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Solution- and Solid-State Structure and Dynamics of Thiophosphonamide Anions: Electronic Tuning of Rotational Barriers

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Carbanionic compounds are indisputably the most powerful and diverse class of reagents for the selective construction of carbon–carbon bonds.[1] In the subclass of heteroatom-stabilized carbanions, those derived from phosphorus have played a dominant role in the construction of C–C double bonds[2] and recently in asymmetric synthesis of chiral (phosphorus-[3] and non-phosphorus-containing[4]) compounds.

R[1]=H, R[2]=Ph: **1**
R[1]= R[2]=Me: **2**

R[1]=H, R[2]=Ph: **3**
R[1]= R[2]=Me: **4**
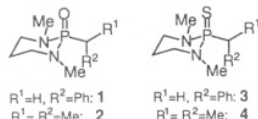
Our interest in the design, development, and application of chiral, phosphorus-based anionic reagents[5] has led to a study of their structure. Recent reports from these laboratories have disclosed the X-ray structures of phosphonamide-stabilized carbanions Li^{+}**1**[-] and Li^{+}**2**[-] along with the solution aggregation and anion hybridization state.[6] In both cases the anions have the following characteristics: (1) dimeric structure, (2) no C–Li contact, (3) nearly planar sp[2] carbanionic carbon, (4) parallel conformation ($\theta = 0$, Figure 1), and (5) a low barrier of rotation around the phosphorus–carbon bond. The low barrier (<8 kcal/mol) was a serious concern for the design of effective chiral auxiliaries. Since the origin of the barrier is the splitting between the $2e_x$ and $2e_y$ acceptor orbitals on phosphorus (which is very small, due to the similar electronegativity of nitrogen and oxygen,[7] Figure 1, X = O), we chose to increase the magnitude of the splitting (and thus the barrier) by enhancing the electronic dissimilarity of the phosphorus ligands and thus turned our attention to *thio*phosphonamides[8-10] **3** and **4** (Figure 1, X = S).
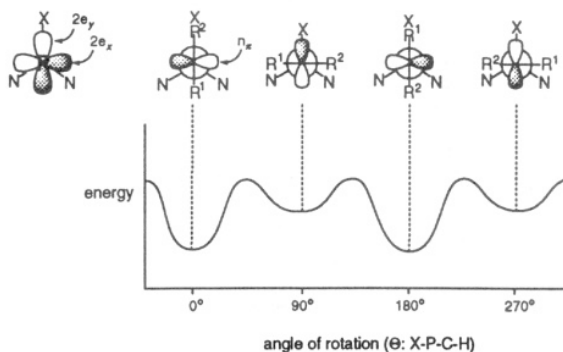

Figure 1. Energy profile of conformation for *P*-stabilized anions.

Since thiophosphonamide anions have not been spectroscopically characterized, comparison of Li^{+}**3**[-] and Li^{+}**4**[-] with the known P=O analogs[6] was undertaken (Table I). Differences in anion structure were immediately apparent from the greater solubility of Li^{+}**3**[-] and Li^{+}**4**[-]. The significant *upfield* [31]P shift upon deprotonation contrasted the phosphonamides, which show a significant *downfield* shift due to polarization of the P=O bond.[11] The [6]Li and ^{7}Li NMR spectra further illustrated fundamental differences between the P=S and P=O anions. Narrow lines were observed at low temperatures in the [7]Li spectra of Li^{+}**3**[-] and Li^{+}**4**[-], indicative of symmetrically solvated lithium (*i.e.*, [Li-(THF)$_4$][+]).[12] Also, the [7]Li chemical shift was found to be in the solvated lithium cation range.[12,13] Further, the [6]Li resonances were very narrow ($W_{1/2}$ = 0.6 to 0.3 Hz), and no phosphorus–lithium coupling was observed.[14] On the other hand, Li^{+}**1**[-] and Li^{+}**2**[-] had broad [7]Li resonances, indicative of an asymmetric ligand sphere, and [6]Li–[31]P coupling was observed.[6] Finally, data from the ^{13}C NMR spectra, in particular the $\Delta^1 J_{CP}$, revealed that the hybridization state of the anionic carbon was the same as in Li^{+}**1**[-] and Li^{+}**2**[-].[15] In all cases, $^1J_{CP}$ increased significantly, indicating an increase in s-character. This was corroborated in Li^{+}**3**[-] by the increase in $^1J_{CH}$[16] which is also indicative of a change in hybridization from sp[3] to sp[2]. *Thus, the spectroscopic data are consistent with monomeric solvent-separated ion pairs (SSIP) for Li^{+}**3**[-] and Li^{+}**4**[-], not disolvated dimers as was found for Li^{+}**1**[-] and Li^{+}**2**[-].*

Further evidence for monomeric solvent-separated ion pairs came from cryoscopic measurements which revealed an aggregation state of 1.2 ± 0.1 for Li^{+}**4**[-].[17] This aggregation state clearly does not support a dimeric structure found in the phosphonamides or separated ions.

The determination of the rotational barrier was best accomplished using Li^{+}**4**[-]. In the slow rotation limit, the anion should adopt a parallel conformation since the $2e_y$ orbital (linear combination of the P–N bonds) should constitute a better acceptor

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Table I.[a] Selected NMR Data for Li⁺1⁻, Li⁺2⁻, Li⁺3⁻, and Li⁺4⁻

compd	$\Delta\delta$ ^{31}P[a]	$\Delta\delta$ ^{13}C C(6)[a]	Δ^1J_{CP}[a,b]	Δ^1J_{CH}[a,c]	δ^7Li[d]	^{7}Li$w_{1/2}$[d]	^{6}Li, mult, $^2J_{LiP}$[e]
Li⁺3⁻	−13.5	6.5	90.0	25.8	−0.064	4.0	s
Li⁺1⁻	18.4	4.6	105.7	21.3	−0.449	10.9	t, 1.2
Li⁺4⁻	−22.8	−11.1	96.2		0.097	3.6	s
Li⁺2⁻	9.4	−17.2	121.4		−0.406	11.5	t, 1.1

[a] Δ datum = (datum anion) − (datum neutral); negative numbers are upfield shifts. [b] 125 MHz ^{13}C, −5 °C; THF-d_8. [c] 100.6 MHz ^{13}C HET2DJ, 2 °C; THF-d_8. [d] 116 MHz ^{7}Li, THF-d_8, −105 °C (LiCl, D₂O external reference). [e] 73.6 MHz ^{6}Li, −105 °C, THF-d_8.

Table II. Thermodynamics of the Barrier to Rotation for Li⁺4⁻

solvent (concn, M)	T_c (°C)	$\Delta G_c^\ddagger$ (kcal/mol)	$\Delta S_c^\ddagger$ (cal/mol K)	$\Delta H_c^\ddagger$ (kcal/mol)
1.6:1 toluene/THF (0.29)	−77.3	9.2 ± 0.3	4.5	10.0
THF (0.33)	−67.6	9.8 ± 0.3	13.6	12.2
THF 4 equiv HMPA (0.34)	−26.9	11.4 ± 0.4	1.7	11.6

than the 2e$_x$ orbital (aligned along the P–S bond). In this limit, R¹ and R² are diastereotopic, and the resulting anisochronicity should be observed as a decoalescence of those nuclei (Figure 1). The variable-temperature ¹H and ¹³C NMR spectra were recorded over a 50–70 °C temperature range in various solvents (Table II). In THF solution, a single P-coupled doublet was observed for the isopropyl methyl signals (both by ¹H and ¹³C NMR) which decoalesced to a pair of differentially P-coupled doublets upon cooling. Complete analysis of the data revealed a significant barrier to rotation of $\Delta G^\ddagger_{205}$ = 9.8 kcal/mol.[18] In toluene–THF, the barrier decreased to $\Delta G^\ddagger_{196}$ = 9.2 kcal/mol. Remarkably, the addition of HMPA raised the barrier to $\Delta G^\ddagger_{246}$ = 11.4 kcal/mol.[19]

The observation of a measurable barrier *clearly indicated that the parallel conformation ($\theta = 0$) must be the ground state orientation of the P-stabilized anion and verified the concept of electronic modulation.* The effect of solvent on the barrier can be understood in terms of the SSIP structure. In the rotational transition state ($\theta \sim 45°$), the attenuated overlap results in an increase in the charge localized on C(6) which may be stabilized by contact with lithium. The attendant desolvation of lithium appears as a positive $\Delta S^\ddagger$. However, addition of HMPA creates free ions.[12] In this case, the strongly solvated lithium cations do not stabilize the rotational transition state, thus leading to a higher barrier ($\Delta G_c^\ddagger$) and a near-zero $\Delta S^\ddagger$.

Attempts to crystallize either Li⁺3⁻ or Li⁺4⁻ from pure THF were unsuccessful. Crystals of Li⁺3⁻ suitable for X-ray analysis were obtained by toluene containing 2 equiv of THF. Quite unexpectedly, the solid-state structure was found to be a C_2-symmetric dimer with each lithium bound to both P=S groups and solvated by two THF molecules (Figure 2).[20] The basic structural features are very similar to Li⁺1⁻.[21] The most significant differences are (1) the extreme planarity of the carbanionic carbon, (2) the equatorial disposition of both *N*-methyl groups, and (3) the idealized parallel conformation of the anion. The sum of the angles around C(6) is 360.0°, the distance of C(6) is above the P(1)–H(6)–C(7) plane (*d*) is 0.009 Å, and the angle (γ) subtended by the C(6)–P(1) vector on the C(6)–H(6)–C(7) plane is 1.3°.[22]

Figure 2. Monomeric unit of [Li⁺3⁻·2THF]₂ from X-ray analysis (40% thermal ellipsoids).

The spectroscopic data clearly show that the planarity of Li⁺3⁻ persists in solution, but the dimeric structure cannot. The lithium dimer is cleaved to solvent-separated lithium cation and thiophosphonamide anion. The equatorial disposition of *both* *N*-methyl groups and the ideal parallel conformation are consistent with the increased role of p-π overlap for anion stabilization. Delocalization of the carbanion into the P–N σ* orbitals raises the energy of these orbitals, thus making the anomeric-type hyperconjugation of the nitrogen lone pair in an equatorial position (axial methyl) unfavorable. This also creates an electronic symmetry in which both P–N σ* orbitals are equally effective acceptors.

In summary, we have found that thiophosphonamide-stabilized anions display significant differences compared their oxygen analogs. Cryoscopy and ⁷Li NMR demonstrated that the lithium cation is not covalently bound to the anion but exists as a solvent-separated ion pair in THF solution. A measurable and significant barrier to rotation was found for Li⁺4⁻. Given the increased barrier to rotation, we expect chiral diamine auxiliaries to afford enhancement in diastereoselectivity in reactions at the carbanionic center.

Supplementary Material Available: Preparation and full spectroscopic characterization of **3** and **4**, tables of ¹H, ⁷Li, ¹³C, and ³¹P NMR spectra for Li⁺3⁻ and Li⁺4⁻; a listing of crystal and positional parameters, bond lengths and angles, and torsional angles for Li⁺3⁻ (36 pages). Ordering information is given on any current masthead page.
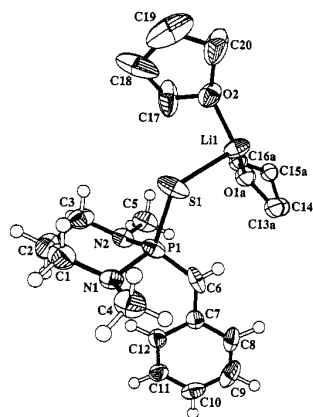
(18) Rates were determined by spectra fitting, see supplimentary material. Friebolin, H. *Basic One- and Two-Dimensional NMR Spectroscopy*; VCH: New York, 1991; pp 263–291.

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(20) Space group *C*2/*c*, *a* = 21.262(3) Å, *b* = 10.820(2) Å, *c* = 19.592(5) Å, β = 96.90(2)°, *Z* = 4, *R* = 0.065, R_w = 0.064 for 1552 reflections with *I* > 2.58σ. The dimer unit has C_2 symmetry.

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(22) For explanation of planar criteria, see ref 6b. Note: for an idealized sp² anion, *d* = 0 Å, γ = 0.0°.