Unexpected direct dilithiation of a prochiral phosphine borane[†]

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Dimethylphenylphosphine borane is readily deprotonated at both methyl groups with tBuLi and (R,R)-TMCDA to the corresponding dilithiated Lewis base adduct, featuring an intriguing structural motif with stabilising Li–H interactions.

Chiral and achiral phosphane ligands have gained huge impact in transition metal-catalyzed reactions such as in Kumada and Suzuki cross-coupling reactions, Heck reaction, enolate arylation and allylation and direct arylation. Especially chiral phosphane ligands have become of great importance due to their application in asymmetric synthesis. Prominent representatives of this class of compounds are BINAP, CHIRAPHOS or DIPAMP, which even belong to the routinely used ligands in enantioselective reactions.¹ In recent years, the (-)-sparteine mediated asymmetric deprotonation of dimethylphoshine boranes with organolithium bases has become the method of choice for the preparation of chiral phosphane ligands.² Typically, these asymmetric lithiations are accomplished with an excess of the lithium base to account for the loss of base due to decomposition of the solvent or the ligand. However, possible side reactions of the excessive alkyllithium reagent, like dilithiations or the formation of aggregates, have never been considered before (Scheme 1), although there are some examples of a direct deprotonation of two methyl groups.³ Generally, such bis-lithiomethyl compounds are only available by metallithium exchange, halide-lithium exchange or reductive cleavage of carbon-sulfur bonds.⁴ For the direct deprotonation elevated temperatures are usually required, which limits the synthetic potential due to side reactions like the decomposition of the additive or the solvent. However, for phosphine borane 1 we observe an exceptional facile deprotonation of both methyl groups which provides high yielding access to interesting building blocks for transition metal complexes.



Scheme 1 Dilithiation (left) and asymmetric deprotonation of 1.^{2g,h}

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Dimethylphenylphosphine borane 1 undergoes a direct α -lithiation of both methyl groups by slowly warming a mixture of the phosphorous compound with two equivalents of tBuLi and 1.5 equivalents of the chiral ligand (1R,2R)-N, N, N', N'-tetramethylcyclohexane-1,2-diamine [(R,R)-TMCDA] in *n*-pentane and diethyl ether from -78 °C to -30 °C (Scheme 2, for further displays see ESI[†]). Thereby, colourless crystals of the dilithiated compound 4 [= $3_2 \cdot 3 (R, R)$ -TMCDA] are formed in 81% isolated yield. The dilithiated phosphine borane 4 crystallises in the triclinic crystal system, space group P1.[‡] 4 features an exceptional structural motif consisting of two molecules of the dilithiated phosphine borane coordinated by three (R,R)-TMCDA molecules (two molecules in the asymmetric unit; one is shown in Fig. 1).⁵ The central unit is formed by a Li-C-P-eight-membered ring, in the centre of which a further lithium atom Li2 is located.⁶ The lithium and carbon atoms build two Li-C-Li-C-four-membered rings, which are connected by one common lithium atom. While Li2 shows four contacts to the lithiated carbon atoms, the lithium atoms of the central ring (Li1 and Li3) are coordinated by the nitrogen atoms of the diamine ligand. The fourth lithium atom, which is located above the Li-C-P-eightmembered ring, is coordinated by the third (R,R)-TMCDA molecule and by the hydrogen atoms of the borane units. Such stabilising Li-H interactions have first been introduced by K. Wade and coworkers who found an analogous coordination sphere in TMEDA coordinated lithium tetrahydroborate.^{7,8} Overall, all lithium atoms possess a coordination number of four. The Li-C distances [2.213(8) to 2.414(8) Å] are longer than in oligomeric organolithium compounds, the Li-N distances in the range of fourfold coordinated alkyllithium bases.⁵ An eye-catching feature of the structure is the almost square-planar coordination of Li2 in the centre of the Li-C-P-eight-membered ring. The angles of 172.4(4) and 166.6(4)° (between Li2 and the carbon atoms opposite each other) differ significantly from the typically observed tetrahedral angles at lithium as are observed for Li1, Li3 and Li4.

The dilithiation of 1 has also been observed with N, N, N', N'tetramethylethylenediamine (TMEDA) and (–)-sparteine as auxiliaries. Due to ligand disorder, crystals obtained from dilithiated phosphine borane and TMEDA were only of poor quality. However, the TMEDA coordinated aggregate showed the same structural motif as 4. Several further phosphine boranes, sulfides and oxides show also dilithiation in the presence of diamine ligands like TMEDA, TMCDA or (–)-sparteine.⁹ 3 is a rare example of a dilithiated species, which is prepared by direct deprotonation of two methyl groups and structurally characterised.^{4,10,11}

The dilithiation of **1** offers access to novel phosphane ligands. Trapping with tributyltin chloride to detect all lithiated spieces

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Scheme 2 Dilithiation of dimethylphosphine borane 1.



Fig. 1 Molecular structure of **4** (some hydrogen atoms are omitted for clarity). Selected bond lengths (Å) and angles (°): C7–Li1 2.213(8),C7–Li2 2.410(8), C8–Li3 2.250(8), C8–Li2 2.269(8), C15–Li3 2.234(8), C15–Li2 2.414(8), C16–Li1 2.227(8), C16–Li2 2.265(8), Li1–N2 2.161(7), Li1–N1 2.171(7), Li1–Li2 2.557(10), Li2–Li3 2.570(10), Li3–N4 2.160(8), Li3–N3 2.195(7), Li4–N6 2.150(7), Li4–N5 2.178(7), B1–Li4 2.479(7), B2–Li4 2.509(8), Li4–H1A 2.17(5), Li4–H1C 1.92(4), Li4–H2C 2.15(5); C8–Li2–C15 108.1(3), C8–Li2–C7 73.0(2), C16–Li2–C8 166.6(4), C16–Li2–C15 73.4(2), C7–Li2–C15 172.4(4).

in the reaction mixture yields the distannylated compound 5 in 74% yield after work-up (Scheme 3).¹² Only traces of the product from monolithiation could be observed. Analogue reactions with silicon electrophiles lead to transmetallation processes in the monosilylated product and thus to product mixtures. Comparable to the monolithiated phosphine borane 2, 3 can also be transferred to dialcohol 6 as crystalline solid by trapping with benzophenone (Scheme 3, Fig. 2). 5 was obtained as a crystalline solid after purification by column chromatography crystallising in the monoclinic crystal system, space group $P2_1/c$. Most interestingly, in the crystal both hydroxyl functions are arranged to one side of the molecule pointing in direction to the borane function and thus indicating a chelating character of the ligand. This might be due to $H^{\delta-}-H^{\delta+}$ interactions between the negatively polarised borane hydrogen atom and the positively polarised hydroxyl hydrogen atom (short H–H distances of 1.97(2) and 2.08(2) Å).

The unusual readiness of dilithiation of **1** even at temperatures below -30 °C prompted us to take a closer glance at the ongoing processes. Therefore, DFT studies with TMEDA as



Scheme 3 Trapping of the dilithiated phosphine borane 3.



Fig. 2 Molecular structure of 6 (for bond lengths and angles, see ESI⁺).

Lewis base (which was also found to support the dilithiation in experiment) were performed to evaluate the reaction barriers of the mono- and dilithiation.¹³ The geometries of the stationary points were initially optimized by using the hybrid B3LYP functional and the 6-31 + G(d) basis set.¹⁴ To identify transition state structures, frequency calculations were carried out on the same level. Monomeric tBuLi-TMEDA was chosen as deprotonation reagent. Such a monomer is reasonable as an analogue adduct has been observed with (R,R)-TMCDA.¹⁵ The calculations (Fig. 3, ESI[†]) indicate a barrier of only 61 kJ mol^{-1} for the deprotonation of the first methyl group and a barrier of 92 kJ mol⁻¹ for the abstraction of the second hydrogen, thus confirming the viability of the mono- and dilithiation at low temperatures. The low barrier of the monolithiation is in accordance with the possible asymmetric deprotonation of dimethylphosphine boranes.² The energy difference of 31 kJ mol⁻¹ between mono- and dilithiation is sufficiently high for a kinetic control of both reactions depending on the reaction temperature and the amount of lithium base.

The barrier of the deprotonation of the second methyl group (92 kJ mol⁻¹) is low enough to be overcome at temperatures below room temperature. As is evident from the optimised transition state structures (Fig. 3) this low reaction barrier can be attributed to the coordination of both lithium atoms by the hydrogen atoms of the borane moiety thus stabilising the transition states. The optimised transition states structures feature Li–H interactions (2.04–2.15 Å) comparable to those found in the crystal structure of **4** (Fig. 1). Compared to a transition state without stabilising Li–H contact (distance greater than 3.80 Å) this interaction leads to a decreased reaction barrier by 12 kJ mol⁻¹ and thus is crucial for the viability of the dilithiation (see ESI†). It is noteworthy, that this low barrier is required for the preparation of the dilithiated compound to exclude side reactions such as



Fig. 3 Optimised transition state structures of the mono- and dilithiation of **1** with *t*BuLi·TMEDA; B3LYP/6-31 + G(d).

decomposition reactions of the solvent or the chiral additive. The deprotonation of the (R,R)-TMCDA ligand for example showed a barrier of 98 kJ mol⁻¹, and lithiation of TMEDA a barrier of 101 kJ mol⁻¹, which are higher than the barrier of the dilithiation.¹⁵ Consequently, the calculations confirm the observed favoritism of the dilithiation over the decomposition of the ligand and the solvent and thus explains the possible direct deprotonation of both methyl groups.

In conclusion, we reported on the unexpected direct dilithiation of the prochiral dimethylphenylphosphine borane **1**. X-ray diffraction analysis of the diamine coordinated, dilithiated product **3** showed an extraordinary structural motif. Computational studies explain the facile deprotonation of both methyl groups by the interaction of the lithium atoms with the hydrogens of the borane moiety. We are currently evaluating the potential of **3** as dilithiated building block for different electrophiles and stepwise addition reactions.

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‡ Crystal data for the dilithiated phosphine borane **4**: C₄₆H₉₀B₂Li₄N₆P₂, M = 838.56 g mol⁻¹, triclinic, P1, a = 13.792(4)Å, b = 14.275(5) Å, c = 16.271(4) Å, $\alpha = 76.327(7)^\circ$, $\beta = 66.351(7)^\circ$, $\gamma = 65.941(5)^\circ$, V = 2669.3(15) Å³, T = 173(2) K, Z = 2, 56322 reflections measured, 18625 independent reflections ($R_{int} = 0.0522$). $R_1 = 0.0603$ [reflections with $I > 2\sigma(I)$], w $R_2 = 0.1555$ (all data). CCDC 746595; Crystal data for dialcohol **8**: C₃₄H₃₄BO₂P, M = 516.39 g mol⁻¹, monoclinic, $P2_1/c$, a = 11.9867(15) Å, b = 13.8915(11) Å, c = 17.6964(16) Å, $\beta = 109.362(12)^\circ$, V = 2780.0(5) Å³, T = 173(2) K, Z = 4, 17640 reflections measured, 5408 independent reflections ($R_{int} = 0.0358$). $R_1 = 0.0371$ [reflections with $I > 2\sigma(I)$], w $R_2 = 0.0727$ (all data). CCDC 746596.

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