

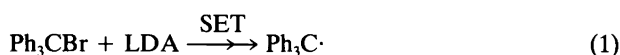
# Competing Radical, Carbanion and Carbene Intermediates in the Reaction of a Primary Alkyl Halide with Lithium Diisopropylamide\*

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Recently we reported evidence for lithium diisopropylamide (LDA) as a one electron donor in its reaction with polynuclear hydrocarbons (e.g. anthracene and perylene), trityl bromide [eqn. (1)] and the cyclizable radical probe, 6-



iodo-5,5-dimethyl-1-hexene, (**1a**).<sup>1</sup> In addition to these results, other groups have reported LDA to be a one electron donor toward heterocyclic compounds,<sup>2</sup>  $\alpha$ -bromo imines<sup>3</sup> and conjugated acetylenes.<sup>4</sup> These results are very intriguing since previously LDA had been used in organic reactions primarily as a strong base.<sup>5</sup> On the other hand, Kowalski<sup>6</sup> and Newcomb<sup>7</sup> proposed the mechanism of reaction of LDA with benzophenone to proceed via a polar mechanism involving hydride transfer from the amide to the carbonyl carbon atoms. It is further known that primary alkyl halides can react with strong bases such as PhLi, PhNa etc. to deprotonate the  $\alpha$ -carbon to form a carbene intermediate<sup>8</sup> and it has been reported that LDA can react with

benzylic halides to form carbenes.<sup>9</sup> Thus there appears to be evidence that LDA can react as a base, a single electron donor and a hydride ion donor.

In an attempt to study the mechanism of reaction of a primary alkyl halide with LDA, we have carried out studies using the model system **1** in which X = I, Br, Cl and OTs [eqn. (2)]. This model system eliminates the unwanted complication of an elimination pathway and greatly lessens the possibility of an S<sub>N</sub>2 pathway so that other potential pathways might be observed. We also used **1** because we have found it to be an excellent probe for a radical intermediate.<sup>10</sup> When we allowed **1a–d** to react with LDA in THF at 0°C, five products **A–E** were formed. The data obtained for the reaction of **1a–d** with LDA in THF at 0°C is recorded in Table 1.

The order of leaving-group ability for polar reactions is I<sup>-</sup> ~ OTs<sup>-</sup> > Br<sup>-</sup> > Cl<sup>-</sup> and for all of the SET reactions in THF that we have studied, it is I<sup>-</sup> > Br<sup>-</sup> > Cl<sup>-</sup> > OTs<sup>-</sup>, an order consistent with a less favourable reduction potential as one proceeds from iodide to tosylate.<sup>11</sup> We now have evidence to support the mechanism below (Scheme 1).

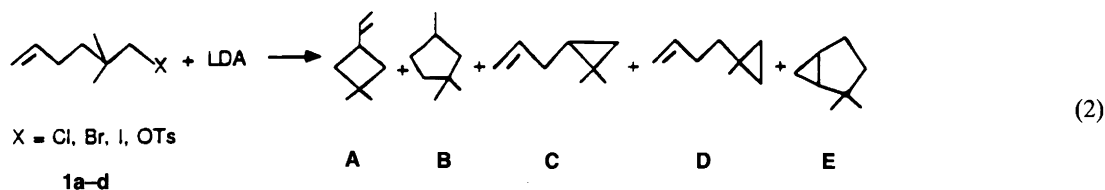
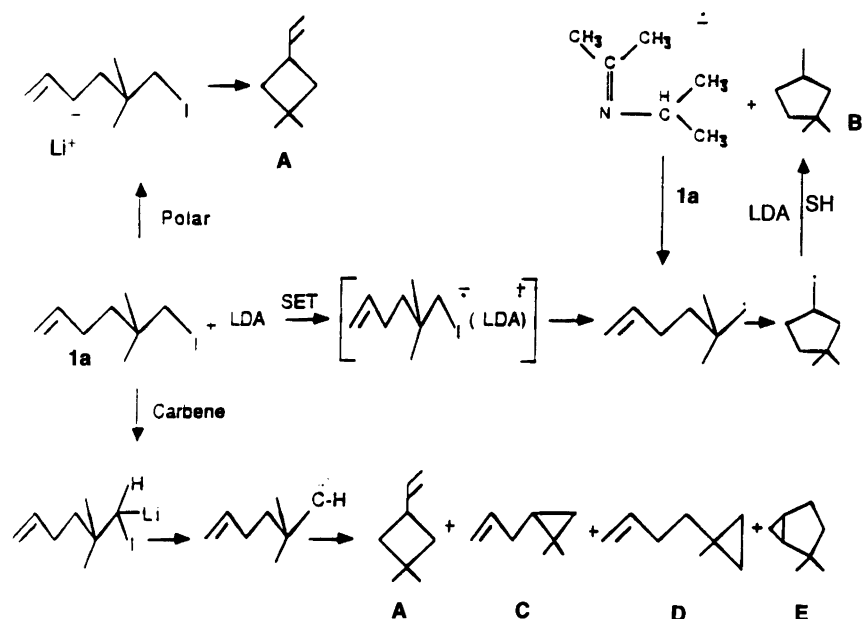


Table 1. Reaction of **1a–d** with LDA in THF at 0°C.

Reaction	Time/h	Recovered RX (%)	Products (%)				
			A	B	C	D	E
I ( <b>1a</b> )	<48	0.0	8.2	48.0	11.3	22.4	10.1
Br ( <b>1b</b> )	72	27.4	19.8	2.1	12.2	31.0	7.5
Cl ( <b>1c</b> )	120	52.6	9.4	0.0	5.6	22.0	10.4
OTs ( <b>1d</b> )	72	99.5	0.0	0.0	0.0	0.0	0.0

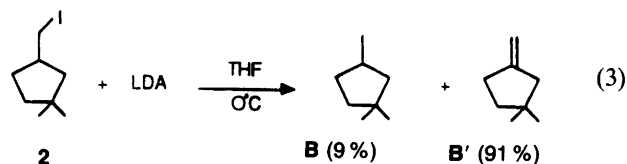
\* Presented as part of a main section lecture at the 32nd IUPAC Congress in Stockholm, Sweden, August 2–7, 1989.



Scheme 1.

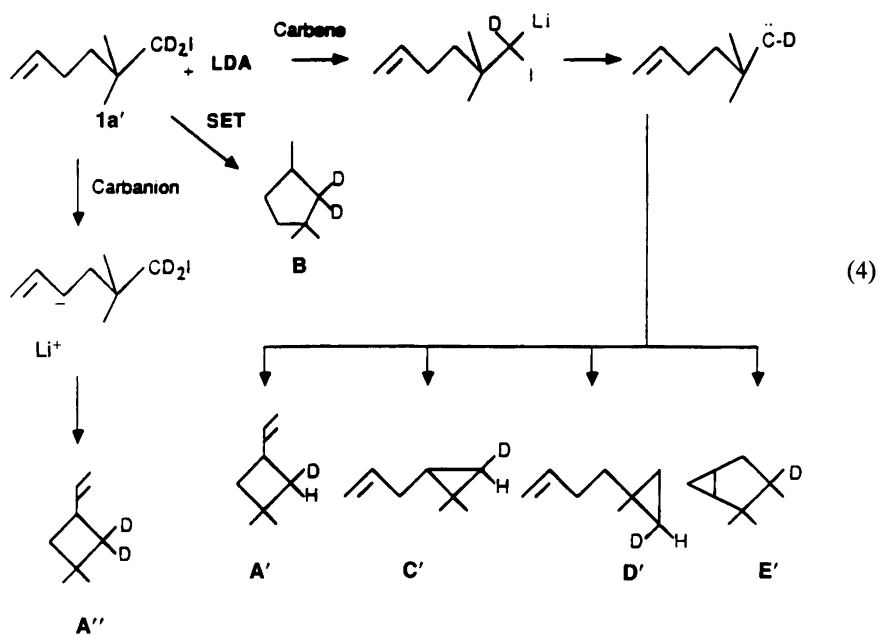
which shows that product **B** is formed via a radical intermediate (involving a radical chain process), products **C**, **D** and **E** are the result of a carbene intermediate, and product **A** is the result of both a carbene and a carbanion intermediate.

Evidence for the formation of **B** via a radical intermediate is based on the following observations: (1) the amount of **B** formed is proportional to the expected reduction potentials of **1a-d**; (2) the amount of **B** decreased when the reaction was carried out in the absence of light whereas the amounts of products **A**, **C**, **D** and **E** remained the same; (3) the amount of **B** decreased when a radical anion scavenger (*p*-dinitrobenzene) and a radical scavenger (*t*-butylnitroxyl radical) were added to the reactions and (4) it is unlikely that **B** was formed by a polar reduction of **2** by LDA in



THF since **B'** was the major product formed in eqn. (3), yet no **B'** was formed in the reaction of **1** with LDA [eqn. (2)].

Evidence for the formation of **A**, **C**, **D** and **E** via a carbene intermediate is based on the following considerations: (1) **A**, **C** and **D** are readily explained by a carbene insertion into the C–H bonds at C3, C4, and insertion into the C–H bonds of the methyl groups at C5, and **E** is the



result of an intramolecular addition to the carbon-carbon double bond of **1** and (2) the reaction of **1a'** with LDA formed **A'**, **B'**, **C'**, **D'** and **E'** with a deuterium content consistent with a carbene pathway [eqn. (4)]. Compounds **C'**, **D'** and **E'** gave 100%  $d_1$ , **B** showed 0%  $d_1$  and 100%  $d_2$ , and **A** showed 10%  $d_1$  (**A'**) and 90%  $d_2$  (**A''**). The 90%  $d_2$  content of **A** can be explained by an isotope effect. Since the C-D bond is stronger than the C-H bond, LDA should have a better chance of abstracting an allylic proton from C3 of **1a'** rather than C3 of **1a**. The resulting lithio compound would then produce **A''** containing two deuterium atoms produced by an intramolecular carbanion displacement of iodide at C6.

The ratio of **A** + **C** + **D** + **E**/**B** is 1.1 for the iodide **1a** and 33.6 for the bromide **1b**. These ratios indicate that for the iodide **1a**, the carbene, radical and carbanion processes occur competitively; however, for the bromide **1b**, which has a less favorable reduction potential than the iodide **1a**, the radical process as a result of SET is much less favorable. When the chloride **1c** was allowed to react with LDA, only the carbene products **A**, **C**, **D** and **E** were formed due to the unfavorable reduction potential of **1c** which makes the formation of **B** by an SET process unlikely.

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## References

1. Ashby, E. C., Goel, A. B. and DePriest, R. N. *J. Org. Chem.* **46** (1981) 2429.
2. Newkome, G. R. and Hager, D. C. *J. Org. Chem.* **47** (1982) 599.
3. Kimpe, N. D., Yao, Z. P. and Schamp, N. *Tetrahedron Lett.* **27** (1986) 1707.
4. Shen, C. and Ainsworth, C. *Tetrahedron Lett.* **20** (1979) 89.
5. (a) House, H. O. *Modern Synthetic Reactions*, 2nd ed., Benjamin, Menlo Park 1972, Chap. 9; (b) Fraser, R. R., Bresse, M. and Mansour, T. S. *J. Chem. Soc., Chem. Commun.* (1983) 620.
6. (a) Kowalski, C., Creary, X., Rollin, A. J. and Burke, M. C. *J. Org. Chem.* **43** (1978) 3101; (b) Kowalski, C., Creary, X., Rollin, A. J. and Burke, M. C. *J. Org. Chem.* **43** (1978) 3101; (c) Kimpe, N. D., Palamareva, M. and Schamp, N. *J. Org. Chem.* **50** (1985) 2993.
7. Newcomb, M. and Burchill, M. T. *J. Am. Chem. Soc.* **106** (1984) 8276.
8. (a) Friedman, L. and Berger, J. G. *J. Am. Chem. Soc.* **82** (1960) 5758; **83** (1961) 492, 500; (b) Kirmse, W. and Doering, W. *Tetrahedron Lett.* **11** (1960) 266.
9. Dougherty, C. M. and Olofson, R. A. *Org. Synth.* **58** (1978) 37; Creary, X. *J. Am. Chem. Soc.* **99** (1977) 7632.
10. Ashby, E. C. and DePriest, R. *J. Org. Chem.* **49** (1984) 3545.
11. Lipshutz, B. H., Wilhelm, R. S., Nugent, S. T., Little, R. D. and Baizer, M. M. *J. Org. Chem.* **48** (1983) 3306.

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