Electronic Supplementary Information for:

Acetaldehyde as an ethanol derived bio-building block: an alternative to Guerbet chemistry

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Materials and methods

Caution, acetaldehyde is a known carcinogen: all manipulations were performed in a properly ventilated fume hood. All chemicals and reagent grade solvents were obtained from commercial vendors and were used as received. ^1H and ^{13}C NMR spectra were obtained at room temperature on a Bruker AV400 MHz spectrometer, with chemical shifts (δ) referenced to the residual solvent signal (^1H and ^{13}C). GC–MS analysis was carried out using a Hewlett-Packard 6890 GC system equipped with a Hewlett-Packard 5973 mass selective detector.

Representative procedure for acetaldehyde condensation

In a stainless steel pressure tube containing a magnetic stirbar, Amberlyst 15 (300 mg), Pd/C (52 mg; 10 wt%, 0.05 mmol Pd), and cyclohexane (4.0 mL) were combined. Cold acetaldehyde (1.45 mmol) was quickly added and the tube was immediately connected to a pressure manifold and pressurized with Ar/H_2 (94/6; 1.7 MPa). The apparatus was heated to 60 °C with stirring (500 rpm) for 1 h, then immediately transferred to another hot plate at 100 °C and stirred (500 rpm). After 1 h, the apparatus was submerged in a cold water bath and allowed to cool for 15 min. At this point the condensation reaction was complete. In order to accurately quantify the yield of the volatile aldehyde product (butyraldehyde), the following workup procedure was employed to convert the aldehydes to diethyl-acetals. The pressure was relieved and ethanol (1.0 mL) was added, then the mixture was stirred (500 rpm) at room temperature for 30 min. The reaction mixture was then transferred to a centrifuge tube and the pressure tube was rinsed with ethyl acetate. After centrifuging, the combined supernatant was decanted from the catalysts and diluted with ethyl acetate in a volumetric flask (10.0 mL). The sample was then analyzed by GCMS and yields were determined using calibration curves generated from authentic standards of the products.

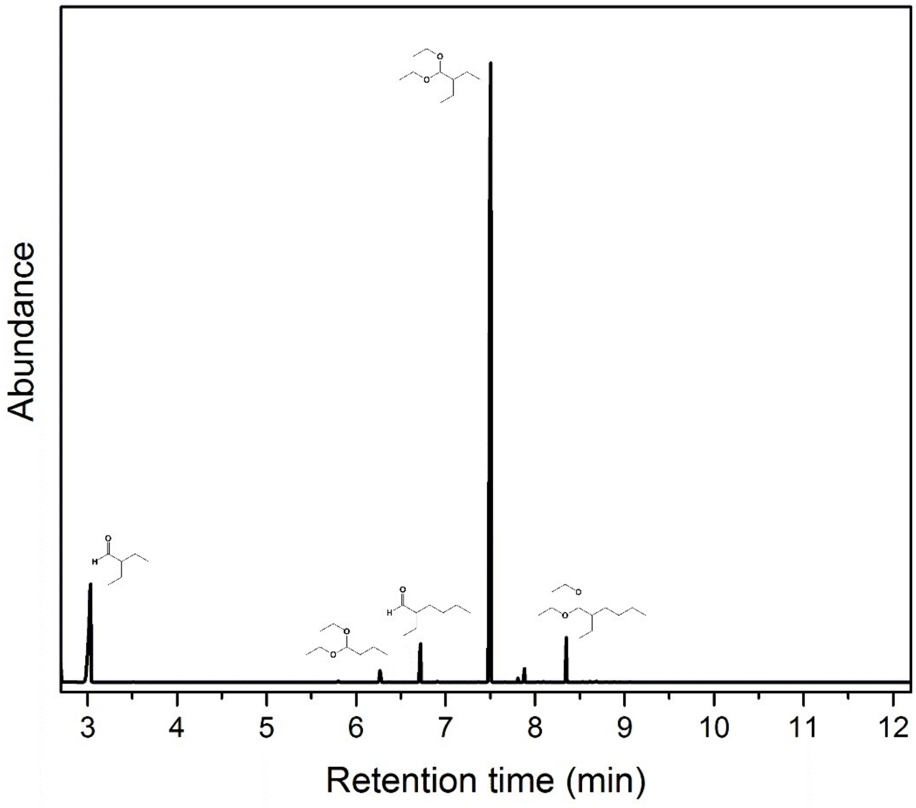


Figure S1. Representative GCMS trace of acetaldehyde condensation products in cyclohexane solution after workup in ethanol. Conditions: Acetaldehyde (3.35 mmol), Amberlyst 15 (0.30 g), Pd/C (10 wt%; 0.05 g), cyclohexane (4.0 mL), Ar/H_2 (94/6; 1.7 Mpa), 60 °C 1 h, 80 °C 3 h.

Calculation of carbon yield

The following equation was used to determine carbon yields from GCMS data:

$$\%\ Carbon\ yield = \frac{(mmol\ product)\ X\ (\#\ of\ C\ atoms)}{(mmol\ acetaldehyde)\ X\ 2} X\ 100$$

Note that for products that were converted to acetals prior to quantification, the -OEt groups were not included in the number of carbon atoms, only those in the carbon chain derived from acetaldehyde.

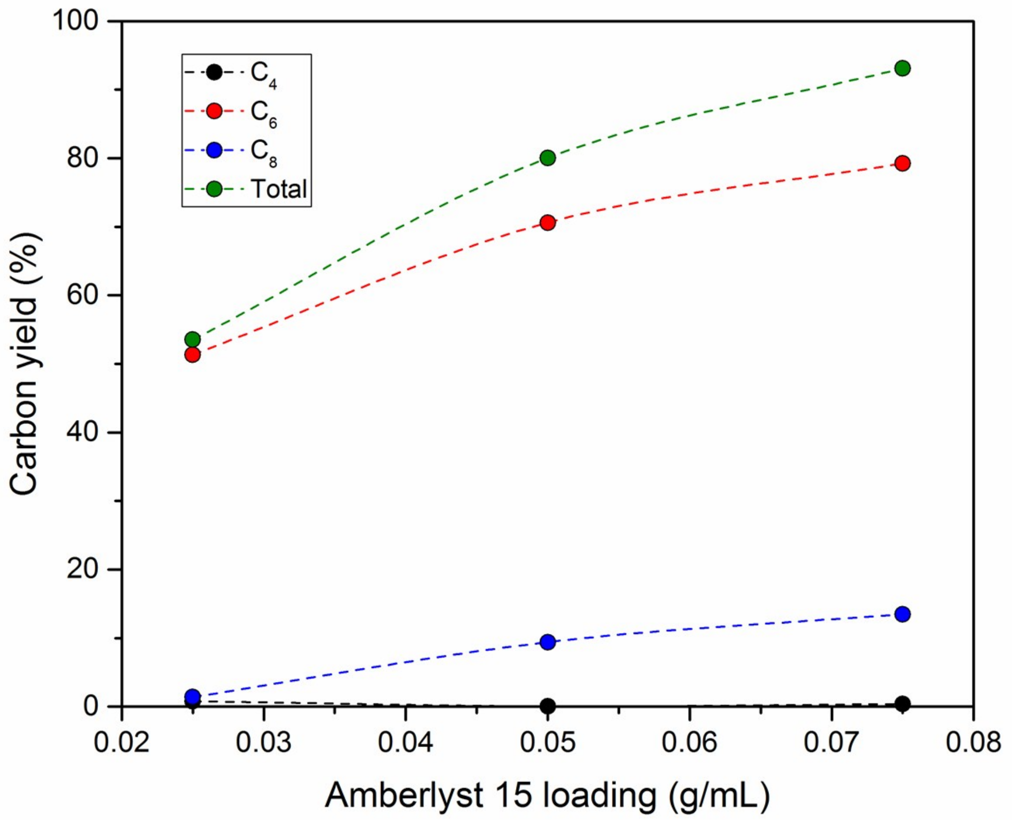
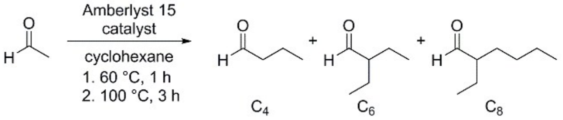


Figure S2. Effect of Amberlyst 15 loading on carbon yield for acetaldehyde condensation products in cyclohexane solution. Conditions: Acetaldehyde (3.35 mmol), Amberlyst 15 (0.10, 0.20, 0.30 g), Pd/C (10 wt%; 0.05 g), cyclohexane (4.0 mL), Ar/H_2 (94/6; 1.7 Mpa), 60 °C 1 h, 100 °C 3 h.



Entry	Catalyst	P (MPa)	Yields (%C):	C_4	C_6	C_8	Total	MBD[a]
1	Pd/C	1.7, Ar/H_2		<1	79	13	92	7
2	Ru/C	1.7, Ar/H_2		<1	2	<1	2	98
3	Ni/SiO_2-Al_2O_3	1.7, Ar/H_2		<1	12	1	13	87
4	CuO/Al_2O_3	1.7, Ar/H_2		<1	12	1	13	87

Table S1. Comparison of metal catalysts for acetaldehyde condensation in cyclohexane solution. Conditions: Acetaldehyde (3.35 mmol), Amberlyst 15 (0.10, 0.20, 0.30 g), catalyst (0.05 g), cyclohexane (4.0 mL), Ar/H_2 (94/6; 1.7 Mpa), 60 °C 1 h, 100 °C 3 h. [a]MBD = mass balance deficiency

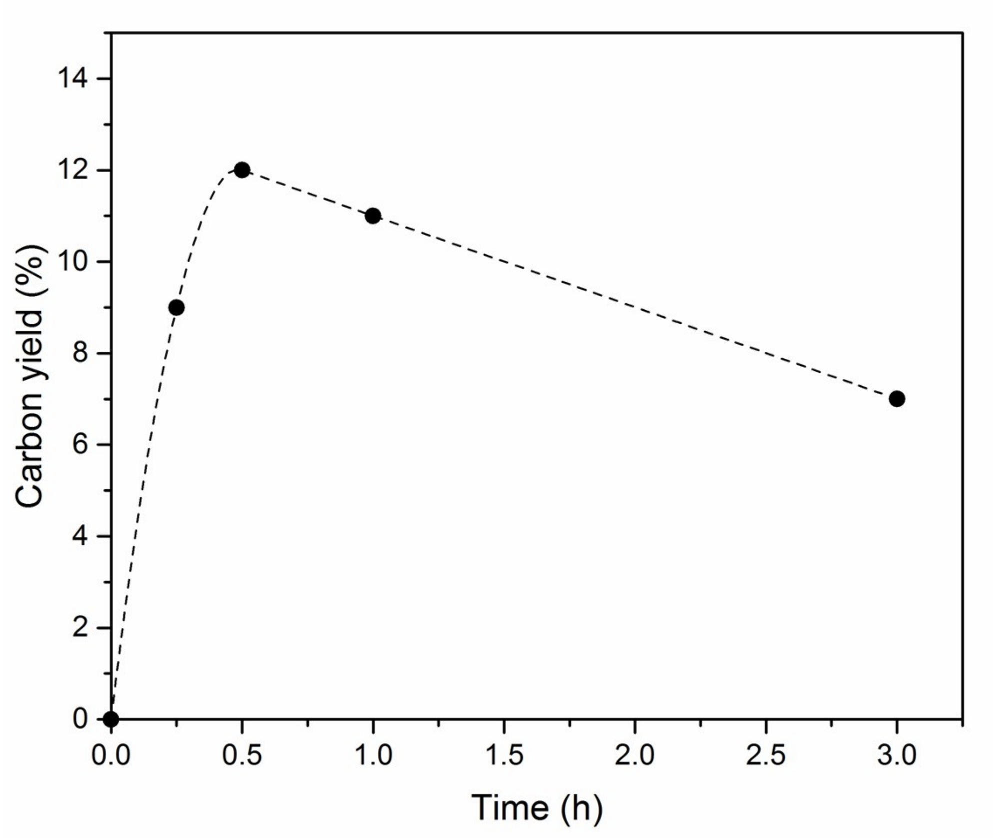


Figure S3. Initial time course for butyraldehyde production from acetaldehyde. Conditions: Acetaldehyde (4.31 mmol), Amberlyst 15 (0.30 g), Pd/C (10 wt%; 0.05 g), cyclohexane (4.0 mL), Ar/H_2 (94/6; 1.7 Mpa), 60 °C.

Condensation of butyraldehyde

In a stainless steel pressure tube containing a magnetic stirbar, Amberlyst 15 (300 mg), Pd/C (52 mg; 10 wt%, 0.05 mmol Pd), and cyclohexane (4.0 mL) were combined. Butyraldehyde (2.90 mmol) was quickly added and the tube was immediately connected to a pressure manifold and pressurized with Ar/H_2 (94/6; 1.7 MPa). The apparatus was heated to 100 °C with stirring (500 rpm). After 3 h, the apparatus was submerged in a cold water bath and allowed to cool for 15 min. The reaction mixture was then transferred to a centrifuge tube and the pressure tube was rinsed with ethyl acetate. After centrifuging, the combined supernatant was decanted from the catalysts and diluted with ethyl acetate in a volumetric flask (10.0 mL). The sample was then analyzed by GCMS and yields were determined using calibration curves generated from authentic standards of the products.

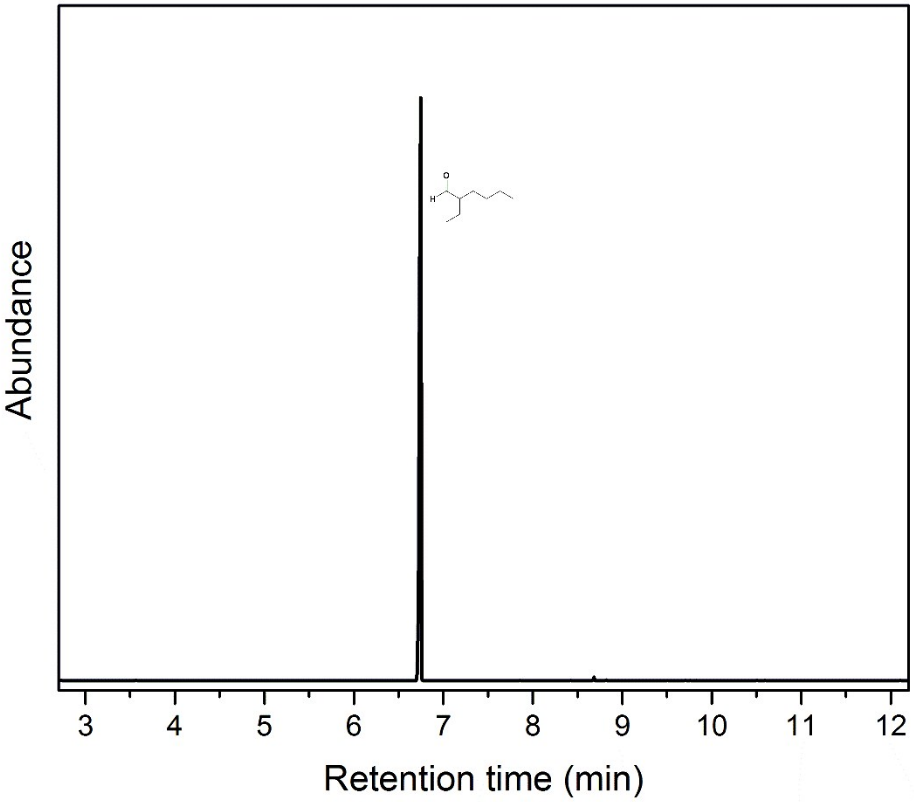


Figure S4. GCMS trace of butyraldehyde condensation products in cyclohexane solution. Conditions: Butyraldehyde (2.90 mmol), Amberlyst 15 (0.30 g), Pd/C (10 wt%; 0.05 g), cyclohexane (4.0 mL), Ar/H_2 (94/6; 1.7 Mpa), 100 °C 3 h.

Hydrogenation of 2-ethylbutyraldehyde

2-Ethylbutyraldehyde (8.0 mL; 65.0 mmol) and Ni/SiO_2-Al_2O_3 (0.40 g; 65 wt% Ni, 4.43 mmol) were loaded into a 100 mL stainless steel bomb reactor fitted with an overhead stirring device. The reactor was connected to a high pressure gas burette (150 mL, 5.0 MPa H_2; *ca.* 760 mmol H_2) to maintain a constant H_2 pressure inside the reactor and monitor H_2 consumption. The reactor was purged with H_2 and then pressurized to 1.4 MPa and heated to 150 $^\circ$C with stirring at 300 rpm. After H_2 consumption ceased (*ca.* 4.5 h), the reactor was cooled and slowly vented. An aliquot of the reaction mixture was analyzed by ^{1}H NMR spectroscopy to reveal >98% conversion to 2-ethyl-1-butanol. The catalyst was removed via filtration to provide 2-ethyl-1-butanol (5.80 g; 87% isolated yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 3.53 (d, *J* = 3.7 Hz, 2H), 1.71 (br s, 1H, OH), 1.43 – 1.24 (m, 5H), 0.88 (t, *J* = 6.9 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 65.00, 43.63, 23.00, 11.21.

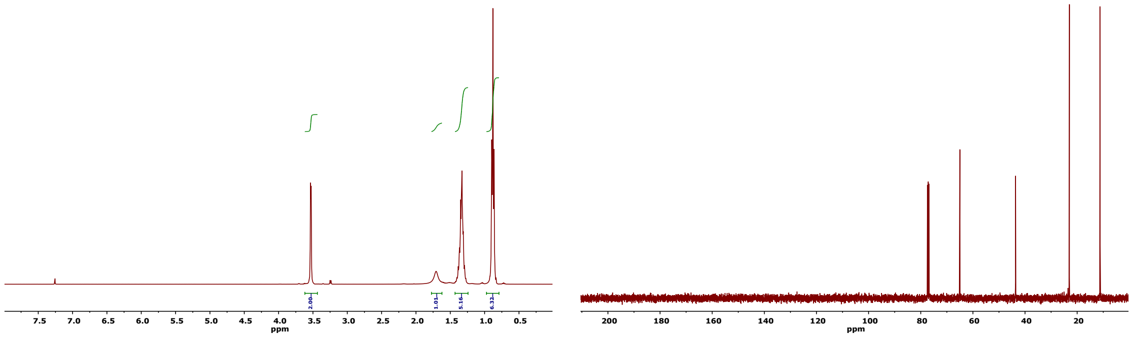


Figure S5. 400 MHz ^1H NMR spectrum (left) and 101 MHz ^{13}C NMR spectrum (right) of as-isolated 2-ethyl-1-butanol.

Hydrogenation of 2-ethylhexanal

2-Ethylhexanal (8.0 mL; 51.3 mmol) and Ni/SiO_2-Al_2O_3 (0.40 g; 65 wt% Ni, 4.43 mmol) were loaded into a 100 mL stainless steel bomb reactor fitted with an overhead stirring device. The reactor was connected to a high pressure gas burette (150 mL, 5.0 MPa H_2; *ca.* 760 mmol H_2) to maintain a constant H_2 pressure inside the reactor and monitor H_2 consumption. The reactor was purged with H_2 and then pressurized to 1.4 MPa and heated to 150 °C with stirring at 300 rpm. After H_2 consumption ceased (*ca.* 4.5 h), the reactor was cooled and slowly vented. An aliquot of the reaction mixture was analyzed by ^1H NMR spectroscopy to reveal >98% conversion to 2-ethyl-1-hexanol. The catalyst was removed via filtration to provide 2-ethyl-1-hexanol (5.19 g; 78% isolated yield).

^1H NMR (400 MHz, $CDCl_3$) δ 3.47 (d, *J* = 4.8 Hz, 2H), 2.73 (br s, 1H OH), 1.45 – 1.13 (m, 9H), 0.84 (dq, *J* = 7.1, 3.4 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 65.08, 42.03, 30.16, 29.17, 23.36, 23.15, 14.08, 11.04.

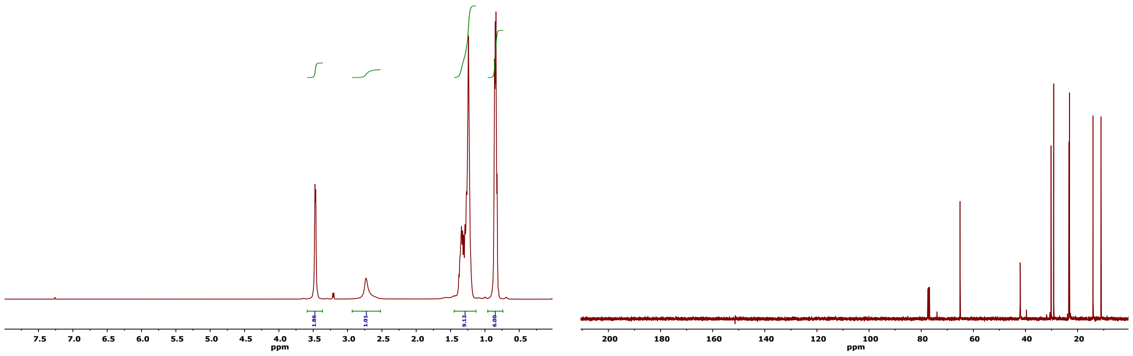


Figure S6. 400 MHz ^1H NMR spectrum (left) and 101 MHz ^{13}C NMR spectrum (right) of as-isolated 2-ethyl-1-hexanol.

Catalyst recycling

A previous study using Amberlyst CH28 (a palladium-doped resin used industrially for MIBK synthesis) reported the deactivation of the resin during acetone condensation catalysis.[1] These studies were conducted in neat acetone and the resin was concluded to be deactivated by water, which is formed during the reaction, rather than coke formation or product inhibition. The above catalyst was found to achieve nearly identical initial activity after drying overnight. To assess the stability of the present catalyst system for acetaldehyde condensation, catalyst recycling experiments were performed. The reaction was set up as described above using cyclohexane solvent and run for 1 hour at 80 °C in order to assess stability under a kinetically-controlled regime. After the reaction, the catalysts were separated from the organic solution via centrifuge, then washed with cyclohexane, suspended in cyclohexane and returned to the reactor. The cyclohexane reaction solution was transferred to an ethanol solution containing additional Amberlyst 15 to convert the products to diethyl-acetals and was analyzed as above by GC-MS. Cold acetaldehyde was added to the catalyst/cyclohexane suspension, the tube was pressurized with Ar/H_2 and re-run for 1 hour. This was repeated for a total of 4 additional cycles. For the final cycle, the catalysts were dried at 110 °C for 1 hour, then subjected to the above reaction conditions. The activity was regained, consistent with water deactivation of the resin during catalysis.

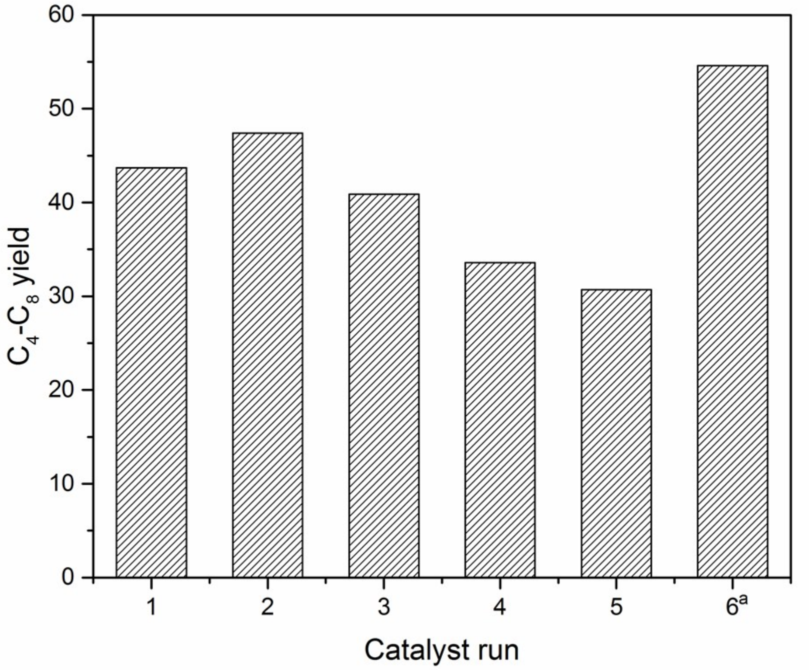


Figure S7. C_4-C_8 condensate yield as a function of catalyst recycle during the acetaldehyde condensation. Conditions: Acetaldehyde (4.31 mmol), Amberlyst 15 (0.30 g), Pd/C (10 wt%; 0.05 g), cyclohexane (4.0 mL), Ar/H_2 (94/6; 1.7 Mpa), 80 °C 1h. ([a]Catalysts dried at 110 C for 1 h prior to re-use).

Reference

1. S. Talwalkar and S. Mahajani, *Appl. Catal. A,* 2006, **302**, 140-148.