Solvent-free efficient synthesis of N,N′-bis(arylmethylidene)-arylmethanediamines from aromatic aldehydes and hexamethyldisilazane

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Dedicated to Professor T. R. Govindachary on his 85th birthday

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Abstract

Reaction of aromatic aldehydes and HMDS under solvent-free as well as mild conditions afforded N,N'-bis(arylmethylidene)arylmethanediamines in excellent yields.

Keywords: Aldehyde, hexamethyldisilazane, hydrobenzamide, methanediamine

Introduction

Reaction of aromatic aldehydes with ammonia leads to the long-known compounds called "hydrobenzamides".[1] Owing to the unique structural features and the reactivity, these compounds have been recognized as potential key intermediates for the synthesis of a variety of nitrogen containing heterocyclic compounds.[2] Recently, Corey et al., while clarifying the structural controversy of amarine, have stressed the importance of N,N'-bis(arylmethylidene)arylmethanediamines in the synthesis of 1,2-disubstituted-1,2-diaminoethanes,[3] which have been used as chiral ligands.[4] Extensive studies on kinetics and mechanism of formation of hydrobenzamides from aromatic aldehydes and ammonia have already been well documented.[5] In spite of such a long history and wide spread applications, no efficient methods for the preparation of these intermediates have been reported. The only conventional method available for the preparation of these compounds involves the reaction of aldehydes with ammonia, a complex reversible reaction which takes days to weeks for completion.[6] Moreover, protic solvents used in this reaction such as methanol or water enhance the reversible conversion of products into starting aldehydes, thereby reducing the yields even after longer reaction times. Therefore, clean and efficient methods for the preparation of these

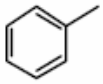
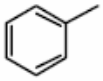
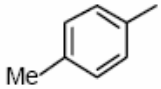
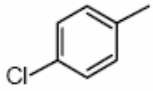
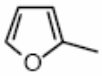
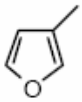
versatile intermediates are highly desirable. Because of economical and environmental reasons, development of the solvent-free reaction is gaining much momentum recently, especially for the large-scale production of widely used compounds. In this context, we reexamined the conventional reaction conditions of aldehydes with ammonia and contemplated a couple of important changes to make the reaction clean and efficient: (i) replacement of harmful and strongly smelling ammonia with hexamethyldisilazane (HMDS) (ii) solvent-free reaction conditions.

In continuation of our efforts to develop new synthetic methods for widely used compounds, we have recently reported the Lewis acid and HMDS-mediated method for the efficient synthesis of N-alkyl- and N-arylmaleimide derivatives.[7] We now report a solvent-free, efficient method for the synthesis of the bis(arylmethylidene)arylmethanediamines from aromatic aldehydes and HMDS.

Results and Discussion

With an eye to developing a more expedient synthetic route to bis(arylmethylidene)arylmethanediamines, we have initially examined the reaction of benzaldehyde with HMDS. Since HMDS was considered as bis(trimethylsilyl)-masked ammonia and also relatively stable and volatile liquid, use of HMDS in place of ammonia would lead to several added advantages in this synthesis. In order to check this concept, an equimolar proportion of benzaldehyde and HMDS was mixed in dry benzene and refluxed. Unfortunately, even after several hours of reflux, only a trace of the product was formed. When the reaction was performed at very high concentration of the reactants in a. benzene solution, the product was formed in 15% yield after 24 h of reflux. Drawing the clue from these reaction conditions, we assumed that the reaction of benzaldehyde and HMDS without solvent might work out well. To our surprise, when benzaldehyde and HMDS (1.2 equiv) was mixed and stirred at 60 °C, the reaction mixture was completely solidified, giving 93% yield of the desired hydrobenzamide. This result triggered us to try the reaction with various aromatic aldehydes. As shown in Table 1, most of the aromatic aldehydes gave the bis(arylmethylidene)-arylmethanediamines in very high yields. However, the yield was low at 60 °C in the case of *p*-tolualdehyde, even using a large excess amount of HMDS. When the reaction was performed at 120 °C in a sealed tube, the yield was significantly improved. However, benzaldehydes having a strong electron-withdrawing group such as *p*-cyano- and *p*nitrobenzaldehydes did not give the desired products.

Table 1. Thermal Reaction of Aromatic Aldehydes and HMDS without Solvent

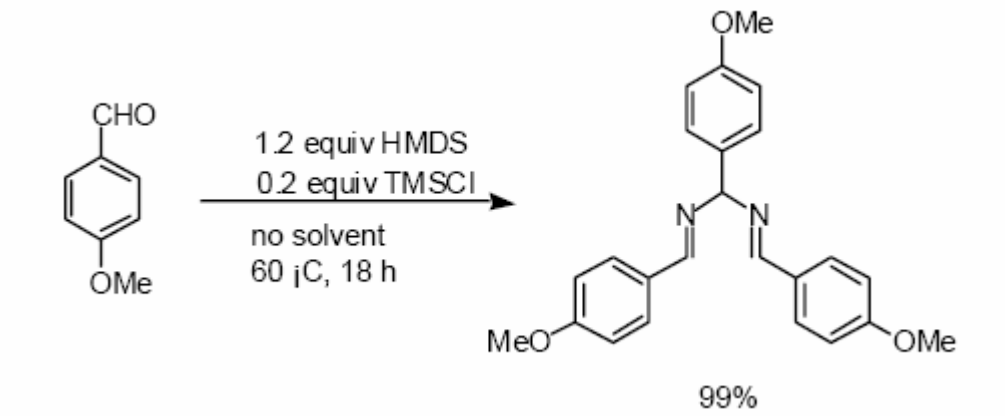
entry	Ar	HMDS (equiv)	reaction time (h)	yield (%)
1		1.2	24[a]	15
2		1.2	6	93
3		1.5	6[b]	98
4		1.2	11[c]	86
5		1.0	6	97
6		1.0	6	91
7		1.1	15	97

a) Refluxed in dry benzene. b) Reaction was carried out at 120 °C in a sealed tube .c) Reaction was carried out at 70 °C.

However, survey of literatures revealed that such attempts had already been made for the synthesis of the bis(arylmethylidene)arylmethanediamines from aldehydes and HMDS in the presence of $ZnCl_2$ in CH_2Cl_2.[7] However, the yields have been reported to be moderate and reaction takes 24 h under these reaction conditions. Moreover, isolation of the moisture- and acid-sensitive products from the complex reaction mixture containing Zn salts by aqueous workup was not suitable.

It is interesting to note that the reaction of *p*-methoxybenzaldehyde did not proceed on treatment with HMDS at 60 °C for 24 h. However, when the reaction was carried out in the presence of a catalytic amount of trimethylsilyl chloride, the reaction was remarkably enhanced, giving an excellent yield of the desired product (Scheme 1). From these results, we infer that trimethylsilyl chloride may play a role in activation of the carbon-oxygen bond, which facilitates nucleophilic attack of HMDS leading to high yield of the product. Other Lewis acids such as $ZnCl_2$ was not so effective that they led to the formation of messy by-products.

Moreover, it is possible to remove all the volatile by-products formed in this reaction, such as bistrimethylsilyl ether and excess HMDS, simply by concentrating and drying the products under vacuum, which would facilitate isolation of the products without any aqueous workup.



Scheme 1

In conclusion, we have developed an efficient method for the preparation of the bis(arylmethylidene)arylmethanediamines, versatile intermediates used in multiple organic transformations. We also claim that this method using HMDS has many advantages over the known conventional liquid ammonia or ammonium hydroxide method. Since the conditions employ no solvents, the products easily precipitate out, which save the efforts of the tedious workup procedure. The reaction of most of the substrates proceeds more rapidly when compared with the traditional methods.

Experimental Section

***N,N′*-Bis(phenylmethylidene)phenylmethanediamine. Representative procedure**
Benzaldehyde (106 mg, 1.0 mmol) and HMDS (193 mg, 1.2 mmol) were heated for 6 h at 60 °C under argon. Then the reaction mixture was cooled to room temperature to give a solid. The solid was triturated with dry hexane (5 mL), filtered, washed with dry hexane, and dried under vacuum to afford 92 mg (93%) of a colorless solid: mp 101.8–102.5 °C (CH_2Cl_2/hexane) (lit.[8] mp 100-101°C); ^{1}H NMR ($CDCl_3$):δ 5.96 (s, 1H), 7.19–7.80 (m, 15H), 8.58 (s, 2H).
***N,N′*-Bis(*p*-methylphenylmethylidene)-*p*-methylhenylmethanediamine.** Mp 95.8-96.4 °C (CH_2Cl_2/hexane) (lit.[8] mp 93-94 °C); ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 3H), 2.42 (s, 6H), 5.96 (s, 1H), 7.19–7.28 (m, 6H), 7.45 (d, J=8.2 Hz, 2H), 7.80 (d, 4H), 8.58 (s, 2H).
***N,N′*-Bis(*p*-chlorophenylmethylidene)-*p*-chlorophenylmethanediamine.** Mp 88.2-89.5 °C (benzene/hexane) (lit.[2b] mp 84.5-85.5 °C); ^{1}H NMR ($CDCl_3$): δ 5.89 (s, 1H), 7.36 (d, *J*=8.3 Hz, 2H), 7.50 (d, *J*=8.6 Hz, 2H), 7.56 (d, *J*=8.5 Hz, 4H), 7.70 (d, *J*=8.5 Hz, 4H), 8.48 (s, 2H).
***N,N′*-Bis(2-furylmethylidene)-2-furylmethanediamine.** Mp 122.5–123.5 °C (benzene/hexane)

(lit.[2b] mp 116-117 °C); ^{1}H NMR ($CDCl_3$): δ 5.96 (s, 1H), 7.19–7.80 (m, 9H), 8.58 (s, 2H).

***N,N′*-Bis(3-furylmethylidene)-3-furylmethanediamine.** Mp 95.4-96.1 °C (benzene/hexane); IR (KBr) 1617 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 5.78 (s, 1H), 6.40 (d, *J* = 1.38 Hz, 1H), 6.92 (d, *J* = 1.70 Hz, 1H), 7.39-7.45 (4H, m), 7.77 (s, 2H), 8.46 (s, 2H); *m/z* 268 (M^+, 5%), 174 (100%);Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.15; H, 4.51; N, 10.44. Found: C, 66.81; H, 4.48; N, 10.31.

***N,N′*-Bis(2-thienylmethylidene)-2-thienylmethanediamine.** Mp 113.0-114.0 °C (CH_2Cl_2/hexane); IR (KBr) 1643 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 6.22 (s, 1H), 6.97-7.47 (m, 9H), 8.31 (2H, s); *m/z* 316 (M^+, 1%), 206 (100%); Anal. Calcd for $C_{15}H_{12}N_2S_3$: C, 56.96; H, 3.82; N, 8.86. Found: C, 56.71; H, 3.84; N, 8.76.

***N,N′*-Bis(*p*-methoxyphenylmethylidine-)-*p*-methoxyphenylmethanediamine.** *p*-Anisaldehyde (222 mg, 1.6 mmol), HMDS (315 mg, 2.0 mmol) and chlorotrimethylsilane (35 mg, 0.3 mmol) were mixed in a sealed tube and heated at 60 °C for 18 h in an oil bath, giving 211 mg (99%) of a colorless solid: mp 126.9-127.4 °C (CH_2Cl_2/hexane) (lit.[8] mp 128-129 °C); ^{1}H NMR ($CDCl_3$): δ 3.79 (s, 3H), 3.84 (s, 6H), 5.83 (s, 1H), 6.89 (d, *J*=8.60 Hz, 2H), 6.92 (d, *J*=8.74 Hz, 4H), 7.42 (d, *J* =8.8 Hz, 2H), 7.79 (d, *J*=8.80 Hz, 4H), 8.58 (s, 2H).

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