Bio-based *N*-alkyl-2-pyrrolidones by Pd-catalyzed reductive *N*-alkylation and decarboxylation of glutamic acid

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Supporting Information

1. General

1.1 Chemicals

L-Glutamic acid (Acros Organics, 99%), L-glutamine (Janssen Chimica, 99%), monosodium glutamate (Sigma-Aldrich, 98%), pyroglutamic acid (Sigma-Aldrich, > 99%), 2-pyrrolidone (Sigma-Aldrich, 99%), *N*-butyl-2-pyrrolidone (TCI Europe, > 98%), propionaldehyde (Acros Organics, > 99%), acetone (Fisher Scientific, 99.99%), butyraldehyde (Acros Organics, 99%), isobutyraldehyde (Sigma-Aldrich, > 99%), 2-butanone (Acros Organics, > 99%), valeraldehyde, (Acros Organics, 98%), 2-pentanone (Acros Organics, > 99%), isovaleraldehyde (Acros Organics, 98%), 2-methylbutyraldehyde (J&K Scientific, 90%), H_3PO_4 (VWR International, 85% in water), NH_3 (Acros Organics, 28-30% in water), acetic acid (VWR International, 99.99%), diglyme (Sigma-Aldrich, 99%), *n*-butyl acetate (Sigma-Aldrich, 99.5%), dimethyl sulfoxide (Acros Organics, > 99%), deuterium oxide (Sigma Aldrich, 99%), Amberlyst-15® (Sigma-Aldrich, hydrogen form) were all used as purchased. Catalysts were prepared from metal precursors and supports: Al_2O_3 (acidic, CONDEA Chemie, Puralox NGa-150), Al_2O_3 (basic, Sigma Aldrich), SiO_2 (Evonik, Aerosil 380), $Pd(NH_3)_4Cl_2{\cdot}H_2O$ (Sigma Aldrich, ≥ 99.99%). Commercial catalysts include 5 wt% Pd/C (Johnson Matthey), 5 wt% Ru/C (Alfa Aesar), 5 wt% Rh/C (Johnson Matthey) and 5wt% $PdBaSO_4$ (Sigma-Aldrich).

1.2 Reductive *N*-alkylation of amino acids

N-*Alkylamino acids*. The reactor was charged with glutamic acid, monosodium glutamate or glutamine (3.4 mmol), aldehyde/ketone (6.8 - 13.6 mmol), 5 wt% Pd/C (2.5 mol% Pd) and water (20 ml). The reactor was sealed, purged 3 times with N_2, 3 times with H_2 and finally pressurized with H_2 (2.5 - 50 bar). Moreover, H_2 was supplied continuously in order to keep the pressure constant during the reaction. The reactor was kept at room temperature or heated at 70 °C while stirring vigorously (830 rpm). Samples were taken at different times by an additional sampling valve. After reaction, the pressure was released and the solid catalyst was removed by centrifugation. The crude reaction mixtures were analyzed with ^{1}H-NMR spectroscopy.

Monosodium N-*alkylglutamate*. The reactor was charged with monosodium glutamate (2.5 g; 14.8 mmol), aldehyde/ketone (20.7 – 88.8 mmol), 5 wt% Pd/C (2 mol% Pd) and water (20 ml). The pH was eventually adjusted with H_3PO_4 or acetic acid. The reactor was sealed, purged 3 times with N_2, 3 times with H_2 and finally pressurized with 60 bar H_2. Reactions were performed at room temperature or 70 °C

while stirring vigorously (830 rpm) for 6 h – 24 h. Afterwards, the reactor was eventually cooled down to room temperature in an ice bath, the pressure was released and the solid catalyst was removed by centrifugation. Evaporation of water, alcohol (obtained by hydrogenation of the aldehyde/ketone) and unreacted aldehyde/ketone was achieved at 60 °C under vacuum, and the solid residue was analyzed with ^{1}H-NMR spectroscopy.

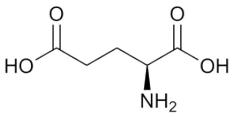
1.3 Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES)

The Pd content of self-prepared Pd catalysts was determined by ICP-AES after complete destruction of the catalyst. To that end, 50 mg catalyst was suspended in 0.5 ml Aqua Regia (1:3 ≡ HNO_3:HCl) and 3 ml HF (40%) in a closed polypropylene recipient. The mixture was stirred for at least 2 h at room temperature in order to obtain complete dissolution. Next, the mixture was diluted with 10 ml Milli-Q water and HF was neutralized by pouring the degradation mixture into an aqueous solution with an excess of H_3BO_3 (1.5 g in a few ml water) in a 50 ml PTFE volumetric flask. The volume was adjusted to 50 ml with Milli-Q water, homogenized and stored overnight. Finally, the samples were diluted (1:10) with a 0.42 N HNO_3 solution. Samples were measured with a Varian 720-ES ICP-AES apparatus at 340.458 nm. Solutions were presented to the spectrometer using the Varian SPS3 Sample Preparation System.

CAUTION: HF is very corrosive and toxic, and is incompatible with many standard laboratory such as glassware. All handling with HF requires special safety precautions to prevent inhalation and contact with skin.

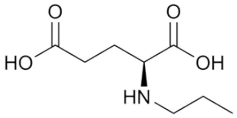
1.4 Product identification

L-Glutamic acid (MW = 147 g mol^{-1})



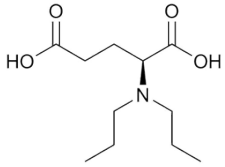
^{1}H-NMR (400 MHz, D_2O): δ 3.70 (dd, ^{3}J(H,H) = 8.04, 4.47 Hz, 1H; (-CH_2)(NH_2)>C**H**-COOH), 2.30 (m, 2H; HOOC-C**H**$_2$-CH_2-), 2.04 (m, 2H; -CH_2-C**H**$_2$-CH<) ppm.

N-Propylglutamic acid (MW = 189 g mol^{-1})



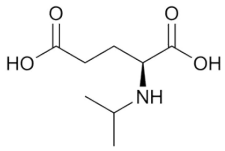
^{1}H-NMR (400 MHz, D_2O): δ 3.57 (t, ^{3}J(H,H) = 6.70 Hz, 1H; (-CH_2)(-NH)>C**H**-COOH), 2.91 (t, ^{3}J(H,H) = 7.44 Hz, 2H; -NH-C**H**$_2$-CH_2-), 2.45 (m, 2H; HOOC-C**H**$_2$-CH_2-), 2.05 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.62 (sex, ^{3}J(H,H) = 7.81 Hz, 2H; -CH_2-C**H**$_2$-CH_3), 0.88 (t, ^{3}J(H,H) = 7.23 Hz, 3H; -CH_2-CH_2-C**H**$_3$) ppm.

_N_,_N_-Dipropylglutamic acid (MW = 231 g mol^{-1})



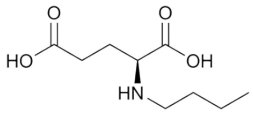
^{1}H-NMR (400 MHz, D_2O): δ 3.66 (m, 1H; (-CH_2)(>N)>C**H**-COOH), 3.07 (m, 4H; -N<(C**H**$_2$-CH_2-CH_3)$_2$), 2.45 (m, 2H; HOOC-C**H**$_2$-CH_2-), 2.05 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.62 (sex, ^{3}J(H,H) = 7.81 Hz, 4H; -N<(CH_2-C**H**$_2$-CH_3)$_2$), 0.88 (t, ^{3}J(H,H) = 7.23 Hz, 6H; -N<(CH_2-CH_2-C**H**$_3$)$_2$) ppm.

_N_-Isopropylglutamic acid (MW = 189 g mol^{-1})



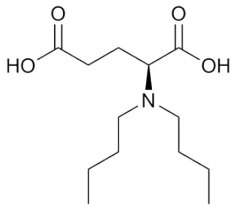
^{1}H-NMR (400 MHz, D_2O): δ 3.76 (t, ^{3}J(H,H) = 5.70 Hz, 1H; (-CH_2)(-NH)>C**H**-COOH), 3.34 (sep, ^{3}J(H,H) = 6.03 Hz, 1H; -NH-C**H**<(CH_3)$_2$), 2.45 (m, 2H; HOOC-C**H**$_2$-CH_2-), 2.03 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.22 (t, ^{3}J(H,H) = 6.03 Hz, 6H; -NH-CH<(C**H**$_3$)$_2$) ppm.

_N_-Butylglutamic acid (MW = 203 g mol^{-1})



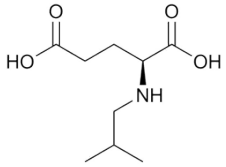
^{1}H-NMR (400 MHz, D_2O): δ 3.58 (t, ^{3}J(H,H) = 5.87 Hz, 1H; (-CH_2)(-NH)>C**H**-COOH), 2.95 (t, ^{3}J(H,H) = 7.96 Hz, 2H; -NH-C**H**$_2$-CH_2-), 2.45 (m, 2H; HOOC-C**H**$_2$-CH_2-), 2.05 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.59 (quin, ^{3}J(H,H) = 7.60 Hz, 2H; -CH_2-C**H**$_2$-CH_2-CH_3), 1.30 (sex, ^{3}J(H,H) = 7.77 Hz, 2H; -CH_2-C**H**$_2$-CH_3), 0.83 (t, ^{3}J(H,H) = 7.25 Hz, 3H; -CH_2-CH_2-C**H**$_3$) ppm.

_N_,_N_-Dibutylglutamic acid (MW = 259 g mol^{-1})



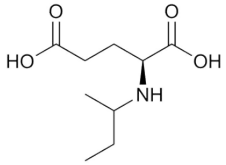
^{1}H-NMR (400 MHz, D_2O): δ 3.66 (m, 1H; (-CH_2)(>N)>C**H**-COOH), 3.1 (m, 4H; -N<(C**H**$_2$-CH_2-CH_2-CH_3)$_2$), 2.45 (m, 2H; HOOC-C**H**$_2$-CH_2-), 2.05 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.59 (quin, ^{3}J(H,H) = 7.60 Hz, 4H; -N<(CH_2-C**H**$_2$-CH_2-CH_3)$_2$), 1.30 (sex, ^{3}J(H,H) = 7.77 Hz, 4H; -N<(CH_2-CH_2-C**H**$_2$-CH_3)$_2$), 0.83 (t, ^{3}J(H,H) = 7.25 Hz, 6H; -N<(CH_2-CH_2-CH_2-C**H**$_3$)$_2$) ppm.

_N_-Isobutylglutamic acid (MW = 203 g mol^{-1})



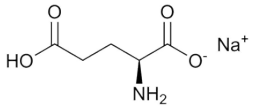
^{1}H-NMR (400 MHz, D_2O): δ 3.57 (t, ^3J(H,H) = 6.36 Hz, 1H; (-CH_2)(-NH)>C**H**-COOH), 2.79 (m, 2H; -NH-C**H**$_2$-CH_2-), 2.47 (m, 2H; HOOC-C**H**$_2$-CH_2-), 2.04 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.92 (sep, ^3J(H,H) = 6.78 Hz, 1H; -CH_2-C**H**<(CH_3)$_2$), 0.90 (d, ^3J(H,H) = 7.36 Hz, 6H; -CH_2-CH<(C**H**$_3$)$_2$) ppm.

_N_-(2-Butyl)glutamic acid (MW = 203 g mol^{-1})



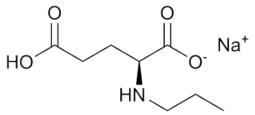
^{1}H-NMR (400 MHz, D_2O): δ 3.66 (m, 1H; (-CH_2)(-NH)>C**H**-COOH), 3.11 (m, 1H; -NH-C**H**<(HCH-CH_3)(CH_3)), 2.47 (m, 2H; HOOC-C**H**$_2$-CH_2-), 2.03 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.72 (m, 1H; -NH-CH<(HC**H**-CH_3)(CH_3)), 1.50 (m, 1H; -NH-CH<(**H**CH-CH_3)(CH_3)), 1.22 (m, 3H; -NH-CH<(HCH-CH_3)(C**H**$_3$)), 0.88 (m, 3H; -NH-CH<(HCH-C**H**$_3$)(CH_3)) ppm.

Monosodium glutamate (MW = 169 g mol^{-1})



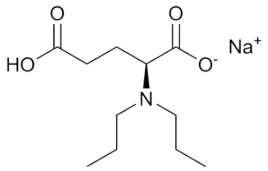
^{1}H-NMR (400 MHz, D_2O): δ 3.66 (t, ^3J(H,H) = 5.99 Hz, 1H; (-CH_2)(NH_2)>C**H**-COOH), 2.27 (t, ^3J(H,H) = 8.38 Hz, 2H; HOOC-C**H**$_2$-CH_2-), 2.00 (m, 2H; -CH_2-C**H**$_2$-CH<) ppm.

Monosodium _N_-propylglutamate (MW = 211 g mol^{-1})



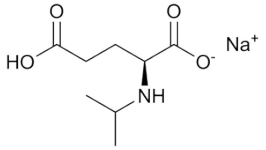
^{1}H-NMR (400 MHz, D_2O): δ 3.51 (t, ^3J(H,H) = 5.82 Hz, 1H; (-CH_2)(-NH)>C**H**-COO^-Na^+), 2.90 (t, ^3J(H,H) = 7.76 Hz, 2H; -NH-C**H**$_2$-CH_2-), 2.30 (t, ^3J(H,H) = 7.27, 2H; HOOC-C**H**$_2$-CH_2-), 1.99 (q, ^3J(H,H) = 6.30 Hz, 2H; -CH_2-C**H**$_2$-CH<), 1.62 (sex, ^3J(H,H) = 7.64 Hz, 2H; -CH_2-C**H**$_2$-CH_3), 0.90 (t, ^3J(H,H) = 7.40 Hz, 3H; -CH_2-CH_2-C**H**$_3$) ppm.

Monosodium _N,N_-dipropylglutamate (MW = 253 g mol^{-1})



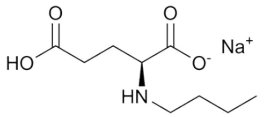
^{1}H-NMR (400 MHz, D_2O): δ 3.60 (m, 1H; (-CH_2)(>N)>C**H**-COO^-Na^+), 3.06 (m, 4H; -N<(C**H**$_2$-CH_2-CH_3)$_2$), 2.30 (m, 2H; HOOC-C**H**$_2$-CH_2-), 1.99 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.62 (sex, ^3J(H,H) = 7.64 Hz, 4H; -N<(CH_2-C**H**$_2$-CH_3)$_2$), 0.90 (t, ^3J(H,H) = 7.40 Hz, 6H; -N<(CH_2-CH_2-C**H**$_3$)$_2$) ppm.

Monosodium *N*-isopropylglutamate (MW = 211 g mol^{-1})



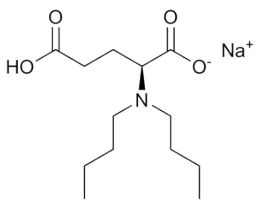
^{1}H-NMR (400 MHz, D_2O): δ 3.59 (t, ^{3}J(H,H) = 5.91 Hz, 1H; (-CH_2)(-NH)>C**H**-COO^-Na^+), 3.31 (sep, ^{3}J(H,H) = 6.64 Hz, 1H; -NH-C**H**<$(CH_3)_2$), 2.35 (m, 2H; HOOC-C**H**$_2$-CH_2-), 1.98 (q, ^{3}J(H,H) = 6.81 Hz, 2H; -CH_2-C**H**$_2$-CH<), 1.22 (dd, ^{3}J(H,H) = 6.64 Hz, 4.64 Hz, 6H; -NH-CH<(C**H**$_3$)$_2$) ppm.

Monosodium *N*-butylglutamate (MW = 225 g mol^{-1})



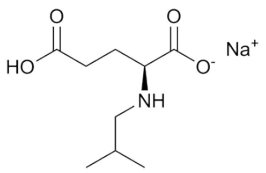
^{1}H-NMR (400 MHz, D_2O): δ 3.53 (t, ^{3}J(H,H) = 5.83 Hz, 1H; (-CH_2)(-NH)>C**H**-COO^-Na^+), 2.96 (t, ^{3}J(H,H) = 7.48 Hz, 2H; -NH-C**H**$_2$-CH_2-), 2.33 (t, ^{3}J(H,H) = 7.38 Hz, 2H; HOOC-C**H**$_2$-CH_2-), 2.02 (q, ^{3}J(H,H) 5.90 Hz, 2H; -CH_2-C**H**$_2$-CH<), 1.61 (quin, ^{3}J(H,H) = 7.77 Hz, 2H; -CH_2-C**H**$_2$-CH_2-CH_3), 1.34 (sex, ^{3}J(H,H) = 7.47 Hz, 2H; -CH_2-C**H**$_2$-CH_3), 0.86 (t, ^{3}J(H,H) = 7.43 Hz, 3H; -CH_2-CH_2-C**H**$_3$) ppm.

Monosodium *N*,*N*-dibutylglutamate (MW =281 g mol^{-1})



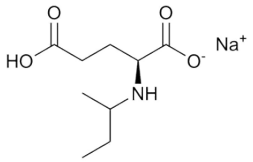
^{1}H-NMR (400 MHz, D_2O): δ 3.64 (q, ^{3}J(H,H) = 4.40 Hz, 1H; (-CH_2)(>N)>C**H**-COO^-Na^+), 3.13 (m, 4H; -N<(C**H**$_2$-CH_2-CH_2-CH_3)$_2$), 2.33 (m, 2H; HOOC-C**H**$_2$-CH_2-), 2.02 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.61 (quin, ^{3}J(H,H) = 7.77 Hz, 4H; -N<(CH_2-C**H**$_2$-CH_2-CH_3)$_2$), 1.34 (sex, ^{3}J(H,H) = 7.47 Hz, 4H; -N<(CH_2-CH_2-C**H**$_2$-CH_3)$_2$), 0.86 (t, ^{3}J(H,H) = 7.43 Hz, 6H; -N<(CH_2-CH_2-CH_2-C**H**$_3$)$_2$) ppm.

Monosodium *N*-isobutylglutamate (MW = 225 g mol^{-1})



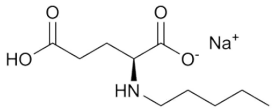
^{1}H-NMR (400 MHz, D_2O): δ 3.48 (t, ^{3}J(H,H) = 5.55 Hz, 1H; (-CH_2)(-NH)>C**H**-COO^-Na^+), 2.79 (m, 2H; -NH-C**H**$_2$-CH<), 2.34 (m, 2H; HOOC-C**H**$_2$-CH_2-), 1.99 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.93 (sep, ^{3}J(H,H) = 6.87 Hz, 1H; -CH_2-C**H**<$(CH_3)_2$), 0.93 (d, ^{3}J(H,H) = 6.64 Hz, 6H; -CH_2-CH<(C**H**$_3$)$_2$) ppm.

Monosodium *N*-(2-butyl)glutamate (MW = 225 g mol^{-1})



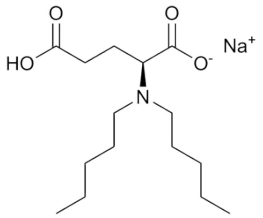
^{1}H-NMR (400 MHz, D_2O): δ 3.61 (t, ^{3}J(H,H) = 5.97 Hz, 1H; (-CH_2)(-NH)>C**H**-COO^-Na^+), 3.10 (m, 1H; -NH-C**H**<(HCH-CH_3)(CH_3)), 2.35 (m, 2H; HOOC-C**H**$_2$-CH_2-), 1.99 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.71 (m, 1H; -NH-CH<(HC**H**-CH_3)(CH_3)), 1.50 (m, 1H; -NH-CH<(**H**CH-CH_3)(CH_3)), 1.20 (m, 3H; -NH-CH<(HCH-CH_3)(C**H**$_3$)), 0.89 (m, 3H; -NH-CH<(HCH-C**H**$_3$)(CH_3)) ppm.

Monosodium *N*-pentylglutamate (MW = 239 g mol^{-1})



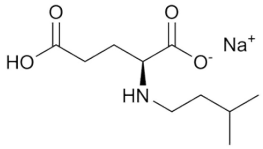
^{1}H-NMR (400 MHz, D_2O): δ 3.51 (t, ^{3}J(H,H) = 6.41 Hz, 1H; (-CH_2)(-NH)>C**H**-COO^-Na^+), 2.93 (t, ^{3}J(H,H) = 7.85 Hz, 2H; -NH-C**H**$_2$-CH_2-), 2.30 (t, ^{3}J(H,H) = 7.25 Hz, 2H; HOOC-C**H**$_2$-CH_2-), 1.99 (q, ^{3}J(H,H) 6.66 Hz, 2H; -CH_2-C**H**$_2$-CH<), 1.61 (quin, ^{3}J(H,H) = 7.13 Hz, 2H; -CH_2-C**H**$_2$-CH_2-CH_2-CH_3), 1.27 (m, 2H; -CH_2-CH_2-C**H**$_2$-CH_2-CH_3), 1.22 (m, ^{3}J(H,H) = 7.47 Hz, 2H; -C**H**$_2$-CH_3), 0.80 (t, ^{3}J(H,H) = 7.04 Hz, 3H; -CH_2-C**H**$_3$) ppm.

Monosodium *N*,*N*-dipentylglutamate (MW = 309 g mol^{-1})



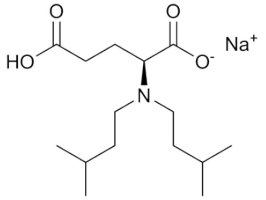
^{1}H-NMR (400 MHz, D_2O): δ 3.61 (t, ^{3}J(H,H) = 4.24 Hz, 1H; (-CH_2)(>N)>C**H**-COO^-Na^+), 3.11 (m, 4H; -N<(C**H**$_2$-CH_2-CH_2-CH_2-CH_3)$_2$), 2.30 (m, 2H; HOOC-C**H**$_2$-CH_2-), 1.99 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.61 (quin, ^{3}J(H,H) = 7.13 Hz, 4H; -N<(CH_2-C**H**$_2$-CH_2-CH_2-CH_3)$_2$), 1.27 (m, 4H; -N<(CH_2-CH_2-C**H**$_2$-CH_2-CH_3)$_2$), 1.22 (m, ^{3}J(H,H) = 7.47 Hz, 4H; -N<(CH_2-CH_2-CH_2-C**H**$_2$-CH_3)$_2$), 0.80 (t, ^{3}J(H,H) = 7.04 Hz, 6H; -N<(CH_2-CH_2-CH_2-CH_2-C**H**$_3$)$_2$) ppm.

Monosodium *N*-isopentylglutamate (MW = 239 g mol^{-1})



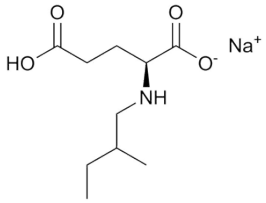
^{1}H-NMR (400 MHz, D_2O): δ 3.51 (t, ^{3}J(H,H) = 5.71 Hz, 1H; (-CH_2)(-NH)>C**H**-COO^-Na^+), 2.96 (t, ^{3}J(H,H) = 7.96 Hz, 2H; -NH-C**H**$_2$-CH_2-), 2.30 (t, ^{3}J(H,H) = 7.00 Hz, 2H; HOOC-C**H**$_2$-CH_2-), 1.99 (q, ^{3}J(H,H) 6.75 Hz, 2H; -CH_2-C**H**$_2$-CH<), 1.58 (m, 1H; -CH_2-CH_2-C**H**-(CH_3)$_2$), 1.50 (m, 2H; -CH_2-C**H**$_2$-CH-(CH_3)$_2$), 0.83 (d, ^{3}J(H,H) = 7.47 Hz, 6H; -CH_2-CH_2-CH-(C**H**$_3$)$_2$) ppm.

Monosodium *N*,*N*-di-isopentylglutamate (MW = 309 g mol^{-1})



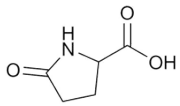
^{1}H-NMR (400 MHz, D_2O): δ 3.61 (q, ^{3}J(H,H) = 4.33 Hz, 1H; (-CH_2)(>N)>C**H**-COO^-Na^+), 3.12 (m, 4H; -N<(-C**H**$_2$-CH_2-CH-(CH_3)$_2$)$_2$), 2.30 (m, 2H; HOOC-C**H**$_2$-CH_2-), 1.99 (m, 2H; -CH_2-C**H**$_2$-CH<), 1.58 (m, 2H; -N<(-CH_2-CH_2-C**H**-(CH_3)$_2$)$_2$), 1.50 (m, 4H; -N<(-CH_2-C**H**$_2$-CH-(CH_3)$_2$)$_2$), 0.83 (d, ^{3}J(H,H) = 7.47 Hz, 12H; -N<(-CH_2-CH_2-CH-(C**H**$_3$)$_2$)$_2$) ppm.

Monosodium *N*-(2-methylbutyl)glutamate (MW = 239 g mol^{-1})



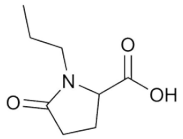
^{1}H-NMR (400 MHz, D_2O): δ 3.47 (t, ^{3}J(H,H) = 5.60 Hz, 1H; (-CH_2)(-NH)>C**H**-COO^-Na^+), 2.80 (m, 2H; -NH-C**H**$_2$-CH-), 2.30 (t, ^{3}J(H,H) = 6.75 Hz, 2H; HOOC-C**H**$_2$-CH_2-), 1.98 (q, ^{3}J(H,H) 6.57 Hz, 2H; -CH_2-C**H**$_2$-CH<), 1.71 (m, 1H; -CH_2-C**H**<(-HCH-CH_3)(CH_3)), 1.42 (m, 1H; -CH_2-CH<(-**H**CH-CH_3)(CH_3)), 1.17 (m, 1H; -CH_2-CH<(-HC**H**-CH_3)(CH_3)), 0.90 (d, ^{3}J(H,H) = 7.00 Hz, 3H; -CH_2-CH<(-HCH-CH_3)(C**H**$_3$)), 0.80 (d, ^{3}J(H,H) = 7.00 Hz, 3H; -CH_2-CH<(-HCH-C**H**$_3$)(CH_3)) ppm.

Pyroglutamic acid (MW = 129 g mol^{-1})



^{1}H-NMR (400 MHz, D_2O): δ 4.33-4.10 (q, ^{3}J(H,H) = 4.82 Hz, 1H; -NH-C**H**-COOH), 2.47 (m, 1H; (-NH)(COOH)>CH-HC**H**-), 2.35-2.33 (m, 2H; -NH-C**H**$_2$-HCH-CH<), 2.09-2.00 (m, 1H; (-NH)(COOH)>CH-**H**CH-) ppm.

***N*-Propylpyroglutamic acid (MW = 171 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 4.34 (m, 1H; (>N)(HCH)>C**H**-COOH), 3.43 (m, 1H; >N-HC**H**-CH_2-CH_3), 2.88 (m, 1H; >N-**H**CH-CH_2-CH_3), 2.46 (m, 1H; (>N)(COOH)>CH-**H**CH-), 2.38 (m, 2H; -C**H**$_2$-CH_2-CH<(COOH)(N<)), 2.04 (m, 1H; (>N)(COOH)>CH-HC**H**-), 1.43 (m, 2H; >N-CH_2-C**H**$_2$-CH_3), 0.76 (t, ^{3}J(H,H) = 7.33 Hz, 3H; >N-CH_2-CH_2-C**H**$_3$) ppm.

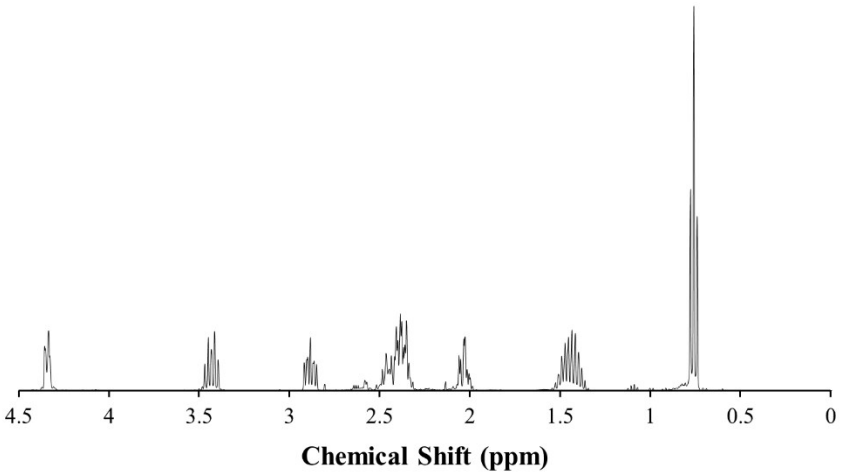
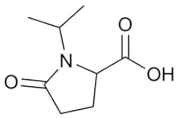


Figure S1 ^{1}H-NMR spectrum (400 MHz, D_2O) of *N*-propylpyroglutamic acid.

Isopropylpyroglutamic acid (MW = 171 g mol^{-1})



^{1}H-NMR (400 MHz, D_2O): δ 4.26 (m, 1H; (>N)(HCH)>C**H**-COOH), 4.00 (sep, ^{3}J(H,H) = 6.70 Hz, 1H; >N-C**H**<(CH_3)$_2$), 2.45 (m, 1H; (>N)(COOH)>CH-**H**CH-), 2.24 (m, 2H; -C**H**$_2$-CH_2-CH<(COOH)(N<)), 1.94 (m, 1H; (>N)(COOH)>CH-HC**H**-), 1.022 (d, ^{3}J(H,H) = 6.70 Hz, 3H; >N-CH<(C**H**$_3$)(CH_3)), 0.96 (d, ^{3}J(H,H) = 6.82 Hz, 3H; >N-CH<(CH_3)(C**H**$_3$)) ppm.

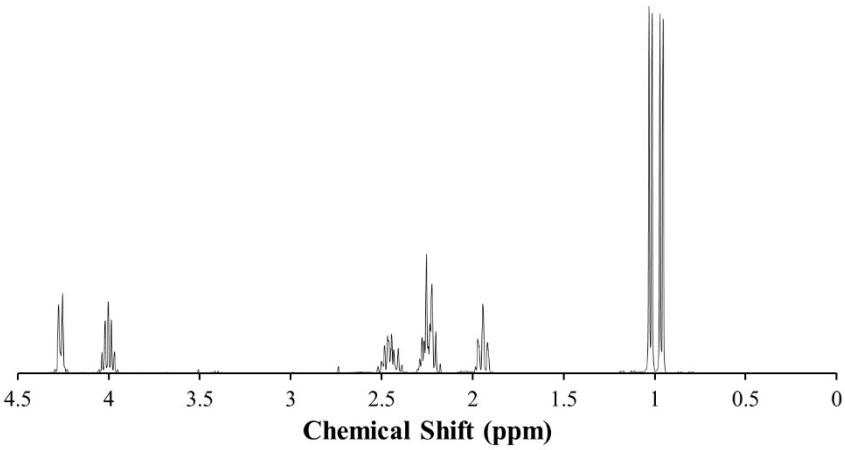
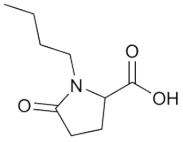


Figure S2 ^{1}H-NMR spectrum (400 MHz, D_2O) of *N*-isopropylpyroglutamic acid.

***N*-Butylpyroglutamic acid (MW = 185 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 4.33 (m, 1H; (>N)(HCH)>C**H**-COOH), 3.49 (m, 1H; >N-HC**H**-CH_2-CH_2-CH_3), 2.88 (m, 1H; >N-**H**CH-CH_2-CH_2-CH_3), 2.46 (m, 1H; (>N)(COOH)>CH-**H**CH-), 2.37 (m, 2H; -C**H**$_2$-CH_2-CH<(COOH)(N<)), 2.02 (m, 1H; (>N)(COOH)>CH-HC**H**-), 1.41 (m, 2H; >N-CH_2-C**H**$_2$-CH_2-CH_3), 1.18 (m, 2H; >N-CH_2-CH_2-C**H**$_2$-CH_3), 0.79 (t, ^{3}J(H,H) = 6.92 Hz, 3H; >N-CH_2-CH_2-CH_2-C**H**$_3$) ppm.

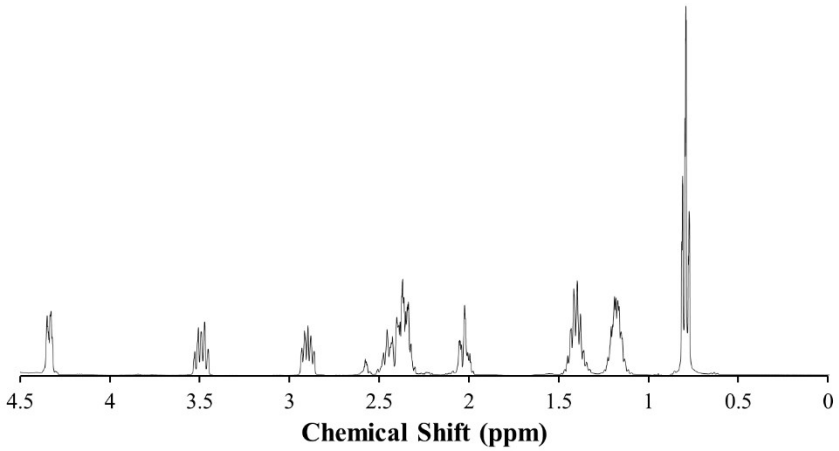
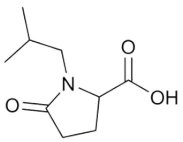


Figure S3 ^{1}H-NMR spectrum (400 MHz, D_2O) of *N*-butylpyroglutamic acid.

***N*-Isobutylpyroglutamic acid (MW = 185 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 4.34 (m, 1H; (>N)(HCH)>C**H**-COOH), 3.29 (dd, ^{3}J(H,H) = 9.33, 14.10 Hz, 1H; >N-HC**H**-CH-$(CH_3)_2$), 2.71 (dd, ^{3}J(H,H) = 14.10, 6.04 Hz, 1H; >N-**H**CH-CH-$(CH_3)_2$), 2.46 (m, 1H; (>N)(COOH)>CH-**H**CH-), 2.40 (m, 2H; -C**H**$_2$-CH_2-CH<(COOH)(N<)), 2.04 (m, 1H; (>N)(COOH)>CH-HC**H**-), 1.81 (m, 2H; >N-CH_2-C**H**-$(CH_3)_2$), 0.81 (d, ^{3}J(H,H) = 6.62 Hz, 3H; >N-CH_2-CH-(C**H**$_3$)(CH_3)), 0.73 (d, ^{3}J(H,H) = 6.62 Hz, 3H; >N-CH_2-CH-(C**H**$_3$)(CH_3)) ppm.

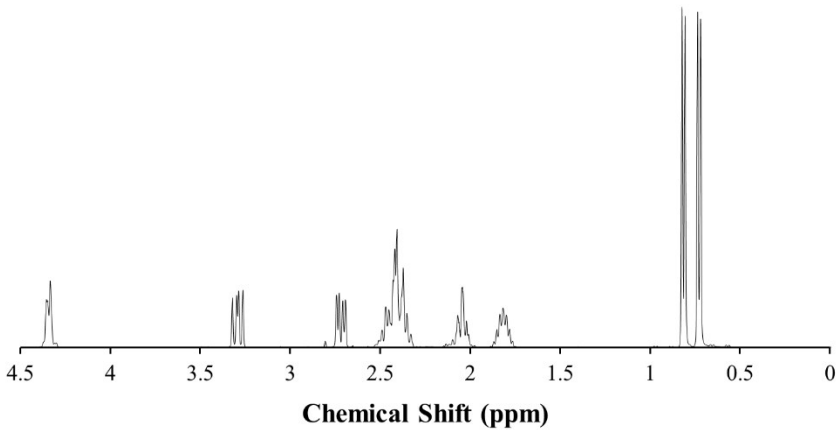
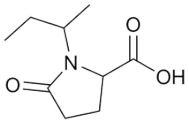


Figure S4 ^{1}H-NMR spectrum (400 MHz, D_2O) of *N*-isobutpyroglutamic acid.

N-(2-Butyl)pyroglutamic acid (MW = 185 g mol^{-1})



^{1}H-NMR (400 MHz, D_2O): δ 4.29 (m, 1H; (>N)(HCH)>C***H**-COOH), 4.24 (m, 1H; (>N)(HCH)>C***H**-COOH), 3.90 (sex, ^{3}J(H,H) = 7.08 Hz, 1H; >N-C***H**<(CH_2-CH_3)(CH_3)), 3.75 (sex, ^{3}J(H,H) = 7.08 Hz, 1H; >N-C***H**<(CH_2-CH_3)(CH_3)), 2.53 (m, 1H; (>N)(COOH)>CH-**H**CH-), 2.32 (m, 2H; -C**H**$_2$-CH_2-CH<(COOH)(N<)), 2.06 (m, 1H; (>N)(COOH)>CH-HC**H**-), 1.46 (m, 2H; >N-C*H<(C**H**$_2$-CH_3)(CH_3)), 1.31 (m, 2H; >N-C*H<(C**H**$_2$-CH_3)(CH_3)), 1.11 (d, ^{3}J(H,H) = 6.70 Hz, 3H; >N-C*H<(CH_2-CH_3)(C**H**$_3$)), 0.99 (d, ^{3}J(H,H) = 6.96 Hz , 3H; >N-C*H<(CH_2-CH_3)(C**H**$_3$)), 0.78 (t, ^{3}J(H,H) = 7.36 Hz , 3H; >N-C*H<(CH_2-C**H**$_3$)(CH_3)), 0.71 (t, ^{3}J(H,H) = 7.43 Hz , 3H; >N-C*H<(CH_2-C**H**$_3$)(CH_3)) ppm.

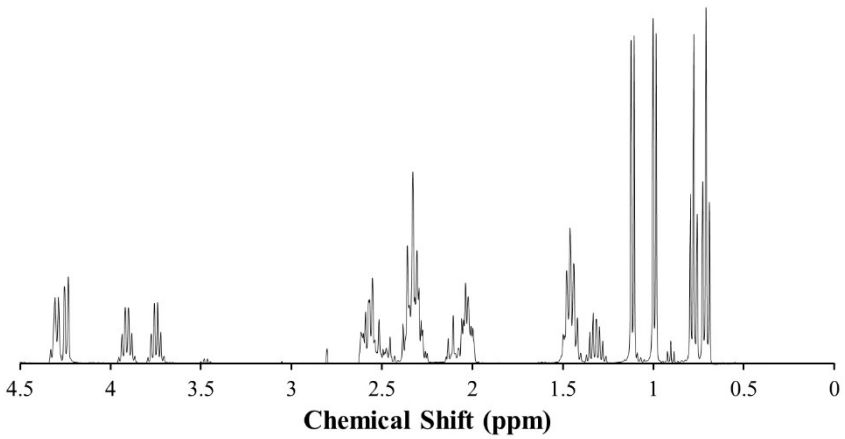
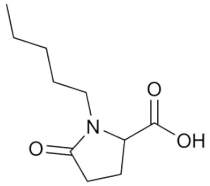


Figure S5 ^{1}H-NMR spectrum (400 MHz, D_2O) of *N*-(2-butyl)pyroglutamic acid.

***N*-Pentylpyroglutamic acid (MW = 199 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 4.34 (m, 1H; (>N)(HCH)>C**H**-COOH), 3.48 (m, 1H; >N-HC**H**-CH_2-CH_2-CH_2-CH_3), 2.90 (m, 1H; >N-**H**CH-CH_2-CH_2-CH_2-CH_3), 2.46 (m, 1H; (>N)(COOH)>CH-**H**CH-), 2.37 (m, 2H; -C**H**$_2$-CH_2-CH<(COOH)(N<)), 2.03 (m, 1H; (>N)(COOH)>CH-HC**H**-), 1.42 (m, 2H; >N-CH_2-C**H**$_2$-CH_2-CH_2-CH_3), 1.20 (m, 2H; >N-CH_2-C**H**$_2$-CH_2-CH_3), 1.16 (m, 2H; >N-CH_2-CH_2-C**H**$_2$-CH_3), 0.77 (t, ^{3}J(H,H) = 6.75 Hz, 3H; >N-CH_2-CH_2-CH_2-C**H**$_3$) ppm.

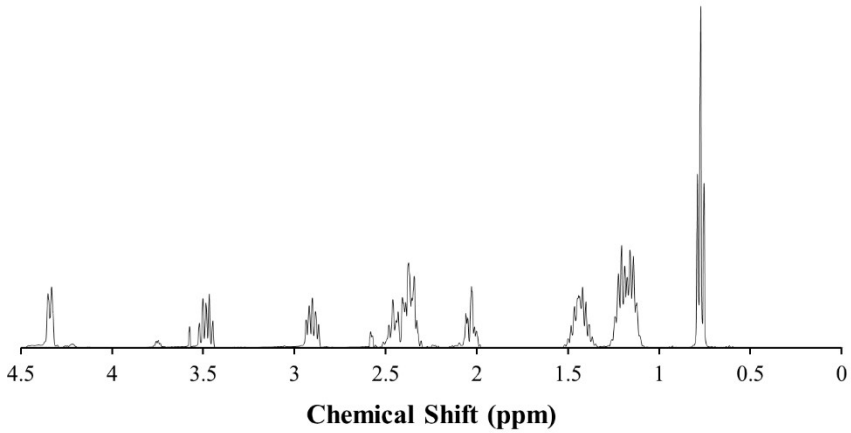
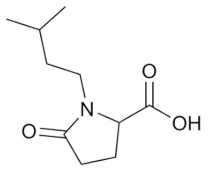


Figure S6 ^{1}H-NMR spectrum (400 MHz, D_2O) of *N*-pentylpyroglutamic acid.

***N*-Isopentylpyroglutamic acid (MW = 199 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 4.34 (m, 1H; (>N)(HCH)>C**H**-COOH), 3.53 (m, 1H; >N-HC**H**-CH_2-CH<$(CH_3)_2$), 2.90 (m, 1H; >N-**H**CH-CH_2-CH<$(CH_3)_2$), 2.46 (m, 1H; (>N)(COOH)>CH-**H**CH-), 2.37 (m, 2H; -C**H**$_2$-CH_2-CH<(COOH)(N<)), 2.03 (m, 1H; (>N)(COOH)>CH-HC**H**-), 1.44 (m, 1H; >N-CH_2-CH_2-C**H**<$(CH_3)_2$), 1.32 (m, 2H; >N-CH_2-C**H**$_2$-CH<$(CH_3)_2$), 0.80 (t, ^{3}J(H,H) = 6.20 Hz, 3H; >N-CH_2-CH_2-CH_2-(CH_3)$_2$) ppm.

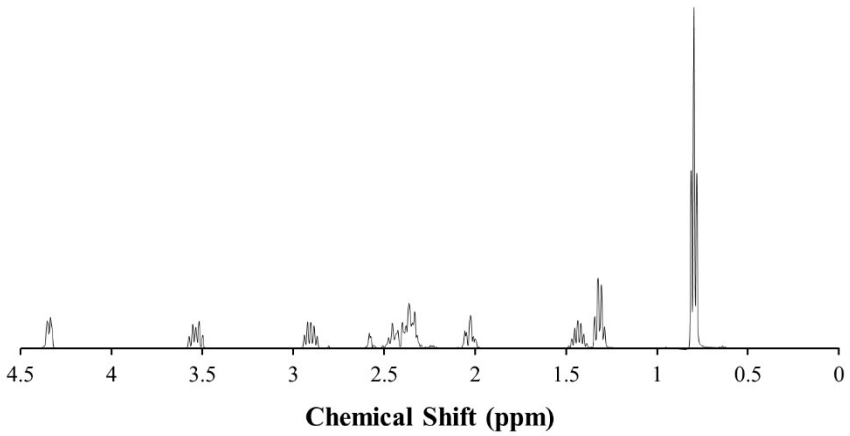
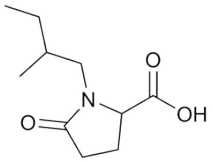


Figure S7 ^{1}H-NMR spectrum (400 MHz, D_2O) of *N*-isopentylpyroglutamic acid.

N-(2-Methylbutyl)pyroglutamic acid (MW = 199 g mol^{-1})



^{1}H-NMR (400 MHz, D_2O): δ 4.33 (m, 1H; (>N)(HCH)>C**H**-COOH), 3.38 (dd, ^{3}J(H,H) = 14.52, 8.93 Hz, 1H; >N-HC**H**-C*H<(CH_3)(CH_2-CH_3)), 3.30 (dd, ^{3}J(H,H) = 13.96, 10.05 Hz, 1H; >N-HC**H**-C*H<(CH_3)(CH_2-CH_3)), 2.79 (dd, ^{3}J(H,H) = 14.14, 5.41 Hz, 1H; >N-**H**CH-C*H<(CH_3)(CH_2-CH_3)), 2.70 (dd, ^{3}J(H,H) = 14.14, 6.13 Hz, 1H; >N-**H**CH-C*H<(CH_3)(CH_2-CH_3)), 2.46 (m, 1H; (>N)(COOH)>CH-**H**CH-), 2.37 (m, 2H; -C**H**$_2$-CH_2-CH<(COOH)(N<)), 2.04 (m, 1H; (>N)(COOH)>CH-HC**H**-), 1.61 (m, 1H; >N-HCH-C***H**<(CH_3)(CH_2-CH_3)), 1.25 (m, 1H; >N-HCH-C*H<(CH_3)(**H**CH-CH_3)), 1.09 (m, 1H; >N-HCH-C*H<(CH_3)(HC**H**-CH_3)), 0.95 (m, 1H; >N-HCH-C*H<(CH_3)(HC**H**-CH_3)), 0.78 (m, 1H; >N-HCH-C*H<(CH_3)(HCH-C**H**$_3$)), 0.77 (d, ^{3}J(H,H) = 6.66 Hz, 3H; >N-HCH-C*H<(C**H**$_3$)(HCH-CH_3)), 0.70 (d, ^{3}J(H,H) = 6.66 Hz, 3H; >N-HCH-C*H<(C**H**$_3$)(HCH-CH_3)) ppm.

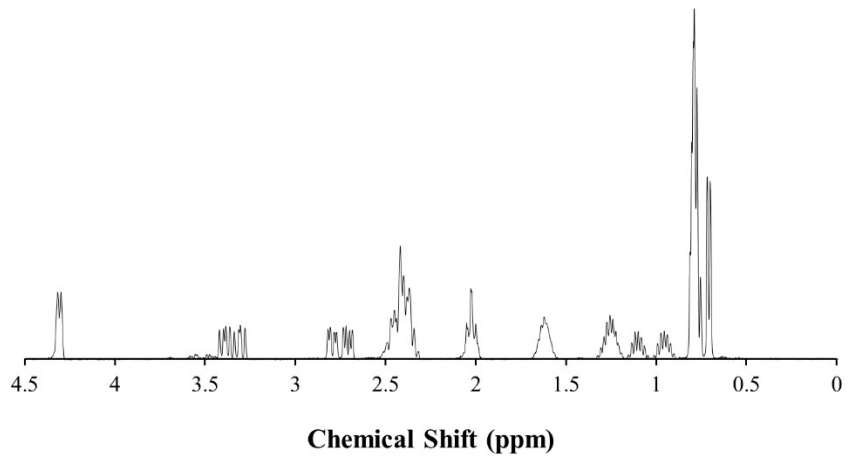
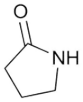


Figure S8 ^{1}H-NMR spectrum (400 MHz, D_2O) of *N*-(2-methylbutyl)pyroglutamic acid.

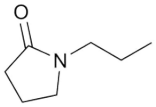
2-Pyrrolidone (MW = 85 g mol^{-1})



^{1}H-NMR (400 MHz, D_2O): δ 3.35 (t, ^{3}J(H,H) = 7.08 Hz, 2H; -CH_2-C**H**$_2$-NH-CO-), 2.28 (t, ^{3}J(H,H) = 8.20 Hz, 2H; -OC-C**H**$_2$-CH_2-CH_2-NH-), 2.06 (quin, ^{3}J(H,H) = 7.82 Hz, 2H; -CH_2-C**H$_2$**-CH_2-NH-) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 85 (100), 84 (23), 56 (8), 42 (18), 41 (19), 40 (5).

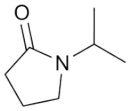
***N*-Propyl-2-pyrrolidone (MW = 127 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 3.40 (t, ^{3}J(H,H) = 7.27 Hz, 2H; CH_2-CH_2-C**H**$_2$-N<(CO-)(CH_2-)), 3.13 (t, ^{3}J(H,H) = 6.97 Hz, 2H; -N<(CO-)(C**H**$_2$-CH_2-CH_3)), 2.35 (t, ^{3}J(H,H) = 8.12 Hz, 2H; -OC-C**H**$_2$-CH_2-CH_2-N<), 1.94 (quin, ^{3}J(H,H) = 7.70 Hz, 2H; OC-CH_2-C**H$_2$**-CH_2-N<), 1.46 (sex, ^{3}J(H,H) =7.27 Hz, 2H; -N<(CO-)(CH_2-C**H**$_2$-CH_3)), 0.75 (t, ^{3}J(H,H) = 7.46 Hz, 3H; CH_2-N<(CO-)(CH_2-CH_2-C**H**$_3$)) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 127 (46), 112 (12), 99 (13), 98 (100), 84 (6), 70 (52), 69 (16), 68 (8), 56 (5), 55 (3), 54 (3), 44 (2), 43 (10), 42 (14), 41 (20), 39 (9).

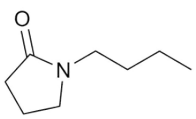
***N*-Isopropyl-2-pyrrolidone (MW = 127 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 4.06 (sep, ^{3}J(H,H) = 6.8 Hz, 1H; -N<(CO-)(C**H**<(CH_3)$_2$)), 3.38 (t, ^{3}J(H,H) = 7.21 Hz, 2H; CH_2-CH_2-C**H**$_2$-N<(CO-)(CH<), 2.33 (t, ^{3}J(H,H) = 8.18 Hz, 2H; -OC-C**H**$_2$-CH_2-CH_2-N<), 1.91 (quin, ^{3}J(H,H) = 7.61 Hz, 2H; OC-CH_2-C**H$_2$**-CH_2-N<), 1.04 (d, ^{3}J(H,H) = 6.79 Hz, 6H; -N<(CO-)(CH<(C**H**$_3$)$_2$)) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 127 (20), 113 (7), 112 (100), 98 (5), 84 (21), 82 (3), 70 (4), 69 (26), 68 (3), 57 (4), 56 (8), 55 (3), 54 (3), 44 (4), 43 (5), 42 (9), 41 (14), 39 (7).

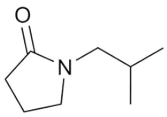
***N*-Butyl-2-pyrrolidone (MW = 141 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 3.34 (t, ^{3}J(H,H) = 7.23 Hz, 2H; CH_2-CH_2-C**H**$_2$-N<(CO-)(CH_2-)), 3.10 (t, ^{3}J(H,H) = 7.23 Hz, 2H; -N<(CO-)(C**H**$_2$-CH_2-CH_2-CH_3)), 2.27 (t, ^{3}J(H,H) = 8.14 Hz, 2H; -OC-C**H**$_2$-CH_2-CH_2-N<), 1.87 (quin, ^{3}J(H,H) = 7.73 Hz, 2H; OC-CH_2-C**H$_2$**-CH_2-N<), 1.37 (quin, ^{3}J(H,H) =7.39 Hz, 2H; -N<(CO-)(CH_2-C**H**$_2$-CH_2-CH_3)), 1.12 (sex, ^{3}J(H,H) =7.49 Hz, 2H; -N<(CO-)(CH_2-CH_2-C**H**$_2$-CH_3)), 0.74 (t, ^{3}J(H,H) = 7.46 Hz, 3H; CH_2-N<(CO-)(CH_2-CH_2-CH_2-C**H**$_3$)) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 141 (32), 126 (11), 112 (14), 99 (38), 98 (100), 86 (4), 84 (4), 71 (3), 70 (33), 69 (12), 68 (6), 56 (4), 43 (5), 42 (8), 47 (13), 39 (6).

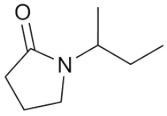
***N*-Isobutyl-2-pyrrolidone (MW = 141 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 3.41 (t, ^{3}J(H,H) = 7.03 Hz, 2H; CH_2-CH_2-C**H**$_2$-N<(CO-)(CH_2-)), 2.96 (d, ^{3}J(H,H) = 7.76 Hz, 2H; -N<(CO-)(C**H**$_2$-CH<(CH_3)$_2$)), 2.36 (t, ^{3}J(H,H) = 8.18 Hz, 2H; -OC-C**H**$_2$-CH_2-CH_2-N<), 1.95 (quin, ^{3}J(H,H) = 7.66 Hz, 2H; OC-CH_2-C**H**$_2$-CH_2-N<), 1.85 (sep, ^{3}J(H,H) =7.06 Hz, 1H; -N<(CO-)(CH_2-C**H**<(CH_3)$_2$)), 0.77 (d, ^{3}J(H,H) = 6.69 Hz, 6H; CH_2-N<(CO-)(CH_2-CH<(C**H**$_3$)$_2$)) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 141 (25), 126 (17), 99 (10), 98 (100), 70 (41), 69 (11), 68 (6), 56 (3), 55 (3), 43 (9), 42 (11), 41 (18), 39 (8).

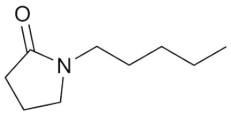
***N*-2-Butyl-2-pyrrolidone (MW = 141 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 3.82 (sex, ^{3}J(H,H) = 7.14 Hz, 1H; -N<(CO-)(C**H**<(CH_3)(CH_2-CH_3))), 3.35 (m, 2H; CH_2-CH_2-C**H**$_2$-N<(CO-)(CH<)), 2.37 (t, ^{3}J(H,H) = 8.17 Hz, 2H; -OC-C**H**$_2$-CH_2-CH_2-N<), 1.94 (quin, ^{3}J(H,H) = 7.64 Hz, 2H; OC-CH_2-C**H**$_2$-CH_2-N<), 1.42 (quin, ^{3}J(H,H) = 7.39 Hz, 2H; -N<(CO-)(CH<(CH_3)(C**H**$_2$-C**H**$_3$))), 1.03 (d, ^{3}J(H,H) = 7.11 Hz, 3H; -N<(CO-)(CH<(C**H**$_3$)(CH_2-CH_3))), 0.70 (t, ^{3}J(H,H) = 7.36 Hz, 3H; -N<(CO-)(CH<(CH_3)(CH_2-C**H**$_3$))) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 141 (8), 126 (10), 113 (8), 112 (100), 98 (4), 86 (5), 84 (14), 70 (3), 69 (21), 56 (7), 55 (3), 42 (6), 41 (11), 39 (5).

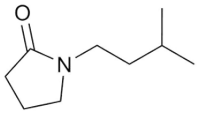
***N*-Pentyl-2-pyrrolidone (MW = 155 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 3.40 (t, ^{3}J(H,H) = 7.36 Hz, 2H; CH_2-CH_2-C**H**$_2$-N<(CO-)(CH_2-)), 3.16 (t, ^{3}J(H,H) = 7.00 Hz, 2H; -N<(CO-)(C**H**$_2$-CH_2-CH_2-CH_2-CH_3)), 2.34 (t, ^{3}J(H,H) = 7.90 Hz, 2H; -OC-C**H**$_2$-CH_2-CH_2-N<), 1.94 (quin, ^{3}J(H,H) = 7.73 Hz, 2H; OC-CH_2-C**H**$_2$-CH_2-N<), 1.45 (quin, ^{3}J(H,H) =7.35 Hz, 2H; -N<(CO-)(CH_2-C**H**$_2$-CH_2-CH_2-CH_3)), 1.20 (quin, ^{3}J(H,H) = 6.82 Hz, 2H; -N<(CO-)(CH_2-CH_2-C**H**$_2$-CH_2-CH_3)), 1.14 (quin, ^{3}J(H,H) = 7.37 Hz, 2H; -N<(CO-)(CH_2-CH_2-CH_2-C**H**$_2$-CH_3)), 0.77 (t, ^{3}J(H,H) = 7.12 Hz, 3H; CH_2-N<(CO-)(CH_2-CH_2-CH_2-CH_2-C**H**$_3$)) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 155 (24), 127 (3), 126 (21), 113 (3), 112 (11), 99 (39), 98 (100), 86 (4), 84 (3), 71 (3), 70 (35), 69 (12), 68 (6), 56 (4), 55 (3), 54 (2), 43 (7), 42 (9), 41 (16), 39 (6).

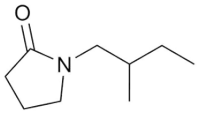
***N*-Isopentyl-2-pyrrolidone (MW = 155 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 3.41 (t, ^{3}J(H,H) = 7.03 Hz, 2H; CH_2-CH_2-C**H**$_2$-N<(CO-)(CH_2-)), 3.19 (t, ^{3}J(H,H) = 7.27 Hz, 2H; -N<(CO-)(C**H**$_2$-CH_2-CH<(CH_3)$_2$)), 2.33 (t, ^{3}J(H,H) = 8.08 Hz, 2H; -OC-C**H**$_2$-CH_2-CH_2-N<), 1.93 (quin, ^{3}J(H,H) = 7.52 Hz, 2H; OC-CH_2-C**H**$_2$-CH_2-N<), 1.43 (m, 1H; -N<(CO-)(CH_2-CH_2-C**H**<(CH_3)$_2$)), 1.33 (t, ^{3}J(H,H) = 7.10 Hz, 2H; -N<(CO-)(CH_2-C**H**$_2$-CH<(CH_3)$_2$)), 0.80 (d, ^{3}J(H,H) = 6.49 Hz, 6H; -N<(CO-)(CH_2-CH_2-CH<(C**H**$_3$)$_2$)) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 155 (11), 140 (9), 112 (10), 100 (4), 99 (64), 98 (100), 86 (10), 84 (3), 71 (3), 70 (34), 69 (12), 68 (5), 56 (5), 55 (5), 44 (2), 43 (9), 42 (10), 41 (18), 39 (7).

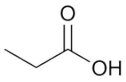
***N*-(2-Methylbutyl)-2-pyrrolidone (MW = 155 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 3.41 (t, ^{3}J(H,H) = 6.51 Hz, 2H; CH_2-CH_2-C**H**$_2$-N<(CO-)(CH_2-)), 3.00 (t, ^{3}J(H,H) = 7.28 Hz, 2H; -N<(CO-)(C**H**$_2$-CH<(HCH-CH_3)(CH_3))), 2.35 (t, ^{3}J(H,H) = 8.05 Hz, 2H; -OC-C**H**$_2$-CH_2-CH_2-N<), 1.95 (quin, ^{3}J(H,H) = 7.66 Hz, 2H; OC-CH_2-C**H**$_2$-CH_2-N<), 1.65 (m, 1H; -N<(CO-)(CH_2-C**H**<(HCH-CH_3)(CH_3))), 1.25 (m, 1H; -N<(CO-)(CH_2-CH<(**H**CH-CH_3)(CH_3))), 1.02 (m, 1H; -N<(CO-)(CH_2-CH<(HC**H**-CH_3)(CH_3))), 0.77 (t, ^{3}J(H,H) = 7.47 Hz, 3H; -N<(CO-)(CH_2-CH<(HCH-CH_3)(C**H**$_3$))), 0.73 (d, ^{3}J(H,H) = 6.51 Hz, 3H; -N<(CO-)(CH_2-CH<(HCH-C**H**$_3$)(CH_3))) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 155 (18), 140 (3), 126 (10), 99 (23), 98 (100), 86 (10), 71 (3), 70 (34), 69 (10), 68 (5), 56 (3), 55 (3), 43 (6), 42 (9), 41 (15), 39 (6).

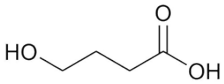
Propionic acid (MW = 74 g mol^{-1})



^{1}H-NMR (400 MHz, D_2O): δ 2.13–2.15 (q, ^{3}J(H,H) = 7.68 Hz, 2H; CH_3-C**H**$_2$-COOH), 0.99 (t, ^{3}J(H,H) = 7.61 Hz, 3H; C**H**$_3$-CH_2-COOH) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 74 (100), 73 (63), 57 (29), 56 (16), 55 (18), 45 (32), 44 (5), 42 (6).

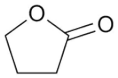
γ-Hydroxybutyric acid (MW = 104 g mol^{-1})



^{1}H-NMR (400 MHz, D_2O): δ 3.35 (t, ^{3}J(H,H) = 6.51 Hz, 2H; HO-C**H**$_2$-CH$_2$-), 2.34 (t, ^{3}J(H,H) = 7.20 Hz, 2H; -CH$_2$-C**H**$_2$-COOH), 1.73 (quin, ^{3}J(H,H) = 7.20 Hz, 2H; -CH$_2$-C**H**$_2$-CH$_2$-) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 86 (44), 85 (19), 57 (10), 56 (37), 55 (12), 44 (11), 43 (11), 42 (100), 41 (87), 40 (20), 39 (17).

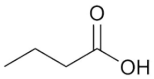
γ-Butyrolactone (MW = 86 g mol^{-1})



^{1}H-NMR (400 MHz, D_2O): δ 4.38 (t, ^{3}J(H,H) = 7.11 Hz, 2H; -CH$_2$-C**H**$_2$-O-), 2.52 (t, ^{3}J(H,H) = 8.15 Hz, 2H; -CH$_2$-C**H**$_2$-CO-), 2.31 (quin, ^{3}J(H,H) = 7.61 Hz, 2H; -CH$_2$-C**H**$_2$-CH$_2$-) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 86 (54), 85 (20), 57 (9), 56 (29), 55 (11), 42 (100), 41 (60), 40 (21), 39 (24), 38 (7).

Butyric acid (MW = 88 g mol^{-1})



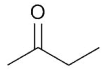
^{1}H-NMR (400 MHz, D_2O): δ 2.10 (t, ^{3}J(H,H) = 7.41 Hz, 2H; -CH$_2$-C**H**$_2$-COOH), 1.49 (sex, ^{3}J(H,H) = 7.41 Hz, 2H; CH$_3$-C**H**$_2$-CH$_2$-), 0.82 (t, ^{3}J(H,H) = 7.47 Hz, 3H; C**H**$_3$-CH$_2$-) ppm.

GC/MS (EI, 70 eV): m/z (rel. int., %): 73 (49), 60 (100), 55 (15), 45 (20), 43 (12), 42 (26), 41 (15), 40 (6), 39 (11), 38 (5).

Methylamine (MW = 31 g mol^{-1})

^{1}H-NMR (600 MHz, D_2O): δ 2.36 (s, 3H; C**H**$_3$-NH$_2$) ppm.

2-Butanone (MW = 72 g mol^{-1})

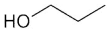


^{1}H-NMR (400 MHz, D_2O): δ 2.49 (q, ^{3}J(H,H) = 7.47 Hz, 2H; -CO-C**H**$_2$-CH$_3$), 2.10 (s, 3H; C**H**$_3$-CO-CH$_2$-), 0.90 (t, ^{3}J(H,H) = 7.33 Hz, 3H; -CO-CH$_2$-C**H**$_3$) ppm.

Acetone (MW = 58 g mol^{-1})

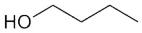
^{1}H-NMR (400 MHz, D_2O): δ 2.13 (s, 6H; CO<(C**H**$_3$)$_2$) ppm.

***n*-Propanol (MW = 60 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 3.46 (t, ^{3}J(H,H) = 6.68 Hz, 2H; HO-C**H**$_2$-CH_2-), 1.45 (sex, ^{3}J(H,H) = 7.11 Hz, 2H; CH_2-C**H**$_2$-CH_3), 0.80 (t, ^{3}J(H,H) = 7.38 Hz, 3H; -CH_2-CH_2-C**H**$_3$).

***n*-Butanol (MW = 74 g mol^{-1})**



^{1}H-NMR (400 MHz, D_2O): δ 3.52 (t, ^{3}J(H,H) = 6.56 Hz, 2H; HO-C**H**$_2$-CH_2-), 1.43 (quin, ^{3}J(H,H) = 7.07 Hz, 2H; HO-CH_2-C**H**$_2$-CH_2-), 1.25 (sex, ^{3}J(H,H) = 7.44 Hz, 2H; -CH_2-C**H**$_2$-CH_3), 0.80 (t, ^{3}J(H,H) = 7.28 Hz, 3H; -CH_2-CH_2-C**H**$_3$) ppm.

2. Catalyst characterisation

Catalyst characterisation of Pd/Al_2O_3 (acidic) and Pd/SiO_2 was partially performed in earlier research of our group.[1]

2.1 Powder X-ray diffraction (XRD)

Powder X-ray diffraction patterns were determined for the synthesized catalysts and their support (in case of Al_2O_3) (Figure S9). After loading the catalysts with palladium, Al_2O_3 maintains its crystallinity. In the case of the Pd/SiO_2 catalyst, clear Pd(0) peaks are present, suggesting that large Pd particles were formed. Additional TEM measurements (Figure S11) demonstrated that Pd particles (7-9 nm) were larger for the Pd/SiO_2 catalyst compared to the Al_2O_3.

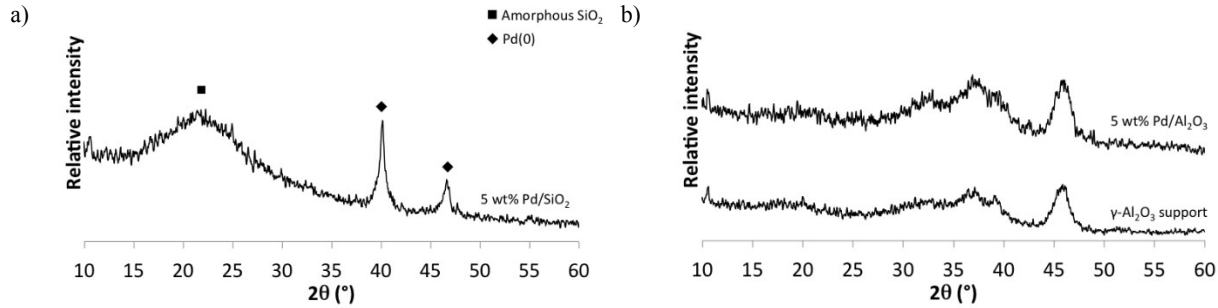


Figure S9 Powder X-ray diffraction patterns of a) 5 wt% Pd/SiO_2, b) commercial Al_2O_3 support and 5 wt% Pd/Al_2O_3.

2.2 Nitrogen physisorption

The textural properties of the synthesized palladium catalysts were determined from nitrogen physisorption measurements at 77 K (Figure S10). The adsorption-desorption isotherms of Pd/SiO_2, Pd/Al_2O_3 (acidic) and Pd/Al_2O_3 (basic) show type IV-behaviour according to the IUPAC classification, which is typical for materials with a limited micropore structure. The isotherms exhibit a hysteresis loop, which is typically associated with a mesoporous structure and originates from the SiO_2 and Al_2O_3 supports.

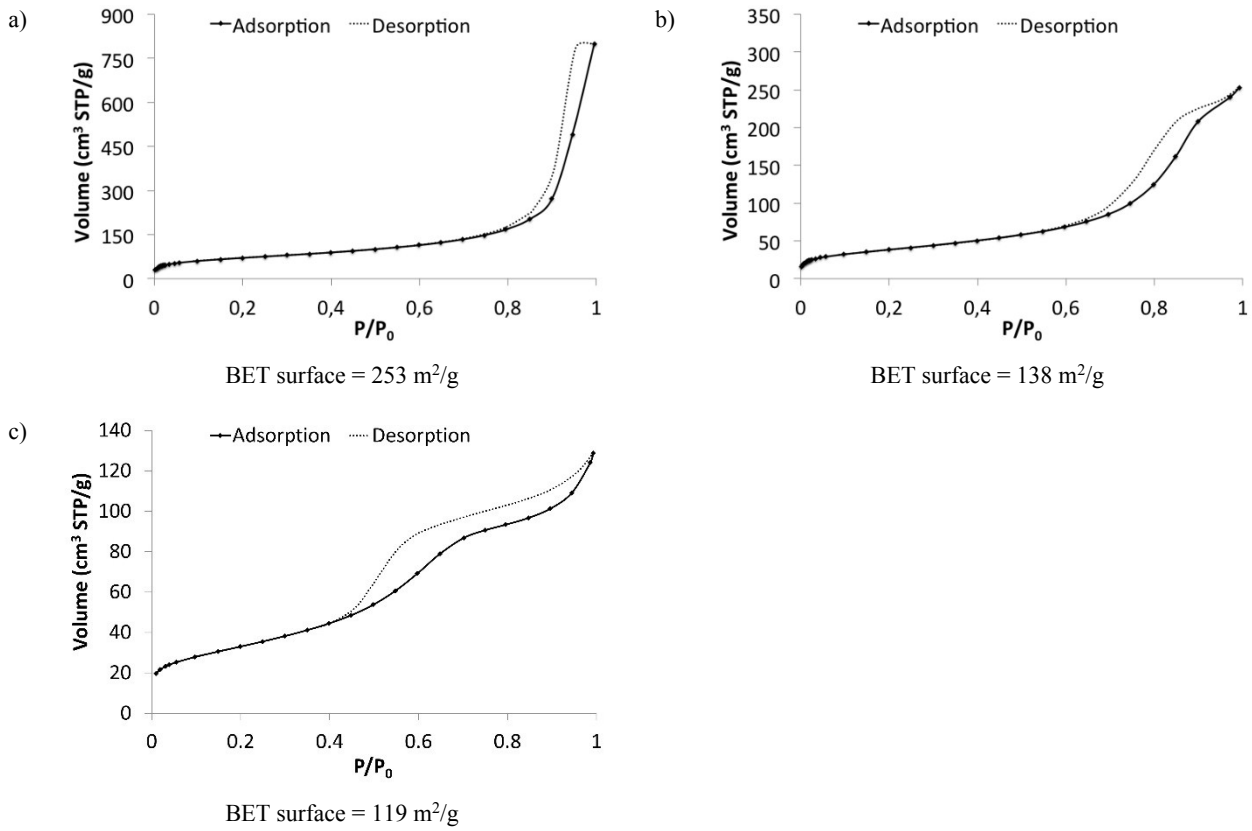
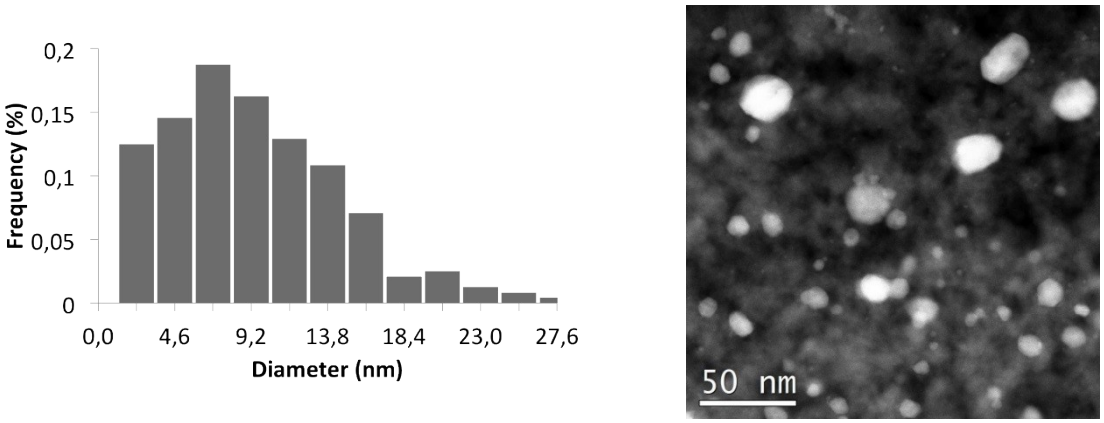


Figure S10 Nitrogen physisorption isotherms and BET surface area of a) Pd/SiO_2, b) Pd/Al_2O_3 (acidic) and c) Pd/Al_2O_3 (basic).

2.3 High Angle Annular Dark Field Scanning Transmission Electron Microscopy (HAADF-STEM) and Energy Dispersive X-ray Spectroscopy (EDX)

HAADF-STEM measurements were performed on Pd/SiO_2 and Pd/Al_2O_3 catalysts to determine the size distribution of the Pd particles on the support surface. For Pd/SiO_2 the particle size distribution was determined with 240 palladium particles. Figure S11 shows that a well-dispersed material was synthesized with rather large palladium particles. The relatively large size of the Pd particles was already suggested by XRD diffractograms, in which the diffraction pattern of Pd(0) was clearly identified. The number average particle diameter of the Pd/SiO_2 equals 8.8 nm. The particle size distribution of Pd/Al_2O_3 was determined with 260 particles. Pd/Al_2O_3 had a narrow distribution containing a large fraction of small particles (< 2.5 nm) and also a substantial fraction of larger particles, leading to a number average particle diameter of 3.7 nm (Figure S12).



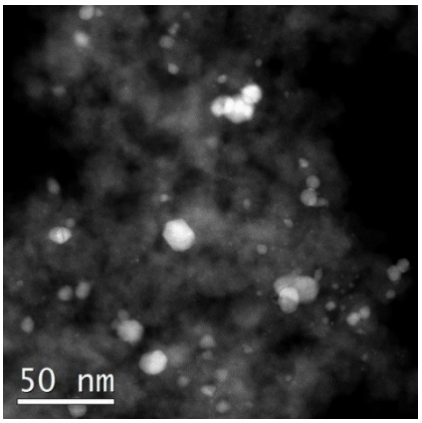
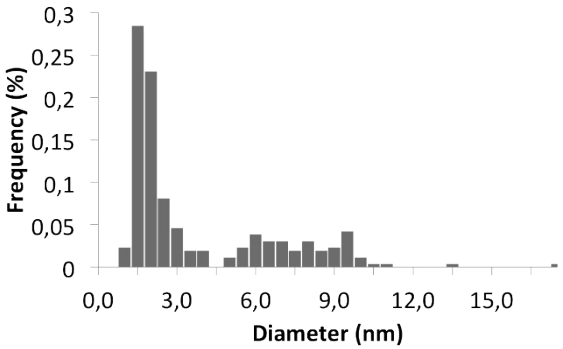


Figure S11 Particle size distribution of Pd/SiO_2 *(left);* HAADF-STEM pictures of Pd/SiO_2 *(right)*.



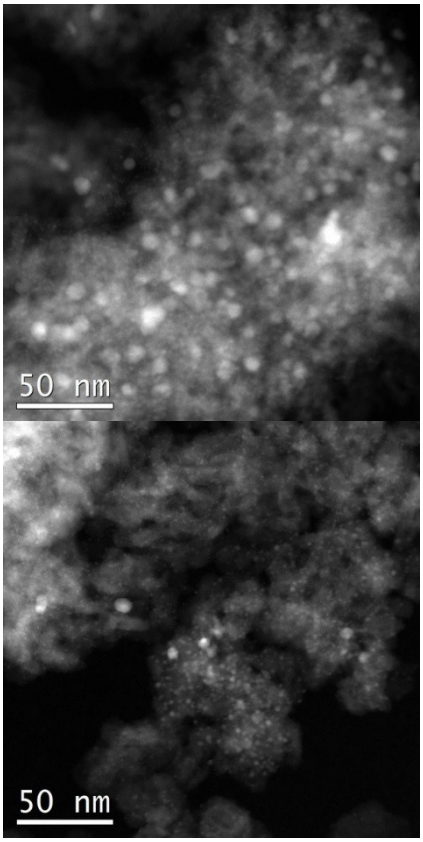


Figure S12 Particle size distribution of Pd/Al_2O_3 (*left*); b) HAADF-STEM pictures of Pd/Al_2O_3 (*right*).

2.4 Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES)

Table S1 Pd content of self-prepared catalysts

Catalyst	Pd content (wt%)
Pd/Al_2O_3 (acidic)	4.8
Pd/Al_2O_3 (basic)	4.7
Pd/SiO_2	5.1

3. Reductive *N*-alkylation of monosodium glutamate: optimization of reaction conditions

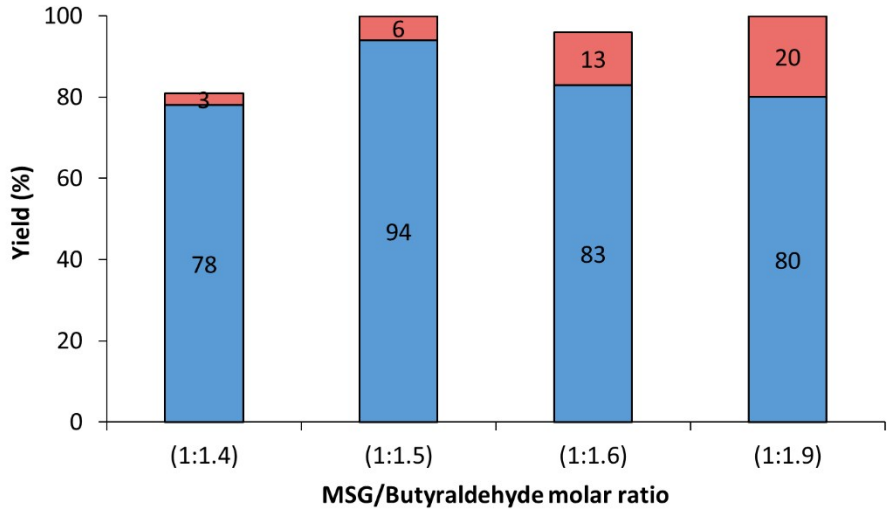


Figure S13 Reductive *N*-butylation of monosodium glutamate (MSG) using various butyraldehyde concentrations at pH 5.7. Conditions: monosodium glutamate (0.74 M in water, 20 ml), butyraldehyde, H_3PO_4 (for pH adjustment), 5 wt% Pd/C (2 mol% Pd), H_2 (60 bar), RT, 6 h. Legend: monosodium *N*-butylglutamate (blue) and monosodium *N*,*N*-dibutylglutamate (red).

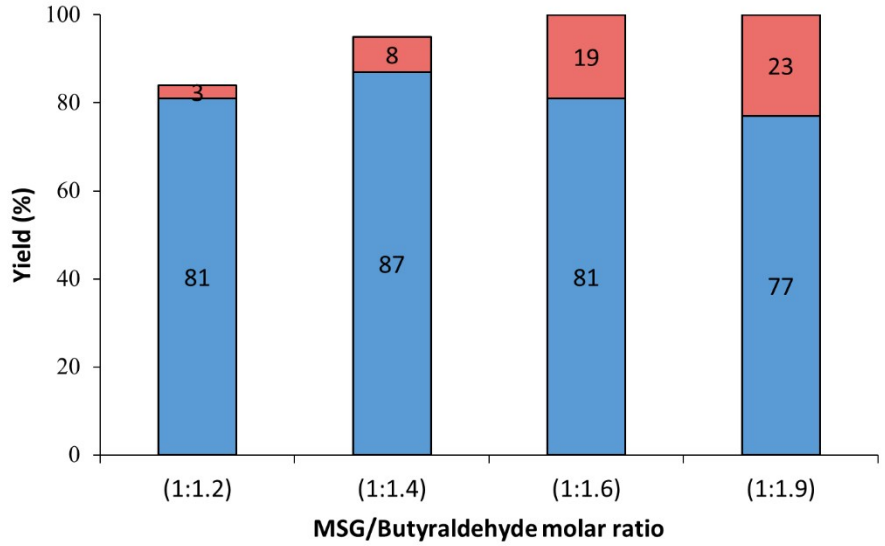


Figure S14 Reductive *N*-butylation of monosodium glutamate (MSG) using various butyraldehyde concentrations. Conditions: monosodium glutamate (0.74 M in water, 20 ml), butyraldehyde, 5 wt% Pd/C (2 mol% Pd), H_2 (60 bar), RT, 6 h. Legend: monosodium *N*-butylglutamate (blue) and monosodium *N*,*N*-dibutylglutamate (red).

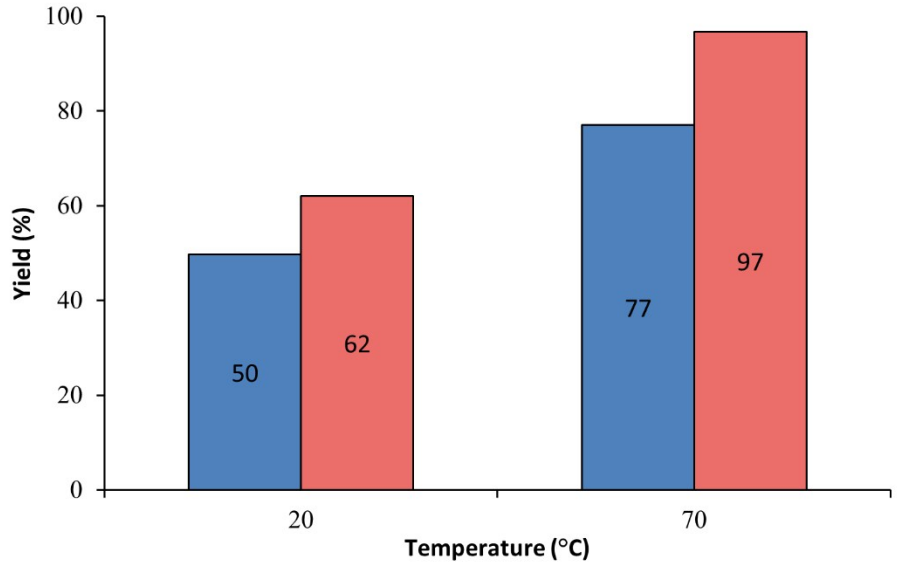


Figure S15 Reductive *N*-isopropylation of monosodium glutamate, eventually in the presence of acetic acid. Conditions: monosodium glutamate (0.74 M in water 20 ml), acetone (5 equiv.), acetic acid (0 or 0.5 equiv.), 5 wt% Pd/C (2 mol% Pd), H_2 (60 bar), RT, 6 h. Legend: reaction of monosodium *N*-isopropylglutamate in the absence of acetic acid (blue) and in the presence of 0.5 equiv. acetic acid (red).

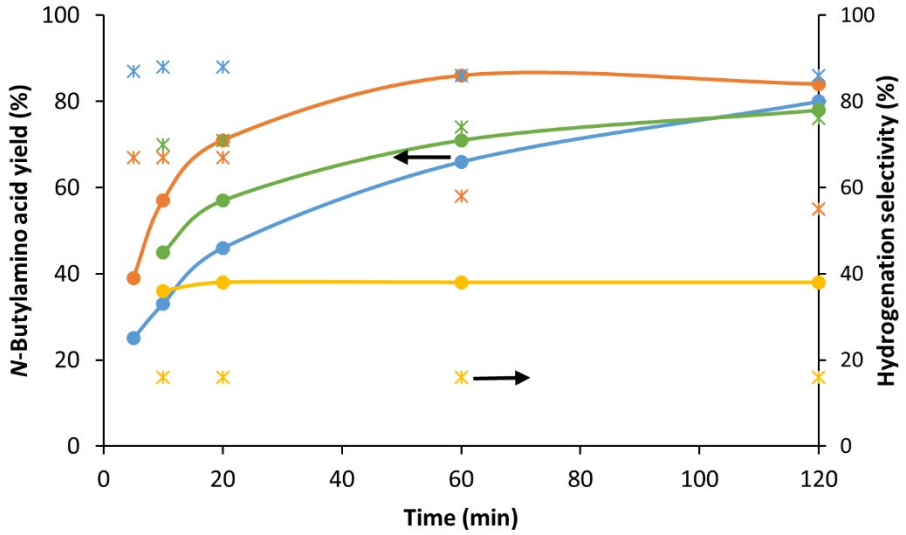


Figure S16 Reductive *N*-butylation of glutamic acid and monosodium glutamate at various H_2 pressures. Conditions: substrate (0.17 M in water, 20 ml), butyraldehyde (2 equiv.), 5 wt% Pd/C (2 mol% Pd), RT. H_2 was supplied continuously in order to keep the pressure constant. Legend: reaction of glutamic acid at 7.5 bar (green) and 50 bar (yellow) and reaction of monosodium glutamate at 7.5 bar (blue) and 50 bar (orange).

4. Decarboxylation of *N*-alkylpyroglutamic acid: time-controlled experiments

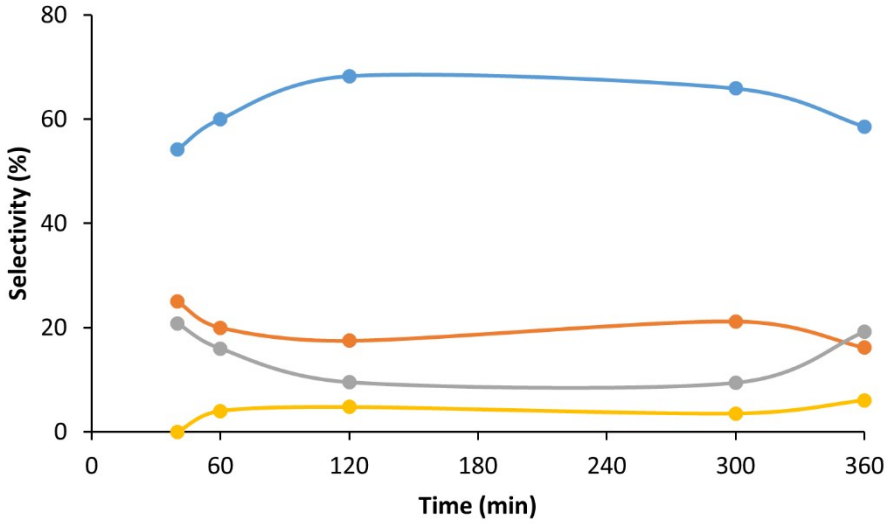


Figure S17 Decarboxylation of *N*-2-butylpyroglutamic acids in function of time. Conditions: *N*-2-butylpyroglutamic acid (0.1 M in water, 20 ml), 5 wt% Pd/Al_2O_3 (4 mol% Pd), N_2 (6 bar), 250 °C, 6 h. Legend: *N*-2-butyl-2-pyrrolidone (blue), 2-pyrrolidone (orange), propionic acid (grey) and others (yellow). Others: γ-butyrolactone, γ-hydroxybutyric acid, butyric acid and non-identified lower molecular weight compounds.

5. Decarboxylation of *N*-alkylpyroglutamic acid: reaction parameter variation

Because many side reactions were initiated by hydrolysis of *N*-alkyl-2-pyrrolidone, the decarboxylation of pyroglutamic acid was performed in other solvents than water. Acetic acid, diglyme (or bis(2-methoxyethyl)ether) and *n*-butyl acetate were selected for their stability towards dehydration, esterification and aqueous reforming under typical reaction conditions However, water remained the preferred solvent, because in these solvents the yield of 2-pyrrolidone was less than 5% after 6 h and other solvent-induced side reactions were observed as well.

The stability of *N*-butyl-2-pyrrolidone in the presence of Pd/C was also evaluated at lower temperatures (Table S2). The eventual decrease in catalytic activity was compensated by prolonging the reaction time from 6 h to 16 h. When *N*-butyl-2-pyrrolidone was treated for 16 h at 230 °C, the extent of degradation was similar to the result after 6 h at 250 °C, with respective conversions of 46% and 44% (entries 3 and 4). *N*-Butyl-2-pyrrolidone was even more stable at 220 °C (entry 2), but the catalytic performance was insufficient; even after 16 h *N*-butylpyroglutamic acid was converted in only 42% and the selectivity dropped drastically to 40% (entry 5). This result can be attributed to the detrimental effect of the high acidity of the medium at low conversions, which will induce hydrolysis and further degradation.

Table S2 Effect of temperature on the degradation of *N*-butyl-2-pyrrolidone and the Pd-catalyzed decarboxylation of *N*-butylpyroglutamic acid in water[a]

Entry	Substrate[b]	Catalyst	Temperature (°C)	Time (h)	Conversion (%)	Yield NBP (%)	Yield 2-pyrrolidone (%)	Yield propionic acid (%)	Yield others[c] (%)
1	NBP	Pd/C	200	16	16	/	9	0	7
2	NBP	Pd/C	220	16	30	/	17	4	9
3	NBP	Pd/C	230	16	46	/	20	7	19
4	NBP	Pd/C	250	6	44	/	19	7	18
5	NBPG	Pd/Al_2O_3 (acidic)	220	16	42	17	13	3	9

[a] Conditions: substrate (0.1 M in water, 20 ml), catalyst (4 mol% Pd), N_2 (6 bar). [b] NBP: *N*-butyl-2-pyrrolidone; NBPG: *N*-butylpyroglutamic acid. [c] Others: γ-butyrolactone, γ-hydroxybutyric acid, butyric acid and non-identified, lower molecular weight compounds.

Product degradation by dehydrogenation of 4-(alkylamino)butyric acid (Manuscript, scheme 1) might be suppressed when H_2 is present in the atmosphere (Table S3). Indeed, the stability of *N*-butyl-2-pyrrolidone substantially increased from 56% to 67% with 1 bar H_2 (entries 1 and 2), and even further to 77% with 15 bar H_2 (entry 4). However, when the Pd-catalyzed decarboxylation of *N*-butylpyroglutamic acid was performed under 15 bar H_2, the yield of *N*-butyl-2-pyrrolidone was only 17% at 52% conversion (entry 5). The selectivity was reduced because amide hydrogenation occurred as a competing side reaction, resulting in 29% yield of *N*-butylpyrrolidine. Since metal-catalyzed hydrogenation of amides is generally difficult[2] and this reaction was not observed with *N*-butyl-2-pyrrolidone, the hydrogenation of the lactam moiety in *N*-butylpyroglutamic acid might be facilitated by the presence of a carboxylic acid. Further decarboxylation of *N*-butylproline probably proceeded fast at 250 °C, because this intermediate was not detected in the product mixture.[3] Nevertheless, the presence of only minor amounts of 2-pyrrolidone and propionic acid clearly demonstrates that the degradation of *N*-alkyl-2-pyrrolidones can be suppressed in the presence of H_2. On the other hand, the conversion decreased because both the substrate and H_2 are in competition for adsorption onto the catalyst surface.

Table S3 Influence of the gas atmosphere on the degradation of *N*-butyl-2-pyrrolidone and the Pd-catalyzed decarboxylation of *N*-butylpyroglutamic acid in water[a]

Entry	Substrate[b]	Catalyst	Atmosphere	Conversion (%)	Yield NBP (%)	Yield 2-pyrrolidone (%)	Yield propionic acid (%)	Yield others[c] (%)
1	NBP	Pd/C	6 bar N_2	44	/	19	7	18
2	NBP	Pd/C	5 N_2 + 1 bar H_2	33	/	16	8	9
3	NBP	Pd/C	6 bar H_2	32	/	13	6	13
4	NBP	Pd/C	15 bar H_2	23	/	4	1	18
5	NBPG	Pd/Al_2O_3 (acidic)	15 bar H_2	52	17	4	2	29[d]

[a] Conditions: substrate (0.1 M in water, 20 ml), catalyst (4 mol% Pd), 250 °C, 6 h. [b] NBP: *N*-butyl-2-pyrrolidone; NBPG: *N*-butylpyroglutamic acid. [c] Others: γ-butyrolactone, γ-hydroxybutyric acid, butyric acid and non-identified, lower molecular weight compounds. [d] Yield of *N*-butylpyrrolidine.

6. References

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2 A. M. Smith and R. Whyman, *Chem. Rev.*, 2014, **114**, 5477–5510.

3 J. Verduyckt, M. Van Hoof, F. De Schouwer, M. Wolberg, M. Kurttepeli, P. Eloy, E. M. Gaigneaux, S. Bals, C. E. A. Kirschhock and D. E. De Vos, *ACS Catal.*, 2016, **6**, 7303–7310.