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## Preparation of Secondary Carbinamines via *N*-Boryl Imines Generated *in situ* from Nitriles and Borane–Tetrahydrofuran

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*N*-Boryl imines obtained from partial reduction of nitriles with borane–tetrahydrofuran have been alkylated with organolithium or Grignard reagents to afford secondary carbinamines in moderate to excellent yields.

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The usefulness of masked imine derivatives of ammonia in the preparation of primary amines<sup>1</sup> as well as  $\beta$ -lactams<sup>2</sup> has been recently demonstrated. *N*-Alkylidenearenesulphenamides were first used by Davis as a masked imine for the synthesis of secondary carbinamines.<sup>1a</sup> *N*-Sulphonylaldehyde imines were found to be useful precursors for the preparation of *N*-protected secondary carbinamines.<sup>1b</sup> *N*-Trimethylsilyl imines have been also utilized by Hirao<sup>3</sup> and Hart<sup>4</sup> in the synthesis of secondary carbinamines. We have also shown the utilization of *N*-

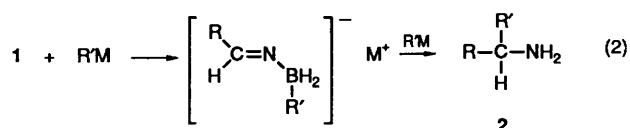
(trimethylsilyl)benzaldehyde imine for the asymmetric synthesis of optically active secondary carbinamines.<sup>5</sup> More recently Panunzio *et al.* have found that *N*-diisobutylaluminium imines, obtained from nitriles and diisobutylaluminium hydride, could be used for the synthesis of secondary carbinamines.<sup>6</sup> Although *N*-metallo imines containing silicon,<sup>2-4</sup> aluminium<sup>6</sup> and tin,<sup>1c</sup> have been studied extensively as shown above, the corresponding *N*-boryl imines have found few synthetic applications.<sup>7</sup> Here we report a convenient one-pot synthesis of secondary

**Table 1** Synthesis of secondary carbinamine from nitrile

Entry	RCN	R'M <sup>a</sup>	Temp. <sup>b</sup> (°C)	Reaction time (h)	Yield <sup>c</sup> (%)	Ref.
a	PhCN	BuLi <sup>d</sup>	-80	2	95	j
b	PhCN	BuLi <sup>d,e</sup>	-80	2	75	j
c	PhCN	BuLi <sup>d</sup>	20	2	70	j
d	PhCN	Bu <sup>3</sup> Li <sup>f</sup>	-80	2	53	k
e	PhCN	Bu <sup>1</sup> Li <sup>g</sup>	-80	1	55	l
f	PhCN	MeLi <sup>h</sup>	-80-0	5	89	m
g	PhCN	PhLi <sup>i</sup>	-80-0	5	73	n
h	PhCN	BuMgBr <sup>i</sup>	-80	5	0	—
i	PhCN	BuMgBr <sup>i</sup>	0	5	34	j
j	PhCN	BuMgBr <sup>i</sup>	20	2	36	j
k	PhCN	PrMgBr <sup>i</sup>	20	2	38	o
l	<i>o</i> -Methylbenzotrile	BuLi <sup>d</sup>	-80	2	72	p
m	<i>o</i> -Chlorobenzotrile	BuLi <sup>d</sup>	-80	2	73	p
n	Thiophene-2-carbonitrile	BuLi <sup>d</sup>	-80	2	53	q
o	EtCN	BuLi <sup>d</sup>	-80	2	69	r
p	PrCN	BuLi <sup>d</sup>	-80	2	57	s

<sup>a</sup> 3 equiv. of R'M were used. <sup>b</sup> Reaction temperature for alkylation. <sup>c</sup> Isolated yield. <sup>d</sup> Hexane solution. <sup>e</sup> 2 equiv. of R'M were used. <sup>f</sup> Cyclohexane solution. <sup>g</sup> Pentane solution. <sup>h</sup> Ether solution. <sup>i</sup> Tetrahydrofuran solution. <sup>j</sup> A. de Roocher and P. de Radzitsky, *Bull. Soc. Chim. Belg.*, 1963, **82**, 195. <sup>k</sup> B. P. Shailendra, *J. Inst. Chem., (India)*, 1981, **51**, 274 (*Chem. Abstr.*, 1982, **97**, 5878). <sup>l</sup> H. Cristol, A. Lavrent and M. Mousseron, *Bull. Chem. Soc. Fr.*, 1961, 2319. <sup>m</sup> R. F. Borch, M. D. Bernstein and H. D. Durst, *J. Am. Chem. Soc.*, 1971, **93**, 2897. <sup>n</sup> J. Kalamán and B. Ryban, *Chem. Zvesti*, 1966, **20**, 79. <sup>o</sup> Y. Yamamoto, H. Shimoda, J. Oda and Y. Inouye, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 3247. <sup>p</sup> Satisfactory NMR spectra were obtained. <sup>q</sup> See ref. 6. <sup>r</sup> J. P. Mahy, G. Bedi, P. Battioni and D. Mansuy, *New J. Chem.*, 1989, **13**, 651. <sup>s</sup> R. M. Southam and M. C. Whiting, *J. Chem. Soc., Perkin Trans.* 2, 1982, 597.

carbinamines by alkylation of *N*-boryl imines **1** using a reaction sequence described in eqns. (1) and (2).



R, R' = alkyl or aryl; M = Li or MgBr

Nitriles are known to be reduced slowly with an excess of borane-tetrahydrofuran to yield primary carbinamines.<sup>8</sup> The use of a controlled quantity of the reagent was found to result in partial reduction of nitrile to give *N*-boryl imine **1** which has potential as alternative masked imine derivative of ammonia. Alkylation of **1** with a variety of alkyl- and aryl-lithium or Grignard reagents followed by an aqueous work-up yielded the corresponding secondary carbinamines. For example, reaction between borane-tetrahydrofuran (1 equiv.) and benzonitrile at 20 °C for 1.5 h led to complete conversion into *N*-(boryl)-benzaldehyde imine **1a** as monitored by TLC analysis and IR spectra. Typical IR spectra showed the absence of the C≡N group and absorptions assigned to C=N stretching near to 1660 cm<sup>-1</sup> and B-H stretching near to 2360 cm<sup>-1</sup>. The *N*-boryl imine structure of **1a** was confirmed from its <sup>1</sup>H NMR spectrum obtained in CDCl<sub>3</sub> solution, which showed the presence of a vinylic proton at 7.6 ppm. For synthetic purposes it is in general more convenient to prepare them *in situ* just before use. Without isolation, **1a** when treated with a hexane solution of butyllithium afforded a secondary carbinamine **2a** after acidic hydrolysis. To our knowledge, this was the first example of a reaction between an *N*-boryl imine and an organometallic compound. Table 1 shows a number of examples of the synthesis of secondary carbinamines. The conditions which must be used for the preparation of secondary carbinamines depend on the structure of the alkylating agents. The alkylation with

organolithium reagents proceeded very rapidly even at -80 °C. Higher reaction temperature lowered the yield of the desired primary amine. Maximum yields of **2** were obtained when 3 equiv. of alkylating agents were used. Alkylation with Grignard reagent required relatively higher temperature to yield amines. Within the time required for the alkylations the amines produced were only secondary carbinamines and not contaminated with the undesired primary amines from complete borane reduction of nitrile.

From the above results, it is clear that enolizable as well as non-enolizable *N*-boryl imines, which can be easily obtained from partial reduction of nitrile with borane in tetrahydrofuran, react with a variety of organometallic reagents to afford good to excellent yields of secondary carbinamines. A further advantage of this method is that *N*-boryl imines possessing reactive B-H bonds have potential for further modification using optically active alcohols or olefins. Studies of an asymmetric variant of this chemistry are currently under investigation.

## Experimental

*Typical Procedure for the Preparation of Secondary Carbinamines from Nitrile.*—To a stirred solution of benzonitrile (1.03 g, 10 mmol) in dry tetrahydrofuran (10 ml) was added a tetrahydrofuran solution of borane-tetrahydrofuran (0.98 mol dm<sup>-3</sup>; 10.2 ml) with cooling in an ice-water bath. After the mixture had been stirred for 1.5 h at 20 °C, TLC analysis showed a single spot corresponding to the *N*-boryl imine instead of one for the nitrile. To the resulting solution containing *N*-boryl imine **1** was added a 1.5 mol dm<sup>-3</sup> hexane solution (20 ml, 30 mmol) of butyllithium at -80 °C *via* a dropping funnel. The resulting red solution was stirred for a further 2 h at the same temperature, and then cautiously hydrolysed with water and 2 mol dm<sup>-3</sup> HCl. The organic layer was removed and the aqueous layer was neutralized with NH<sub>4</sub>OH and extracted with ether (3 × 30 ml). The combined extracts were dried (MgSO<sub>4</sub>) and concentrated under reduced pressure to give an oil (1.55 g, 95%), identified as 1-phenylpentylamine. The amine obtained by this procedure prior to distillation was 95% pure as indicated by <sup>1</sup>H NMR and GLC.

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