These flash/quench methods provide a wide time window to study highly reactive forms of the enzyme. Both $[P_{Cys}Fe^{II}(OH_2)]^-$ and $[P^{\bullet+}_{Cys}Fe^{III}(OH_2)]^+$ are formed in about 0.1 ms and persist for approximately 100 ms. Improved design of sensitizers, quenchers, linkers, and substrates may lead to even faster electron and hole injection into P450 and other redox-active enzymes.

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Structural Investigation of a Dilithiated Phosphonate in the Solid State

Jürgen F. K. Müller,* Markus Neuburger, and Bernhard Spingler

The structural determination of reaction intermediates in organophosphonate anion chemistry has been stimulated by the extraordinary synthetic utility of these reagents.[1] A great body of information about the solid-state and solution structures of phosphorus-stabilized anions has been collected during recent years, and include lithiated phosphonates,[2] phosphinoxides,[3] phosphonamides, and thiophosphonamides.[4] Even though a more detailed picture of the characteristics was achieved, and important conclusions about the related reactivity were drawn, there some open questions still remain. For example, a general problem in the reactions of such monolithiated reagents with electrophiles occurs when more acidic products are formed. This usually leads to the formation of unwanted side products. To overcome this limitation, an attractive strategy that takes advantage of a dianionic intermediate has been developed.[5] Dicarbanions have already been used in several cases as supernucleophiles, and even in asymmetric reactions.[6] Despite the synthetic value of these reagents, there is still a demand for more information about the structures.[6l, 7] Our interest in the study of such dilithiophosphonates is an extension of our work in the development and application of chiral substituted dianions.[6l] Here we present the first solid-state structure of a geminal dilithiated phosphonate.

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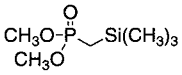
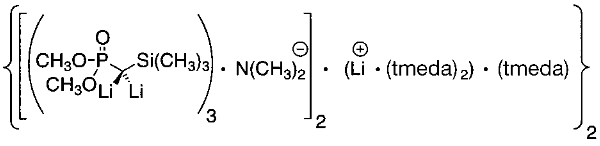


$CH_3O\text{-}\overset{O}{\underset{CH_3O}{P}}\text{-}CH_2\text{-}Si(CH_3)_3$

1



$\left\{\left[\left(CH_3O\text{-}\overset{O}{\underset{CH_3O}{P}}\text{-}C(Li)(Li)\text{-}Si(CH_3)_3\right)_3 \cdot N(CH_3)_2^{\ominus}\right]_2 \cdot (Li^{\oplus} \cdot (tmeda)_2) \cdot (tmeda)\right\}_2$

2

Treatment of a clear solution of **1** in tmeda (*N,N,N′,N′*-tetramethyl-1,2-ethane diamine) at −78 °C with 2.5 equivalents of *n*BuLi in hexane gave a yellow–green solution from which yellow crystals were obtained after 24 h at room temperature. These crystals decomposed during storage for longer periods and were pyrophoric upon exposure to moist air. The lithium cluster **2** crystallizes in the space group $P\bar{1}$ as a hexameric aggregate, which consists of six dilithiated phosphonate units and two molecules of dimethylamide.[8] In addition, two Li$^+$ ions are coordinated by four tmeda ligands in a distorted tetrahedral fashion, which balances the remaining two negative charges (Figure 1). The core of the aggregate is characterized by a Li-O-Li-O four-membered ring that contains the crystallographic inversion center. Such a structural motif has been found to be an essential feature in such monolithiated phosphonates that do not contain C–Li bonds.[2] Up to six six-membered rings (Li4-O11-Li1-C1-P1-O1, Li4-O11-Li2-C1-P1-O1, O1-Li2-C21-P21-O21-Li4, Li1-O11-Li4-O21-Li3-N27, Li4-O21-Li11-O2-P1-O1, and Li2-O11-P11-O12-Li21-C21) are fused to opposite sides of the central four-membered ring (Scheme 1), to form an overall puckered-ladder structure, which is known for certain lithium siloxides.[9]

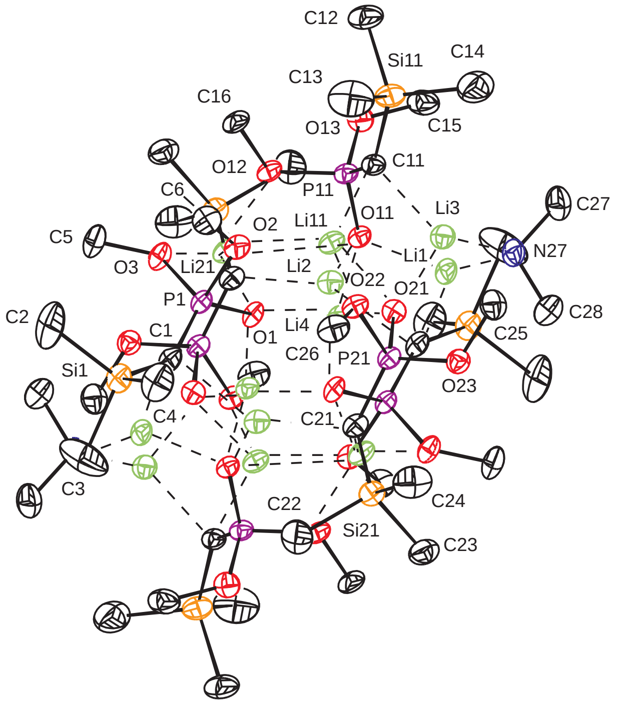
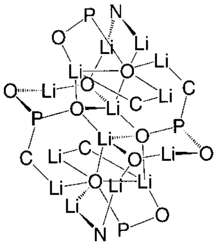


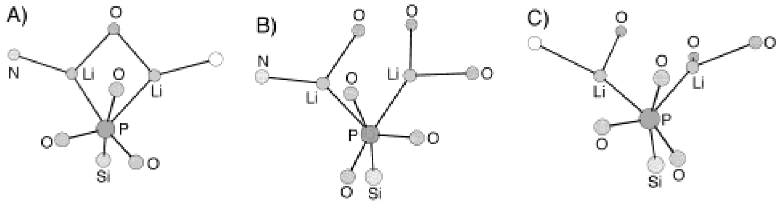
Figure 1. Molecular structure of **2** in the crystal. All hydrogen atoms, two tmeda molecules, and two $[Li(tmeda)_2]^+$ complexes are omitted for clarity. The thermal ellipsoids are drawn at the 30 % probability level.



Scheme 1. Schematic representation of the central Li-O-Li-O four-membered ring in **2**. Tmeda, methyl, methoxy, and trimethylsilyl groups have been omitted for clarity; only selected connectivities are shown.

There are three different dilithiated carbon atoms in the asymmetric unit, each connected to two Li$^+$ ions and distinctly pyramidalized. These geminal bound Li$^+$ ions coordinate in a similar fashion to a neighboring phosphonate oxygen atom to form C-Li-O-Li four-membered ring motifs. However, they differ in their detailed coordination mode: Li3 and Li21 show heteroatom coordination (N,O versus O,O), whereas the others have one additional C–Li bond and a Li–N or Li–O contact. In the second case, one Li$^+$ ion bridges two different dimetalated carbon atoms and leads to a O1-Li21-C21-Li2-C1-Li1-N27 zig-zag chain. The Li$^+$ ion in the bridging position complements its three-coordination by complexation to a phosphonate oxygen atom. A similar three-coordination is found for Li1 and Li3. Another unusual coordination mode is found for Li21, which is surrounded by an array of four oxygen atoms and one dianionic carbon atom, which leads to a distorted trigonal bipyramidal geometry. The incorporation of lithium dimethylamide into the aggregate arises from the use of an excess of *n*BuLi in tmeda, which leads to the decomposition products *N,N*-dimethylvinylamine and lithium dimethylamide at elevated temperatures.[10] However, lithium dimethylamide is essential for the formation of the aggregate, because it acts as a bridge between the trigonal coordinated Li1 and Li3 atoms. The Li–C bond lengths (2.13(1)–2.28(1) Å) are similar to those in monolithiated phosphonates, which have Li–C bond lengths of 2.21–2.26 Å.[2] The Li–O bond lengths within each C-Li-O-Li chelate (1.95(1)–2.85(1) Å) are significantly longer than those within the $(Li–O)_2$ core (1.895(9) and 1.903(9) Å, respectively). A striking feature is the extremely short P–C bonds (1.587(6), 1.604(5), and 1.619(6) Å) compared to neutral (1.80 Å) and monolithiated phosphonates (ca. 1.68 Å).[2] This additional contraction can be explained with the threefold and/or fourfold Li$^+$ ion coordination of each phosphonate oxygen atom and the additional complexation of the methoxy groups to one Li$^+$ ion, which leads to an increased coulombic attraction of the negatively charged $C^{(\alpha)}$ atom.[6, 7] A closer look along the C–P bonds demonstrates that the phosphonate oxygen atoms adopt a *gauche* conformation between the geminal Li$^+$ ions, which clearly indicates a significant degree of pyramidalization (Scheme 2). This view is supported by the examination of the dihedral angles (Li21-C21-P21-O21 25.7°, Li2-C21-P21-O21 65.2°, Li2-C1-P1-O1 27.4°, Li1-C1-P1-O1 48.8°, Li11-C11-P11-O11 58.1°, and Li3-C11-P11-O11 19.7°).

The question remains, how does the organization of such a highly aggregated species occur? The foundation of this



Scheme 2. Newman projections along the P1 – C1 (A), P11 – C11 (B), and P21 – C21 bonds (**C**) in **2**.

aggregate seems to be the central (Li – O)$_2$ core, which is related to the fundamental structural unit that is derived from several monolithiophosphonates. Based on this, we conclude that after the formation of the typical four-membered rhomboid motif, the incorporation of the second lithium ion affects only the aggregation sphere outside of the (Li – O)$_2$ core. This is supported by the fact that nearly every available coordination partner is linked to at least one lithium ion, except the phosphonate oxygen atoms in the center, which leads finally to this hexameric aggregate. However, it is interesting to note in this context that, despite the large excess of tmeda no such ligand has been incorporated within the aggregate as a coordination partner.[11]

Experimental Section

2: A solution of **1** (236 mg, 1.2 mmol) in tmeda (2 mL) was treated with *n*BuLi in hexane (1.2 mL, 2.48 M, 3 mmol) at – 78 °C. After 24 h at room temperature yellow crystals of **2** formed, which were suitable for X-ray analysis (211 mg, 63 %).

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[8] X-ray crystal data for **2**: $C_{38}H_{99}Li_7N_7O_9P_3Si_3$, $M_r = 1024.01$, triclinic, space group $P\bar{1}$, $a = 4.359(4)$, $b = 14.555(4)$, $c = 16.465(5)$ Å, $\alpha = 78.02(3)$, $\beta = 71.00(2)$, $\gamma = 77.33(2)^\circ$, $V = 3139.7(16)$ Å^3, $Z = 2$, $F(000) = 1112$, $\rho_{calcd} = 1.08\ Mg\,m^{-3}$, $\mu = 1.79\ cm^{-1}$, crystal dimensions $= 0.3 \times 0.4 \times 0.5$ mm, $T = 193$ K, radiation $Cu_{K\alpha}$ ($\lambda = 1.54180$ Å), scan type $\omega/2\Theta$, $\Theta_{max} = 74.33^\circ$, no. of measured reflections = 10510, no. of independent reflections = 10170, no. of reflections in refinement = 6117, $I > 3.00\sigma(I)$, no. of parameters = 660, $R = 0.0792$, $R_w = 0.0955$, weighting scheme $\omega(1 - (\delta F/6\sigma F)^2)^2$, $\Delta\rho = 0.45/-1.10$ e Å^{-3}, $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $R_w = \{\Sigma(|F_o| - |F_c|)^2\omega)/\Sigma F_o^2\omega\}^{1/2}$. A crystal of **2** was stuck with perfluoropolyether to a glass fibre and mounted on the diffractometer. Unit cell parameters were determined by careful centering of 21 independent strong reflections with $11 \leq \Theta \leq 20^\circ$. Data collection was carried out on an Enraf – Nonius CAD4 diffractometer equipped with a graphite monochromator, and 10510 reflections with $2.88 \leq \Theta \leq 74.33^\circ$ were measured, three of which, monitored every 2 h, showed an intensity loss of 24.60 %. The usual corrections were applied. Absorption correction was carried out with φ scans (minimum and maximum transmission: 0.51/1.00). The structure was solved by direct methods with the program SIR92.[12] An anisotropic least squares full matrix refinement was carried out on all non-hydrogen atoms with the program CRYSTALS.[13] The positions of the hydrogen atoms were determined geometrically. The disordered tmeda ligand was refined with appropriate restraints. Chebychev polynomial weights were used to complete the refinement.[14] Scattering factors were taken from the International Tables, Vol. IV, Table 2.2B. Crystallographic data (excluding structure factors) for the structure reported in this publication have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-102686. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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