

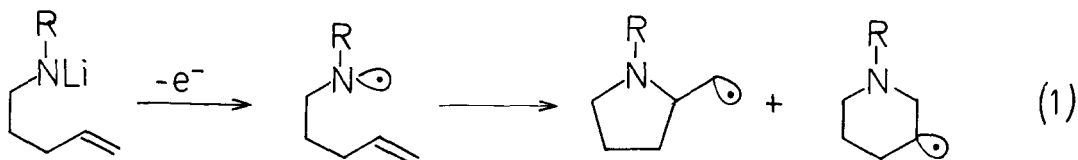
ISOMERIZATION REACTIONS OF LITHIUM N-BUTYL-4-PENTENYLAMIDE

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**Abstract** Lithium N-butyl-4-pentenylamide (**1**) in tetrahydrofuran at 22 °C rearranged smoothly to give a mixture (after protonation) of 1-butyl-2-methylpyrrolidine, formed by an unusual cyclization process, and *cis*- and *trans*-N-butyl-3-pentenylamine, in the presence of 2.0 molar equiv of hexamethylphosphoramide, the total rate of isomerization was accelerated by a factor of 2.5

The potential utility of small ring lithium dialkylamides to serve as mechanistic probes for electron transfer processes in reactions of lithium dialkylamides and the rearrangements of these species were discussed in the accompanying communication. In this communication we present the results of our preliminary studies of lithium N-butyl-4-pentenylamide (**1**), a representative member of another class of potential mechanistic probes for such electron transfer processes. Species such as **1** could undergo the sequence of reactions shown in eq 1 to give, ultimately, cyclized products. Although there is no doubt that analogous carbon-centered 5-hexenyl radicals cyclize,<sup>2</sup> the cyclizations of 4-pentenylaminy radicals, step two in eq 1, is still questionable. Cyclization of the N-propyl-4-pentenylaminy radical (**2**) formed upon thermolysis of the corresponding tetrazine<sup>3,4</sup> has been reported as has cyclization of **2** formed by photolysis of the corresponding N-chloroamine.<sup>5</sup> However, when **2** was prepared by the reaction of the parent amine with photochemically generated *tert*-butoxyl radicals, Maeda and Ingold saw no indication of cyclization in EPR studies at low temperatures,<sup>6</sup> but recent results suggest that there may have been experimental problems in these studies.<sup>7</sup> On balance, we felt that the potential for aminyl radical cyclization warranted a study of the lithium amide **1**.



*N*-Butyl-4-pentenylamine<sup>8</sup> in tetrahydrofuran (THF) was treated with 0.9 molar equiv of *n*-butyllithium in hexane at -78 °C to give lithium amide **1**. When solutions of **1** were warmed to 22 °C and subsequently quenched by the rapid addition of water, we observed that the parent amine had isomerized to give a mixture of 1-butyl-2-methylpyrrolidine (**3**)<sup>9</sup> and *cis*- and *trans*-*N*-butyl-3-pentenylamine (*cis*- and *trans*-**4**)<sup>11</sup>. Kinetic studies in which reaction aliquots were removed periodically and rapidly added to water and the resulting mixtures were analyzed by gc showed that the rearrangements of amide **1** proceeded smoothly. Over 3.5 half-lives at 22 °C, amide **1** in THF (0.10 N) rearranged by first order processes with a total rate constant for disappearance of  $4.7 \times 10^{-4} \text{ sec}^{-1}$  ( $r^2 = 0.9991$ ). When 2.0 molar equivalents of hexamethylphosphoramide (HMPA) per lithium species was added to the reaction mixture at -78 °C, the rate constant for loss of amide **1** at 22 °C was accelerated to  $1.04 \times 10^{-3} \text{ sec}^{-1}$  ( $r^2 = 0.993$ , data was collected over 3.0 half-lives). The percentages of products **3**, *cis*-**4** and *trans*-**4** at representative times during these reactions are given in the Table. The double bond isomerization reactions were accelerated more by the addition of HMPA than was the cyclization reaction.

Table Percentage of amines from the reactions of **1** in THF at 22 °C<sup>a</sup>

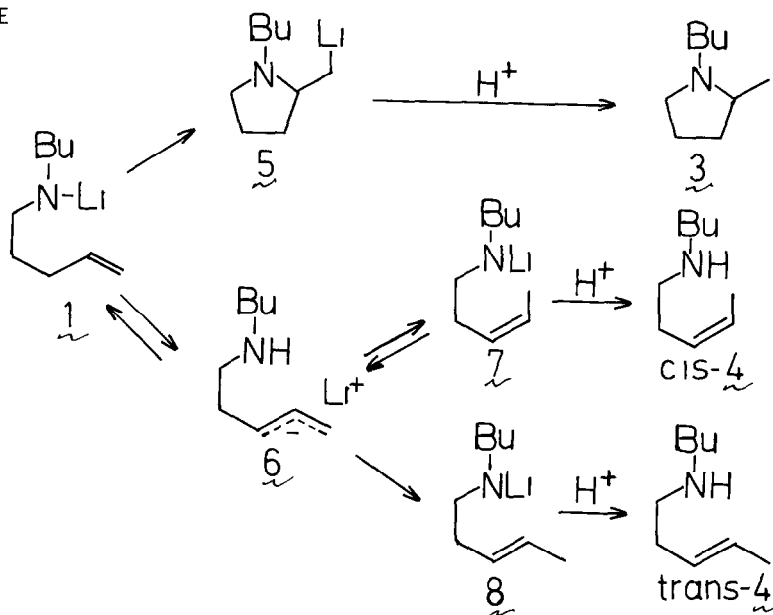
HMPA/Li <sup>+</sup>	time (h)	% Yield <sup>b</sup>				rel % Yield		
		parent amine	<b>3</b>	<i>cis</i> - <b>4</b>	<i>trans</i> - <b>4</b>	<b>3</b>	<i>cis</i> - <b>4</b>	<i>trans</i> - <b>4</b>
0	0.41	51	27	18	4	55	37	8
0	0.81	26	36	32	5	49	44	7
0	2.12	6	48	37	8	52	40	9
2.0	0.15	52	18	24	5	38	51	11
2.0	0.38	23	26	43	9	33	55	11
2.0	0.93	5	31	53	11	32	56	12
2.0	28	2	53	12	28	57	13	30

<sup>a</sup>Lithium amide **1** (0.10 N) in THF was warmed to 22 °C, and aliquots from the reaction mixtures were removed periodically and rapidly added to water.

<sup>b</sup>Absolute yields were determined by gc using an internal standard of *n*-nonane.

The processes in the Scheme can account for the loss of lithium amide **1**. Cyclization of **1** produces a primary organolithium species (**5**) which may deprotonate THF<sup>13</sup> to give **3**. Alternatively, internal deprotonation of **1** would give **6** which can lead to **7** or **8**. The *cis* amide **7** is formed faster than the *trans* amide **8** as would be expected for an internal reprotonation of the allyl anion moiety by the amine portion of **6**. The product distribution at 28 h from the reaction run in the presence of HMPA shows that the formation of **7** from **6** and the formation of **6** from **1** are reversible. From our data we cannot determine whether or not the formation of **8** from **6** is reversible. Control experiments showed that no isomerization of the olefin moiety of the parent amine by *n*-butyllithium occurred before deprotonation of the amine, when solutions of **1** were maintained at -78 °C for several hours and then quenched, we observed no formation of

SCHEME



**3** or **4**, and in the early kinetic points from the 22 °C reactions only small amounts of **4** were present

The cyclization of lithium amide **1** to **5** is somewhat unusual. Although the addition of alkali metal amides to dienes or styrenes are well known,<sup>14</sup> we are aware of only one report of cyclizations involving additions of a lithium amide moiety to an olefin to give an unstabilized carbanion, those cyclizations involved transannular bond forming reactions across seven- and eight-membered rings with bond formation to the substituted carbons of 1,1-diphenylethylene moieties and may have occurred by radical chain processes.<sup>15</sup> The cyclization of **1** to **5** could involve an oxidation--radical closure--reduction sequence or a two-electron, nucleophilic addition, the reproducibility of the rates of rearrangement of **1** in different reactions in which we took no unusual precautions to exclude traces of oxygen (the reactions were run under argon) and the smooth kinetic behavior we observed suggests to us that the mechanism of cyclization does not involve a radical chain process.

Although the cyclization reaction of **1** to give product **3** was unexpected, the rate of this reaction and those of the olefin isomerization reactions of **1** are too slow to cause problems in the application of **1** as a mechanistic probe since most reactions of hindered lithium dialkylamide bases are rapidly completed at lower temperatures than 22 °C. In fact, when reactions of hindered amide bases are observed to occur over hours or days at room temperature, it is quite possible that secondary reactions involving products from the reaction of the amide base with the ethereal solvent are important. Thus, species such as **1** should serve as useful mechanistic probes for electron transfer processes in reactions of hindered dialkylamide bases provided that the radical cyclizations are fast.

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- 8) Prepared by the following sequence treatment of allylmagnesium chloride with ethylene oxide, tosylation in pyridine (56%), reaction with butylamine (71%)
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- 11) cis-4 was purified by preparative gc (Carbowax 20M) and was identified by  $^1\text{H}$  NMR Spectroscopy (200 MHz) employing decoupling experiments. Consistent with expected values,<sup>12</sup> cis-4 exhibited the following coupling constants to the vinyl protons  $^3\text{J}_{\text{H-H}} = 10.8$  Hz and  $^4\text{J}_{\text{H-H}}$ 's = 1.6 and 1.3 Hz for the methyl and methylene groups, respectively. trans-4 has been tentatively identified by the similarity of its gc retention time to that of cis-4 and by  $^1\text{H}$  NMR spectroscopy of an impure sample collected by preparative gc
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