Dynamic processes in organolithium chemistry: tetrameric and 'open' tetrameric chiral α-amino lithium alkoxides

David R. Armstrong,[a] John E. Davies,[b] Robert P. Davies,[b] Paul R. Raithby,[b] Ronald Snaith[b] and Andrew E. H. Wheatley*[b]

[a] *Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow, UK G1 1XL*
[b] *Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge, UK CB2 1EW*

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Lithium *N*,*N*,*N*′-trimethylethylenediamide, LiN(Me)$(CH_2)_2NMe_2$, **1**-Li, reacts with 1 equiv. of benzaldehyde to afford the corresponding chiral α-amino lithium alkoxide **2**, which in the solid state is a conventional pseudo-cubane tetramer. Reaction of **1**-Li with *o*-methoxybenzaldehyde affords instead a novel 'open' pseudo-cubane tetramer **3**, wherein the coordinative mode of the potentially bidentate *N*,*N*,*N*′-trimethylethylenediamino moiety can be related to ligand chirality. Employment of *p*-methoxybenzaldehyde results in the isolation of a tetramer **4**, whose solid-state structure is intermediate between those of **2** and **3** and therefore suggests that fluxional processes may operate. Extensive studies of **2**–**4** in non-donor solution indicate diverse and complex behaviour.

Introduction

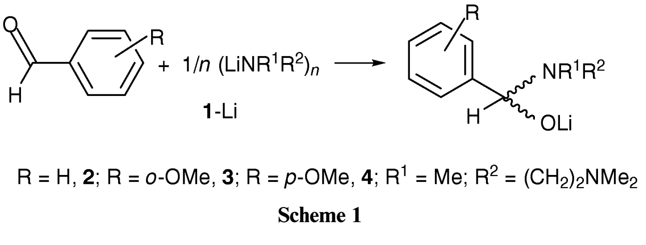
While the extensive use of chiral organolithium reagents in organic synthesis in general has been noted,[1] attempts to regiospecifically metallate aromatic systems[2] have led to the utilisation of chiral α-amino lithium alkoxides for the metallation of arylaldehydes.[3] Generally, reaction of a lithium dialkylamide with either a heterocyclic arylaldehyde[4] or substituted benzaldehyde[3,5] has afforded an intermediate which, while it contains a superior aldehyde protecting group, is also capable of directing a second equivalent of lithium to the *ortho*-ring position. The structural nature of such intermediates has attracted surprisingly little attention in spite of their demonstrable utility, only a few examples of solution studies,[6,7] solid-state structures (of β-amino lithium alkoxides)[6] and theoretical investigations having been reported.[8] It is this paucity of data which prompted us to investigate chiral α-amino lithium alkoxides in order to establish not only their overall structures but also the coordinative modes adopted by the metal centres in the presence of the amino moiety N-centres.

Results and discussion

Solid-state studies

We report here the solid-state and solution structures of three tetrameric α-amino lithium alkoxide species, afforded in good yield by the simple 1 : 1 reaction of lithium *N*,*N*,*N*′-trimethylethylenediamide, **1**-Li, with the corresponding benzaldehyde (Scheme 1).

The simplest dialkylamino lithium alkoxide to incorporate both the bifunctional *N*,*N*,*N*′-trimethylethylenediamino and benzoid aromatic moieties, **2**, results from the treatment of *in situ*-generated lithium *N*,*N*,*N*′-trimethylethylenediamide (**1**-Li) with 1 equivalent of benzaldehyde. X-Ray crystallography shows that the crystals deposited when the yellow solution resulting from reflux of the reaction mixture is stored at +80 °C have an apparently simple solid-state tetrameric structure wherein each metal centre is made four-coordinate by virtue of α-N-centre coordination (Fig. 1). To facilitate the discussion, the tetrameric aggregates reported here will be considered to be comprised of four monomeric units wherein each monomer is defined as a moiety containing a four-membered N–C–O–Li ring. While intact $(LiO)_4$ pseudo-cubanes which show intra-monomer N-stabilisation[6,9] of the



R = H, **2**; R = *o*-OMe, **3**; R = *p*-OMe, **4**; R^1 = Me; R^2 = $(CH_2)_2NMe_2$

Scheme 1

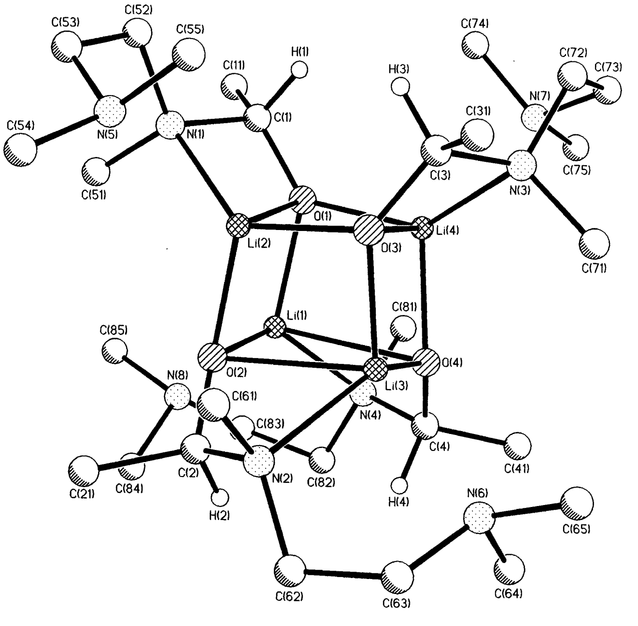


Fig. 1 Structure of the $(LiO)_4$ pseudo-cubane core of **2**; hydrogen atoms (except the protected aldehyde hydrogen atoms) have been omitted for clarity and only the *ipso*-carbon atoms of the aromatic rings are shown.

metal centres (including two diastereomeric β-amino lithium alkoxides)[6] have been reported previously, **2** is rendered interesting by virtue of the fact that *in situ* protection of the aldehyde renders the consequent α-amino lithium alkoxide *monomers* chiral. The solid-state structure of **2** can be viewed as a tetrameric racemate comprised of two stacked dimers (Fig. 1, top to bottom), wherein the four-membered N–C–O–Li rings associated with the two (*S*)-ligands are staggered with respect to the lower (*R*)-associated ones. Like other N–C–O–Li chelated[7a] $(LiO)_4$ structures, cubane distortion affords two *intra-dimer* Li–O bond types, wherein (presumably by virtue of ring strain in the four-membered chelates) the mean *intra*-chelate distance is appreciably longer than the mean *inter*-chelate one [2.339(7) and 1.908(6) Å respectively]. At a mean of 1.893(7) Å, *inter-dimer* Li–O interactions are nominally the shortest in the pseudo-cubane core. It is clear from an analysis of the different Li–N distances that only the α-N-centres interact significantly with the metal centres [Li–N = 2.109(6) and 2.131 Å mean *intra*-(*S*)- and (*R*)-chelate respectively]. However, while at 2.650(7) Å (mean) the δ-N···Li distances are substantially too long to be regarded as having significant bonding relevance, Fig. 1 shows that for any given *N*,*N*,*N*′-trimethylethylenediamino moiety the orientation of the δ-N-centre is towards the same metal as the α-one coordinates, suggesting that the δ-N-centres are not completely independent of the metal centres.

The reaction of **1**-Li in THF at −78 °C with *o*-methoxybenzaldehyde affords **3** which, unlike, the conventional pseudo-cube of **2**, is revealed by X-ray crystallography to be a novel 'open' pseudo-cubane tetramer in the solid state (Fig. 2): the molecule occupies a crystallographic two-fold axis which passes through the Li(1)O(2)Li(1A)O(2A) and Li(2)O(4)Li(2A)O(4A) planes of the 'open' cube. Each metal centre achieves four-fold coordination, the fashion in which this is done being related to the *chirality* of the ligand at the protected aldehyde carbon atom.[10] Coordination of the metal centres by the dialkylamino moieties, which is responsible for the exclusion of THF from the product, is either mono- or bis-depending upon whether they are associated with (*S*)- or (*R*)-ligands respectively, with bis-coordination by the (*R*)-ligands incurring the opening of one end of the pseudo-cubane and necessarily introducing significant variations in core Li–O distances. The solid-state structure of **3** can be viewed as an aggregate in which a dimeric pair of (*R*)-ligands lies next to a dimeric pair of (*S*)-ligands (Fig. 2, right to left), the inter-dimer Li–O distances varying between 1.909(8) Å [Li(2)–O(2)] and 1.852(8) Å [Li(1A)–O(4)]. The closed face of the pseudo-cubane incorporates the four-membered $(LiO)_2$ ring which results from dimerisation of the two (*S*)-ligands and is itself composed of two types of Li–O bond, the *inter*-(*S*)-monomer ones [*i.e.* Li(1)–O(2) = 1.903(8) Å] being much shorter than those in the four-membered *intra*-(*S*)-monomer chelate rings [*i.e.* Li(1A)O(2)C(6)N(1), Li(1A)–O(2) = 2.303(8) Å] which result from mono-coordination of the α-amino moieties and which constitute *anti*-geometrical isomers with respect to the C–N interaction. While at 2.101(8) Å, the Li(1A)–N(1) distance is consistent with distances found in related mono-complexed species,[5,6,7c,7d,7f] the non-bonding Li(1)···N(2A) distance is 2.754 Å. Unlike their (*S*)-counterparts, the two (*R*)-ligands bis-coordinate the metal centres *via* both α- and δ-N-centre donation, two eclipsed *intra-monomer* Li–O bonds in the pseudo-cubane core having concomitantly cleaved [*i.e.* Li(2)···O(4A) = 2.723 Å]. The result is that instead of each (*R*)-ligand incorporating a four-membered Li–O–C–N chelate ring, both (*R*)-ligands combine with two intact edges of the open pseudo-cubane, affording an eight-membered $(Li–O–C–N)_2$ ring in a boat conformation, *anti*-geometrical isomerism being observed again about the C–N bonds. The absence of significant strain in the eight-membered boat is probably responsible for the observation of Li–O bonds [Li(2)–O(4)] which, at only 1.872(8) Å, are somewhat shorter than those in the four-membered mono-chelate rings associated with the two (*S*)-isomers. The α-N–Li distance [Li(2)–N(4A) = 2.118(8) Å] is not significantly different to the analogous interactions in the mono-chelated (*S*)-ligands, and is somewhat shorter than the δ-N–Li bond lengths [Li(2)–N(3A) = 2.365(9) Å].

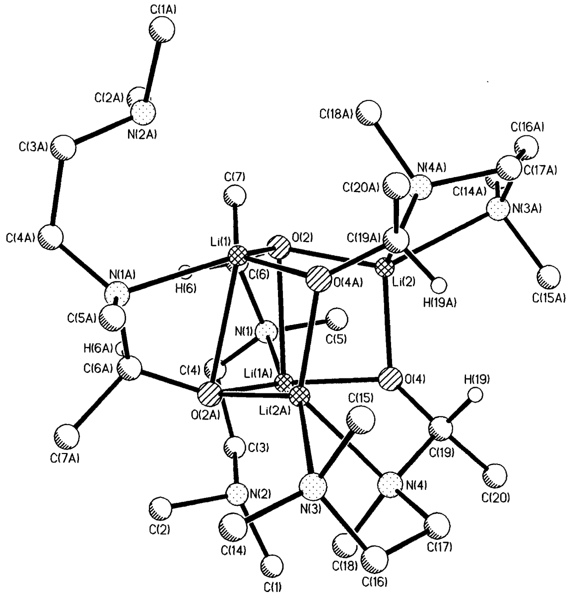


Fig. 2 Structure of the $(LiO)_4$ 'open' pseudo-cubane core of **3**; hydrogen atoms (except the protected aldehyde hydrogen atoms) have been omitted for clarity and only the *ipso*-carbon atoms of the aromatic rings are shown. The symmetry operation which relates original atoms to their 'A' equivalents is $1 - x, y, \frac{1}{2} - z$.

The non-bonded Li(2)···O(4A) distance is, at 2.723(8) Å, rather shorter than that of 3.14 Å observed in the only other known example of an 'open' $(LiO)_4$ pseudo-cubane, $(PhOLi \cdot THF)_4 \cdot PhOH$.[11] The two tetramers further differ in that opening of only *one* pseudo-cubane bond (by virtue of the inclusion of a non-lithiated phenol molecule whose hydroxyl group bridges one cubane edge) is demonstrated by the latter structure. Cleavage of a single pseudo-cubane bond has also been reported in the $(LiN)_4$-containing structure of {6lithio(trimethylsilyl)diazomethane · 2lithio[4,5-bis(trimethylsilyl)triazine] · 7diethyl ether}.[12] More extensive fragmentation has been recorded in polymeric $(LiBr \cdot THF)_\infty$,[13] this species representing the only previous example of an 'open' pseudo-cubane in which, as for **3**, *two eclipsed* Li–X bonds are missing. Some features in common with **3** are also demonstrated by $Li_6Cl_6 \cdot 2TMEDA \cdot 4/2TMEDA$, wherein variations in the mode of external solvation incur the cleavage of *two* Li–Cl bonds between $(LiCl)_3$ rings at either end of a hexameric aggregate.[14]

The reaction of **1**-Li can be extended to the remaining *m*- and *p*-methoxybenzaldehyde isomers, in the latter case diffraction-quality crystals of **4** being afforded with the resultant structure demonstrating features characteristic of both **2** *and* **3**. Superficially, the solid-state structure of **4** is based (like that of **2**) on a complete tetrameric pseudo-cubane racemate composed of a staggered stack of enantiomerically pure (*S*)- and (*R*)-dimers (Fig. 3, top to bottom). However, a closer analysis of bond lengths in the aggregate core reveals a more intriguing pattern. There exist, within the $(LiO)_4$ core, four types of Li–O bond, the first being the *inter-dimer* interactions [1.893(5) Å mean]. Next, within either enantiomerically pure dimer there are *inter-monomer* bonds which are essentially equivalent [1.908(5) Å mean] *irrespective* of ligand chirality. However, *intra-monomer* Li–O interactions show a pronounced dependence both upon ligand chirality and upon the

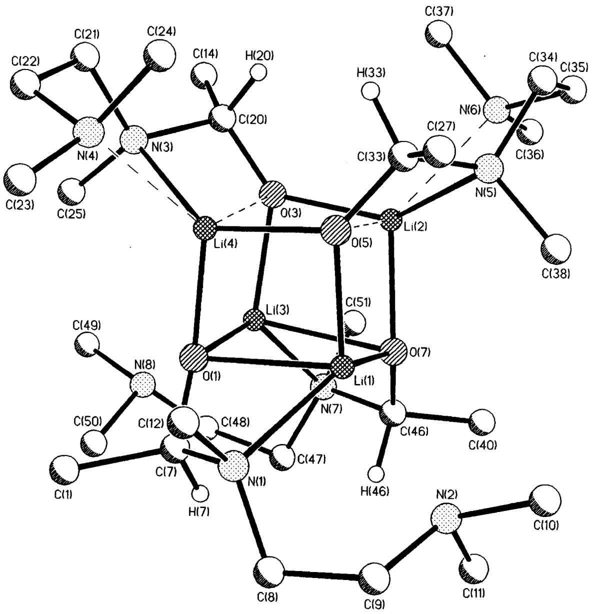
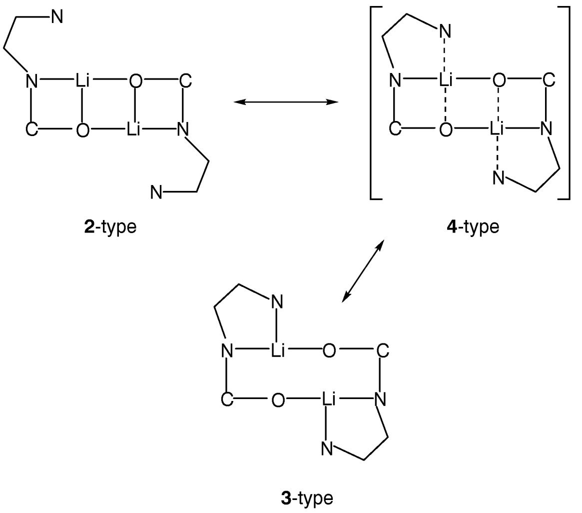


Fig. 3 Structure of the $(\text{LiO})_4$ pseudo-cubane core of **4**; hydrogen atoms (except the protected aldehyde hydrogen atoms) have been omitted for clarity and only the *ipso*-carbon atoms of the aromatic rings are shown.

coordinative mode of the dialkylamino moiety. In common with the solid-state structure of **2**, the two (*R*)-ligands demonstrate mono-coordination of the metal centres *via* α-N-centre donation [2.133(5) Å mean], relatively long Li–O interactions [2.162(5) Å mean] in the consequent (presumably) strained four-membered Li–O–C–N chelates and no δ-N-coordination [mean $\text{Li}\cdots\text{N} = 2.941(5)$ Å]. However, bearing in mind the novel structure of **3**, the behaviour of the (*S*),(*S*)-dimer is particularly salient. Here the question of whether dialkylamine coordination is mono- or bi-dentate is rather vexed. Stabilisation of the lithium centres *via* α-N-centre coordination is again manifest [2.145(5) Å mean]. However, what should be the consequent Li–O–C–N four-membered rings show unexpectedly long lithium–oxygen distances {2.327(5) [Li(2)–O(5)] and 2.527(5) [Li(4)–O(3)] Å}, leading to the conclusion that these are best viewed as only partial interactions. It is noticeable, however, that these bond extensions correlate with the observation of corresponding (albeit weak) interactions between the metal centres and the δ-N-ones {2.544(5) [Li(2)–N(6)] and 2.435(5) [Li(4)–N(4)] Å}. Furthermore, the *shorter* of these δ-N–Li partial interactions [Li(4)–N(4)] involves the same metal centre as the *longer* of the partial Li–O bonds [Li(4)–O(3)] and, conversely, the *longer* δ-N–Li partial interaction [Li(2)–N(6)] involves the same lithium centre as the *shorter* Li–O one [Li(2)–O(5)]. This observation suggests that species such as these, if they can exist in solution without deaggregating significantly, will be rapidly fluxional.[16] Furthermore, the solid-state structure of **4** represents an intermediate state in the interconversion of the structural types represented by **2** and **3** (Scheme 2).

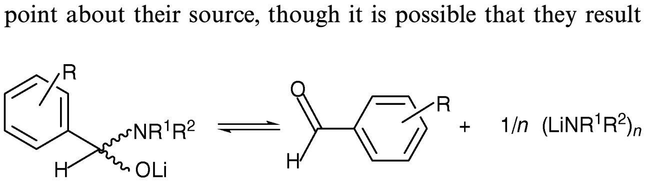
Solution studies

While **2** is only nominally soluble in aromatic solvents, it is possible to record the ^{1}H NMR spectrum. It affords the protected aldehyde resonance as a singlet at δ 5.87. However, the solution properties of **2** specifically (and the α-amino lithium alkoxides reported here in general) are rather complex. Over and above the expected aggregation/deaggregation behaviour (see below, compounds **3** and **4**) these species exhibit apparently concentration dependent solution equilibria between the intact α-amino lithium alkoxide and its constituent lithium dialkylamide and free aldehyde (Scheme 3; for **2**, R = H). Hence, for **2**, which is only sparingly soluble in non-donor aromatic media, equilibrium is moved towards the right-hand side, affording a free aldehyde : protected aldehyde ratio by ^{1}H NMR spectroscopy immediately after sample preparation of 1 : 5.

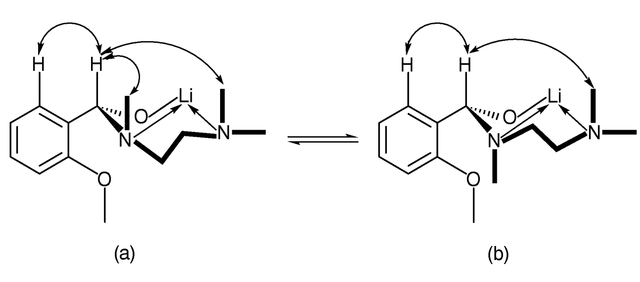


Scheme 2

According to multinuclear NMR studies, **3** exhibits extremely complex solution behaviour. In the first instance, the solution equilibrium demonstrated by **2** is repeated. However, apparently by virtue of the slightly greater solubility of **3**, the position of equilibrium is shifted less significantly towards an aldehyde/**1**-Li mixture. At ambient temperature ^{1}H NMR spectroscopy in [^{2}H$_6$]benzene (*ca.* 2 mg ml^{-1}) shows a main protected aldehyde singlet at δ 6.48 and five much less significant satellites in the range δ 6.12–6.01, all of which correlate with the protected aldehyde carbon centre at δ 88.6 in the HMQC spectrum. ^{1}H DPFGSE NOE spectroscopy[15] ($\tau_m = 0.7$ s) shows a weak NOE (2.8%) between the δ 6.46 singlet and the aromatic doublet at δ 8.14. More interestingly, salient NOEs are observed to both of the dominant α- and δ-N-methyl groups (2.4 and 4.8% respectively). This suggests that, in non-donor solution, not only is bis-chelation of the metal centres favoured but that the δ-NMe$_2$ group adopts an *endo*-orientation with respect to the resultant chelate ring [Scheme 4(a)]. It is, nevertheless, apparent that the NOE to the α-NMe group is not consistent with the *anti*-isomerism demonstrated by the Li–O–C–N chelate rings in the solid-state structure of **3** [Scheme 4(b)]. Tentatively, therefore, it can be suggested that the observation of this NOE is evidence for the existence of small amounts of *syn*-isomers in solution. It is only possible to speculate at this point about their source, though it is possible that they result



Scheme 3



Scheme 4

from the recombination of free aldehyde and **1**-Li (formed when trace amounts of **3** dissociate in solution).

The ^{1}H NMR spectrum at ambient temperature is essentially the same in [^{2}H$_{8}$]toluene as it is in [^{2}H$_{6}$]benzene, and in both cases the relative free aldehyde singlet : protected aldehyde multiplet ratio is approximately 1 : 50 immediately after preparation. That this ratio does not change on cooling the probe-head to −80 °C or on returning it to ambient temperature points to the equilibrium being neither temperature nor (in this case; see discussion for **4**, below) time dependent. These observations allow ^{7}Li NMR spectroscopy to be undertaken over the same temperature range and on the same timescale. The first and most obvious result to be had from ^{7}Li NMR spectroscopy is that, at the same concentration and at ambient temperature, **3** fails to exhibit two lithium environments in a 1 : 1 ratio and, therefore, on the NMR timescale the (*R*)- and (*S*)-monomers do not retain their solid-state differences. This suggests either that the tetramer is rapidly fluxional or that it deaggregates. Cryoscopy in benzene[17] favours the latter explanation, results suggesting (Table 1) that over the concentration range 1.3–3.9 mg ml^{-1} the mean aggregation state varies only from 1.4 ± 0.3 to 1.5 ± 0.2, and therefore that in non-polar solution a monomer–dimer equilibrium is dominant. In fact the ^{7}Li NMR spectroscopic results bear out this view. While at ambient temperature in [^{2}H$_{6}$]benzene two major features in a 3.8 : 1 ratio (δ −0.35 and −0.47) are observed, variable-temperature ^{7}Li NMR spectroscopy in [^{2}H$_{8}$]toluene allows these (now observed at δ −0.42 and −0.55) to be assigned respectively as dimer and monomer. At sub-ambient temperatures the high-field signal is absent, the low-field one having moved to δ −0.33 at −25 °C and δ −0.26 at −80 °C (Table 2).

Compared to **3**, **4** is very soluble in non-donor aromatic media and, furthermore, it tends not to deaggregate as significantly. Hence by cryoscopy in benzene (Table 3) the average aggregation state increases only from 2.9 ± 0.7 to 3.5 ± 0.1 over a wide concentration range (1.7–30.1 mg ml^{-1}) and *n* is 3.4 ± 0.1 at 10.2 mg ml^{-1}. This value of *n* correlates well with ^{7}Li NMR spectroscopy wherein a 10.0 mg ml^{-1} sample of **4** in [^{2}H$_{8}$]toluene at 0 °C shows three lithium signals in roughly a 2 : 9 : 1 ratio (Table 4). The dominant δ 0.25 resonance, observable at all temperatures from 90 to −95 °C can, by virtue of its being the *only* signal to remain at low temperatures (below −50 °C), be considered to be the most aggregated species in solution, which, judging from cryoscopic data, is the tetramer. Of the two other signals (δ 0.44 and 0.14 at 0 °C) the low-field one is nominally favoured at higher temperatures, allowing it to be assigned as the lower aggregation state species, the dimer, the remaining signal being attributable to the trimer. Calculation of the average formula mass and aggregation state at 10.0 mg ml^{-1} in [^{2}H$_{8}$]toluene at 0 °C affords values which, at 817 and 3.3 respectively, correlate closely with crysocopic data. Indeed, the closeness of this agreement, combined with the observation that the adoption of monomer and dimer respectively as the two remaining species afford poor concordance with cryoscopic data, demonstrate that the monomer is not viable in non-donor solution at this temperature and concentration. Nevertheless the slightly tentative nature of the dimer/trimer assignments is demonstrated by the fact that good correlation with cryoscopy can also be had if the two assignments are swapped, leading to a calculated average formula mass and aggregation state of 857 and 3.5 respectively.

Table 1 Cryoscopic data for **3** in benzene in the concentration range 1.3–3.9 mg ml^{-1}

Conc./mg ml^{-1}	Av. mol. mass	*n*
1.3	345 ± 65	1.4 ± 0.3
2.7	376 ± 33	1.5 ± 0.2
3.9	362 ± 50	1.5 ± 0.2

Table 2 ^{7}Li NMR data for **3** in [^{2}H$_{8}$]toluene over the range 25 to −80 °C. (—) indicates that the signal was not observable at that temperature

T/°C	δ	
25	−0.42(3.5)	−0.55(1)
0	−0.38(4.9)	−0.50(1)
−25	−0.33(1)	—
−50	−0.29(1)	—
−80	−0.26(1)	—

0 ppm = PhLi in [^{2}H$_{8}$]toluene at 25 °C. Integrals given in parentheses

Table 3 Cryoscopic data for **4** in benzene in the concentration range 1.7–30.1 mg ml^{-1}

Conc./mg ml^{-1}	Av. mol. mass	*n*
1.7	701 ± 224	2.9 ± 0.7
2.6	748 ± 152	3.1 ± 0.6
3.8	762 ± 101	3.1 ± 0.4
6.0	712 ± 77	2.9 ± 0.3
8.2	716 ± 78	2.9 ± 0.3
10.2	840 ± 26	3.4 ± 0.1
20.2	845 ± 26	3.5 ± 0.1
30.1	848 ± 18	3.5 ± 0.1

^{1}H NMR spectroscopy demonstrates that, like both **2** and **3**, **4** is in equilibrium with its constituents at low concentration. The enhanced solubility of **4** affords the chance, however, to study this solution behaviour more closely and to this end spectra obtained at low, intermediate and high concentrations (0.5, 2.0 and 10.0 mg ml^{-1} respectively) both immediately after sample preparation and (for low and high concentrations) after a six-hour delay have been recorded (Table 5). While a *p*-methoxybenzaldehyde/**1**-H control spectrum shows a free aldehyde singlet at δ 9.69, that of **4** (at 10.0 mg ml^{-1}) has the protected aldehyde as a dominant resonance at δ 5.89 (which correlates with the ^{13}C NMR spectroscopy singlet at δ 95.5 by HMQC spectroscopy) accompanied by a less significant complex multiplet in the range δ 5.86–5.83. The essential stability of **4** at high concentration is demonstrated by the fact that the 1 : 15 free aldehyde : protected aldehyde ratio immediately after preparation decreases only to 1 : 10 after 6 h. At intermediate concentration the initial ratio is 1 : 5, and at low concentration it is 1 : 1.75 with *only* free aldehyde observable after 6 h. The ^{7}Li NMR spectra also reflect these changes (Table 6). The high concentration spectrum does not change significantly with time, while at lower concentration a signal

Table 4 ^{7}Li NMR data for **4** in [^{2}H$_{8}$]toluene (10.0 mg ml^{-1}), over the range 90 to −95 °C. (—) indicates that the signal was not observable at that temperature

T/°C	δ			
90	—	0.27*(1)	0.21(1.5)	—
80	—	0.33(1.5)	0.21(2)	0.15(1)
60	0.46(1)	0.35(4)	0.21(8)	0.11(2)
40	0.42(1)	0.37(4.5)	0.22(9)	0.11(1)
25	—	0.40(2)	0.23(5)	0.11(1)
0	—	0.44(2)	0.25(9)	0.14*(1)
−25	—	0.47*(1)	0.28(7)	—
−50	—	—	0.30(1)	—
−75	—	—	0.31(1)	—
−95	—	—	0.33(1)	—

0 ppm = PhLi in [^{2}H$_{8}$]toluene at 25 °C. Integrals given in parentheses. *Shoulder.

Table 5 ^{1}H NMR data for concentrated (10.0 mg ml^{-1}), intermediate (2.0 mg ml^{-1}) and dilute (0.5 mg ml^{-1}) samples of **4** in [^{2}H$_6$]benzene at 25 °C

Assignment	*p*-Methoxybenz-aldehyde + **1**-H	**4** (conc.) $t = 0$ h	**4** (conc.) $t = 6$ h	**4** (int.) $t = 0$ h	**4** (dil.) $t = 0$ h	**4** (dil.) $t = 6$ h
C(O)H	9.69, s, 1H	9.71, s, 0.07H	9.71, s, 0.1H	9.69, s, 0.2H	9.69, s, 0.6H	9.69, s, 1H
Ar*	—	7.59, d, 2H	7.59, d, 2H	7.59, d, 2H	7.59, d, 2H	—
Ar	7.55, d, 2H	7.55, d, 0.13H	7.55, d, 0.2H	7.54, d, 0.4H	7.54, d, 1.14H	7.55, d, 2H
Ar*	—	7.02, d, 2H	7.02, d, 2H	7.02, d, 2H	7.02, d, 2H	—
Ar	6.55, d, 2H	6.54, d, 0.13H	6.54, d, 0.2H	6.54, d, 0.4H	6.54, d, 1.14H	6.54, d, 2H
ArC(*H*)(O)N*	—	5.89, 5.86–5.83, m, 1H	5.89,5.86–5.83, m, 1H	5.89, s, 1H	5.89, s, 1H	—
$\mathrm{OCH_3}$*	—	3.42, s, 3H	3.43, s, 3H	3.42, s, 3H	3.42, s, 3H	—
$\mathrm{N(CH_3)C}H_2$*	—	3.25, m, 1H	3.26, m, 1H	3.26, m, 1H	3.29, m, 1H	—
$\mathrm{OCH_3}$	3.13, s, 3H	3.09, s, 0.2H	3.09, s, 0.3H	3.08, s, 0.6H	3.08, s, 1.71H	3.08, s, 3H
$\mathrm{N(CH_3)C}H_2$*	—	2.63, m, 1H	2.63, m, 1H	2.64, m, 1H	2.63, m, 1H	—
$\mathrm{N(CH_3)C}H_2$	2.52, t, 2H	2.53, td, 0.13H	2.53, td, 0.2H	2.53, td, 0.4H	2.53, td, 1.15H	2.53, td, 2H
$\mathrm{NCH_3}$	2.31, s, 3H	2.31, d, 0.2H	2.32, d, 0.3H	2.32, d, 0.6H	2.32, d, 1.71H	2.32, d, 3H
$\mathrm{N(CH_3)_2C}H_2$	2.28, t, 2H	2.30, td, 0.13H	2.30, td, 0.2H	2.30, td, 0.4H	2.30, td, 1.14H	2.30, td, 2H
$\mathrm{N(CH_3)C}H_2$*	—	2.25–2.20, m, 1H	2.25–2.20, m, 1H	2.25–2.21, m, 1H	2.25–2.21, m, 1H	—
$\mathrm{NCH_3}$*	—	2.18, s, 3H	2.18, s, 3H	2.18, s, 3H	2.18, s, 3H	—
$\mathrm{N(CH_3)_2}$	2.04, s, 6H	2.06, s, 0.4H	2.07, s, 0.6H	2.05, s, 1.2H	2.05, s, 3.4H	2.05, s, 6H
$\mathrm{N(CH_3)_2}$*	—	2.04, s, 6H	2.04, s, 6H	2.04, s, 6H	2.04, s, 6H	—
$\mathrm{N(CH_3)_2C}H_2$*	—	1.95, dt, 1H	1.95, dt, 1H	1.95, dt, 1H	1.95, dt, 1H	—
NH	1.22, s, 1H	—	—	—	—	—

The concentrated and dilute samples are re-observed after a time delay (t) of 6 hours. Signals marked * are due to **4**

at δ 0.23, consistent with **4**, is initially dominant, but is replaced by a broad low-field signal with time.

Conclusion

Reactions of $\mathrm{LiN(Me)(CH_2)_2NMe_2}$, **1**-Li, with benzaldehyde, *o*- and *p*-methoxybenzaldehyde afford complexes **2**, **3** and **4** respectively. Their solid-state structures (the first of chiral α-amino lithium alkoxides) have, in essence, pseudo-cubane $\mathrm{(LiO)_4}$ cores. However, variations in the coordination modes adopted by the bis(amino) moieties incur significant differences in the spatial orientations of the organic peripheries and also in the precise structural features of the $\mathrm{(LiO)_4}$ cores. In all three structures the α-N centres of the bis(amino) groups are coordinated to the lithium cations, and in **2** the δ-N centres are distanced from these cations so that the $\mathrm{(LiO)_4}$ cube is intact. However, in **3** two of the four bis(amino) groups show δ-N–Li coordination, causing opening of two eclipsed Li–O edges of the cube. The structure of **4** is intermediate between those of **2** and **3**, with two weak δ-N–Li interactions leading to significant lengthening of two Li–O cube edges.

The solution natures of these three chiral α-amino lithium alkoxides have been studied extensively by variable-concentration cryoscopic relative molecular mass measurements and by linked variable-concentration/-temperature ^{1}H and ^{7}Li NMR spectroscopy. All three species exhibit dissociative equilibria involving their constituents (**1**-Li + free aldehyde) and also equilibria involving tetrameric and lower aggregates and monomers. The precise conformations of these various solution species will be probed further in an attempt to explain the known specificity, mainly *ortho*, of further lithiations of these intermediates.

Experimental

Synthesis of 2

Bu^{n}Li (1.88 ml, 1.6 M in hexanes, 3.0 mmol) was added to *N*,*N*,*N*′-trimethylethylenediamine (**1**-H, 0.38 ml, 3.0 mmol) in toluene (13 ml) at −78 °C under nitrogen. After stirring for 10 min, benzaldehyde (0.30 ml, 3.0 mmol) was added. After a further 10 min at −78 °C the solution was warmed to room temperature yielding a white suspension which dissolved at reflux. After filtration, storage of the resultant yellow solution for 12 h at +80 °C afforded colourless blocks of **2**, mp 203–205 °C, yield, 55%. Found: C 66.61, H 8.71, N 12.27. Calc. for $\mathrm{C_{12}H_{19}LiN_2O}$: C 67.29, H 8.88, N 13.08%. ^{1}H NMR (500.130 MHz, [^{2}H$_6$]benzene), δ 7.61 (d, 2H, 2-Ph, $^3J_{\mathrm{HH}} = 7.01$ Hz), 7.34 (t, 1H, 4-Ph, $^3J_{\mathrm{HH}} = 7.55$ Hz), 7.21 (dt, 2H, 3-Ph, $^3J_{\mathrm{HH}} = 7.28$ Hz), 5.87 [s, 1H PhC(*H*)(O)N], 3.24–2.28, (m, 4H, $\mathrm{CH_2}$), 2.13–2.12 (m, 3H, $\mathrm{NCH_3}$), 2.05–1.91 [m, 6H, $\mathrm{N(CH_3)_2}$]. ^{13}C NMR (100.614 MHz, [^{2}H$_6$]benzene), δ 129.2, 127.2, 126.4 (Ph), 95.9 [Ph*C*(H)(O)N)], 59.5–57.0 ($\mathrm{CH_2}$), 50.2 ($\mathrm{CH_2}$), 46.4–45.6 [m, $\mathrm{N(CH_3)_2}$], 36.9 (m, $\mathrm{NCH_3}$).

Synthesis of 3

Bu^{n}Li (1.88 ml, 1.6 M in hexanes, 3.0 mmol) was added to **1**-H (0.38 ml, 3.0 mmol) in THF (4 ml) at −78 °C under nitrogen. After stirring for 10 min, *o*-methoxybenzaldehyde (0.36 ml, 3.0 mmol) was added and the resultant colourless solution was stirred for a further 10 min at −78 °C. Warming to room temperature gave a white suspension, which afforded a yellow solution on gentle heating. Storage at room temperature for one day resulted in the deposition of colourless, rectangular crystals of **3**, mp 160–161 °C, yield, 82%. Found: C 63.65, H

Table 6 ^{7}Li NMR data for concentrated (10.0 mg ml^{-1}), intermediate (2.0 mg ml^{-1}) and dilute (0.5 mg ml^{-1}) samples of **4** in [^{2}H$_6$]benzene at 25 °C

Conc., $t = 0$ h	Conc., $t = 6$ h	Int., $t = 0$ h	Dil., $t = 0$ h	Dil., $t = 6$ h
0.42(2)	0.41(2)	—	—	—
—	—	0.30*(1)	0.45*(1.8)	0.59*(1)
0.22(5)	0.22(5)	0.23(2)	0.23(1)	—
0.11(1)	0.11(1)	—	—	—

Concentrated and dilute samples re-observed after a time delay (t) of 6 hours. 0 ppm = PhLi in [^{2}H$_6$]benzene at 25 °C. Integrals given in parentheses. *Broad.

Table 7 Crystallographic data for **2**, **3** and **4**

	2	**3**	**4**
Formula	$C_{48}H_{76}Li_4N_8O_4$	$C_{52}H_{84}Li_4N_8O_8$	$C_{52}H_{84}Li_4N_8O_8$
M_r	856.92	977.03	976.24
Space group	$P\bar{1}$	$C2/c$	$P\bar{1}$
a/Å	11.132(2)	21.795(6)	12.753(6)
b/Å	11.120(2)	12.828(4)	20.394(7)
c/Å	20.726(5)	20.754(7)	11.090(6)
α/°	77.81(2)	90	98.18(4)
β/°	83.31(2)	105.19(2)	105.19(2)
γ/°	89.950(14)	90	85.50(4)
V/Å^3	2490.0(9)	5600(3)	2714(2)
Z	2	4	2
D_c/g cm^{-3}	1.143	1.159	1.196
Crystal size/mm	0.3 × 0.3 × 0.1	0.4 × 0.3 × 0.15	0.4 × 0.3 × 0.25
Radiation (λ/Å)	Mo-Kα(0.71069)	Mo-Kα(0.71069)	Mo-Kα(0.71069)
μ/mm^{-1}	0.072	0.077	0.079
F(000)	844	2112	1056
T/K	180	150	150
Scan mode	ω–2θ	ω–2θ	ω
2θ range/°	8.10–50.02	5.12–39.96	5.00–50.16
Measured reflections	11154	2707	10001
Unique reflections	8730	2604	9536
R_{int}	0.1348	0.0335	0.0922
Reflections with $I > 2\sigma(I)$	8713	2595	9515
Final $R(F)$, $wR(F^2)$	0.0698, 0.2719	0.0536, 0.1412	0.0571, 0.1585
Goodness-of-fit	1.031	1.045	1.014
Max. peak, hole/e Å^{-3}	0.396, −0.351	0.172, −0.186	0.252, −0.258

8.39, N 11.12. Calc. for $C_{20}H_{21}LiN_2O_2$: C 63.93, H 8.61, N 11.48%. ^{1}H NMR (500.130 MHz, [$^2H_6$]benzene), δ 8.14 (d, 1H, 2-Ar, $^3J_{HH}$ = 6.57 Hz). 7.18 (d, 1H, 5-Ar, $^3J_{HH}$ = 7.35 Hz), 7.14 (dd, 1H, 4-Ar, $^3J_{HH}$ = 7.45 Hz), 6.78 (dd, 1H, 3-Ar, $^3J_{HH}$ = 7.78 Hz), 6.48–6.01 [m, 1H, ArC(*H*)(O)N], 3.72–3.31 (m, 3H, OCH_3), 2.75–2.69, 2.32 (m, 2H, CH_2), 2.68–2.21 (m, 3H, NCH_3), 2.53–2.49 (m, 2H, CH_2), 2.41–1.92 [m 6H, $N(CH_3)_2$]. ^{13}C NMR (100.614 MHz, [$^2H_6$]benzene), δ 157.0, 135.8, (1-/2-Ar), 130.6 (2-Ar), 126.8 (5-Ar), 119.9 (4-Ar), 110.0 (3-Ar), 88.6 [Ar*C*(H)(O)NR_2], 59.0 (CH_2), 54.9 (OCH_3), 52.1 (CH_2), 46.7–45.5 [m, $N(CH_3)_2$], 36.9–34.7 (m, NCH_3). ^{7}Li NMR (155.508 MHz, [$^2H_6$]benzene, 0 ppm = PhLi in [$^2H_6$]benzene at 25 °C), δ −0.35 (s, 3.8Li), −0.47 (s, 1Li). ^{1}H DPFGSE NOE (500.130 MHz, [$^2H_6$]benzene), irradiation at δ 6.46 (τ_m = 0.7 s) gives a 2.8% NOE at δ = 8.14, a 2.4% NOE at δ 2.68–2.21 and a 4.8% NOE at δ 2.41–1.92.

Synthesis of 4

Bu^{n}Li (1.88 ml, 1.6 M in hexanes, 3.0 mmol) was added to **1**-H (0.38 ml, 3.0 mmol) in 8 : 1 toluene–THF (2 : 0.25 ml) at −78 °C under nitrogen. The resultant yellow solution was stirred for 10 min at −78 °C whereupon *p*-methoxybenzaldehyde (0.36 ml, 3.0 mmol) was added. After a further 10 min at this temperature the solution was allowed to warm to room temperature, yielding a white suspension which was dissolved by gentle heating. Storage at room temperature for 12 h afforded colourless blocks of **4**, mp 164–166 °C, yield, 75%. Found: C 63.79, H 8.74, N 11.57. Calc. for $C_{20}H_{21}LiN_2O_2$: C 63.93, H 8.61, N 11.48%. ^{1}H NMR (400.134 MHz, [$^2H_6$]benzene), δ 7.59 (d, 2H, Ar, $^3J_{HH}$ = 8.49 Hz), 7.02 (d, 2H, Ar, $^3J_{HH}$ = 8.51 Hz), 5.89, 5.86, 5.84, 5.83 [m, 1H, ArC(*H*)(O)N], 3.42 (s, 3H, OCH_3), 3.25 (br, m 1H, CH_2), 2.63 (dt, 1H, CH_2, $^3J_{HH}$ = 11.80, $^3J_{HH}$ = 3.23 Hz), 2.25–2.20 (m, 1H, CH_2), 2.18 (s, 3H, NCH_3), 2.04 [s, 6H, $N(CH_3)_2$], 1.95 (dt, 1H, CH_2, $^3J_{HH}$ = 12.48 Hz, $^3J_{HH}$ = 3.12 Hz). ^{13}C NMR (100.614 MHz, [$^2H_6$]benzene), δ 158.8, 139.4, (Ar-CH) 112.7 (Ar-C), 95.5 [Ar*C*(H)(O)NR_2], 58.3 (CH_2), 54.7 (OCH_3), 52.4 (CH_2), 46.5 [$N(CH_3)_2$], 33.9 (NCH_3). ^{7}Li NMR (155.508 MHz, [$^2H_6$]benzene, 0 ppm = PhLi in [$^2H_6$]benzene at 25 °C), δ 0.42 (s, 2Li), 0.22 (s, 5Li), 0.11 (1Li).

X-Ray crystallography

Essential crystallographic details are given in Table 7. Data for **2** were collected on a Stoe-Siemens four-circle diffractometer with data for **3** and **4** being collected on a Rigaku AFC5R four-circle diffractometer. All three structures were solved using direct methods[18] and subsequent Fourier difference syntheses and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for all non-hydrogen atoms.[19] A riding model with idealised geometry was employed for H-atom refinement. CCDC reference number 440/085. See http://www.rsc.org/suppdata/njc1999/35/for crystallographic files in .cif format.

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