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ELECTRON TRANSFER PROCESSES IN REACTIONS OF LITHIUM DIALKYLAMIDES. USE OF THE N-PROPYLCYCLOBUTYLAMINYL RADICAL RING OPENING AS A PROBE REACTION

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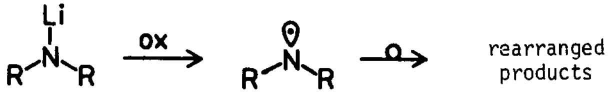
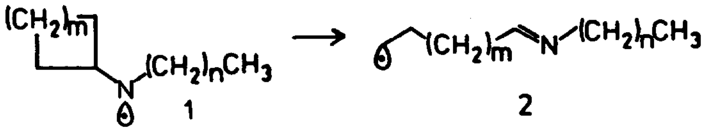
Summary: N-Lithio-N-propylcyclobutylamine has been used as a qualitative mechanistic probe for electron transfer processes in several reactions.

During the last several years evidence has been accumulating that reactions of strong bases and nucleophiles with selected organic substrates can involve an electron transfer step. There is now evidence that ketones,[2] an oxaziridine,[3] alkyl sulfonates,[4] alkyl halides,[5] polycyclic aromatics,[5] and pyridine[6] may react with lithium dialkylamide bases by such an electron transfer process. In each of the studies which led to these conclusions, the reduced products were analyzed. We have initiated a program in which we concentrate on the oxidized products of these reactions, aminyl radicals. If a probe is properly designed the aminyl radical formed by oxidation could undergo a characteristic skeletal rearrangement (Eq 1). The observation of rearranged products would provide qualitative or possibly quantitative evidence which supports an electron transfer process.



(1)

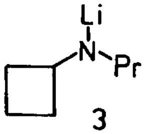
One class of probes which might be employed in Eq 1 is the small ring lithium cycloalkylamides. Ingold has reported the rates of ring opening of aminyl radicals **1**[7] (Eq 2). We have previously reported studies of the thermal stability of the corresponding lithium amides.[8] N-Lithio-N-propylcyclobutylamine (**3**) is stable enough to permit its application as a mechanistic probe at low temperatures in tetrahydrofuran (THF).[9]



1 **2**

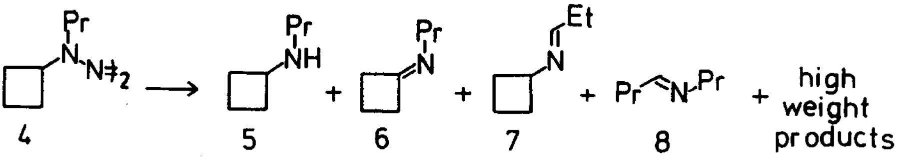
(2)

a: m = 1, n = 2
b: m = 0, n = 3



3

Before we could attempt to use **3** as a probe it was necessary to determine the product distribution from radical **1a**. Toward that end, tetrazene **4**[11] was prepared by conversion of the parent amine to the corresponding hydrazine[11] ($NaNO_2$, H^+; $LiAlH_4$ in THF; 36% overall) and subsequent oxidative coupling[12] (HgO in THF, 57%) to give **4** (bp 123-127 °C, 0.05 Torr). Tetrazene **4** was relatively stable when stored as a dilute (<0.08 M) solution in cyclohexane in the dark at 0 °C. As with other tetrazenes,[13] *neat* tetrazene **4** decomposed rapidly by induced decomposition.



(3)

Eq 3 shows the products which might be expected from decomposition of tetrazene **4**. Yields of products **5-8** resulting from thermal and photochemical decomposition of tetrazene **4** in various solvents are reported in Table 1. Aminyl radicals are poor hydrogen atom abstractors[13] so we had hoped that the ring opening of **1a** would be efficient and that carbon radical **2a** would then abstract a hydrogen atom from solvent to give imine **8**. Although good yields of imine **8** were obtained, it is clear that coupling reactions consumed a large amount of the radical products since good yields of unidentified high weight products were formed in these reactions.[14]

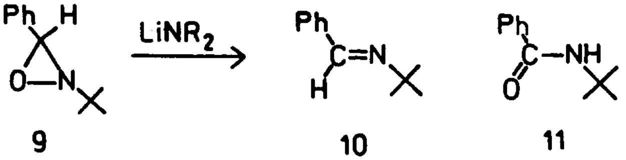
Table 1. Products from Decomposition of Tetrazene **4**.[a]

Solvent	(conditions)	% Yield[b]			
		5	**6**	**7**	**8**
c-C_6H_{12}	(131 °C, 1.7 h)	0	0	0.4	32.4
c-C_6H_{12}	(143 °C, 2.0 h)	0	0	0	38.3
c-C_6H_{12}	(163 °C, 0.6 h)	1.3	0	0	44.6
THF	(135 °C, 2.6 h)	0	0	0	47.8
tetraglyme	(131 °C, 4.5 h)	0	0	0.3	37.7
c-C_6H_{12}	(h , 0.5 h)	17.0	0	9.9	17.0
THF	(h , 0.8 h)	8.6	0	0.4	29.3
tetraglyme	(h , 0.3 h)	15.4	0	3.6	16.1

[a] Solutions (0.06 *M*) of **4** were added to tubes. After several freeze-thaw cycles, the tubes were sealed *in vacuo*. The reaction tubes were heated at the listed temperature or photolyzed (high pressure mercury lamp, Pyrex, 25 °C). The reactions were stopped at various times; the results in the table give conversions at 4-5 half-lifes of **4**. All reactions (except the final one in the table) were repeated; no substantial change in yields was observed.

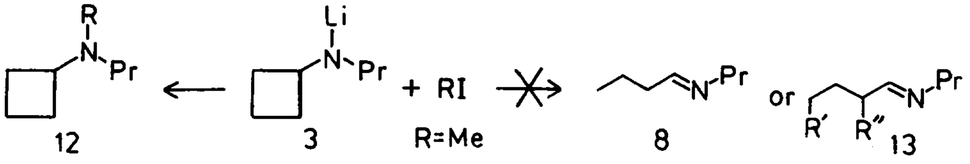
[b] Absolute yields were determined by gc using a nonane standard added immediately after the reaction.

Lithium amide **3** was tested as a mechanistic probe in the reaction with (E)-2-*tert*-butyl-3-phenyloxaziridine (**9**), a compound which appears to react with lithium dialkylamides in part by an electron transfer process that gives imine **10**[3,10] (Eq 4). One-half of an equivalent of oxaziridine **9** was added to 0.1 N **3** in THF at -20 °C. After 30 sec, the reaction mixture was quenched with 10% water in THF. We obtained products **5-8** in 87, 2.6, 6.7, and 2.0% yields, respectively, and from oxaziridine **9** we observed imine **10**, benzaldehyde, and amide **11** in 15, 39, and 24% yields, respectively. In control reactions, (1) the product ratios were unchanged after 0.5 h at -20 °C, and (2) no **8** (<0.1%) was formed when **9** was not added to **3**. From the ratio of reagents and the conservative assumption that all of oxaziridine **9** not converted to amide **11** reacted by an electron transfer process, imine **8** was found in 5% yield relative to the amount of electron transfer. Probe **3** also was also found to test positive for aminyl radical formation in reactions with the thianthrene radical cation at -78 °C giving 11-13% yield of **8**.[16] It is clear that **3** does function as a qualitative probe for an electron transfer pathway, but apparently it cannot provide quantitative information about the extent of such a process.



(4)

Probe **3** was next employed in reactions with weak oxidizing agents; aryl ketones, pyridine, and iodomethane. For each of these species there exists some evidence that an electron transfer process can occur in reactions with lithium dialkylamides, but that evidence is circumstantial.[2,5,6] We found no indication that **3** was oxidized to **1a**. Thus, (1) reactions of **3** with benzophenone at -78 °C or -20 °C gave benzhydrol and imines **6** and **7** but no **8**; (2) reaction of **3** with dimesityl ketone at -78 °C or -20 °C gave no **8**; (3) reaction of **3** with pyridine at -78 °C gave no **8**; and (4) reaction of **3** with iodomethane at -78 °C gave N-alkylated cyclic amine product **12**, but we did not detect **8** or the alkylated imines **13** (R' = CH_3, R" = H; R' = H, R" = CH_3; R' = R" = CH_3). Our results suggest that electron transfer processes involving the lithium amide base **3** are *not* important under these conditions. In the cases where oxidant-derived radical anions have been detected,[2,6] we infer that secondary reactions may have produced these radical anions. Indeed, the formation of benzophenone ketyl in the reaction of benzophenone with lithium dialkylamides by a route not involving electron transfer from the base has recently been implicated in other studies in our laboratory.[17]



In summary, we have demonstrated that the known ring opening of a cyclobutylaminyl radical can be exploited successfully in the mechanistic probe **3**. The detection of imine **8** from reactions of **3** with an oxidant is a qualitative indication of an electron transfer process. For the weak oxidants benzophenone, dimesityl ketone, pyridine and iodomethane, our results suggest that electron transfer reactions with **3** did not occur; for the first three of these substrates our conclusions concerning the viability of electron transfer processes are the opposite of those reached by others who studied the products arising from the oxidants, and it would appear that further mechanistic studies of these reactions are in order.

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