

# Inhibition of the Cyclotrimerization of Benzonitrile and the Likely Mechanism of the Cyclotrimerization Process: Structure of a New Tetrameric $\alpha$ -Amino Lithium Imide Demonstrating *Intramolecular* Stabilization of the Metal Centers

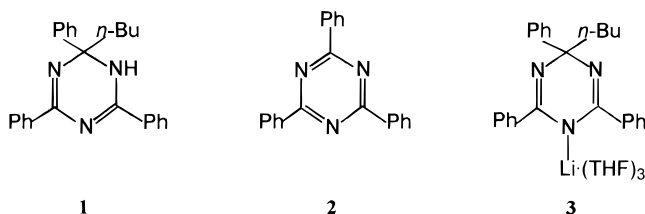
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Received December 19, 1996<sup>®</sup>

**Summary:** Reaction of ((2-(dimethylamino)ethyl)methylamino)lithium (**4**) with benzonitrile gives a new  $\alpha$ -amino lithium imide, **5**, which in the solid state is a tetrameric cubane. Aggregation is accompanied by chelation of each metal center using a tertiary amino function, yielding stable seven-membered rings. The stability of **5** limits cyclotrimerization of the benzonitrile moiety to 2,4,6-triphenyl-1,3,5-triazine, thereby suggesting a likely mechanism for the cyclotrimerization process.

That organolithium reagents (RLi) such as *n*-butyllithium induce the cyclotrimerization of benzonitrile to give a monosubstituted dihydrotriazine such as **1** has long been recognized.<sup>1,2</sup> Furthermore, it has been estab-



lished recently<sup>3,4</sup> that the fully unsaturated 2,4,6-triphenyl-1,3,5-triazine (**2**) can be obtained in good yield (50%+) from the 3:1 reaction of benzonitrile with *n*-butyllithium in hexane. However when *n*- or *tert*-butyllithium in THF is used, it is found that formation of a lithio-1,4-dihydrotriazine complex, **3**, is favored, so that the cyclotrimerization process appears to be a solvent-dependent one. Despite these findings, the precise mechanism of such organolithium-induced benzonitrile cyclotrimerization reactions remains obscure. One presumes that the initial intermediate is an imidolithium species, Ph(R)C=NLi, which then adds across another benzonitrile. This paper reports findings which test this presumption and which appear to prove it.

We report the isolation and structural characterization of an imidolithium derivative of benzonitrile,<sup>5</sup> obtained in good yield by the partial inhibition of cyclotrimerization. Reaction of *in situ* generated ((2-(dimethylamino)ethyl)methylamino)lithium (**4**) with 1 equiv of nitrile in toluene/THF solvent results in the

high-yield formation of an  $\alpha$ -amino lithium imide, **5** (Scheme 1),<sup>6</sup> in the complete absence of any isolable trimer **2**. X-ray crystallography<sup>7</sup> demonstrates that, unlike previously observed  $\alpha$ -amino lithium imides which have all been hexamers in the solid state (*viz.* [Ph(Me<sub>2</sub>N)C=NLi]<sub>6</sub>, [(Me<sub>2</sub>N)<sub>2</sub>C=NLi]<sub>6</sub>),<sup>6</sup> **5** is a tetrameric cubane (Figure 1). While the aforementioned hexamers demonstrated 3-fold coordination of the lithium centers and no involvement of the Me<sub>2</sub>N groups, those in tetramer **5** are four-coordinate, lower aggregation being facilitated by stabilization of the metal centers by *intramolecular* chelation of the  $\delta$ -N' centers. While such intramolecular complexation is common in lithium amide, alkyl, alkoxide, and enolate chemistry,<sup>5</sup> it has not been observed previously for lithium imides. The inability of the  $\alpha$ -amino centers to interact with the metal centers is expected, while involvement of the internal  $\delta$ -N' centers can be compared with that of

(5) *n*-Butyllithium (0.94 mL, 1.6 M in hexanes, 1.5 mmol) was added to *N,N,N*-trimethylethylenediamine (0.19 mL, 1.5 mmol) in 1:1 toluene/THF (2:2 mL) at  $-78^\circ\text{C}$ . After the mixture was stirred for 10 min, benzonitrile (0.15 mL, 1.5 mmol) was added and the resultant yellow solution was stirred for a further 10 min at  $-78^\circ\text{C}$ . Warming to room temperature gave a yellow suspension, which afforded a yellow solution on gentle heating. Storage at room temperature for 1 day afforded yellow cubic crystals of **5**: mp  $163\text{--}164^\circ\text{C}$ ; yield 82%. Anal. Found: C, 67.7; H, 8.6; N, 19.9. Calcd for C<sub>12</sub>H<sub>18</sub>N<sub>3</sub>Li: C, 68.2; H, 8.5; N, 19.9. <sup>1</sup>H NMR spectroscopy (250 MHz, 25  $^\circ\text{C}$ , C<sub>6</sub>D<sub>6</sub>):  $\delta$  1.84 (s, 6H, NMe<sub>2</sub>), 2.18 (t, 2H,  $\beta$ -CH<sub>2</sub>), 2.78 (s, 3H, NMe), 3.37 (s, br, 2H,  $\alpha$ -CH<sub>2</sub>), 7.17 (m, 1H, *p*-Ph), 7.36 (t, 2H, *m*-Ph), 7.66 (d, 2H, *o*-Ph).

(6) For other imidolithium derivatives of benzonitrile see: (a) Clegg, W.; Snaith, R.; Shearer, H. M. M.; Wade, K.; Whitehead, G. *J. Chem. Soc., Dalton Trans.* **1983**, 1309–1317. (b) Barr, D.; Clegg, W.; Mulvey, R. E.; Snaith, R.; Wade, K. *J. Chem. Soc., Chem. Commun.* **1986**, 295–297. (c) Armstrong, D. R.; Barr, D.; Snaith, R.; Clegg, W.; Mulvey, R. E.; Wade, K.; Reed, D. *J. Chem. Soc., Dalton Trans.* **1987**, 1071–1081. (d) Gregory, K.; Schleyer, P. v. R.; Snaith, R. *Adv. Inorg. Chem.* **1991**, 37, 47–142. (e) Mulvey, R. E. *Chem. Soc. Rev.* **1991**, 20, 167–209.

(7) Crystal data for **5**: C<sub>48</sub>H<sub>72</sub>Li<sub>4</sub>N<sub>12</sub>, triclinic, space group P1 (No. 2),  $a = 11.138(10)$  Å,  $b = 11.151(11)$  Å,  $c = 22.14(3)$  Å,  $\alpha = 90.56(9)^\circ$ ,  $\beta = 100.55(8)^\circ$ ,  $\gamma = 112.24(8)^\circ$ ,  $M_r = 844.92$ ,  $Z = 2$ ,  $D_c = 1.126$  Mg m<sup>-3</sup>,  $\mu(\text{Mo K}\alpha) = 0.067$  mm<sup>-1</sup>,  $F(000) = 912$ . Data were collected by the  $\omega/\theta$  scan method on a Stoe-Siemens four-circle diffractometer at 153(2) K using graphite-monochromated Mo K $\alpha$  radiation ( $\lambda = 0.71073$  Å) in the range  $7.16 < 2\theta < 50.30^\circ$ ,  $\pm h, \pm k, \pm l$  15 901 reflections were collected, of which 8337 were independent ( $R_{\text{int}} = 0.10$ ) and were used in all calculations. The structure was solved using direct methods<sup>8</sup> and subsequent Fourier difference syntheses and refined<sup>9</sup> by full-matrix least squares on  $F^2$  with anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms were placed in geometrically idealized positions and refined using a riding model or as rigid methyl groups. In the final cycles of refinement a weighting scheme of the form  $w^{-1} = [\sigma^2(F_o^2) + (0.0745P)^2 + 1.58P]$ , where  $P = (F_o^2 + 2F_c^2)/3$ , was employed, which produced a flat analysis of variance: final  $R(F) = 0.0623$ , and  $R_w(F^2) = 0.1500$  for 6054 observed reflections ( $I > 2\sigma(I)$ );  $R(F) = 0.0914$ , and  $R_w(F^2) = 0.1750$  for all data; 589 parameters; GOF = 1.035; maximum  $\Delta\sigma = 0.001$ ; maximum peak and hole in final Fourier difference map 0.43 and  $-0.27$  e Å<sup>-3</sup>, respectively.

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(9) Sheldrick, G. M. SHELXL-93, Program for Crystal Structure Refinement; University of Göttingen, Göttingen, Germany, 1993.

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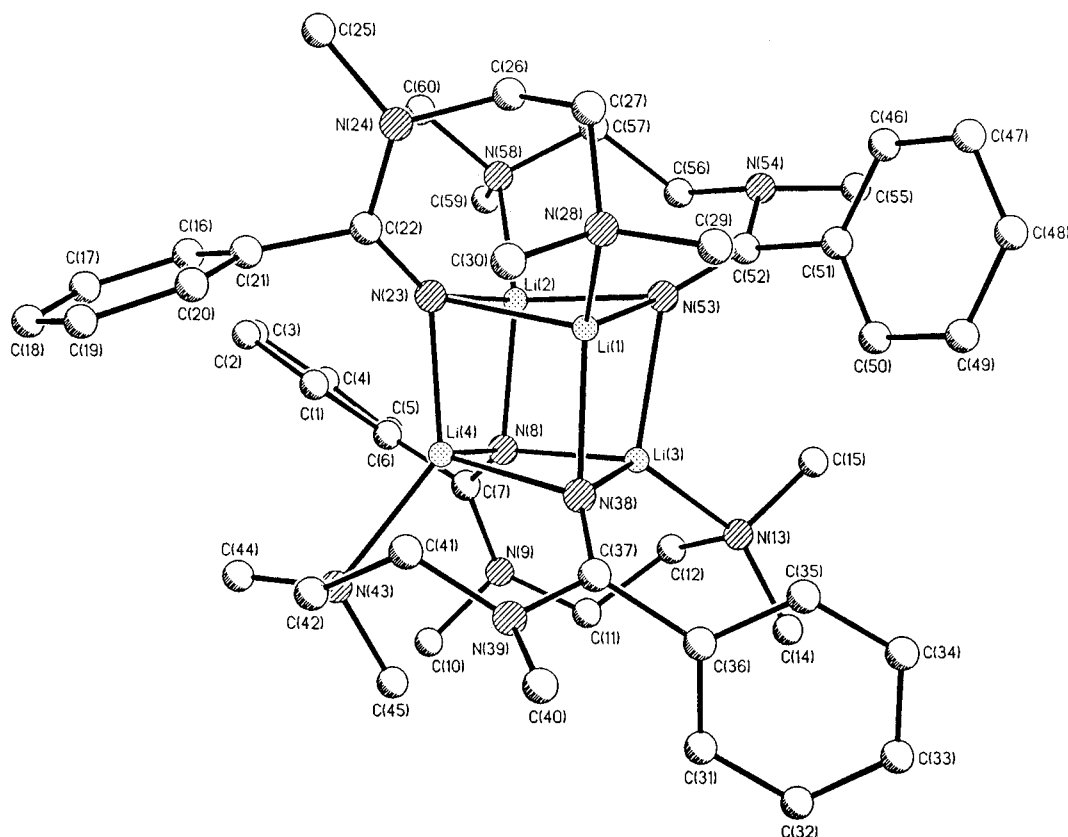
<sup>®</sup> Abstract published in *Advance ACS Abstracts*, April 15, 1997.

(1) Anker, R. M.; Cook, A. H. *J. Chem. Soc.* **1941**, 323–331.

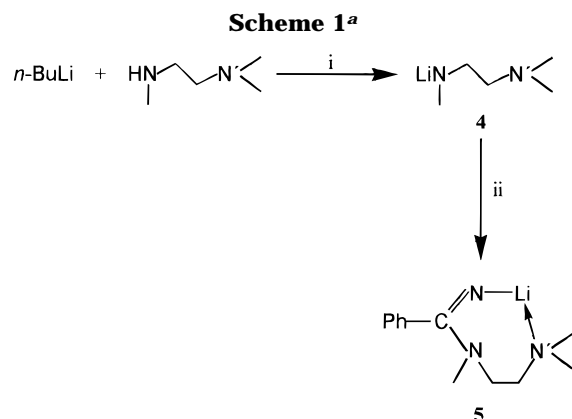
(2) Cook, L. S.; Wakefield, B. J. *J. Chem. Soc., Perkin Trans. 1* **1980**, 2392–2397.

(3) Armstrong, D. R.; Clegg, W.; MacGregor, M.; Mulvey, R. E.; O'Neil, P. A. *J. Chem. Soc., Chem. Commun.* **1993**, 608–610.

(4) Armstrong, D. R.; Henderson, K. W.; MacGregor, M.; Mulvey, R. E.; Ross, M. J.; Clegg, W.; O'Neil, P. A. *J. Organomet. Chem.* **1995**, 486, 79–93.



**Figure 1.** Molecular structure of **5**; hydrogen atoms omitted for clarity.



<sup>a</sup> Reagents and conditions: (i) 1/1 toluene/THF,  $-78\text{ }^{\circ}\text{C}$ ; (ii) 1 equiv of PhCN.

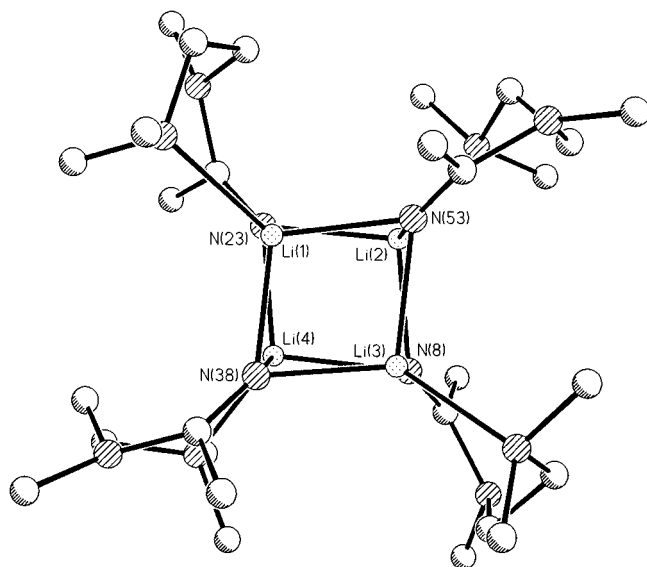
added pyridine solvent in the tetrameric cubane  $[\text{Ph}_2\text{C}=\text{NLi}\cdot\text{py}]_4$ <sup>10</sup> (py = pyridine). However, the favorability of chelate formation in **5** precludes and resists external solvation, even by extremely good Lewis bases. For example, effecting the reactions in Scheme 1 in the presence of HMPA (hexamethylphosphoramide,  $\text{O}=\text{P}(\text{NMe}_2)_3$ ) gives **5**, albeit in depleted yield (32%); no HMPA complex could be isolated.<sup>11</sup> It is also apparent that the surprising and exceptional stability of this chelate is highly dependent upon ring size. It is found, for example, that replacement of *N,N,N*-trimethylethylenediamine with *N,N,N*-trimethylpropanediamine, in an attempt to form the eight-membered chelate analogue of **5**, serves to generate only **2** in 32% yield, with

(10) Barr, D.; Clegg, W.; Mulvey, R. E.; Snaith, R. *J. Chem. Soc., Chem. Commun.* **1984**, 79–80.

(11) Reaction of 1 mmol of *n*-butyllithium with 1 mmol of *N,N,N*-trimethylethylenediamine in the presence of 1 equiv of HMPA in hexane (2 mL), followed by the addition of 1 equiv of benzonitrile, gave **5** as the only isolable product.

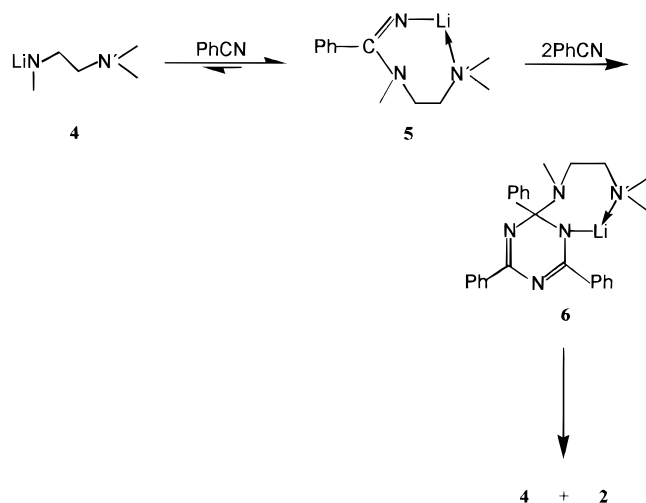
no imidolithium being isolated; *i.e.*, cyclotrimerization of benzonitrile now proceeds.

The tetramer can be considered as comprising two stacked dimers (Figure 1, top to bottom). It is apparent, on closer analysis, that in spite of their superficial similarity, the four chelate rings are not identical. As a consequence of this, the cubane core of the aggregate is significantly distorted, with N–Li interactions adopting a range of values. Two interdimer N–Li interactions, located on opposite edges of the cubane, are of intermediate length (Li(1)–N(38) = 2.035(5) Å, Li(2)–N(8) = 2.038(5) Å), while the remaining two such interactions show a marked variation; one is anomalously long (Li(3)–N(53) = 2.131(5) Å) and the other short (Li(4)–N(23) = 2.005(5) Å). Truncation of this latter interaction appears to have no adverse effect on the strength with which Li(4) is chelated; indeed, rather the reverse, since  $\delta\text{-N}'\text{-Li}$  bonding shows little variation, with the exception of Li(4)–N(43) which, surprisingly, is anomalously short at 2.149(5) Å (the remaining  $\delta\text{-N}'\text{-Li}$  bonds have a mean value of 2.182(5) Å). Distortion of the cubane core is probably attributable to steric interactions between ligands. Interestingly, the two dimers stack in an eclipsed fashion rather than in a staggered one. Necessarily, therefore, within each dimeric pair the chelated monomers are oriented differently. While each of the chelate rings is folded, one is inclined toward its partner in the dimeric arrangement. This partner then minimizes steric interaction by folding toward the second dimeric pair, thus explaining in part the inequivalence of the  $\delta\text{-N}'\text{-Li}$  interactions. The consequence of this is that the aggregate adopts a “wheel” configuration (Figure 2). Some confirmation that it is reasonable to view the solid-state aggregate as two stacked dimers comes from cryoscopic measurements in benzene, which indicate solution equilibria dominated by dimeric aggregation. The mean value of



**Figure 2.** End-on view of **5** demonstrating the relative orientations of the seven-membered chelate rings; only the  $\alpha$ -carbon atoms of the phenyl rings are shown.

### Scheme 2

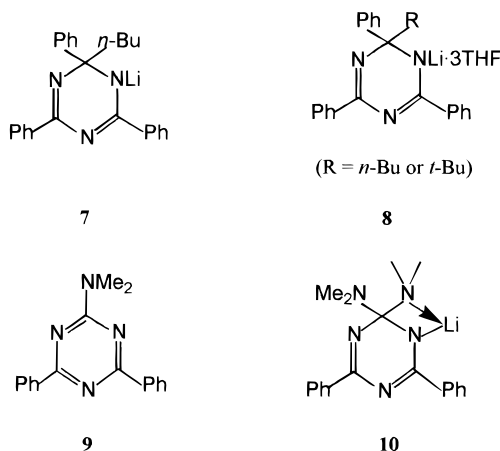


$n$  varies only from 2.13 to 2.45 over the concentration range 0.01–0.12 M.

Reaction of **4** with 3 equiv of benzonitrile in toluene has also been studied. As previously described,<sup>3,4</sup> *n*-butyllithium reacts with benzonitrile in nonpolar solvents to yield **2** as the sole isolable crystalline product. Interestingly, **4** also is found to induce cyclotrimerization in the presence of 3 equiv of benzonitrile, but now both **2** and **5** are recoverable in high relative yields from the mother liquor.<sup>12</sup> Clearly, this suggests that, despite its inherent stability, **5** in solution participates in the cyclotrimerization of excess nitrile, probably leading to the lithio-1,2-dihydrotriazine intermediate **6** (Scheme 2). Some of species **6** (which is itself somewhat stabilized by intramolecular chelation) can eliminate **4** and so produce the fully unsaturated triazine **2**, and the eliminated **4** can reenter the reaction cycle, thus giving more of **5** and, hence, the isolation of both compounds. Such a mechanistic scenario appears to explain many previous results in this area.<sup>1–4</sup> Thus, as noted, the

(12) The addition of 1 mmol of *n*-butyllithium to 1 equiv of *N,N,N'*,*N'*-trimethylethylenediamine in toluene (4 mL), followed by 3 equiv of benzonitrile, gave **5** and **2** in yields of 62 and 97%, respectively. The latter yield was calculated by assuming that only the 2 mmol excess of nitrile was available for cyclotrimerization.

reaction between *n*-butyllithium and 3 equiv of benzonitrile in a noninvolved solvent such as hexane affords **2** only: the hitherto presumed imidolithium intermediate,  $\text{Ph}(n\text{-Bu})\text{C}=\text{NLi}$  (cf. **5**), and the lithio-1,2-dihydrotriazine product precursor **7** (cf. **6**) both lack stabilization by chelation or external solvation. Thus, the imidolithium compound reacts freely with the two extra benzonitrile equivalents and **7** eliminates *n*-butyllithium



readily. However, if the same reaction (or one using *tert*-butyllithium) is carried out in THF, the product is **3**, a tris-THF-complexed lithio-1,4-dihydrotriazine. This is now understandable, given our mechanistic model. Tricomplexation by added THF (cf. internal complexation by one  $\text{Me}_2\text{N}$  unit in **6**) to give **8** is impossible sterically. Hence, it results in a shift of the  $\text{Li}(\text{THF})_3$  unit to the 4-position, where  $\text{RLi}$  elimination to give **2** is implausible: hence, **3** is isolated as the sole product. In contrast—but again in agreement with our proposed mechanism—reaction of  $(\text{Me}_2\text{N})_2\text{C}=\text{NLi}$  with 2 equiv of benzonitrile in hexane/toluene or in THF gives the fully unsaturated triazine **9**.<sup>4</sup> This is now understandable given that the immediate precursor will be the chelated and stabilized 1,2-species **10**, akin to **6**.<sup>6,7</sup>  $^6/7\text{Li}$  NMR spectroscopy would appear to offer the best chance of elucidating the cyclotrimerization process further. Accordingly, therefore, this is being utilized in conjunction with attempts at isolating other trimerization-related lithio intermediates.

In conclusion, **5** represents the successful derivatization of benzonitrile as a lithium imide by limitation of the cyclotrimerization reaction of this nitrile. Nevertheless, in the presence of excess nitrile, formation of a product mixture suggests that the first stage of the cyclotrimerization proceeds *via* the reaction of a classical lithium imide with unreacted nitrile and that consequently **5** can be regarded as a likely first-stage intermediate in cyclotrimerization. The solid-state structure of **5** shows it to be the first example of an  $\alpha$ -amino lithium imide to demonstrate intramolecular coordination of the metal centers.

**Acknowledgment.** We thank the U.K. EPSRC (R.P.D., G.P.S., and A.E.H.W.), the Cambridge Crystallographic Data Centre (G.P.S.), and The Royal Society (P.R.R.) for financial support.

**Supporting Information Available:** Details of the X-ray structure determination for compound **5** and tables of X-ray crystallographic data (14 pages). Ordering information is given on any current masthead page.

OM961082W