

On-column reduction of aldehyde with diMe-Imd-BH₃: simultaneous reaction and purification by flash chromatography

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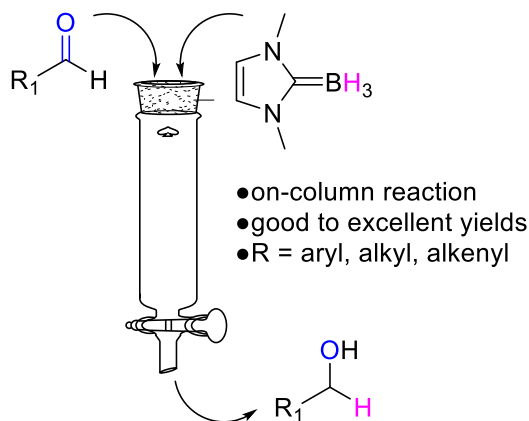
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Abstract

In this study, an on-column reduction of aldehydes using 1,3-dimethylimidazol-2-ylidene trihydroborate is described. The aldehyde and the reductant were mixed prior to loading onto a column packed with silica gel. Upon elution, the corresponding alcohol was obtained in good to excellent yield, while the unreacted reductant was recovered. This approach combines reaction and purification into a single process. Owing to the stability of the reductant and the simplicity of the procedure, this protocol represents an alternative for organic reductions.

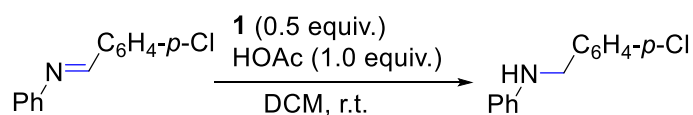


Keywords: Aldehyde, reduction, 1,3-dimethylimidazol-2-ylidene trihydroborate, on-column, silica gel.

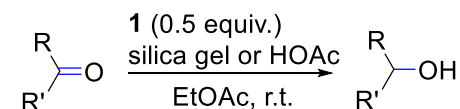
Introduction

Following its introduction in 2010, 1,3-dimethylimidazol-2-ylidene borane (diMe-lmd-BH₃, **1**) has quickly become one of the most important NHC-boranes.¹ It is a typical crystalline solid and is easy to handle. It is stable in air, in strong bases, in mild acids and under chromatographic conditions.² Its role as a useful building blocks for formation of new types of borane-containing compounds has been well developed so far.³⁻¹⁶ As a hydrogen atom donor, **1** has been used in reduction reactions¹⁷⁻²³ and cascade reactions^{24, 25}. Since the discovery of borane (BH₃) as reducing agent in H.C. Brown's lab, developing milder and more selective borane compounds as reducing agent has been research focus.²⁶ For example, sodium borohydride has been widely used as an economical and mild reducing agent.^{27, 28} However, it is normally performed in protic solvents, and the reactions are sluggish.²⁸ Curran's group has measured the 'nucleophilicity parameters' (N value)²⁹ of **1**, which is even higher than that of cyanoborate anion and reductive animation was reported therein (Scheme 1a).²⁹ They have reported reduction of aldehydes and ketones with **1** promoted by silica gel (Scheme 1b)³⁰ and by acetic acid as well (Scheme 1b)³¹. Reduction of 4-anisaldehyde with **1** catalyzed by iodine was reported and no reduction product was detected without iodine (Scheme 1c).²⁴ It is believed that typical aldehyde or ketones are not electrophilic enough for direct reduction by **1**.³⁰

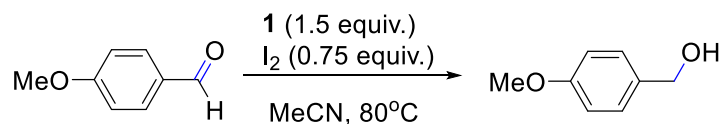
1a. Reduction of imine (Horn, M. *et al.* 2012)



1b. Reduction of aldehydes and ketones (Taniguchi, T. *et al.* 2012&Lamm, V. *et al.* 2013)



1c. Reduction of anisaldehyde (Kawamoto, T. *et al.* 2013)



Scheme 1. Prior diMe-lmd-BH₃-mediated reduction.

Results and Discussion

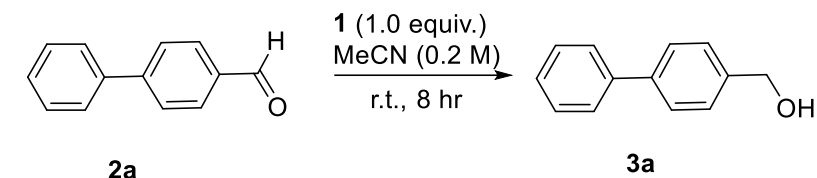
Based on the previous reports, we are curious whether the acidic catalyst is essential for this reduction, if value of **1** is even higher than cyanoborate anion²⁹. Therefore, the reduction of aldehydes by **1** without acidic catalyst has been carried out in our lab. And we are reporting our findings here.

First of all, **1** was prepared according to Curran's procedure.^{23, 32, 33} Using 4-phenylbenzaldehyde as the model substrate, we set two steps to survey.

Step 1. To eliminate the possible reduction happening during purification with silica gel column, **1** was quenched with diluted HCl after the reaction. Table 1 shows a survey of conditions. The outcome of the solvents is as follows: MeCN>DMSO>DCM (anhydrous)>DCM>Toluene. Polar solvents gave better results than

nonpolar solvents. The result is slightly better when the solvent is anhydrous (Table 1, entries 3&4). When the amount of **1** was reduced to 0.5 equivalents, the yield was decreased dramatically. (Table 1, entry 2) The presence of oxygen does not affect the reaction significantly, shown by reaction in an open flask, the yield was only slight decreased. (Table 1, entry 7)

Table 1 Reduction of 4-phenylbenzaldehyde (**2a**) with diMe-Imd-BH₃ (**1**) followed by quenching with HCl (diluted).

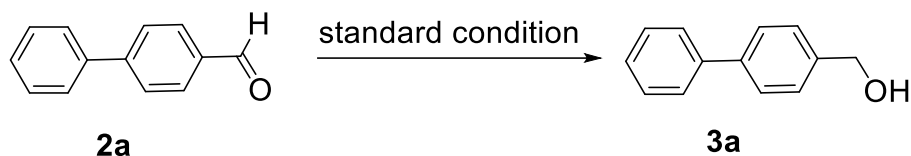


Entry	Deviation from the standard conditions	Yield (%) ^a
1	None	98
2	0.5 Equiv. of 1	64
3	DCM instead of MeCN	18
4	Anhydrous DCM instead of MeCN	20
5	DMSO instead of MeCN	83
6	Toluene instead of MeCN	8
7	In an open flask	96

^a Isolated yield.

Step 2. To test how much the nature of the silica gel would affect the reduction, we have carried out the reaction for 24 hr, which was purified with neutral alumina column (PE/EA as eluent) after concentration to afford 38% of **3a**. (Table 2, entry 4) Direct loading the mixture of **2a** and **1** in DCM still afforded 7% of **3a** was obtained still. (Table 2, entry 3) These two results showed that the reduction could be realized without catalysis and prolonging the reaction time was beneficial to the yield of the reaction. However, the yields were rather poor. It was clear that silica gel could improve the reduction substantially given the work reported by Curran's group³⁰. Then we wondered what would happen if the mixture of **2a** and **1** was directly applied onto the silica gel column followed directly with flash chromatography. Interestingly, **3a** was achieved in 79% yield. (Table 2, entry 2) What was more interesting was that we noticed that *R_f* values of **1** and **2a** were much closer in DCM than in EA/PA when we did thin layer chromatography (TLC) analysis. (SI-4b&c) It occurred to us that if we switched to MeOH/DCM eluting system, the outcome of the reduction might be different. As expected, the yield has been increased to 92%. (Table 2, entry 1) Halving the amount of reductant **1** led to a decrease in yield. (Table 2, entry 5) Although one equiv. of **1** was initially charged (as an excess), 1/3 of it was consumed (matching the theoretical requirement), while the remaining 2/3 was recovered. Reducing the length of the column led a poor result. (Table 2, entry 6) when a narrower column was used, it turned out that the isolated yield was only moderate, because there was an inseparable mixture of **3a** with **1**. (Table 2, entry 7). Considering the loading might be too high, we tried a quarter loading, and the isolated yield was increased. (Table 2, entry 8)

Table 2 Optimizing reduction of 4-phenylbenzaldehyde (**2a**) with diMe-Imd-BH₃ (**1**) ^a.

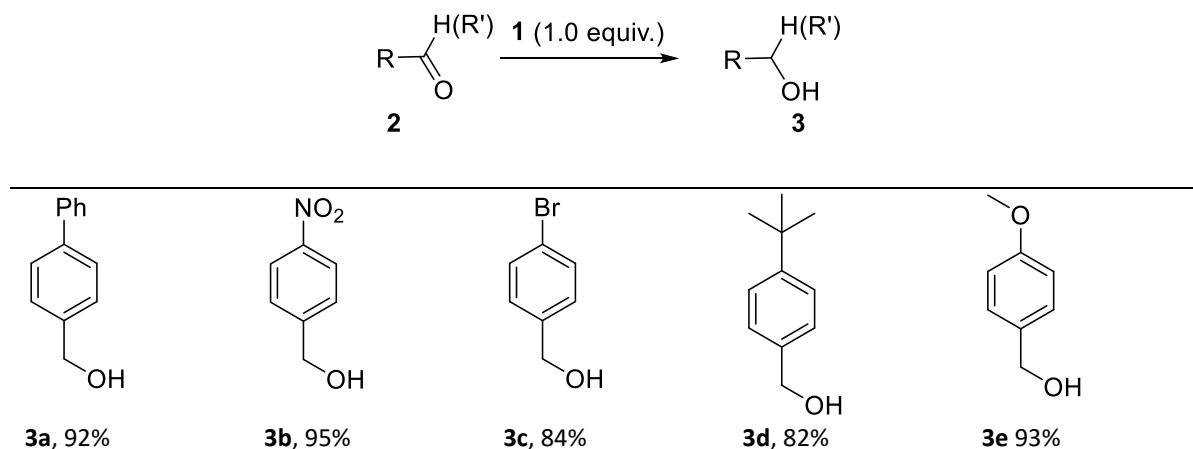


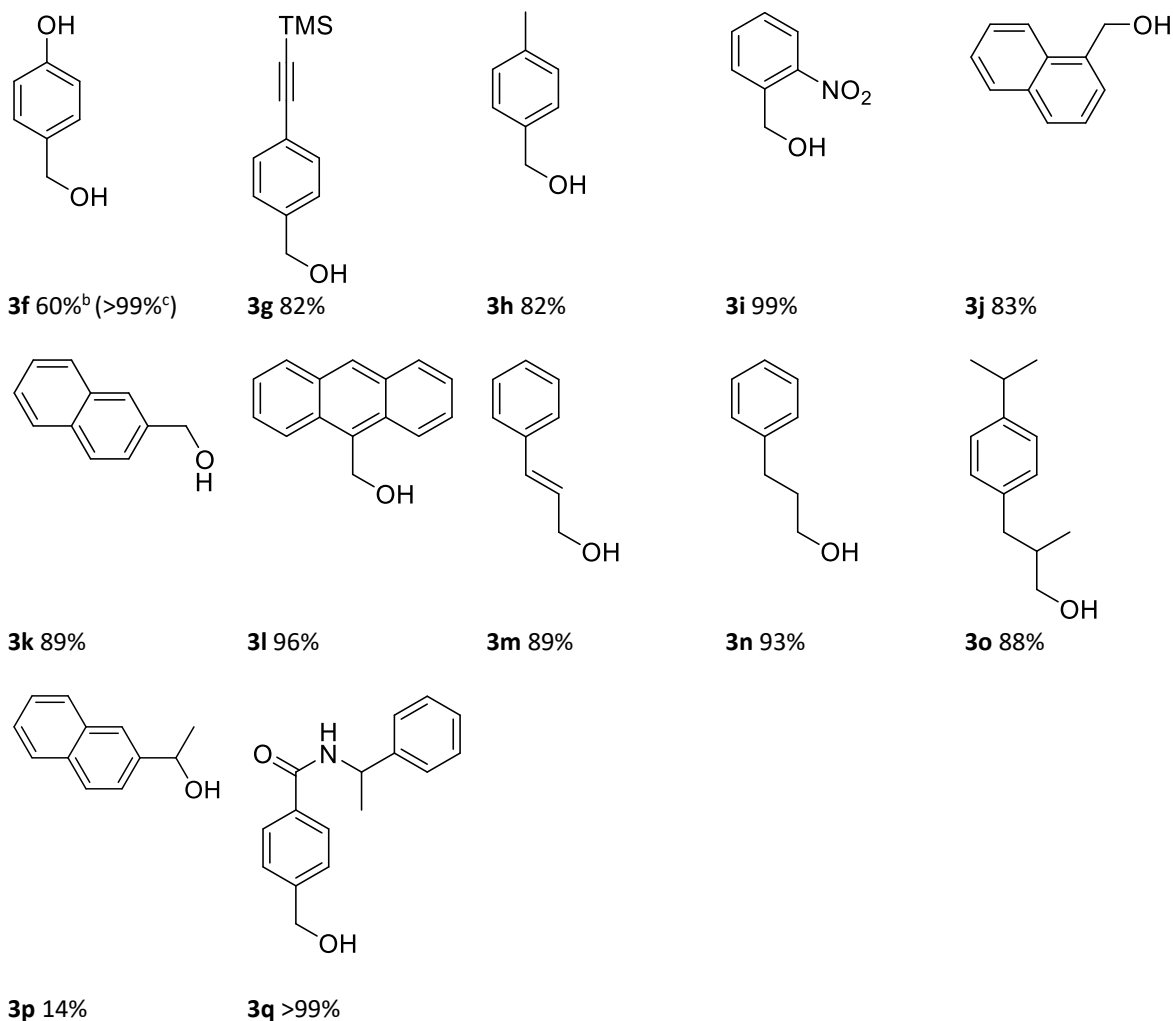
Entry	Deviation from the standard conditions	^b Yield (%)
1	None	92
2	EA/PE as eluent	79
3	EA/PE as eluent and alumina column	7
4	The mixture of 2a and 1 in ACN were stirred for 24 hr under N ₂ before it was loaded to alumina column and eluted with EA/PE	38
5	0.5 Equiv. of 1	78
6	Column length was 8.5 cm	88
7	A narrower column was used ^c	68 ^d
8	Narrower column with lower loading ^e	88

^a Standard condition: 4-Biphenylcarboxaldehyde (**2a**, 1.0 mmol) and **1** (1.0 mmol, 1.0 equiv.) were dissolved in DCM (5 mL) and loaded to the silica gel column (inner diameter is 2.6 cm, length is 18 cm) directly and eluted with a gradient of DCM/MeOH (from pure DCM to 100:1, then to 50:1). ^b Isolated yield. ^c Column (inner diameter is 1.6 cm, length is 18 cm). ^d The inseparable mixture of **3a** and **1** was excluded from the yield calculation. ^e On the scale of 0.25 mmol (**2a**).

Unexpectedly, we have developed an on-column reaction for reduction of aldehyde with **1**. The mixture of aldehyde **2a** with **1** in DCM was loaded onto silica gel column, rinsing with MeOH/DCM in gradient. The whole process took about 40 min (10 min retention + 30 min rinsing) and alcohol was collected straightforwardly in excellent yield. Next, we evaluated this reduction's scope, and the results are summarized (Table 3).

Table 3. Scope for on-column reduction of carbonyls by diMe-lmd-BH₃ (**1**).





^a Standard condition: 4-Biphenylcarboxaldehyde (1.0 mmol) and **1** (1.0 mmol, 1.0 equiv.) were dissolved in DCM (5 mL) and were loaded onto the silica gel column (diameter 3.0 cm, and length 18 cm) directly and eluted with a gradient of DCM/MeOH (from pure DCM to 100:1, then to 50:1). The yields were isolated yields. ^bElution with a gradient of DCM/MeOH (50:1, 25:1, 15:1, then 10:1). ^cConversion-based yield.

Aromatic, alkenyl and alkyl aldehydes could be reduced in moderate to excellent yields. The yield of 4-hydroxybenzyl alcohol (**3f**) was only moderate, due to the high polarity of 4-hydroxybenzaldehyde (**2f**), which resulted in a larger ΔR_f value between **2f** and **1**. (SI-4d) However if we double its elution period, the yield has been increased to 71% with the compromised separation efficiency. C(sp²)-C(sp²) and C(sp)-C(sp) bonds were untouched under this reaction. (**3g&m**) Steric hindrance is detrimental for the reaction, as yield of cyclamen alcohol (**3o**) is poorer than 3-phenylpropanol (**3n**). The ability to reduce ketone is very poor, as indicated by 1-(2-naphthyl)ethanol (**3p**), due to the poorer nucleophilicity of carbonyl group in ketone than that in aldehyde. And the amide bond remains stable under this condition (**3q**). The whole process for each substrate listed took about 40 min.

Conclusions

Finally, initiated by our curiosity whether the reduction of carbonyl compounds with **1** without catalysis could be realized or not and how much the silica gel would affect the reaction, we have developed an on-column reduction unexpectedly. It is applicable to various aldehydes in good to excellent yields, and limited application in aldehyde bearing polar groups and ketones. This protocol represents an alternative for organic

reductions with organic boranes. But the length and diameter of a column also need to be taken into account for optimal reaction results.

Experimental Section

General. All the commercial reagents were used without further purification. ^1H and ^{13}C NMR spectra were recorded on Bruker 400 UltraShield™ spectrometer (400 MHz for ^1H NMR, 101 MHz for ^{13}C NMR); IR spectra were recorded on a Nicolet Avatar 370 DTGS spectrometer. High-resolution mass spectrometry (HRMS) was recorded on a Q-TOF (AB SCIEX X500R with ESI source, and Agilent 7250 with EI source), which combines quadrupole precursor ion selection and a high-resolution accurate-mass (HR/AM) Time of Flight mass analyzer to deliver mass accuracy. Flash chromatography was packed with SiO_2 (silica gel 60, 200~300 mesh) or alimina (neutral, 200-300 mesh). Melting points were recorded on the microscope with hot plate with thermometer.

General procedure for on-column reduction of aldehydes with diMe-Imd-BH₃. 4-Biphenylcarboxaldehyde (1.0 mmol) and diMe-Imd-BH₃ (**1**, 1.0 mmol, 1.0 equiv.) were dissolved in DCM (5 mL) and were loaded to the silica gel column (diameter = 3.0 cm, and the length = 18 cm) directly and the eluent was mixture of DCM and MeOH to afford **[1,1'-biphenyl]-4-methanol (3a)**.

[1,1'-Biphenyl]-4-methanol (3a).³⁴ Bright white solid (170 mg, 92%). Mp 101.5-102.5 °C (ref³⁴. 101-102 °C). R_f = 0.38 (PE/EA 3:1). ^1H NMR (400 MHz, CDCl_3) δ 7.64-7.58 (m, 4H), 7.48-7.42 (m, 4H), 7.39-7.33 (m, 1H), 4.75 (s, 2H), 1.76 (br s, 1H); ^{13}C NMR (101 MHz, CDCl_3) δ 140.9, 140.7, 140.0, 128.9, 127.6, 127.42, 127.40, 127.2, 65.1. FT-IR (KBr pellet) ν 3254, 3054, 2923, 1403, 1039, 998, 818, 754 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_{13}\text{H}_{12}\text{O}$ ($[\text{M}]^+$) 184.0883, found 184.0884.

4-Nitrobenzyl alcohol (3b).³⁵ White solid (145 mg, 95% yield), Mp 87~91.4 °C (ref³⁵94-96 °C). R_f = 0.44 (DCM/MeOH 50:1). ^1H NMR (400 MHz, CDCl_3): δ 8.22 (d, J 8.8 Hz, 2H), 7.54 (d, J 8.8 Hz, 2H), 4.84 (s, 2H), 1.96 (s, 1H); ^{13}C NMR (101 MHz, CDCl_3): δ 148.4, 147.3, 127.1, 123.8, 64.0. FT-IR (KBr pellet) ν 3521 (s), 3081, 2925, 2869, 1511, 1343, 1196, 1057, 737 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_7\text{H}_7\text{NNaO}_3$ ($[\text{M}+\text{Na}]^+$) 176.0318, found 176.0314

4-Bromobenzyl alcohol (3c).²⁸ White solid (159 mg, 84% yield), Mp 74.5~77.1 °C (ref.²⁸ 76-78 °C). R_f = 0.47 (PE/EA 2:1). ^1H NMR (400 MHz, CDCl_3): δ 7.48 (d, J 8.4 Hz, 2H), 7.24 (d, J 8.4 Hz, 2H), 4.65 (d, J 5.2 Hz, 2H), 1.77-1.69 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3): δ 139.9, 131.7, 128.7, 121.5, 64.6. FT-IR (KBr pellet) ν 3375 (s), 3081, 2922, 1486, 1068, 1009, 828 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_7\text{H}_7\text{BrO}$ ($[\text{M}]^+$) 185.9675, found 185.9675.

4-tert-Butylbenzyl alcohol (3d)³⁶ Colorless oil (143 mg, 82% yield). R_f = 0.52 (PE/EA 2:1). ^1H NMR (400 MHz, CDCl_3): δ 7.40 (d, J 8.8 Hz, 2H), 7.31 (d, J 8.8 Hz, 2H), 4.67 (s, 2H), 1.63 (s, 1H), 1.33 (s, 9H); ^{13}C NMR (101 MHz, CDCl_3): δ 150.8, 138.0, 127.0, 125.6, , 65.3, 34.7, 31.5. FT-IR (KBr film) ν 3343 (s), 3026, 2962, 1513, 1462, 1363, 1269, 1013, 834 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_{11}\text{H}_{16}\text{O}$ ($[\text{M}]^+$) 164.1196; found 164.1195.

4-Methoxybenzyl alcohol (3e).³⁶ Colorless oil (132 mg, 93% yield). R_f = 0.42 (PE/EA 2:1). ^1H NMR (400 MHz, CDCl_3): δ 7.30 (d, J 8.8 Hz, 2H), 6.89 (d, J 8.4 Hz, 2H), 4.62 (s, 2H), 3.81 (s, 3H), 1.62 (s, 1H); ^{13}C NMR (101 MHz, CDCl_3): δ 159.2, 133.2, 128.7, 114.0, 65.0, 55.4. FT-IR (KBr film) ν 3381 (s), 3001, 2935, 1612, 1513, 1248, 1033, 816 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_8\text{H}_{10}\text{O}_2$ ($[\text{M}]^+$) 138.0675; found 138.0677.

4-Hydroxybenzyl alcohol (3f).³⁷ White solid (74 mg, 60% yield). 4-Hydroxybenzaldehyde (recovered SM, 49 mg, 40%). Mp 117-121.7 °C (ref.³⁷ 118-119 °C). R_f = 0.35 (DCM/MeOH 10:1). ^1H NMR (400 MHz, $\text{DMSO}-d_6$): δ 9.24 (br s, 1H), 7.10 (d, J 8.4 Hz, 2H), 6.70 (d, J 8.4 Hz, 2H), 4.93 (br s, 1H), 4.37 (s, 2H); ^{13}C NMR (101 MHz,

DMSO- d_6): δ 156.3, 132.8, 128.2, 114.9, 62.9. FT-IR (KBr pellet) ν 3386 (br s), 3123, 2925, 1613, 1597, 1518, 1207, 993, 886 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_7\text{H}_8\text{O}_2$ ($[\text{M}]^+$) 124.0519; found 124.0521.

4-[2-(Trimethylsilyl)ethynyl]benzenemethanol (3g).³⁸ White solid (168 mg, 82% yield). Mp 69.6-70.9 °C (ref.³⁸ 62-64 °C). R_f = 0.40 (PE/EA 3:1). ^1H NMR (400 MHz, CDCl_3): δ 7.45 (d, J 8.4 Hz, 2H), 7.29 (d, J 8.4 Hz, 2H), 4.67 (d, J 5.6 Hz, 2H), 1.91-1.56 (m, 1H), 0.25 (s, 9H); ^{13}C NMR (101 MHz, CDCl_3): δ 141.3, 132.2, 126.7, 122.4, 105.1, 94.3, 64.9, 0.1. FT-IR (KBr pellet) ν 3296, 2959, 2155, 1507, 1250, 1034, 842 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_{12}\text{H}_{16}\text{OSi}$ ($[\text{M}]^+$) 204.0965; found 204.0966

4-Methylbenzyl alcohol (3h).³⁹ White solid (113 mg, 82% yield). Mp 53.0-57.8 °C (ref.³⁹ 57-58 °C). R_f = 0.50 (PE/EA 2:1). ^1H NMR (400 MHz, CDCl_3): δ 7.26 (d, J 8.0 Hz, 2H), 7.17 (d, J 8.0 Hz, 2H), 4.64 (s, 2H), 2.36 (s, 3H), 1.77-1.62 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3): δ 138.0, 137.4, 129.3, 127.2, 65.2, 21.2. FT-IR (KBr pellet) ν 3285 (s), 3020, 2923, 1516, 1446, 1032, 804 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_8\text{H}_{10}\text{O}$ ($[\text{M}]^+$) 122.0726; found 122.0726.

2-Nitrobenzyl alcohol (3i).³⁷ White solid (154 mg, 99% yield). Mp 65.5-69.0 °C (ref.³⁷ 69-70 °C). R_f = 0.52 (PE/EA 2:1). ^1H NMR (400 MHz, CDCl_3): δ 8.10 (d, J 8.0 Hz, 1H), 7.74 (d, J 8.0 Hz, 1H), 7.68 (t, J 7.6 Hz, 1H), 7.48 (t, J 7.6 Hz, 1H), 4.97 (s, 2H), 2.62 (br s, 1H); ^{13}C NMR (101 MHz, CDCl_3): δ 147.6, 136.9, 134.2, 129.9, 128.5, 125.1, 62.5. FT-IR (KBr pellet) ν 3326, 2928, 1525, 1338, 1036, 724 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_7\text{H}_7\text{NO}_3$ ($[\text{M}+\text{NH}_4]^+$) 171.0764; found 171.0765.

1-Naphthylmethanol (3j).³⁷ White solid (143 mg, 83% yield). Mp 55-58.6 °C (ref.³⁷ 58-59 °C). R_f = 0.52 (PE/EA 2:1). ^1H NMR (400 MHz, CDCl_3): δ 8.13 (d, J 8.4 Hz, 1H), 7.89 (d, J 8.8 Hz, 1H), 7.82 (d, J 8.4 Hz, 1H), 7.59-7.43 (m, 4H), 5.16 (s, 2H), 1.72 (s, 1H); ^{13}C NMR (101 MHz, CDCl_3): δ 136.3, 133.9, 131.3, 128.7, 128.6, 126.4, 126.0, 125.5, 125.4, 123.7, 63.7. FT-IR (KBr pellet) ν 3373 (br s), 3048, 2883, 1510, 1003, 800 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_{11}\text{H}_{14}\text{NO}$ ($[\text{M}+\text{NH}_4]^+$) 176.1070; found 176.1060.

2-Naphthylmethanol.⁴⁰ White solid (142 mg, 89% yield). Mp 77.5-79.6 °C (ref.⁴⁰ 79-81 °C). R_f = 0.45 (PE/EA 2:1). ^1H NMR (400 MHz, CDCl_3): δ 7.89-7.79 (m, 4H), 7.52-7.45 (m, 3H), 4.88-4.83 (m, 2H), 1.97-1.59 (m, 1H); ^{13}C NMR (101 MHz, CDCl_3): δ 138.4, 133.4, 133.0, 128.4, 128.0, 127.8, 126.3, 126.0, 125.5, 125.3, 65.4. FT-IR (KBr pellet) ν 3254 (br s), 3051, 2860, 1508, 1041, 815 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_{11}\text{H}_{10}\text{O}$ ($[\text{M}]^+$) 158.0726; found 158.0729.

9-Anthracenemethanol (3l).⁴¹ Yellow solid (201 mg, 96% yield). Mp 156-159.5 °C (ref.⁴¹ 185-160 °C). R_f = 0.47 (PE/EA 2:1). ^1H NMR (400 MHz, CDCl_3): δ 8.46 (s, 1H), 8.41 (d, J 8.8 Hz, 2H), 8.03 (d, J 8.4 Hz, 2H), 7.57 (t, J 8.8 Hz, 2H), 7.49 (t, J 8.4 Hz, 2H), 5.66 (s, 2H), 1.75 (br s, 1H); ^{13}C NMR (101 MHz, CDCl_3): δ 131.7, 131.1, 130.4, 129.3, 128.5, 126.6, 125.2, 124.0, 57.5. FT-IR (KBr pellet) ν 3408, 3042, 2949, 1435, 1273, 1046, 978, 884, 733 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_{15}\text{H}_{12}\text{NaO}$ ($[\text{M}+\text{Na}]^+$) 231.0780; found 231.0778.

Cinnamyl alcohol (3m).⁴² Colorless oil (128 mg, 89% yield). R_f = 0.43 (PE/EA 2:1). ^1H NMR (400 MHz, CDCl_3): δ 7.40-7.38 (m, 2H), 7.34-7.30 (m, 2H), 7.27-7.23 (m, 1H), 6.62 (dt, J 16.0, 1.6 Hz, 1H), 6.37 (dt, J 16.0, 5.6 Hz, 1H), 4.33 (dd, J 5.6, 1.6 Hz, 1H); ^{13}C NMR (101 MHz, CDCl_3): δ 136.8, 131.1, 128.7, 128.6, 127.8, 126.6, 63.7. FT-IR (KBr film) ν 3355 (br s), 3026, 2923, 1494, 1092, 967, 735 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_8\text{H}_{10}\text{O}$ ($[\text{M}]^+$) 134.0726; found 134.0727.

3-Phenylpropanol (3n).⁴² Colorless oil (137 mg, 93% yield). R_f = 0.43 (PE/EA 2:1). ^1H NMR (400 MHz, CDCl_3): δ 7.32-7.27 (m, 2H), 7.23-7.17 (m, 3H), 3.68 (t, J 6.4 Hz, 2H), 2.72 (t, J 7.6 Hz, 2H), 1.90 (tt, J 7.6, 6.4 Hz, 2H), 1.39 (br s, 1H); ^{13}C NMR (101 MHz, CDCl_3): δ 141.9, 128.51, 128.48, 125.9, 62.3, 34.3, 32.2. FT-IR (KBr film) ν 3340 (br s), 3027, 2938, 1454, 1059, 1034, 745, 699 cm^{-1} . HRMS (EI) Calcd for $\text{C}_9\text{H}_{12}\text{O}$ ($[\text{M}]^+$) 136.0883, found 136.0885.

Cyclamen alcohol (3o).⁴³ Colorless oil (170 mg, 88% yield). R_f = 0.35 (PE/EA 5:1). ^1H NMR (400 MHz, CDCl_3): δ 7.15 (d, J 8.0 Hz, 2H), 7.10 (d, J 8.0 Hz, 2H), 3.54 (dd, J 10.4, 6.0 Hz, 1H), 3.47 (dd, J 10.4, 6.0 Hz, 1H), 2.88 (sept,

J 6.8 Hz, 1H), 2.71 (dd, J 13.6, 6.4 Hz, 1H), 2.40 (dd, J 13.6, 8.0 Hz, 1H), 1.94 (octet, J 6.8 Hz, 1H), 1.52 (br s, 1H), 1.24 (d, J 6.8 Hz, 6H), 0.93 (d, J 6.8 Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 146.4, 137.9, 129.1, 126.3, 67.7, 39.3, 37.8, 33.7, 24.1, 16.6. FT-IR (KBr film) ν 3364 (br s), 3009, 2959, 1511, 1460, 1034, 846 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_{13}\text{H}_{20}\text{O}$ ($[\text{M}]^+$) 192.1509; found 192.1508.

1-(2-Naphthyl)ethanol (3p).⁴² White solid (24 mg, 14% yield). Mp 70.5–73.0 °C (ref.⁴² 72.3–73.0 °C). R_f = 0.39 (PE/EA 3:1). ^1H NMR (400 MHz, CDCl_3): δ 7.88–7.80 (m, 4H), 7.54–7.44 (m, 3H), 5.12–5.04 (m, 1H), 2.02 (br s, 1H), 1.59 (d, J 6.4 Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 143.3, 133.4, 133.0, 128.4, 128.0, 127.8, 126.2, 125.9, 123.94, 123.91, 70.6, 25.2. FR-IR (KBr pellet) ν 3311 (br s). 3052, 2971, 1507, 1364, 1124, 1075, 825, 742 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_{12}\text{H}_{12}\text{O}$ ($[\text{M}]^+$) 172.0883, found 172.0885.

4-Hydroxymethyl-*N*-(1-phenylethyl)benzamide (3q). White solid (255 mg, >99% yield). Mp 102.5–105.0 °C; R_f = 0.36 (PE/EA 1:1). ^1H NMR (400 MHz, CDCl_3): δ 7.74 (br s, 1H), 7.72 (br s, 1H), 7.43 – 7.33 (m, 6H), 7.31–7.27 (m, 1H), 6.37 (d, J 8.0 Hz, 1H), 5.32 (pent, J 7.2 Hz, 1H), 4.72 (s, 2H), 2.10 (br s, 1H), 1.61 (d, J 6.8 Hz, 3H); ^{13}C NMR (101 MHz, CDCl_3): δ 166.9, 144.9, 143.2, 133.3, 128.7, 127.4, 127.1, 126.6, 126.3, 64.3, 49.3, 21.8. FR-IR (KBr pellet) ν 3300, 3028, 2930, 1635, 1613, 1531, 999, 698 cm^{-1} . HRMS (ESI) Calcd. for $\text{C}_{16}\text{H}_{18}\text{NO}_2$ ($[\text{M}+\text{H}]^+$) 256.1332, found 256.1327.

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Supplementary Material

Experimental details, NMR data can be accessed on the publisher's website.

References

- Walton, J. C.; Brahmi, M. M.; Fensterbank, L.; Lacôte, E.; Malacria, M.; Chu, Q.; Ueng, S.-H.; Solov'yev, A.; Curran, D. P. *J. Am. Chem. Soc.* **2010**, 132, 2350–2358.
- Curran, D. P.; Solov'yev, A.; Makhlouf Brahmi, M.; Fensterbank, L.; Malacria, M.; Lacôte, E. *Angew. Chem. Int. Ed.* **2011**, 50, 10294–10317.
- Komatsu, R.; Morioka, T.; Kamimura, A.; Matsubara, H.; Curran, D. P.; Kawamoto, T. *Org. Lett.* **2026**, 28, 260–264.
- Xie, F. K.; Mao, Z.; Curran, D. P.; Liang, H. L.; Dai, W. *Angew. Chem. Int. Ed.* **2023**, 62, e202306846.
- Li, G.; Huang, G.; Sun, R.; Curran, D. P.; Dai, W. *Org. Lett.* **2021**, 23, 4353–4357.
- Kawamoto, T.; Morioka, T.; Noguchi, K.; Curran, D. P.; Kamimura, A. *Org. Lett.* **2021**, 23, 1825–1828.
- Takahashi, K.; Geib, S. J.; Maeda, K.; Curran, D. P.; Taniguchi, T. *Org. Lett.* **2021**, 23, 1071–1075.
- Bolt, D. A.; Curran, D. P. *Adv. Synth. Catal.* **2020**, 362, 2238–2244.
- Dai, W.; Geib, S. J.; Curran, D. P. *J. Am. Chem. Soc.* **2020**, 142, 6261–6267.
- Walton, J. C.; Dai, W.; Curran, D. P. *J. Org. Chem.* **2020**, 85, 4248–4255.
- Takahashi, K.; Shimoi, M.; Watanabe, T.; Maeda, K.; Geib, S. J.; Curran, D. P.; Taniguchi, T. *Org. Lett.* **2020**, 22, 2054–2059.
- Chen, C.; Li, Y. L.; Xia, J. B. *Org. Lett.* **2026**, 28, 2553–2559.
- Zhang, X.; Zhang, B.; Wang, Y.-P.; Tang, M.-L.; Zhang, Q.-X.; Liu, H.; Hu, J.-T.; Qi, T.; Li, J.-L. *Org. Biomol. Chem.* **2025**, 23, 9624–9634.

14. Xie, J.; Zhu, C.; Yao, S. *Synthesis* **2023**, 56, 1711-1718.
15. Zheng, H.; Lu, H.; Su, C.; Yang, R.; Zhao, L.; Liu, X.; Cao, H. *Chin. J. Chem.* **2022**, 41, 193-198.
16. Zhou, Y.; Liu, B. *Org. Chem. Front.* **2025**, 12, 142-147.
17. Ueng, S.-H.; Fensterbank, L.; Lacôte, E.; Malacria, M.; Curran, D. P. *Org. Lett.* **2010**, 12, 3002-3005.
18. Ueng, S.-H.; Fensterbank, L.; Lacôte, E.; Malacria, M.; Curran, D. P. *Org. Biomol. Chem.* **2011**, 9, 3415-3420.
19. Pan, X.; Lacôte, E.; Lalevée, J.; Curran, D. P. *J. Am. Chem. Soc.* **2012**, 134, 5669-5674.
20. Studer, A.; Curran, D. P. *Angew. Chem. Int. Ed.* **2016**, 55, 58-102.
21. Pan, X.; Lalevée, J.; Lacote, E.; Curran, D. P. *Adv. Synth. Catal.* **2013**, 355, 3522-3526.
22. Watanabe, T.; Geib, S. J.; Curran, D. P.; Taniguchi, T. *J. Org. Chem.* **2017**, 82, 13034-13042.
23. Kaneko, T.; Ito, R.; Okamura, T.; Sato, T. *Org. Lett.* **2025**, 27, 2042-2048.
24. Kawamoto, T.; Okada, T.; Curran, D. P.; Rye, I. *Org. Lett.* **2013**, 15, 2144-2147.
25. Wan, T.; Ciszewski, Ł. W.; Ravelli, D.; Capaldo, L. *Org. Lett.* **2024**, 26, 5839-5843.
26. Burkhardt, E. R.; Matos, K. *Chem. Rev.* **2006**, 106, 2617-2650.
27. Li, Z. *Synlett* **2004**, 2005, 182-183.
28. Naimi-Jamal, M. R.; Mokhtari, J.; Dekamin, M. G.; Kaupp, G. *Eur. J. Org. Chem.* **2009**, 3567-3572.
29. Horn, M.; Mayr, H.; Lacote, E.; Merling, E.; Deaner, J.; Wells, S.; McFadden, T.; Curran, D. P. *Org. Lett.* **2012**, 14, 82-85.
30. Taniguchi, T.; Curran, D. P. *Org. Lett.* **2012**, 14, 4540-4543.
31. Lamm, V.; Pan, X.; Taniguchi, T.; Curran, D. P. *Beilstein J. Org. Chem.* **2013**, 9, 675-680.
32. Gardner, S.; Kawamoto, T.; Curran, D. P. *J. Org. Chem.* **2015**, 80, 9794-9797.
33. Gardner, S.; Kawamoto, T.; Curran, D. P. *Org. Synth.* **2015**, 92, 342-355.
34. Mao, S.; Chen, Z.; Wang, L.; Khadka, D. B.; Xin, M.; Li, P.; Zhang, S.-Q. *J. Org. Chem.* **2018**, 84, 463-471.
35. Zheng, X.-A.; Kong, R.; Huang, H.-S.; Wei, J.-Y.; Chen, J.-Z.; Gong, S.-S.; Sun, Q. *Synthesis* **2018**, 51, 944-952.
36. Xu, J.; Liu, N.; Zou, L.; Cheng, F.; Shen, X.; Liu, T.; Lv, H.; Khan, R.; Fan, B. *Asian J. Org. Chem.* **2019**, 8, 261-264.
37. Wang, R.; Tang, Y.; Xu, M.; Meng, C.; Li, F. *J. Org. Chem.* **2018**, 83, 2274-2281.
38. Voronin, V. V.; Ledovskaya, M. S.; Rodygin, K. S.; Ananikov, V. P. *Org. Chem. Front.* **2020**, 7, 1334-1342.
39. Yang, M. H.; Hunt, J. R.; Sharifi, N.; Altman, R. A. *Angew. Chem. Int. Ed.* **2016**, 55, 9080-9083.
40. Okuda, Y.; Nagaoka, M.; Yamamoto, T. *ChemCatChem* **2020**, 12, 6291-6300.
41. Singh, M. D.; Ningombam, A. *Indian J. Chem.* **2010**, 49B, 77-83.
42. Yang, Y. Q.; Lu, Z.; Xu, X. *Asian J. Org. Chem.* **2019**, 8, 2192-2195.
43. Manojveer, S.; Salahi, S.; Wendt, O. F.; Johnson, M. T. *J. Org. Chem.* **2018**, 83, 10864-10870.

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