

**Continuous catalytic “one-pot” multi-step synthesis of 2-ethylhexanal from crotonaldehyde**

Tsunetake Seki,<sup>†</sup> Jan-Dierk Grunwaldt and Alfons Baiker\*

*Department of Chemistry and Applied Biosciences, ETH Zurich,  
Hönggerberg, CH-8093 Zurich, Switzerland*

<sup>†</sup>*Research Fellow of the Japan Society for the Promotion of Science*

## 1. Experimental details

### 1.1. Catalyst preparation

As a typical example, the preparation method of 1% Pd/Amberlyst-15 is described. [Pd(NH<sub>3</sub>)<sub>4</sub>]Cl<sub>2</sub> (ABCR, 99%; 0.0466 g, 0.190 mmol) and deionized water (20.0 g) were mixed in a 50-mL flask containing a stirring bar. After stirring the mixture for homogenization, Amberlyst® 15 (Fluka, 20–50 mesh, dry (moisture ~5%), product number: 06423, lot number: 1166065; 2.00 g) was added, and the resultant heterogeneous mixture was stirred at 80 °C for 24 h. The solid material was separated by filtration, washed with deionized water (15 mL), and dried at 100–110 °C overnight. The reduction of the material under an H<sub>2</sub>/N<sub>2</sub> flow at 100 °C for 1 h yielded an active catalyst of 1% Pd/Amberlyst-15, which was subsequently used for a catalytic reaction.

### 1.2. Commercially available catalyst

1% Pd/C (Engelhard, 5109) was crushed and used as sieved fractions (ca. 0.5–1.4 mm). This catalyst was pre-reduced at 100 °C for 1 h under an H<sub>2</sub>/N<sub>2</sub> flow just before the use for a reaction.

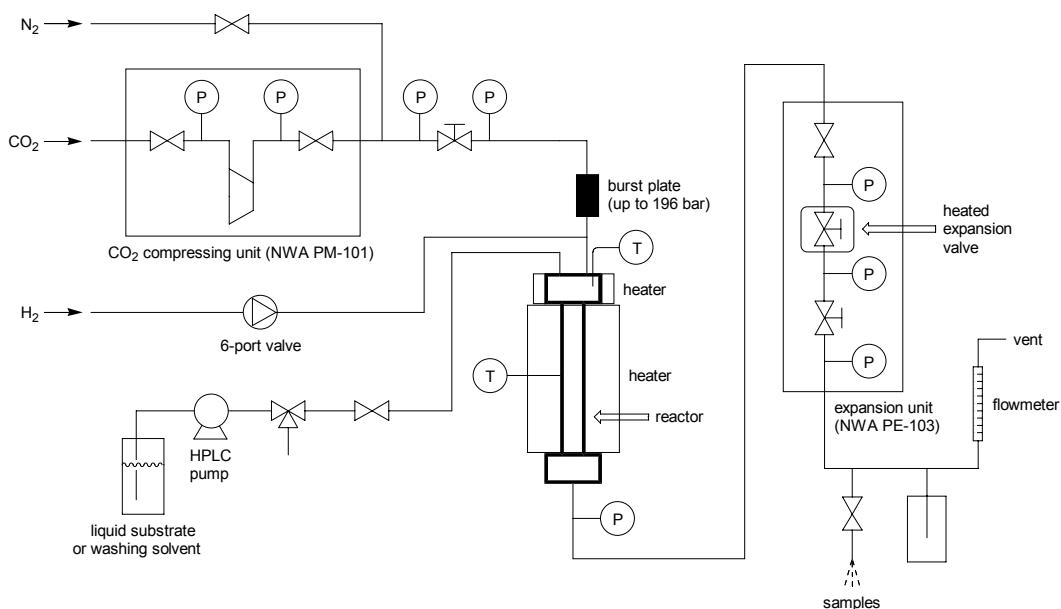
### 1.3. Organic reagent

Commercially available high-grade crotonaldehyde (Fluka, ≥99.5%, *cis:trans* = ~1:20, stabilizers: ~0.1% 2,6-di-*tert*-butyl-*p*-cresol and ~1% H<sub>2</sub>O) was used without further purification.

#### 1.4. Continuous-flow reactor and reaction procedures

The continuous-flow reactor system employed in the present research is shown in Figure S1. Commercially available CO<sub>2</sub> (Pangas, 99.9%) and H<sub>2</sub> (Pangas, 99.995%) were used as received. The reactions were performed with a tubular reactor (ETH-workshop) of which inner diameter and volume were 13 mm and 35 mL, respectively. Glass beads were placed above the catalyst to ensure an optimum flow distribution and mixing of the substrate at the entrance of the catalyst bed.

Hydrogen was introduced through a six-port switching valve (Rheodyne, model 7000) dosing 0.05 mL pulses at high pressure and constant frequency. Freshly opened liquid substrate was fed to the reactor using an HPLC pump (Gilson, model 305). The total pressure was adjusted to a constant value during the reactions with the pressure regulator connected to the CO<sub>2</sub>-compressing unit and the total fluid flow was controlled at the expansion unit.



**Figure S1.** Continuous-flow reactor system used in the present research.

The product samples, which were taken every 20 min, were collected in a glass vial containing a known amount of toluene (internal standard substance). The mixture was subsequently diluted with ethyl acetate and subjected to analysis by GC equipped with FID (Hewlett Packard, model HP 6890) that had an HP-5 column (J&W Scientific, 30 m × 0.32 mm × 0.25 μm) to determine the composition. The column temperature was as follows: 50 °C (10 min) → 20 °C min<sup>-1</sup> → 250 °C (5 min). After the steady state conditions were reached after ca. 3 h from the first sampling, the conversion, yield and selectivity were determined by the following equations.

Conversion (%) = [(mol of **2**) + (mol of 1-butanol) + {2 × (mol of **3**)} + {2 × (mol of **4**)}] / [(mol of **7**) + (mol of **2**) + (mol of 1-butanol) + {2 × (mol of **3**)} + {2 × (mol of **4**)}] × 100

Selectivity to **2** (%) = (mol of **2**) / [(mol of **2**) + (mol of 1-butanol) + {2 × (mol of **3**)} + {2 × (mol of **4**)}] × 100

Selectivity to 1-butanol (%) = (mol of 1-butanol) / [(mol of **2**) + (mol of 1-butanol) + {2 × (mol of **3**)} + {2 × (mol of **4**)}] × 100

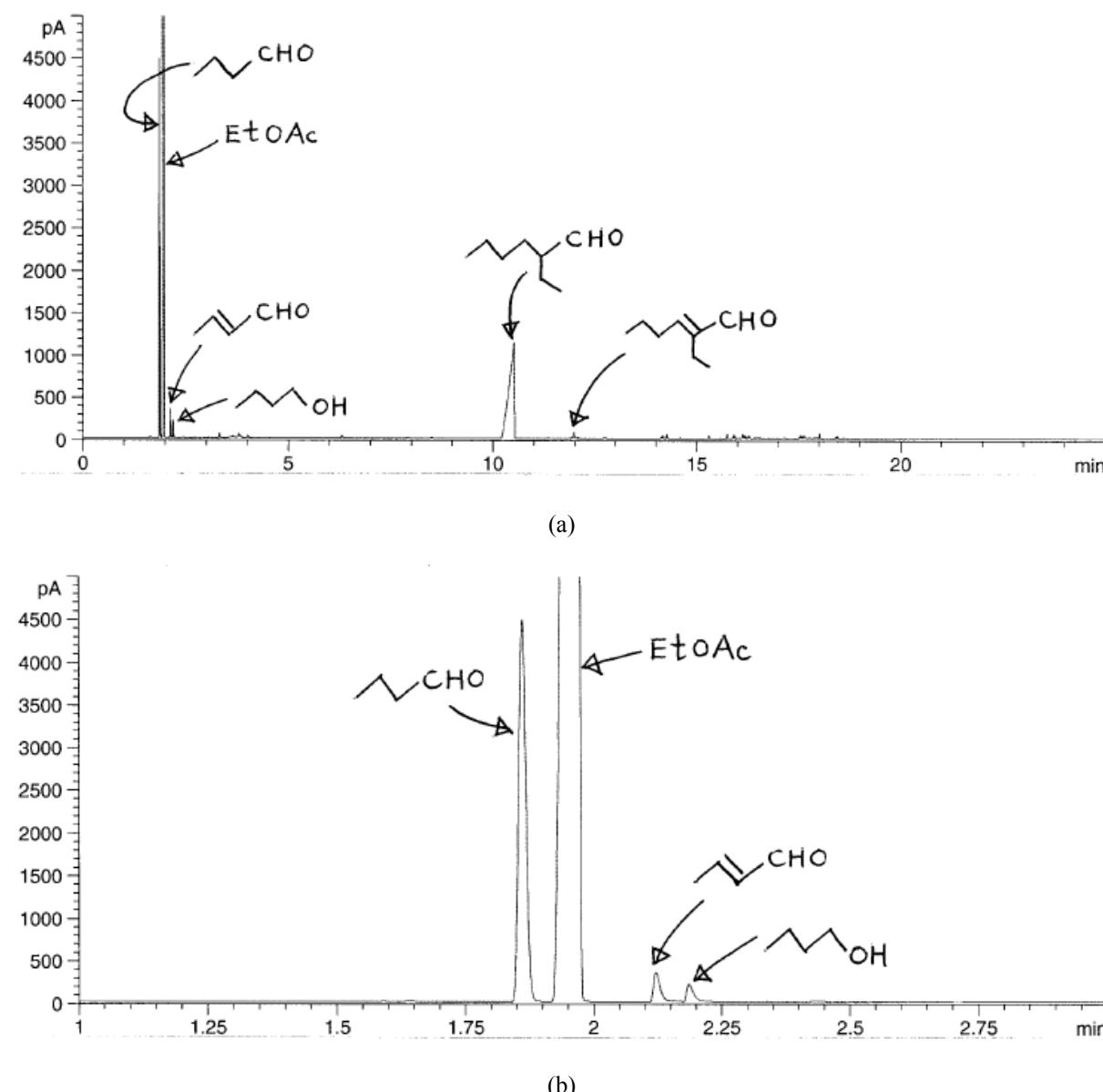
Selectivity to **3** (%) = {2 × (mol of **3**)} / [(mol of **2**) + (mol of 1-butanol) + {2 × (mol of **3**)} + {2 × (mol of **4**)}] × 100

Selectivity to **4** (%) = {2 × (mol of **4**)} / [(mol of **2**) + (mol of 1-butanol) + {2 × (mol of **3**)} + {2 × (mol of **4**)}] × 100

Generally, the average conversions, yields and selectivities obtained from four samples are quoted as the results. The identification of the products was performed by comparing the GC retention times with authentic samples (all the products commercially available), GC-MS (Hewlett Packard, model HP 5973) with an analyzing program (Enhanced ChemStation, G1701BA, Version B.01.00, Hewlett Packard) and NMR spectroscopy. The intense GC-MS peaks of 2-ethylhexanal **4** were as follows: *m/z* 41, 43, 57, 72; the program proposed the structure in preference to the others. The NMR analysis of **4** was performed as follows. Several samples obtained under the condition of entry 4 in Table 1 were collected in a flask and the components with lower boiling points were evaporated off to obtain the concentrated **4**, which was subsequently applied to NMR analysis. The crude product showed the characteristic <sup>13</sup>C NMR peaks attributed to **4**: <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 11.48, 13.91, 21.90, 22.81, 28.22, 29.28, 53.46, 205.73.

**2. GC profile of the product sample.**

Figures S2 shows the GC profile of the product sample obtained under the condition of entry 4 in Table 1.



**Figure S2.** GC profile of the product sample obtained under the condition of entry 4 in Table 1. (a) Full view; (b) magnified view. Note that this is a sample without an internal standard substance. The peak attributed to toluene as an internal standard substance appears at a retention time of ca. 3.30 min.