

## Butyllithium-induced Cyclotrimerisation Reactions of Organic Nitriles: Solvent Dependency, Crystal and Solution Structures of Lithio Triazine Intermediates and an Unexpected Rearrangement of Dihydrotriazino Anions

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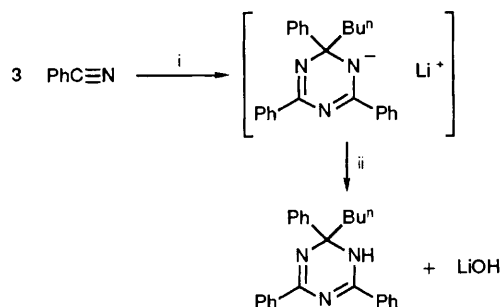
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Sequential addition of Bu<sup>n</sup>C≡N and PhC≡N (2 equiv.) to Bu<sup>n</sup>Li in the presence of tetrahydrofuran (THF) produces an isolable lithio 1,4-dihydrotriazine tris(THF) solvate, characterised by both NMR spectroscopic and X-ray crystallographic methods, which converts to a 1,2-dihydro arrangement on methanolysis.

As long ago as 1941, *n*-butyllithium was reported to cyclotrimerise benzonitrile to give a dihydrotriazine product (Scheme 1).<sup>1</sup> Surprisingly this observation inspired no further research until some forty years later when a more quantitative analysis showed that yields were low (29%, maximum) and that the reaction gave other products besides a dihydrotriazine.<sup>2</sup> Both studies adopted a similar approach in that the triazines were obtained following hydrolysis of the original reaction mixtures and subsequent work-up procedures. In contrast, by deliberately avoiding hydrolysis, we have managed to isolate and characterise an intermediate, a lithiotriazine complex, from a related cyclotrimerisation process. From this direct approach, we have learned that the heteroatomic (CN)<sub>3</sub> ring 'isomerises' from a 1,4-dihydro type to a 1,2-dihydro type on protonating the reactive lithio intermediate—information that would have remained concealed if, as is the norm, the reaction was performed *in situ*, then quenched. Our studies have also revealed that the cyclotrimerisation reaction is solvent dependent.

A 3 : 1 molar mixture of benzonitrile and *n*-butyllithium in hexane solution gave a red oil which redissolved on dropwise addition of tetrahydrofuran (THF). On refrigeration, this

solution deposited colourless needle crystals which proved not to be a lithiodihydrotriazine, as expected from the earlier work,<sup>1,2</sup> but the known, fully unsaturated 2,4,6-triphenyl-1,3,5-triazine, **1**. Previously **1** was identified as a minor side-product (yield, 2%) from the hydrolysed reaction mix-

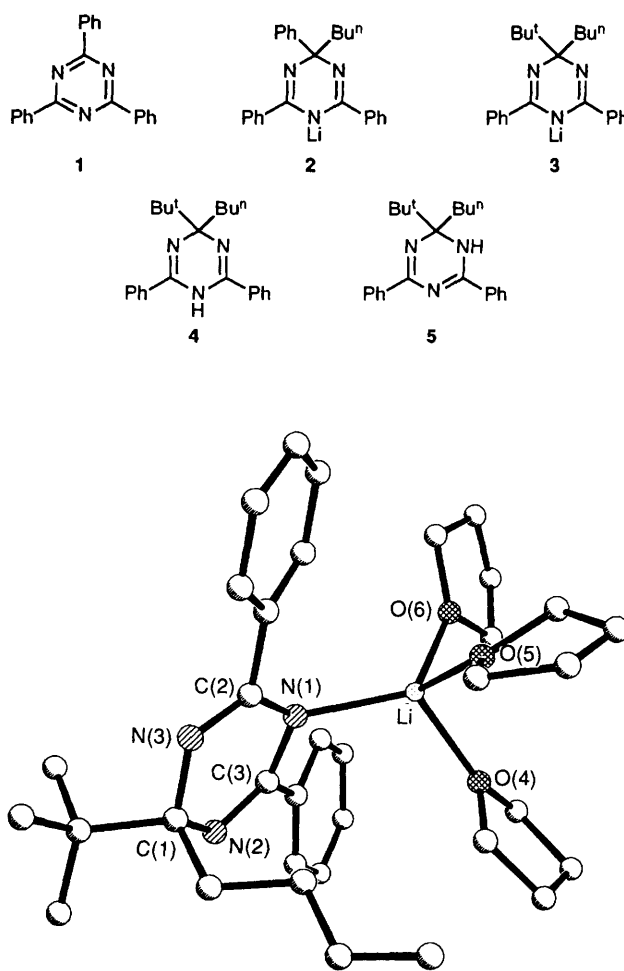


**Scheme 1** Reagents and conditions: i, Bu<sup>n</sup>Li (1 equiv.), benzene solvent, dry nitrogen atmosphere; ii, H<sub>2</sub>O. The 1,2-dihydrotriazine is shown but the data at the time could not distinguish between 1,2- and 1,4-dihydro structures.

ture in benzene solution.<sup>2</sup> However, by our improved method, significant yields in excess of 50% are possible directly from 'active' organolithium-containing media.

On further examination, a marked solvent effect was detected. This operates when hexane is replaced by THF in the butyllithium solution prior to adding benzonitrile, resulting in the formation of the crystalline THF solvate of the lithio 1,4-dihydrotriazine **2** in high yield.<sup>†</sup> Its 1,4-dihydro identity is discernible from a <sup>1</sup>H NMR spectrum (*vide infra*). The Li<sup>+</sup> cation is complexed by the oxygen atoms of three THF molecules. This feature would appear to be an important factor in the solvent dependency of the cyclotrimerisation process, for whereas THF molecules can coordinatively saturate the Li<sup>+</sup> centre when it is fixed to the (CN)<sub>3</sub> ring, non-complexing hexane molecules have no means of doing so. But there must be another factor involved as the reaction that produces the closely related intermediate **3**·(THF)<sub>3</sub> does not exhibit this solvent dependency. In this case, butyllithium was treated with a different nitrile (Bu<sup>t</sup>C≡N, trimethylacetone nitrile) in hexane solution to give the ketimide [Bu<sup>n</sup>(Bu<sup>t</sup>C=NLi)]<sub>n</sub>. Treating this, in turn, with two equiv. of benzonitrile afforded an oil, which redissolved on addition of warm THF. Crystalline **3**·(THF)<sub>3</sub> was obtained on cooling the solution.<sup>†</sup> Given that the solvent effect is therefore substituent dependent (*i.e.* replacing a Ph group by a Bu<sup>t</sup> group renders it inoperative), it must, in part, be influenced by the stability of product **1**. The major factor in this regard is resonance delocalisation which, because of the three Ph substituents, is feasible over the entire framework of the molecule. Previously reported reactions of nitriles with lithium amides<sup>3</sup> support this view as fully-unsaturated triazines were also obtained with Ph and *para* Me(C<sub>6</sub>H<sub>4</sub>) substituents.

An X-ray crystallographic study of **3**·(THF)<sub>3</sub><sup>‡</sup> reveals a structure consistent with the solution structure implied by the NMR spectroscopic data on **2**·(THF)<sub>3</sub> and **3**·(THF)<sub>3</sub>. The monomeric arrangement (Fig. 1) has the pseudo-tetrahedral lithium centre tris(coordinated) by THF molecules and terminally attached to the (CN)<sub>3</sub> ring at N(1). Dimensions



**Fig. 1** Molecular structure of **3**·(THF)<sub>3</sub>, without hydrogen atoms, and with important atoms labelled. Key dimensions: Li–N(1) 2.059(8), Li–O(4) 2.025(10), Li–O(5) 1.958(13), Li–O(6) 2.091(10), N(1)–C(2) 1.386(4), N(1)–C(3) 1.371(4), N(2)–C(1) 1.475(4), N(2)–C(3) 1.291(4), N(3)–C(1) 1.457(5), N(3)–C(2) 1.287(5) Å; O(4)–Li–N(1) 115.0(6), O(5)–Li–N(1) 116.9(5), O(6)–Li–N(1) 122.4(5), C(2)–N(1)–C(3) 111.6(3), C(1)–N(2)–C(3) 117.2(3), C(1)–N(3)–C(2) 118.2(3), N(2)–C(1)–N(3) 114.5(3), N(1)–C(2)–N(3) 127.6(3), N(1)–C(3)–N(2) 128.4(3)°.

<sup>†</sup> The air- and moisture-sensitive nature of organolithium compounds necessitated the use of protective argon blankets during all preparations. Satisfactory analyses (C, H, Li, N) were obtained for all products. For **2**·(THF)<sub>3</sub>, m.p., 102 °C; yield, 79%. For **3**·(THF)<sub>3</sub>, m.p., 82 °C; yield 88%. For **5**, m.p., 108 °C; yield 41%.

<sup>1</sup>H NMR spectra (400 MHz), 25 °C. For **2**·(THF)<sub>3</sub>, [<sup>2</sup>H<sub>8</sub>]THF solution, δ 0.82 (t, 3H, Me), 1.27 (m, 2H, γ-CH<sub>2</sub>), 1.39 (m, 2H, β-CH<sub>2</sub>), 1.76 (t, 12H, CH<sub>2</sub>-THF), 1.88 (m, 2H, α-CH<sub>2</sub>), 3.62 (m, 12H, CH<sub>2</sub>O-THF), 6.95 (t, 1H, *p*-Ph'), 7.09 (m, 2H, *m*-Ph'), 7.28 (m, 6H, *m*-, *p*-Ph), 7.84 (d, 2H, *o*-Ph'), 8.27 (d, 4H, *o*-Ph).

For **3**·(THF)<sub>3</sub>, [<sup>2</sup>H<sub>8</sub>]THF solution, δ 0.81 (t, 3H, Me), 1.02 (s, 9H, Bu<sup>t</sup>), 1.23 (m, 2H, β-CH<sub>2</sub>), 1.32 (m, 2H, γ-CH<sub>2</sub>), 1.61 (m, 2H, α-CH<sub>2</sub>), 1.76 (m, 12H, CH<sub>2</sub>-THF), 3.62 (m, 12H, CH<sub>2</sub>O-THF), 7.23 (m, 6H, *m*-, *p*-Ph), 8.05 (d, 4H, *o*-Ph).

For **5**·(HOME), [<sup>2</sup>H<sub>6</sub>]benzene solution, δ 0.77 (t, 3H, Me), 0.93 (s, 9H, Bu<sup>t</sup>), 1.24 (m, 2H, γ-CH<sub>2</sub>), 1.38 (s, 3H, CH<sub>3</sub>OH), 1.54 (m, 2H, β-CH<sub>2</sub>), 1.97 (m, 1H, α-CH-Bu), 2.13 (m, 1H, α-CH'-Bu), 4.88 (s, 1H, NH), 7.13 (m, 2H, *m*-Ph), 7.20 (m, 1H, *p*-Ph), 7.27 (m, 1H, *p*-Ph'), 7.34 (m, 2H, *m*-Ph'), 7.82 (d, 2H, *o*-Ph'), 8.83 (d, 2H, *o*-Ph) (OH not found) relative to SiMe<sub>4</sub>.

<sup>‡</sup> Crystal data for **3**·(THF)<sub>3</sub>: C<sub>35</sub>H<sub>52</sub>LiN<sub>3</sub>O<sub>3</sub>, *M* = 569.7, monoclinic, space group *P*2<sub>1</sub>/*n*, *a* = 10.917(2), *b* = 15.893(3), *c* = 20.227(4) Å, β = 100.30(2)°, *U* = 3452.9(11) Å<sup>3</sup>, *Z* = 4, *D*<sub>c</sub> = 1.096 g cm<sup>-3</sup>. 5736 independent reflections were measured on a Siemens AED2 diffractometer using graphite monochromated Cu-Kα radiation (λ = 1.54184 Å), μ(Cu-Kα) = 0.54 mm<sup>-1</sup>, with ω-θ scans and on-line profile fitting.<sup>4</sup> *F*(000) = 1240. Structure solution was by direct methods, refinement by full-matrix least-squares on *F*<sup>2</sup> for all independent reflections,<sup>5</sup> with some restraints on disordered THF ligands. *R*<sup>1</sup> = {Σ[w(*F*<sub>o</sub><sup>2</sup> - *F*<sub>c</sub><sup>2</sup>)]/Σ[w(*F*<sub>o</sub><sup>2</sup>)]}<sup>1/2</sup> = 0.3356 for all data, conventional *R* [on *F* values for 3508 reflections with *I* > 2σ(*I*)] = 0.0917. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

within the triazine ring reflect its 1,4-dihydro nature: the formal double bonds [C(2)–N(3), C(3)–N(2)] are shortest, the (anionic) nitrogen–carbon bonds [C(2)–N(1), C(3)–N(1)] are intermediate, while those involving the saturated carbon atom [C(1)–N(2), C(1)–N(3)] are longest (mean lengths: 1.289, 1.378 and 1.466 Å, respectively). The C<sub>3</sub>N<sub>3</sub> ring is only approximately planar: C(1) lies 0.219 Å out of the mean plane of the other five atoms (rms deviation, 0.029 Å). Other key dimensions are given in the legend to Fig. 1.

With the Li<sup>+</sup> centre so heavily solvated, preference for the 1,4- over the 1,2-dihydro structure is undoubtedly sterically borne. Interestingly, however, methanolysis of **3**·(THF)<sub>3</sub> does not produce the 1,4-dihydrotriazine **4**, but the 1,2-dihydro analogue **5**, isolated as the monomethanolate, **5**·(HOME).<sup>†</sup> Proof of its 1,2-dihydro form comes from the two distinct Ph groups and the diastereotopic protons of the α-CH<sub>2</sub> of the Bu<sup>n</sup> group (indicating a chiral centre) observed in the <sup>1</sup>H NMR spectrum. *Ab initio* MO calculations are in hand to determine the mechanism of this Li<sup>+</sup>-H<sup>+</sup> exchange process.

Many syntheses involving organolithium reagents are evaluated indirectly by substituting H<sup>+</sup> for Li<sup>+</sup> in the final step of a reaction sequence, but the work highlighted here shows that potentially valuable chemical information can be overlooked

by adopting this approach and assuming that the anion  $R^-$  in the isolated, studied product  $R-H^+$  corresponds to  $R^-$  in the *in situ* species  $R-Li^+$ .

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