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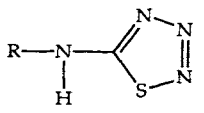
[9] In principle, there are least four conformations in which the linker arm can join the uppermost melamine ring in **4** to the central benzene "hub" [2]. Additionally, adjacent melamine rings in each arm of the Hub(MMM)$_3$ unit can lie in eclipsed or staggered conformations, resulting in a total of at least 16 discrete conformers.
[10] Supramolecular aggregates based on a single $CA_3 \cdot M_3$ rosette often exist as mixtures of different geometrical isomers. The exchange between these structures can be slowed to reveal the separate isomers by ^{1}H NMR at temperatures below ambient; M. Wazeer, J. P. Mathias, E. E. Simanek, G. M. Whitesides, unpublished results.
[11] The traces from **4** in the GPC are significantly broader than those of previously reported double-layer aggregates, such as that between the hexamelamine derivative Hub(MM)$_3$ and six equivalent of neohexylisocyanurate, Hub(MM)$_3$ · 6*neo*hex(CA). The reduction in stability for **4** suggested by this observation places this aggregate close to the lower limit of stability that can be observed successfully by GPC.
[12] Chloroform was Aldrich HPLC grade. No attempt was made to monitor its moisture content during analysis by VPO.

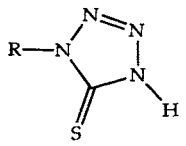
The First Structure of a Lithiated Cyanamide; Synthesis of (PhNCNLi · HMPA)$_n$ by Extrusion of N_2 and S from 5-Phenylamino-1,2,3,4-thiatriazole with Li Reagents and HMPA**

By *David R. Armstrong, F. Adele Banbury, Ian Cragg-Hine, Matthew G. Davidson, Francis S. Mair, Ehmke Pohl, Paul R. Raithby*, and *Ronald Snaith**

We described recently the product resulting from the reaction of solid $Ba(OH)_2$ with aminothiatriazole (**AH**; R = naphthyl) and HMPA [O=P(NMe$_2$)$_3$] dissolved in toluene.[1] Instead of the expected aqua complex, (**A**)$_2$Ba · 2H$_2$O · *x* HMPA,[2] a rearrangement occurs to give the thioxotetrazole derivative, (**B**)$_2$Ba · 3HMPA, in 60% yield. This rearrangement has been known for a long time[3] as has the fact that compounds of the type **AH** react with excess aqueous NaOH along two different paths: the first path involves the degradation of the heterocycle **AH** to give RNCS and azide; the RNCS is subsequently hydrolyzed to the corresponding amine. The second path involves the isomerization of the thiatriazole **AH** to the thioxotetrazolyl anion (**B**$^-$). Path 1 is favored when an excess of OH^- ions and H_2O is used. In contrast, our recent study[1] showed that in the presence of HMPA ligands, the use of stoichiometric amounts of solid $Ba(OH)_2$ and **AH** prevent the hydrolysis step in path 1, and indeed, constructively favor path 2: the rearrangement increases the distance of the R group (naphthyl) from the $(N\cdots C\cdots S)^-$ unit which chelates the large $Ba(HMPA)_3^{2+}$ fragment.



AH



BH

Here we report a third, and rather more spectacular, pathway for the deprotonation of aminothiatriazoles **AH**: extrusion of N_2 and S at ambient temperature lead to metal complexes of the anion of R–N(H)–C≡N. Thus, in this way complex **1**, whose solid-state structure—the first of a lithiated cyanamide—was determined, was formed from **AH** (R = phenyl). Deprotonations of 5-(phenylamino)-1,2,3,4-thiatriazole (**AH**; R = Ph) were performed with a range of lithium bases. In general, equimolar amounts of **AH** and HMPA are dissolved in toluene at −78 °C, and then one equivalent of the chosen base (LiOH, MeOLi, $LiNH_2$, *i*Pr$_2$NLi as solids; *n*BuLi as a solution in hexane; see the Experimental Procedure for specific details) is added. Warming the mixture to room temperature causes dissolution of any solid, usually accompanied by visible gas evolution. Refrigeration of the resulting solution gives crystals of **1** (20–60% yield) except when the base used for the reaction is solid LiOH. In this case crystals of (**B**)Li · H_2O · HMPA are isolated initially; that is those containing the rearranged, rather than the extruded, anion. However, subsequent treatment of these crystals with additional LiOH/HMPA, or with *n*BuLi/HMPA, affords **1**. Interestingly, the reaction of **BH** with *n*BuLi/HMPA affords (**B**)Li · HMPA rather than **1**. The most immediate evidence for an extrusion product [$(RNCN)_x \cdot M^{x+} \cdot y$ ligand] is the appearance of a strong $\nu(N\cdots C\cdots N)^-$ stretch in the IR spectrum; for **1**, this band appears at 2147 cm^{-1}. The products of the reactions of **AH** (R = naphthyl) with HMPA and all the above-mentioned lithium bases show a similar absorption. However, treatment of HMPA and **AH** (R = Ph) in toluene with the highly reactive system $Ba/Ba(NH_2)_2$ (obtained by evaporating a solution of metallic Ba in liquid NH_3) affords a product having no such band. In this case the rearrangement product (**B**)$_2$Ba · 3HMPA (R = Ph) is formed. This product is akin to that [R = naphthyl in **B**] obtained from a similar reaction in which rather unreactive solid $Ba(OH)_2$ is used.[1] Thus it seems that formation of extrusion products is dependent on the metal atom attached to the base (switch from Ba to Li) rather than on the R group (switch from R = naphthyl to R = Ph in **AH**), or on a change in the general reactivity of the metalating reagent used.

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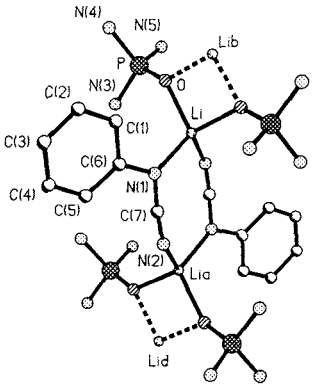


Fig. 1. The molecular structure of **1**, showing the central $(LiNCN)_2$ ring and adjacent $(LiO)_2$ rings.

The solid-state structure of **1** has been resolved by X-ray crystallography.[4] The most important structural feature (Fig. 1) is a $(LiNCN)_2$ ring [distances: Li–N1 2.061(4) Å; Lia–N2 1.984(4) Å]. The distances along the near-linear N1-C7-N2 portion of the anion are N1–C7 1.303(3) and C7–N2 1.157(3) Å, suggesting that the anion is best considered as $[Ph\text{-}N\cdots C\equiv\!\!=N]^-$. The eight-membered ring itself is slightly chair-shaped [internal angles: 106.4(2) at Li, 111.3(2) at N1, 175.7(2) at C7, and 142.8(2)° at N2; Li and Lia are 0.311 Å above and below the mean plane defined by N1-C7-N2].

Each Li is also coordinated to two HMPA molecules [Li–O 1.958(4) Å, Lib–O 1.973(4) Å] which in turn bridge to a Li atom in a neighboring $(LiNCN)_2$ ring. This leads to the formation of polymeric strands (Fig. 2) consisting of alternating and orthogonal eight-membered $(LiNCN)_2$ and four-membered $(LiO)_2$ rings.

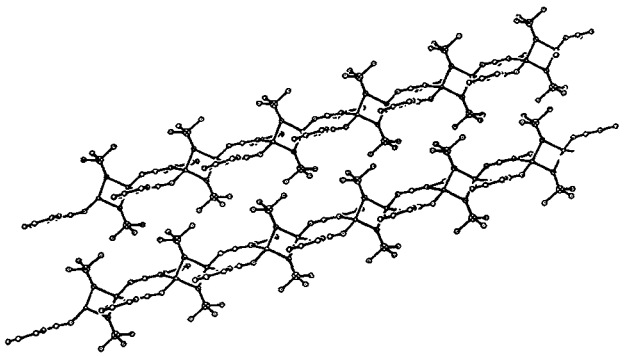
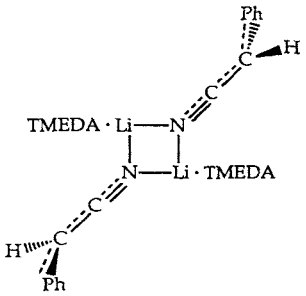
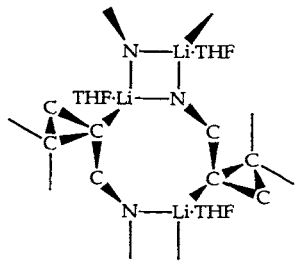


Fig. 2. Two polymeric strands of **1** showing alternating and orthogonal eight- and four-membered rings.

The structure of **1** is the first for a lithium cyanamide and as such it is unique, although certain of its features have analogies. For example, eight-membered rings of type $(LiXYZ)_2$ are well known in dimeric systems such as the lithium thiobenzoate $[PhC(=O)SLi \cdot TMEDA]_2$ with a $(LiOCS)_2$ ring[5] and the lithiosulfones $[PhSO_2CH(R)Li \cdot TMEDA]_2$ (R = H,[6] R = Ph[7, 8]) with $(LiOSO)_2$ rings. However, in comparison with the near-linear NCN^- unit in **1**, in all these structures an acute angle is found at atom Y. More akin to cyanamides, lithiated nitriles might be expected to contain eight-membered $(LiCCN)_2$ rings. MNDO calculations predict such a feature for uncomplexed $(LiCH_2CN)_2$.[9] However, on complexation a ketenimine structure $(H_2C\cdots C\equiv\!\!=NLi \cdot OH_2)_2$ with a four-membered $(NLi)_2$ ring is favored; such was indeed found for the first structurally characterized lithionitrile $[PhC(H)\cdots C\equiv\!\!=NLi \cdot TMEDA]_2$ (**C**).[8, 10] An example of the eight-membered $(LiCCN)_2$ unit is found in the structure of the 1-cyano-2,2-dimethylcyclopropyllithium complex (**D**).[8, 11] Here, the anionic α-C atom of the cyclopropyl unit is coordinated to the Li center so that an eight-membered $(LiCCN)_2$ ring results. The N atoms of each such ring bridge to the lithium atoms of neighboring eight-membered rings, resulting in alternating eight- and four-membered rings sharing a common LiN edge. In contrast, in **1**, the alternating rings share merely a common Li atom.

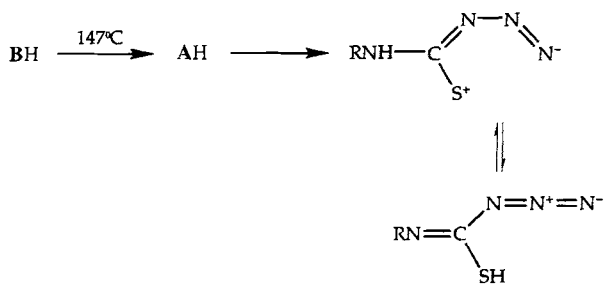


C



D

It has not yet been possible to explain the rather dramatic extrusion reactions that occur when thiatriazoles **AH** are treated with HMPA and lithium bases. An earlier report[3] noted that a mercaptotetrazole **BH** (R = Ph) degraded violently at its melting point (147 °C), evolving N_2 and forming sulfur and unidentified organic product(s). It was suggested that isomerization to the thiatriazole **AH** occurs first, followed by bond cleavage and an "explosive internal oxidition–reduction" between the thiol and azido groups (Scheme 1).



Scheme 1.

Our results here imply that the unidentified organic product of the earlier study was PhNHC≡N. However, a striking difference between the two studies is that all the reactions we describe occur at or below room temperature. Furthermore, it is clear that the metal cation and the added ligand play crucial roles. The different reactions of **AH** and HMPA with lithium (extrusion) and with barium (rearrangement) reagents have been noted; however, **AH**, $LiNH_2$, and the ligand PMDETA $[(Me_2NCH_2CH_2)_2NMe]$ react to give a rearrangement product containing $\mathbf{B}^-$. In addition, some of the reactions of **AH** and HMPA with lithium bases (e.g., with $LiNH_2$, *n*BuLi) proceed through numerous color changes, but others (e.g., with MeOLi, iPr_2NLi) do not. Further experiments are planned in the hope of elucidating the mechanisms of these unusual reactions.

Experimental Procedure

Typical syntheses of **1**: 1) With *n*BuLi. Solid **AH** (R = Ph; 0.89 g, 5 mmol) was dissolved under nitrogen in a mixture of HMPA (0.89 g, 5 mmol) and toluene (10 mL). The solution was cooled to −78 °C in an acetone/dry ice bath, and

*n*BuLi solution (5 mmol; in hexane) added. On warming to room temperature the original yellow solution changed color from green to reddish-brown, and gas evolution was observed. After the mixture had been stirred at room temperature for 30 min the resulting clear yellow solution was refrigerated overnight. This afforded very pale yellow crystals of **1** [first batch yield, 0.76 g, 50%; m.p. 132–135 C; correct analysis for $C_{13}H_{23}LiN_5OP$; ^1H NMR (CD_3CN, 250 MHz, 25 C): δ = 7.03 (m, 2H), 6.78 (m, 2H), 6.53 (m, 1H), 2.58 (d, 18H, HMPA)]. – 2) With $LiNH_2$. To a chilled solution of **AH** and HMPA in toluene [as in 1)] was added solid $LiNH_2$ (0.12 g, 5 mmol). On warming to room temperature with stirring the yellow solution became first green and then blue, with gradual dissolution of the white solid. Stirring the blue solution at room temperature for a further 45 min gave, after a green color, a yellow solution. Storage at 25 C over 2 days afforded yellow crystals of **1** (first batch yield, 0.30 g, 20%).

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[4] X-ray crystal data for $(C_6H_5NCNLi \cdot HMPA)_n$ (**1**): $C_{13}H_{23}N_5OPLi$, M = 303.27, triclinic, space group $P\bar{1}$, a = 7.3531(12), b = 10.6051(15), c = 11.462(3) Å, α = 82.210(12), β = 79.700(12), γ = 72.610(9)°, V = 836.0(3) Å^3, Z = 2, ϱ_{calcd} = 1.205 Mg m^{-3}, $F(000)$ = 324, $\lambda(Mo_{K\alpha})$ = 0.71073 Å, $\mu(Mo_{K\alpha})$ = 0.169 mm^{-1}, T = 193.0(20) K. Data were collected on a Stoe-Siemens diffractometer in the range $8° \leq 2\theta \leq 52°$, 2625 unique reflections measured. The structure was solved by direct methods and refined by full-matrix least-squares techniques (SHELX 92, G. M. Sheldrick, Universität Göttingen; all non-hydrogen atoms were refined anisotropically and hydrogen atoms were included in calculated positions) to R_1 = 0.0414, wR_2 = 0.0905, 2025 observed reflections, [$F > 4\sigma(F)$]. Further details of the crystal structure investigation are available on request from the Director of the Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge, CB2 1EZ (UK), on quoting the full journal citation.
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Synthesis and Reactivity of α,α-Dichloroglycyl Peptides**

By *Stefan Jaroch, Thomas Schwarz, Wolfgang Steglich,** and *Peter Zistler*

Dedicated to Professor Heinrich Nöth on the occasion of his 65th birthday

We recently introduced a new method for the synthesis of α-chloroglycyl peptides which makes it possible to prepare interesting peptide modifications.[1, 2] We now describe for the first time an approach to peptide derivatives that contain the α,α-dichloroglycine residue.

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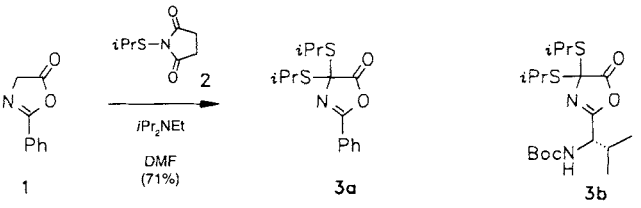
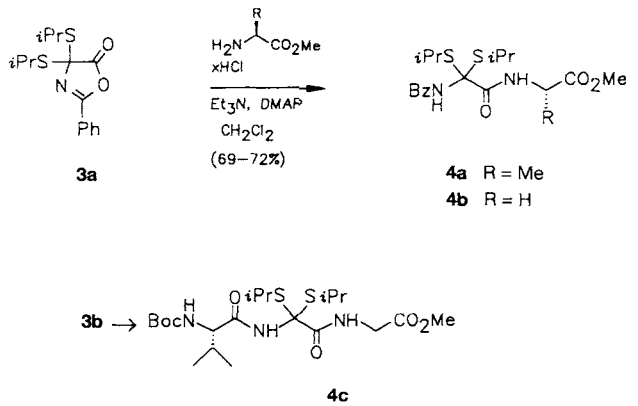
The synthesis of these peptide derivatives begins with 2-phenyl-5(4*H*)-oxazolone (**1**),[3] which reacts readily with *N*-sulfenylsuccinimides such as **2**[4] to give 4,4-di(isopropylthio)oxazolones **3**.[5] If this reaction is conducted with the azlactone of Boc-Val-Gly-OH,[6] the doubly sulfurated peptide azlactone **3b**[5] is obtained in 37% yield. The oxazolones **3** can be stored at approximately −20 °C for several days without decomposition. We found that the five-membered ring of 4,4-disubstituted oxazolones **3** opens to give *N*-acyl peptides **4** containing an α,α-di(isopropylthio)glycine residue (see Table 1) when amino acid esters are added in the presence of catalytic quantities of 4-dimethylaminopyridine (DMAP). Reaction of a peptide azlactone such as **3b** provides peptide derivatives of type **4c**, in which the α,α-di(isopropylthio)glycine residue is not located terminally but within the peptide chain. These compounds are generally obtained as stable solids that can be purified by chromatography or recrystallization.





In analogy to the mono(alkylthio)glycine derivatives,[1, 2] when **4** is treated with sulfuryl chloride the alkylthio residues are readily exchanged for chlorine substituents. In this way