Organolithium Chemistry

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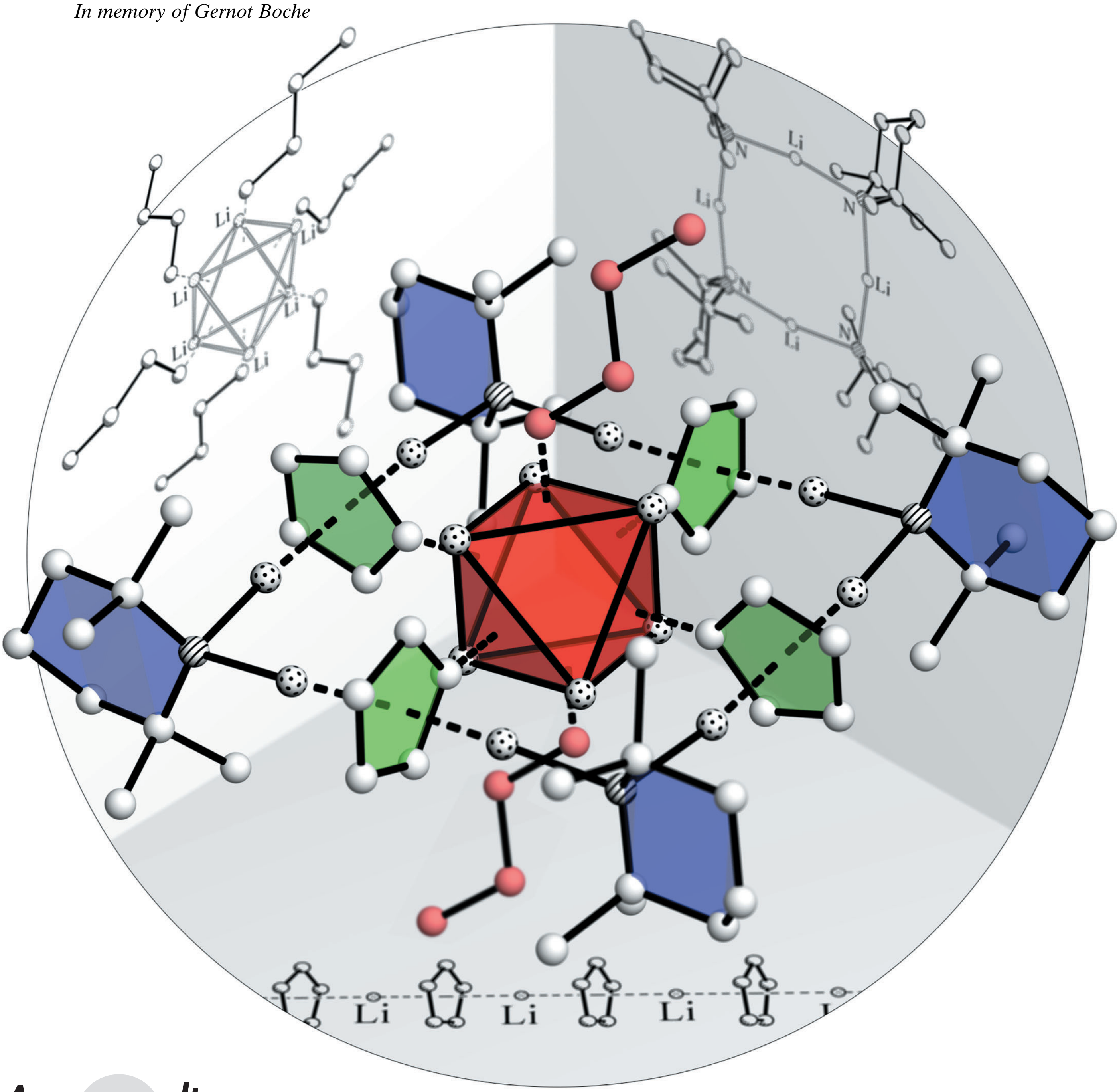
Crossing Organolithium Compounds with Organolithium Compounds: Molecular Squares and a Cage-Encapsulating Reaction**

Andrew A. Fyfe, Alan R. Kennedy, Jan Klett, and Robert E. Mulvey*

In memory of Gernot Boche



Angewandte Chemie

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In reporting the first organolithium compounds nearly a century ago,[1] Schlenk's legacy was to gift to the world functional and fascinating tools that have evolved to play a monumental part in the development of modern chemistry. Synthetic chemists, whether in academia or industry, use them routinely, generally as bases or as nucleophiles for bond construction. One of their special fascinations lies in the vast variety of structures adopted by them; however, it is the dynamic interplay between these structures that pose many challenging mechanistic questions. With more than one thousand solid-state organolithium structures documented, several reviews have appeared, including excellent contributions by Schleyer,[2] Seebach,[3] Boche,[4] Weiss,[5] and Stalke.[6] Ring and cage architectures are common among organolithium aggregates, as eloquently explained by Snaith through his "ring-stacking and ring-laddering principles".[7] Herein, we present novel organolithium "cross-complexes" synthesized by crossing two or three different organolithium complexes. We show how combining a dicross-complex having a molecular square ring structure hollow at its center with a 3D cage complex of the appropriate size can cause an unprecedented shape-controlled reaction that produces a tricross-complex with a remarkable cage-encapsulated ring structure. This new chemistry is all the more extraordinary as the compounds crossed to generate these structures, *n*BuLi, LiTMP (TMP = 2,2,6,6-tetramethylpiperidide), and LiCp (Cp = *c*-C_5H_5) are three of the most widely utilized organometallic reagents in synthesis and belong to the three most popular classes of organolithium reagent (namely lithium alkyls, amides, and cyclopentadienyls).

Our starting point in this study was the serendipitous crossing of LiTMP and LiCp to construct the molecular square complex [{Li(μ-TMP)Li(μ-Cp)}$_4$] (**1**; Figure 1).[8] The intention was to dimetalate the metallocene $CoCp_2$ with the lithium TMP magnesiate base [(TMEDA)Li(TMP)Mg(CH_2SiMe_3)$_2$],[9] but octanuclear **1** formed as a byproduct. Apparently, in contrast to ferrocene,[9a] cobaltocene is not stable enough to tolerate such attempted dimetalation. Rational crossings of LiTMP and LiCp in methylcyclohexane or toluene solution were then studied. The former produced a microcrystalline product that precluded structural analysis, but as NMR studies confirmed a 1:1 LiTMP/LiCp composition and the product has good solubility in low-polarity solvents, it can be assumed to be tetrameric **1**. Further evidence for the reproducibility of **1** came from the latter reaction that did afford crystals suitable for X-ray structural determination, which through several unit-cell checks were confirmed as **1**. Formally, this two-compound crossing can be regarded as an insertion reaction of four LiCp monomers into the parent tetrameric ring structure of LiTMP (Scheme 1).[10]

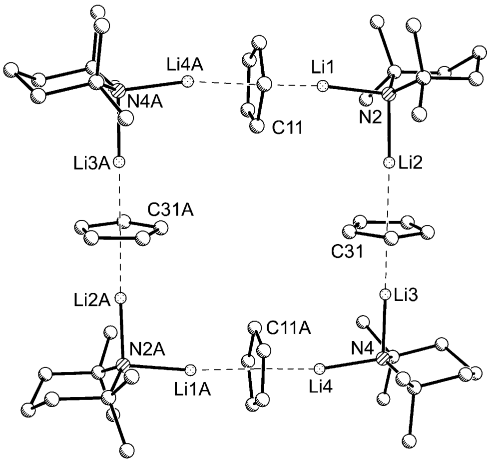
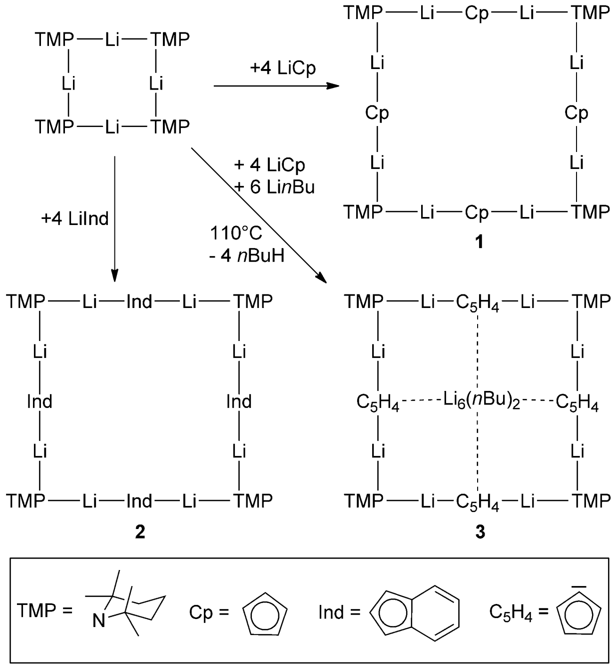


Figure 1. Molecular structure of **1** with selected atom labeling and H atoms omitted for clarity.

Reasoning that the reaction may be extendable to other Cp-like ligands capable of ditopic ligation, we crossed indenyllithium[11] with LiTMP to produce [{Li(μ-TMP)Li(μ-Ind)}$_4$] (**2**; Figure 2), another molecular square complex.[8]

With the hollow center of **1** inviting the exciting prospect of its filling by a suitably sized organolithium cage, we treated a mixture of **1** in situ with excess *n*BuLi, a classic hexameric cage in the solid state. Apart from cage encapsulation, success in this quest would realize a novel three-compound crossing. This was duly achieved through formation of the yellow crystalline product [{Li(μ-TMP)Li(μ-C_5H_4)}$_4$Li$_6$(*n*Bu)$_2$] (**3**; Scheme 1, Figure 3).[8] Inspection of the formula of this



Scheme 1. Synthesis of cross-complexes **1**, **2**, and **3**. All reactions were performed in methylcyclohexane, and *n*BuLi was used in excess.

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[*] A. A. Fyfe, Dr. A. R. Kennedy, Dr. J. Klett, Prof. R. E. Mulvey
WestCHEM, Department of Pure and Applied Chemistry
University of Strathclyde, Glasgow G1 1XL (UK)
E-mail: jan.klett@strath.ac.uk

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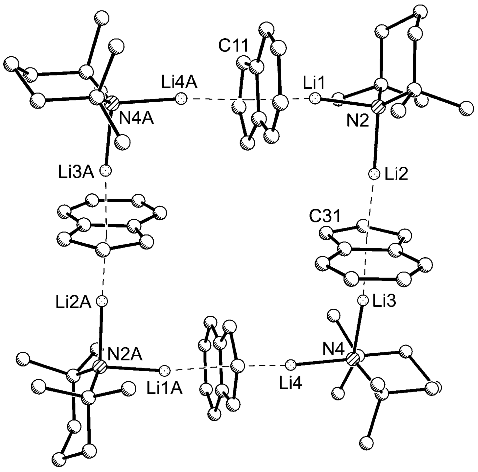

Figure 2. Molecular structure of **2** with selected atom labeling and H atoms omitted for clarity.

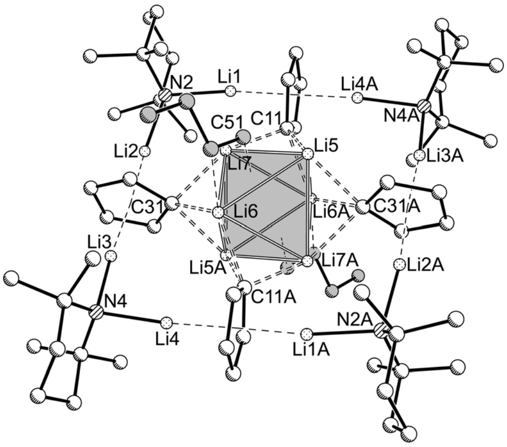

Figure 3. Molecular structure of **3** with selected atom labeling and H atoms omitted for clarity. The central Li_6 octahedron and the carbon atoms of the *n*-butyl groups are shaded for emphasis. The co-crystallized and heavily disordered methylcyclohexane molecule was omitted.

mixed alkyl–amido–cyclopentadienyl lithium complex shows the tri-crossing involves a remarkable deprotonation of the Cp^- anion to the $C_5H_4^{2-}$ dianion accompanied by the loss of four units of butane. While Cp(H) has a pK_a value of about 15[12] and accordingly is easy to metalate, to the best of our knowledge, the pK_a of Cp^- is unknown, though it must be exceedingly high. Significantly, neither LiTMP nor *n*BuLi when separate from each other can metalate Cp^-,[13] thus the deprotonation must have its origin in a structurally dictated multicomponent synergic effect more usually associated with mixed-metal reagents.[14] It is therefore important to analyze the molecular structures involved both before and after the special deprotonation.

Both dicross-complexes **1** and **2** crystallize in the $P2_1/c$ space group and feature molecular centrosymmetric squares. Counting aromatic ligands as single carbon centroids (C*), the molecular squares comprise 16-membered $(LiNLiC^*)_4$ rings made up of TMP corners joined together by linear Li−C*−Li sides, the Li atoms of which bind η^5 to both faces of the Cp/Ind anions. Note these Li−η^5Cp/Li−η^5Ind interactions mirror those in the linear polymeric parent structures of $(LiCp)_\infty$[15] and $(LiInd)_\infty$.[11] In **2**, the six-membered rings of the Ind ligands project orthogonally to the molecular square (displaced by 82.2° and 116.8° from the Li···Li axis). The TMP chairs of **1** (note that of N31 is disordered over two sites in a 9:1 ratio) are all orientated similarly with respect to the $(LiNLiC^*)_4$ ring, but those in **2** are displaced from each other in a paddle-wheel arrangement. In neither case is the cyclotetramer a perfect square, with small deviations in the side lengths (N2−N4/N4−N2A 7.785/7.645 Å for **1**, 7.700/7.611 Å for **2**) and angles (N2−N4−N2A/N4−N2A−N4A 88.29/91.71° for **1**, 90.29/89.71° for **2**). Both 16-membered rings are modestly puckered (RMS deviation from plane of Li, N, and C centroids are 0.07 Å and 0.17 Å for **1** and **2**, respectively). Furthermore, separation distances between opposite-facing Cp centroids are unequal at 8.226 Å and 7.658 Å, as one pair points toward a C−H bond while the other points a C(H)−C(H) edge towards the inversion center. A similar disparity is observed in the opposite-facing Ind centroids of its five-membered rings (corresponding separations 8.115 Å and 7.497 Å).

The best analogy to **1** and **2**, reported when this manuscript was being drafted, is the lithium boratabenzene–lithium 1,1,1,3,3,3-hexamethyldisilazide (LiHMDS) compound $[\{Li(\mu\text{-}HMDS)Li(\mu\text{-}Et_2NBC_5H_5)\}_4]$.[16] Emerging unexpectedly from a reaction of $LiNEt_2$ and an *ansa*-heteroborabenzene ytterbium amide, this other centrosymmetric square compound could, following the interpretation here, also be categorized as a dicross-complex between two distinct lithium compounds. Selected dimensions in this compound and those in **1** and **2** are compared in the Supporting Information.

Tricross-complex **3** crystallizes in the space group $C2/c$.[8] As for **1** and **2**, the molecular structure of **3** is centrosymmetric and it retains the $(LiNLiC^*)_4$ square-like ring feature, the dimensions of which are generally similar to those in **1** (see Supporting Information), though the doubling of the charge on the $C_5H_4^{2-}$ rings compared to that of $C_5H_5^-$ rings generally leads to a modest compression of the Li···C_5 centroid distances (mean values: **3** 1.900 Å, **1** 1.924 Å). Significantly, the mean transannular centroid–centroid C_5···C_5 distances across the filled cavity of **3** and the empty cavity of **1** are nearly identical (7.928 Å and 7.942 Å, respectively), showing that the molecular square is an ideal receptor for the partially deligated $(nBuLi)_6$ cage. This fact is substantiated further by the remarkable similarity of the distorted octahedral Li_6 deltahedron compared to that in Stalke's classical $(nBuLi)_6$ structure (see metrical comparison in Figure 4),[17] as the deprotonated sp^2 carbon atoms of $C_5H_4^{2-}$ in bridging these Li_3 faces mimic the role of the sp^3 α-C atoms of the "missing" *n*Bu ligands. Consistent with additional steric constraints, the puckering of the (LiNLiC*) ring is more pronounced in **3** (RMS deviation from plane of Li, N, and C centroids is 0.19 Å) than in **1**. The structure of **3** is completed by two μ_3-*n*Bu ligands (β-C−Li contacts as well as α-C−Li contacts are implicated: see Figure 3), which sit symmetrically above and below the molecular square. ^1H, ^7Li, and ^{13}C NMR spectra of **1**, **2**, and **3** in C_6D_6 solution were consistent with their solid-

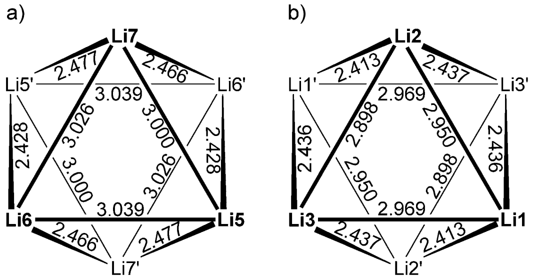

Figure 4. Comparison of interatomic distances [Å] in the central Li_6 octahedron for a) compound **3** and b) Stalke's $(n\text{BuLi})_6$ from Ref. [17].

state structures (full details are in the Supporting Information). A notable feature is the strong shielding of the ring lithium atoms in **1** sandwiched between Cp and TMP ligands which appear at $\delta = -6.52$ ppm in the ^{7}Li NMR spectrum. These move even more upfield to $\delta = -7.07$ ppm in **3** while the cage Li atoms appear downfield at $\delta = 3.72$ ppm.

In summary, this study has introduced aesthetically appealing octanuclear and cage-encapsulated tetradecanuclear organolithium structures made by crossing utility organolithium reagents. By locking the Cp^- ligand into the framework of a molecular square, its deprotonation to $C_5H_4^{2-}$ is enabled in a novel reaction outside the scope of free Cp^-. While the literature contains many examples of mixed-anion organolithium species, crossing organolithium compounds to construct fixed architectures that can induce special reactions impossible with separated organolithium compounds brings a new slant to mixed anion chemistry that potentially opens up an exciting new frontier ripe for future development.

Experimental Section

n-Hexane and methylcyclohexane were distilled from sodium/benzophenone. All synthetic work was carried out under an inert argon atmosphere using standard Schlenk and glove-box techniques. *n*BuLi (in *n*-hexane, 1.6 M) and LiCp were purchased from Sigma–Aldrich.

[{Li(μ-TMP)Li(μ-Cp)}$_4$] (**1**): LiTMP was prepared by reaction of *n*BuLi (1.25 mL, 2.0 mmol) with TMP(H) (0.34 mL, 2.0 mmol) in methylcyclohexane (40 mL). Solid LiCp (0.14 g, 2.0 mmol) was added and the mixture heated to 110 °C for 2.5 h. The solution was filtered hot and concentrated under vacuum; the product could be isolated as an off-white crystalline powder (0.17 g, 38.8 %). Crystals suitable for X-ray diffractometry could be obtained by performing the reaction in toluene. ^{1}H NMR (400 MHz, C_6D_6, TMS): $\delta = 5.99$ (s, 5H; Cp), 1.73 (m, 2H; γ-TMP), 1.15 (m, 4H; β-TMP), 0.88 ppm (s, 12H; Me-TMP); ^{7}Li NMR (155.5 MHz, C_6D_6, LiCl): $\delta = -6.52$ ppm; ^{13}C NMR (100.6 MHz, C_6D_6, TMS): $\delta = 105.6$ (Cp), 50.3 (α-TMP), 41.1 (β-TMP), 35.6 (Me-TMP), 20.2 ppm (γ-TMP). Elemental analysis (%) calcd for $C_{56}H_{92}Li_8N_4$ ($M = 876.86\ \text{g mol}^{-1}$): C 76.7, H 10.6, N 6.4; found: C 76.3, H 10.8, N 6.0. [{Li(μ-TMP)Li(μ-Ind)}$_4$] (**2**): LiTMP and indenyllithium were prepared by reaction of *n*BuLi (2.5 mL, 4.0 mmol) with TMP(H) (0.34 mL, 2.0 mmol) and indene (0.23 mL, 2.0 mmol) in methylcyclohexane (40 mL). The yellowish clear solution was heated to 110 °C for 1 h. After cooling, an off-white crystalline powder precipitated and was isolated by filtration (0.47 g, 88.7 %). ^{1}H NMR (400 MHz, C_6D_6, TMS): $\delta = 7.70$ (m, 2H; Ind), 7.07 (m, 2H; Ind), 6.81 (m, 1H; Ind), 6.36 (m, 2H; Ind), 1.44 (m, 2H; γ-TMP), 0.73 (m, 4H; β-TMP), 0.41 ppm (s, 12H; Me-TMP); ^{7}Li NMR (155.5 MHz, C_6D_6, LiCl): $\delta = -6.74$ ppm; ^{13}C NMR (100.6 MHz, C_6D_6, TMS): $\delta = 122.2$ (Ind), 121.3 (Ind), 92.5 (Ind), 49.8 (α-TMP), 40.9 (β-TMP), 34.8 (Me-TMP), 19.8 ppm (γ-TMP). Elemental analysis (%) calcd for $C_{72}H_{100}Li_8N_4$, ($M = 1077.08\ \text{g mol}^{-1}$): C 80.3, H 9.4, N 5.2; found: C 79.7, H 9.7, N 5.3. [{Li(μ-TMP)Li(μ-C_5H_4)}$_4$Li$_6$(*n*Bu)$_2$] (**3**): TMP(H) (0.17 mL, 1.0 mmol) and LiCp (0.07 g, 1.0 mmol) were added to a solution of *n*BuLi (4.0 mL, 6.4 mmol) in methylcyclohexane (20 mL). The mixture was heated to 110 °C for 2.5 h to give a yellow solution. After cooling and filtering, some solvent was removed in vacuum. The solution was allowed to stand for 1 day; a crop of yellow crystals was obtained (0.17 g, 66.1 %). When the solution with crystals was allowed to stand for several weeks, large yellow rhombus-shaped crystals were formed (0.07 g, 24.8 %), containing one equivalent of methylcyclohexane, which is lost when the crystals are stored without mother liquid. ^{1}H NMR (400 MHz, C_6D_6, TMS): $\delta = 6.32$ (s, 5H; Cp), 2.07 (m, 2H; β-*n*Bu), 1.80 (m, 2H; γ-*n*Bu), 1.68 (m, 2H; γ-TMP), 1.20 (t, 2H; δ-*n*Bu), 1.08 (m, 4H; β-TMP), 0.85 (s, 12H; Me-TMP), 0.10 ppm (m, 3H; α-*n*Bu); ^{7}Li NMR (155.5 MHz, C_6D_6, LiCl): $\delta = 3.72, -7.07$ ppm; ^{13}C NMR (100.6 MHz, C_6D_6, TMS): $\delta = 117.9$ (C_5H_4), 111.2 (C_5H_4), 50.3 (α-TMP), 40.8 (β-TMP), 35.7 (Me-TMP), 33.4 (β-*n*Bu), 32.2 (γ-*n*Bu), 20.1 (γ-TMP), 13.9 ppm (α-*n*Bu, δ-*n*Bu). Elemental analysis (%) calcd for $C_{64}H_{106}Li_{14}N_4$ ($M = 1028.69\ \text{g mol}^{-1}$): C 74.7, H 10.4, N 5.4; found: C 74.9, H 10.7, N 5.3.

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[8] Crystal data for **1**: $C_{56}H_{92}Li_8N_4$, $M_r = 876.86$, monoclinic, space group $P2_1/c$, $a = 15.4971(13)$, $b = 14.0761(8)$, $c = 15.1572(13)$ Å, $\beta = 118.687(11)°$, $V = 2900.5(4)$ Å^3, $Z = 2$, $\rho_{\text{calcd}} = 1.004\ \text{g cm}^{-3}$, $T = 123(2)$ K, $\mu(\text{Mo}_{K\alpha}) = 0.055\ \text{mm}^{-1}$ ($\lambda = 0.71073$ Å); 26765 reflections measured, 6996 unique, $R_{\text{int}} = 0.0474$; R (F, $F^2 > 2\sigma$) $= 0.0448$, wR (F^2, all data) $= 0.1071$, S (F^2) $= 0.867$, 347 refined parameters, constrained H atoms, difference map extremes $+0.222$ and -0.188 e Å^{-3}. Crystal data for **2**: $C_{72}H_{100}Li_8N_4$, $M_r = 1077.08$, monoclinic, space group $P2_1/c$, $a = 14.8875(4)$, $b = 18.8428(3)$, $c = 13.0762(3)$ Å, $\beta = 115.809(3)°$, $V = 3302.26(13)$ Å^3, $Z = 2$, $\rho_{\text{calcd}} = 1.083\ \text{g cm}^{-3}$, $T = 123$ K, μ-(Cu$_{K\alpha}$) $= 0.441\ \text{mm}^{-1}$ ($\lambda = 1.5418$ Å); 15553 reflections measured, 5981 unique, $R_{\text{int}} = 0.0256$; R (F, $F^2 > 2\sigma$) $= 0.0610$, wR (F^2, all data) $= 0.1713$, S (F^2) $= 1.035$, 387 refined parameters, constrained H atoms, difference map extremes $+0.381$ and -0.229 e Å^{-3}. Crystal data for **3**: $C_{71}H_{120}Li_{14}N_4$, $M_r = 1126.93$, monoclinic, space group $C2/c$, $a = 22.2393(2)$, $b = 15.0824(2)$, $c = 23.2338(3)$ Å, $\beta = 106.953(1)°$, $V = 7454.47(15)$ Å^3, $Z = 4$, $\lambda = 1.5418$ Å; 32591 reflections measured, 7471 unique, $R_{\text{int}} =$

0.018; R (F, $F^2 > 2\sigma$) = 0.0540, wR (F^2, all data) = 0.1608, S (F^2) = 1.080, 387 refined parameters, constrained H atoms, difference map extremes +0.561 and −0.227 e Å^{-3}. The PLATON SQUEEZE routine was used to remove traces of disordered methylcyclohexane from the structure; see: A. L. Spek, *J. Appl. Crystallogr.* **2003**, *36*, 7. Compound **3** was also obtained in a second crystalline phase without co-crystallized methylcyclohexane, producing a model of low quality: $C_{64}H_{106}Li_{14}N_4$, $M_r = 1028.69$, triclinic, $a = 12.8933$, $b = 20.7896$, $c = 25.8503$ Å, $\alpha = 90.0855$, $\beta = 100.8985°$, $\gamma = 96.6906$, $V = 6755.80$ Å^3. CCDC 822182 (**1**), CCDC 822181 (**2**), and CCDC 822180 (**3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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