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REACTIONS OF BIS(SILYL-SUBSTITUTED) METHYLLITHIUM WITH α-HYDROGEN-FREE NITRILES INTO 1,3,5-TRIAZINES

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Abstract –Bis(silyl-substituted) methyllithium has been found to catalyze a conversion of α-hydrogen-free nitriles directly to yield 2,4,6-trisubsituted *s*-triazines. The generally high yields and relatively mild reaction conditions of this procedure suggest an alternative to other aromatic nitrile cyclotrimerization reactions. Silicotropic rearrangements from C to N or N to N and an unusual elimination of $LiCR_2R'$ (R=$SiMe_3$, R'=$SiMe_2NMe_2$) were observed.

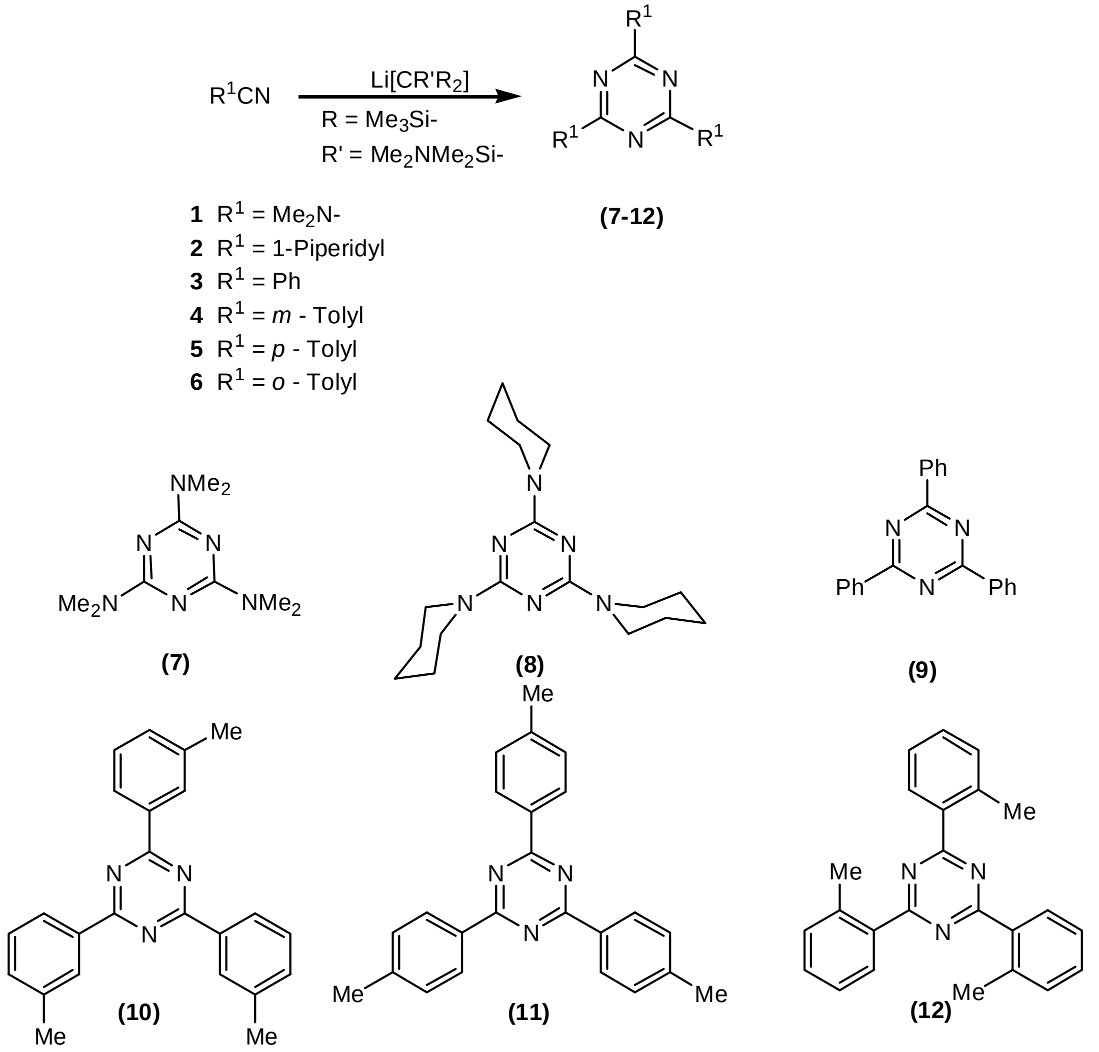
INTRODUCTION

A series of studies on the reactions of $Li[CH_{3-n}R_n]$ (n=1, 2, or 3 and R=$SiMe_3$) with α-hydrogen-free nitriles showed that different kinds of addition products such as 1-azaallyl-, β-diketiminato- or 1,3-diazaallyllithium compounds could be yielded.[1-5] Normally, as a troublesome side reaction, the *N*-lithioimine could add further to molecules of nitrile, leading to aggregate or cyclic products such as pyrimidines and triazines.[6-9] However, the triazines were often in limited amount; the mechanism of their formation was sometimes obscure.[10-11]

In our early investigation it was shown that addition reactions of bis(trimethylsilyl)methyllithium reagent $Li[CHR_2]$ (R = $SiMe_3$) or 1-azaallyllithium $[\overline{\text{LiN(R)C(Bu-}t\text{)CHR}}]_2$ with cyanoamines R''CN (R'' = Me_2N, 1-piperidyl or *p*-pyridyl)[12] led to β-diketiminatolithium and uniformed or mixed 2,4,6-trisubsituted triazines. However, if other α-hydrogen- free nitriles *e.g.* PhCN or substituted PhCN were used instead of the cyanoamines the triazine products were not observed. Treatment of $LiCR_3(thf)_2$ (R=$SiMe_3$) with PhCN afforded the 1-azaallyl $[Li\{N(R)C(Ph)CR_2\}(thf)]$ other than β-diketiminate or triazine[13,14] It is our interesting to renovate the limit of this type reaction by using other lithium analogous such as dimethylaminodimethylsilyl-bis(trimethylsilyl)methyllithium $LiCR_2R'$ (R=$SiMe_3$, R'=$SiMe_2NMe_2$). We proved that the reaction routes involve silicotropic rearrangements from C to N or N to N and an unusual elimination reaction. The paper describes an improved procedure for the preparation of 1,3,5-*s*-triazine derivatives under mild reaction conditions in context of α-hydrogen-free nitriles and using $LiCR_2R'$ as a catalyst.

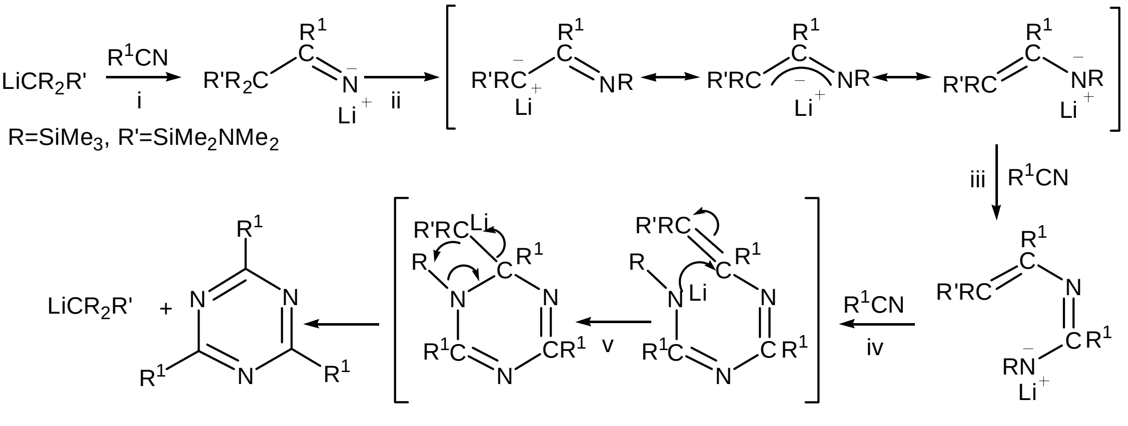
RESULTS AND DISCUSSION

The reaction of various α-hydrogen-free nitriles R^1CN (R^1 = Me_2N or 1-piperidyl) with $Li[CHR_2]$ (R=$SiMe_3$,) in hexane gave symmetrical 2,4,6-(tri)(dimethylamino)-*s*-triazine or 2,4,6-(tri)(1-piperidinyl)-*s*-triazine in good yield (>90%). However, the different interaction of $Li[CHR_2]$ with aromatic nitriles had been reported to give different kinds of addition products such as 1-azaallyl- and β-diketiminato-lithium compounds.[1-5] But if $LiCR_2R'$, the analogue of $Li[CHR_2]$, was been used instead of $Li[CHR_2]$, the 2,4,6-trisubsituted *s*-triazines (**7-12)** were also obtained (**Scheme 1**).



Scheme 1

In order to investigate the catalyst effect of the lithium reagent, the reaction of $LiCR_2R'$ with excessive α-hydrogen-free nitriles R^1CN (**1-6**) and *t*-BuCN was studied. High yields of triazine compounds (**7-11**) were obtained. Minor product (**12**) was formed and there were no triazine products produced from the reaction of $LiCR_2R'$ and *t*-BuCN. We supposed that the steric effect was the main reason. A proposed mechanism is given in **Scheme 2** as steps i-v: (i) C-C coupling, (ii) silyl migration, (iii) the first time of N-C coupling and silyl group migration, (iv) the second time of N-C coupling and silyl group migration, (v) the third time of N-C coupling and silyl migration finally an $LiCR_2R'$ elimination to give triazines.



(7-12)

Scheme 2 Schematic process of formation of triazine (**7-12**)

In conclusion, the reaction of organic lithium reagents with various sterically less-hindered α-hydrogen-free nitriles provides a simple and convenient one-pot process from the readily available materials to uniformed and mixed 2,4,6-trisubsituted *s*-triazines in the mild conditions. A new and simple direct synthetic method for s-triazines was supplied from the reaction catalyzed by lithium complex.

EXPERIMENTAL

All manipulations were carried out under argon, using standard Schlenk technique. Solvents (hexane, ether) were distilled from drying agents and degassed with argon prior to use. ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Bruker DKX300 apparatus. Elemental analyses were performed by Vario-III analyzer.

2,4,6-Tri(dimethylamino)-1,3,5-triazine (7).

Dimethyl cyanamide (0.50 mL, 6.00 mmol) was added by syringe to a stirred solution of $[(SiMe_3)_2CSiMe_2NMe_2]Li(TMEDA)$ (1.10 g, 2.89 mmol) in hexane (*ca.* 20 mL) at 0 °C. The mixture was warmed to rt, stirred for 12 h, concentrated and the residue was crystallized from hexane at –30 °C to give white crystalline pure complex (**7**) (0.38 g, 91%): mp 170-173 °C; ^{1}H NMR (300 MHz, C_6D_6): δ =3.09 (s, 18H, NMe_2); ^{13}C NMR (75 MHz, C_6D_6): δ 36.54 (s, NMe_2), 167.26 (s, *ipso*-C of ring). Anal. Calcd for $C_9H_{18}N_6$: C, 51.41; H, 8.63; N, 39.97. Found: C, 51.25; H, 8.75; N, 39.14.

2,4,6-Tri(1-piperidinyl)-1,3,5-triazine (8).

$[(SiMe_3)_2CSiMe_2NMe_2]Li(TMEDA)$ (0.12 g, 0.31 mmol) was added to a stirred solution of 1-piperidinecarbonnitrile (0.55 mL, 4.75 mmol) in hexane (*ca.* 15 mL) at the rt. After stirring for 6 h, the solvent was removed in *vacuo*. The residue was dissolved in ether (*ca.* 10 mL) and filtered. The filtrate was concentrated and stored at –30 °C to give colorless crystals (from ether) of compound (**8**) (0.47 g, 89%): mp 215-216 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 4.43 (s, 12H, NCH_2), 2.25 (m, 18H,CH_2); ^{13}C NMR (75 MHz, $CDCl_3$): δ=165.98 (*ipso*-C of triazine ring), 44.59(*o*-CH_2), 26.37, 25.64 (*m*-CH_2 and *p*-CH_2). Anal. Calcd for $C_{18}H_{30}N_6$: C, 65.42; H, 9.15; N, 25.43. Found: C, 65.40; H, 9.00; N, 25.17.

2,4,6-Tri(phenyl)-1,3,5-triazine (9).

$[(SiMe_3)_2CSiMe_2NMe_2]Li(TMEDA)$ (0.50 g, 1.31 mmol) was dissolved in hexane *(ca.* 20 mL). PhCN (1.07 g, 10.4 mmol) was injected into the solution at 0 °C and the solution changed into yellow immediately. The mixture was warmed to rt. After overnight reaction, it gave some white or light yellow precipitate. The solvent was removed in *vacuo*. The remained solid was dissolved in ether (*ca.* 10 mL) and filtered. The filtrate was concentrated and stored at –30 °C to give pure colorless crystalline (from ether) triphenyltriazine (**9**) (0.97 g, 91%): mp 234-235 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 8.86 (d, J=6.9 Hz, 6H, *o*-CH), 7.67 (m, 9H, *m*- and *p*-CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.63 (*ipso*-C of triazine ring), 137.23 (*ipso*-C of phenyl), 133.46 (*o*-CH), 129.93, 129.60 (*m*-CH and *p*-CH). Anal. Calcd for $C_{21}H_{15}N_3$: C, 81.55; H, 4.85; N 13.59. Found: C, 81.52; H, 4.83; N, 13.69.

2,4,6-Tri(*m*-tolyl)-1,3,5-triazine (10).

$[(SiMe_3)_2CSiMe_2NMe_2]Li(TMEDA)$ (0.23 g, 0.6 mmol) was dissolved in hexane (*ca.* 20 mL). *m*-Tolunitrile (0.70 g, 6.0 mmol) was injected into the solution at 0 °C. The mixture was warmed to rt. for further reaction. After overnight reaction, some light yellow precipitate were formed. The solvent was then removed in *vacuo*. The remaining solid was dissolved in ether (*ca.* 10 mL) and filtered. The filtrate was concentrated and stored at –30 °C to give light yellow product (from ether) (**10**) (0.69 g, 98%): mp 146-147 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 8.60 (s, 6H, phenyl), 7.49 (m, 6H, phenyl), 2.56 (s, 9H; *m*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.64 (*ipso*-C of triazine ring), 139.25, 137.23 (*ipso*-C of phenyl), 134.24, 130.37, 129.50, 127.19 (CH of phenyl), 22.57 (CH_3). Anal. Calcd for $C_{21}H_{21}N_3$: C, 82.05; H, 5.98; N 11.96. Found: C, 81.83; H, 6.19; N, 11.81.

2,4,6-Tri(*p*-tolyl)-1,3,5-triazine (11).

p-Tolunitrile (0.86 g, 7.31 mmol) was injected into the solution of $[(SiMe_3)_2CSiMe_2NMe_2]Li(TMEDA)$ (0.36 g, 0.94 mmol) in hexane (*ca.* 20 mL). Some light yellow precipitate were formed. The solvent was removed in *vacuo*. The remained solid was dissolved in ether (*ca.* 10 mL) and filtered. The filtrate was concentrated and stored at –30 °C to give pure light yellow product (from ether) (**11**) (0.82 g, 96%): mp 283-285 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55 (d, J=9.0 Hz, 6H; *o*-CH of phenyl), 7.25 (t, J=9.0 Hz, 6H; *m*-CH of pheny), 2.42 (s, 9H; *p*-CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.65 (*ipso*-C of triazine ring), 143.71, 139.30 (*ipso*-C of phenyl), 132.05, 129.84 (CH of phenyl), 21.85 (CH_3). Anal. Calcd for $C_{21}H_{21}N_3$: C, 82.05; H, 5.98; N 11.96. Found: C, 82.04; H, 6.02; N, 11.94.

2,4,6-Tri(*o*-tolyl)- 1,3,5-triazine (12).

$[(SiMe_3)_2CSiMe_2NMe_2]Li(TMEDA)$ (0.44 g, 1.15 mmol) was dissolved in hexane (ca. 20 mL). *o*-Tolunitrile (1.20 g, 10.24 mmol) was injected into the solution at 0 °C. The mixture was warmed to rt and reacted overnight. Some light yellow precipitate were formed. The solvent was then removed in *vacuo*. The remaining solid was dissolved in ether (*ca.* 10 mL) and filtered. The filtrate was concentrated and stored at –30 °C to give pure light yellow product (from ether) (**12**) (0.23 g, 19%): mp 110-111°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90-7.32 (m, 12H; phenyl), 2.61-2.45 (m, 9H; *o*-Me); ^{13}C NMR (75 MHz, $CDCl_3$): δ 175.50 (*ipso*-C of triazine ring), 142.90, 138.81 (*ipso*-C of phenyl), 133.59, 131.57,130.98,129.76,128.76 (CH of phenyl), 21.42 (CH_3). Anal. Calcd for $C_{21}H_{21}N_3$: C, 82.05; H, 5.98; N 11.96. Found: C, 81.95; H, 5.89; N, 12.05.

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