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Chemoselective hydrogenation of nitrobenzyl ethers to aminobenzyl ethers catalyzed by palladium–nickel bimetallic nanoparticles

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ABSTRACT

A highly efficient and chemoselective hydrogenation of nitrobenzyl ethers to aminobenzyl ethers was developed by using a novel palladium–nickel bimetallic nanocatalyst. Since the catalytic selectivity was resulted from the synergistic effects between two metals rather than the traditional catalyst poisons, the hydrogenation proceeded smoothly under additive-free conditions. Thus, the work-up procedure was as simple as to recover the catalyst by a magnetic separation and then to evaporate the solvent.

1. Introduction

In the past decade, the compounds containing the subunit of aminobenzyl ether **1** have been found as important applications in organic synthesis, drug discovery and material sciences. As shown in Fig. 1, iteamine (*o*-aminobenzyl β-D-glucopyranoside) is a natural product isolated recently from *itea virginica*.[1] The compound SB1578 (as a potent inhibitor of JAK2/FLT3 at phase I clinical trials) is developed for the treatment of rheumatoid arthritis.[2] 3,5-Bis(methoxymethyl)-aniline is a main building block for the synthesis of the cationic dendrons in the discovery of dye-sensitized solar cells.[3]

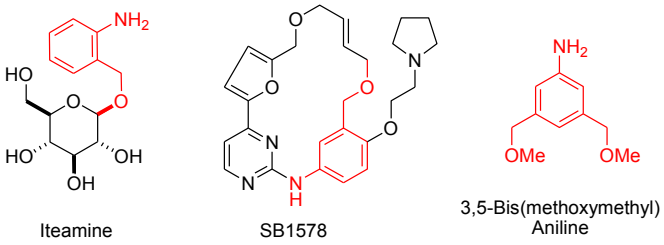
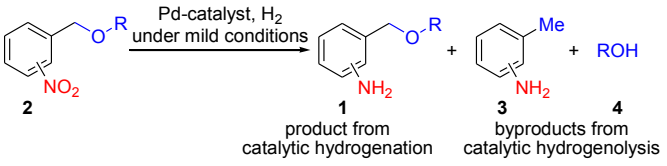


Fig. 1. Some important aminobenzyl ethers.

In literature, aminobenzyl ethers **1** are routinely synthesized by chemoselective reduction of the corresponding nitrobenzyl ethers **2**. Investigation showed that Pd-catalyzed hydrogenation is the most efficient, convenient and clean method to convert nitrobenzenes into anilines in laboratories.[4] But, the most often used methods for the transformation of **2** to **1** are catalytic transfer hydrogenation[5] and dissolving metal reduction.[6] As shown in Scheme 1, this situation was caused by the fact that Pd-catalysts also have a strong ability to catalyze the hydrogenolysis[7] of benzyl ethers under similar conditions for the hydrogenation of nitrobenzene. Thus, low chemoselectivity and efficiency were obtained often in the Pd-catalyzed hydrogenation of nitrobenzyl ethers **2**.[8]



Scheme 1. Pd-catalyzed hydrogenation and hydrogenolysis.

Herein, we would like to report a novel palladium–nickel bimetallic nanocatalyst, by which highly chemoselective and efficient hydrogenation of **2** to **1** was achieved under room temperature and atmospheric pressure.

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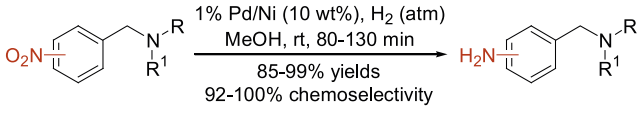
0040-4020/

2. Results and discussion

In routine organic synthesis, Pd-catalyzed hydrogenolysis of benzyl ethers is so efficient that it is a major method for O-debenzylation when benzyl ether served as a protective group for alcohols or phenols.[9] Therefore, much less attention was paid to inhibit this transformation in literature. In a few methods that dealt specifically with this purpose,[10] amines were used as poisons for the Pd-catalysts with two characteristics: (a) aliphatic amines were suitable poisons, but aromatic amines were not; (b) the hydrogenolysis of alkyl benzyl ethers could be inhibited, but aryl benzyl ethers could not. Therefore, it is necessary to develop new catalysts and general processes for the chemoselective hydrogenation of **2** to **1**.

In recent years, the catalytic applications of bimetallic nanoparticles have made great progress.[11] Since the formation of heteromeltallic bonds and the changes of average metal–metal bond lengths, bimetallic nanoparticles have typically shown different electronic effect (or ligand effect) and geometric effect (or strain effect) from their parent metals. In our recent work,[12a] a novel 1% Pd/Ni (containing 1 wt % of Pd) bimetallic nanoparticle was prepared by simply boiling the mixture of Na_2PdCl_4 and Raney-Ni in water. As shown in Scheme 2, when it was used as a catalyst, nitrobenzylamine was chemoselectively hydrogenated to the corresponding aminobenzylamine based on its synergistic effects.



Scheme 2. Chemoselective hydrogenation of nitrobenzylamines.

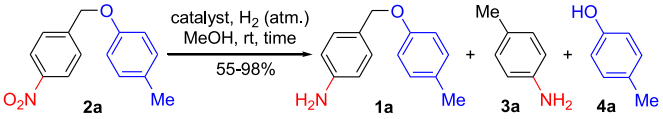
Thus, we were encouraged to test further the catalytic selectivity of this Pd/Ni bimetallic nanocatalyst in the hydrogenation of nitrobenzyl ethers. As shown in Table 1, 4-methylphenyl 4-nitrobenzyl ether (**2a**) was chosen as a model substrate due to the fact that phenyl benzyl ether is highly sensitive to Pd-catalyzed hydrogenolysis. Under room temperature and atmospheric pressure, the desired product **1a** was obtained in 71% yield and 75% chemoselectivity over Pd/C catalyst (entry 1). By using Raney-Ni as a catalyst, the hydrogenation stopped automatically within 3 h to give **1a** in 55% yield with recovery of **2a** in 41% yield (entry 2). However, **1a** was obtained in 93% yield and 95% chemoselectivity in the presence of 50 wt % of the Pd/Ni bimetallic catalyst (entry 3). Much higher chemoselectivity was achieved even though the amount of palladium metal (net weight) in entry 3 was used more than that in entry 1. To our delight, quantitative yield and chemoselectivity of **1a** were obtained in the presence of 30 wt % of Pd/Ni bimetallic catalyst (entry 4). The results in entries 5–8 indicated that the chemoselectivity was not influenced by using lower ratios of Pd/Ni bimetallic catalyst, but the conversion was decreased and prolonged times were required. However, these problems can be solved easily by increasing the hydrogen pressure a little.

As shown in Table 2, the catalytic activity of the Pd/Ni bimetallic catalyst was influenced significantly by the reaction solvents. The all tested alcohols proved to be excellent solvents for this hydrogenation (entries 1–3) and MeOH was the best one (entry 1). We interestingly observed that the Pd/Ni bimetallic nanoparticles were all attracted to the surface of the standing magnetic stirring bar in the alcohol solvents. After the magnetic stirring bar was spinning, the nanoparticles were dispersed fully into the alcohol solvents. However, only parts of nanoparticles were dispersed into the non-alcohol solvents (entries 4–7) and most of them were still attracted to the surface of the spinning magnetic stirring bar.

Since nickel metal is ferromagnetic, the Pd/Ni bimetallic nanoparticles could be recovered conveniently by use of a magnetic stirring bar (a magnetic separation) in work-up procedure and reused in the subsequent rounds. As shown in Table 3, a recycling study shows that the catalytic activity of the Pd/Ni bimetallic catalyst decreased steadily (entries 1–4). Although the chemoselectivity was not influenced in the fourth round, the conversion could not be completed even prolonged reaction time was used (entry 4). These results may be caused by the fact that some of palladium metals were peeled off from the surface of the Pd/Ni bimetallic nanoparticles in each round. Thus, they were converted from 'the magnetic palladium' into 'the non-magnetic palladium' and were lost in the work-up procedures by a magnetic separation. The ICP analyses of the catalyst after fourth round also showed that the percentage of palladium is 0.74%, which gave a strong support to our hypothesis.

Finally, the scope was tested by using different substrates as shown in Scheme 3. Although the aryl benzyl ethers (R=aryl) were extremely sensitive to hydrogenolysis, excellent yields and chemoselectivity were obtained for the conversion of **2a**–**2j** into **1a**–**1j**. No influence was observed for the substituted position of the nitro-group on the benzene ring (**1a**–**1c**). It seemed that the

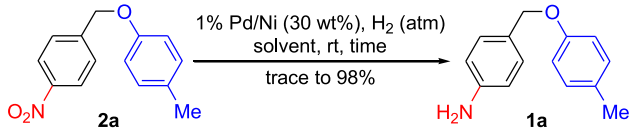
Table 1
Hydrogenations of **2a** by using different catalysts[a]



Entry	Catalyst (wt %)	Net weight of metal (mg)	Pressure (psi)	Time (h)[b]	Yield of **1a** (%)[c]	Selectivity of **1a** (%)[d]
1	5% Pd/C (5)	Pd (0.61)	—	1	71	75
2	Raney-Ni (50)	Ni (122)	—	3	55	100
3	1% Pd/Ni (50)	Pd (1.22), Ni (122)	—	1	93	95
4	1% Pd/Ni (30)	Pd (0.73), Ni (73)	—	1.5	98	100
5	1% Pd/Ni (20)	Pd (0.49), Ni (49)	—	4.5	91	100
6[e]	1% Pd/Ni (20)	Pd (0.49), Ni (49)	45	4.5	98	100
7[e]	1% Pd/Ni (10)	Pd (0.24), Ni (24)	45	6	90	100
8[e]	1% Pd/Ni (10)	Pd (0.24), Ni (24)	90	6	98	100

[a] A mixture of **2a** (1 mmol) and catalyst in MeOH (10 mL) was stirred under H_2 at room temperature and atmospheric pressure (on an atmospheric pressure hydrogenation apparatus).
[b] The time is when the absorption of hydrogen ceased automatically except for the hydrogenation in entry 1.
[c] Isolated yield was obtained.
[d] It was determined by ^1H NMR spectra of the crude products.
[e] The experiments proceeded on a Parr-hydrogenator.

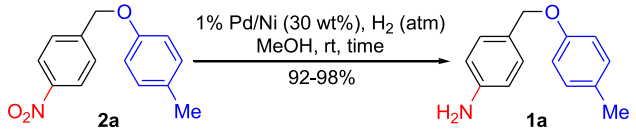
Table 2
Effect of the solvents on the hydrogenations of **2a**[a]



Entry	Solvent	Time (h)[b]	Yield of **1a** (%)[c]
1	MeOH	1.5	98
2	EtOH	2.1	97
3	i-PrOH	3.1	92
4	EtOAc	7	85
5	THF	10	80
6	Cyclohexane	3	Trace
7	Toluene	3	Trace

[a] A mixture of **2a** (1 mmol) and Pd/Ni bimetallic catalyst in MeOH (10 mL) was stirred under H_2 at room temperature and atmospheric pressure (on an atmospheric pressure hydrogenation apparatus).
[b] The time was when the absorption of hydrogen ceased automatically.
[c] Isolated yield was obtained.

Table 3
Recycling study of the Pd/Ni bimetallic catalyst[a]

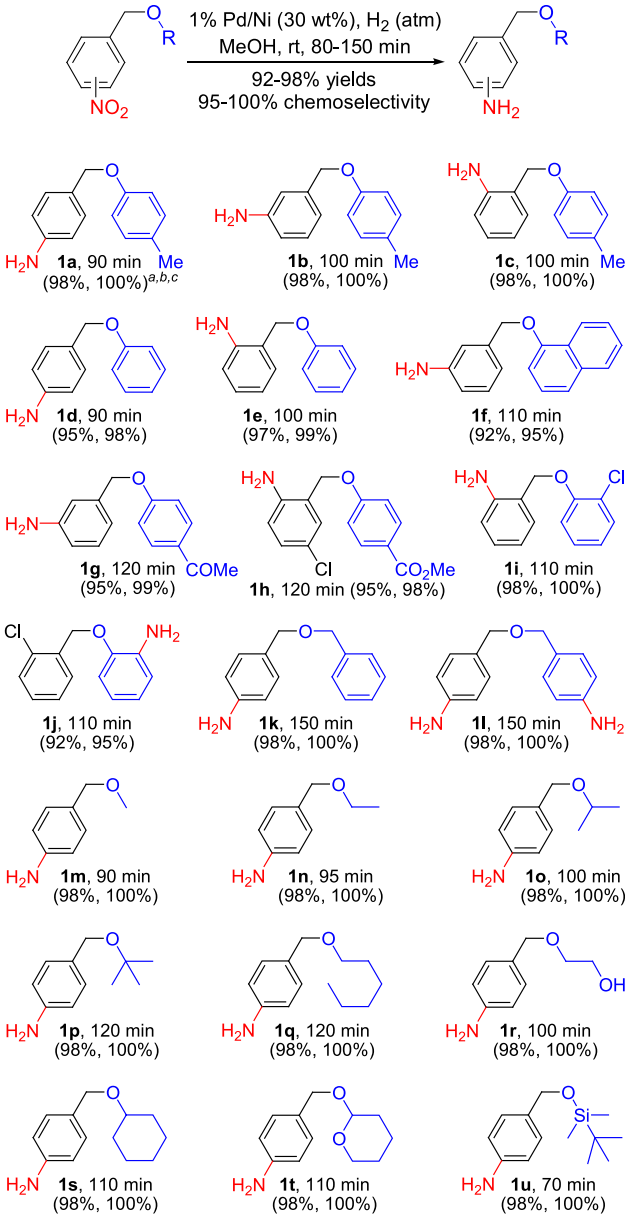


Recycle times	Time (h)[b]	Yield of **1a** (%)[c]
1	1.5	98
2	3.5	97
3	7.5	95
4	15	92[d]

[a] A mixture of **2a** (1 mmol) and Pd/Ni bimetallic catalyst in MeOH (10 mL) was stirred under H_2 at room temperature and atmospheric pressure (on an atmospheric pressure hydrogenation apparatus).
[b] The time was when the absorption of hydrogen ceased automatically.
[c] Isolated yield was obtained.
[d] Only **1a** and **2a** were detected in the reaction mixture.

chemoselectivity could be influenced by the aryl group size (**1d**–**1f**). Since the hydrogenation proceeded under neutral conditions, the ketone and ester groups survived well (**1g**–**1h**) during the hydrogenation. As was expected, all tested alkyl benzyl ethers gave quantitative yield and chemoselectivity (**1k**-**1u**). It is well-known that the *tert*-butyl ether (**1p**), tetrahydropyranyl ether (**1t**), and TBDMS ether (**1u**) are very sensitive to acidic or basic conditions, but they remained intact throughout because the hydrogenation proceeded under additive-free conditions.

When this method was performed at a 5-g scale under the standard conditions, **2a** was hydrogenated into **1a** in 90% yield within 10 h. However, the same reaction gave **1a** in 98% yield within 2 h under 60 psi hydrogen pressures, which can be easily performed on a Parr-hydrogenator.



[a] The numbers in the parathesis are the yield and the chemoselctivity, respectively.
[b] Separated yield is obtained. [c] Chemoselectivity is determined by ^{1}H NMR spectra.

Scheme 3. Scope of the method.

3. Conclusion

A general method for highly efficient and chemoselective hydrogenation of nitrobenzyl ethers into aminobenzyl ethers were developed by using a novel Pd/Ni bimetallic catalyst. This work provides further examples to prove that our Pd/Ni bimetallic nanoparticles are a reliable catalyst to reduce or stop the hydrogenolysis risks of the benzyl-heteroatom bonds in catalytic hydrogenations. Since the catalytic selectivity came from the synergistic effects of the Pd/Ni bimetallic catalyst rather than from the catalytic poisons, no additive was added into the reaction systems except the catalyst and the substance. The work-up procedure was as simple as to recover the catalyst by a magnetic separation and then to evaporate the solvent.

4. Experimental section

4.1. General information

All melting points were determined on a Yanaco melting point apparatus and were uncorrected. IR spectra were recorded as KBr pellets on a Nicolet FTIR 5DX spectrometer. All spectra of ^{1}H NMR and ^{13}C NMR were recorded on a JEOL JNM-ECA 300 or 400 spectrometers in $CDCl_3$ and TMS was used as an internal reference. HRMS were obtained on a Bruker micrOTOF-Q II spectrometer. The 1% Pd/Ni bimetallic catalyst was prepared by our previous procedure.[12a]

4.2. Typical procedure for hydrogenation of 4-methylphenyl 4-nitrobenzyl ether (2a) to 4-methylphenyl 4-aminobenzyl ether (1a)

A mixture of **2a** (243 mg, 1 mmol) and 1% Pd/Ni bimetallic catalyst (73 mg, 30 wt %) in MeOH (10 mL) was stirred under H_2 at room temperature and atmospheric pressure (on an atmospheric pressure hydrogenation apparatus) until the absorption of hydrogen ceased (90 min). After the catalyst was removed off by a magnetic stirring bar, the solution was evaporated on a rotavapor to give the product **1a** as yellowish oil (210 mg, 98%), which is pure enough for ^{1}H and ^{13}C NMR determinations. IR (KBr) ν 3372, 1623, 1519, 1233 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.26–7.20 (m, 2H), 7.06 (d, 2H, J=11.0 Hz), 6.87 (d, 2H, J=11.0 Hz), 6.69 (d, 2H, J=11.0 Hz), 4.90 (s, 2H), 3.69 (s, 2H), 2.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.8, 146.3, 129.7 (2C), 126.8, 115.0 (2C), 114.6 (2C), 70.1, 20.4. HRMS (ESI-TOF) (m/z): calcd for $C_{14}H_{15}NO$, $[M+Na]^+$: 236.1046, found: 236.1044.

The similar procedure was used for the chemoselective hydrogenation of **2b**–**2u** to **1b**–**1u**. In some cases, flash chromatography was required for the purification of the products.

4.3. 4-Methylphenyl 3-aminobenzyl ether (1b)

Yellowish oil. IR (KBr) ν 3304, 1607, 1510, 1239 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.15–7.05 (m, 3H), 6.87–6.76 (m, 5H), 4.95 (s, 2H), 3.67 (s, 2H), 2.28 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.7, 146.6, 138.5, 130.0 (2C), 129.9, 129.5, 117.5, 114.7 (2C), 114.6, 113.9, 70.0, 20.5. HRMS (ESI-TOF) (m/z): calcd for $C_{14}H_{15}NO$, $[M+H]^+$: 214.1226, found: 214.1227.

4.4. 4-Methylphenyl 2-aminobenzyl ether (1c)

Yellowish oil. IR (KBr) ν 3395, 1616, 1484, 1277 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.19–7.07 (m, 4H), 6.95–6.86 (m, 2H), 6.80–6.70 (m, 2H), 5.00 (s, 2H), 4.09 (s, 2H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.2, 145.8, 130.2, 129.8 (3C), 129.4, 121.2, 118.2, 116.0, 114.6 (2C), 69.1, 20.3. HRMS (ESI-TOF) (m/z): calcd for $C_{14}H_{15}NO$, $[M+H]^+$: 214.1226, found: 214.1228.

4.5. Phenyl 4-aminobenzyl ether (1d)

Yellowish oil.[13a] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28–7.21 (m, 4H), 6.98–6.95 (m, 3H), 6.70–6.67 (m, 2H), 4.92 (s, 2H), 3.69 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.9, 146.3, 129.3 (2C), 129.3 (2C), 126.6, 120.6, 114.9 (2C), 114.7 (2C), 69.9.

4.6. Phenyl 2-aminobenzyl ether (1e)

Yellowish oil.[13b] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30–7.25 (m, 4H), 7.02–6.99 (m, 3H), 6.80–6.70 (m, 2H), 5.03 (s, 2H), 4.06 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.3, 146.1, 130.1, 129.7, 129.4 (2C), 121.1, 120.1, 118.2, 116.0, 114.8 (2C), 69.0.

4.7. 1-Naphthyl 3-aminobenzyl ether (1f)

Yellowish oil.[13c] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.37–8.34 (m, 1H), 7.81–7.80 (m, 1H), 7.54–7.16 (m, 5H), 6.95–6.85 (m, 3H), 6.69–6.65 (m, 1H), 5.17 (s, 2H), 3.70 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 154.3, 146.5, 138.1, 134.3, 129.3, 127.3, 126.3, 125.7, 125.5, 125.0, 122.0, 120.2, 117.1, 114.4, 113.6, 105.0, 69.8.

4.8. 4-Acetophenyl 3-aminobenzyl ether (1g)

Yellowish solid, mp 152–153 °C (lit.[13d] mp 153–154 °C). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.94–7.91 (m, 2H), 7.17–7.14 (m, 1H), 7.01–6.98 (m, 2H), 6.80–6.75 (m, 3H), 5.04 (s, 2H), 3.71 (s, 2H), 2.55 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 196.8, 162.6, 146.7, 137.3, 130.5 (2C), 130.3, 129.5, 117.3, 114.8, 114.4 (2C), 113.7, 70.0, 26.2.

4.9. 4-Methoxycarbonylphenyl 5-chloro-2-aminobenzyl ether (1h)

Yellowish oil.[13e] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.02–7.99 (m, 2H), 7.19–6.98 (m, 4H), 6.67–6.64 (m, 1H), 5.02 (s, 2H), 4.01 (s, 2H), 3.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.6, 161.7, 144.4, 131.5 (2C), 129.6, 129.5, 123.2, 122.7, 121.6, 117.3, 114.3 (2C), 68.3, 51.8.

4.10. 2-Chlorophenyl 2-aminobenzyl ether (1i)

Yellowish oil. IR (KBr) ν 3442, 1622, 1511, 1235 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.73–7.27 (m, 8H), 5.14 (s, 2H), 4.25 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 153.6, 146.5, 130.3, 130.1, 129.9, 127.6, 123.2, 121.9, 120.4, 118.1, 116.3, 114.3, 70.4. HRMS (ESI-TOF) (m/z): calcd for $C_{13}H_{12}ClNO$, $[M+H]^+$: 234.0680, found: 234.0676.

4.11. 2-Aminophenyl 2-chlorobenzyl ether (1j)

Yellowish oil.[13f] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.58–7.51 (m, 1H), 7.42–7.38 (m, 1H), 7.30–7.26 (m, 2H), 6.88–6.68 (m, 4H), 5.19 (s, 2H), 3.85 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.1, 136.6, 134.8, 132.8, 129.4, 129.0, 128.9, 126.9, 121.8, 118.4, 115.3, 112.3, 67.7.

4.12. Benzyl 4-aminobenzyl ether (1k)

Yellowish oil.[13g] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36–7.24 (m, 5H), 7.15–7.14 (m, 2H), 6.65–6.64 (m, 2H), 4.50 (s, 2H), 4.40 (s, 2H), 3.65 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.4, 138.3, 129.4, 129.1 (2C), 128.1 (2C), 127.6 (2C), 127.3 (2C), 115.1, 71.8, 71.4.

4.13. Di(4-aminobenzyl) ether (1l)

Yellowish solid, mp 189–190 °C (lit.[5c] mp 189–190 °C); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.13 (d, 4H, J=12.0 Hz), 6.65 (d, 4H, J=12.4 Hz), 4.39 (s, 4H), 3.65 (s, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.9 (2C), 129.5 (4C), 128.3 (2C), 114.9 (4C), 71.4 (2C).

4.14. Methyl 4-aminobenzyl ether (1m)

Yellowish oil.[13h] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.12 (d, 2H, J=12.0 Hz), 6.65 (d, 2H, J=12.4 Hz), 4.33 (s, 2H), 3.65 (s, 2H), 3.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.0, 129.4 (2C), 128.0, 114.9 (2C), 74.6, 57.6.

4.15. Ethyl 4-aminobenzyl ether (1n)

Yellowish oil. IR (KBr) ν 2973, 1625, 1518, 1284 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.13 (d, 2H, J=8.91 Hz), 6.65 (d, 2H, J=8.94 Hz), 4.37 (s, 2H), 3.64 (s, 2H), 3.50 (q, 2H, J=7.2 Hz), 1.21 (t, 3H, J=6.87 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.9, 129.3 (2C), 128.4, 114.9 (2C), 72.6, 65.1, 15.2. HRMS (ESI-TOF) (m/z): calcd for $C_9H_{13}NO$, $[M+H]^+$: 152.1070; found: 152.1075.

4.16. Isopropanyl 4-aminobenzyl ether (1o)

Yellowish oil. IR (KBr) ν 2971, 1627, 1519, 1374 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.13 (d, 2H, J=8.22 Hz), 6.65 (d, 2H, J=8.25 Hz), 4.38 (s, 2H), 3.64–3.69 (m, 1H), 1.18 (d, 6H, J=6.18 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.8, 129.1 (2C), 128.9, 114.9 (2C), 70.2, 69.8, 22.1 (2C). HRMS (ESI-TOF) (m/z): calcd for $C_{10}H_{15}NO$, $[M+Na]^+$: 188.1046; found: 188.1047.

4.17. *tert*-Butyl 4-aminobenzyl ether (1p)

Yellowish oil. IR (KBr) ν 2931, 1629, 1519, 1374 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.13 (d, 2H, J=11.0 Hz), 6.64 (d, 2H, J=11.4 Hz), 4.31 (s, 2H), 3.59 (s, 2H), 1.27 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.5, 129.8, 128.9 (2C), 115.0 (2C), 73.1, 64.0, 27.7 (3C). HRMS (ESI-TOF) (m/z): calcd for $C_{11}H_{17}NO$, $[M+Na]^+$ 202.1202; found 202.1203.

4.18. *n*-Hexyl 4-aminobenzyl ether (1q)

Yellowish oil. IR (KBr) ν 2930, 1624, 1518, 1374 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.13 (d, 2H, J=11.36 Hz), 6.64 (d, 2H, J=11.44 Hz), 4.37 (s, 2H), 3.64 (s, 2H), 3.41 (t, 2H, J=8.68 Hz), 1.60–1.28 (m, 8H), 0.88 (t, 3H, J=9.16 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.9, 129.3 (2C), 128.5, 114.9 (2C), 72.7, 70.0, 31.7, 29.7, 25.8, 22.6, 14.0. HRMS (ESI-TOF) (m/z): calcd for $C_{13}H_{21}NO$, $[M+Na]^+$ 230.1515; found: 230.1518.

4.19. 2-Hydroxyethyl 2-aminobenzyl ether (1r)

Yellow oil.[8c] ^1H NMR ($CDCl_3$, 300 MHz) δ 7.13 (d, 2H, J=8.25 Hz), 6.66 (d, 2H, J=8.25 Hz), 4.44 (s, 2H), 3.73 (t, 2H, J=4.20 Hz), 3.73 (t, 2H, J=4.80 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.1, 129.4 (2C), 127.6, 114.9 (2C), 73.0, 70.8, 61.6.

4.20. Cyclohexyl 4-aminobenzyl ether (1s)

Yellow oil. IR (KBr) ν 2930, 1624, 1517, 1374 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.13 (d, 2H, J=11.0 Hz), 6.64 (d, 2H, J=11.4 Hz), 4.42 (s, 2H), 3.62 (s, 2H), 3.34–3.29 (m, 1H), 1.20–1.99 (m, 10H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.7, 129.0 (3C), 114.9 (2C), 76.3, 69.4, 32.2 (2C), 25.8, 24.1 (2C). HRMS (ESI-TOF) (m/z): calcd for $C_{13}H_{19}NO$, $[M+Na]^+$ 228.1359; found: 228.1356.

4.21. Tetrahydro-2*H*-pyran-4-yl 4-aminobenzyl ether (1t)

Yellow oil.[13i] ^1H NMR ($CDCl_3$, 300 MHz) δ 7.16 (d, 2H, J=8.25 Hz), 6.65 (d, 2H, J=8.24 Hz), 4.68–4.64 (m, 2H), 4.40–4.36 (m, 1H), 3.93–3.90 (m, 1H), 3.65 (s, 2H), 3.51–3.55 (m, 1H), 1.61–1.52 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 145.9, 129.5 (2C), 127.8, 114.8 (2C), 97.1, 68.6, 62.0, 30.5, 25.4, 19.3.

4.22. *tert*-Butyldimethylsily 4-aminobenzyl ether (1u)

Yellow oil.[13j] ^1H NMR ($CDCl_3$, 300 MHz) δ 7.11 (d, 2H, J=8.25 Hz), 6.64 (d, 2H, J=8.25 Hz), 4.61 (s, 2H), 3.60 (s, 2H), 0.92 (s, 9H), 0.07 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 145.3, 131.4, 127.6 (2C), 114.9 (2C), 65.0, 25.9 (3C), 18.4, −5.18 (2C).

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.10.037.

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