



Heterogeneous bimetallic Pt–Sn/ γ -Al₂O₃ catalyzed direct synthesis of diamines from N-alkylation of amines with diols through a borrowing hydrogen strategy

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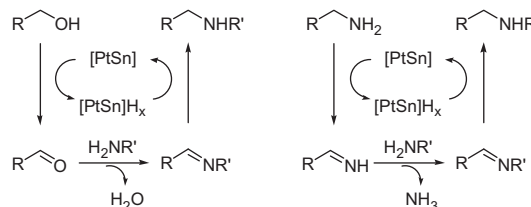
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ABSTRACT

Direct synthesis of diamines has been efficiently realized from the N-alkylation of amines with diols by means of heterogeneous bimetallic Pt–Sn/ γ -Al₂O₃ catalyst (0.5 wt % Pt, molar ratio Pt:Sn = 1:3) through a ‘Borrowing Hydrogen’ strategy under ligand-free conditions. The present methodology provides an environmentally benign route to diamines.

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Amines are a class of important organic compounds and are extensively utilized in organic synthesis and chemical industry.¹ Amination using primary amines and organic halides has been applied as the major method to prepare secondary and tertiary amines, but this method often arouses environmental problems with low selectivity for the desired products. Reductive amination of aldehydes or ketones with amines by using high pressure hydrogen as reductant is another way for this purpose. Recently, transition metal complex-catalyzed direct N-alkylation of amines^{2–4} and ammonia⁵ with alcohols has been reported as an alternative to amines through a ‘Borrowing Hydrogen’ (BH) strategy.² Through such a process, new amines,^{2–5} imines,⁶ and amides⁷ can be produced, and deaminative N-alkylation between two amines may also occur.⁸ Transition metal complex-catalyzed N-alkylation of amines with long-chain diols was occasionally reported.^{3d,7b} However, only very limited work has been directed toward supported catalysts in this area.⁹ Very recently, in the search for a readily available, applicable, and highly active catalyst for a BH process, we found that a heterogeneous bimetallic Pt–Sn/ γ -Al₂O₃ catalyst can be applied for the efficient direct synthesis of secondary and tertiary amines and imines from the reactions of amines with alcohols or between amines.¹⁰ Pt–Sn/ γ -Al₂O₃ has been known as the catalyst for alkane dehydrogenation,¹¹ reforming processes,¹² and hydrogenation¹³ in petroleum industry. Pt@TiO₂ can promote photoirradiation of *o*-arylenediamines in very dilute alcohol solution.^{4e} Primary amines interacted with methanol over γ -Al₂O₃ in the gas phase at >200 °C, yielding an amine mixture.¹⁴ Herein, we report direct synthesis of diamines from the reactions of amines with middle to long-chain diols by using a Pt–Sn/ γ -Al₂O₃ catalyst (0.5 wt % Pt, molar ratio Pt:Sn = 1:3) for the first time (Scheme 1).



Scheme 1. Pt–Sn/ γ -Al₂O₃ catalyzed direct N-alkylation of amines with alcohols and amines through a BH strategy.¹⁰

The reaction of ethylene glycol (**1a**) with aniline (**2a**) in a 1:2 molar ratio was initially conducted at 145 °C in a 15-mL sealed glass tube reactor with Pt–Sn/ γ -Al₂O₃ as catalyst (200 mg, 0.5 mol % Pt) and *o*-xylene as solvent under a nitrogen atmosphere. Over a period of 24 h, the corresponding product diamine **3a** was isolated in 20% yield (Table 1, entry 1), suggesting potential application of the present heterogeneous catalyst in N-alkylation of amines by diols.¹⁵ Thus, short to long-chain diols were investigated in the direct N-alkylation of aniline **2a** (Table 1).¹⁶ With 1,3-propanediol (**1b**) as the alcohol, the desired product **3b** was only collected in a 11% yield and *N*-propylaniline (**4**), the result of monoamination, dehydration, and reduction¹⁷ was obtained in a 28% yield (entry 2). Inter- and intramolecular N-alkylation of **2a** with diols 1,4-butanediol (**1c**) and 1,5-pentanediol (**1d**) occurred to form cyclic tertiary amines **5a** and **5b** in 66–76% yields (entries 3 and 4), respectively. As the carbon-chain was extended to 1,6-hexanediol (**1e**), the reaction of **1e** and **2a** afforded both the diamine product **3c** (21%) and cyclic tertiary amine **5c** (71%) (entry 5), revealing a remarkable effect of the carbon-chain of a diol (entries 1–5). Further extending the carbon-chain of a diol substrate, for example, from C₇ to C₁₂, led to the desired diamine products **3d–h** in excellent yields (87–94%, entries 6–10). The reaction of

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Table 1
Direct synthesis of diamines (**3**) from the reactions of diols (**1**) and aniline (**2a**)^a

$\text{HO}-(\text{CH}_2)_n-\text{OH} + 2 \text{PhNH}_2 \xrightarrow[\text{-H}_2\text{O}]{\text{Pt-Sn}/\gamma\text{-Al}_2\text{O}_3} \text{PhHN}-(\text{CH}_2)_n-\text{NHPH} \quad (1)$		
Entry	Diol (1)	Product ^b (%)
1	1a	3a (18)
2	1b	3b (11)
	1c	4 (28)
3	1d	5a (66)
4	1e	5b (76)
5	1f	3c (21)
	1k	5c (71)
6	1g	3d (89)
7	1h	3e (87)
8	1i	3f (88)
9	1j	3g (91)
10	1k	3h (94)
11	1l	3i (79)
12	1m	3j (93)
13	1n	3k (50)
14	1o	3l (20)
15	1p	3m (29)

^a Reaction conditions: diol **1**, 1.0 mmol; amine **2a**, 2.0 mmol; Pt-Sn/ γ -Al₂O₃ catalyst, 200 mg (0.5 mol % Pt); *o*-xylene, 5 mL; 0.1 MPa N₂ atmosphere, 145 °C, 24 h.

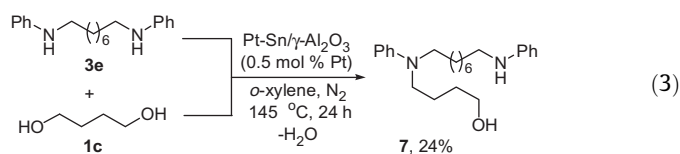
^b Isolated yields.

1,4-cyclohexanediol (**1k**) reacted with **2a** formed diamine **3i** (79%), while N-alkylation of **2a** by diol **1l** with a longer chain produced diamine product **3j** in an excellent yield (93%) (entries 11 and 12). Using *O*-tethered diol **1m**, only the monoamination product **3k** was isolated in a moderate yield (50%), and increasing the number of tethering oxygen atoms lessened the reaction efficiency (entries 13–15), which is presumably attributed to multiple coordination of the tethering oxygen atoms to the catalytically active Pt metal center, reducing the catalyst activity.

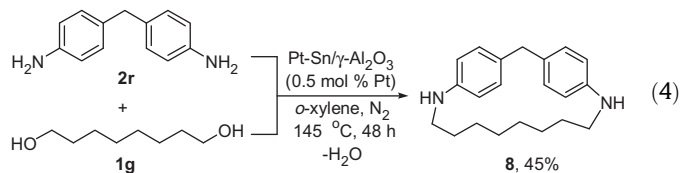
The successful N-alkylation of aniline **2a** with middle to long-chain diols has revealed that the present Pt-Sn/ γ -Al₂O₃ catalyst is very efficient for the direct synthesis of diamines (Table 1). Next, N-alkylation of diverse amines **2** with 1,8-octanediol (**1g**) was

investigated to probe into the protocol generality (Table 2). Methyl-substituted anilines **2b–e** efficiently reacted with **1g** to afford the desired products, that is, diamines **3n–q** in 87–91% yields (Table 2, entries 1–4), while the corresponding chloro-substituted anilines **2f–i** reacted less efficiently to form diamines **3r–u** in low yields (7–20%) with monoamination products **3r'–u'** (55–61%) as the major products (entries 5–8), suggesting an obvious electronic effect of the substituents from amines **2**. However, the reaction of 4-fluoroaniline (**2j**) gave diamine **3v** in a good yield (79%, entry 9). Naphthylamine (**2k**) was also efficiently alkylated by **1g** (entry 10). The reaction of 3-aminopyridine (**2l**) gave the mono- and diamination products in 47% and 24% yields, respectively, while 2-aminopyridine did not undergo the same reaction (entry 11). N-Alkylation of secondary amine *N*-methylaniline (**2m**) formed the monoamination product **3y'** (55%) as the major product with the desired diamine **3y** (17%) as the minor product, revealing a steric/electronic effect from the amine substrate (entry 12). Aliphatic long-chain primary amine, for example, 1-hexylamine (**2n**), made the reaction complicated, while benzylamine (**2o**) underwent deaminative self-coupling to afford dibenzylamine **6** (54%) which reacted less efficiently with **1g** to give the desired product **3z** (18%) (entries 13–15). Cyclic secondary amine piperidine (**2p**) behaved more efficiently than **6** to afford both the desired and monoamination products **3z1** (31%) and **3z1'** (40%), whereas the reaction of morpholine (**2q**) produced the desired product **3z2** in an 84% yield, suggesting that the ether oxygen atom obviously increases the reactivity of amine **2q** (entries 16 and 17).

In order to explore the double N-alkylation of a diamine with a diol, the 1:1 molar ratio reaction of di(secondary amine) **3e** with diol **1c** was carried out under the standard

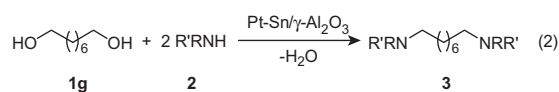


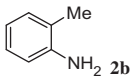
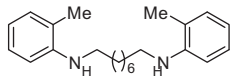
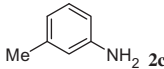
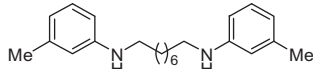
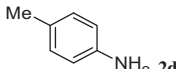
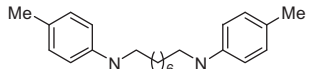
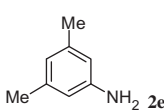
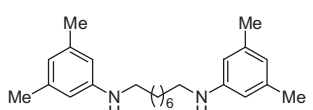
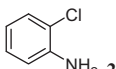
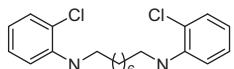
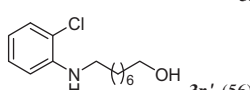
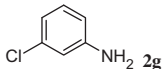
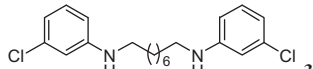
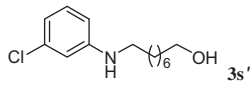
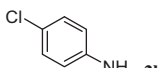
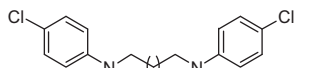
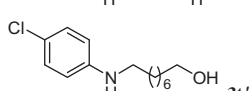
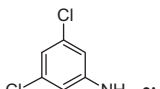
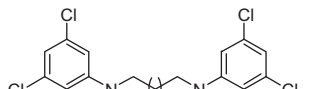
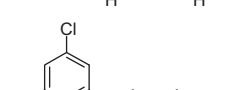
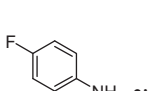
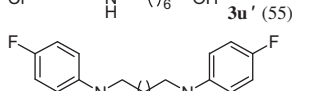
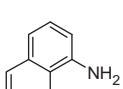
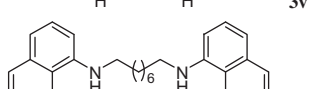
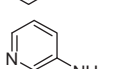
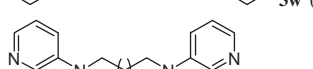
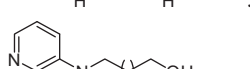
reaction conditions (Eq. 3). Over a period of 24 h, the monoamination product **7** was obtained in 24% yield and subsequent intramolecular cyclization of **7** did not occur. When a di(primary amine), that is, **2r**, was applied in the reaction with diol **1g**, inter- and intramolecular N-alkylation successively underwent to form the cyclization product **8**¹⁸ (45%) (Eq. 4), further revealing that di(primary amine) is more reactive than its secondary analogue. This method can provide an easy access to macrocyclic diamines.



Recycling the catalyst was carried out in the N-alkylation of aniline **2a** with 1,7-heptanediol (**1f**) under the standard conditions shown in Tables 1 and 2. The catalyst was easily recycled by centrifugation and did not lose activity during the first three run reactions, while in the fourth run reaction its catalytic activity was reduced by about 25%. Analysis of the supernatant from each-run reaction mixture by ICP-AES technology revealed no Pt metal leaching into the liquid phase. Decrease of the catalytic activity is presumably attributed to the aggregation of Pt metal particles on γ -Al₂O₃ support during the catalyst reuse.

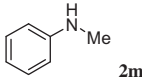
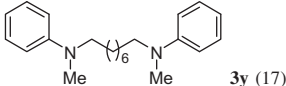
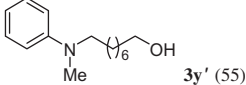
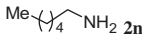
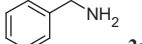
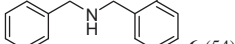
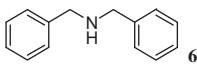
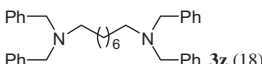
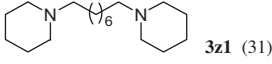
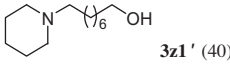
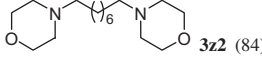
In summary, we have developed an efficient protocol to synthesize diamines from the direct N-alkylation of amines with middle to long-chain diols with heterogeneous bimetallic Pt-Sn/ γ -Al₂O₃ catalyst through a Hydrogen Borrowing strategy. That the catalyst

Table 2Direct synthesis of diamines (**3**) from the reactions of 1,8-octanediol (**1g**) and amines (**2**)^a

Entry	Amine (2)	Diamine 3 ^b (%)
1	 2b	 3n (90)
2	 2c	 3o (91)
3	 2d	 3p (87)
4	 2e	 3q (90)
5	 2f	 3r (19)
		 3r' (56)
6	 2g	 3s (20)
		 3s' (60)
7	 2h	 3t (9)
		 3t' (61)
8	 2i	 3u (7)
		 3u' (55)
9	 2j	 3v (79)
10	 2k	 3w (72)
11	 2l	 3x (47)
		 3x' (24)

(continued on next page)

Table 2 (continued)

Entry	Amine (2)	Diamine 3 ^b (%)
12	 2m	 3y (17)  3y' (55)
13	 2n	Complicated
14	 2o	 6 (54)
15	 6	 3z (18)
16	 2p	 3z1 (31)  3z1' (40)
17	 2q	 3z2 (84)

^a Reaction conditions: diol **1g**, 1.0 mmol; amine **2**, 2.0 mmol; Pt–Sn/ γ -Al₂O₃ catalyst, 200 mg (0.5 mol % Pt); *o*-xylene, 5 mL; 0.1 MPa N₂ atmosphere, 145 °C, 24 h.

^b Isolated yields.

is recyclable and the procedure is environmentally benign and ligand-free is the feature of the methodology.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.tetlet.2011.10.100](https://doi.org/10.1016/j.tetlet.2011.10.100).

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- A general procedure for the direct synthesis of diamines **3** from the N-alkylation of amines **2** with diols **1**: Under nitrogen atmosphere, to a 15-mL Pyrex glass screw-cap tube were added diol **1** (1.0 mmol), amine **2** (2.0 mmol), Pt–Sn/ γ -Al₂O₃ catalyst (200 mg, 0.5 mol % Pt), and *o*-xylene (5 mL). The resultant mixture was stirred in the sealed tube at 145 °C for 24 h. After cooled to ambient temperature, the catalyst was removed by centrifugation and washed with CH₂Cl₂ (3 × 5 mL). The combined supernatant was condensed under reduced pressure and subjected to purification by silica gel

- column chromatography (eluent: petroleum ether (60–90 °C)/EtOAc = 20:1, v/v), affording diamine **3**. The known compounds were identified by comparison of their NMR features with the reported data or of their GC traces with those of the authentic samples. The spectroscopic features of these known compounds are in good agreement with those reported in the literatures. All the new products were characterized by NMR and HRMS techniques.
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18. **Compound 8**: ^1H NMR (CDCl_3 , 400 MHz, 23 °C) δ 6.97 and 6.54 (d each, 4:4H, J = 8.3 Hz, aromatic CH), 3.78 (s, 2H, ArCH_2Ar), 3.47 (br, 2H, $2 \times \text{NH}$), 3.08 (t, 4H, $2 \times \text{NCH}_2$), 1.59 and 1.28 (m each, 4:8 H, $6 \times \text{CH}_2$); $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3 , 100 MHz, 23 °C) δ 146.7 (Cq, HN–C), 130.8 (Cq, C_6H_4), 129.7 and 112.9 (aromatic CH), 44.4 (HN– CH_2), 40.2 (ArCH_2Ar), 29.7, 29.5 and 27.2 ($6 \times \text{CH}_2$). HRMS calcd for $\text{C}_{21}\text{H}_{28}\text{N}_2$: 308.2252; found: 308.2252.