Electronic Supplementary Material (ESI) for Catalysis Science & Technology.

Supporting Information

Iron-Catalyzed Highly Efficient, General Hydrogenation of Aldehydes

*Thomas Zell, Yehoshoa Ben-David and David Milstein**

Department of Organic Chemistry, Weizmann Institute of Science, 76100 Rehovot, Israel

* E-mail: david.milstein@weizmann.ac.il

The Supporting Information contents:

1. General considerations
2. General procedures for the catalytic hydrogenation reactions
3. Analysis of the hydrogenation reaction mixtures
4. Additional tables

    Table S1. The effect of different additives on the hydrogenation reaction of benzaldehyde.

    Table S2. The effect of different solvents on the hydrogenation reaction of benzaldehyde.

    Table S3. The effect of different temperatures on the hydrogenation reaction of benzaldehyde.

    Table S4. The effect of KO*t*Bu concentration on the hydrogenation reaction of benzaldehyde.

    Table S5. Poisoning effects on the hydrogenation reaction of cuminaldehyde.

5. References

1. General considerations

All reactions were performed under a nitrogen or argon atmosphere in a glovebox or using standard Schlenk techniques. All solvents were reagent grade or better. Tetrahydrofuran (THF), toluene, 1,4-dioxane, and diethylether (Et_2O) were refluxed over sodium and distilled under argon atmosphere. Triethylamine was refluxed over potassium and distilled under nitrogen atmosphere. Methanol (MeOH), ethanol (EtOH), and *iso*-propanol (*i*PrOH) were degassed by freeze-pump thaw cycles and stored in the glovebox over the appropriate molecular sieves. KO*t*Bu was purchased from Sigma Aldrich and used without any further purification. All aldehydes and acetophenone were obtained from commercial sources and purified prior reaction. Acetophenone was distilled under reduced pressure. The aldehydes were dissolved in diethylether, washed with $NaHCO_3$ solution (3x), water (2x), and brine (3x). The organic phase was dried over $MgSO_4$ or Na_2SO_4, filtered and distilled or sublimed under reduced pressure. Deuterated solvents and other commercially available reagents were used as received.

NMR spectra were recorded using Bruker AMX-300 and AMX-400 NMR spectrometers. ^1H and $^{13}C\{^1H\}$ NMR chemical shifts are reported in ppm downfield from tetramethylsilane. When required, ^1H-COSY, ^1H-^{13}C-HSQC, ^1H-^{13}C-HMBC, and ^{13}C-DEPTQ NMR spectra were recorded to assist the assignment of the ^1H resonances. GC-MS analysis were carried out on HP 6890 / 5973 (MS detector) instruments equipped with a 30 m column (Restek 5MS, 0.32 mm internal diameter) with a 5% phenylmethylsilicone coating (0.25 mm) and helium as carrier gas. GC analysis were carried out using a Carboxen 1000 column on a HP 690 series GC system or HP-5 cross linked 5% phenylmethylsilicone column (30m × 0.32mm × 0.25 μm film thickness, FID) on a HP 6890 series GC system.

Complex **1**[1] and **2**[2] were prepared as reported previously.

2. General procedures for the catalytic hydrogenation reactions

In a N_2 filled glovebox the reaction vessel (45 mL Parr autoclave type 341) was charged with the corresponding (pre)catalyst (stock solution in the corresponding solvent), the corresponding additive (e.g. triethylamine), substrate, and KO*t*Bu (stock solution in the corresponding solvent). The autoclave was sealed and pressurized at room temperature with H_2 at the specified pressure. The solution was stirred in an oil bath at the specified temperature for the specified time. Mesitylene was added as internal standard and the reaction mixtures were analyzed by ^{1}H NMR, GC and GC-MS. The conversions were determined by integration of ^{1}H resonances and the yields were determined by the integration ratio of the ^{1}H resonances (vs. mesitylene) or by GC calibration using mesitylene as an external standard.

3. Analysis of the hydrogenation reaction mixtures

The reaction mixtures were analyzed by ^{1}H NMR (performed in $CDCl_3$), GC, and GC-MS. Where necessary a full NMR analysis by ^{1}H-^{1}H-COSY, ^{1}H-^{13}C-HSQC, ^{1}H-^{13}C-HMBC, and ^{13}C-DEPTQ NMR spectroscopy were performed. The yields were determined by the integration ratio of the ^{1}H resonances (vs. mesitylene) or by GC calibration using mesitylene as external standard. The ^{1}H NMR spectra were compared to the literature[3] or to samples of the alcohols in $CDCl_3$ solutions.

Benzyl alcohol. ^{1}H NMR (300.1 MHz, $CDCl_3$, 23 °C) δ = 4.62 (s, 2H, C*H*$_2$), 7.30 (m, 5H, aryl-*H*). **MS** (*m*/*z, pos.*): 108 (M^+).

4-Methylbenzyl alcohol. ^{1}H NMR (300.1 MHz, $CDCl_3$, 23 °C) δ = 2.31 (s, 3H, C*H*$_3$), 4.57 (s, 2H, C*H*$_2$), 7.11 (d, 2H, $^{3}J_{HH}$ = 7.9 Hz, aryl-*H*), 7.21 (d, 2H, $^{3}J_{HH}$ = 7.9 Hz, aryl-*H*). **MS** (*m*/*z, pos.*): 122 (M^+).

4-*Iso*propylbenzyl alcohol. ^{1}H NMR (300.1 MHz, $CDCl_3$, 23 °C) δ = 1.22 (d, 6H, $^{3}J_{HH}$ = 7.0 Hz, C*H*$_3$), 2.89 (sept, 1H, $^{3}J_{HH}$ = 6.9 Hz, C*H*), 4.62 (s, 2H, C*H*$_2$), 7.20 (d, 2H, $^{3}J_{HH}$ = 8.2 Hz, aryl-*H*), 7.28 (d, 2H, $^{3}J_{HH}$ = 8.1 Hz, aryl-*H*). **MS** (*m*/*z, pos.*): 150 (M^+).

4-Methoxybenzyl alcohol. ^{1}H NMR (300.1 MHz, $CDCl_3$, 23 °C) δ = 3.75 (s, 3H, OC*H*$_3$), 4.53 (s, 2H, C*H*$_2$), 6.83 (d, 2H, $^{3}J_{HH}$ = 8.6 Hz, aryl-*H*), 7.24 (d, 2H, $^{3}J_{HH}$ = 8.2 Hz, aryl-*H*). **MS** (*m*/*z, pos.*): 138 (M^+).

4-Dimethylaminobenzyl alcohol. **^{1}H NMR** (300.1 MHz, $CDCl_3$, 23 °C) δ = 2.90 (s, 6H, NC*H*$_3$), 4.51 (s, 2H, C*H*$_2$), 6.69 (d, 2H, $^3J_{HH}$ = 8.5 Hz, aryl-*H*), 7.20 (d, 2H, $^3J_{HH}$ = 8.5 Hz, aryl-*H*).

Mesitylmethanol. **^{1}H NMR** (300.1 MHz, $CDCl_3$, 23 °C) δ = 2.24 (s, 3H, C*H*$_3$), 2.37 (s, 6H, C*H*$_3$), 4.67 (d, 2H, $^3J_{HH}$ = 4.8 Hz, C*H*$_2$), 6.85 (s, 2H, aryl-*H*). **MS** (*m/z, pos.*): 150 (M^+).

3,4,5-Trimethoxybenzyl alcohol. **^{1}H NMR** (300.1 MHz, $CDCl_3$, 23 °C) δ = 3.81 (s, 3H, C*H*$_3$), 3.84 (s, 3H, C*H*$_3$), 4.59 (s, 2H, C*H*$_2$), 6.58 (s, 2H, aryl-*H*). **MS** (*m/z, pos.*): 198 (M^+).

1-Naphthalenemethanol. **^{1}H NMR** (300.1 MHz, $CDCl_3$, 23 °C) δ = 5.10 (s, 2H, C*H*$_2$), 7.46 (m, 4H, aryl-*H*), 7.78 (d, br, 1H, $^3J_{HH}$ = 8.1 Hz, aryl-*H*), 7.85 (dd, 1H, $^3J_{HH}$ = 7.1 Hz, $^4J_{HH}$ = 2.1 Hz, aryl-*H*), 8.10 (d, 1H, $^3J_{HH}$ = 8.0 Hz, aryl-*H*). **MS** (*m/z, pos.*): 158 (M^+).

1,3-Benzodioxazole-5-methanol. **^{1}H NMR** (300.1 MHz, $CDCl_3$, 23 °C) δ = 4.51 (s, 2H, C*H*$_2$OH), 5.91 (s, 2H, OC*H*$_2$O), 6.73 (d, 1H, $^3J_{HH}$ = 8.0 Hz, aryl-*H*), 6.77 (d, 1H, $^3J_{HH}$ = 8.0 Hz, aryl-*H*), 6.84 (m, 1H, aryl-*H*). **MS** (*m/z, pos.*): 152 (M^+).

***Iso*-butanol.** **^{1}H NMR** (300.1 MHz, $CDCl_3$, 23 °C) δ = 0.89 (d, 6H, $^3J_{HH}$ = 6.7 Hz, C*H*$_3$), 1.72 (sept, 1H, $^3J_{HH}$ = 6.6 Hz, C*H*), 2.14 (s, 2H, C*H*$_2$). **MS** (*m/z, pos.*): 74 (M^+).

2,6-Dimethylhept-5-en-1-ol. **^{1}H NMR** (400.1 MHz, $CDCl_3$, 23 °C) δ = 0.90 (d, 3H, $^3J_{HH}$ = 6.7 Hz, C*H*$_3$-CH), 1.27 (m, 2H, C*H*$_2$-CH(Me)(CH_2OH)), 1.59 (s, 3H, C*H*$_3$C=C), 1.62 (m, 1H, C*H*), 1.66 (s, 3H, C*H*$_3$C=C), 1.99 (m, 2H, C*H*$_2$-CH=CMe_2), 3.43 (m, 2H, C*H*$_2$-OH), 5.08 (tt, 1H, $^3J_{HH}$ = 7.2 Hz, $^4J_{HH}$ = 0.9 Hz,). **^{13}C{^{1}H} NMR** (100.7 MHz, $CDCl_3$, 23 °C) δ = 16.4 (s, C*H*$_3$-CH), 17.5 (s, 3H, *C*H$_3$C=C), 25.3 (s, *C*H$_2$-CH=CMe_2), 25.7 (s, *C*H$_3$C=C), 33.2 (s, *C*H$_2$-

CH(Me)(CH_2OH)), 35.2 (s, *C*H(Me)(CH_2OH)), 68.1 (s, *C*H_2OH), 124.5 (s, *C*HR=CMe_2), 131.3 (s, CHR=*C*Me_2). **MS** (*m/z, pos.*): 142 (M^+).

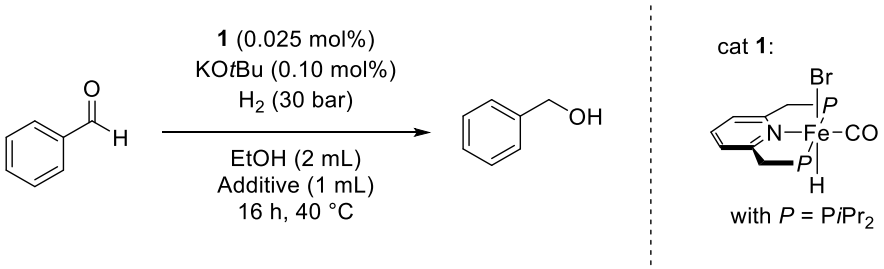
Neopentyl alcohol. **^{1}H NMR** (300.1 MHz, $CDCl_3$, 23 °C) δ = 0.90 (s, 9H, C*H*$_3$), 3.27 (s, 2H, C*H*$_2$). **MS** (*m/z, pos.*): 88 (M^+).

(Z)-2-pentylnon-2-en-1-ol. **^{1}H NMR** (400.1 MHz, $CDCl_3$, 23 °C) δ = 0.90 (m, br, 6H, 2xC*H*$_3$), 1.29 (m, br, 14H, 7xC*H*$_2$), 2.05 (m, 4H, 2xC*H*$_2$-C=), 4.01 (s, 2H, C*H*$_2$), 5.40 (t, 1H, $^3J_{HH}$ = 6.5 Hz, R*H*C=CR'R''). **^{13}C{^{1}H} NMR** (100.7 MHz, $CDCl_3$, 23 °C) δ = 13.9 (s, C*H*$_3$), 14.0 (s, C*H*$_3$), 22.5 (s, *C*H_2), 22.6 (s, *C*H_2), 27.4 (s, *C*H_2), 27.9 (s, *C*H_2), 28.3 (s, *C*H_2), 29.1 (s, *C*H_2), 29.7 (s, *C*H_2), 31.7 (s, *C*H_2), 32.0 (s, *C*H_2), 67.1 (s, *C*H_2-OH), 126.9 (s, RH*C*=CR'R''), 139.1 (s, RHC=*C*R'R''). **MS** (*m/z, pos.*): 212 (M^+).

Heptanol. **^{1}H NMR** (300.1 MHz, $CDCl_3$, 23 °C) δ = 0.88 (m, 3H, C*H*$_3$), 1.30 (m, br, 6H, C*H*$_2$), 1.43 (br, 2H, C*H*$_2$), 1.55 (m, 2H, C*H*$_2$), 3.64 (t, 2H, $^3J_{HH}$ = 6.6 Hz, C*H*$_2$-OH). **MS** (*m/z, pos.*): 115 ($[M-H]^+$).

4. Additional tables

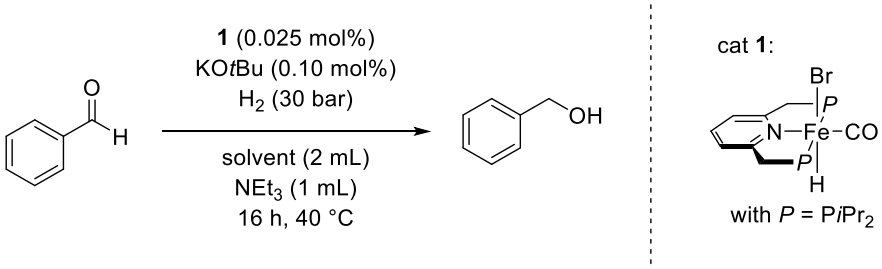
Table S1. The effect of various additives on the hydrogenation reaction of benzaldehyde.[a]



Entry	Additive, (1mL)	Conversion, [%][b]	TON
1	NEt_3	31	1240
2	pyridine	<1	<40
3[c]	DBU	<1	<40
4	NBu_3	<1	<40
5	Me_2NHex	35	1400

[a] Reaction conditions: Benzaldehyde (5.0 mmol), 0.025 mol% **1**, 0.10 mol% KO*t*Bu, $p(H_2)$ = 30 bar, 40°C, 16 h, EtOH (2 mL), additive (1 mL), performed in a Parr autoclave (45 mL). [b] Based on integration of the ^1H NMR spectra. [c] Unidentified side products were observed.

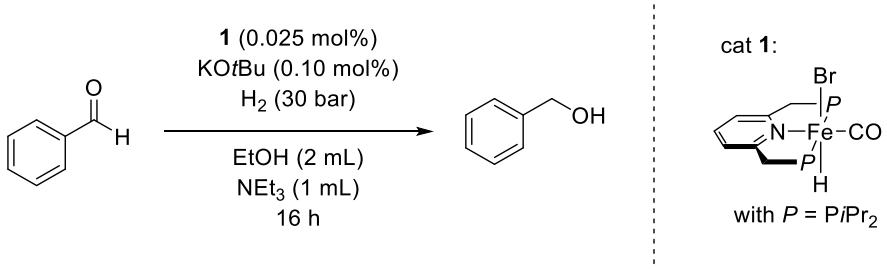
Table S2. The effect of different solvents on the hydrogenation reaction of benzaldehyde.[a]



Entry	Solvent, (2 mL)	Conversion, [%][b]	TON
1	EtOH	31	1240
2[c]	-	<1	<40
3	MeOH	30	1200
4	^{i}PrOH	8	320

[a] Reaction conditions: Benzaldehyde (5.0 mmol), 0.025 mol% **1**, 0.10 mol% KO*t*Bu, $p(H_2)$ = 30 bar, 40°C, 16 h, solvent (2 mL), NEt_3 (1 mL), performed in a Parr autoclave (45 mL). [b] Based on integration of the ^{1}H NMR spectra. [c] Reaction performed in 2 mL of NEt_3 in the absence of any other solvent.

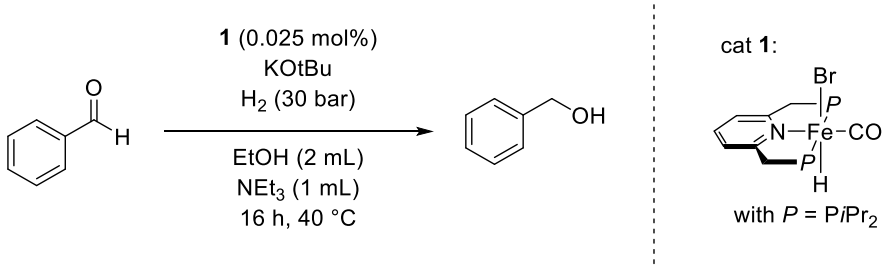
Table S3. The effect of temperature on the hydrogenation reaction of benzaldehyde. [a]



Entry	T, [°C]	Conversion, [%][b]	TON
1	23	12	480
2	40	31	1240
3	60	29	1160

[a] Reaction conditions: Benzaldehyde (5.0 mmol), 0.025 mol% **1**, 0.10 mol% KO*t*Bu, $p(H_2)$ = 30 bar, 16 h, EtOH (2 mL), NEt_3 (1 mL), performed in a Parr autoclave (45 mL). [b] Based on integration of the ^1H NMR spectra.

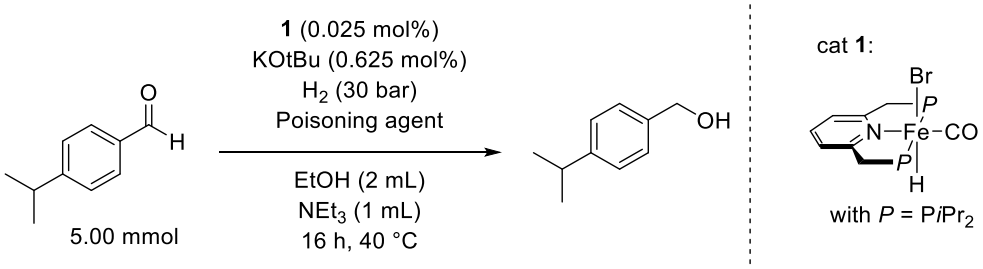
Table S4. The effect of KO*t*Bu concentration on the hydrogenation reaction of benzaldehyde.[a]



Entry	KO*t*Bu, [mol%]	Conversion, [%][b]	TON
1	0.03	1	40
2	0.10	31	1240
3	0.25	65	2560
4	0.375	91	3640
5	0.625	>99	4000
6	1.0	16	640

[a] Reaction conditions: Benzaldehyde (5.0 mmol), 0.025 mol% **1**, $p(H_2)$ = 30 bar, 40 °C, 16 h, EtOH (2 mL), NEt_3 (1 mL), performed in a Parr autoclave (45 mL). [b] Based on integration of the ^1H NMR spectra.

Table S5. Poisoning effects on the hydrogenation reaction of Cuminaldehyde.[a]



Entry	Poisoning agent, ([mol%])	Conversion, [%][b]	Yield, [%][c]	TON
1	-	>99	>99	4000
2[d]	Hg (excess)	>99	>99	4000
3	PMe_3 (0.008)	>99	>99	4000
4	PhCOOH (0.025)	>99	>99	4000
5	PhCOOH (0.25)	15	15	600

[a] Reaction conditions: Cuminaldehyde (5.0 mmol), 0.025 mol% **1**, 0.625 mol% KO*t*Bu, $p(H_2)$ = 30 bar, 40 °C, 16 h, EtOH (2 mL), NEt_3 (1 mL), poisoning agent, performed in a Parr autoclave (45 mL). [b] Based on integration of the ^1H NMR spectra. [c] Based on integration of the ^1H NMR spectra with mesitylene as standard. [d] Performed in the presence of ~2 g of mercury.

5. References

1 (a) R. Langer, G. Leitus, Y. Ben-David and D. Milstein, *Angew. Chem.*, 2011, **123**, 2168; (b) R. Langer, G. Leitus, Y. Ben-David and D. Milstein, *Angew. Chem. Int. Ed.*, 2011, **50**, 2120.

2 R. Langer, M. A. Iron, L. Konstantinovski, Y. Diskin-Posner, G. Leitus, Y. Ben-David and D. Milstein, *Chem.—Eur. J.*, 2012, **18**, 7196.

3 Homepage of the Spectral Database for Organic Compounds. Link: http://sdbs.db.aist.go.jp/sdbs/cgi-bin/cre_index.cgi