Proton−Lithium Binding Behavior of Tris(2-((pyrid-2-ylmethyl)uredio)ethyl)amine

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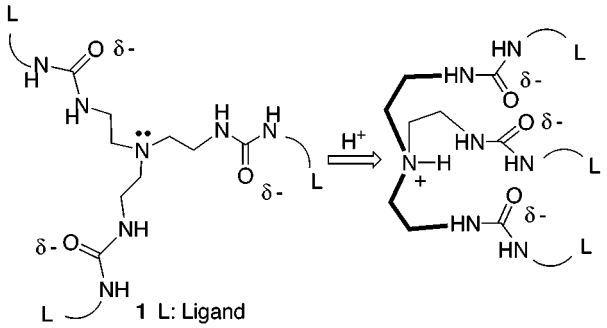
Tris(2-((pyrid-2-ylmethyl)uredio)ethyl)amine (**2**) and its perchlorate salt, **2**·$HClO_4$, bind with Li^+ in nitromethane in a 1:1 fashion. The stability constants of $K(Li^+)$ and $K^H(Li^+)$ were found to be 112 ± 25 and 130 ± 30 M^{-1} in CD_3NO_2, respectively. Formation of the 1:1 complexes were further evidenced by electrospray ionization mass spectrometry (ESI-MS). The slight increase, or at least the same order of magnitude, of $K^H(Li^+)$ compared to $K(Li^+)$ points to a remarkable preorganization of the protonated podand in **2**·$HClO_4$, that essentially overcomes the increased Columbic repulsion occurring on complexation to Li^+.

Because of the actual and potential applications of Li^+ in science, medicine, and technology, there is growing interest in designing artificial lithium ionophores.[1] Since Li^+ is a typical hard Lewis acid, Li^+ complexation would be predominately controlled by electrostatic interactions if hard donors such as O- or N-donor ligands are involved. Our current interest is to design various kinds of host that bind guest molecules or ions cooperatively through electrostatic interactions. The proton-sensitive lithium hosts are of particular interest because their binding behavior is controlled by the acidity of the environment. Podand **1** intrigues several organic research teams because of its ability in binding with a variety of cations as well as anions.[2−11] Since ureas and cyclic derivatives thereof are known to possess powerful ligating abilities



that are due primarily to their highly polarized carbonyl groups, macrocycles and podands incorporating ureas as the ligands have been extensively studied. However, ureas as ligands have still received much less attention[2−11,13−32] compared to their polyoxa, polyoxo, and polyaza congeners. In our study, we are interested in using podand **1** as a host for Li^+. This type of podand has been developed as a host for K^+ and Na^+ binding.[3] According to the results of previous studies,[10,18,26] we

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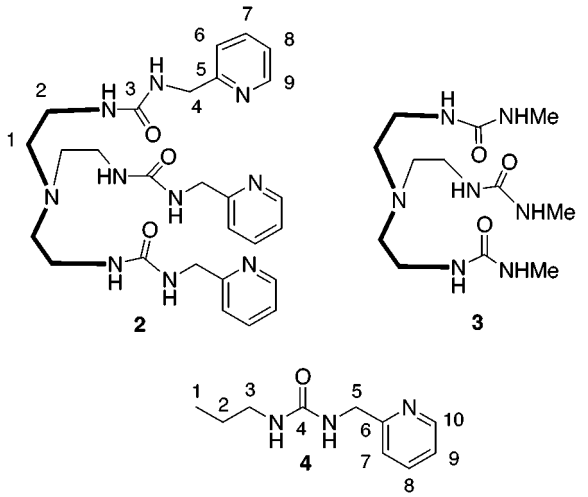
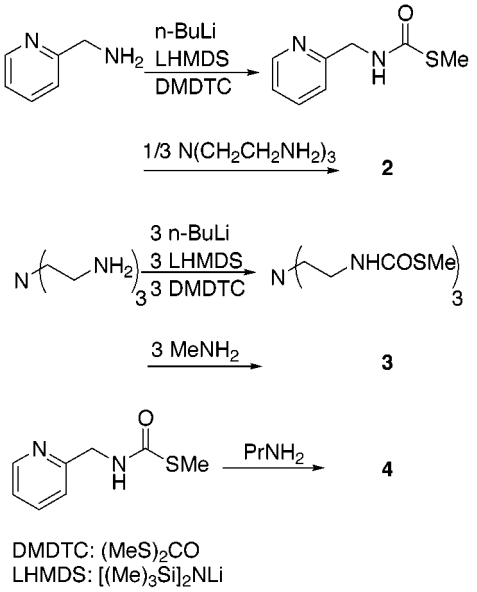
believe that protonation at the locus would establish an electrostatic attraction, gathering the dipolar sidearms together to form a new cavity for binding. To form a cavity for Li^+ cation, we introduce a pyridyl ligand on each of the sidearms. It has been known that pyridine-containing macrocycles are good hosts for Li^+ complexation.[33,34] In this paper, we report an interesting proton−lithium binding behavior of **2**.



To examine the aforementioned design, podands **2** and **3** and a model of the sidearm **4**[35] were prepared through two-step thiocarbamate synthetic sequences (Scheme 1).[36] Single crystal X-ray crystallographic analysis clearly demonstrated that **3** possesses an extended conformation in the crystal lattice with the dipolar groups pointing away from the axial nitrogen (Figure 1). The distances between the axial nitrogen N(1) and the carbonyl oxygen atoms O(1), O(2), and O(3) are 4.591 (54), 4.953 (37), and 3.431 (41) Å, respectively. This conformation is particularly favored because the offending lone-pair dipole repulsion could be reduced. A three-dimensional network of **3** through intramolecular and intermolecular hydrogen bonds is formed in the crystal lattice. As shown in Figure 1, the carbonyl oxygen O(1) is hydrogen-bonded to N(5′)H with a distance of 2.062 (3) Å. In addition, O(3) is

Scheme 1



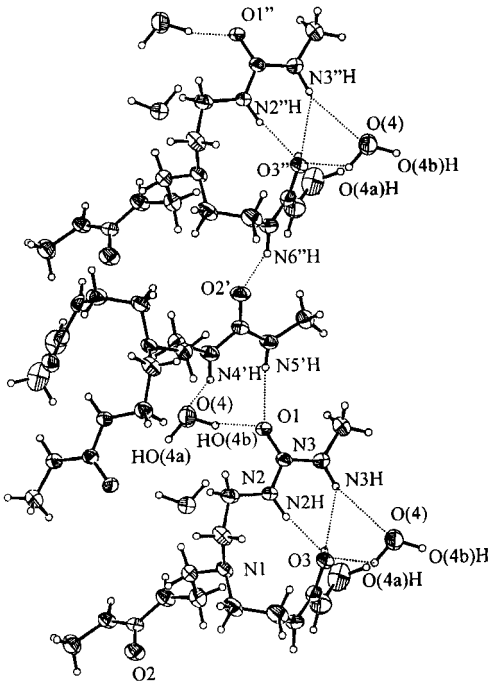


Figure 1. ORTEP drawing of podand **3**.

hydrogen-bonded asymmetrically to N(2)H and N(3)H with a distance of 2.025 (3) and 2.558 (12), respectively. Furthermore, the third set of hydrogen bond between N(6")H and O(2′) with a distance of 1.953 (3) Å is observed. Hydrogen bonds between the ureyleno groups and H_2O in the crystal lattice have also been evidenced.

In contrast, **3**·$HClO_4$ possesses a contracted form with the axial proton being closely surrounded by the ureyleno groups (Figure 2). A propeller-like arrangement for the sidearms is shown in Figure 2b when viewed down the "C3" axis. Relatively short distances between the axial nitrogen N(3) and the carbonyl oxygen atoms O(1), O(2), and O(3) are obtained with distances of 3.312 (7), 4.326 (7), and 2.677 (5) Å, respectively. This conformation with shorter NLO distances optimizes the cation-dipole attractions between the central positive charge and the dipolar sidearms. Unlike the cases of tripodal proton-

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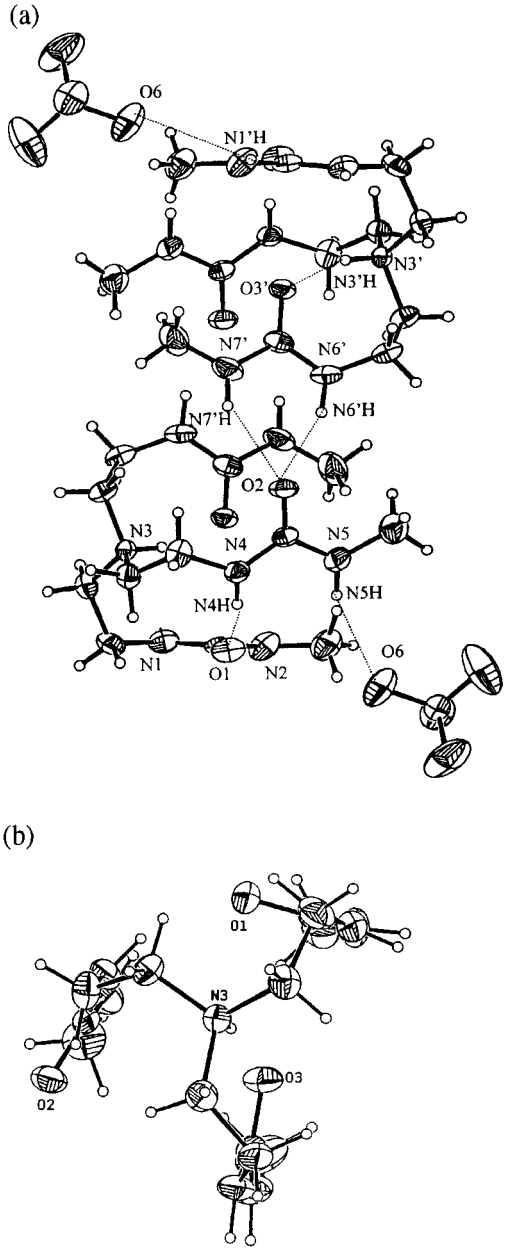

Figure 2. ORTEP drawings of the protonated podand **3** (**3**·$HClO_4$): (a) side view; (b) top view along the C_3 axis.

metal co-complexes reported in the literature,[10,11] the axial proton in this case is not symmetically trifurcated with the C=O groups. Examination of the crystal structure revealed that a hydrogen-bonded dimeric pair of **3**·H^+ is formed in the crystal lattice. The ureyleno oxygen O(1) on the first sidearm is hydrogen-bonded to N(4)H with a distance of 1.991 (3) Å while O(6) of perchlorate ions are hydrogen bonded to N(1′)H and N(5)H with a distance of 2.475 (4) and 2.398 (4) Å, respectively. On the other hand, intermolecular hydrogen bonds are formed between O(2) and N(6′)H and N(7′)H with a distance of 2.040 (3) and 2.338 (3) Å. Finally, a relatively strong intramolecular hydrogen bond is observed between O(3′) and the axial proton N(3′)H with a short distance of 1.813 (2) Å. Hydrogen-bond arrays derived from urea functional groups have been discussed extensively in recent literature.[37]

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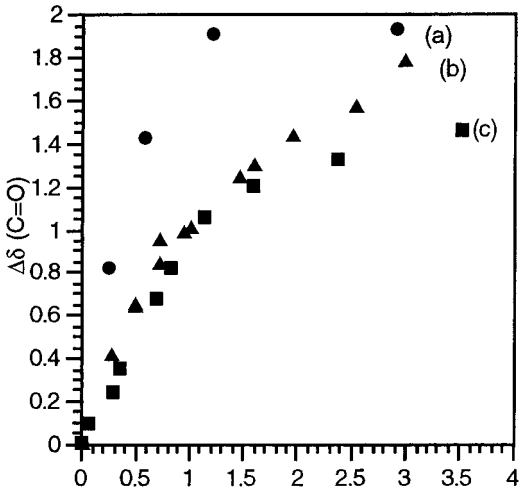
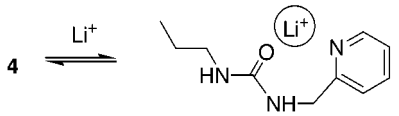


Figure 3. Titration curves of **2** (▲, curve b), **2**·$HClO_4$ (■, curve c), and **4** (●, curve a) with $LiClO_4$ at 24.0 °C. The concentrations of **2**, **2**·$HClO_4$, and **4** were kept at $(2.1 \pm 0.1) \times 10^{-2}$ M.

Table 1. Lithium Complexation Induced ^{13}C NMR Upfield and Downfield Shifts of 4

	Δδ (ppm)									
Li^+/**4**	C6	C4	C10	C8	C9	C7	C5	C3	C2	C1
0.23	−0.32	0.81	0.11	0.83	0.55	1.02	−0.05	0.06	−0.17	−0.04
0.57	−0.46	1.42	0.21	1.54	1.03	1.87	−0.03	0.08	−0.28	−0.07
0.95	−0.62	1.89	0.28	2.18	1.40	2.67	0.01	0.13	−0.41	−0.12
1.90	−0.72	1.90	0.26	2.28	1.43	2.76	−0.18	0.14	−0.46	−0.14
2.91	−0.66	1.94	0.30	2.28	1.45	2.75	−0.13	0.13	−0.43	−0.14

Although ^{1}H and ^{7}Li NMR are commonly used as tools for complexation study,[38] ^{13}C NMR spectroscopy is adapted in our experiments because it could provide more structural information about the complexes. The unambiguous assignments for the ^{13}C signals of **2**, **2**·$HClO_4$, and **4** were achieved on the basis of their 2D-COSY, HMBC, and HMQC spectra. To reduce the interference arising from $LiClO_4$ ion-pair formation[39] as well as hydrogen-bonded aggregation,[40] dilute solutions of **2**, **2**·$HClO_4$, and **4** (about 0.02 M) in CD_3NO_2 were used in the titration experiments. The results of the titration of **4** by gradually addition of $LiClO_4$ indicated that **4** favors to bind Li^+ ion in a 1:1 fashion (Figure 3, curve a). During the titration, the δ value of the carbonyl carbon was gradually shifted toward downfield region while the δ values of the pyridyl carbons were gradually shifted either toward upfield or downfield regions (Table 1). Limiting chemical shifts were reached at 1:1 **4**/Li^+ mole-ratio. It is noteworthy to mention that signals of the alkyl portion remain almost unchanged (less than 0.5 ppm) during titration. These observations suggest a 1:1 **4**/Li^+ complex formation with the Li^+ ion coincidentally binds with the pyridyl and the carbonyl groups.



Significant changes in the chemical shifts of **2**·$HClO_4$ were also observed on addition of Li^+ (Table 2). The Job

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Table 2. Lithium Complexation Induced ^{13}C NMR Upfield and Downfield Shifts of 2·HClO$_4$

	Δδ (ppm)								
Li$^+$/**2**·H$^+$	C3	C5	C9	C7	C8	C6	C1	C4	C2
0.07	0.09	−0.06	0.01	0.10	0.07	0.10	0.02	0.02	−0.01
0.30	0.23	−0.21	−0.01	0.31	0.20	0.30	0.20	0.08	−0.03
0.35	0.35	−0.22	0.10	0.33	0.24	0.39	0.11	0.14	0.00
0.70	0.68	−0.35	0.27	0.61	0.46	0.81	0.29	0.29	−0.02
0.83	0.81	−0.46	0.31	0.80	0.58	1.01	0.53	0.39	0.00
1.15	1.06	−0.52	0.51	1.02	0.76	1.36	0.74	0.53	−0.02
1.59	1.20	−0.65	0.52	1.32	0.95	1.72	0.79	0.54	0.05
2.37	1.35	−0.77	0.55	1.62	1.14	2.05	0.77	0.54	0.11
2.35	1.31	−0.71	0.62	1.50	1.07	1.97	0.61	0.52	0.17
3.52	1.45	−0.81	0.69	1.78	1.21	2.20	0.65	0.44	0.14

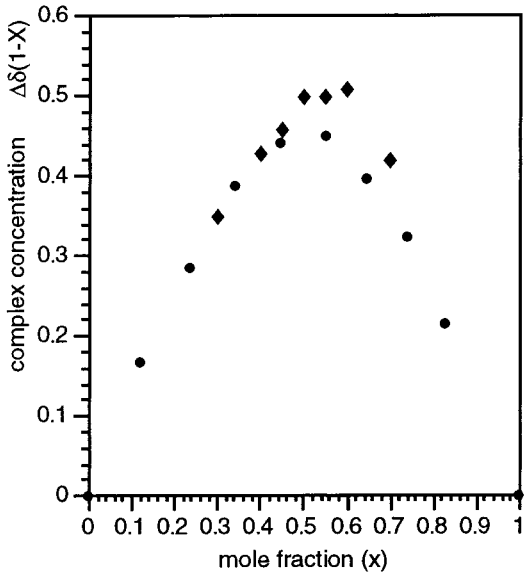


Figure 4. Job plot of **2**·HClO$_4$ (•) and **2** (◆) with LiClO$_4$ at 21.0 °C in CD$_3$NO$_2$, using the chemical shift of the C=O carbon as an index for complexation. The total concentration of **2**·HClO$_4$ is (2.0 ± 0.1) × 10^{-2} M. The total concentration of **2** is (1.9 ± 0.1) × 10^{-2} M.

plot[41] using a resonance of the carbonyl carbon for complexation between **2**·HClO$_4$ and Li$^+$ has a maximum at mole fraction of 0.5 indicative of formation of a 1:1 complex **5** (Figure 4). A nonlinear least-squares analysis of the ^{13}C NMR titration curve (Figure 3, curve c) gave the stability constant, K^H(Li$^+$) of 130 ± 30 M^{-1} in CD$_3$NO$_2$. The infinite complexation-induced shift (CIS) value calculated is 1.6 ± 0.1 ppm.

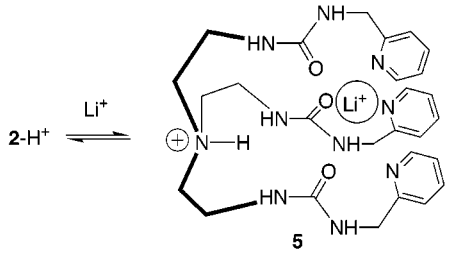
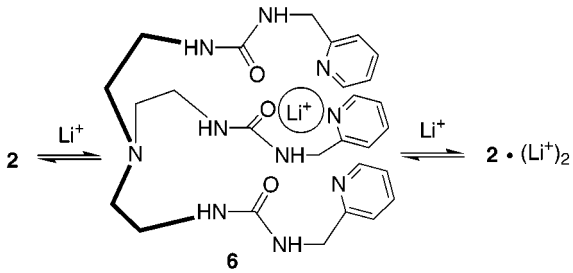


Table 3. Lithium Complexation Induced ^{13}C NMR Upfield and Downfield Shifts of 2

	Δδ (ppm)								
Li$^+$/**2**	C5	C3	C9	C7	C6	C8	C1[a]	C4	C2[a]
0.27	−0.45	0.42	0.10	0.39	0.30	0.41	−0.18	0.17	0.09
0.29	−0.43	0.40	0.12	0.39	0.30	0.43	−0.08	0.31	0.15
0.49	−0.70	0.71	0.18	0.67	0.52	0.75	−0.20	0.30	0.26
0.51	−0.70	0.63	0.15	0.66	0.49	0.71	−0.24	0.21	0.08
0.73	−0.92	0.91	0.24	0.92	0.70	1.03	−0.30	0.36	0.38
0.73	−0.92	0.85	0.16	0.92	0.68	1.00	−0.30	0.18	0.29
0.96	−0.97	1.05	0.30	1.23	0.91	1.39		0.42	0.35
1.02	−1.02	1.01	0.27	1.25	0.91	1.40		0.35	−0.01
1.47	−1.15	1.24	0.31	1.62	1.16	1.78		0.38	0.02
1.60	−1.11	1.36	0.36	1.63	1.24	2.01		0.48	0.35
1.97	−1.18	1.50	0.39	1.89	1.34	2.20		0.47	
2.53	−1.30	1.63	0.43	2.02	1.42	2.35		0.46	
2.98	−1.47	1.78	0.48	2.14	1.50	2.50		0.39	

[a] Due to the line-broadening effect, the chemical shift could not be further followed.

In comparison to the binding behavior of **2**·HClO$_4$, podand **2** shows a similar trend in the titration (Figure 3, curve b), indicating the formation of a 1:1 complex **6**. The possibility of accommodating the Li$^+$ in the inner cavity was eliminated because the chemical shifts of the −CH$_2$CH$_2$− groups remains almost unchanged (less than 0.4 ppm) during titration, in comparison to the large CIS of the carbonyl carbon as well as the pyridyl carbons (Table 3). A nonlinear least-squares analysis of the ^{13}C NMR titration curve (Figure 3, curve b) gave the stability constant, K(Li$^+$), of 112 ± 25 M^{-1} in CD$_3$NO$_2$. The infinite CIS value calculated for the carbonyl carbon is 2.1 ± 0.1 ppm.



The slight increase, or at least the same order of magnitude, of K^H(Li$^+$) compared to K(Li$^+$) points to a remarkable preorganization of the protonated podand in **2**·HClO$_4$, that essentially overcomes the increased Columbic repulsion occurring on complexation to Li$^+$.[10,18,26,42,43] More interesting is the fact that the Job plot (Figure 4) for the formation of **6** has a maximum slightly deviated from the mole fraction of 0.5 indicative of formation of higher complexes. One of the possible explanations for this observation is that the weak strength complex **6** partially disintegrates in the presence of large excess of Li$^+$ to form higher complexes at the later stage of the Job-plot experiment. In contrast, prealigned and held by the extra attractions between the central ammonium group and the ureyleno sidearms, complex **5** is relatively stable and the integrity of the complex could be maintained even in the presence of excess amounts of Li$^+$. Moreover, the higher Columbic repulsion arising from the doubly charged **5** would also prevent it from binding with additional Li$^+$.

(39) According to the literature, less than 10% of LiClO$_4$ contact ion-pair would be formed under our conditions. For references see: (a) Cahen, Y. M.; Handy, P. R.; Roach, E. T.; Popov, A. I. *J. Phys. Chem.* **1975**, *79*, 80. (b) Berman, H. A.; Stengle, T. R. *J. Phys. Chem.* **1975**, *79*, 1001.

(40) Within our dilute concentration range, the pattern of the ^{1}H NMR spectra is concentration independent, indicating that the possibility of intermolecular hydrogen-bonding aggregate formation has been eliminated.

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The Li^+ complexation behavior of **2** and **2**·$HClO_4$ was also evaluated by electrospray ionization mass spectroscopy (ESI-MS).[44] Although mass spectrometry only reflects the properties of gas-phase species, it has been known that the correlation between gas phase and solution is often good for ESI-MS.[45] Under the conditions we selected for our experiments, the concentration dependent complexation behavior could be clearly observed. According to the spectrum of a 1:1 **2**/$LiClO_4$ solution, formation of [**2**·Li]$^+$ is clearly demonstrated on the basis of the peak at $m/z = 555$ (100). When the stoichiometry of Li^+/**2** increased from a ratio of 1:1 to 3:1, the relative signal intensity at $m/z = 661$ for [**2** + Li + $LiClO_4$]$^+$ increased from 1% to 12%. This result is consistent with the proposal of higher complex formation in the presence of excess lithium ions.

In comparison, the spectrum of a 1:1 **2**·$HClO_4$/$LiClO_4$ solution is more complicated and shows a strong peak at m/z = [**2**·H]$^+$ (77) along with a base peak at m/z = [**2**·Li]$^+$. When the stoichiometry of Li^+/**2**·$HClO_4$ increased from a ratio of 1:1 to 3:1, the relative signal intensity for [**2**·H]$^+$ decreased from 77% to 9% while the signal for [**2**·Li]$^+$ remains as the base peak. Probably due to the relatively lower stability of [**2**·Li·H]$^{2+}$ in gas phase and further fragmentation may occur in the ionization process, the signal for [**2** + Li + $HClO_4$]$^+$ (about 20%) is not the most intense as expected. Nevertheless, the formation of [**2**·Li·H]$^{2+}$ is undoubtedly evidenced. Indeed further investigation of the fragmentation behavior of [**2** + Li + $HClO_4$]$^+$ byproduct-ion mass spectrometry (PIMS) revealed that [**2** + Li + $HClO_4$]$^+$ fragments exclusively to give [**2**·Li]$^+$ in the MS. Furthermore, the constant intensity-ratio of [**2**·Li]$^+$/[**2** + Li + $HClO_4$]$^+$ in the MS, independent of the original stoichiometry of Li^+/**2**·$HClO_4$, clearly explains the origin of [**2**·Li]$^+$. Since the complex of [**2**·Li·H]$^{2+}$ would be favorably formed in nitromethane-d_3 but not in the gas phase, we tentatively suggest the necessity of a polar environment that is essential for the stabilization of the doubly charged [**2**·Li·H]$^{2+}$ complex. Again, significant amounts of higher complexes such as [**2** + H + 2$LiClO_4$]$^+$ were also observed in the presence of excess lithium ions in the ESI-MS.

In summary, our note reports unusual lithium complexation of **2** to give **2**·Li^+ in nitromethane. Since the columbic repulsion between the proton and lithium ion is partially compensated by the ion−dipole interactions, along with an entropically favored cavity-preorganization, the [**2**·Li·H]$^{2+}$ complex could also be formed effectively in solution.

Experimental Section

Materials. Amines were commercially available and used as received. *S,S*-Dimethyl dithiocarbonate (DMDTC) was prepared according to the procedures reported literatures.[36]

Tris(2-((pyrid-2-ylmethyl)uredio)ethyl)amine (2). To a solution of 2-aminomethylpyridine (21.0 g, 195 mmol) and 1,1,1,3,3,3-hexamethyldisilazane (32.4 g, 201 mmol) in THF (125 mL) at −78 °C was added *n*-BuLi (248 mL, 1.6 M in hexane, 400 mmol) under N_2. After addition, the solution was stirred at −78 °C for 0.5 h, followed by addition of a solution of DMDTC (23.8 g, 195 mmol) in THF (35 mL). The solution was then allowed to warmed gradually to room temperature and further reacted for 17 h. The reaction was quenched by pouring into ice−water. The crude product was extracted with $CHCl_3$ for three times, washed with brine, dried over anhydrous $MgSO_4$, concentrated under reduced pressure to provide crude solid. The crude solid was purified through a silica gel column, using a mixture of MeOH and CH_2Cl_2 (1:20) as the eluent to afford *S*-methyl (*N*-pyrid-2-ylmethyl)thiocarbamate as colorless crystals (9.8 g, 54 mmol, 28%): mp 100−101 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, J = 4.5 Hz, 1H), 7.60 (m, 1H), 7.42 (bs, 1H), 7.24 (m, 1H), 7.13 (m, 1H), 4.52 (d, J = 5.4 Hz, 2H), 2.29 (s, 3H); ^{13}C NMR (75 MHz, d_6-DMSO) 166.8, 158.2, 148.9, 136.7, 122.2, 120.9, 45.9, 11.6; IR (KBr) cm^{-1} 3165, 2929, 1672; MS (EI, 20 eV) m/z 183 (M^+ + H, 22). Anal. Calcd for $C_8H_{10}N_2OS$: C, 52.75; H, 5.49; N 15.38. Found: C, 52.64; H, 5.52; N 15.38.

To a solution of *S*-methyl (*N*-pyrid-2-ylmethyl)thiocarbamate (8.0 g, 44 mmol) in MeOH (96 mL) was added tris(2-aminoethyl)amine (1.84 g, 12.4 mmol). The reaction mixture was heated at reflux temperature for 48 h and then concentrated under reduced pressure to provide a crude solid. The crude solid was washed with EtOAc and further purified by recrystallization from nitromethane to afford **2** as a colorless solid (6.48 g, 11.8 mmol, 94%). Noteworthy to mention is that recrystallization of **2** from nitromethane gives colorless a gel-like solid that holds up certain amounts of solvent. Removal of the solvent under vacuum affords a slightly hygroscopic rock-like solid. Therefore, samples prepared for NMR measurements have to be dried under vacuum at 70 °C for 24 h before use: mp 210−211 °C; ^{1}H NMR (200 MHz, d_6-DMSO) δ 8.45 (d, J = 3.7 Hz, 3H), 7.69 (m, 3H), 7.19−7.26 (m, 6H), 6.56 (bt, 3H), 5.94 (bt, 3H), 4.28 (d, J = 5.4 Hz, 6H), 3.08 (m, 6H), 2.49 (m, 6H); ^{13}C NMR (100 MHz, CD_3NO_2) δ 158.7, 158.4 (C=O), 148.0, 135.9, 121.1, 120.5, 53.8, 44.1, 37.3; IR (KBr) cm^{-1} 3331, 1628, 1585; FAB (NBA) 549.3 (M^+ + H). Anal. Calcd for $C_{27}H_{36}N_{10}O_3$: C, 59.11; H, 6.61; N, 25.53. Found: C, 57.74; H, 6.73; N, 24.95.

Tris((2-(pyrid-2-ylmethyl)uredio)ethyl)amine Hydrogen Perchlorate (2·$HClO_4$). To a solution of **2** (1 g, 1.82 mmol) in MeOH (26 mL) was added $HClO_4$ (70%, 11.2 M, 0.163 mL, 0.27 g). After the mixture was stirred overnight, MeOH was removed under reduced pressure to provide a glassy solid. We conclude that protonation occurs on the central tertiary amine on the basis of the significant $\Delta\delta$ of the ethano groups before and after protonation. Since the compound is slightly hygroscopic, samples prepared for NMR measurements were dried under vacuum at 70 °C for 24 h before use: ^{1}H NMR (300 MHz, DMSO) δ 8.46 (d, J = 3.6 Hz, 3H), 7.72 (t, J = 7.8 Hz, 3H), 7.21−7.23 (m, 6H), 6.83 (bt, 3H), 6.46 (bt, 3H), 4.31 (d, J = 5.7 Hz, 6H), 3.35 (m, 6H), 3.22 (m, 6H); ^{13}C NMR (100 MHz, CD_3NO_2) δ 158.8 (C=O), 157.7, 147.7, 136.5, 121.5, 121.0, 55.1, 44.0, 35.2. FAB (NBA) 549.3 (M^+ + H).

Tris(2-(methyluredio)ethyl)amine (3). To a solution of tris(2-aminoethyl)amine (3.2 g, 22 mmol) and 1,1,1,3,3,3-hexamethyldisilazane (10.6 g, 66 mmol) in THF (70 mL) at −78 °C was added *n*-BuLi (81 mL, 1.6 M in hexane, 130 mmol) under N_2. After addition, the solution was stirred at −78 °C for 0.5 h, followed by addition of a solution of DMDTC (8.1 g, 66 mmol) in THF (20 mL). The solution was then allowed to react at room temperature for 6 h. The reaction was quenched by pouring it into ice−water. The crude product was extracted with CH_2Cl_2, washed with brine, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to provide crude solid. The crude solid was purified through a silica gel column, using a mixture of MeOH and CH_2Cl_2 (1:10) as the eluent to afford tris(2-(methylthiocarbonylamino)ethyl)amine (TMTCEA) as colorless crystals (4.0 g, 50%): mp 116−118 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.37(s, 3H), 3.30−3.33 (m, 6H), 2.53−2.55 (m, 6H), 2.35 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 54.04, 39.2, 12.5; IR (KBr) cm^{-1} 3263, 1651, 1637; MS

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FAB (NBA) 369 ($M^+ + H$). Anal. Calcd for $C_4H_{24}N_4O_3S_3$: C, 39.10; H, 6.56; N, 15.20. Found: C, 38.98; H, 6.56; N, 15.21.

To a solution of TMTCEA (280 mg, 0.76 mmol) in MeOH (5 mL) was added methylamine (2 M in MeOH, 2 mL, 4 mmol). The solution was allowed to heat at reflux temperature for 12 h. The reaction mixture was then concentrated under reduced pressure to provide a crude solid. The crude solid was purified by recrystallization, using MeOH−CH_2Cl_2 as a solvent to afford **3** as colorless crystals (209 mg, 0.66 mmol, 87%): mp 191−193 °C; ^{1}H NMR (200 MHz, D_2O) δ 2.99 (t, $J = 6$ Hz, 6 H), 2.46 (s, 9H), 2.42 (t, $J = 6$ Hz, 6 H); ^{13}C NMR (100 MHz, D_2O, CH_3CN as the internal standard: δ 1.00, 118.25) δ 160.4, 52.4, 36.7, 25.5; IR (KBr) cm^{-1} 3352, 1630, 1593; FAB (NBA) 318.3 ($M^+ + H$). Anal. Calcd for $C_{12}H_{27}N_7O_3$: C, 45.41; H, 8.57; N, 30.89. Found: C, 45.25; H, 85.3; N, 30.74.

***N*-(Pyrid-2-ylmethyl)-*N*′-propylurea (4).**[35] To a solution of *S*-methyl (*N*-pyrid-2-ylmethyl)-thiocarbamate (0.48 g, 2.6 mmol) in MeOH (2 mL) was added 1-propylamine (1.6 g, 26 mmol). The solution was allowed reacted at 60 °C for 9 h. The reaction mixture was then concentrated under reduced pressure to provide a crude solid. The crude solid was purified by recrystallization, using $CHCl_3$-EtOAc as a solvent to afford colorless crystals (0.3 g, 1.6 mmol, 59%): mp 90−91 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.48 (m, 1H), 7.63 (m, 1H), 7.26 (d, $J = 8.0$ Hz, 1H), 7.15 (m, 1H), 5.61 (bs, 1H), 4.86 (bs, 1H), 4.46 (d, $J = 5.4$ Hz, 2H), 3.13 (q, $J = 6.5$ Hz, 2H), 1.40−1.58 (m, 2H), 0.89 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (100 MHz, CD_3NO_2) δ 158.6, 157.5, 148.0, 135.7, 121.0, 120.2, 44.4, 40.9, 22.3, 9.4; IR (KBr) cm^{-1} 3332, 2955, 1626, 1588; MS (EI, 20 eV) *m*/*z* 193 (M^+, 38), 135 (93), 92 (100); HMRS (EI, 70 eV) calcd for $C_{10}H_{15}N_3O$ 193.1215, obsd 193.1209. Anal. Calcd for $C_{10}H_{15}N_3O$: C, 62.14; H, 7.83; N, 21.75. Found: C, 62.00; H, 7.69; N, 21.56.

Preparation of Single Crystals of Tris(2-(methylureido)ethyl)amine (3). Vapor diffusion of diethyl ether into a solution of **3** in methanol−H_2O (95:5) affords colorless crystals which are suitable for X-ray crystallographic analysis.

Preparation of Single Crystals of Tris(2-(methylureido)ethyl)amine Hydrogen Perchlorate (3·HClO$_4$). To a stirred solution of **3** (33 mg, 0.10 mmol) in methanol was added hydrogen perchlorate (70%) (11.2 M, 15 mg, 0.10 mmol). The mixture was concentrated under reduced pressure to afford a colorless solid. Vapor diffusion of diethyl ether into a solution of **3** in MeOH affords colorless crystals that are suitable for X-ray crystallographic analysis.

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Supporting Information Available: ^{1}H NMR and ^{13}C NMR spectra of **2** and **2**·HClO$_4$, the ^{13}C NMR assignments for **2** and **2**·HClO$_4$, procedures and data for ESI-MS experiments, and crystallography data for **3** and **3**·HClO$_4$. This material is available free of charge via the Internet at http://pubs.acs.org.

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