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Supplementary Material (ESI) for Green Chemistry

Supporting Information

How ultrasound is improving the conversion of nitro compounds to amines catalyzed by Pd/C using a mixture of sodium hypophosphite and hypophosphorous acid as reducing agent

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Nitrostyrene



In a round bottom flask, benzaldehyde (4 g, 37,7 mmol, 1.0 eq) and ammonium acetate (1.31 g, 17 mmol, 0.45 eq) suspended in nitromethane (55 mL, 1.02 mol, 27 eq), were heated to reflux during 5 hours under argon. After cooling to room temperature, the reaction mixture was washed with water (100 mL) and the aqueous phase was extracted with ethyl acetate (3 x 25 mL). The combined organic layers were washed with brine (10 mL), dried

over magnesium sulfate. The dried organic phase was filtered and concentrated under reduced pressure to get a brown viscous oil. The crude residue was chromatographied on silica (gradient: cyclohexane (100%) to cyclohexane / ethyl acetate (98/2, v/v) and recrystallized in ethanol to provide yellow needles (4.50 g, 80%). ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 7.44-7.57 (m, 5H, H_{arom}), 7.60 (d, 1H, *J* =12.0 Hz, H_{alkene}), 8.02 (d, 1H, *J* =12.0 Hz, H_{alkene}).



<u>β-nitroethylbenzene</u>

In a round bottom flask, sodium borohydride (0.38 g, 10.06 mmol, 3.0 eq) was suspended in tetrahydrofurane (10



mL) and methanol (2.6 mL) under argon. Then a solution of nitrostyrene (0.5 g, 3.35 mmol, 1.0 eq) in tetrahydrofurane (10 mL) was added dropwise to the reaction mixture maintained at 0°C with an ice bath. After the end of the addition, the reaction mixture were stirred 20 min at 0°C. Then the reaction was quenched with water (10 mL) and neutralised with a solution of HCL 10%. The mixture was filtered on celite. The aqueous and organic phases were separated and the aqueous phase was extracted by ethyl

acetate (3 x 25 mL). The combined organic layers were washed with brine (10 mL), dried over magnesium sulfate. The dried organic phase was filtered and concentrated under reduced pressure to get a yellow liquid. The crude residue was chromatographied on silica (gradient: cyclohexane (100%) to cyclohexane / ethyl acetate (9/1, v/v) to provide a pale yellow liquid (0.26 g, 52%). ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 3.34 (t, 2H, *J* = 8.0 Hz, CH₂), (4.63, 2H, *J* = 8.0 Hz, CH₂), 7.21-7.23 (m, 2H,

¹H NMR (400 MHz, CDCl₃) δ (ppm) = 3.34 (t, 2H, *J* = 8.0 Hz, CH₂), (4.63, 2H, *J* = 8.0 Hz, CH₂), 7.21-7.23 (m, 2H, H_{arom}), 7.29-7.37 (m, 3H, H_{arom}). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 33.6 (CH₂), 76.4 (CH₂), 127.6 (CH_{arom}), 128.7 (CH_{arom}), 129.1 (CH_{arom}), 135.8 (C_{qarom}).



Phenylethylamine



In a closed tube, 1-(2-nitroethyl)benzene (151 mg, 1 mmol, 1.0 eq) was solubilized in solvent (water or 2-methyltetrahydrofurane) (1 mL) and Pd/C (5% wt, 50% in water) (27 mg, 0.6 mol %) was added. After addition of a mixture of sodium hypophosphite monohydrate (424 mg, 4 mmol, 4.0 eq) and hypophosphorous acid (50% in water) (0.109mL, 1 mmol, 1.0 eq) solubilized in water (2 ml), the reaction mixture was stirred

for 16 hours at 60°C. After cooling down to room temperature, the reaction mixture was diluted with ethyl acetate (20 mL), basified with a 2.5 M sodium hydroxide solution (10 mL) and filtered on celite[®]. The aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine (10 mL), and dried over magnesium sulfate. The dried organic phase was filtered and concentrated under reduced pressure to get a yellow crude product. The crude residue was chromatographied on silica (gradient: cyclohexane (100%) to cyclohexane / ethyl acetate (7/3, v/v) to provide a pale yellow liquid. ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 1.47 (s, 2H, NH₂), 2.76 (d, 2H, *J* = 8.0 Hz, CH₂), 2.98 (d, 2H, *J* = 8.0 Hz, CH₂), 7.20-7.24 (m, 3H, H_{arom}), 7.29-7.33 (m, 2H, H_{arom}). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 40.2 (CH₂), 43.7 (CH₂), 126.3 (CH_{arom}), 128.6 (CH_{arom}), 129.0 (CH_{arom}), 139.9 (C_{garom}).



(1-methyl-2-nitroethyl)benzene



To a solution of nitrostyrene (2 g, 13.4 mmol, 1.0 eq) in tetrahydrofurane (25 mL) at -45°C was added dropwise a solution of methylmagnesium bromide in Et₂O (3.0 M) (11.2 mL, 33.6 mmol, 2.5 eq), the solution was slowly warmed to room temperature for 3 hours. The reaction was quenched with saturated aqueous ammonium chloride (25 mL). The aqueous phase was extracted with diethyl ether (3 x 50 mL). The combined organic

layers were washed with brine (30 mL), dried over magnesium sulfate, filtered and concentrated under reduced pressure to provide the crude compound as a yellow/orange liquid. The crude residue was chromatographied on silica (gradient: cyclohexane (100%) to cyclohexane / ethyl acetate (95/5, v/v) to provide a pale yellow liquid (1.77 g, 80%). ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 1.40 (d, 3H, *J* = 4.0 Hz, CH₃), 3.66 (m, 1H, CH), 4.48-4.60 (m, 2H, CH₂NO₂), 7.24-7.32 (m, 3H, H_{arom}), 7.35-7.39 (m, 2H, H_{arom}). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 18.9 (CH₃), 38.8 (CH), 82.0 (CH₂), 127.0 (CH_{arom}), 127.7 (CH_{arom}), 129.1 (CH_{arom}), 141.0 (C_{qarom}).



3-(1-Methyl-2-nitro-ethyl)-1H-indole



To a solution of 3-(2-nitrovinyl)indole (2 g, 10.6 mmol, 1.0 eq) in tetrahydrofurane (25 mL) at -45°C was added dropwise a solution of methylmagnesium bromide in Et_2O (3.0 M) (8.8 mL, 26.5 mmol, 2.5 eq). The reaction mixture was slowly warmed to room temperature for 3 hours. The reaction was quenched with saturated aqueous ammonium chloride (50 mL). The aqueous phase was extracted with ethyl acetate (3 x 30 mL). The combined organic layers were washed with brine (25 mL), dried over magnesium sulfate, filtered and concentrated under reduced pressure to provide the

crude compound as a brown liquid. The crude residue was chromatographied on silica (gradient: cyclohexane (100%) to cyclohexane / ethyl acetate (7/3, v/v) and recrystallized in ethanol to provide a yellow solid (1.95 g, 90%). ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 1.53 (d, 3 H, *J* = 8 Hz), 4.00 (m, 1 H, CH), 4.51 (dd, 1 H, *J* = 8.0 Hz, *J* = 12.0 Hz, CHNO₂), 4.76 (dd, 1 H, *J* = 4.0 Hz, *J* = 12.0 Hz, CHNO₂), 7.06 (d, 1 H, H_{arom}), 7.17-7.28 (m, 2 H, H_{arom}), 7.40 (d, 1 H, *J* = 8.0 Hz, H_{arom}), 7.68 (d, 1 H, *J* = 8.0 Hz, H_{arom}), 8.09 (s, 1 H, NH). ¹³C NMR (100 MHz, CDCl₃) δ (ppm) = 18.2 (CH₃), 30.8 (CH), 81.6 (CH₂), 111.7 (CH), 116.0 (Cq), 118.7 (CH_{arom}), 120.0 (CH_{arom}), 121.2 (CH_{arom}), 122.7 (CH_{arom}), 126.0 (Cq).





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3-(2-nitroethyl)-1H-indole



In a round bottom flask, sodium borohydride (0.602 g, 15.9 mmol, 3.0 eq) was suspended in tetrahydrofurane (16 mL) and methanol (4 mL) under argon. Then a solution of 3-(2-nitrovinyl)-1H-indole (1 g, 5.3 mmol, 1.0 eq) in tetrahydrofurane (16 mL) was added dropwise to the reaction mixture maintained at 0°C with an ice bath. After the end of the addition, the reaction mixture were stirred 3 hours at 0°C. Then the

reaction was quenched with water (15 mL) and neutralised with an aqueous solution of HCl 10%. The mixture was filtered on celite. The aqueous and organic phases were separated and the aqueous phase was extracted by diethyl ether (3 x 30 mL). The combined organic layers were washed with brine (20 mL), dried over magnesium sulfate. The dried organic phase was filtered and concentrated under reduced pressure to get a yellow/orange oil. The crude residue was chromatographied on silica (gradient: cyclohexane (100%) to cyclohexane / ethyl acetate (7/3, v/v) to provide a yellow liquid which crystallized in cold ethanol to get a pale yellow solid (0.655g, 65%). ¹H NMR (400 MHz, CDCl₃) δ (ppm) = 3.71 (t, 2 H, *J* = 8.0 Hz, CH₂), 4.88 (t, 2 H, *J* = 8.0 Hz, CH₂), 7.26 (d, 1 H, H_{arom}), 7.38 (t, 1 H, *J* = 8.0 Hz, H_{arom}), 7.45 (t, 1 H, *J* = 8.0 Hz, H_{arom}), 7.59 (d, 1 H, *J* = 8.0 Hz, H_{arom}), 7.80 (d, 1 H, *J* = 8.0 Hz, H_{arom}), 8.28 (s, 1 H, NH).



General procedure to determine the yields by RMN

To determine the yields by ¹H NMR, the crude product and a known amount of a pure internal standard are mixed together and dissolved in a deuterated solvent. The quantity of product in the RMN tube can be calculated from the ratio between the areas of the peaks of the analyte and those of the internal standard. Then, the yield was established from the amount of internal standard introduced in the NMR tube, the number of protons and the molecular weights of the sample and the internal standard.

Determination of the acoustic power of the sonotrode

The acoustic power is rarely given in papers published in the literature. Yet, it is the power actually dissipated in the irradiated fluid, independently of the device used. We therefore characterized our ultrasonic equipment by the determination of the acoustic power of the sonotrode to allow a better reproducibility of experiments, even performed with another type of equipment.

Experimental process

The acoustic power of the sonotrode (P_{acous} (W)) was determined by a calorimetric method¹. Indeed, above the cavitation threshold, part of the acoustic energy is converted into heat by absorption. The sonotrode was plunged in a reactor containing 10 mL of distilled water. This volume of liquid was sonicated for 5 min. Under the effect of the ultrasounds, its temperature progressively increased. Then the ultrasonic activation was stopped and the temperature of the solution decreased. The initial temperature rise per unit time ((dT / dt) to K.s⁻¹) induced by the ultrasounds was determined by the addition of the slope of the temperature rise line and the slope of the temperature cooling line, in absolute value.

This study was repeated three times to check its repeatability. Finally, the acoustic power was determined by the formula : $P_{acous} = m x cp x (dT/dt)_{t0}$ with the specific heat capacity of water, $cp_{water} = 4,18 \text{ J.g}^{-1}$.K⁻¹ and the mass of sonicated water, $m_{water} = 10 \text{ g.}$

The acoustic power can be reported to the volume to express the volumic acoustic power ($P_{acous.vol}$ (W.L⁻¹)): $P_{acous.vol}$ (W.L⁻¹) = P_{acous} / V



Result

According to the graph, the initial temperature rise per unit time $(dT/dt)_{t0} = 0.0745+0.0227 = 0.0942 \text{ K.s}^{-1}$ Thus, $P_{acous} = m x cp x (dT/dt)_{t0} = 3.94 \text{ W}$ and $P_{acous.vol}$ (W.L⁻¹) = $P_{acous} / V = 394 \text{ W.L}^{-1}$

¹ H. Guéguen, Ann. Chim. **1963**, 8, 667–713.