$$K_2 = \frac{(OD_0 - OD_\infty)}{OD_\infty[MeO^-]}$$

In the case of the cation **1a**, owing to the absorbance contribution of the 2*H* adduct **1c**. the observed OD_∞ value (OD_∞^{obsd}) must be corrected by the equation

$$OD_\infty = \frac{OD_\infty^{obsd}\epsilon_{1a} - OD_0\epsilon_{1c}}{\epsilon_{1a} - \epsilon_{1c}}$$

where ϵ_{1a} and ϵ_{1c} are the molar absorbances for **1a** and **1c** at λ = 330 nm, respectively. The buffers used were triethylamine/triethylammonium (pK_a = 10.88)[31] for cations **2a**-**7a** and chloroacetic acid/chloroacetate (pK_a = 7.7)[40] for cations **1a** and **2a**. The methoxide ion concentration of each buffer was calculated from the methanol autoprotolysis constant (pK_s = 16.92 at 25 °C).[41] The K_2 value for the cation **7a** was also obtained with diluted solutions of sodium methoxide ([MeO^-] ~ 10^{-4} to 10^{-3} M). The ionic strength was always lower than 2×10^{-3} M. The concentration of the substrates was in the range (1-4) $\times 10^{-5}$ M. The absorbance measurements were carried out with Teflon-stoppered 1-cm quartz cells, with the exception of cations **2a** (with triethylamine/triethylammonium buffer) and **3a** for which 10-cm quartz cells were used.

(40) Clare, B. W.; Cook, D.; Ko, E. C. F.; Mac, Y. C.; Parker, A. J. *J. Am. Chem. Soc.* **1966**, *88*, 1911.
(41) Koskikallio, J. *Suom. Kemistil. B* **1957**, *30*, 111.

Note Added in Proof. M.L.D.V., G.D., and G.E. remember with great sorrow the sudden decease of their inspiring teacher Prof. Gabriello Illuminati.

Acknowledgment. We wish to thank Prof. C. A. Bunton and Prof. F. Stegel for criticisms and suggestions, G. Frachey for the technical assistance in NMR measurements, and the Servizio di Microanalisi, Area della Ricerca di Roma del C.N.R., for elemental analyses.

Supplementary Material Available: Tables S1-S8 summarizing all the kinetic measurements (4 pages). Ordering information is given on any current masthead page.

Solid-State and Solution Studies of Lithiated 2-Carbomethoxycyclohexanone Dimethylhydrazone and Lithiated Cyclohexanone Phenylimine

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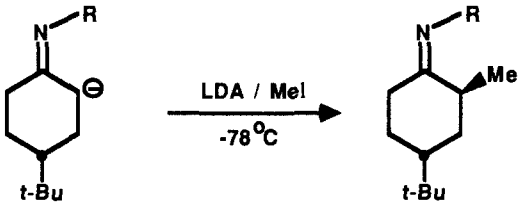
Abstract: Treatment of 2-carbomethoxycyclohexanone dimethylhydrazone with lithium diisopropylamide as a hydrocarbon solution afforded the corresponding lithiated hydrazone as a tetrahydrofuran solvate **1**. An X-ray crystallographic structure determination showed **1** to be dimeric in the solid state. Solution molecular weight and spectroscopic studies in aromatic hydrocarbon solvents uncovered a dissociative process involving either monomer-dimer equilibrium or solvent dissociation. Treatment of cyclohexanone phenylimine with lithium diisopropylamide in hydrocarbon solution afforded the corresponding lithiated derivative as the diisopropylamine solvate **2**. An X-ray crystallographic structure determination showed **2** to exist as a dimer with significant disorder in the cyclohexenyl and phenyl moieties. Lithium-carbon contacts of the η^3-azaallyl type were not observed. ^{6}Li and ^{13}C NMR studies showed **2** to exist as a 2:1 mixture of two rapidly equilibrating forms. By titration of the corresponding solvent-free anion ($\mathbf{2}_{solvent\text{-}free}$) with diisopropylamine, the two species were shown to be bis-solvated dimers in close analogy to the solid-state structure. The structures are discussed in light of the stereochemistry of imine alkylation and the syn effect of lithiated imines.

We became interested in the mechanism of the alkylations of metalated Schiff's bases (azaallyllithiums).[1,2] Although on first inspection the C=N-R moiety and C=O ketone carbonyl group appear to be interchangeable, studies by Corey, Enders, Fraser, and others uncovered some notable differences in the alkylation stereoselectivities.[3,4] For example, metalated Schiff's bases derived from conformationally anchored cyclohexanones exhibit axial alkylation selectivities of a significantly greater magnitude than those of the corresponding ketone enolates (eq 1).[5] In the specific case of dimethylhydrazone alkylation, the axial selectivities are sensitive to substituents on the carbanionic carbon. Cyano- and (methylthio)-substituted lithiated hydrazones alkylate with high axial selectivities. However, the corresponding carbomethoxy-substituted derivative exhibits a lower selectivity more characteristic of ketone enolates. Equally intriguing is the propensity of the 3- and 6-substituted lithiated cyclohexanone dimethylhydrazones to alkylate from the *more* hindered face.[1]

(1) Collum, D. B.; Kahne, D.; Gut, S. A.; DePue, R. T.; Mohamadi, F.; Wanat, R. A.; Clardy, J.; Van Duyne, G. *J. Am. Chem. Soc.* **1985**, *106*, 4865.
(2) Wanat, R. A.; Collum, D. B. *J. Am. Chem. Soc.* **1985**, *107*, 2078.
(3) Reviews of the chemistry of metalated Schiff's bases: (a) Hickmott, P. W. *Tetrahedron* **1982**, *38*, 1975. (b) Enders, D. In *Current Trends in Organic Synthesis*; Nozaki, H., Ed.; Pergamon: New York, 1983. (c) Whitesell, J. K.; Whitesell, M. A. *Synthesis* **1983**, 517. (d) Fraser, R. R. In *Comprehensive Carbanion Chemistry*; Elsevior: New York, 1980.
(4) The nitroso derivatives of 4-*tert*-butylpiperidines exhibit high alkylation stereoselectivities that seem to imply a close mechanistic relationship to lithiated Schiff's base alkylations (cf. ref 3d).
(5) Huff, B. J. L.; Tuller, F. N.; Caine, D. *J. Org. Chem.* **1969**, *34*, 3070. House, H. O.; Umen, M. J. *J. Org. Chem.* **1973**, *38*, 1000. Howe, R.; McQuillin, F. J. *J. Chem. Soc.* **1958**, 1194. Kuwajima, I.; Nakamura, E. *J. Am. Chem. Soc.* **1975**, *97*, 3257. Djerassi, C.; Osiecki, J.; Eisenbraun, E. J. *J. Am. Chem. Soc.* **1961**, *83*, 4433. House, H. O.; Tefertiller, B. A.; Olmstead, H. D. *J. Org. Chem.* **1968**, *33*, 935. Kuehne, M. E. *J. Org. Chem.* **1970**, *35*, 171. Kuwajima, I.; Nakamura, E.; Shimizu, M. *J. Am. Chem. Soc.* **1982**, *104*, 1025.

0002-7863/86/1508-3415$01.50/0



(1)

> 95% axial

Elegant spectroscopic studies by Bergbreiter, Fraser, Newcomb, Enders, and others have elucidated many structural details of azaallyllithiums.[3] However, the origins of the surprising alkylation selectivities and the structural or electronic differences between lithium enolates and lithiated hydrazones that cause such divergent reactivities have remained obscure. Our studies of lithiated hydrazone crystal structures, molecular weights, alkylation aggregation effects, and solution kinetics led to a model to explain the empirical observations.[2]

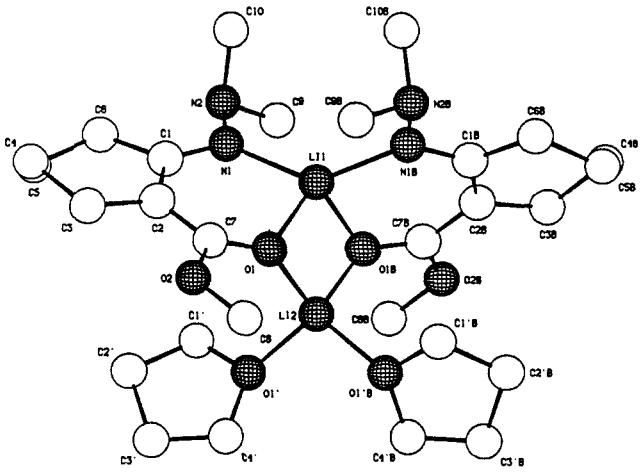
To further understand the structures of azaallyllithiums and their relationships to the corresponding enolates, we have investigated the solid-state and solution structures of lithiated cyclohexanone phenylimine–diisopropylamine solvate and lithiated 2-carbomethoxycyclohexanone dimethylhydrazone–tetrahydrofuran solvate.[6]

Results and Discussion

Molecular Structure of [Li(2-carbomethoxycyclohexanone dimethylhydrazone)·THF]$_2$ (1). Treatment of 2-carbomethoxycyclohexanone *N*,*N*-dimethylhydrazone with lithium diisopropylamide in THF/hexane solution afforded the corresponding lithiated derivative **1** as a colorless crystalline solid. Figure 1 is a computer generated perspective drawing of the X-ray crystal structure of **1**. Selected bond distances are listed in Table I. In the solid-state dimeric structure, a crystallographic twofold axis relates the two halves of the molecule. The two Li's are on the twofold axis and are separated by 2.61 Å. The closest contacts around the Li's are Li1–N1, 2.023 Å; Li1–O1, 1.919 Å; Li2–O1, 1.927 Å; and Li2–O_{THF}, 1.929 Å. The coordination geometries around both Li's are approximately tetrahedral. The tetrahedron about Li1 is slightly flattened with an N1–Li1–N1′ angle of 137°. Some bond distances include N1–C1, 1.305 Å; C1–C2, 1.453 Å; and C2–C7, 1.386 Å. The N1–C1–C2–C7 torsional angle is −16° with C2 planar within experimental error.

Solution Structure of 1: NMR and Molecular Weight Studies. The proton noise decoupled ^{13}C NMR spectrum of organolithium **1** (toluene-d_8, 25 °C) exhibited 10 sharp resonances consistent with a single species (see Experimental Section). When the probe was sequentially cooled to −93 °C, no fluctional processes deriving from solvent exchange or aggregate equilibration could be frozen out. (The single resonance corresponding to the NMe_2 moiety broadened considerably at low temperatures relative to the other resonances.) In the presence of 3.0 equiv of added tetrahydrofuran (THF), exchange of free and coordinated THF was fast on the NMR time scales at all temperatures. The ^7Li NMR spectrum of **1** in toluene-d_8 at −85 °C showed a broad resonance ($\Delta\nu_{1/2}$ = 35 Hz) centered at 0.26 ppm relative to 0.3 M LiCl in MeOH.

The corresponding ^6Li-labeled material (**1**-^6Li) was prepared from 99.5% *n*-Bu^6Li in the hope that improved resolution due to the low quadrupolar moment of ^6Li would increase the probability of observing ^6Li–^{13}C and ^6Li–^6Li coupling.[7,8] The ^{13}C NMR spectrum of **1**-^6Li showed no sign of ^6Li–^{13}C coupling at −93 °C. At 20 °C, the ^6Li NMR spectrum **1**-^6Li showed a sharp singlet



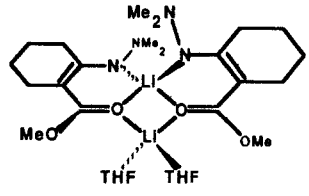


Figure 1. X-ray crystal structure of dimeric lithiated 2-carbomethoxycyclohexanone dimethylhydrazone THF solvate **1**. Hydrogens have been calculated but omitted for clarity.

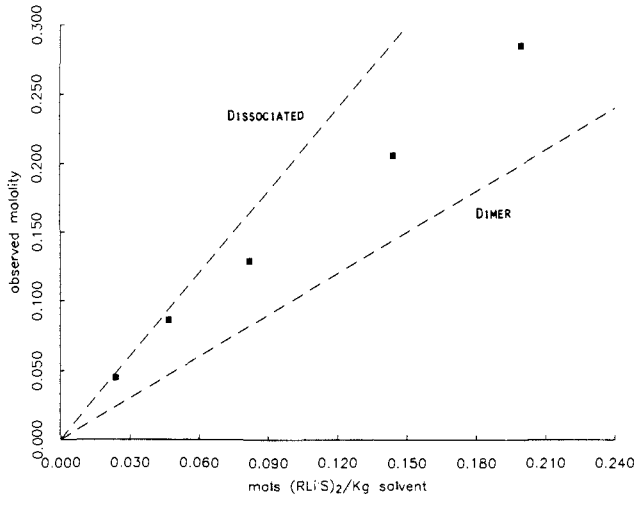


Figure 2. Observed molality measured as a function of the concentration of dimeric **1** in benzene. The dashed lines (---) represent calculated plots if **1** dissolved with and without dissociation.

Table I. Selected Bond Distances for Lithiated Hydrazone **1**

C1–C2	1.453 (5)	C8–O2	1.427 (6)
C1–C6	1.509 (6)	C9–N2	1.409 (6)
C1–N1	1.305 (5)	C10–N2	1.434 (7)
C2–C3	1.509 (6)	N1–N2	1.452 (5)
C2–C7	1.386 (5)	O*–C1*	1.418 (6)
C3–C4	1.503 (7)	O*–C4*	1.413 (7)
C4–C5	1.470 (7)	C1*–C2*	1.512 (11)
C5–C6	1.514 (7)	C2*–C3*	1.431 (12)
C7–O1	1.262 (4)	C3*–C4*	1.446 (11)
C7–O2	1.367 (5)		

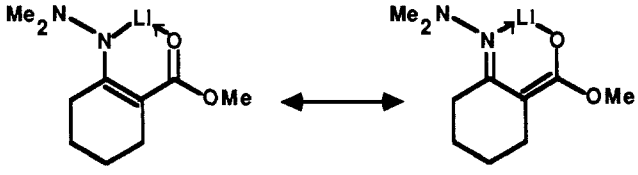
(6) Reviews of structural and mechanistic organolithium chemistry: Seebach, D. In *Proceedings of the Robert A. Welch Foundation Conferences on Chemical Research XXVII*; 1984, p 93. Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: New York, 1974; Chapter 1. Wardell, J. J. In *Comprehensive Organometallic Chemistry*; Stone, F. G. A.; Wilkinson, G.; Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. I. Fraser, R. R. In *Comprehensive Carbanion Chemistry*; Buncel, E., Durst, T., Eds.; Elsevior: New York, 1980. Cram, D. J. In *Fundamentals of Carbanion Chemistry*; Academic Press: New York, 1965. Schleyer, P. v. R. *Pure Appl. Chem.* **1984**, *56*, 151. Jackman, L. M.; Lange, B. C. *Tetrahedron* **1977**, *33*, 2737. Brown, T. L. *Pure Appl. Chem.* **1970**, *23*, 447. Streitwieser, A., Jr. *Acc. Chem. Res.* **1984**, *17*, 353.

(7) For the first report of ^6Li NMR spectroscopic studies of alkyllithiums, see: Wehrli, F. *J. Magn. Reson.* **1978**, *30*, 193.

at 1.12 ppm relative to 0.3 M ^{6}LiCl in MeOH. Upon sequential cooling of the probe, only peak broadening could be observed down to −89 °C.

Solution molecular weights were determined cryoscopically in benzene by using a modification of an apparatus described by Seebach that affords molecular weights of standard organic unknowns within 2–5% error.[9] The nonlinear dependence of the measured molality on the concentration of added **1** was consistent with a dissociative equilibrium (Figure 2); extensive dissociation was evident at high dilution. The absence of any coalescences in the ^{13}C NMR spectra down to −93 °C indicated that the equilibrium was fast relative to NMR time scales.[10-12]

We originally proposed that the poor stereoselectivities observed in the alkylations of the carbomethoxy-substituted hydrazones arose from the intervention of chelated structures i, in which π complexation of the lithium counterion to the azaallyl fragment did not occur.[1,2] To this extent, it was gratifying to find that such chelated structures do exist in the solid state as shown in Figure 1. It is also interesting that the −16° N1–C1–C2–C7 torsion angle and the relatively long (1.453 Å) C1–C2 (compared to 1.360 Å for lithiated cyclohexanone dimethylhydrazone[1]) implicate a significant contribution from resonance structure ii. Structure ii is more akin to ester enolates than lithiated hydrazones.



I II

It is not clear, however, whether the dissociation of the dimeric form of **1** that was detected in the molecular weight studies is a monomer–dimer equilibrium or simply dissociation of a molecule of THF from the lithium coordination sphere (eq 2). Additional

$$2\ [RLi\cdot THF] \overset{???}{\rightleftharpoons} [RLi\cdot THF]_2 \overset{???}{\rightleftharpoons} (RLi)_2 THF + THF \qquad (2)$$

studies of the solution structures and alkylation dynamics will be required to define the important structure–reactivity relationships.

Molecular Structure of [Li(cyclohexanone phenylimine)·diisopropylamine]$_2$ (2). Treatment of cyclohexanone phenylimine with lithium diisopropylamide in hexane solution afforded the corresponding lithiated derivative **2** as a crystalline diisopropylamine solvate in a 50% yield. Figure 3 is a computer generated perspective drawing of the final X-ray model of the lithiated imine **2** with the hydrogens omitted for clarity. The molecular unit is composed of a dimer whose two halves are related by a molecular, but noncrystallographic, inversion center. The inversion center is midway between the Li atoms that are separated by 2.53 (3) Å. The Li–N distance of 2.10 Å is similar to those found in closely related dimeric lithium amide structures.[13,14] The structure appears to be disordered in the sense that it is not easy to distinguish the phenyl ring from the cyclohexene ring. This could reflect either a spatial disordering between the phenyl and cyclohexenyl rings (vide infra) or poor definition of the carbon atoms furthest from N7 arising from large thermal vibrations. The average isotropic thermal parameter for the twelve cyclohexenyl

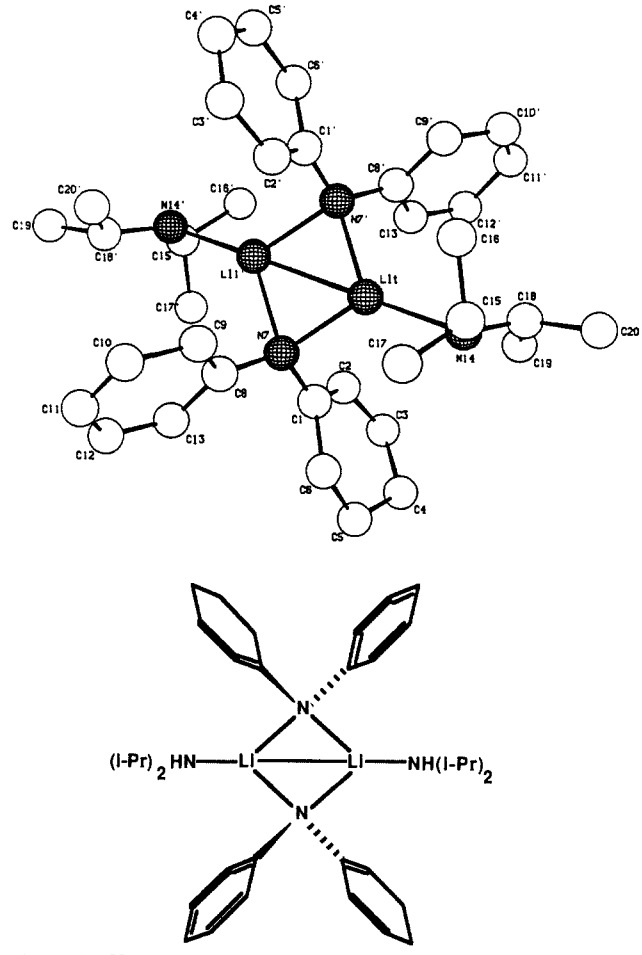


Figure 3. X-ray crystal structure of dimeric lithiated cyclohexanone phenylimine diisopropylamine solvate **2**. Hydrogens have been calculated but omitted for clarity.

Table II. Selected Bond Distances for Lithiated Imine **2**

C1–Li	2.569 (21)	Li–C9′	3.583 (22)
C1–Li′	3.158 (19)	Li–Li′	2.527 (26)
C2–Li	2.992 (22)	C1′–Li′	2.567 (21)
C2–Li′	3.498 (19)	C2′–Li′	2.971 (21)
N7–Li	2.012 (22)	Li–C2′	3.437 (19)
N7–Li′	2.078 (18)	Li–N7′	2.065 (18)
C8–Li	3.189 (23)	N7′–Li′	2.028 (21)
C8–Li′	2.688 (21)	Li–C8′	2.677 (21)
C9–Li	3.578 (23)	C8′–Li′	3.209 (23)
C9–Li′	3.137 (22)	N14′–Li′	2.094 (21)
N14–Li	2.124 (21)	Li–C1′	3.130 (19)

(8) Additional leading references to ^{6}Li NMR spectroscopy, see: (a) Seebach, D.; Hässig, R.; Gabriel, J. *Helv. Chim. Acta* **1983**, *66*, 308. (b) Fraenkel, G.; Fraenkel, A. M.; Geckle, M. J.; Schloss, F. *J. Am. Chem. Soc.* **1979**, *101*, 4745. (c) Najera, C.; Yus, M.; Hässig, R.; Seebach, D. *Helv. Chim. Acta* **1984**, *67*, 1100. (d) Seebach, D.; Gabriel, J.; Hässig, R. *Helv. Chim. Acta* **1984**, *67*, 1083. (e) Rajca, A.; Tolbert, L. M. *J. Am. Chem. Soc.* **1985**, *107*, 2969. (f) Fraenkel, G.; Henrichs, M.; Hewitt, J. M.; Su, B. M.; Geckle, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 3345.

(9) Seebach, D.; Bauer, von W. *Helv. Chim. Acta* **1984**, *67*, 1972.

(10) Comparison of the NMR and molecular weight data must be done cautiously, however, because of the dramatic temperature differences. Negative entropies of solvation often dominate the entropy terms which, in turn, cause the more highly aggregated forms to be favored at higher temperatures.[8a,11] However, for lithiated hydrazone **1**, the dissociative equilibrium does not appear to involve external coordinating ligands. In this case, the dissociated form would be favored at higher temperatures.

(11) McGarrity, J. F.; Ogle, C. A. *J. Am. Chem. Soc.* **1985**, *107*, 1805. See, also: Arnett, E. M.; Maroldo, S. G.; Schriver, G. W.; Schilling, S. L.; Troughton, E. B. *J. Am. Chem. Soc.* **1985**, *107*, 2091. Kimura, B. Y.; Brown, T. L. *J. Organomet. Chem.* **1971**, *26*, 57.

(12) Preliminary studies of the molecular weight of benzene solutions of **1** containing varying quantities of added THF provided evidence of THF association. However, by themselves, these studies provide little information about the actual species being additionally solvated.

(13) Dimeric lithium amides: Lappert, M. F.; Slade, M. J.; Singh, A.; Atwood, J. L.; Rogers, R. D.; Shakir, R. *J. Am. Chem. Soc.* **1983**, *105*, 302. Engelhardt, L. M.; May, A. S.; Raston, C. L.; White, A. H. *J. Chem. Soc., Dalton Trans.* **1983**, 1671. Seebach, D.; Bauer, W.; Hansen, J.; Laube, T.; Schweizer, W. B.; Dunitz, J. D. *J. Chem. Soc., Chem. Commun.* **1984**, 853. Cetinkaya, B.; Hitchcock, P. B.; Lappert, M. F.; Misra, M. L.; Thorne, A. J. *J. Chem. Soc., Chem. Commun.* **1984**, 148.

(14) For representative examples and leading references to other structurally characterized N-lithiated species see: Fjeldberg, T.; Hitchcock, P. B.; Lappert, M. F.; Thorne, A. J. *J. Chem. Soc., Chem. Commun.* **1984**, 823. Power, P. P.; Xiaojie, X. *J. Chem. Soc., Chem. Commun.* **1984**, 358. Barr, B.; Clegg, W.; Mulvey, R. E.; Snaith, R. *J. Chem. Soc., Chem. Commun.* **1984**, 79. *Ibid.* **1984**, 226. *Ibid.* **1984**, 469.

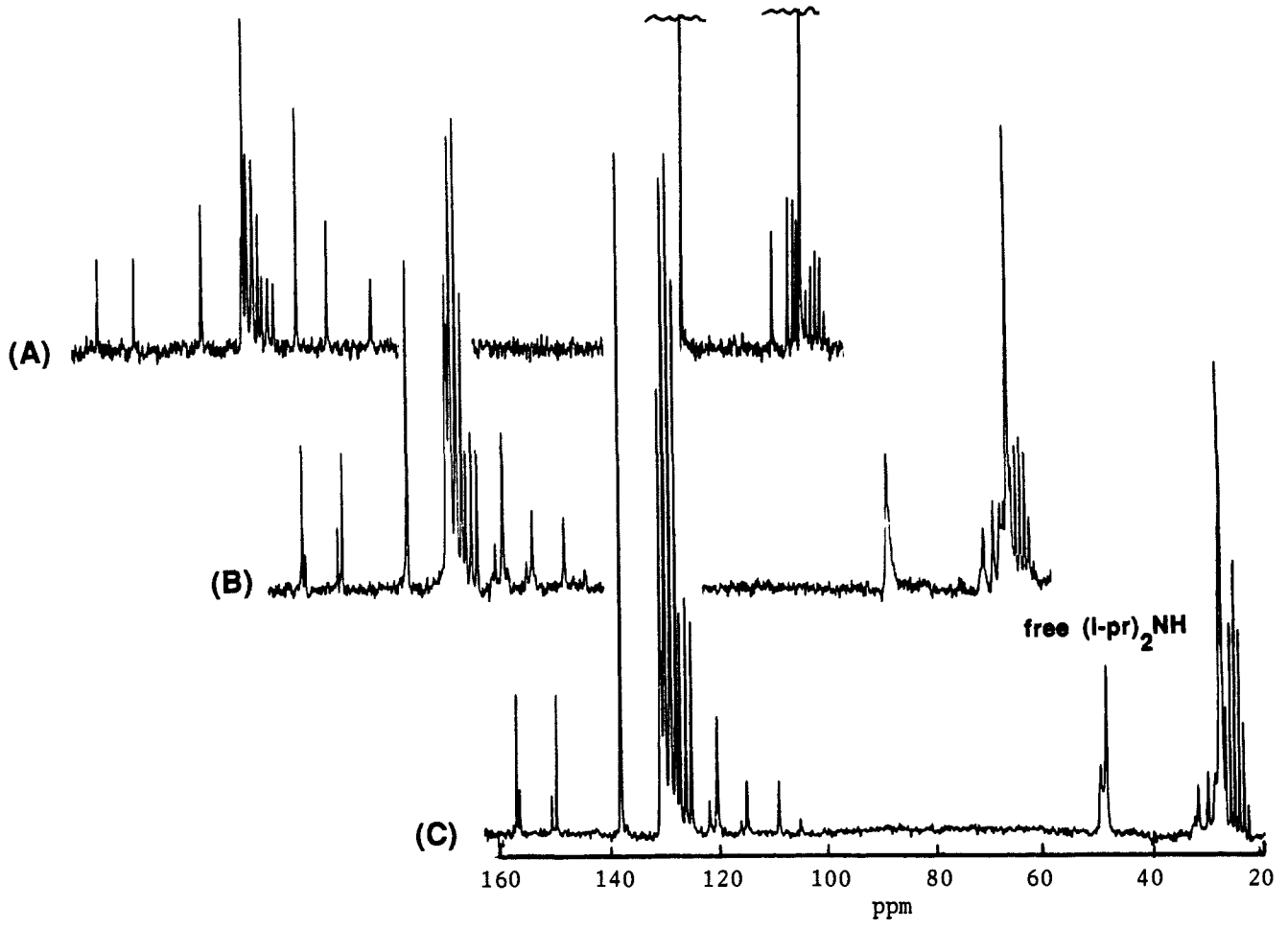


Figure 4. $^{13}C\{^1H\}$ NMR spectra of 0.50 molar toluene-d_8 solutions of (A) **2** at 25 °C, (B) **2** at −54 °C, and (C) $\mathbf{2}_{\text{solvent-free}}$ and diisopropylamine (2.0 equiv per lithium) at −54 °C. The spectrum in (C) is from a sample that was 99.5% ^{6}Li enriched.

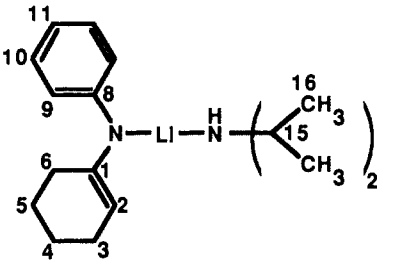
carbons is 10.4 (13). For comparison, the average isotropic thermal parameter of the Li's and N's is 7.1 (10). The cyclohexene ring appears to be the one numbered C1 through C6, and the phenyl ring is C8 through C13. The C1–N7 distance is 1.37 (1) Å and the C8–N7 distance is 1.40 (1) Å. Selected bond distances are summarized in Table II. The long Li–C distances indicate the absence of an η^3-π-allyl type interaction. For example, some of the distances include the following: Li–N7, 2.01 Å; Li–C1, 2.57 Å; Li–C2, 3.00 Å.

Two structural features of **2** stand out as being important to the understanding of the reactivity of lithiated imines. To the best of our knowledge, the diisopropylamine solvate is the first direct evidence that the free diisopropylamine might not be an innocent spectator in the reactions employing lithium diisopropylamide.[15] (In the absence of additional solvating ligands, a benzene solution of **2** alkylates with methyl iodide within seconds at 25 °C. In contrast, benzene solutions of the corresponding lithiated dimethylhydrazone containing diisopropylamine required added ethereal solvents to alkylate.[2]) Secondly, the phenyl rings of **2** reside approximately 40° out of the plane defined by the azaallyl atoms. (The C8–N7–C1–C2 dihedral angle is 142°.) This contrasts with literature reports proposing a dihedral angle of 0° (syn orientation) for lithiated imines in solution. This point will be discussed further (vide infra).

Solution Structure of 2: NMR, Molecular Weight, and Solubility Studies. Crystalline **2** was sufficiently soluble in hydrocarbon solvents to obtain spectral data in the absence of additional co-

(15) Several X-ray crystal structures of lithium enolates solvated by the secondary amine, *N,N,N'*-trimethylethylenediamine, were recently reported. The authors included a postulated structure of a lithium enolate solvated by diisopropylamine. Laube, T.; Dunitz, J. D.; Seebach, D. *Helv. Chim. Acta* **1985**, *68*, 1373.

Table III. ^{13}C NMR Spectroscopic Data on Lithiated Imine **2** in Toluene-d_8[a]



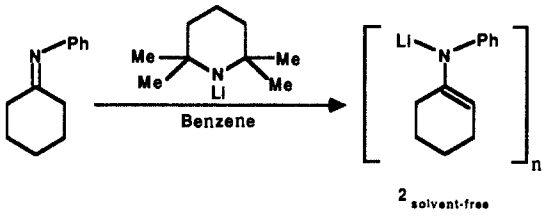
carbon[b]	25 °C[c]	−54 °C[c] major isomer	−54 °C[c] minor isomer
1, 8	157.5	157.4	156.8
1, 8	150.5	149.8	150.7
2	105.7	107.6	103.6
9, 10, 11	129.6	129.7	*e*
9, 10, 11	119.7	119.3	120.7
9, 10, 11	114.1	113.7	114.8
15	46.1	*f*	*f*
3, 4, 5, 6	28.8	*d*	*d*
3, 4, 5, 6	25.8	*d*	*d*
3, 4, 5, 6	24.7	*d*	*d*
3, 4, 5, 6	24.0	*d*	*d*
16	23.2	*f*	*f*

[a] Assignments were made through a variety of techniques briefly described in ref 18. [b] Numbering derives from the crystallographic data found in Figure 3 and Table II. [c] Figure 3. [d] Poor resolution of the envelope of resonances from 28–23 ppm and the aromatic solvent resonances precluded precise assignments. Cf. Figure 3. [e] The resonance was not located. [f] Broadening and poorly defined fine structure was observed. Cf. Figure 3.

ordinating solvent. The ^1H NMR spectrum of **2** in toluene-d_8 was relatively uninformative (see Experimental Section).[16,17] The proton noise decoupled ^{13}C NMR spectrum recorded at 20 °C is reproduced in Figure 4 (part A) and Table III.[18] A reversible coalescence was observed at approximately −15 °C with the slow exchange spectra below −20 °C showing two discrete species (Figure 4, part B). The resonance corresponding to the diisopropyl-amino methine carbon at 46.0 ppm appeared in the low-temperature-limiting spectrum as a sharp singlet superimposed upon a seemingly complex broader peak. Neither resonance corresponded to noncoordinated diisopropylamine. The ratio of the two compounds remained unchanged when the absolute concentration was varied over a 12-fold range, indicating that the two equilibrating species were equivalently aggregated. (This was corroborated by molecular weight studies, vide infra.) Although at −15 °C we observed a singlet ($\Delta\nu_{1/2}$ = 42 Hz) at 1.15 ppm downfield of 0.30 M LiCl in MeOH in the ^7Li NMR spectrum of **2**, significant peak broadening precluded acquisition of additional structural information at lower temperatures.

The ^6Li-labeled derivative (**2**-^{6}Li) was prepared from cyclohexanone phenylimine and 99.5% ^6Li-labeled lithium diisopropylamide. At 20 °C, the ^6Li NMR spectrum of **2**-^{6}Li in toluene-d_8 displayed a singlet at 0.75 ppm relative to 0.3 M ^6LiCl in MeOH.[8] A coalescence was observed between −50 and −57 °C; the low-temperature-limiting spectrum (−69 °C) displayed two singlets at 0.84 and 0.71 ppm in an approximate 2:1 ratio. Additional cooling simply increased the peak broadening. No ^6Li–^{13}C coupling was observed in the low-temperature ^{13}C NMR spectra of **2**-^{6}Li.

In order to systematically and quantitatively study the amine solvation of **2** in solution, we prepared the corresponding solvent-free lithium salt ($\mathbf{2}_{\text{solvent-free}}$) by reacting cyclohexanone phenylimine with lithium tetramethylpiperidide in hexane/benzene (eq 3). Compound $\mathbf{2}_{\text{solvent-free}}$ was isolated as a hydrocarbon



(3)

$\mathbf{2}_{\text{solvent-free}}$

insoluble, analytically pure white powder. The ^1H NMR spectrum of $\mathbf{2}_{\text{solvent-free}}$ in benzene-d_6 charged with 3.0 equiv of THF per lithium to dissolve the sample contained no resonances corresponding to the tetramethylpiperidyl fragment.

Data on the solvation of lithiated cyclohexanone phenylimine were obtained by titrating a suspension of $\mathbf{2}_{\text{solvent-free}}$ in hydrocarbon solvents with diisopropylamine. Toluene or benzene suspensions of $\mathbf{2}_{\text{solvent-free}}$ became homogeneous upon addition of 1.10–1.20 equiv of amine. When the incremental amine additions to a toluene-d_8 suspension of $\mathbf{2}_{\text{solvent-free}}$ were monitored by ^{13}C NMR spectroscopy at −54 °C, the only spectroscopically observable change that occurred upon adding up to 1.10 equiv was an increasing signal-to-noise ratio arising from the increasing solubility. The homogeneous solution of $\mathbf{2}_{\text{solvent-free}}$ in the presence of 1.20 equiv of added diisopropylamine showed traces of noncoordinated amine in addition to the two previously observed species. Samples containing 1.2–10.0 equiv of added diisopropylamine exhibited proportional increases in the intensity of the ^{13}C resonance of uncoordinated amine at 45.5 ppm (Figure 4, part C). Addition of up to 10 equiv of added amine (an estimated overall increase in uncoordinated amine concentration of at least 50-fold) did not affect the temperature of the coalescence or alter the relative

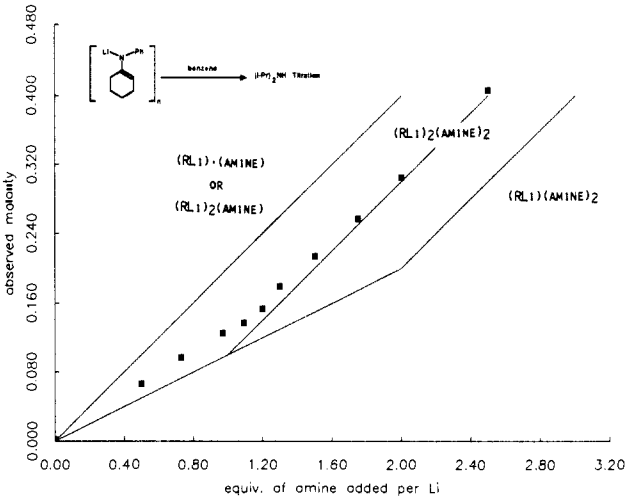


Figure 5. Observed molality measured as a function of added diisopropylamine for suspensions of $\mathbf{2}_{\text{solvent-free}}$ in benzene. The solid lines represent the calculated plots for models based on mono- and bis-solvated monomers and dimers as labeled.

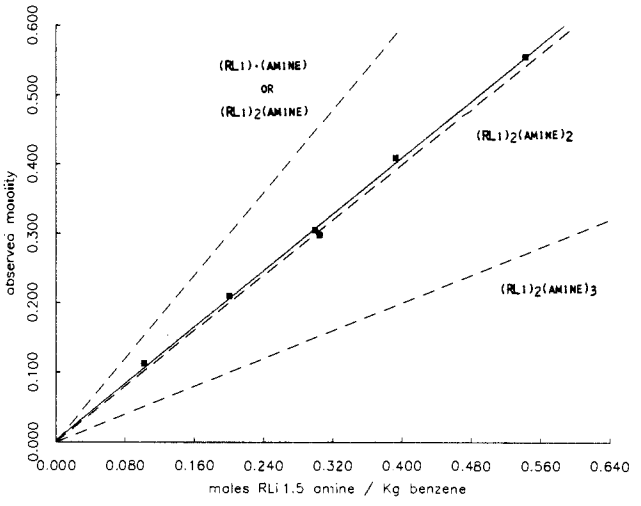


Figure 6. Observed molality measured as a function of $\mathbf{2}_{\text{solvent-free}}$. Each sample contained 1.50 equiv of diisopropylamine (per lithium). The dashed lines (---) represent the calculated plots for models based on several different degrees of solvation and aggregation as labeled.

abundances of the two visible species. The absence of a mass-action effect was consistent with the two organolithium species having the same number of coordinated amines.

To gain further insight into the solvation of the lithium counterions, the incremental diisopropylamine additions were monitored by cryoscopic molecular weight determination in benzene. Figure 5 is a plot of the observed molalities of $\mathbf{2}_{\text{solvent-free}}$ as a function of added diisopropylamine. The measurements between 0.0 and 1.10 equiv were made on the partially dissolved suspension of $\mathbf{2}_{\text{solvent-free}}$. We have included the calculated plots if $\mathbf{2}_{\text{solvent-free}}$ was dissolving to form (A) monosolvated monomers or monosolvated dimers, (B) bis-solvated dimers, and (C) bis-solvated monomers. The discontinuities represent the points at which saturation of the coordination sphere would occur and additional solvent would remain uncoordinated in solution.[19] The subtle discontinuity in the observed data coincided with the quantity of amine required to attain homogeneity of the samples.

Figure 6 is a plot of measured solution molality as a function of the absolute concentration of **2**. For each data point compound $\mathbf{2}_{\text{solvent-free}}$ was dissolved by adding 1.50 equiv of diisopropylamine per lithium counterion. The dashed lines represent the calculated

(16) The ^1H NMR spectroscopic data on lithiated cyclohexanone phenylimine has been described.[17]

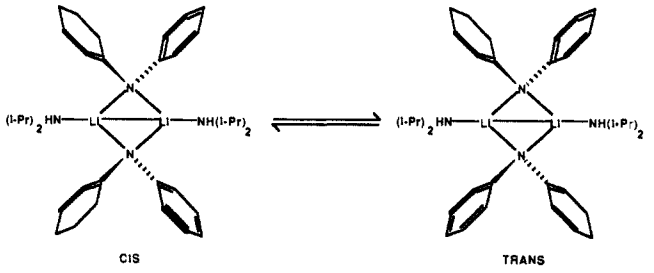
(17) Knorr, R. Weib, Löw, P.; Räpple, E. *Chem. Ber.* **1980**, *113*, 2462.

(18) ^{13}C NMR spectra are assigned with the aid of off-resonance decoupling and INEPT pulse sequences. Preparation of **2**-d_5 starting from aniline-d_5 distinguished the assignments of the aromatic and vinylic resonances. We thank Neil Kallman for preparing the deuterated derivative.

(19) Control experiments showed that benzene solutions of diisopropylamine exhibited freezing point depressions consistent within 2–4% calculated for the non-hydrogen bonded monomeric form.

plots expected if the dissolved lithiated imine existed as (A) monosolvated monomers or monosolvated dimers (the two lines superimpose), (B) bis-solvated dimers, or (C) tris-solvated dimers. The solid line represents a linear least-squares fit of the observed data. The calculated slope (1.02 ± 0.02) is within experimental error of the 1.00 slope calculated for the model based on bis-solvated dimers in solution.[20]

The spectroscopic, solubility, and molecular weight data fit the bis-solvated dimer model. Given the lack of ^{13}C–^{6}Li or ^{13}C–^{7}Li coupling providing (albeit inconclusive[8f]) evidence against direct carbon–lithium contacts, the two most rational structures would be the cis and trans stereoisomeric dimers shown in eq 4. Further



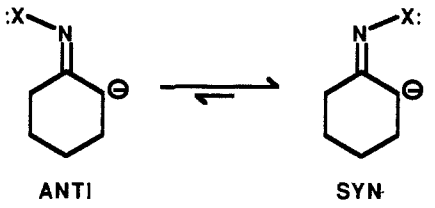
(4)

support comes from the apparent disorder in the crystal structure of **2** attributable to an analogous cis/trans mixture in the lattice.[21]

These assignments require some qualification. The discontinuities observed in the solubility, spectroscopic, and molecular weight studies indicated that 10–20% more amine was being consumed than would be expected for a 1:1 solvent/lithium stoichiometry. The complicated amine methine carbon resonances in the ^{13}C NMR spectra of the solvated imine anions appeared to arise from more than two distinct kinds of coordinated amine. Comparison of the amine resonances centered at 46 ppm in spectra B and C of Figure 4 leads us to believe that some of the coordinated amines may be in rapid exchange with the free amine. Therefore, additional dynamic phenomena appear to be occurring to at least a limited extent. Further solvation studies on $\mathbf{2}_{\text{solvent-free}}$ are underway to clarify this point.

On the Stereochemistry of Imine Alkylation. Lithiated imines exhibit high alkylation selectivities similar to those observed for lithiated oximes, oximino ethers, and hydrazones. The stereochemical model that we proposed earlier to explain the stereoselectivities of hydrazone and related Schiff's base alkylations hinged upon a π-complexed azaallyl structure in the (spectroscopically invisible) reactive intermediates and transition states. Two crystallographic analyses showed η^4-π-complexation of the lithium counterion in lithiated hydrazones.[1] In contrast, the structure of lithiated imine **2** showed no carbon–lithium contacts (Figure 3). The solution studies indicated that the crystal structure of **2** adequately reflected the structure of **2** is solution. A detailed discussion of the stereoselectivities of imine alkylations will require elucidation of the relationships of the lithiated structures in solution with the structures of the reactive intermediates undergoing the alkylation. We note, however, that Raston et al. reported that the azaallyllithium moieties found in monomeric and dimeric lithiomethylpyridines exhibit η^3-complexation of the lithium counterion.[22]

On the Syn Effect. Mechanistic investigations of azaallyllithiums have focused on the syn effect, i.e., the propensity of the imine substituent to adopt the syn orientation relative to the carbanionic carbon (eq 5).[3d] Early explanations for the 4–5 kcal



(5)

syn preference in azaallyllithiums were based on either lithium chelation effects or orbital symmetry control and depended critically on the presence of a heteroatomic substituent on the nitrogen. These hypotheses became suspect when lithiated imines were shown to alkylate with exceptional syn selectivities despite the absence of such a heteroatomic substituent.[23]

In 1980, Knorr et al. reported ^{1}H NMR spectroscopic studies of lithiated phenyl- and cyclohexylimines in several different solvents.[17] Although interconversion of the *E* and *Z* carbon–carbon double bond stereochemistry was readily observed for the lithiated imines derived from acyclic ketones, they found no evidence of dynamic processes attributable to syn/anti interconversion. (Some peak broadening ascribed to changes in ion pairing was observed, however.) In 1981, Fraser and co-workers reported ^{13}C NMR studies of lithiated imines derived from several aldehydes and ketones.[24] For example, the lithiated isopropylimine of acetaldehyde appeared as a single species at 25 °C and as two species below −20 °C. Extensive studies led to the suggestion that the two species observed in the low-temperature limit were rotameric forms of the syn oriented anion (eq 6). Backed by molecular

(6)

orbital calculations, an explanation for the syn effect based on predominantly electron repulsion arguments[25] was adopted in preference to the chelation and orbital symmetry models.

From crystallographic studies, we revitalized the model that credited lithium chelation as a significant contributor to syn stabilization for lithiated hydrazones.[1] The solid and solution structural studies of lithiated cyclohexanone phenylimine provide further insights. Due to the similarities of our results with Fraser's, we suggest that the two lithiated imine structures observed by Fraser in THF were stereoisomeric aggregates analogous to those in eq 4.[20] Since the orientations of the phenyl substituents in dimer **2** are 140° away from the syn alignment, the phenyl substituents are in neither the syn nor the anti orientations.[26] In contrast to the corresponding lithiated hydrazones studied in detail by Bergbreiter et al.,[27] conclusions that the syn effect in lithiated imines is a spectroscopically observable ground-state phenomenon may require reevaluation. The syn–anti nomenclature may not be appropriate to describe the observable ground-state structures of lithiated imines. Well documented high syn alkylation selectivities[23] would have to derive from either syn selectivities in spectroscopically invisible (monomeric?) reactive intermediates or from effects found exclusively in the alkylation transition states.

(20) Preliminary results from titrations of $\mathbf{2}_{\text{solvent-free}}$ with THF indicate aggregation behavior most readily attributable to tris-solvated trimers. Detailed spectroscopic studies are in progress. Collum, D. B.; Kallman, N.; Wanat, R. A., unpublished results.

(21) Aluminum amides [$R_2AlN(R)R'$] have also been shown to exist as analogous mixtures of stereoisomeric bridging dimers in both the solution and solid state. Amirkhalili, S.; Hitchcock, P. B.; Jenkins, A. D.; Nyathi, J. Z.; Smith, J. D. *J. Chem. Soc., Dalton Trans.* **1981**, 377 and references cited therein.

(22) Colgan, D.; Papasergio, R. I.; Raston, C. L.; White, A. H. *J. Chem. Soc., Chem. Commun.* **1984**, 1708.

(23) Fraser, R. R.; Banville, J.; Dhawan, K. L. *J. Am. Chem. Soc.* **1978**, *100*, 7999 and references cited therein.

(24) Fraser, R. R.; Chuaqui-Offermanns, N.; Houk, K. N.; Rondan, N. G. *J. Organomet. Chem.* **1981**, *206*, 131. For related investigations see: Fraser, R. R.; Chuaqui-Offermanns, N. *Can. J. Chem.* **1981**, *59*, 3007. Lee, J. Y.; Lynch, T. J.; Mao, D. T.; Bergbreiter, D. E.; Newcomb, M. *J. Am. Chem. Soc.* **1981**, *103*, 6215.

(25) Houk, K. N.; Strozier, R. W.; Rondan, N. G.; Fraser, R. R.; Chuaqui-Offermanns, N. *J. Am. Chem. Soc.* **1980**, *102*, 1427 and references cited therein.

(26) The syn orientational requirement could in principle be fulfilled by treating the phenylamide as the azaallylic moiety and the cyclohexene as the innocent imine substituent. Even in this instance, however, there is still no evidence of syn orientation in the ground-state structures.

(27) Davenport, K. G.; Eichenauer, H.; Enders, D.; Newcomb, M.; Bergbreiter, D. E. *J. Am. Chem. Soc.* **1979**, *101*, 5654.

In any event, an understanding of the structure-reactivity relationships in lithiated imines must be founded on a more complete understanding of the solvation and aggregation effects.

Summary

We have described the solid-state and solution structures of lithiated 2-carbomethoxycyclohexanone dimethylhydrazone **1** and lithiated cyclohexanone phenylimine **2**. Both compounds exist as bis-solvated dimers in the solid state. In hydrocarbon solution, **1** undergoes considerable dissociation either to monomers or to a monosolvated dimer and free THF. Lithiated imine **2** dissolves to afford an approximate 2:1 mixture of two equilibrating bis-solvated dimers that appear to be two stereosiomers of the dimeric form observed in the solid-state structure. Understanding the complex behavior of **2** in solution was made considerably easier by titrating the corresponding solvent-free material with the ligating solvent in conjunction with spectroscopic studies and extensive molecular weight analyses. The stereoselectivities of the alkylations of lithiated derivatives related to **1** and **2** were briefly addressed. A detailed analysis of the structure-reactivity relationships was deferred until a more detailed understanding of the dynamics of the alkylations is obtained.

Experimental Section

Instrumentation. Routine ^1H NMR spectra were recorded on a Varian CFT-20 (80 MHz) spectrometer. ^{13}C and ^7Li NMR spectra were recorded on a JEOL FX90Q spectrometer operating at 22.49 and 34.77 MHz, respectively. ^6Li NMR spectra were recorded on a Bruker WP 300 spectrometer operating at 44.15 MHz. ^1H and ^{13}C NMR chemical shifts are reported in ppm down field of tetramethylsilane. The ^6Li and ^7Li NMR chemical shifts are reported in ppm downfield of an external 0.30 M LiCl/methanol standard. Probe temperatures were monitored with a thermocouple and are accurate to within 1.0 °C. Microanalyses were performed by Alfred Bernhardt Analytisches Laboratorien (Elbach, West Germany).

Solvents and Materials. Benzene and hexane were distilled from benzophenone ketyl containing 1% tetraglyme to dissolve the ketyl. The benzene used in molecular weight determinations was refluxed over CaH_2 for at least 7 days, distilled under argon, and degassed by 3 freeze–pump–thaw cycles. Toluene was distilled from neat *n*-BuLi. Toluene-d_8 and benzene-d_6 were distilled from sodium/benzophenone ketyl. Diisopropylamine and tetramethylpiperidine were distilled from CaH_2. ^6Li metal (99.5%) was obtained from Oak Ridge National Laboratory. The *n*-Bu^{6}Li was prepared by the standard literature procedure.[28] Air and moisture sensitive materials were manipulated by using standard glovebox and vacuum line techniques with the aid of gas tight syringes.

Molecular Weight Determinations. Molecular weights were measured by using the freezing point depression technique in a modification of an apparatus described by Seebach.[9] Details of these modifications will be described elsewhere.[29] Samples were prepared in a glovebox and measurements were made under N_2 by using standard inert atmosphere techniques. Calibrations were performed by using known concentrations of naphthalene in benzene.

Nuclear Magnetic Resonance Studies. The following is a representative procedure for preparing samples for spectroscopic analysis. In a glovebox, a 10-mm NMR tube was charged sequentially with $\mathbf{2}_{\text{solvent-free}}$ (250 mg, 1.40 mmol), toluene-d_8 (1.750 g), and diisopropylamine (184 mg, 1.82 mmol). The NMR tube containing the resulting clear, colorless solution was placed under septum and sealed with a flame under reduced pressure.

Lithiated 2-Carbomethoxycyclohexanone Dimethylhydrazone (1). To a solution of diisopropylamine (0.366 mL, 2.40 mmol) in 14 mL of hexane and 1.40 mL of THF under N_2 was added 2.0 M *n*-BuLi (1.20 mL, 2.40 mmol) by gas tight syringe. The clear, colorless solution was cooled to −78 °C and 2-carbomethoxycyclohexanone dimethylhydrazone (0.540 mL, 2.40 mmol) was added neat. The stirring was stopped, and the solution was immediately warmed to 20 °C. Colorless crystals of **1** that deposited within 1 h were filtered and dried in vacuo (525 mg, 79% yield): ^1H NMR (C_6D_6, 25 °C) δ 3.61 (s, 3 H), 3.50 (m, 4 H), 3.05–2.65 (m, 4 H), 2.44 (s, 6 H), 1.58 (m, 4 H), 1.44 (m, 4 H); $^{13}C\{^1H\}$ NMR (toluene-d_8, 25 °C) δ 172.70 (q C), 166.4 (q C), 78.8 (CH), 68.1 (CH_2), 50.2 (CH_3), 48.2 (CH_3), 27.9 (CH_2), 25.7 (CH_2), 24.8 (CH_2), 23.8 (CH_2); $^{13}C\{^1H\}$ NMR (toluene-d_8, −85 °C) δ 170.3, 166.0, 76.7, 50.0, 48.7 (br), 28–23 (br envelope); ^7Li NMR (toluene-d_8, 20 °C) δ 1.12; ^6Li NMR (toluene-d_8, 20 °C) δ 1.12; ^6Li NMR (toluene-d_8, −40 °C) δ 0.95.

Single-Crystal X-ray Diffraction Analysis of 1. A single crystal of **1** was mounted in a thin-walled glass capillary and preliminary X-ray photographs showed monoclinic symmetry. Accurate lattice constants, determined from a least-squares analysis of 15 moderate 2θ-values, were a = 14.587 (3) Å, b = 11.559 (2) Å, c = 19.292 (4) Å, and β = 91.83 (2)°. Systematic extinctions and crystal density were consistent with space group $C2/c$ with a unit of composition $C_{14}H_{25}O_3N_2Li$ forming the asymmetric unit. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a computer controlled four-circle diffractometer by using graphite monochromated Cu Kα radiation (1.5417 Å) and variable speed, 1° ω-scans. Of the 1894 reflections collected in this manner, 1587 (84%) were judged observed ($F_o \geq 3\sigma(F_o)$) after correction for Lorentz, polarization, and background effects.[30] A phasing model was found by using a multisolution sign-determining procedure, and all non-hydrogen atoms were located in E-syntheses. Block diagonal least-squares refinements with anisotropic non-hydrogen atoms and fixed isotropic hydrogens have converged to a current crystallographic residual of 0.078 for the observed reflections. Additional crystallographic details are available and are described in the supplementary material paragraph.

Lithiated Imine 2: Preparative Scale. To a solution of 2.0 M *n*-BuLi (7.5 mL, 15 mmol) under nitrogen was added diisopropylamine (2.10 mL, 15 mmol). After 15 min, the hexane solution of lithium diisopropylamide was treated with neat cyclohexanone phenylimine (2.60 mL, 15 mmol). The vessel was immediately warmed to 25 °C and stirring was ceased. The large mass of solid that deposited between 1 and 48 h was collected by filtration, washed once with hexane, and evacuated to afford 2.1 g (50% yield) of lithiated imine **2** as white crystals: ^1H NMR (C_6D_6) δ 7.4–6.5 (m, 5 H), 5.23 (br t, J_{HH} = 4–6 Hz, 1 H), 2.38 (m, 6 H), 1.70 (m, 4 H), 0.84 (d, J_{HH} = 6 Hz, 12 H), 0.41 (br t, J_{HH} = 6 Hz, 1 H); ^7Li NMR (toluene-d_8, −15 °C) δ 1.1 ppm; ^6Li NMR (toluene-d_8, 20 °C) δ 0.75 ppm; ^6Li NMR (toluene-d_8, −57 °C) δ 0.83 (minor), 0.70 (major). For ^{13}C NMR$\{^1H\}$ spectral data see Table III in text.

X-ray Crystal Structure of Lithiated Imine 2. Crystals were grown by treatment of cyclohexanone phenylimine (0.172 mL, 1.00 mmol) with lithium diisopropylamide (1.00 mmol) in hexane (2.0 mL) in a sealed ampule at 25 °C over 12 h. A crystal of **2** was sealed in a thin-walled glass capillary tube and preliminary X-ray photographs showed that it belonged to the monoclinic system. Accurate lattice constants of a = 10.082 (1) Å, b = 16.988 (1) Å, c = 21.224 (1) Å, and β = 101.16 (1)° were determined from a least-squares fit of fifteen diffractometer measured 2θ-values. Systematic extinctions and a plausible crystal density were accommodated by space group $P2_1/n$ with an asymmetric unit of $C_{36}H_{56}N_4Li_2$. All unique diffraction maxima with $2\theta \leq 100$ °C were collected on a computer controlled four-circle diffractometer by using graphite monochromated Cu Kα radiation (1.54178 Å) and variable speed, 1° ω-scans. After correction for Lorentz, polarization, and background effects, were judged observed ($F_o \geq 3\sigma(F_o)$). The structure was solved routinely by using a multisolution sign determining procedure.[30] Block-diagonal least-squares refinements with anisotropic non-hydrogen and fixed isotropic hydrogens have converged to a conventional crystallographic residual of 0.074 for the observed reflections. Additional crystallographic details are available and are described in the supplementary material paragraph.

Solvent-Free Lithiated Cyclohexanone Phenylimine ($\mathbf{2}_{\text{solvent-free}}$). To a solution of tetramethylpiperidine (2.36 mL, 14.0 mmol) in 4:1 hexane/benzene (25 mL) at 0 °C under N_2 was added 2.0 M *n*-BuLi in hexane (6.86 mL, 13.7 mmol). To the resulting slurry of lithium tetramethylpiperidide at 0 °C was added cyclohexanone phenylimine (2.60 mL, 15 mmol) neat. The vessel was warmed to 25 °C, and the slurry was stirred for 48 h. Isolating by filtration, washing twice with pentane, and drying in vacuo afforded 1.70 g (63% yield) of $\mathbf{2}_{\text{solvent-free}}$ as a white amorphous powder. Anal. Calcd for $C_{12}H_{14}NLi$: C, 80.43; H, 7.87; N, 7.83; Li, 3.87. Found: C, 80.16; H, 7.76; N, 7.60; Li, 3.82. $\mathbf{2}_{\text{solvent-free}}$ was in-

(28) Amonoo-Neizer, E. H.; Shaw, R. A.; Skovlin, D. O.; Smith, B. C. *Inorg. Synth.* **1966**, *8*, 20.

(29) Wanat, R. A. Ph.D. Dissertation, Cornell University, Ithaca, New York, in press.

(30) All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were the following: REDUCE and UNIQUE, data reduction programs by Leonowicz, M. E., Cornell University, 1978; MULTAN78 and -80, a system of computer programs for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations including Patterson syntheses) written by Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; DeClercq, J. P.; Woolfson, M. M., University of York, England, 1978; BLS78A an anisotropic block-diagonal least-squares refinement written by Hirotsu, K.; Arnold, E., Cornell University, 1980; PLUTO78, a crystallographic illustration program by Motherwell, W. D. S., Cambridge Crystallographic Data Center, 1978; and BOND, a program to calculate molecular parameters and prepare tables written by Hirotsu, K., Cornell University.

soluble in hydrocarbon solvents. ^{13}C NMR in toluene-d_8 charged with 3.0 equiv of THF contained no resonances attributable to the tetramethylpiperidyl residue. ^{13}C NMR spectra of $\mathbf{2}_{solvent\text{-}free}$ with added diisopropylamine were indistinguishable from the spectra derived from the corresponding solvated material **2** prepared as described above.

Acknowledgment. We thank the National Institutes of Health for generous financial support of this work. Acknowledgment is made to the National Science Foundation Instrumentation Program (CHE 7904825 and PCM 8018643) for support of the Cornell Nuclear Magnetic Resonance Facility.

Registry No. Lithium-6, 14258-72-1; lithium 2-carbomethoxycyclohexanone dimethylhydrazone, 101773-94-8; dimeric lithium 2-carbomethoxycyclohexanone dimethylhydrazone, 101773-97-1; dimeric lithiated cyclohexanone phenylimine, 101773-98-2; lithium cyclohexanone phenylimine, 101773-95-9; 2-carbomethoxycyclohexanone dimethylhydrazone, 101773-96-0; cyclohexanone phenylimine, 1132-38-3.

Supplementary Material Available: Fractional coordinates, bond angles, and bond distances for lithiated derivatives **1** and **2** (10 pages). Ordering information is given on any current masthead page.

Stereochemistry of the Reactions of Substituted Allylboronates with Chiral Aldehydes. Factors Influencing Aldehyde Diastereofacial Selectivity[1]

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Abstract: The stereochemistry of the reactions of substituted allylboronates **5–9** with D-glyceraldehyde acetonide (**4**) and L-4-deoxythreose cyclohexyl ketal (**2**) is described. The reactions involving (*Z*)-crotylboronates **5** and **6** are exceptionally stereoselective, with selectivity for the major 3,4-syn,4,5-anti adducts **19**, **23**, **27**, and **31** approaching the limit defined by the isomeric purity of the reagents. The level of aldehyde diastereofacial selectivity is at least 20:1 with **4** and 90:1 in reactions with **2**. In contrast, the reactions of (*E*)-crotylboronates **7** and **8** afford roughly 1:1 mixtures of anti,anti (**20**, **24**, **28**, **32**) and anti,syn (**21**, **25**, **29**, **33**) adducts differing in the facial sense of reagent addition to the aldehyde. Interestingly, the diastereofacial selectivity of the reactions of allylboronate **9** with these aldehydes is intermediate (4:1 with **4**, 9:1 with **9**). Stereochemical assignments for **19–33** were established by unambiguous chemical correlations with compounds synthesized by stereochemically defined methods. These results clearly show that the substitution pattern at C(3) of the reagent is a significant and previously unappreciated variable in determining diastereofacial selectivity. This effect is a consequence of the nonbonded interactions that the C(3) substituents experience in the competing reaction transition states A–D. These interactions are fundamental in nature and are likely to have a significant influence on the diastereofacial selectivity of other reactions that proceed via cyclic transition states including the aldol reaction and sigmatropic processes such as the Claisen rearrangement. A second variable that influences the extent and direction of diastereofacial selectivity is the electronic structure of the aldehyde. Comparison of the results of reactions of allylic boronates **1**, **5**, **7**, and **9** with glyceraldehyde acetonide (**4**), benzyl lactaldehyde (**78**), and 2-methylbutyraldehyde (**79**) shows (a) that anti diastereofacial selectivity is always greater with **4** than with **78** or **79** (**4** > **78** > **79**) in reactions with each reagent and (b) that for each aldehyde anti diastereofacial selectivity is greater in reactions involving (*Z*)-crotylboronates **1** or **5** than allylboronate **9** or (*E*)-crotylboronate **7** (**1**, **5** > **9** > **7**).

Introduction

The reactions of crotylmetal reagents with chiral carbonyl compounds are of considerable interest in the context of acyclic stereoselective synthesis.[3,4] This transformation, like the aldol reaction,[5] generates two new stereochemical relationships and, potentially, four diastereomeric products (Figure 1). One objective of research in this area, required to support applications in natural products synthesis, is the development of methodology and/or reagents suitable for synthesis of each diastereomeric relationship with exceptional selectivity and control.[6] Although considerable effort has been devoted to the elucidation of the stereochemistry of the reactions of crotylmetal compounds with achiral aldehydes,[3] only recently have studies begun in earnest to probe the factors influencing aldehyde diastereofacial selectivity.[7-9] Consequently, the full potential of allylmetal compounds

(1) Taken in part from the Ph.D. Theses of M. A. Adam and A. E. Walts, Massachusetts Institute of Technology, Cambridge, MA, 1985.
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