

An *N*-lithio-indole from the reaction of  $\text{LiCH}(\text{TMS})_2$  and  $\text{PhNC}$ Manuel A. Fernandes,<sup>a</sup> Michael F. Lappert,<sup>b</sup> Marcus Layh\*<sup>a</sup> and Bernard Omondia<sup>a</sup> Molecular Science Institute, School of Chemistry, University of the Witwatersrand, Private Bag 3, Wits, 2050 Johannesburg, South Africa. E-mail: marcus@aurum.chem.wits.ac.za; Fax: +27 11 7176749; Tel: +27 11 7176744<sup>b</sup> The Chemistry Laboratory, University of Sussex, Brighton, UK BN1 9QJ. E-mail: M.F.Lappert@sussex.ac.uk; Tel: +44 1273 678316

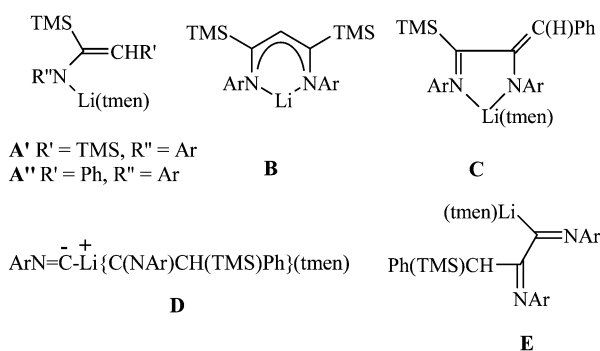
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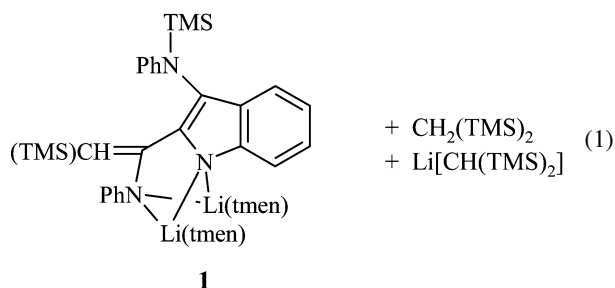
The reaction of  $\text{LiCH}(\text{TMS})_2$  with phenyl isocyanide  $\text{PhNC}$  has unexpectedly led to the *N*-lithio-indole derivative **1**, that has been fully characterised including its X-ray crystal structure determination.

Reactions between a lithium alkyl and an organic isocyanide have been investigated in considerable detail, especially by Walborsky and co-workers, who have used these for the synthesis of aldehydes, ketones, hydroxy-ketones, substituted carboxylic acids and various heterocycles.<sup>1</sup>

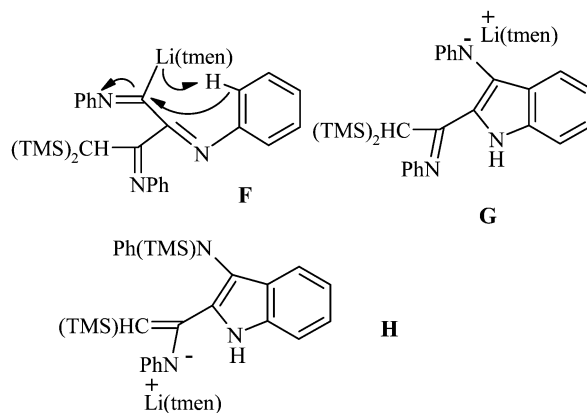
Recently we described the synthesis of the lithium-1-azaallyl **A'** and **A''**, the lithium  $\beta$ -diketiminate **B** and the 1-azabuta-1,3-dienyl-3-amide **C**, from the reaction of  $\text{Li}[\text{CH}(\text{TMS})\text{R}']$  and the bulky  $\alpha$ -H-free isocyanide  $\text{ArNC}$  ( $\text{R}' = \text{TMS}$  or  $\text{Ph}$ ,  $\text{Ar} = \text{C}_6\text{H}_3\text{Me}_2$ -2,6).<sup>2</sup> The compounds **A'** and **A''** were intermediates to **B** and **C**, respectively. The conversion of **A'**  $\rightarrow$  **B** was exceedingly slow; whereas the less bulky **A'** rapidly reacted with  $\text{ArNC}$  yielding **C**, via **D** and **E** as intermediates.



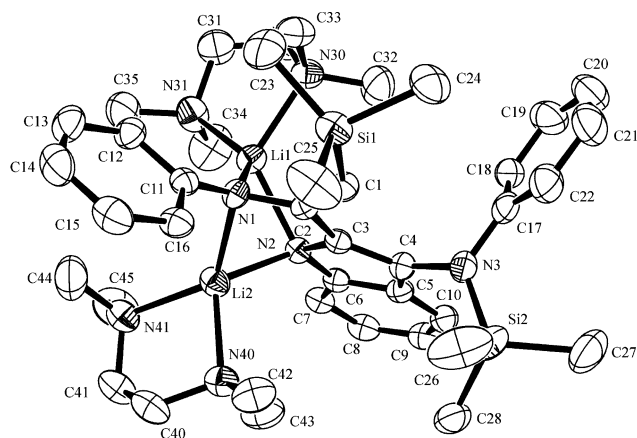
We now report that using the less bulky  $\text{PhNC}$  and  $\text{LiCH}(\text{TMS})_2$  in the presence of *tmen* [1,2-bis(dimethylamino)ethane] the product was the *N*-lithio-indole **1** [eqn. (1)]. The reaction was sensitive to conditions employed. Optimally, it was carried out in a 1:1:1 stoichiometry, the reagents were mixed at  $-90^\circ\text{C}$  in pentane and the mixture slowly brought to ambient temperature, the yield being 64% based on  $\text{PhNC}$ , which was not improved by using the 2:3:2 stoichiometry. When the reaction was carried out in diethyl ether, compound **1** was not isolated.



Consistent with our earlier studies on the  $\text{LiCH}(\text{TMS})_2/2,6\text{-Me}_2\text{C}_6\text{H}_3\text{NC}$  system,<sup>2</sup> we suggest that the reaction of eqn. (1) implicates an intermediate similar to **E** but with  $\text{Ar} = \text{Ph}$ . This, being less hindered than **E**, undergoes a final  $\text{PhNC}$  (likewise less sterically hindered than  $\text{ArNC}$ ) insertion giving **F**. The latter, by electrocyclic rearrangement followed by prototropy is believed to yield **G**, which by 1,5-TMS  $\text{C} \rightarrow \text{N}$  migration gives **H**, that is readily metallated by  $\text{LiCH}(\text{TMS})_2$  affording **1** +  $\text{CH}_2(\text{TMS})_2$ .



The yellow crystalline compound **1** gave satisfactory mass spectrometric and ambient temperature multinuclear NMR spectra,<sup>†</sup> as well as single crystal X-ray data.<sup>‡</sup> It crystallised in two polymorphic forms: one (*P* $\bar{1}$ , from hexane at  $-60^\circ\text{C}$ ) with one molecule in the asymmetric unit, the other (*P* $2_1/c$ , grown at ambient temperature from hexane) with two independent molecules (Fig. 1) in the unit cell and one molecule of solvent occupying an inversion centre. The molecular arrangement in both polymorphs is essentially identical.<sup>§</sup> The close to planar indole moiety<sup>§</sup> [largest deviation from plane C8 {C58} 0.023(2) {0.013(2)} Å] is approximately coplanar to the adjacent enamido group [torsion angle N1-C2-C3-N2 {N4-C52-C53-N5} 2.1(3) {-5.6(3)}°]. The two lithium atoms are above and below this plane and bind slightly asymmetrically (Fig. 1) to the two negatively charged nitrogen atoms N1 and N2. Both lithium atoms bind additionally to two nitrogen atoms of a neutral *tmen* ligand leading to a distorted tetrahedral coordination sphere around each lithium atom. The amino group attached to the indole ring is minimising steric strains by being orientated in such a way that the trimethylsilyl- and phenyl- substituent are above and below the ring plane [torsion angle Si2-N3-C4-C5 {Si4-N6-C54-C55} -81.6(3) {79.0(3)}°]. As a consequence the environments of the two lithium atoms are magnetically different (as also indicated by the observation of two signals in the  $^7\text{Li}\{-^1\text{H}\}$ -NMR spectrum in  $\text{C}_7\text{D}_8$ . The overall arrangement of **1** and the Li-N bond distances closely resemble those found in the dilithiated 1,4-diaza-1,3-dienes [ $(\text{Et}_2\text{OLi}\{\text{N}(p\text{-Tol})\text{C}(\text{CNMePh})\text{C}=\text{C}(\text{NMePh})\text{N}(p\text{-Tol})\})\text{Li}(\text{OEt}_2)_2$ ],<sup>3</sup> [(*thf*) $_2\text{Li}\{\text{N}(\text{R}')\text{C}(\text{Ph})=\text{C}(\text{Ph})\text{N}(\text{R}')\}\text{Li}(\text{thf})_2$ ],<sup>4</sup> and the *N,N'*-dilithium ethylenediamides [ $\text{Li}\{\text{N}(\text{Bu}^t)\text{CH}_2\text{CH}_2\text{N}$ -



**Fig. 1** Molecular structure of **1** (polymorph II, one independent molecule only): Li1–N1 2.036(5), Li1–N2 2.102(5), Li1–N30 2.090(5), Li1–N31 2.187(5), Li2–N1 2.074(5), Li2–N2 2.027(5), Li2–N40 2.101(5), Li2–N41 2.149(5), N1–C2 1.392(3), N2–C3 1.393(3), C1–C2 1.363(3), C2–C3 1.509(3).

(Bu<sup>t</sup>)<sub>2</sub>Li<sub>2</sub>,<sup>5</sup> [Li{N(Ph)CH<sub>2</sub>CH<sub>2</sub>N(Ph)}Li(hmpa)]<sub>3</sub>.<sup>6</sup> The two prior examples of simple lithio-indoles, namely [(Li{μ-*N*-indolyL})<sub>2</sub>] [L = tmen<sup>7</sup> or (thf)<sub>2</sub><sup>8</sup>], are binuclear.

Variable temperature NMR spectral studies of **1** in C<sub>7</sub>D<sub>8</sub> at ambient temperature indicate that the solid-state structure is retained in solution.† The <sup>1</sup>H-NMR spectrum showed a characteristic signal for the CH(TMS) group at δ 5.67 and 3 broad signals for the coordinated tmen ligands, the latter indicating that tmen was participating in a dynamic exchange process. The two signals in the <sup>7</sup>Li-{<sup>1</sup>H}-NMR spectrum observed at ca. 300 K converged at 333 K into a singlet, indicating a rapid exchange between the two lithium atoms. Likewise in the <sup>1</sup>H-NMR spectrum at 333 K the tmen protons were observed as a single broad feature. When the sample was cooled, a second exchange process was observed. Thus, at 233 K the <sup>7</sup>Li-{<sup>1</sup>H}-NMR signal was a broad peak, which at 193 K split into four separate signals, while the tmen protons were also found as four equal intensity signals at 213 K. As other signals in the <sup>1</sup>H-NMR spectrum were essentially unaffected by changes in temperature, we attribute the above fluxional effects to conformational changes in the Li(tmen) metallacycles.

In conclusion, we have discovered a novel synthesis of an indole derivative based on PhNC. The reaction between Bu<sup>t</sup>NC and an acylarene in presence of BF<sub>3</sub>(OEt<sub>2</sub>) has previously been shown to give α-*t*-butylamidindoles in low yield.<sup>9</sup>

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## Notes and references

† *Synthesis and characterisation of 1*: A solution of PhNC (0.38 g, 3.67 mmol) pentane (5 cm<sup>3</sup>) was added to a solution of LiCHR<sub>2</sub> (0.61 g, 3.67 mmol) in pentane (30 cm<sup>3</sup>) and tmen (0.55 cm<sup>3</sup>, 3.67 mmol) at –90 °C. The reaction mixture was slowly warmed to RT, stirred for 12 h yielding a red

solution with a yellow precipitate. The solvent was removed *in vacuo* and the residue extracted with pentane. The yellow residue that remained after filtration was found to be pure **1** (0.56 g, 64% based on PhNC) mp 160 °C (decomp.). Mass spectrum [*m/z* (%): 469 (7 [HLL]<sup>+</sup>), 454 (12 [HLL – Me]<sup>+</sup>), 377 (12 [HLL – Ph]<sup>+</sup>); <sup>1</sup>H-NMR (C<sub>6</sub>D<sub>6</sub>, 300 K): δ 0.22 (s, 9 H, CSiMe<sub>3</sub>), 0.57 (s, 9 H, NSiMe<sub>3</sub>), 1.44, 1.45, 1.60, 1.69 (s, 32 H, tmen), 5.67 (s, 1 H, CHSiMe<sub>3</sub>), 6.71 (t, 1 H, *p*-Ph, <sup>3</sup>*J* = 7.15), 6.88 (t, 1 H, *p*-Ph, <sup>3</sup>*J* = 7.25), 7.09–7.31 (m, 9 H, Ph), 7.48 (d, 2 H, Ph, *J* = 7.62), 7.95 (m, 1 H, H-10 of indole ring, *c.f.* Fig. 1); <sup>13</sup>C-NMR (C<sub>6</sub>D<sub>6</sub>, 300 K): δ 2.3 (SiMe<sub>3</sub>), 3.1 (SiMe<sub>3</sub>), 45.6 (NMe), 56.5 (NCH<sub>2</sub>), 86.5 (CH), 115.6 115.8, 117.3, 118.5, 119.1, 120.3, 122.5, 124.6, 127.2, 129.1 (CH, aromatic C), 135.1, 144.2, 146.2, 151.6, 157.7, 159.3 (quart. C, signal at 120.3 overlaps with CH); <sup>7</sup>Li-{<sup>1</sup>H}-NMR (C<sub>6</sub>D<sub>6</sub>, 300 K): δ 0.87, 1.05; <sup>29</sup>Si-{<sup>1</sup>H}-NMR (C<sub>6</sub>D<sub>6</sub>, 300 K): δ –14.32 (s, CSiMe<sub>3</sub>), 4.86 (NSiMe<sub>3</sub>).

‡ *Crystallographic data for 1 (polymorph I/II)*: C<sub>40</sub>H<sub>65</sub>Li<sub>2</sub>N<sub>7</sub>Si<sub>2</sub>/[C<sub>40</sub>H<sub>65</sub>Li<sub>2</sub>N<sub>7</sub>Si<sub>2</sub>(C<sub>3</sub>H<sub>7</sub>)<sub>2</sub>], *M* = 714.05/1471.19, triclinic/monoclinic, space group *P*1̄ (No. 2)/*P*2<sub>1</sub>/*c* (No. 14), *a* = 12.453(2)/34.405(5), *b* = 12.473(2)/13.594(2), *c* = 16.775(2)/19.865(3) Å, α = 88.096(3)/90°, β = 80.581(3)/92.106(2), γ = 61.552(2)/90°, *U* = 2257.1(5)/9285(3) Å<sup>3</sup>, *Z* = 2/4, *D*<sub>c</sub> = 1.051/1.052 Mg/m<sup>3</sup>, *F*(000) = 776/3204, λ (Mo-Kα) = 0.71073 Å, μ = 0.112/0.110 mm<sup>–1</sup>. Data were collected at 173(2) K on a Bruker SMART 1K CCD area detector diffractometer<sup>10</sup> using ω scans of width 0.3° for the range of 1.23 < θ < 25.50° (I) or 1.18 < θ < 25.00° (II). The structures were solved by direct methods using SHELXTL<sup>11</sup> and refined with full matrix least-squares on all *F*<sup>2</sup> (SHELXTL). All non-hydrogen atoms were refined anisotropically, and hydrogen atoms were positioned geometrically and allowed to ride on their respective parent atoms. Atoms C40, C41, N41, C44 and C45 on one of the tmen groups of polymorph I were found to be disordered and were modelled by a partial occupancy model over two sites as C40, C41, N41, C44 and C45 and C40A, C41A, N41A, C44A and C45A, with site occupancy factors of 0.545(6) and 0.455(6), respectively. Appropriate restraints were applied to bond distances and angles involving the disordered atoms. In polymorph II one molecule of hexane was found on an inversion centre. Final residuals for 8322/16216 independent reflections were *R*<sub>1</sub> = 0.125/0.095, *wR*<sub>2</sub> = 0.264/0.149 and for the 5332/10839 with *I* > 2σ(*I*), *R*<sub>1</sub> = 0.084/0.056, *wR*<sub>2</sub> = 0.236/0.128. CCDC 199140 and 199141. See <http://www.rsc.org/suppdata/cc/b2/b212103d/> for crystallographic files in CIF or other electronic format.

§ Values in bracket refer to the second independent molecule.

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