W. accompanying paper in this issue.
- Products were identified by comparison with authentic samples (ref. 6) unless otherwise noted. Mixtures were analyzed by GLC under conditions affording baseline separation of components [20-ft, 20% SE-30 on Anakrom A (80/100 mesh) column] and, unless otherwise indicated, yields were corrected for detector response under the conditions of the analysis using samples of pure product and standard.
- Beckwith, A. L. *J. Tetrahedron* 1981, **37**, 3073 and references therein.
- Bailey, W. F.; Patricia, J. J.; Delgobbo, V. C.; Jarret, R. M.; Okarma, P. J. *J. Org. Chem.* 1985, **50**, 1999.
- Garst, J. F.; Barton, F. E., III *J. Am. Chem. Soc.* 1974, **96**, 523.

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