lithium and a single amide, an equilibrium constant for formation of the complex of 300 ± 50 can be obtained from the data. The most straightforward possibility is that **4** is converted directly to **5**; however, it is also possible that **5** could be formed by reaction of **3** with a small amount of *sec*-butyllithium monomer in equilibrium with the tetramer.[10] Over a range of 0.03–0.24 M *sec*-butyllithium at 0.0048 M **3**, the observed rate constant decreases exponentially, a result that suggests that neither of these processes by themselves provides a complete description of the reaction.[11]

The present results provide the first direct observation of, and quantitative information about, an initially formed complex in the α' metalation of amides. To the best of our knowledge, this is the first such study of a directed lithiation, and the approach should be applicable to a number of systems. A reasonable inference is that similar complexes may be observed in other directed lithiations, including α' metalations of other amides,[12] ortho metalations of aromatic amides,[13] β' metalations of α,β-unsaturated amides,[14] and α' metalations of amidines.[15,16]

Acknowledgment. We are grateful to the National Science Foundation and the National Institute of Health for support of this work. We also thank Professor A. I. Meyers for informing us of his related work, which appears in the following communication.

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[10] For example, the addition of methyllithium to a ketone is 0.25 order in methyl lithium. Smith, S. G.; Charbonneau, L. F.; Novak, D. P.; Brown, T. L. *J. Am. Chem. Soc.* **1972**, *44*, 1059. See: Schlosser, M. "Struktur and Reaktivität Polarer Organometalle"; Springer Verlag: Berlin, 1973; pp 129–38, for other cases.

[11] While such a result might be explained by some combination of the two pathways, among other possibilities, we prefer not to speculate until more information is available.

[12] Reitz, D. B.; Beak, P.; Tse, A. *J. Org. Chem.* **1981**, *46*, 4316 and references cited therein.

[13] Beak, P.; Brown, R. A. *J. Org. Chem.* **1982**, *47*, 34. Beak, P.; Snieckus, V. *Acc. Chem. Res.* **1982**, *15*, 306.

[14] Kempf, D. J.; Wilson, K. D.; Beak, P. *J. Org. Chem.* **1982**, *47*, 1610.

[15] Meyers, A. I.; TenHoeve, W. *J. Am. Chem. Soc.* **1980**, *102*, 7125. Meyers, A. I.; Rieker, W. F.; Fuentes, L. M. *Ibid.*, following paper in this issue.

[16] A recent study of deuterium isotope effects by Miller and Saunders suggests such species are important in enolate formation from ketones. Miller, D. J.; Saunders, W. H., Jr. *J. Org. Chem.* **1982**, *47*, 5041.

Initial Complex and the Role of Solvent in Metalations Leading to Dipole-Stabilized Anions

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The use of dipole-stabilized anions as a synthetic tool for forming C–C bonds is now well documented[1] although there is no experimental evidence to support the postulated pathway. The proposal that there is coordination between the lithium base and the heteroatom necessary for carbanion formation has now been verified by infrared spectroscopy using a stopped-flow technique.[2] In this fashion the equilibrium constant for the complex and the rate constant leading to metalation have been measured. Furthermore, a recent report describes, via X-ray and NMR data, the intramolecular chelation of the heteroatoms with the lithium as well as the intermolecular chelation with solvent molecules.[3] However, this study does not address processes *prior* to formation of the carbanion.

Scheme I

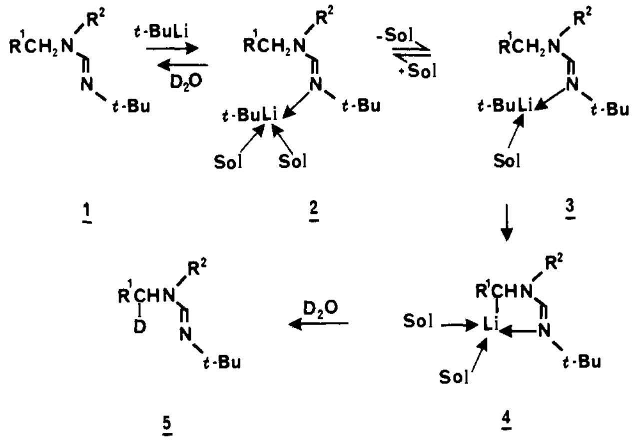
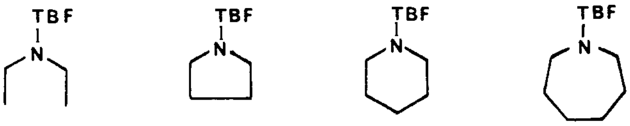


Table I. Metalation–Deuteration of *tert*-Butylformamidines (TBF) in Various Solvents[a]



solvent	D, %	D, %	D, %	D, %
DME	0.05[b]	12.8[b]	0.05[b]	1.0[c]
THF	14.5	98.6	25.8	69.4
DMTHF	54.1	94.6	91.0	93.9
ether	64.2	95.6	92.2	94.4

[a] Isolated yields of *tert*-butylformamidines (TBF) were 60–99%. Reactions performed in 0.5 M solutions at -25 ± 5 °C for 20 min and then quenched with D_2O. Percent deuteration was determined by mass spectroscopy (ratio of M^+ and $M + 1$). [b] A white to light yellow solid appeared at −25 °C, prior to D_2O addition. [c] A clear viscous oil separated at −25 °C prior to addition of D_2O.

We now report the direct observation of complex **2** (Scheme I), which precipitates from solution, and infrared data that corroborate the structure of the complex. We also describe the critical role of various solvents necessary for metalation to **4**. The formamidines **1** (0.5 M in solvent) when treated with an equimolar amount of *t*-BuLi at −25 °C are known to give carbanions that alkylate or deuterate smoothly to **5**.[1c] A series of formamidines derived from secondary amines (Table I) were subjected to treatment with *tert*-butyllithium in various solvents and gave widely variable yields of deuterium incorporation on quenching with D_2O. As seen from the table, ether and 2,5-dimethyltetrahydrofuran (DMTHF)[4] gave good to excellent yields of the α-D compounds, whereas THF allowed efficient deuteration for the pyrrolidine and the hexahydroazepine derivatives. Conversely, dimethoxyethane (DME) gave poor to virtually no deuterium incorporation on D_2O quench. Thus addition of *tert*-butyllithium to DME solutions of all the amine formamidines in Table I resulted in a light-colored powdery precipitates (a viscous oil in the case of the azepine), which when quenched with D_2O, provided very low levels of D incorporation.

Verification of the lack of formamidine metalation was further found when benzaldehyde was added to the viscous oil designated as complex **2**. Isolation of the reaction products provided benzyl alcohol and benzyl benzoate (~50%) along with starting azepine formamidine. Furthermore, when this reaction was performed in THF, an 83% yield of the expected carbinol amine (from the

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[1] Deprotonation leading to carbanions adjacent to nitrogen have been generated via (a) amides: Beak, P.; Reitz, D. B. *Chem. Rev.* **1978**, *78*, 275. Beak, P.; Brown, R. A. *J. Org. Chem.* **1982**, *47*, 34. (b) Nitrosamines: Seebach, D.; Enders, D. *Angew. Chem., Int. Ed Engl.* **1975**, *14*, 1101. (c) Formamidines: Meyers, A. I.; Hellring, S. *J. Org. Chem.* **1982**, *47*, 2229 and earlier references cited.

[2] Al-Aseer, M.; Beak, P.; Hay, D.; Kempf, D. J.; Mills, S.; Smith, S. G. *J. Am. Chem. Soc.*, preceding paper in this issue.

[3] Jastrzebski, T. B. H.; van Koten, G.; Konijn, M.; Stam, C. H. *J. Am. Chem. Soc.* **1982**, *104*, 5490.

[4] Aldrich Chemical Co.

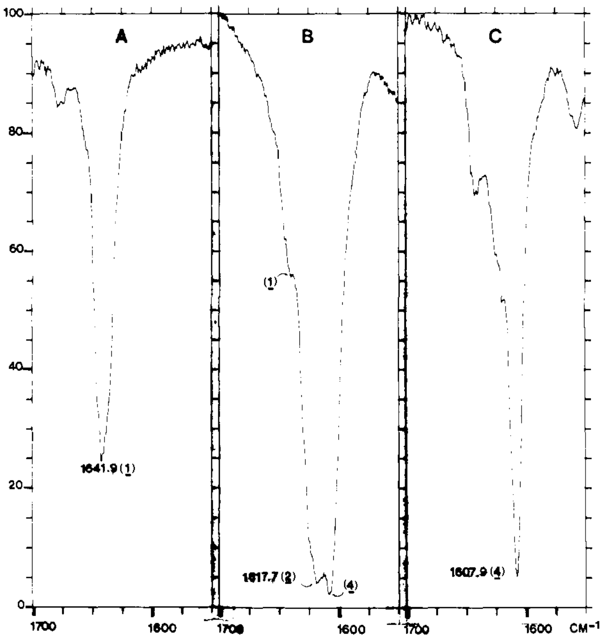

Figure 1. IR spectra (C=N stretch) of *N'-tert*-butylhexahydroazepine formamidine: (A) formamidine in THF; (B) formamidine in THF with *t*-BuLi at room temperature (*t* = 0 min); (C) formamidine in THF with *t*-BuLi at room temperature (*t* = 15 min).

α-amino carbanion and benzaldehyde in a 1:1 erythro–threo ratio) was obtained. Thus, in DME, the complex **2** proceeded to give a normal Cannizzaro reaction between benzaldehyde and *t*-BuLi. In fact, the exact same results were obtained in DME, in the absence of the azepine formamidine.[5,6]

The other solvents depicted in Table I furnished clear, lightly colored solutions when the formamidines were treated with *tert*-butyllithium. The formation of the precipitates (in DME) and their lack of D incorporation indicate strongly that these species are complexes (**2**) that involve only formamidine, the base, and solvent. The unique behavior of DME is attributed to its bidentate nature, which forms a very stable complex and does not allow dissociation to **3** which exposes one of the lithium sites of coordination. When the latter occurs, metalation ensues leading to carbanion **4**. This premise is reinforced by the behavior of the other solvents in Table I. Both ether and DMTHF are sterically encumbered ligands that form weaker solvates thus allowing dissociation (**2** to **3**) and ultimately metalation. The lower rates of metalation in THF for the diethyl- and piperidinylformamidines probably reflect entropic factors.[7]

The formation of complex **2** and the resulting carbanion **4**, except in DME, was also observable in the infrared. The salient features are given in Figure 1, which shows the behavior of the formamidine of hexahydroazepine. Thus, the C=N stretch for the formamidine in THF shows a band at 1641.9 cm^{-1} (curve A), and a new band appears at 1617.7 cm^{-1} <1 min after addition of *t*-BuLi (curve B) along with another band at 1607.9 cm^{-1} due to the carbanion. After 15 min, the complex at 1617.7 cm^{-1} is virtually gone, leaving only the carbanion at 1607.9 cm^{-1} (curve C).[8] In DME the addition of *t*-BuLi to the azepine formamidine after removal of solvent gave a viscous oil[6] that exhibited only the *t*-BuLi–formamidine complex **2** as a borad band at 1636 cm^{-1} but no carbanion band at lower wavenumbers. This spectral behavior for formamidines is in good agreement[2] with the absorptions of hindered tertiary amides (1650 cm^{-1}), *sec*-butyllithium-complexed amides (1625 cm^{-1}), and the α-carbanions derived from these amides (1588 cm^{-1}).[2]

Table II. Metalation of Piperidine-TBF in Ether-THF Mixtures[a]

ether, %	10	20	35	50	80	90
THF, %	90	80	65	50	20	10
D, %[b]	32.2	43.4	53.4	85.6	94.4	97.7

[a] Reactions performed at −25 ±5 °C for 20 min using 1.1 equiv of *t*-BuLi and quenching with D_2O. [b] Determined by mass spectroscopy.

Finally, to further support the premise that dissociation of the complex is necessary prior to metalation (**2** to **3**), the piperidine formamidine was treated with *t*-BuLi at −25 °C for 20 min using different ratios of ether and THF (Table II). The dramatic increase in D incorporation on going from 10% ether–THF to 90% ether–THF argues strongly for the poorer ligand properties of ether (thus greater dissociation to **3**) as compared to THF.

The observations reported here coupled with those obtained by Beak are consistent with the notion of a complex prior to metalation; this process may be halted or allowed to proceed depending on the solvents employed. This selectivity will undoubtedly find use in syntheses involving dipole-stabilized anions.

Acknowledgment. We are grateful to the National Science Foundation for support of this work and to the National Institutes of Health for a postdoctoral fellowship (to L.M.F.). Warm thanks are due to Professor J. R. Norton, Jeffrey M. Sullivan, and Bruce D. Martin for their infrared capabilitities and assistance. Finally, we acknowledge helpful discussions with Professor Peter Beak and his kind willingess to delay his paper so that we could publish simultaneously.

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(5) When a 0.5 M *t*-BuLi solution in DME was added (−78 to −25 °C) to benzaldehyde, quenched, and worked up, there was isolated (~50%) a 3:1 ratio of benzyl alcohol and benzyl benzoate.

(6) Additional evidence for complexed *t*-BuLi in **2** was also gathered by titration (*sec*-BuOH, phenanthroline as indicator) and showed roughly 40% *t*-BuLi present after 20 min at −25 °C.

(7) All reactions were run for 20 min. For longer reaction time with *t*-BuLi, much higher deuteration levels were achieved.

(8) The carbanion band in Figure 1 (C) was verified by D_2O quench of the spectrum sample furnishing the α-D azepine formamidine in 70% yield.

Tetralithiotetrahedrane: Is It a Minimum?[†]

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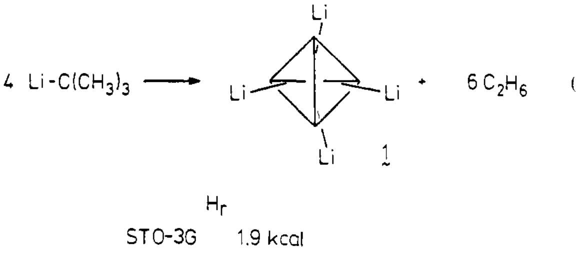
Recent quantum mechanical calculations have suggested that lithiocarbons possess structures having no precedent in hydrocarbon chemistry.[1,2] Probably the most striking of the unusual structures proposed for lithiocarbons are those of the tetralithiotetrahedranes. Schleyer and co-workers have found that calculations favor the face-lithiated tetralithiotetrahedrane, **1**, over the classical corner-lithiated tetralithiotetrahedrane by 65.2 kcal at the STO-3G level.[3] Although **1** is the lowest energy tetralithiotetrahedrane, other C_4Li_4 isomers lie lower in energy.[3] Using eq 1, Schleyer and co-workers suggested that **1** possesses little or



(1)

[†] This work was conducted under the auspices of the U.S. Department of Energy.

(1) A complete list of references would be too long to list here; the papers contained in ref 2, however, provide extensive citations.

(2) (a) Jemmins, E. D.; Chandrasekhar, J.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1979**, *101*, 2848-2856. (b) Kos, A. J.; Schleyer, P. v. R. *Ibid.* **1980**, *102*, 7928-7929. (c) Apeloig, Y.; Clark, T.; Kos, A. J.; Jemmins, E. D.; Schleyer, P. v. R. *Isr. J. Chem.* **1980**, *20*, 43-50. (d) Kos, A. J.; Jemmins, E. D.; Schleyer, P. v. R.; Gleiter, R.; Fischbach, U.; Pople, J. A. *J. Am. Chem. Soc.* **1981**, *103*, 4996-5002.

(3) Rauscher, G.; Clark, T.; Poppinger, D.; Schleyer, P. v. R. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 276-278.

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