

Solid-state and solution structures of hetero-aggregates formed between *n*BuLi and NCN pincer aryl lithium†‡

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The reaction of NCNLi pincers (NCN = [2,6-(R₂NCH₂)₂C₆H₃]⁻, R = Me (**3**), Et (**4**)) with various equivalents of *n*BuLi in non-polar solvent results in the generation of novel mixed alkyl-aryl organolithium hetero-aggregates. The identification (variable temperature ¹H, ¹³C, ⁷Li and 2D NMR spectroscopy and X-ray crystallography) of multiple, equilibrating mixed-aggregates that form in these reactions has been achieved. Fluxional processes in the parent [NCNLi]₂ dimeric homo-aggregates were re-evaluated and Li–N bond rupture was found to be in operation, a prerequisite towards further aggregation chemistry. The crystallized aggregates, with the formula **3**₂·[*n*BuLi]₂ or **4**₂·[*n*BuLi]₂, shows one amine arm from each NCNLi fragment stabilizing a [*n*BuLi]₂ dimer. The core of the aggregates exhibit a roughly cubic Li₄C₄ configuration with each aryl carbanion η³ coordinated to Li₃ triangular faces. Dissolution of microcrystalline powders of **3**₂·[*n*BuLi]₂ or **4**₂·[*n*BuLi]₂ regenerates the observed equilibria. Based on the NMR data, the remaining mixed aggregates are proposed to have the formula **3**·[*n*BuLi]₃ and **4**·[*n*BuLi]₃, respectively; the solution structure is again based on a Li₄C₄ cluster. The relative concentration of the constituents in these equilibria was found to vary depending on the steric size of the amine groups. In the case of **3**, the predominant species is the **3**₂·[*n*BuLi]₂ aggregate while for **4**, the dimer **4**₂ is favoured.

Introduction

Organolithium species are amongst the most widely used reagents for C–C bond forming reactions, particularly in the synthesis of complex molecules.^{1–8} While often denoted as simple ‘RLi’-type compounds, they usually exist as equilibrating mixtures of aggregates (dimers, trimers, tetramers or higher oligomers) in solution⁹ and have similar structures in the solid state.¹⁰ It is now generally accepted that the reactivity and selectivity of organolithium reagents is strongly dependent on the forms of aggregates present.¹¹ Organolithium hetero-aggregates, mixed species containing two or more different carbanionic organic fragments, also have a rich history^{12–19} and are important because the hetero-aggregates often display disparate reactivity compared to the component homo-aggregates.^{20–23} For example, an equimolar mixture of *t*BuLi and

*i*PrLi was found to be an order of magnitude more reactive than *t*BuLi alone.²¹ Numerous examples from the closely related areas of lithium amide, alkoxide and halide hetero-aggregate chemistry also exhibit differences in reactivity dependent on aggregate composition.^{16,22,24–40} One of the best known examples are the ‘superbases’, most commonly LiR–KOR mixtures, which have exceedingly powerful deprotonating abilities.^{33–37} As there is the potential to elucidate meaningful structure–activity relationships, the solution and solid state structures of organolithium hetero-aggregates are topics of current interest.^{41–52} One issue often ignored is the potential impact of these aggregates on the *synthesis* of organolithium reagents and their subsequent reactivity, as these are often generated and employed *in situ*.^{53–55}

Our research group has performed a number of investigations on the organolithium chemistry of 2,6-bis-[(dialkylamino)methyl]aryl-1-lithium species (the potentially terdentate NCN ‘pincers’)^{56–59} **1** and have reported some of their hetero-aggregate chemistry with *n*BuLi.^{60–64} Recently, the reactivity and stereoselective self-assembly of the homo and hetero-aggregates of chiral and achiral bidentate 2-[(dialkylamino)methyl]aryl-1-lithium species **2**, containing an NC donor set, have also been reported.^{65–76}

From these studies, a number of interesting chemical and structural features are apparent. In apolar, non-coordinating solvents, homo-aggregates of type **1** generally form dimeric species in solution and also in the solid state, whereas type **2** compounds tend to form isomeric tetramers based on a cubic Li₄C₄ core, see Fig. 1. The addition of *n*BuLi serves to disrupt or alter these bonding motifs by either the addition of *n*BuLi fragments to the aggregates or *via* replacement of the pincer Li groups, generally resulting in the formation of complexes with a cubic Li₄C₄ core. However, some exceptions, such as an open ladderane-type

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† Dedicated to Prof. Ken Wade on the occasion of his 75th birthday in recognition of his early and excellent contributions to organolithium, boron and cluster chemistry

‡ Electronic supplementary information (ESI) available: Full experimental details, figures depicting exchanges processes and NMR spectra. CCDC reference numbers 615196–615197 (**3**₂·[*n*BuLi]₂ and **3**₂) and 249825 (**4**₂·[*n*BuLi]₂). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b805092a

§ Contact for inquires pertaining to crystallographic studies

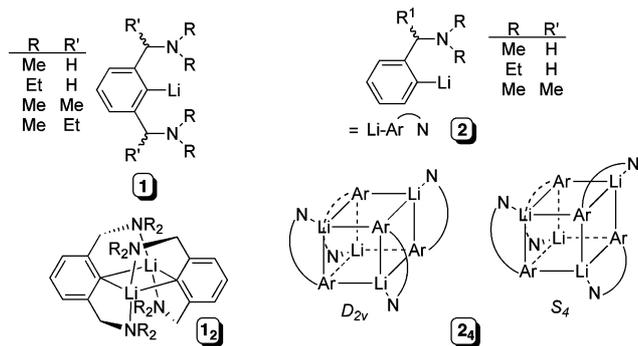


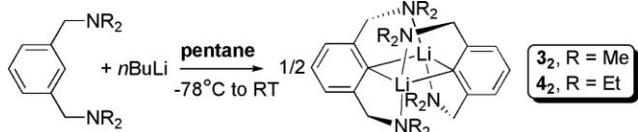
Fig. 1 Structures of the model NCN (**1**) and NC (**2**) pincer ligand aggregates.

structure, have also been observed.⁶² These aggregates can have unforeseen effects on the subsequent chemistry. For example, attempts to lithiate a chiral NCN ligand ($R = \text{Me}$, $R' = \text{Et}$ for **1** in Fig. 1) required 2 equivalents of $n\text{BuLi}$ due to the formation of a $[\text{NCNLi}]_2[n\text{BuLi}]_2$ aggregate that is kinetically unreactive towards the starting 1,3-diaminoarene. This investigation details our efforts to unravel the aspects of hetero-aggregate chemistry associated with the progenitor NCNLi pincer species and $n\text{BuLi}$.

Results and discussion

Synthesis and fluxional processes

The lithiated species incorporating dimethyl and diethylaminomethyl groups, **3**₂⁷⁷ and **4**₂,⁷⁸ respectively, were synthesized *via* selective deprotonation in the 2-position (*ortho-ortho* to the benzylic carbon atoms) of the parent arenes in pentane at low temperature (LT) utilizing 1 equivalent of $n\text{BuLi}$, Scheme 1.⁷⁹ Only a single equivalent of $n\text{BuLi}$ was necessary for quantitative Li–H exchange and no mixed aggregates were observed under these conditions. Due to their relatively rigid structures, both the benzylic CH_2 and NR_2 groups are diastereotopic in the dimers, a feature that is observed in LT NMR spectra. For **3**₂, dynamic processes that exchange the NMe methyl groups and benzylic CH_2N protons were both found to have a ΔG^\ddagger value of 56.1 kJ mol^{-1} .⁷⁷ In the case of **4**₂, a similar value was reported previously by Hey-Hawkins *et al.* ($56.4 \pm 0.2 \text{ kJ mol}^{-1}$).⁷⁸ However, it has never been explicitly stated that Li–N bond scission occurs in this process, a potentially important step for aggregate formation. For exchange of the alkyl groups of the NR_2 amine, simple Li–N dissociation, pyramidal inversion at N and re-coordination is proposed.⁸⁰ Exchange of the methylene proton signals is also proposed to be initiated by Li–N bond dissociation, followed by either rotation about the Ar–Li bonds to give co-planar arenes in the transition state or rotation about the Ar– CH_2 bonds, see Fig. S1 and Fig. S2.† The ΔG^\ddagger values are almost identical for **3**₂, **4**₂ and for a similar process in a 2,6-bis(oxazolonyl)phenyl-1-lithium derivative⁸¹ (57 kJ mol^{-1}).



Scheme 1 Synthesis and schematic structures of **3**₂ and **4**₂

If all the Li–N bonds were intact, the difference in steric bulk at the N center would greatly impact the barrier for exchange of the benzylic methylene protons through the previously proposed co-planar $\text{Li}_2\text{arene}_2$ transition state.⁸¹ So it appears that the main contribution to the ΔG^\ddagger , regardless of pathway, is the strength of the Li–N bonds, which are likely to be similar in these cases and that rupture of the Li–N bond is the rate limiting step.⁸²

It is well known that Lewis bases disrupt the bonding in organolithium aggregates; for example, the addition of Et_2O or TMEDA to apolar solutions of $n\text{BuLi}$ results in the formation of tetramers and dimers, a situation that leads to enhanced reactivity.^{82–87} Here, free amine functionalities are transiently accessible for coordination to incoming $[n\text{BuLi}]_x$ fragments. In addition, the Li centers become coordinatively unsaturated and are available for aggregate formation.

The addition of varying equivalents of $n\text{BuLi}$ to toluene solutions of **3**₂ or **4**₂ gave rise to NMR spectra indicative of the presence of a number of aggregates in equilibrium. In addition, the extra $n\text{BuLi}$ could not be removed by crystallization, suggesting the generation of stable mixed aggregates. Extensive variable temperature (VT), multi-nuclear (^1H , ^{13}C , ^7Li) and 2D (^1H – ^1H COSY, ^1H – ^{13}C HETCOR) NMR experiments were employed to identify the species present in solution. The analysis of a 1 : 2 mixture of **3**₂ or **4**₂ with $n\text{BuLi}$ or a 1 : 1 ratio of NCNLi to $n\text{BuLi}$ by VT NMR spectroscopy in toluene- d_8 revealed unreacted, intact homo-aggregate dimers and multiple mixed aryl–alkyl hetero-aggregates $[\text{NCNLi}]_x[n\text{BuLi}]_y$, Fig. 2. Notably, the peaks for the parent dimer **4**₂ do not coalesce with those of the mixed aggregates, even up to 90°C (*vide infra*). However, due to the complexity of the LT spectra for reactions with **3**₂ and **4**₂, potential structures of these mixed aggregates could not be easily elucidated and further information was needed.

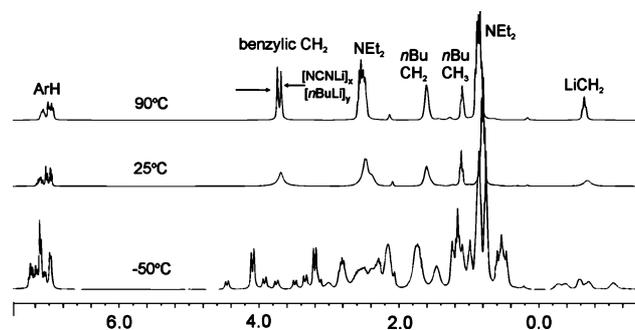


Fig. 2 ^1H NMR spectra of **4**₂ and 2 equiv. of $n\text{BuLi}$ in toluene- d_8 at three different temperatures.

Solid state structures of **3**₂· $[n\text{BuLi}]_2$ and **4**₂· $[n\text{BuLi}]_2$

Fortunately, the cooling of a pentane solution of a mixture of **3**₂ or **4**₂ with 2 equiv. of $n\text{BuLi}$ resulted in the formation of clear, colorless single crystals. The X-ray crystal structures,¶ shown in

¶ Crystal structure determinations: X-ray intensities were measured using a Nonius Kappa CCD diffractometer with rotating anode ($\text{Mo K}\alpha$, graphite monochromator, $\lambda = 0.71073 \text{ \AA}$) at a temperature of 150 K . The structures were solved and refined with the SHELXS-97/SHELXD/SHELXL-97 programs.¹⁰⁶ **3**₂· $(n\text{BuLi})_2$: $\text{C}_{32}\text{H}_{58}\text{Li}_2\text{N}_4$, FW = 524.57, colorless plates, $0.45 \times 0.39 \times 0.12 \text{ mm}^3$, triclinic, P1 (No. 2), $a =$

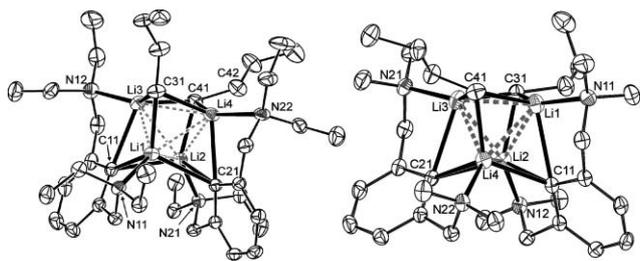


Fig. 3 Molecular representation of $3_2 \cdot [n\text{BuLi}]_2$ (right) and $4_2 \cdot [n\text{BuLi}]_2$ (left) in the crystal with ellipsoids drawn at the 30% probability level and H atoms omitted for clarity. For both, only the major disorder component of the *n*-butyl at C31 is shown. Selected bond lengths (Å) and angles (°) for $3_2 \cdot [n\text{BuLi}]_2$: C11–Li1 2.563(3), C11–Li2 2.304(3), C11–Li4 2.369(3), C21–Li2 2.387(3), C21–Li3 2.541(3), C21–Li4 2.315(3), C31–Li1 2.192(3), C31–Li2 2.206(3), C31–Li3 2.278(3), C41–Li1 2.311(3), C41–Li3 2.168(3), C41–Li4 2.189(3), N11–Li1 2.072(3), N12–Li2 1.994(3), N21–Li4 1.996(3), N22–Li3 2.063(3), Li–Li 2.454(4)–2.561(4); Li2–C11–Li4 63.34(10), Li2–C21–Li4 62.91(10), C11–Li2–C21 106.97(12), C11–Li4–C21 107.22(11), Li1–C31–Li3 68.48(11), Li1–C41–Li3 68.26(11), C31–Li1–C41 108.42(12), C31–Li3–C41 110.53(13). Selected bond lengths (Å) and angles (°) for $4_2 \cdot [n\text{BuLi}]_2$: C11–Li1 2.276(6), C11–Li2 2.388(6), C11–Li3 2.497(6), C21–Li1 2.432(6), C21–Li2 2.318(5), C21–Li4 2.466(5), C31–Li1 2.209(5), C31–Li3 2.185(6), C31–Li4 2.317(6), C41–Li2 2.195(5), C41–Li3 2.286(6), C41–Li4 2.249(6), C42–Li4 2.423(6), N11–Li1 1.982(5), N21–Li2 1.991(5), N12–Li3 2.074(6), N22–Li4 2.097(5), Average Li–Li 2.444(7)–2.622(7); Li1–C11–Li2 65.26(18), Li1–C21–Li2 63.94(17), C11–Li1–C21 103.7(2), C11–Li2–C21 103.9(2), Li3–C31–Li4 71.2(2), Li3–C41–Li4 70.6(2), C31–Li3–C41 106.1(3), C31–Li4–C41 103.0(2).

Fig. 3 with selected bond lengths and angles, reveals the structures of the 2 : 2 mixed aryl–alkyl hetero-aggregates. Both are quite similar and only the specifics of $4_2 \cdot [n\text{BuLi}]_2$ are discussed in detail. This species contains a Li_4 tetrahedral core (average Li–Li = 2.514(5) Å) surrounded by two formal NCN pincer aryl anions and two butyl carbanions also arranged in a tetrahedral environment, giving an overall distorted Li_4C_4 cube. The structure is reminiscent of the previously reported mixed aggregate **5a**, see Fig. 4, which differs from $4_2 \cdot [n\text{BuLi}]_2$ by the presence of a benzylic CH_2Li instead of a direct Ar–Li bond.⁶⁰ Similarly, the structure of the single arm NC aggregate **5b** also exhibits this type of aggregate bonding and coordination of two external Et_2O molecules.⁶⁶ In

9.4158(6), $b = 10.4587(5)$, $c = 17.6551(8)$ Å, $\alpha = 95.909(3)$, $\beta = 97.918(3)$, $\gamma = 104.638(3)^\circ$, $V = 1648.85(15)$ Å³, $Z = 2$, $D_{\text{calcd}} = 1.057$ g cm⁻³, $\mu = 0.06$ mm⁻¹, 24 123 measured reflections up to a resolution of $(\sin\theta/\lambda)_{\text{max}} = 0.65$ Å⁻¹, 7487 unique reflections ($R_{\text{int}} = 0.0363$). 399 refined parameters, 3 restraints. R ($I > 2\sigma(I)$): $R_1 = 0.0528$, $wR_2 = 0.1257$. R (all data), $R_1 = 0.0823$, $wR_2 = 0.1419$. $S = 1.051$. $4_2 \cdot (n\text{BuLi})_2$: $\text{C}_{40}\text{H}_{72}\text{Li}_4\text{N}_4$, FW = 636.78, colorless triangular blocks, $0.30 \times 0.30 \times 0.18$ mm³, triclinic, $P\bar{1}$ (No. 2), $a = 10.2596(1)$, $b = 10.7254(2)$, $c = 19.3963(3)$ Å, $\alpha = 88.6961(7)$, $\beta = 89.1097(8)$, $\gamma = 74.9462(6)^\circ$, $V = 2060.45(5)$ Å³, $Z = 2$, $D_{\text{calcd}} = 1.026$ g cm⁻³, $\mu = 0.06$ mm⁻¹, 36 961 measured reflections up to a resolution of $(\sin\theta/\lambda)_{\text{max}} = 0.54$ Å⁻¹, 5465 unique reflections ($R_{\text{int}} = 0.1114$). 471 refined parameters, 49 restraints. R ($I > 2\sigma(I)$): $R_1 = 0.0648$, $wR_2 = 0.1839$. R (all data): $R_1 = 0.0824$, $wR_2 = 0.1977$. $S = 1.087$. 3_2 : $\text{C}_{24}\text{H}_{38}\text{Li}_2\text{N}_4$, FW = 396.46, colorless plates, $0.60 \times 0.51 \times 0.06$ mm³, monoclinic, $P2/c$ (No. 13), $a = 41.945(2)$, $b = 10.4363(4)$, $c = 17.8074(5)$ Å, $\beta = 102.196(3)^\circ$, $V = 7619.4(5)$ Å³, $Z = 12$, $D_{\text{calcd}} = 1.037$ g cm⁻³, $\mu = 0.06$ mm⁻¹, 42 242 measured reflections up to a resolution of $(\sin\theta/\lambda)_{\text{max}} = 0.50$ Å⁻¹, 8191 unique reflections ($R_{\text{int}} = 0.0651$). The structure was refined as pseudo-orthorhombic twin with (1,0,1/0,-1/0,0,-1) as twin matrix, resulting in a twin fraction of 0.4251(16). 838 refined parameters, 1176 restraints. R ($I > 2\sigma(I)$): $R_1 = 0.0706$, $wR_2 = 0.1681$. R (all data): $R_1 = 0.0878$, $wR_2 = 0.1823$. $S = 1.107$.

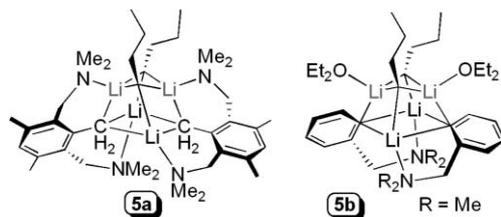


Fig. 4 Schematic structures of mixed hetero-aggregates **5a** and **5b**.

$4_2 \cdot [n\text{BuLi}]_2$, two of the amine arms are stabilizing a $[n\text{BuLi}]_2$ dimer (Li3–N12 = 2.074(6), Li4–N22 = 2.097(5) Å) and acting as an internal base similar to THF or TMEDA.^{82–87} The remaining Li–N interactions are somewhat shorter and remain associated with the NCNLi fragment (Li1–N11 = 1.982(5), Li2–N21 = 1.991(5) Å). The formal aryl and butyl carbanions are η^3 bonded to the Li_3 triangular faces and occupy non-central positions. The pendant N-donor atoms cap the four Li vertexes. An agostic Li–H interaction with the $\beta\text{-CH}_2$ of one butyl fragment is suggested by the data by a short Li–C distance (Li4–C42 = 2.423(6) Å) and supported by the slightly longer bond length of Li4–N22 vs. Li3–N12. Notably, dissolution of the crystals of isolated $3_2 \cdot [n\text{BuLi}]_2$ or $4_2 \cdot [n\text{BuLi}]_2$ back into toluene- d_8 regenerates the same NMR spectra of the originally observed equilibrium mixture, indicating that this species is likely to be isolable only because of its low inherent solubility in pentane.

Assignment of solution structures

Armed with the molecular structures of $3_2 \cdot [n\text{BuLi}]_2$ and $4_2 \cdot [n\text{BuLi}]_2$, re-evaluation of the solution NMR data allowed for the identification of the remaining species in solution. Fig. 5 shows selected regions of the LT ¹H NMR spectra for the reaction of 4_2 with varying amounts of *n*BuLi. For reactions involving either 3_2 or 4_2 with 2 equivalents of *n*BuLi, eight separate doublet signals assigned to the benzylic NCH_2 groups were observed in the LT ¹H NMR spectrum. Each doublet represents one of the diastereotopic protons of a single CH_2N group, which gives rise to an AX spin system with geminal coupling constants of 11–12 Hz. Fig. 6 contains the schematic structures of $3_2 \cdot [n\text{BuLi}]_2$ and $4_2 \cdot [n\text{BuLi}]_2$, highlighting the diastereotopic benzylic protons. Those labelled H_{in} are directed towards the inner Li_4C_4 core. As shown in Fig. 5, two doublets correspond to the homo-aggregate dimer 4_2 , four doublets were assigned to the in-equivalent benzylic CH_2 groups of $4_2 \cdot [n\text{BuLi}]_2$ and the final two doublets to a third

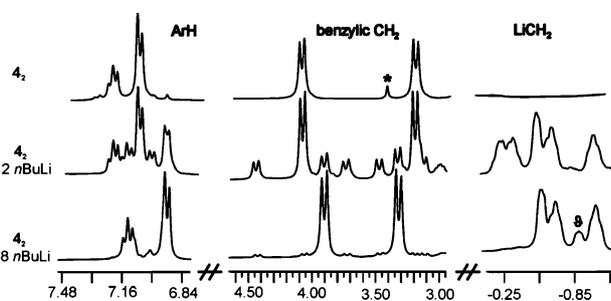


Fig. 5 Aryl CH, benzylic CH_2 and LiCH_2 regions of the ¹H NMR spectra of 4_2 with varying amounts of *n*BuLi at -50 °C in toluene- d_8 . In the top spectrum, the signal at * is due to a small amount of unreacted NCN(H). In the bottom spectrum, ϑ denotes LiCH_2 protons of free *n*BuLi.

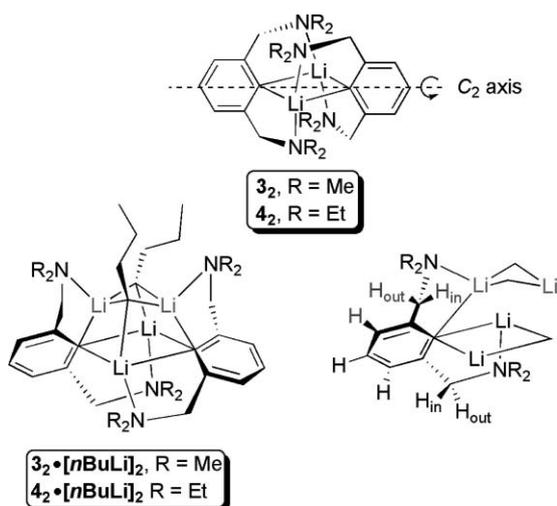


Fig. 6 Structures of $3_2 \cdot [n\text{BuLi}]_2$ and $4_2 \cdot [n\text{BuLi}]_2$ highlighting diastereotopic benzylic protons.

aggregate **7** with the base formula $\{[\text{NCNLi}][n\text{BuLi}]_3\}$ (*vide infra*). The assignment of the benzylic protons was confirmed by ^1H - ^1H COSY experiments, Fig. 7. Integration of the LiCH_2 signals of the formal butyl anion for the individual aggregates quantified the amount of entrapped $n\text{BuLi}$ in each species. Table 1 and 2 give a listing of selected ^1H , $^7\text{Li}\{^1\text{H}\}$ and $^{13}\text{C}\{^1\text{H}\}$ NMR data for the aggregates containing **3** and **4**, respectively. All the spectra are included in the ESI.† In accordance with the crystal structure of $4_2 \cdot [n\text{BuLi}]_2$, the LT ^1H NMR signals for the aryl protons *meta* to the Li centers are in-equivalent due to the disruption of the C_2 rotation axis present in the parent dimers, see Fig. 6. These signals appear as two doublets at δ 7.07 and 6.96 ppm and the *para*-CH resonates at δ 7.21 ppm. The LiCH_2 protons of the $n\text{Bu}$ groups are diastereotopic and appear as broad multiplets, due to coupling with the spin active Li centers, at δ -0.21 and -0.34 ppm (^6Li ; $I = \frac{1}{2}$, 7.5%, ^7Li ; $I = 1$, 92.5%). Also in agreement with the proposed structure, the LT $^7\text{Li}\{^1\text{H}\}$ NMR spectrum contains two resonances corresponding for the $4_2 \cdot [n\text{BuLi}]_2$ aggregate (δ 0.76 and 0.10 ppm). Equivalent signals for $3_2 \cdot [n\text{BuLi}]_2$ appear at δ 0.87 and 0.44 ppm. Salient features of the LT ^{13}C NMR spectrum of $4_2 \cdot [n\text{BuLi}]_2$ include the presence of six signals for the aryl rings and two different benzylic carbons at δ 64.3 and 62.5 ppm,

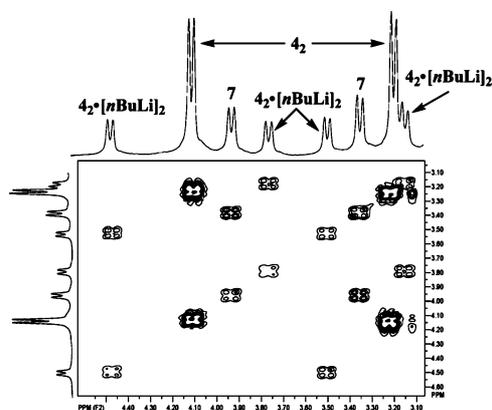


Fig. 7 ^1H - ^1H COSY NMR spectrum at -50°C of the benzylic region of the equilibrium mixture generated from **4**, with 2 equivalents of $n\text{BuLi}$.

confirming the presence of in-equivalent benzylamine groups and a lowering of the molecular symmetry found in **4**. Also, there are four separate NCH_2 and terminal methyl resonances for the NEt_2 groups, indicating that all four ethyl chains of one NCN pincer are also in-equivalent. Essentially, identical spectra are observed in the NMR spectra containing $3_2 \cdot [n\text{BuLi}]_2$, with the exception of a somewhat less complicated alkyl region, and together the NMR data strongly suggests retention of a tetrameric $[\text{NCNLi}]_2[n\text{BuLi}]_2$ structure in solution that is closely related to that of $3_2 \cdot [n\text{BuLi}]_2$ or $4_2 \cdot [n\text{BuLi}]_2$ found in the solid state.

The remainder of the resonances in the spectra match up with a complex with the base formula $[\text{NCNLi}][n\text{BuLi}]_3$ and correspond to the new species **6** and **7**, respectively. In the LT ^1H NMR spectrum of **7**, portions of which are shown in Fig. 5, the aryl region exhibits a triplet (1H) and a doublet (2H) resonance and indicate mirror or rotational symmetry in the arene, similar to the parent homo-aggregate dimers. The benzylic region contains two doublets, characteristic of diastereotopic CH_2 protons ($J_{\text{gem}} = 12$ Hz). The alkyl groups of the NR_2 amine are also in-equivalent at low temperature, which suggests that the NCN pincer is in a stereochemically rigid environment presumably with the amine nitrogen atoms tightly bound to the Li atoms on the NMR time scale. For **6**, the two signals found in the LT ^1H NMR spectrum at δ 2.17 and 1.73 ppm for the amino methyl groups collapse into a single resonance δ 1.93 ppm at room temperature. In **7**, similar temperature dependant behavior is noted for the amino methylene and terminal methyl signals for the NEt_2 group. Due to symmetry considerations, each CH_2 proton of the NEt_2 groups is diastereotopic, which is confirmed by the presence of four signals in the LT ^1H NMR spectrum of **7**. These coalesce into a broad signal at δ 2.61 ppm and a virtual quintet at δ 2.40 ppm, suggesting restricted rotation about the N-C bond. Further, the LT ^{13}C NMR spectrum exhibits only four resonances in the aryl region and, in **7**, two signals are found for the methylene carbons of the NEt_2 groups at δ 33.1 and 32.9 ppm. However, the LT $^7\text{Li}\{^1\text{H}\}$ NMR spectrum contains three signals for species **7** (δ 0.54, 0.08, and -1.29 ppm) in a 2 : 1 : 1 ratio and, in the LT ^1H NMR spectrum, there are three signals corresponding to the LiCH_2 of the $n\text{Bu}$ groups, two of which show coupling *via* ^1H - ^1H COSY cross-peaks. These protons are attached to the same carbon center, as shown by coincident cross-peaks in the ^1H - ^{13}C HETCOR. Based on the NMR data, a structure is proposed based on a Li_4 tetrahedron where one triangular face is bonded to a NCN pincer fragment and the remaining three faces coordinate carbanionic $n\text{Bu}$ units, Fig. 8. The two amine arms coordinate to

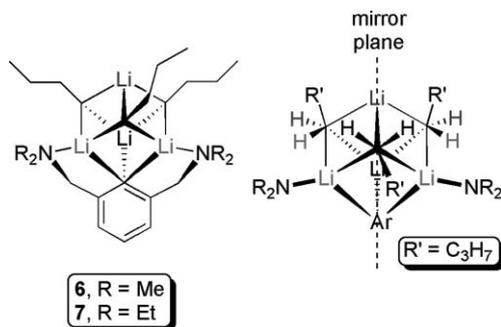


Fig. 8 Schematic structures of $[\text{NCNLi}][n\text{BuLi}]_3$ adducts **6** and **7**.

Table 1 Selected NMR data for aryl-alkyl hetero-aggregates of **3** in toluene- d_6

Compound	^1H δ /ppm				$^{13}\text{C}\{^1\text{H}\}$ δ /ppm				$^7\text{Li}\{^1\text{H}\}$ δ /ppm
	ArH	Benzylic CH	NMe	LiCH	ArCLi	Benzylic C	NM	LiCH ₂	
3₂	7.27 (t, 2H) 7.11 (d, 4H)	4.06 (d, 4H) 2.89 (d, 4H)	1.94 (s, 12H) 1.79 (s, 12H)		188.9	73.0	47. 43.5		0.99
3₂·[<i>n</i>BuLi]₂	7.14 (m, 2H)	4.44 (d, 2H) 3.89 (d, 2H)	2.30 (s, 6H)	-0.30 (2H)	178.8	70.3	46.6 45.0 43.1 42.5	10.9	0.87 (2Li) 0.44 (2Li)
	6.95 (d, 2H) 6.93 (d, 2H)	2.87 (d, 2H) 2.56 (2, 2H)	1.82 (s, 12H) 1.74 (s, 6H)	-0.54 (2H) -0.63 (2H)		68.7			
6	7.15 (m, 1H) 6.90 (d, 2H)	4.11 (d, 2H) 2.74 (d, 2H)	2.17 (s, 6H) 1.73 (s, 6H)	-0.76 (2H) -1.03 (2H)	178.2	69.5	46.1 42.5	9.6 (2C) 8.3	0.44 (2Li) 0.07 (1Li) -1.36 (1Li)

Table 2 Selected NMR data for aryl-alkyl hetero-aggregates of **4** in toluene- d_6

Compound	^1H δ /ppm					$^{13}\text{C}\{^1\text{H}\}$ δ /ppm					$^7\text{Li}\{^1\text{H}\}$ δ /ppm
	ArH	Benzylic CH	NCH ₂ CH ₃	NCH ₂ CH ₃	LiCH	ArCLi	Benzylic CH	NCH ₂	NCH ₂ CH ₃	LiCH ₂	
4₂	7.28 (t, 2H) 7.14 (d, 4H)	4.12 (d, 4H) 3.22 (d, 4H)	2.53 (d of q, 4H) 2.31 (m, 4H) 2.17 (m, 8H)	0.89 (t, 12H) 0.79 (t, 12H)	—	190.0	60.1	48.2 44.6	13.0 4.6	—	0.59
4₂·[<i>n</i>BuLi]₂	7.21 (t, 2H) 7.07 (d, 2H) 6.96 (d, 2H)	4.47 (d, 2H) 3.93 (d, 2H) 3.77 (d, 2H) 3.15 (d, 2H)	3.03 (m, 2H) 2.68–2.52 (m, 10H) 2.18 (m, 4H)	1.12 (t, 6H) 0.91 (t, 6H) 0.61 (t, 6H) 0.48 (t, 6H)	-0.21 (2H) -0.34 (2H)	180.1	64.3 62.5	45.7 44.8 44.6 39.0	11.9 (2C) 4.4 3.8	9.5	0.76 0.10
7	7.17 (t, 1H) 6.97 (d, 2H)	3.94 (d, 2H) 3.36 (d, 2H)	2.80 (vq, 2H) ^a 2.50 (m, 2H) 2.38 (m, 4H)	1.01 (t, 6H) 0.57 (t, 6H)	-0.56 (2H) -0.68 (2H) -1.02 (2H)	179.4	63.8	45.8 39.1	11.8 5.2	9.5 (3C)	0.54 (2Li) 0.08 (1Li) -1.29 (1Li)

^a vq = virtual quintet.

adjacent Li atoms generating a symmetry plane bisecting the two amine coordinated Li centers. This Li–N coordination also gives rise to the observed diastereotopic benzylic CH₂ protons and alkyl amino groups. The remaining two coordinatively unsaturated Li centers are in-equivalent as one shares a four center, two-electron bond with the NCN pincer group while the other Li atom interacts exclusively with *n*Bu anions. In addition, there are two distinct *n*Bu groups; the α -CH₂ of one lies on the mirror plane while the remaining two are equivalent by mirror plane symmetry. The methylene CH protons of the two symmetry related *n*Bu groups are also diastereotopic by virtue of the coordinated amines. The

remainder of the $^{13}\text{C}\{^1\text{H}\}$ and 2D NMR spectroscopic data are also consistent with the proposed formulation. Notably, the Li₄R₄ structural motif is well known for aggregates with equivalent R groups¹⁰ but relatively rare for mixed aggregates.^{23,88–91}

The identity of **6** and **7** was further verified by increasing the concentration of *n*BuLi and shifting the equilibrium towards the *n*BuLi-rich aggregates. The addition of slightly more than 3 equivalents of *n*BuLi to either **3₂·[*n*BuLi]₂** or **4₂·[*n*BuLi]₂**, giving a 4 : 1 ratio of *n*BuLi to NCNLi, shifts the observed equilibria in favour of **6** or **7**, respectively. One equivalent of free [*n*BuLi]₆ is also observed, suggesting that no further *n*BuLi-enriched

aggregates are present or thermodynamically stable enough to allow observation. As shown in Fig. 5, a peak for the LiCH₂ protons of free *n*BuLi is readily observed and its presence is also confirmed in the ⁷Li{¹H} and ¹³C{¹H} NMR spectra.

As all the products generated in this equilibrium have been identified and a number of complimentary crystal structures along this trajectory have been obtained, this provides a relatively unique opportunity to assess the impact of variation of steric factors on aggregate stability in these clusters. In addition to the structures of mixed aggregates **3**₂·[*n*BuLi]₂ and **4**₂·[*n*BuLi]₂, the molecular structure of the simple parent **3**₂ dimer has also been obtained. § As shown in Fig. 9, the dimeric structure is anchored about a trapazoidal Li₂C₂ core and is essentially identical to that of **4**₂ and other related NCNLi structures.^{62,78,81,92–94} For **3**₂, the unit cell contains four distinct molecules that vary only in the slight differences in relative twists of the aryl rings with respect to each other and thus only one of the four is shown. A quaternion fit⁹⁵ of one molecule of **3**₂ with **4**₂ emphasizes the similarities between these two structures.

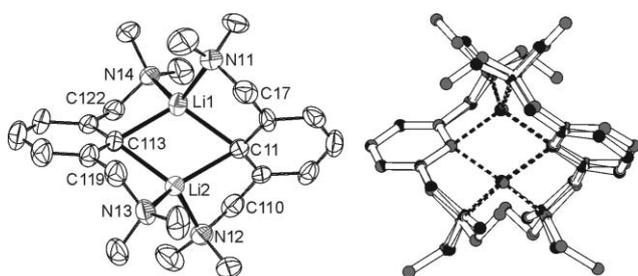
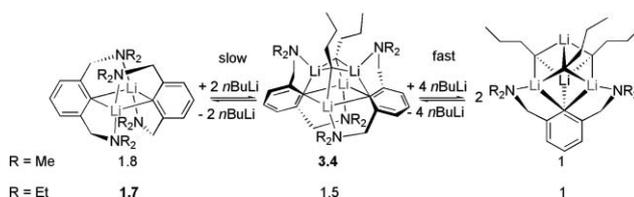


Fig. 9 Molecular representation (left) of one molecule of **3**₂ in the crystal with ellipsoids drawn at the 30% probability level and H atoms omitted for clarity. Only one of four independent molecules is shown. C11–Li11 2.206(9), C11–Li12 2.171(10), C113–Li11 2.207(10), C113–Li12 2.222(9), N11–Li11 2.121(10), N12–Li12 2.099(9), N13–Li12 2.129(10), N14–Li11 2.114(9), Li11–C11–Li12 67.9(3), Li11–C113–Li12 66.9(3), C11–Li11–C113 112.2(4), C11–Li12–C113 113.0(4). Quaternion fit (right) of **3**₂ and **4**₂.

The ratios of the individual products in the equilibrium indicate the relative stabilities of the parent dimers and subsequently mixed aggregates. As previously mentioned, the lithiation of the chiral NCN pincer containing ethyl groups in the benzylic position was complicated by preferential formation of a mixed hetero-aggregate. Substitution of ethyl to methyl destabilizes the mixed aggregate and lithiation proceeds normally.^{23,62,64} In this case, a similar but more subtle steric control of aggregate stability is also apparent. The integration of the well separated benzylic protons for the 1 : 1 molar reaction of **3** and *n*BuLi gives relative ratios for **3**₂ to **3**₂·[*n*BuLi]₂ to **6** of 1.8 : 3.4 : 1. At identical temperature (–50 °C) and concentration (0.2 M), the concurrent values for **4** are 1.7 : 1.5 : 1, see Scheme 2. For the NMe₂ system, the mixed aggregate **3**₂·[*n*BuLi]₂ is the most stable species, whereas the parent dimer **4**₂ is preferred in the NEt₂ case. Complex **3**₂·[*n*BuLi]₂ is stabilized with respect to **4**₂·[*n*BuLi]₂ due to steric interactions of the NR₂ groups coordinated to the NCNLi fragments. Upon entrainment of the *n*BuLi, the aryl rings push away from the complexed *n*BuLi dimer. This forces two of the NR₂ groups into closer proximity and thus the effect of the smaller steric size of Me vs. Et is amplified. This allows the lower amino groups of



Scheme 2 Relative ratios of products in equilibria processes.

3₂·[*n*BuLi]₂ to penetrate further under the Li₄C₄ core. As shown in Fig. 10, this is manifested by a pitching and twisting of the aryl rings; in **3**₂·[*n*BuLi]₂ the relative orientation of the aryl rings is more spread than that of **4**₂·[*n*BuLi]₂ again indicating somewhat less steric pressure in **3**₂·[*n*BuLi]₂. Additional evidence for the manifestation of subtle steric control in the aggregates stems from the fact that, in the presence of an excess of *n*BuLi and **6**, significant quantities of **3**₂ and **3**₂·[*n*BuLi]₂ remain. With **7**, only traces of **4**₂ and **4**₂·[*n*BuLi]₂ are present. Notably, **6** and **7** are the least stable of the clusters in the respective equilibria, likely due to the presence of coordinatively unsaturated Li centers. Reich *et al.* noted that similar steric factors are important in aggregate formation of aryl Li species with potentially chelating donor ‘arms’ of varying tether length.^{96,97}

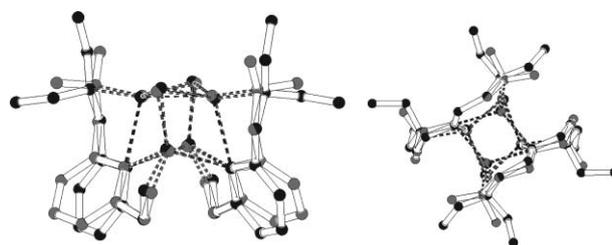
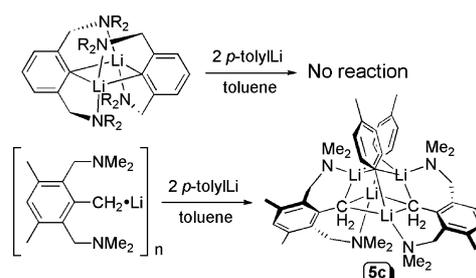


Fig. 10 Quaternion fit of **3**₂·[*n*BuLi]₂ with **4**₂·[*n*BuLi]₂. Left: *n*Bu groups, lower *N* alkyl groups and H atoms have been removed for clarity. Right: *n*Bu groups, *meta* and *para* carbon atoms and H atoms have been removed for clarity.

Attempts were also made to determine if other hetero-aggregates could form by varying the nature of the organolithium salts. This was observed with related systems as the *p*-tolyl variant of **5a** was observed by NMR experiments, (**5c**, see Scheme 3).⁶⁰ In this work, neither **3**₂ nor **4**₂ interact with *p*-tolyl lithium in toluene-d₈ at a variety of temperatures in the NMR tube experiments. In the case of **5c**, the benzene insoluble *p*-tolyl lithium is drawn into solution by the NCNLi aggregate whereas here, it remains as a solid in the NMR tube. This is perhaps not overly surprising as mixed aryl–aryl Li aggregates are relatively rare while mixed alkyl–aryl hetero-aggregates are fairly well studied.^{10,23}



Scheme 3 Reactions of NCNLi aggregates with *p*-tolyl lithium.

Conclusions

The identification of a number of equilibrating mixed alkyl–aryl hetero-aggregates has been accomplished. These data have allowed for the delineation of steric effects on aggregate stability in which subtle changes in steric bulk of the amino groups affects the concentration of the various components in equilibrium. Due to their relatively similar stabilities, NCNLi–*n*BuLi aggregates of a given NCN pincer generate a number of spectroscopically observable and potentially isolable species along such a reaction coordinate. In the case of selective *ortho*–*ortho* deprotonation of NCN(H), **6** and **7** are potential structural models of the aggregates formed during the initial deprotonation step *via* Li–H exchange. This also correlates with the solvent dependence of the reaction^{56,64} as additional basic donors would disrupt the *N,N*-chelate of the pincer arene ligand, which presumably directs the regiochemistry. However, lower order transient aggregates may also be mechanistically important.^{43,98} This chemistry is, of course, an example of the important directed *ortho*-metalation reaction.^{7,8,99–104}

The chemistry of aryl and alkyl lithium species with pendant donor groups can exhibit a stunning degree of complexity, which is highly dependant on a number of factors such as solvent, nature and position of the donor heteroatom and steric bulk of the component anions as well as at the complexing donors. As these changes can be quite subtle, it is difficult to predict *a priori* whether formation of hetero-aggregates will interfere with lithiation and thus, studies should be taken on a case-by-case basis. As a cautionary note, there is certainly a potential for such aggregates to play havoc with yield optimization experiments, especially when attempts are made to maximize the yield of a desired organolithium species by the addition of excess organolithium reagents (*e.g.* *n*BuLi). Even after crystallization, the excess reagent organolithium can become entrapped with the desired species.^{23,105} In this study, a single [NCNLi]₂ dimer is shown to sequester up to 6 equivalents of *n*BuLi in toluene and the additional *n*BuLi cannot be readily removed from the aggregates. Protocols incorporating excess organolithium reagents to facilitate complete metalation, either *via* Li–Br or Li–H exchange reactions, may result in the formation of undesirable and stable mixed species of unpredictable reactivity.²³

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