However chlorodiphenyl compounds were not detected by the analytical method used in this study. It indicates that greater amount of phenyl radical is produced than chlorophenyl radical in the reaction by attack of Cl radical to chlorobenzene as in reaction (3).

In summary, phenol and chloride ion were produced as main products along with benzene, 2-phenylphenol, 3-phenylphenol, 4-phenylphenol and biphenyl in the irradiation of 3.54×10^{-3} M deoxygenated aqueous chlorobenzene solution using 253.7 nm UV light. The initial quantum yield of the products was found to be nearly same regardless of the absence or presence of air. Most of the electronically excited chlorobenzene by the absorption of 253.7 nm UV light was decomposed to phenol by the attack of the water in the solution. In addition to this photochemical decomposition process, small part of the electronically excited chlorobenzene can also splitted into the phenyl and chlorophenyl radicals, and the radicals produced take part in the formation of the benzene, 2-phenylphenol, 3-phenylphenol, 4-phenylphenol and biphenyl. During the reaction by attack of Cl radical to chlorobenzene, Cl atom is more easily abstracted from the chlorobenzen molecule rather than H atom.

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Reductive Amination of Aldehydes and Ketones with Dimethylamine Using Borohydride Exchange Resin (BER)

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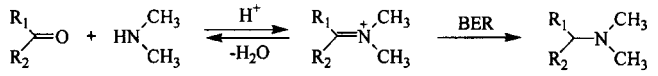
The synthesis of amines is an important theme in chemical research because of their versatile utility as intermediates for drugs and agrochemicals.[1] The *N,N*-dimethylalkylamines are particularly useful as ligands[2] in homogeneous catalytic asymmetric transformations, and as buffers[3] in sequential anaylsis of proteins and peptides among other applications.[4] The most direct approach for the synthesis of *N,N*-dimethylated tertiary amines is the reductive amination of appropriate aldehydes or ketones. Among the reducing reagents, sodium cyanoborohydride[5] has been widely used to effect this transformation. However, it is expensive and highly toxic, and also risks the presence of residual cyanide in the product. Therefore, borane pyridine (BAP),[6] sodium triacetoxyborohydride[7] and borohydride exchange resin (BER)[8] were reported as alternatives, less expensive, and less toxic reagents. Recently an efficient method for the reductive amination of aldehydes and ketones was reported using the combination of titanium(IV) isopropoxide and sodium borohydride.[9] However, this system needs titanium(IV) isopropoxide as Lewis acid and requires a considerably long reaction time. This prompted us to apply our earlier method[8] for the synthesis of *N,N*-dimethylalkylamines. Previously we

studied the reductive amination of aldehydes and ketones in general using BER and did not concentrate our attention to the synthesis of *N,N*-dimethylalkylamines. We obtained only 68% yield of *N,N*-dimethyl-2-heptylamine (only one example of *N,N*-dimethylamine synthesis). Therefore we examined representative aldehydes and ketones for the reductive amination with dimethylamine to obtain the higher yields of the corresponding *N,N*-dimethylalkylamines.

The procedure is simple. To the substrate aldehyde or ketone in 95% ethanol, dimethylamine (5 eq) in ethanol, Et_3NHCl (2 eq), and BER (1 eq) were added successively and stirred at room temperature. After 1-2 h, the acidic solution was neutralized with NaOH. Then the resin was removed by filtration, and the solvent was evaporated under reduced pressure. The crude products were chromatographed on silica gel.



R_1 = alkyl, aryl
R_2 = alkyl, hydrogen

Scheme 1

The results are summarized in Table 1. As shown in Table 1, all the aldehydes and ketones examined were readily aminated to the corresponding *N,N*-dimethylalkylamines in excellet yields in 1-2 h at room temperature. But in the case of acetophenone, the reaction was very sluggish giving only 10% of the product in 2 h and did not proceed appreciably even in 24 h (entry 17). In contrast, *p*-nitroacetophenone reacted smoothly (entry 18). Apparently the increase of positive charge on carbonyl carbon of *p*-nitroacetophenone resulted in the faster reaction. In order to circumvent this difficulty of acetophenone, we tried the reaction in the presence of metal salts, and found $ZnCl_2$ is the best. Thus in the presence of 3 eq of $ZnCl_2$ and using 10 eq of dimethylamine, we obtained 85% yield of *N,N*-dimethyl-1-phenylethylamine. The present method tolerates many functional groups such as chloro, cyano, methoxy, nitro, ester and amido group (entries 6-11 and 18). Isolated and conjugated double bonds were also inert to this system (entries 3 and 4). In the case of norcamphor (entry 16), *N,N*-dimethyl-*endo*-norbornylamine was obtained in an excellent yield without contaminating with *exo*-isomer. The use of sodium cyanoborohydride has been reported for the transformation of aldehydes and ketones to give the corresponding *N,N*-dimethylamine derivatives in 40-70% yields,[4] and titanium (IV) isopropoxide-$NaBH_4$ gave excellent yields of *N,N*-dimethyamine derivatives from aldehydes but only moderate yields from ketones.[9] Finally this method was applied to the reductive amination of benzaldehyde with other secondary amines such as diethylamines and *N*-methylaniline. We obtained an excellent yield (95%) of *N,N*-diethylbenzylamine, but less than 10% yield of *N,N*-benzylmethylaniline.

In conclusion, this method gives excellent yields of the corresponding amines from carbonyl compounds tolerating many functional groups, and has an advantage of simple work-up. Therefore for the synthesis of *N,N*-dimethylalkylamines, BER is a good alternative to cyanoborohydride, BAP, $NaBH(OAc)_3$ and titanium (IV) isopropoxide-$NaBH_4$.

Experimental

General Procedure. Synthesis of *N,N*-dimethylhexylamine from hexanal is representative (entry 1). To 3 mL of 1.0 M hexanal (0.30 g, 3.0 mmol) solution in 95% ethanol in a 50 mL flask, 2.75 mL of 5.6 M dimethylamine (15.0 mmol) solution in ethanol (Fluka), 0.83 g of Et_3NHCl (6.0 mmol), and 1.14 g (3.0 mmol) of BER were successively added. After stirring for 1 h at room temperature, the acidic solution was neutralized with NaOH. Then the resin

Table 1. Reductive amination of aldehydes and ketones with dimethylamine using BER at room temperature[a]

Entry	Substrate	Product	Yield (%)[b]
1	hexanal	*N,N*-dimethylhexylamine	95
2	cyclohexanecarboxaldehyde	*N,N*-dimethylcyclohexylmethylamine	93
3	3-cyclohexene-1-carboxaldehyde	*N,N*-dimethyl-3-cyclohexenylmethylamine	92
4	cinnamaldehyde	*N,N*-dimethylcinnamylamine	95
5	benzaldehyde	*N,N*-dimethylbenzylamine	94
6	*p*-chlorobenzaldehyde	*N,N*-dimethyl-*p*-chlorobenzylamine	95
7	*p*-cyanobenzaldehyde	*N,N*-dimethyl-*p*-cyanobenzylamine	95
8	*p*-methoxybenzaldehyde	*N,N*-dimethyl-*p*-methoxybenzylamine	98
9	*p*-nitrobenzaldehyde	*N,N*-dimethyl-*p*-nitrobenzylamine	94
10	*p*-carbomethoxybenzaldehyde	*N,N*-dimethyl-*p*-carbomethoxybenzylamine	93
11	*p*-acetamidobenzaldehyde	*N,N*-dimethyl-*p*-acetamidobenzylamine	96
12	2-heptanone	*N,N*-dimethyl-2-heptylamine	92[c]
13	cyclopentanone	*N,N*-dimethylcyclopentylamine	94[c]
14	cyclohexanone	*N,N*-dimethylcyclohexylamine	94[c]
15	cyclootanone	*N,N*-dimethylcyclootylamine	92[c]
16	norcamphor	*N,N*-dimethyl-2-endo-norbornylamine	92[c]
17	acetophenone	*N,N*-dimethyl-1-phenylethylamine	10(85)[d]
18	*p*-nitroacetophenone	*N,N*-dimethyl-*p*-nitro-1-phenylethylamine	91[c]

[a] Aldehydes or ketones (3 mmol) were reacted with *N,N*-dimethylamine (15 mmol), Et_3NHCl (6 mmol) and BER (3 mmol) for 1 h in 95% ethanol. [b] Isolated yields. [c] Reactions were carried out for 2 h. [d] 15 h reaction with $ZnCl_2$ (3 eq) and dimethylamine (10 eq).

was removed by filtration, and the solvent evaporated under reduced pressure. The crude residue was chromatographed on silica gel (CH_2Cl_2 : MeOH, 9 : 1) to give the pure *N,N*-dimethylhexylamine (0.36 g, 95%) (entry 1): ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.88 (t, 3H, J=6.4 Hz), 1.39 (m, 8H), 2.20 (s, 6H), 2.23 (t, 2H, J=7.3 Hz); IR (neat) 3400, 2950, 2800, 1490, 1050 cm^{-1}; MS m/z (relative intensity) (EI, 70 eV) 129 (M^+, 63), 59 (4), 58 (100), 42 (5).

***N,N*-Dimethyl-3-cyclohexenylmethylamine.** (entry 3) ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.07 (m, 6H), 2.11 (m, 1H), 2.83 (s, 6H), 2.92 (d, 2H, J=6.8 Hz), 5.68 (brs, 2H); IR (neat) 3623, 2960, 2570, 1730, 1690, 1265 cm^{-1}; MS m/z (relative intensity) (EI, 70 eV) 139 (M^+, 3), 79 (2), 77 (1), 59 (4), 58 (100); Anal. Calcd for $C_9H_{17}N$: C, 77.63; H, 12.31; N, 10.06. Found: C, 77.54; H, 12.70; N, 10.05.

***N,N*-Dimethyl-*p*-carbomethoxybenzylamine.** (entry 10) ^{1}H NMR (200 MHz, $CDCl_3$): δ 2.24 (s, 6H), 3.47 (s, 2H), 3.91 (s, 2H), 7.38 (d, 2H, J=7.8 Hz), 7.99 (d, 2H, J=8.06 Hz); IR (neat) 2976, 2817, 1720, 1435, 757 cm^{-1}; MS m/z (relative intensity) (EI, 70 eV) 193 (M^+, 46), 192 (30), 149 (10), 89 (6), 58 (100); Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.78; H, 8.07; N, 6.76.

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An Efficient Synthesis of Ethylenimine Dendrimer

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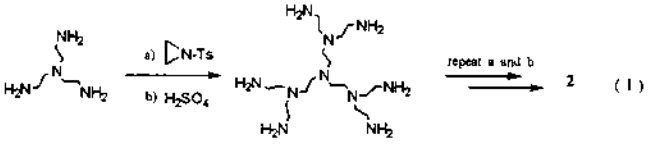
Because of their potential in cancer chemotherapy,[1] siderophores,[2] immobilization of enzyme,[3] gene delivery,[4] anion-exchange chromatography,[5] and skeleton of artificial enzyme,[6] poly(ethylenimine) (**1**)[7] derivatives have received a great deal of attention from synthetic chemists. Amongst them, ethylenimine dendrimer (**2**) is our recent interest because various biomimetic functional molecules can be designed by attaching appropriate chemical moieties to it. Dendrimer with hydrophilic exteriors and hydrophobic interiors like **2** may be regarded as covalently bonded assemblies of amphiles such as micells[8] or vesicles[9] possessing well-defined structures.

We used **2** for the study of biomimetic catalyst in our previous publication.[10] For further application of **2**, we need to improve the synthetic procedure because it was not easy to get enough amount of **2** by the known procedure.[11] Tomalia *et al.* synthesized **2** as shown in equation 1. They used *N*-(*p*-toluenesulfonyl)aziridine (Ts-aziridine) as a repeating unit. However, the deprotection of *p*-toluenesulfonyl (Ts) group with H_2SO_4 was inefficient due to the complex procedure and low yield (~30%) in each deprotection step.



(1)

In this paper, we report an efficient procedure for the synthesis of dendrimer **2**. The key step for this synthesis is deprotection. If we can use the *N*-benzyloxycarbonylaziridine (Cbz-aziridine) (**4**) as a repeating unit, the deprotection procedure will be more efficient and simpler than otherwise because the Cbz can be removed by catalytic hydrogenolysis. **4** was synthesized from β-aminoethylsulfuric acid as shown in equation 2. The reaction of **4** with benzylamine was examined in order to establish the reaction conditions. The