J. Am. Chem. Soc. **1993,** *115,* 3826–3827

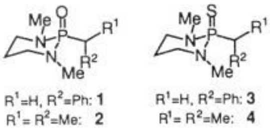
Solution- and Solid-State Structure and Dynamics of Thiophosphonamide Anions: Electronic Tuning of Rotational Barriers

Scott E. Denmark,* Kevin A. Swiss, and Scott R. Wilson

Roger Adams Laboratory, Department of Chemistry
University of Illinois, Urbana, Illinois 61801

Received January 14, 1993

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=H, R^2=Ph: **3**
R^1= R^2=Me: **2** 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).

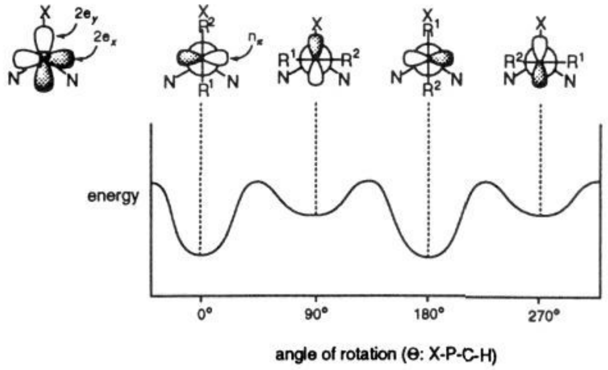


Figure 1. Energy profile of conformation for *P*-stabilized anions.

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 ^6Li and ^7Li NMR spectra further illustrated fundamental differences between the P═S and P═O anions. Narrow lines were observed at low temperatures in the ^7Li spectra of Li^+**3**$^-$ and Li^+**4**$^-$, indicative of symmetrically solvated lithium (*i.e.*, $[Li(THF)_4]^+$).[12] Also, the ^7Li chemical shift was found to be in the solvated lithium cation range.[12,13] Further, the ^6Li 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 ^7Li resonances, indicative of an asymmetric ligand sphere, and ^6Li–^{31}P coupling was observed.[6] Finally, data from the ^{13}C NMR spectra, in particular the Δ^1J_{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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[1] See, for example: (a) *Comprehensive Organic Synthesis, Vols. 1, 2 Additions to C–X π Bonds*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991. (b) *Comprehensive Carbanion Chemistry, Part B*; Buncel, E., Durst, T., Ed.; Elsevier: Amsterdam, 1984. (c) *Modern Synthetic Methods 1992*; Scheffold, R., Ed.; Verlag Helvetica Chemica Acta: Basel, 1992.

[2] (a) *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic Press: New York, 1980. (b) Wadsworth, W. S., Jr. *Org. React.* **1977**, *25*, 73. (c) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863.

[3] Denmark, S. E.; Chatani, N.; Pansare, S. V. *Tetrahedron* **1992**, *46*, 6974 and references cited therein.

[4] Denmark, S. E.; Chen, C.-T. *J. Am. Chem. Soc.* **1992**, *114*, 10647 and references cited therein.

[5] (a) Denmark, S. E.; Marlin, J. E. *J. Org. Chem.* **1987**, *52*, 5742. (b) Denmark, S. E.; Rajendra, G.; Marlin, J. E. *Tetrahedron Lett.* **1989**, *30*, 2469. (c) Denmark, S. E.; Dorow, R. L. *J. Org. Chem.* **1990**, *55*, 5926. (d) Denmark, S. E.; Stadler, H.; Dorow, R. L.; Kim, J. H. *J. Org. Chem.* **1991**, *56*, 5063.

[6] (a) Denmark, S. E.; Dorow, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 864. (b) Denmark, S. E.; Miller, P. C.; Wilson, S. R. *J. Am. Chem. Soc.* **1991**, *113*, 1468.

[7] (a) Albright, T. A.; Burdett, J. K.; Whangbo, M.-H. *Orbital Interactions in Chemistry*; Wiley-Interscience: New York, 1985; Chapter 10. (b) Cram, D. J. *Fundamentals of Carbanion Chemistry*; Academic Press: New York, 1965; pp 71–113. (c) Mitchell, D. J.; Wolfe, S.; Schlegel, H. B. *Can. J. Chem.* **1981**, *59*, 3280.

[8] For a recent theoretical treatment of the bonding in P═S vs P═O compounds, see: Basch, H.; Krauss, M.; Stevens, W. J. *J. Mol. Struct.* (THEOCHEM) **1991**, *235*, 277.

[9] For thiophosphonates, see: Corey, E. J.; Kwiatkowski, G. T. *J. Am. Chem. Soc.* **1966**, *88*, 5654. For thiophosphinamides, see: Johnson, C. R.; Elliott, R. C. *J. Am. Chem. Soc.* **1982**, *104*, 7041. For bis(phosphine sulfides), see: Goli, M. B.; Grim, S. O. *Tetrahedron Lett.* **1991**, 3631.

[10] Substrates **3** and **4** were prepared from the corresponding thiophosphoryl dichlorides. See supplementary material for full characterization.

[11] (a) Denmark, S. E.; Cramer, C. J. *J. Org. Chem.* **1990**, *55*, 1806. (b) Bernardi, F. Schlegel, H. B.; Whangbo, M.-H.; Wolfe, S. *J. Am. Chem. Soc.* **1977**, *99*, 5633.

[12] Since ^7Li has a medium quadrapole moment (Q = –0.037, $I = ^3/_2$), narrow ^7Li lines usually indicate symmetric (tetrahedral) environments, see: Reich, H. J.; Green, D. P. *J. Am. Chem. Soc.* **1989**, *111*, 8729.

[13] Fraenkel reports shifts for solvated Li cations that range from δ +0.1 to –1.7 (LiCl/D_2O reference): Fraenkel, G.; Hallden-Abberton, M. P. *J. Am. Chem. Soc.* **1981**, *103*, 5657. Cox, R. H.; Terry, H. W. *J. Magn. Reson.* **1974**, *14*, 317.

[14] No published value could be found for $^2J_{P(S)Li}$.

[15] Albright, T. A. *Org. Magn. Reson.* **1976**, *8*, 489. Duangthai, S.; Webb, G. A. *Ibid.* **1983**, *21*, 125. Webb, G. A.; Simonnin, M.-P.; Seyden-Penne, J.; Bottin-Strzalko, T. *Magn. Reson. Chem.* **1985**, *23*, 48.

[16] Breitmaier, E.; Voelter, W. *Carbon-13 NMR Spectroscopy*; VCH: New York, 1990; pp 134–140.

[17] Cryoscopy was performed by F. Haller (G. Boche, Martburg). All determinations take into account the ΔT due to the presence of 1 molal equiv of *n*-butane from the *n*-BuLi.

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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, D_2O 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, R^1 and R^2 are diastereotopic, and the resulting anisochronicity should be observed as a decoalescence of those nuclei (Figure 1). The variable-temperature ^{1}H and ^{13}C 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 ^{1}H and ^{13}C 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 (θ = 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]

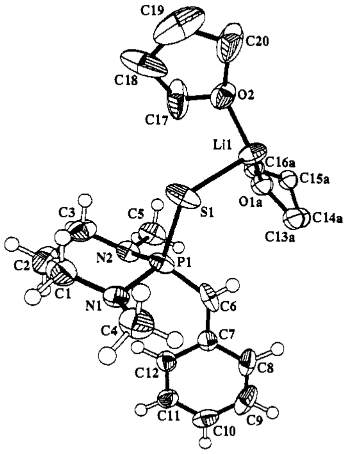

Figure 2. Monomeric unit of [Li$^+$**3**$^-$·2THF]$_2$ from X-ray analysis (40% thermal ellipsoids).

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 ^{7}Li 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.

Acknowledgment. We are grateful to the National Institutes of Health (GM 45532) for generous support of this research. We are indebted to Prof. G. Boche and Friederike Haller (Phillips Universtät Marburg) for obtaining the cryoscopic measurements. We acknowledge Dr. Vera Mainz for NMR technical assistance and the Molecular Spectroscopy Laboratory funded by NIH Grant 1531957 and NSF Grant 85-14500.

Supplementary Material Available: Preparation and full spectroscopic characterization of **3** and **4**, tables of ^{1}H, ^{7}Li, ^{13}C, and ^{31}PNMR 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.

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(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.

(19) For other barriers (a), see: Gais, H.-J.; Hellmann, G.; Günther, H.; Lopez, F.; Lindner, H. J.; Braun, S. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1025. (b) Gais, H.-J.; Hellmann, G.; Lindner, H. J. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 100. (c) Martin, J.; Robert, J. B. *Tetrahedron Lett.* **1976**, 2475.

(20) Space group $C2/c$, 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 $I > 2.58\sigma$. The dimer unit has C_2 symmetry.

(21) (a) Karsch, H. H. *Chem. Ber.* **1982**, *115*, 818. (b) Grim, S. O.; Gilardi, R. D.; Sangokoya, S. A. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 254. (c) Self, M. F.; Lee, B.; Sangokoya, S. A.; Pennington, W. T.; Robinson, G. H. *Polyhedron* **1990**, *9*, 313.

(22) For explanation of planar criteria, see ref 6b. Note: for an idealized sp^2 anion, d = 0 Å, γ = 0.0°.