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METAL-HALOGEN INTERCHANGE BETWEEN t-BUTYLLITHIUM AND 1-IODO-5-HEXENES PROVIDES NO EVIDENCE FOR SINGLE-ELECTRON TRANSFER

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Abstract: No products attributable to cyclization of 5-hexen-1-yl radicals have been detected in reactions of t-butyllithium with 1-iodo-5-hexenes at -78°C. Such experiments provide no evidence for the intermediacy of free-radicals in the metal-halogen interchange of primary alkyl-iodides with t-C_4H_9Li.

The mechanism of the metal-halogen interchange has been the subject of a number of recent studies employing so-called "radical probes" to investigate the possible intermediacy of free radicals in the reaction.[1-3] Such radical probes are alkyl halide substrates which, if converted to a free radical in the course of the interchange, will undergo a characteristic intramolecular rearrangement.[4] The intermediacy of free radicals does not, however, follow as a logical consequence of the simple observation of rearranged products. Clearly, the conclusion that free radicals are responsible for an observed isomerization is valid only to the extent that other plausible intermediates can be shown not to undergo similar rearrangement. This factor is of particular significance in mechanistic studies of the metal-halogen interchange for two reasons: (1) the product organolithium may be capable of isomerization that mimics the radical mediated process, and; (2) to the extent that the organolithium is persistent, anionic rearrangement can occur at a relatively slow rate well after the interchange is complete and produce non-negligible quantities of isomerized product. We have recently demonstrated such behavior for the organolithium corresponding to the prototypical 5-hexen-1-yl radical probe.[5] Thus, 1-lithio-5-hexene (1) undergoes isomerization analogous to that of the 5-hexen-1-yl radical, albeit more slowly, to give cyclopentylmethyllithium (2) in a process characterized[5] by a $\Delta H^{\neq} = -11.8 \pm 0.5$ kcal/mol and $\Delta S^{\neq} = +30 \pm 2$ eu.

Recently Ashby and co-workers[2] reported on an investigation of the metal-halogen interchange between t-butyllithium (t-BuLi) and alkyl halide substrates that incorporated the 5-hexen-1-yl system. The reactions were conducted at low temperature ($\leq$ -78°C) in a solution of n-pentane-diethyl ether and, following quenching with water, significant quantities (ca 10-20%) of product containing the cyclopentylmethyl moiety were observed. On this basis, the authors concluded that the interchange proceeds via a single-electron transfer (SET) mechanism involving free 5-hexen-1-yl radicals.[2] However, as detailed below, we have explored the metal-halogen interchange reactions of a variety of 1-iodo-5-hexenes with t-BuLi and, *under conditions seemingly identical to those employed by Ashby and co-workers, we find no products attributable to*

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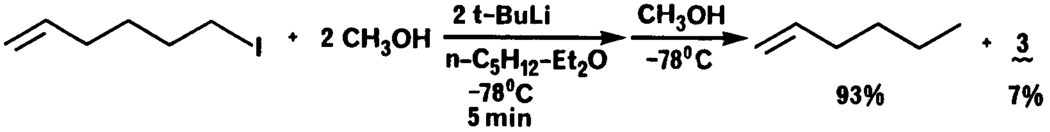
the cyclization of 5-hexen-1-yl radicals.

Metal-halogen interchange reactions were performed at -78°C under an atmosphere of oxygen-free argon by slow addition (3-4 min) of 2.0 equiv[6] of freshly prepared *t*-BuLi in *n*-pentane[7] to a 0.1 *M* solution of the appropriate iodide in dry solvent containing an accurately weighed quantity of cyclohexane (internal standard). Reaction mixtures were stirred for 5 min at -78°C and quenched at -78°C by addition of an excess of anhydrous, oxygen-free methanol. After warming to room temperature, the organic phase was washed with water, dried and analyzed by GLC[1] to give the results presented in Table I. The material balance for the reactions was virtually quantitative ($\geq$ 95%) and in no instance was more than a trace ($\leq$ 0.8%) of a methylcyclopentane produced in the interchange.

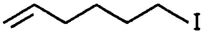
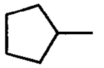
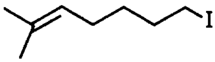
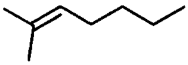
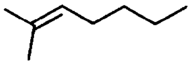
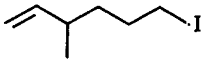
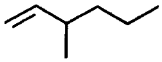
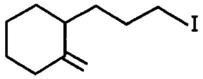
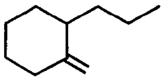
The small quantity of methylcyclopentane detected from reactions involving **3** (Table I, entries 1-4) may well be a consequence of the exothermicity of the interchange resulting in the anionic cyclization of **1** → **2** due to local heating during the addition of *t*-BuLi to the iodide (*vide infra*). It is of interest to note that no rearranged product is observed in reactions of 1-iodo-6-methyl-5-heptene (**6**) with *t*-BuLi (Table I, entries 5-6) even though a radical generated from this substrate is known to cyclize even more rapidly than the parent 5-hexen-1-yl radical.[4] The alkyllithium produced from **6** would be expected to be rather more resistant than **1** to isomerization since it would produce a tertiary alkyllithium upon cyclization to give a five-membered ring.

The metal-halogen interchange of a primary iodide with *t*-BuLi is virtually instantaneous on the laboratory time scale. Indeed, interchange effectively competes with proton transfer from CH_3OH to *t*-BuLi: when a solution of **3** in *n*-C_5H_{12}-Et_2O (3:2 by vol) containing 2 equiv of CH_3OH is treated with *t*-BuLi at -78°, more than 90% of the iodide is converted to the alkyllithium.[8]



The experiments summarized in Table I provide no evidence for the intermediacy of 5-hexen-1-yl radicals in the metal-halogen interchange reaction of primary alkyl iodides with *t*-BuLi.[9] These results suggest that Ashby and co-workers may have inadvertently observed anionic cyclization of initially formed 1-lithio-5-hexenes to cyclopentylmethyllithiums in their study of the metal-halogen interchange.[2] The isomerization of **1** to **2** is fairly rapid at 0°C (k ∿ 5 × 10^{-4} s^{-1}; $t_{1/2}$ ∿ 23 min)[5] and the fact that the Ashby group used water to quench the reaction[2] implies that initially formed products reached temperatures near 0°C before protonation occurred. Indeed, we have been able to reproduce the observations of Ashby and co-workers by simply allowing a reaction mixture to warm to 0°C prior to quenching. Thus, when the product generated upon interchange of **3** with *t*-BuLi in *n*-C_5H_{12}-Et_2O at -78°C (Table I, entry 1) was allowed to warm over 8 min to 0°C before the addition of H_2O, 14% of the initially formed 1-lithio-5-hexene (**1**) rearranged to cyclopentylmethyllithium (**2**).

Table I. Reactions of 1-Iodo-5-hexenes with *t*-BuLi at -78°C

Entry	Iodide	Conditions[a]	Products[b] (Yield, %)
1	 (**3**)	*n*-C_5H_{12}-Et_2O[c]	 (97.2) +  (<0.2) **4** **5**
2	**3**	*n*-C_5H_{12}-Et_2O,[c] inverse addition[d]	**4** (99.4) + **5** (<0.3)
3	**3**	*n*-C_5H_{12}-Et_2O,[c] 4 hr at -78°C	**4** (91.9) + **5** (<0.2) +  (ca.7)
4	**3**	Et_2O	**4** (98.4) + **5** (<0.8)
5	 (**6**)	*n*-C_5H_{12}-Et_2O[c]	 (99.8)
6	**6**	Et_2O	 (99.8)
7		*n*-C_5H_{12}-Et_2O[c]	 (>96)
8		*n*-C_5H_{12}-Et_2O[c]	 (98)

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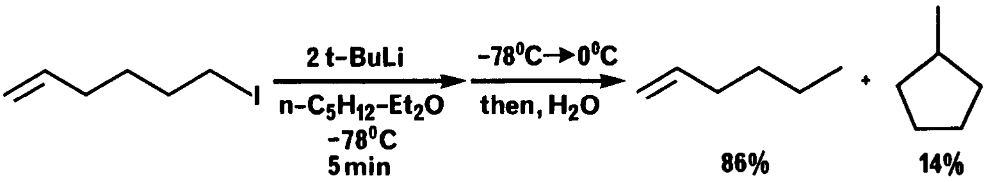
[a] Except where otherwise indicated, reactions were performed at -78°C by slow addition of 2 equiv of *t*-BuLi to 0.1 *M* solutions of iodide.

[b] Yields of products formed upon addition of anhydrous, oxygen-free CH_3OH to the reaction mixture at -78°C determined by GLC analysis using an internal standard and correction for detector response.

[c] 3:2 by volume.

[d] Reaction performed at -78°C by slow addition of **3** to 2.0 equiv of *t*-BuLi in *n*-pentane.



This result serves to reinforce the caveat, noted elsewhere,[5] that, "observation of products containing the cyclopentylmethyl group from reactions employing 5-hexen-1-yl substrates is not sufficient evidence to establish the intermediacy of radicals particularly when organometallic species may be involved".

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References and Notes

1. Bailey, W. F.; Gagnier, R. P.; Patricia, J. J. *J. Org. Chem.* 1984, 49, 2098.
2. Ashby, E. C.; Pham, T. N.; Park, B. *Tetrahedron Lett.* 1985, 26, 4691.
3. Newcomb, M.; Williams, W. G.; Crumpacker, E. L. *Tetrahedron Lett.* 1985, 26, 1183.
4. (a) Beckwith, A. L. J.; Ingold, K. U. in "Rearrangements in Ground and Excited States"; deMayo, P., Ed.; Academic Press: New York, 1980; Vol. 1, Chpt. 4.
   (b) Surzur, J-M. in "Reactive Intermediates", Abramovitch, R. A., Ed.; Plenum Press: New York, 1982; Vol. 2, Chpt. 3.
5. Bailey, W. F.; Patricia, J. J.; DelGobbo, V. C.; Jarret, R. M.; Okarma, P. J. *J. Org. Chem.* 1985, 50, 1999.
6. t-BuLi (1 equiv) is consumed by formal reaction with the t-BuI generated in the interchange. Although both isobutane and isobutylene have been identified as products of this reaction, the mechanism by which t-BuLi is consumed has not been established.
7. Solutions of t-BuLi in pure n-pentane were prepared by the method of Kamienski and Esmay (*J. Org. Chem.* 1960, 25, 1807) and titrated immediately prior to use (Lipton, M. F.; Sorensen, C. M.; Sadler, A. C.; Shapiro, R. H. *J. Organomet. Chem.* 1980, 186, 155). Commercial samples of "t-BuLi in pentane" were not used in the present study because, regardless of source, they were invariably found to contain a small but significant quantity of methylcyclopentane which, presumably, was present in the pentane solvent used in their preparation.
8. See also: Stein, C. A.; Morton, T. H. *Tetrahedron Lett.* 1973, 4933.
9. The behavior of primary alkyl iodides when treated with t-BuLi should not be interpreted as illustrative of the general metal-halogen interchange reaction. The disparate behavior of alkyl bromides and iodides in reactions with organolithiums has been detailed elsewhere (Ref. 1) and the mechanism of the metal-halogen interchange has been shown to be halogen dependent. See: Bailey, W. F.; Patricia, J. J.; Nurmi, T. T. , accompanying paper in this issue.

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