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Structure and Reactivity of a Lithium Complex with a Tridentate Amide Ligand, $[Li(Et_2NCH_2CH_2NCH_2CH_2NEt_2)]_2$

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Summary: The structure of $[Li(Et_2NCH_2CH_2NCH_2CH_2NEt_2)]_2$ has been determined by X-ray diffraction analysis and NMR spectroscopy, and its reactivity with ketones has been investigated.

Lithium amides have been widely used in the deprotonation of ketones and organic carbonyl compounds.[1] Much research on the structures and reactivities of lithium amides has been conducted to ascertain their role in organic synthesis.[2] Most of the lithium amide compounds characterized to date involve either secondary amines or diamines, including the most popular, lithium diisopropylamide (LDA).[1,2] One common problem associated with these lithium amides is their tendency to form polymeric species which may result in low solubility and poor reactivity in hydrocarbon solvents, although recent study has suggested that LDA displays appreciable reactivity in hydrocarbon solvents.[3] To overcome this problem, lithium amides are often employed in coordinating solvents such as THF or in the presence of either amines such as tetramethylethylenediamine (TMEDA) or hexamethylphosphoric triamide (HMPA). We report here a new lithium amide complex with a tridentate amide ligand $[Et_2NCH_2CH_2NCH_2CH_2NEt_2]^{1-}$ (tetraethyldiethylenetriamine,[4] TEDTA) and its excellent reactivity in nonpolar solvents such as hexane.

Results and Discussion

The lithium TEDTA complex was isolated as a colorless crystalline material in good yield from a concentrated solution of the reaction mixture of *n*-butyllithium with $Et_2NCH_2CH_2NHCH_2CH_2NEt_2$ in hexane under nitrogen atmosphere. The structure of this complex was determined by single crystal X-ray diffraction analysis. Positional and thermal parameters are given in Table II. Bond distances and angles are listed in Table IIIa,b, respectively.

Table I. Crystallographic Data

formula	$C_{24}H_{56}Li_2N_6$
fw	442.6
space group	$P2_1/a$
a, Å	13.618(5)
b, Å	13.240(5)
c, Å	17.748(7)
β, deg	107.397(3)
V, Å^3	3053(2)
Z	4
d_{calc}, g cm^{-3}	0.96
μ(Mo Kα), cm^{-1}	0.53
(Mo K$\alpha\lambda$, Å radiation)	0.710 69
temp, °C	22
2θ range, deg	3–45
no. of reflns measd	3491
no. of reflns, $F_o^2 \geq 3\sigma(F_o^2)$	731
no. of params refined	129
R^a	0.102
R_w^b	0.110
largest shift/esd, final cycle	0.068
largest peak, e/Å^3	0.275
goodness-of-fit indicator,[c] S	3.445

[a] $R = \sum_{i=1}^{n}(|F_o|_i - |F_o|_i)/\sum_{i=1}^{n}|F_o|_i$. [b] $R_w = (\sum_{i=1}^{n}W_i(|F_o|_i - |F_c|_i)^2/\sum_{i=1}^{n}w_i|F_o|_i^2)^{1/2}$, $w = 1/\sigma^2(F_o)$. [c] $S = [\sum_{i=1}^{n}(|F_o|_i - |F_c|_i)/\sigma]/(N_{obs} - N_{para})$.

As shown in Figure 1, the lithium TEDTA compound has a dimeric structure in the solid state with the formula of $[Li(TEDTA)]_2$. This compound is a chiral molecule with an approximate D_2 symmetry. The two Li atoms are bridged by two nitrogen atoms with a very short Li–Li separation (2.43(5) Å). Similar short Li–Li distances have been observed previously in dimeric lithium amide compounds.[2] Each lithium center is also coordinated by two amino groups with normal Li–N bond lengths. The distorted tetrahedral geometry of the lithium atom in the molecule has been observed frequently in dimeric lithium complexes. Due to the lack of an inversion center or a reflection plane in the $[Li(TEDTA)]_2$ molecule, the two ethyl substituents on each amino group are inequivalent. If the dimer retains the same structure in solution, six types of carbon atoms (two from CH_3, two from CH_2 of the ethyl, and two from CH_2 of the ethylene) should be detected by ^{13}C NMR spectroscopy. Indeed, at 223 K, six ^{13}C chemical shifts with nearly equal intensity were observed. The two CH_3 signals coalesced at about 273 K, and the coalescence temperature for the two CH_2 signals of the ethyl occurred a few degrees higher. At 293 K, only one CH_3 signal and one CH_2 signal of the ethyl group were observed (Figure 2). This suggests that the $[Li(TEDTA)]_2$ dimer undergoes enantiomer interconversion in solution, as illustrated by Scheme I. The activation energy for this process is about 11 kcal mol^{-1}. Only one ^7Li chemical shift was observed at 298 and 183 K in the ^7Li NMR spectra of $[Li(TEDTA)]_2$, which further supports that this compound does not undergo dissociation or polymerization in solution. Dimeric lithium amide species such as $[Li(diisopropylamide)L]_2$ have been observed frequently in solution where the presence of excess ligands L (L = THF or TMEDA) is necessary to stabilize the dimer.[2,5] In contrast, the $[Li(TEDTA)]_2$ compound does not undergo dissociation in noncoordinating solvents such as toluene

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Table II. Positional and Thermal Parameters for $[Li(TEDTA)]_2$

atom	*x*	*y*	*z*	*B*(eq),[a] Å^2
N1	0.970(1)	0.078(1)	0.840(1)	4.4(4)
N2	0.848(1)	−0.088(1)	0.7580(9)	3.4(4)
N3	0.647(1)	−0.169(1)	0.658(1)	5.3(5)
N4	0.637(1)	−0.065(1)	0.855(1)	4.5(4)
N5	0.681(1)	0.090(1)	0.747(1)	4.2(4)
N6	0.802(1)	0.169(1)	0.650(1)	4.5(4)
C1	0.963(1)	−0.017(2)	0.878(1)	4.6(5)
C2	0.940(2)	−0.103(2)	0.822(1)	5.6(6)
C3	0.838(2)	−0.168(2)	0.699(1)	5.9(6)
C4	0.742(2)	−0.160(2)	0.633(1)	5.8(6)
C5	1.048(2)	0.078(2)	0.799(1)	5.7(6)
C6	1.160(2)	0.054(2)	0.844(1)	6.8(7)
C7	0.993(2)	0.166(2)	0.895(1)	8.1(8)
C8	0.915(2)	0.209(2)	0.917(1)	8.8(8)
C9	0.642(2)	−0.267(2)	0.697(1)	6.5(7)
C10	0.630(2)	−0.360(2)	0.647(2)	12(1)
C11	0.558(2)	−0.142(2)	0.594(1)	8.4(8)
C12	0.473(2)	−0.099(2)	0.603(2)	10.2(9)
C13	0.663(2)	0.043(2)	0.875(1)	5.6(6)
C14	0.631(2)	0.113(2)	0.805(1)	7.6(7)
C15	0.639(2)	0.154(2)	0.682(1)	6.0(6)
C16	0.694(2)	0.151(2)	0.621(1)	5.9(6)
C17	0.691(2)	−0.122(2)	0.927(2)	8.3(8)
C18	0.720(2)	−0.220(2)	0.921(2)	12(1)
C19	0.533(2)	−0.086(2)	0.827(1)	6.5(7)
C20	0.463(2)	−0.059(2)	0.879(2)	9.9(9)
C21	0.827(2)	0.265(2)	0.687(1)	7.2(7)
C22	0.790(2)	0.362(2)	0.636(2)	11(1)
C23	0.861(2)	0.158(2)	0.591(2)	11(1)
C24	0.885(2)	0.065(3)	0.575(2)	12(1)
Li1	0.827(3)	0.060(3)	0.750(2)	4(1)
Li2	0.698(3)	−0.066(3)	0.751(2)	4.0(9)

[a] $B_{eq} = (8\pi^2/3)\sum_{i=1}^{3}\sum_{j=1}^{3}U_{ij}a_i^*a_j^*\vec{a}_i\cdot\vec{a}_j$.

and hexane in the absence of additional ligands. The high stability of the $[Li(TEDTA)]_2$ dimer structure can be ascribed to the chelating and steric effects imposed by the bulky TEDTA ligand.

Although several lithium amide complexes with internal coordinating amino groups have been reported previously, they are limited to diamines which contain one amido site and one amino site.[6] To our knowledge, lithium complexes involving a triamine ligand which coordinates to the lithium center through two amino groups and one amido group, such as the TEDTA ligand, are previously unknown.

$[Li(TEDTA)]_2$ is soluble in hexane. Our preliminary studies indicate that this compound is a very reactive deprotonation reagent in hexane. For example, it reacts rapidly with acetophenone or propiophenone to form the corresponding lithium enolates. Although we have not been able to determine the structures of the enolates due to the lack of suitable crystals, ^1H and ^{13}C NMR spectroscopic studies (Table IV) unambiguously established that the neutral TEDTA-H ligand is still coordinated to the metal center in the lithium enolates. From the reaction of propiophenone with $[Li(TEDTA)]_2$ in hexane, only one enolate isomer was obtained, as indicated by the ^1H NMR spectrum. This enolate reacted with trimethylsilyl chloride in hexane at 23 °C and was converted to (*Z*)-1-phenyl-1-[(trimethylsilyl)oxy]-1-propene nearly quantitatively after a few hours, as monitored by ^1H NMR spectroscopy.

Table III. Bond Lengths (Å) and Angles (deg)

a. Distances

N1–C1	1.44(2)	N5–Li2	2.07(4)
N1–C5	1.46(2)	N6–C16	1.42(2)
N1–C7	1.49(3)	N6–C21	1.43(3)
N1–Li1	2.13(4)	N6–C23	1.51(3)
N2–C2	1.43(2)	N6–Li1	2.24(4)
N2–C3	1.46(2)	C1–C2	1.49(3)
N2–Li1	1.99(4)	C3–C4	1.47(3)
N2–Li2	2.03(3)	C5–C6	1.53(3)
N3–C4	1.50(2)	C7–C8	1.37(3)
N3–C9	1.47(3)	C9–C10	1.51(3)
N3–C11	1.43(3)	C11–C12	1.35(3)
N3–Li2	2.10(4)	C13–C14	1.50(3)
N4–C13	1.49(2)	C15–C16	1.48(3)
N4–C17	1.48(3)	C17–C18	1.37(3)
N4–C19	1.37(2)	C19–C20	1.56(3)
N4–Li2	2.23(4)	C21–C22	1.57(3)
N5–C14	1.43(2)	C23–C24	1.33(4)
N5–C15	1.40(2)	N5–Li1	2.01(3)

b. Angles

C1–N1–C5	113(2)	C14–N5–Li2	105(2)
C1–N1–C7	114(2)	C15–N5–Li1	107(2)
C1–N1–Li1	95(2)	C15–N5–Li2	130(2)
C5–N1–C7	106(2)	Li1–N5–Li2	73(1)
C5–N1–Li1	105(2)	C16–N6–C21	113(2)
C7–N1–Li1	123(2)	C16–N6–C23	117(2)
C2–N2–C3	110(2)	C16–N6–Li1	94(1)
C2–N2–Li1	105(2)	C21–N6–C23	108(2)
C2–N2–Li2	134(2)	C21–N6–Li1	104(2)
C3–N2–Li1	133(2)	C23–N6–Li1	120(2)
C3–N2–Li2	101(2)	N1–C1–C2	113(2)
Li1–N2–Li2	75(2)	N2–C2–C1	113(2)
C4–N3–C9	112(2)	N2–C3–C4	112(2)
C4–N3–C11	110(2)	N3–C4–C3	114(2)
C4–N3–Li2	94(2)	N1–C5–C6	119(2)
C9–N3–C11	117(2)	N1–C7–C8	119(2)
C9–N3–Li2	105(2)	N3–C9–C10	117(2)
C11–N3–Li2	118(2)	N3–C11–C12	124(2)
C13–N4–C17	105(2)	N4–C13–C14	114(2)
C13–N4–C19	115(2)	N5–C14–C13	113(2)
C13–N4–Li2	95(2)	N5–C15–C16	114(2)
C17–N4–C19	113(2)	N6–C16–C15	115(2)
C17–N4–Li2	120(2)	N4–C17–C18	120(2)
C19–N4–Li2	107(2)	N4–C19–C20	119(2)
C14–N5–C15	108(2)	N6–C21–C22	118(2)
C14–N5–Li1	134(2)	N6–C23–C24	117(3)
N1–Li1–N2	89(2)	N2–Li2–N3	92(1)
N1–Li1–N5	133(2)	N2–Li2–N4	125(2)
N1–Li1–N6	115(2)	N2–Li2–N5	104(2)
N2–Li1–N5	108(2)	N3–Li2–N4	122(2)
N2–Li1–N6	133(2)	N3–Li2–N5	127(2)
N5–Li1–N6	86(1)	N4–Li2–N5	88(1)

Table IV. ^{13}C NMR Data for TEDTA-H Ligand (C_6D_6, δ, ppm, 293 K)

free ligand	12.56, 47.52, 48.61, 53.69
with $Li(CH_2{=}C(O)Ph)$	11.98, 47.05, 47.89, 53.23
with $Li(CH_3CH{=}C(O)Ph)$	11.28, 46.35, 46.57, 52.23

The selective formation of the *Z* isomer is not unexpected since the similar selectivity was observed for LDA.[2,7]

Although it is not clear yet whether or not $[Li(TEDTA)]_2$ is superior to the traditional LDA, the high stability, high solubility, and high reactivity with ketones of this compound in noncoordinating solvents certainly provides a new alternative in organic synthesis where the performance of traditional lithium amides may not be satisfactory.

Experimental Section

All reactions were carried out under a nitrogen atmosphere. All solvents were freshly dried and distilled prior to use. The tetraethyldiethylenetriamine (TEDTA-H)

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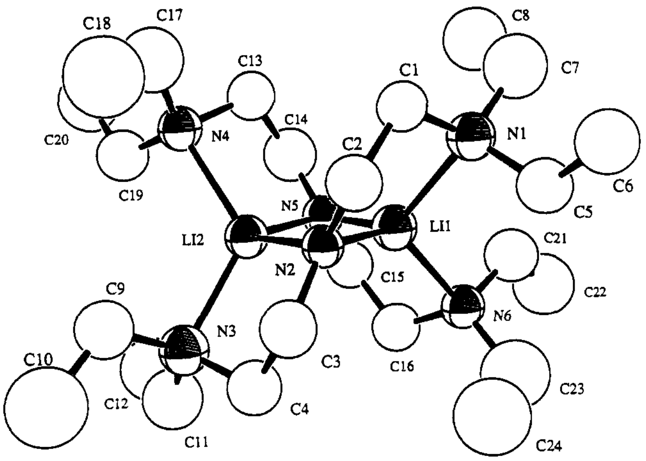


Figure 1. ORTEP diagram for [Li(TEDTA)]$_2$ with labeling scheme and 50% thermal ellipsoids.

ligand was prepared according to published procedures.[4] n-Butyllithium, acetophenone, propiophenone, and trimethylsilyl chloride were purchased from Aldrich. NMR spectra were recorded on a Brüker AC-300 spectrometer.

Synthesis of [Li(TEDTA)]$_2$. A 1.16-mL (1.86-mmol) aliquot of 1.6 M ^{n}BuLi was added to a hexane solution containing 0.40 g (1.86 mmol) of TEDTA-H at 23 °C. After being stirred for 1 h, the volume of the solution was reduced by vacuum. The solid was collected by filtration and washed several times with hexane to remove the yellow impurities. The isolated yield of the colorless, crystalline compound [Li(TEDTA)]$_2$ was about 40%. The yield can be improved by further reducing the volume of the filtrate and collecting the precipitated product. ^{13}C NMR data for [Li(TEDTA)]$_2$ (toluene-d_8, δ, ppm): (223 K) 5.08, 13.53, 43.13, 48.84, 52.09, 57.75; (273 K) 47.36 (br), 53.47, 57.64; (293 K) 9.11, 45.58, 53.91, 57.59. ^{7}Li NMR data for [Li(TEDTA)]$_2$ (toluene-d_8, ^{7}LiCl as reference): (183 K) −1.00; (298 K) −0.69.

Reaction of [Li(TEDTA)]$_2$ with Propiophenone. Propiophenone (0.060 g, 0.45 mmol) was added dropwise to the hexane solution containing 0.100 g (0.23 mmol) of [Li(TEDTA)]$_2$ at −78 °C. The solution was stirred for 1 h. A portion of the solution was transferred to another flask and evaporated to dryness by vacuum. The yellow oil obtained was dissolved in C_6D_6. NMR spectra indicated that the propiophenone has been completely deprotonated to form the lithium enolate. The reaction with acetophenone was performed similarly. ^{1}H NMR data (benzene-d_6, 293 K): δ, for Li(CH$_2$=C(O)Ph) 4.07 (CH), 4.67 (CH); for Li(CH$_3$CH=C(O)Ph) 2.11 (d, CH$_3$, J = 6 Hz, 5.10 (q, CH, J = 6 Hz).

Reaction of Me$_3$SiCl with Lithium Enolate. A stoichiometric amount of Me$_3$SiCl was added to the lithium enolate solution described above at −78 °C. The solution was then allowed to warm to 23 °C. A colorless solid formed. The content of the solution was monitored by NMR spectroscopy by removing a portion of the solution to another flask and pumping it to dryness by vacuum. The NMR spectrum of the residue was taken in C_6D_6 and $CDCl_3$. After about 5 h, the lithium enolate was converted to (Z)-1-phenyl-1-[(trimethylsily)oxy]-1-propene nearly quantitatively. ^{1}H NMR data for (Z)-CH$_3$CH=C(OSiMe$_3$)Ph (CDCl$_3$, 293 K): δ 1.70 (d, CH$_3$, J = 6 Hz), 5.29 (q, CH, J = 6 Hz).

X-ray Crystallography. Single crystals of [Li(TEDTA)]$_2$ were obtained from a concentrated toluene solution.

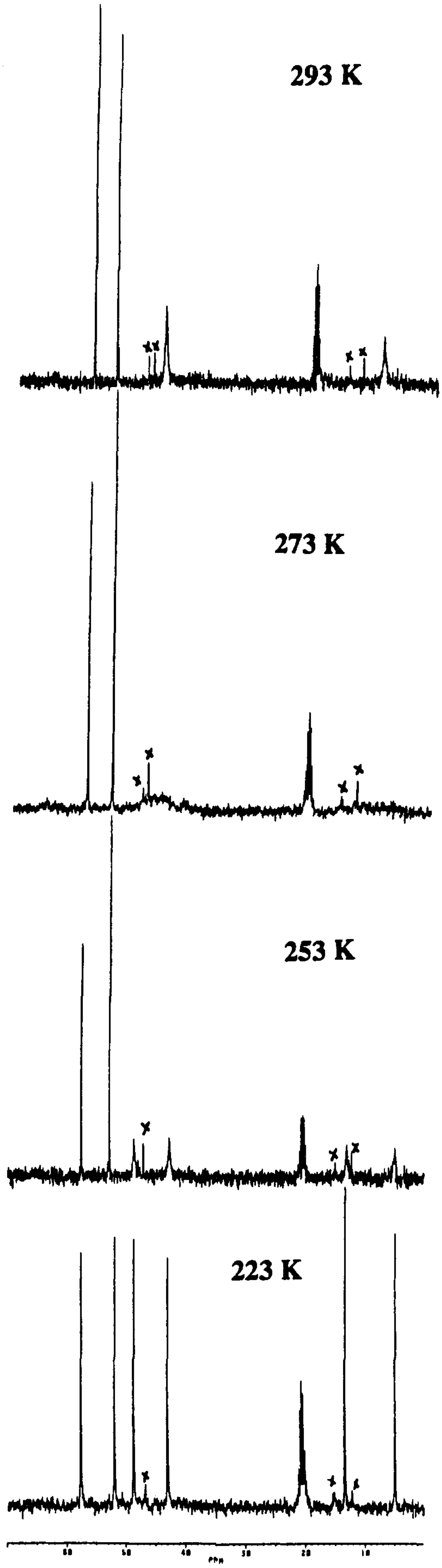
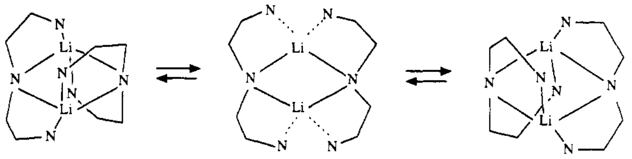


Figure 2. Variable temperature ^{13}C NMR spectra for [Li(TEDTA)]$_2$ in toluene-d_8.

Scheme I



The crystal was mounted and sealed in a 0.5-mm capillary. Data were collected at 23 °C over the range of $3 < 2\theta < 45°$ on a Rigaku AFC6-S diffractometer with graphite-monochromated Mo Kα radiation operated at 50 kV and 35 mA. The initial orientation matrix was obtained from 20 reflections ($10 < 2\theta < 16°$), located by the SEARCH routine. No high angle cell refinement was performed. Three standard reflections were measured every 147 reflections. No significant decay during the data collection period was observed. Data were processed on a VAX workstation 3520 using the TEXSAN crystallographic package (version 5.0). Data were corrected for Lorentz–polarization effects. Neutral-atom scattering factors were taken from Cromer and Waber.[8]

The crystal of [Li(TEDTA)]$_2$ belongs to the monoclinic crystal system. The space group $P2_1/a$ was unambiguously determined by the systematic absences. The structure was solved by the direct methods of the SHELXS option. Full-matrix least squares refinements were applied. Due to the low data/variable ratio all atoms were refined isotropically. The positions of hydrogen atoms were calculated. Their temperature factors were tied to the temperature factors of the carbon atoms to which they are bonded (multiplied by 1.10). Their contribution in structure factors calculations was included. The high R factor is believed to be caused by the lack of sufficient data. The data for the X-ray diffraction analysis are given in Table I.

Acknowledgment. We thank Professor James R. Green for his helpful discussions on lithium amide chemistry and the NSERC (Canada) for financial support.

Supplementary Material Available: Tables of H atom coordinates and isotropic thermal parameters, bond distances, and bond angles (6 pages). Ordering information is given on any current masthead page.

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