J. Chem. Research (S),
1999, 330–331†

Lithium Perchlorate Mediated Three Component Reaction for the Preparation of Primary Amines†

Mohammad R. Saidi,* Shahrzad Javanshir and Mohammad M. Mojtahedi

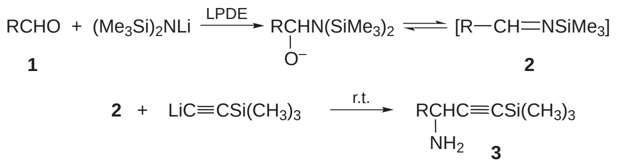
Department of Chemistry, Sharif University of Technology P.O. Box 11356-9516, Teheran, I.R. of Iran

In the presence of lithium perchlorate in diethyl ether, LPDE, a three-component reaction between aldehydes, sodium hexamethyldisilazane or lithium hexamethyldisilazane, LHMDS, and different nucleophiles proceeds smoothly to afford primary amines in good yields.

Addition reactions of carbonyl and related compounds are the most useful and important reactions in organic chemistry.[1] Also, synthesis of amines by the Mannich reaction has been extensively studied by organic chemists. Since the classical Mannich reaction has many limitations, numerous attempts have been made to overcome these, owing to the importance of the products.[2–5]

The synthesis of primary amines is of interest due to their different uses.[6–8] One approach involves addition of organometallic reagents to imines, but the low electrophilicity of the imine carbon has frequently hindered these reactions. The reactivity of imines has been improved by complexation with Lewis acids, or by preparation of 'masked' imine derivatives of ammonia. They react with organometallic reagents followed by the removal of the protecting group to give primary amines.[9–13]

Recently, we reported the lithium perchlorate mediated one pot three-component aminosilylation of aldehydes **1**, with lithium hexamethyldisilazane or sodium hexamethyldisilazane and a nucleophiles with a silicon protecting group, for the preparation of trimethylsilyl amines **3**, in good yields,[14] Scheme 1.



$$\underset{\mathbf{1}}{RCHO} + (Me_3Si)_2NLi \xrightarrow{LPDE} \underset{O^-}{RCHN(SiMe_3)_2} \rightleftharpoons \underset{\mathbf{2}}{[R{-}CH{=}NSiMe_3]}$$

$$\mathbf{2} + LiC{\equiv}CSi(CH_3)_3 \xrightarrow{r.t.} \underset{NH_2}{RCHC{\equiv}CSi(CH_3)_3}\ \mathbf{3}$$

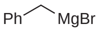
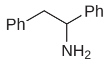
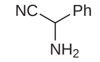
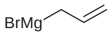
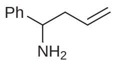
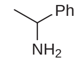
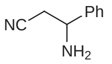
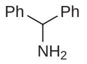
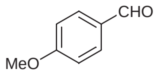
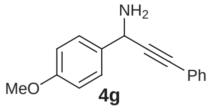
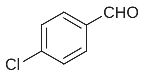
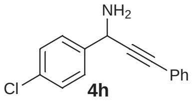
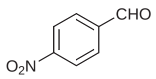
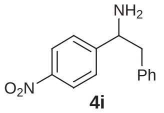
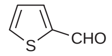
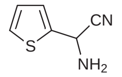
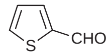
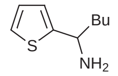
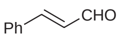
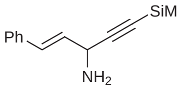
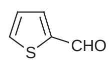
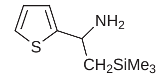
Scheme 1

On the basis of this idea, in this paper we report a simple method for the synthesis of several primary amines from the preformed imines, mediated by lithium perchlorate, which avoids multistep procedures. Aldehyde **1** reacts with sodium hexamethyldisilazane or LHMDS in the presence of a 5 M solution of lithium perchlorate in diethyl ether at r.t. to produce imine **2**, *in situ*, in about 30 min. Reaction of organolithium and other nucleophiles with **2** at r.t. affords the corresponding primary amines **4** in good to moderate yields, Scheme 2.

The structures and the yields of the products are shown in Table 1. When the reaction was carried out without using 5 M LPDE, compound **4** was produced in very low yields (up to 10%).

In conclusion, we have devised a synthesis for primary amines by nucleophilic addition of organometallic reagents to aldimines mediated by 5 M LPDE. Most of the crude amine products are of sufficient purity for subsequent use.

Table 1 The structure and yields of the primary amines

Entry	Aldehyde	Nucleophile	Product	Yield(%)
1	PhCHO		 **4a**	57
2	PhCHO	$NCSiMe_3$	 **4b**	60
3	PhCHO		 **4c**	87
4	PhCHO	MeLi	 **4d**	43
5	PhCHO	$LiCH_2CN$	 **4e**	86
6	PhCHO	PhLi	 **4d**	83
7		LiC≡CPh	 **4g**	74
8		LiC≡CPh	 **4h**	30
9		$LiCH_2Ph$	 **4i**	31
10		$NCSiMe_3$	 **4j**	60
11		BuLi	 **4k**	55
12		$LiC{\equiv}CSiMe_3$	 **4l**	75
13		$BrMgCH_2SiMe_3$	 **4m**	60

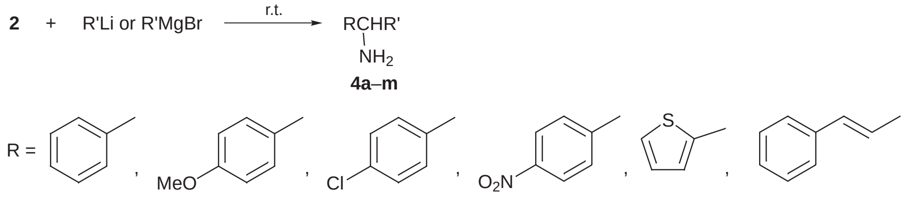
Experimental

General.—$LiClO_4$ (Fluka) was dried at 160 °C and 10^{-1} Torr for 48 h, diethyl ether over Na benzophenone under argon. IR spectra

---

[*] To receive any correspondence.

[†] This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1999, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.



R' = Me, Ph, *n*-Bu, PhCH$_2$, CN, CH$_2$CN, CH$_2$SiMe$_3$, PhC≡C, Me$_3$SiC≡C

Scheme 2

were taken on a Matt Son 1000 Unicam FTIR, ^{1}H and ^{13}C NMR spectra on a Bruker AC 80 spectrometer. All reactions were performed under argon. Chemicals were purchased from Fluka and used as received.

Caution: Although we did not have any accidents using LiClO$_4$, it is advised to dry lithium perchlorate in a hood using a suitable lab-shield. The ether solution should be freshly prepared and not stored.

Procedure for the Preparation of Primary Amines (*Entries* 1–13 *in Table* 1).—Hexamethyldisilazane, HMDS (3.3 mmol, 0.54 g), was placed in a two-necked flask fitted with a condenser and a stirring bar, under argon, 3.5 mmol of sodium hydride (60–65%, after washing with light petroleum) or 3.3 mmol of methyllithium in diethyl ether were added, and the mixture was stirred for about 5 min. Then 3 mL solution of 5 M LPDE and 2 mmol of aldehyde were added *via* a syringe. After stirring for 30 min, organometallic reagent or other nucleophile (4 mmol) was added *via* syringe, and the mixture stirred for 30 min. Water (10 mL) was added and the product extracted with ether (2 × 10 mL). The organic layer was separated and extracted with cold 0.5 M HCl solution. Neutralization with a 2.0 M solution of KOH gave the desired product. Further purification was by preparative gas chromatography if needed. The structures of the new compounds were determined by their IR, ^{1}H, ^{13}C NMR and compared with those reported.[10–12] All new products showed satisfactory C and H analyses.

Selected Spectroscopic Data.—**4b**: ^{1}H NMR (CDCl$_3$) δ 7.00–7.41 (m, 5 H), 5.35 (s, 1 H), 1.12 (s, 2 H); IR (neat) ν 3392, 3320, 2238 cm^{-1}. **4g**: ^{1}H NMR (CDCl$_3$) δ 6.61–7.80 (m, 9 H), 5.38 (s, 1 H), 3.62 (s, 3 H), 1.10 (s, 2 H); IR (neat), ν 3384, 3321, 2261 cm^{-1}. **4j**: ^{1}H NMR (CDCl$_3$) δ 6.48–7.51 (m, 3 H), 5.61 (s, 1 H), 1.13 (s, 2 H); IR (neat) ν 3410, 3338, 2250 cm^{-1}. **4i**: ^{1}H NMR (CDCl$_3$) δ 0.22 (s, 9 H), 2.32 (br s, 2 H), 5.04 (d, $J = 6.0$, 1 H), 6.28 (dd, $J = 16.0$, 5.7, 1 H), 6.76 (d, $J = 16.0$, 1 H), 7.34 (m, 5 H); ^{13}C NMR (CDCl$_3$) δ −0.16 (CH$_3$), 63.22 (CH), 93.50 (C), 104.48 (C), 126.78 (CH), 128.02 (CH), 128.54 (CH), 129.41 (CH), 131.92 (CH), 136.15 (C); IR (neat) ν 3434, 2173, 843 cm^{-1}. **4m**: ^{1}H NMR (CDCl$_3$) δ 0.00 (s, 9 H), 1.30 (d, $J = 7.4$, 2 H), 3.26 (br s, 2 H), 5.06 (t, $J = 7.4$ 1 H), 6.80–7.47 (m, 3 H); ^{13}C NMR (CDCl$_3$) δ −1.13 (CH$_3$), 28.88 (CH$_2$), 67.67 (CH), 123.26 (CH), 124.19 (CH), 126.27 (CH), 151.20 (C); IR (neat) ν 3394, 1251, 852 cm^{-1}.

We acknowledge Volkswagen-Stiftung, Federal Republic of Germany for financial support to purchase laboratory chemicals. We also thank the Research Council of the Sharif University of Technology for its partial financial support of this work.

Received, 30th October 1998; Accepted, 2nd February 1999
Paper E/8/08424F

References

1 S. Kobayashi and S. Nagayama, *J. Org. Chem.*, 1997, **62**, 232.
2 E. F. Kleinman, in *Comprehensive Organic Synthesis*, eds. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, vol. 2, pp. 893–951.
3 A. R. Katritzky and P. A. Harris, *Tetrahedron*, 1990, **46**, 987.
4 D. Seebach, C. Bestschuart and M. Schiess, *Helv. Chim. Acta*, 1984, **67**, 1593.
5 M. Arend and N. Risch, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 2639.
6 S. Toyoshima, Y. Fukushima, N. Yagi, H. Tomioka, M. Fukuma and Y. Seto, *Chem. Abstr.*, 1981, 94,114438v; M. Kolb and J. Barth, *Leibigs Ann. Chem.*, 1983, 1679.
7 B. B. Snider, R. S. E. Conn and M. Karras, *Tetrahedron Lett.*, 1979, 1679; R. S. E. Conn, M. Karras and B. B. Snider, *Isr. J. Chem.*, 1984, **24**, 108.
8 C. Sahlberg, S. B. Ross, I. Fagerwall, A. L. Ask and A. J. Claesson, *Med. Chem.*, 1983, **26**, 1036.
9 R. L. White, R. A. Smith and A. Krantz, *Biochem. Pharmacol.*, 1983, **32**, 3361.
10 S. S. Nikan and K. K. Wang, *J. Org. Chem.*, 1996, **50**, 2193.
11 J. Wang, Y. Zhang and W. Bao, *Synth. Commun.*, 1996, **26**, 2473.
12 A. R. Katritzky, L. Xie and G. Zhang, *Tetrahedron Lett.*, 1997, **38**, 7011.
13 F. Gyenes, K. E. Bergmann and J. T. Welch, *J. Org. Chem.*, 1998, **63**, 2824.
14 M. R. Saidi, M. M. Mojtahedi and M. Bolourtchian, *Tetrahedron Lett.*, 1997, **63**, 8071 and references therein.