

estimated to be 11.7 Å long, 8.6 Å wide, and 3.6 Å thick, as drawn in Figure 2(b). Using the known bond lengths, bond angles, van der Waals atomic radii, and the approximate distance between the sulfur atom and the gold surface,<sup>20</sup> the thickness of the AQ-CONH-C2-SH monolayer on gold is estimated to be 11.8 and 13.3 Å, respectively, when the tilt and twist angles determined from the RAIR spectra for the samples prepared in 10<sup>-6</sup> and 10<sup>-3</sup> M solutions were invoked. It would be desirable to compare these values with the ellipsometric measurement, albeit a direct comparison may be controversial due to the various uncertainties in the ellipsometry measurement (*i.e.*, oxide formation and ambient contamination). Since the solution of the ellipsometry equations, *i.e.*, refractive index and thickness, could not be obtained simultaneously, a refractive index of 1.45 was assumed for the estimation of thickness. From a three phase optical model, the ellipsometric parameters corresponded to the thicknesses of 9.6±1.1 Å and 10.8±0.5 Å for the samples prepared in 10<sup>-6</sup> and 10<sup>-3</sup> M solutions, respectively. Although the predicted thicknesses from the RAIR spectral feature do not agree with the measured thicknesses, it is nonetheless informative that the predicted difference in the thicknesses of the AQ-CONH-C2-SH monolayers prepared in 10<sup>-6</sup> and 10<sup>-3</sup> M solutions is quite comparable to that measured by ellipsometry.

In summary, we have found that AQ-CONH-C2-SH should chemisorb well on a gold surface. The AQ moiety is concluded to be tilted and twisted with respect to the surface normal in a full surface coverage limit. The present information will be useful in the investigation of the adsorption kinetics and the spectroelectrochemical characteristics of various AQ derivatives, and eventually in the preparation of AQ-containing electroactive devices that could be applied as a biosensor.

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## Direct Synthesis of Benzylamine Derivatives from Aldehydes and Ketones via Phenylhydrazones Using BER-Pd(OAc)<sub>2</sub>

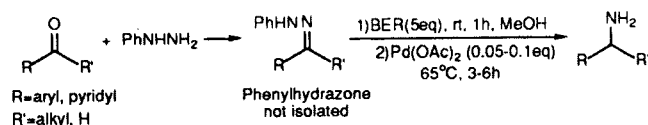
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Reductive amination is commonly carried out using cyanoborohydrides.<sup>1-3</sup> Borane pyridine (BAP),<sup>4</sup> sodium triacetoxyborohydride<sup>5</sup> and borohydride exchange resin (BER)<sup>6</sup> were also reported as alternative, less expensive and less

toxic reagents. Using these methods, secondary and tertiary amines are prepared in very good yields; however, primary amines are obtained in poor to moderate yields using cyanoborohydride<sup>1b</sup> or BER.<sup>6</sup> Alternatively primary amines



Scheme 1

are prepared by the reduction of oximes with  $\text{NaBH}_4/\text{NiCl}_2^7$  or  $\text{BER-Ni(OAc)}_2^8$ , however oxime intermediates must first be isolated.

Recently, we have reported that  $\text{BER-Ni(OAc)}_2$  in methanol is also a good reducing system for the synthesis of primary amines by the reductive amination of aldehydes and ketones via hydrazones using  $\text{BER-Ni(OAc)}_2$  in methanol,<sup>9</sup> but a large excess of BER (20 eq) and  $\text{Ni(OAc)}_2$  (1 eq) was needed in this reduction. During these studies, we tried the reductive amination of aldehydes and ketones with phenylhydrazine using  $\text{BER-Ni(OAc)}_2$ .<sup>10</sup> 2-Heptylamine was obtained in 85% yields, but  $\alpha$ -methylbenzylamine was obtained only in 40% yield. In contrast, using  $\text{BER-Pd(OAc)}_2$ , 2-heptylamine was obtained in poor yield (15%), but  $\alpha$ -methylbenzylamine was obtained in 88% yield. Therefore, we decided to study the synthesis of benzylamine derivatives by the reductive amination of aldehydes and ketones via phenylhydrazones using  $\text{BER-Pd(OAc)}_2$ .

We tested fifteen carbonyl compounds to examine the generality of this benzylamine derivative synthesis. The methanol solution of the crude phenylhydrazone, which was prepared from equimolar amounts of the carbonyl compound and phenylhydrazine was treated with BER (5 eq) in methanol for 1 h at room temperature. The BER became black immediately by adding  $\text{Pd(OAc)}_2$  (0.05-0.1 eq) and reacted at 65 °C for 3-6 h. Without the prior reduction with BER, the yields of the primary amines dropped 10-20%, suggesting the prior reduction of carbon-nitrogen double bond is necessary before the cleavage of nitrogen-nitrogen bond by  $\text{BER-Pd}$ .

The results are summarized in Table 1. As shown in Table 1, yields were relatively good compared with other reported data. Benzylamine was obtained in 88% yield using 0.05 eq of  $\text{Pd(OAc)}_2$  (entry 1); while only a 70% yield was obtained by a large amount of BER (20 eq) in the  $\text{BER-Ni(OAc)}_2$  system. In the case of phenyl ketones such as acetophenone, heptanophenone, isobutyrophenone, cyclopentyl phenyl ketone, and *p*-methoxyacetophenone (entries 7-11), the corresponding amines were produced in high yields (88-89%) using 0.1 eq of  $\text{Pd(OAc)}_2$ . For example  $\alpha$ -isopropylbenzylamine was obtained in 88% yield (entry 9), however only 59% yield was obtained using  $\text{NaBH}_3\text{CN}^1$ . In the case of substituted benzaldehydes (entries 2-5), to our surprise, we obtained an about 1:1 mixture of the expected benzylamines and the corresponding toluenes, deaminated products. Fortunately, the desired products, substituted benzylamines, could be obtained in good yields (82-89%), when the reactions were carried out in ethanol. This deamination reaction could be carried out cleanly using a twice amount of  $\text{Pd(OAc)}_2$  (0.1 eq). The two pyridine derivatives tested, 2-pyridinecarboxaldehyde and 4-acetylpyridine, also gave good yields of the corresponding amines (entries 12 and 13). Aliphatic compounds such as hexanal and cy-

**Table 1.** Direct Synthesis of Benzylamine Derivatives from Aldehydes and Ketones via Phenylhydrazones using Borohydride Exchange Resin (BER)- $\text{Pd(OAc)}_2^a$

Entry	Substrate	Product	Time (h) <sup>b</sup>	Yield (%) <sup>c</sup>
1	benzaldehyde	benzylamine	6	88
2	<i>p</i> -acetamidobenzaldehyde	<i>p</i> -acetamidobenzylamine <i>p</i> -acetamidotoluene	3	88 <sup>d</sup> 3 88 <sup>e</sup>
3	<i>p</i> -carbomethoxybenzaldehyde	<i>p</i> -carboethoxybenzylamine <i>p</i> -carbomethoxytoluene	3	89 <sup>d</sup> 3 90 <sup>e</sup>
4	<i>p</i> -dimethylamino benzaldehyde	<i>p</i> -dimethylamino benzylamine <i>p</i> -dimethylaminotoluene	3	88 <sup>d</sup> 3 88 <sup>e</sup>
5	<i>p</i> -cyanobenzaldehyde	<i>p</i> -cyanobenzylamine	6	82 <sup>d</sup>
6	hexanal	hexylamine	3	(40)
7	acetophenone	$\alpha$ -methylbenzylamine	3	88 <sup>e</sup>
8	heptanophenone	$\alpha$ -hexylbenzylamine	3	89 <sup>e</sup>
9	isobutyrophenone	$\alpha$ -isopropylbenzylamine	6	88 <sup>e</sup>
10	cyclopentanophenone	$\alpha$ -cyclopentylbenzylamine	6	88 <sup>e</sup>
11	<i>p</i> -methoxyacetophenone benzylamine	$\alpha$ -methyl- <i>p</i> -methoxy-	3	88 <sup>e</sup>
12	2-pyridinecarboxaldehyde	2-pyridylmethylamine	3	84
13	4-acetylpyridine	1-(4-pyridyl)-ethylamine	3	90 <sup>e</sup>
14	cyclohexanone	cyclohexylamine	3	(10)
15	2-acetylthiophene		3	NR

<sup>a</sup>The corresponding phenylhydrazones (3 mmol), prepared in situ, were reacted with BER (15 mmol) at room temperature for 1 h, and further reacted at 65 °C after the addition of  $\text{Pd(OAc)}_2$  (0.15 mmol) in methanol. <sup>b</sup>Reaction time at 65 °C. <sup>c</sup>Isolated yields. Figures in parenthesis are GC yields. <sup>d</sup>At 78 °C in ethanol. <sup>e</sup> $\text{Pd(OAc)}_2$  (0.3 mmol) was used.

clohexanone gave only poor yields (entries 6 and 14). 2-Acetylthiophene phenylhydrazone was inert to this reducing system (entry 15).

In conclusion, the synthesis of benzylamine derivatives by the present method is a good alternative to the cyanoborohydride method or  $\text{BER-Ni(OAc)}_2$  method which require either expensive and toxic or large amounts of reagents.

## Experimental

**General Procedure.** The synthesis of benzylamine from benzaldehyde is representative. Benzaldehyde phenylhydrazone was prepared from benzaldehyde (0.318 g, 3 mmol) and phenylhydrazine (0.324 g, 3 mmol) by heating in water bath for 1 h,<sup>11</sup> and the crude product was dissolved in methanol (24 mL) without isolation and reacted with BER (5.18 g, 15 mmol) at room temperature. After 1 h, a methanol solution (12 mL) of  $\text{Pd(OAc)}_2$  (0.034 g, 0.15 mmol) was added to the mixture and reacted at 65 °C for 6 h. The resin was removed by filtration, and methanol was evaporated under reduced pressure. The crude residue was chromatographed on a silicagel (eluent 20%  $\text{MeOH/CH}_2\text{Cl}_2$ ) to give the pure benzylamine (0.28 g, 88%).

***p*-Acetamidobenzylamine.** <sup>1</sup>H NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.46 (s, 2H), 2.15 (s, 3H), 3.82 (s, 2H), 7.24 (d, 2H,  $J=8.4\text{Hz}$ ), 7.45 (d, 2H,  $J=8.4\text{Hz}$ ), 7.54 (s, 1H); IR

(neat) 3344, 3257, 1712, 1566, 1290, 767  $\text{cm}^{-1}$ ; MS  $m/z$  (relative intensity) (EI, 70 eV) 164 ( $M^+$ , 15), 163 (8), 149 (0.3), 121 (100), 106 (37), 94 (18), 77 (10); Anal Calcd for  $\text{C}_9\text{H}_{12}\text{ON}_2$ : C, 65.83; H, 7.37; N, 17.06. Found: C, 65.97; H, 7.38; N, 16.78.

**p-Carboethoxybenzylamine.**  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.35 (t, 3H,  $J=7.1$  Hz), 1.66 (s, 2H), 3.89 (s, 2H), 4.33 (q, 2H,  $J=7.1$  Hz), 7.34 (d, 2H,  $J=8.1$  Hz), 7.97 (d, 2H,  $J=8.1$  Hz); IR (neat) 3340, 2949, 1716, 1303, 1149, 738  $\text{cm}^{-1}$ ; MS  $m/z$  (relative intensity) (EI, 70 eV), 179 ( $M^+$ , 4), 178 (15), 150 (45), 134 (35), 133 (23), 132 (19), 123 (7), 106 (100), 105 (29), 89 (18), 79 (18), 77 (19); Anal Calcd for  $\text{C}_{10}\text{H}_{13}\text{O}_2\text{N}$ : C, 67.02; H, 7.31; N, 7.82. Found: C, 67.16; H, 7.15; N, 7.80.

**p-Cyanobenzylamine.**  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.61 (s, 2H), 3.92 (s, 2H), 7.40 (d, 2H,  $J=8.1$  Hz), 7.58 (d, 2H,  $J=8.1$  Hz); IR (neat) 3377, 3304, 2919, 2858, 2232, 1608, 814  $\text{cm}^{-1}$ ; MS  $m/z$  (relative intensity) (EI, 70 eV), 132 ( $M^+$ , 78), 131 (100), 116 (7), 104 (51), 89 (7), 77 (15); Anal Calcd for  $\text{C}_8\text{H}_8\text{N}_2$ : C, 72.71; H, 6.10; N, 21.19. Found: C, 72.82; H, 6.21; N, 20.97.

**1-(4-Pyridyl)-ethylamine.**  $^1\text{H}$  NMR (200 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.36 (d, 3H,  $J=6.6$  Hz), 1.74 (s, 2H), 4.09 (q, 1H,  $J=6.6$  Hz), 7.25 (d, 2H,  $J=5.9$  Hz), 8.51 (d, 2H,  $J=5.9$  Hz); IR (neat) 3319, 2945, 1572, 1394, 921, 848  $\text{cm}^{-1}$ ; MS  $m/z$  (relative intensity) (EI, 70 eV), 122 ( $M^+$ , 1), 121 (3), 108 (7), 107 (100), 80 (23), 78 (7), 51 (13); Anal Calcd for  $\text{C}_7\text{H}_{10}\text{N}_2$ : C, 68.82; H, 8.25; N, 22.93. Found: C, 69.01; H, 8.39; N, 22.60.

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