

be also quite high before a slowdown below collision rates is observed for gas phase ion-molecule reactions.^{2,21-24} Therefore, although the dip in the rate constant plot for (CHT)Fe(CO)₃ is smaller than those for Bd and CHD shown in Figure 3, still a substantial geometry change is indicated by the plot.

The rate constant plots for (COT)Fe(CO)₃ and (CHT)Cr(CO)₃, shown in Figure 5, exhibit essentially no decrease of rates at near zero exoergicities. A very small dip would be expected from the consideration that the forward rate should go down to half of the collision rate when the exoergicities is exactly equal to

zero. Thus, the results in Figure 5 are consistent with the small ΔS^\ddagger for (COT)Fe(CO)₃ and (CHT)Cr(CO)₃ of 8.7 and 5 cal K⁻¹ mol⁻¹, Table II, and the expected small geometry changes deduced in the preceding section from the observed changes of bonding in the neutral molecule and the negative ion.

Acknowledgment. Financial support by the Canadian Natural Sciences and Engineering Research Council is gratefully acknowledged.

Communications to the Editor

Metalation of Imines by Lithium Diisopropylamide Solvated by *N,N,N',N'*-Tetramethylethylenediamine: Evidence for Solvent-Free Open Dimer Reactive Intermediates

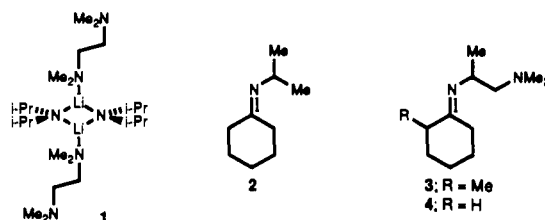
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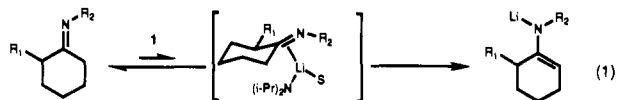
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Previous rate studies of *N,N*-dimethylhydrazone metalations by LDA in THF/hexane or TMEDA/hexane (TMEDA = *N,N,N',N'*-tetramethylethylenediamine) implicated mechanisms involving deaggregation of LDA dimers without participation by additional donor solvent (eq 1, R₁ = Me, R₂ = NMe₂).^{1,2} We concluded that TMEDA functions as a monodentate rather than bidentate ligand in both the ground state (e.g., **1**) and the transition state.² Furthermore, the surprisingly low affinity of TMEDA for LDA led us to question the mode of action of TMEDA as a ligand for lithium in a more general sense.³ In this communication we will provide evidence that LDA/TMEDA-mediated metalations of simple *N*-isopropyl imine **2** proceed by a mechanism involving a dimer-monomer pre-equilibrium akin to that observed for the isostructural *N,N*-dimethylhydrazones. In contrast, metalation of imine **3** bearing a pendant NMe₂ moiety is extremely rapid and proceeds by a mechanism involving facile dissociation of both TMEDA ligands from LDA dimer **1** followed by direct reaction of the LDA dimer. We ascribe the change in the rate equation to the Me₂N moiety. The kinetics provide clear evidence of a ligand-assisted metalation (complex-induced proximity effect; CIPE)⁴ and gives experimental support to speculations that lithium amide open dimers may be important reactive intermediates.⁵⁻⁷

Metalations of imine **2** and the 2,2,6,6-tetradeuterio derivative **2-d₄** by LDA in TMEDA/hexane mixtures, maintained at 0 °C



with an ice bath, were monitored using an FT-IR continuous-flow method described previously.^{1,2} The primary kinetic isotope effect ($k_H/k_D = 7.7 \pm 1.0$) and rate equation (eq 2) are consistent with a mechanism involving dimer dissociation (eq 1, R₁ = H, R₂ = CHMe₂).^{1,2} Moreover, the completely analogous rate equations for metalation of *N,N*-dimethylhydrazones and *N*-isopropyl imines indicate that the Me₂N moieties of the hydrazones do *not* function as obligatory ligands during the metalation.



$$-d[2]/dt = k[\text{substrate}][\text{LDA}]^{1/2}[\text{TMEDA}]^0 \quad (2)$$

We investigated the possibility that inclusion of a second ligand on the imine *N*-alkyl substituent might, through chelation, cause an increased metalation rate characteristic of a CIPE.⁴ Such a CIPE should be accompanied by a fundamental change in the mathematical form of the rate equation. The metalations of **4** and **4-d₄** proved to be too fast to monitor within the restrictions of the continuous-flow IR cell, clearly demonstrating that the pendant Me₂N of **4** facilitates the metalation relative to **2**. Fortunately, reduced metalation rates of the methylated derivatives **3** and **3-d₃** allowed for reasonably precise rate measurements.¹⁰ An unusually small kinetic isotope effect ($k_H/k_D = 2.0 \pm 0.1$) was accompanied by a substantial change in the rate equation (eq 3).⁸ The first-order dependence on [LDA] and first-order dependence on [3]⁹ implicate a direct metalation by the intact LDA dimer fragment. The inverse second-order dependence on [TMEDA] (Figure 1) causes a striking exponential increase in metalation rate with decreasing TMEDA concentration and points to a mechanism involving dissociation of both η¹-TMEDA ligands prior to metalation. In previous studies we had shown that THF is superior to TMEDA as a ligand for LDA. Indeed, addition of 2% by volume THF to metalations of **3** in TMEDA or TME-

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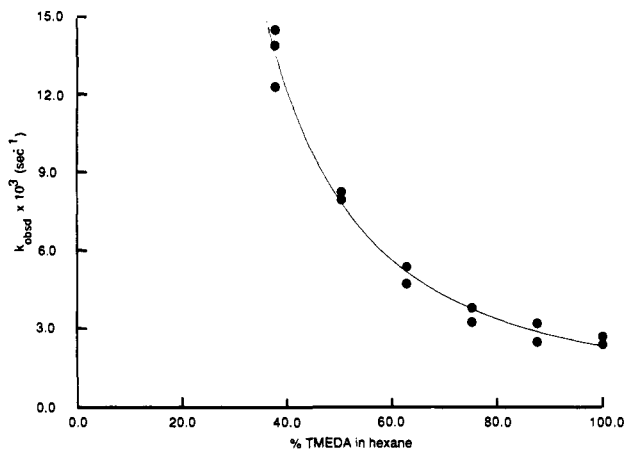
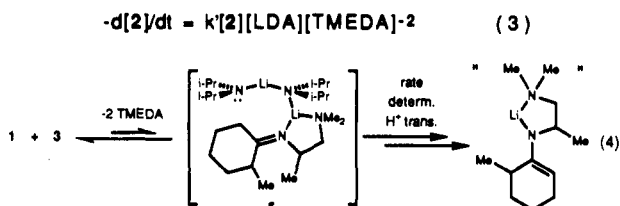


Figure 1. Plot of k_{obsd} versus [TMEDA] in hexane cosolvent for the metalation of imine **3** (0.004 M) by LDA (0.13 M) at 0.0 ± 0.5 °C. The curve depicts the result of an unweighted nonlinear least-squares fit to the general expression $k_{\text{obsd}} = k[\text{TMEDA}]^n + k''$. The adjustable parameter n corresponds to the order in TMEDA (-2.02 ± 0.01). The parameter k'' (0.52 ± 10^{-3}) corresponds to the observed rate constant for the metalation via monomers (eq 1).¹⁰

DA/hexane mixtures causes essentially complete inhibition of the metalation.¹⁰

In the context of MNDO calculations we noted that open dimers could provide a viable pathway for reaction of lithium amide dimers without intervening deaggregation.^{6,11} We now present such a mechanism as consistent with the rate data (eq 4). Open dimer **5** is certainly not the only possible intermediate; however, despite little precedence for open dimers in the literature prior to 1990,¹¹ recent spectroscopic,^{5,12} computational,⁶ and crystallographic⁷ support for lithium amide open dimers makes **5** highly plausible. As to the origin of the double TMEDA dissociation, MNDO calculations predicted quite unequivocally that lithium amide open dimers are viable intermediates only when unsolvated on the internal lithium.⁶ Moreover, the 8-membered-ring transition state has been shown to be optimal for related internal proton abstractions.¹³ We hasten to add that the mechanism depicted in eq 4 is not generally available to **3**; metalation of **3** in THF displays rate behavior consistent with the mechanism specified by eqs 1 and 2.¹⁰



In summary, a number of features of the mechanism depicted in eq 4 are without precedent or contrary to conventional wisdom. These include (1) the high lability of TMEDA toward dissociation; (2) a TMEDA-dependent rate acceleration stemming from dissociation of two TMEDA ligands; (3) metalation via an LDA dimer rather than monomer; and (4) promotion of aggregate (relative to monomer) reactivity by a bidentate interaction with the substrate. The observed change in the mathematical form

(10) Metalations of **3** in dimethylethylamine—an isostructural analog of TMEDA incapable of bidentate coordination²—display the same rate profile and small KIE. These and other studies will be described in due course.

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of the rate equation provides an important criterion for invoking participation by internal ligands.⁴

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Supplementary Material Available: Kinetic plots affording reaction orders for metalation of **2** and **3** (2 pages). Ordering information is given on any current masthead page.

Tuning Exo/Endo Stereoselectivity in Ene Reactions

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We have reported the startling observation that a lone pair on a dienophile can have a very large effect on the exo/endo selectivity in Diels–Alder reactions.¹ The large preference for the transition structure with the nitrogen lone pair exo was attributed to a repulsive interaction between the π -system of butadiene and the nitrogen lone pair in the endo transition structure. We have found that related electrostatic interactions in other reactions may be attractive or repulsive, depending on the charge densities at various sites in the transition structures.

The ene reaction of propene with formaldehyde imine can proceed with CC bond formation and hydrogen transfer to the nitrogen or with CN bond formation and hydrogen transfer to the methylene group of formaldehyde imine. Experimentally, there are far fewer examples of ene reactions with imines as the enophile than alkenes or carbonyls.² These types of reactions typically fall into three groups: (1) reactions of imines with electron-withdrawing groups attached to the nitrogen³ such as reaction A; (2) retro-ene reactions of amines⁴ such as reactions B and C; and (3) intramolecular ene reactions of *N*-acyl imines with CN bond formation (D)⁵ (Scheme I).

Ab initio molecular orbital calculations were performed on the simplest parent reaction with GAUSSIAN 90.⁶ The geometries of the reactants and transition structures were optimized using restricted Hartree–Fock theory and the 3-21G and 6-31G* basis sets.^{7,8} Harmonic vibrational frequency calculations were performed to confirm the nature of all stationary points. Energies of each RHF/6-31G* stationary point were calculated with inclusion of electron correlation using second-order Møller–Plesset theory⁹ and the 6-31G* basis set. The CHELPG program was

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