1,2,3-Trimethoxypropane a glycerol-based solvent with low toxicity: new utilization for the reduction of nitrile, nitro, ester, acid functional groups with TMDS and a metal catalyst
Marc Sutter, Leyla Pehlivan, Romain Lafon, Wissam Dayoub, Yann Raoul, Estelle Métay and Marc Lemaire*

SUPPORTING INFORMATION

Table of Contents

Experimental procedures ........................................................................................................................................S2
Preparation 1,2,3-TMP: GC of the crude, GC of the pure product and GC of the by-products........S6
Short description of toxicological tests of 1,2,3-TMP (OECD guidelines)..................................................S8
Catalyst and hydride source screening for the reduction of benzonitrile ..................................................S12
$^1$H NMR spectra of the reduction of 4-hydroxybenzylamine in 2-MeTHF and 1,2,3-TMP ..........S13
Products characterizations ..........................................................................................................................S14
NMR $^1$H, $^{13}$C and $^{13}$C DEPT 135 Spectra ............................................................................................S20
References ..................................................................................................................................................S40
Experimental

General

All reagents were used as received from the chemical company. Substrates and metal complexes were supplied by Acros, Sigma-Aldrich, Alfa Aesar and TCI. Glycerol, 99 %, Reagentplus® was purchased from Sigma-Aldrich.

\(^1\)H NMR and \(^{13}\)C NMR spectra were recorded on a BRUKER DRX 300 or BRUKER ALS 300 (\(^1\)H 300 MHz, \(^{13}\)C 75 MHz) in CDCl\(_3\) (except when mentioned) and chemical shifts are given in ppm. \(J\) values are given in Hertz (Hz). Abbreviations are defined as follows: \(br\) = broad singlet, \(s\) = singlet, \(d\) = doublet, \(dd\) = doublet of doublets, \(t\) = triplet, \(q\) = quadruplet, \(m\) = multiplet.

IR spectra were recorded on a Spectro Nicolet IS10 Smart ITR with an ATR diamond.

The HRMS-ESI mass spectra were recorded in positive-ion mode on a hybrid quadrupole time-of-flight mass spectrometer (MicroTOFQ-II, Bruker Daltonics, Bremen) with an Electrospray Ionization (ESI) ion source. The flow of spray gas was at 0.6 bar and the capillary voltage was 4.5kV. The solutions were infused at 180\(\mu\)L/h in a mixture of solvents (methanol / dichloromethane / water 45/40/15). The mass range of the analysis was 50-1000m/z and the calibration was done with sodium formate.

The HRMS-CI (Chemical Ionization) and HRMS-EI (Electron Ionization) mass spectra were recorded on a high resolution double-focusing (reversed Nier-Johns B/E geometry) mass spectrometer (ThermoFinnigan MAT95XL, Bremen, Germany) equipped with a chemical ionization (CI) and an electron ionization (EI) ion sources. The reagent gas for the CI was isobutane and the calibration for high resolution mass spectra was done with perfluorotributylamine (FC43). For the EI an electron energy of 70eV was used and the calibration was done with perfluorokerosene (PFK).

The GC-MS analysis were performed on a Focus GC (Thermo Electron Corporation, Bremen, Germany) equipped with a DB-5MS capillary column (30m, 0.25mm i.d., 0.25\(\mu\)m film thickness) and a DSQ mass spectrometer as a detector (Thermo Electron corporation, Bremen, Germany). The carrier gas was helium, at a flow rate of 1 mL/min. Column temperature was initially 70 °C for 2 min, then gradually increased to 310°C at 15 °C/min and finally kept at 310 °C for 10min. The injector temperature was 220 °C and the transfer line temperature was 280 °C. For GC-MS detection an electron ionization system was used with electron energy of 70 eV, and the mass analyzer was a simple quadrupole.

The GC analysis for the preparation of 1,2,3-TMP were performed on a GC-2025 Gas Chromatograph (Shimadzu) equipped with a ZB-5-MS column (30.0m, 0.25mm i.d., 025\(\mu\)m film thickness). The carrier gas was N\(_2\), at a flow rate of 1.27 mL/min. Column temperature was initially 40 °C for 4 min, then gradually increased to 200 °C at 15 °C/min and finally kept at 200 °C for 15 min. The injector temperature was 250 °C and for detection a FID was used (280 °C).
Preparation of 1,2,3-Trimethoxypropane by phase transfer catalysis:

In a 2 L double walled glass reactor equipped with a cooling system (water stream) and a mechanical anchor Teflon stirrer, glycerol (139 g, 111 mL, 1.51 mol, 1 eq.), 142 g of KOH pellets 85% (2.53 mol, 1.65 eq.) and 5.28 g of (n-Bu)₄NHSO₄ (15.6 mmol, 10 mol%) were successively introduced in small portions under stirring. The mixture was then stirred at room temperature for 30 min until the medium became more homogeneous. After cooling down the reactor to 15 °C by a cold water stream, dimethyl sulfate (166 g, 125 mL, 1.30 mol, 0.85 eq) was carefully added dropwise to the reaction medium. Next, the rest of KOH was slowly added (142 g, 2.53 mol, 1.65 eq) before adding the remaining DMS dropwise (166 g, 125 mL, 1.30 mol, 0.85 eq). The basicity of the mixture was then checked by pH measurement, and the medium was vigorously stirred at room temperature for 24 h to 36 h. Pentane was then added to the crude and the salts (Na₂SO₄) were filtered and washed several times with pentane. Next, the salts were engaged in a Soxhlet extractor overnight with pentane as extraction solvent. The solutions obtained after filtration and Soxhlet extraction were concentrated and finally distillated under reduced pressure over CaH₂ to remove pentane at 35 °C / 950 mbar. Finally, 1,2,3-Trimethoxypropane 2 was obtained at 66-69 °C / 90 mbar in 79 % yield (161 g) as a colorless liquid. Without Soxhlet extraction of the salts, 1,2,3-TMP was isolated in 57% yield.

Reduction of substrates 1a-4a in 1,2,3-TMP with LiAlH₄ as hydride source:

In a double-neck round bottom flask under an inert atmosphere of argon was added a suspension of LiAlH₄ (2.4 to 4 mmol) in 1.5 mL of 1,2,3-TMP. Next, a solution of substrate 1a-4a (2 mmol) in 0.5 mL of 1,2,3-TMP was carefully added dropwise to the reaction medium at 0°C. The reaction was allowed to warm to room temperature and stirred for 2 h. The mixture was cooled at 0°C and water (0.1 mL), followed by an aqueous solution of NaOH 1N (0.2 mL) and water (0.3 mL) were added in the crude. The reaction was allowed to warm to room temperature and stirred for 1 h. Then, 10 mL of CH₂Cl₂ were added and the salts were filtered. 5 mL of a saturated aqueous solution of NaCl were added and the mixture was extracted with CH₂Cl₂ (3×20 mL). After concentration under reduced pressure, the crude was purified by column chromatography on silica gel to afford reduced product 1b-4b (eluent: cyclohexane/ethyl acetate = 99:1~9:1 for products 1b and 2b and methanol/CH₂Cl₂ = 95:5~5:1 for products 3b and 4b).

Reduction of nitro compounds 5a-7a in 1,2,3-TMP with Fe(acac)₃ in association with TMDS:
In a sealed tube under an inert atmosphere of argon was added a magnetic stirring bar, followed by a solution of nitro compound 5a-7a (2 mmol) in 1,2,3-TMP (2 mL, [1 M]), Fe(acac)$_3$ (10 mol%, 70 mg) and TMDS (2 equiv., 0.71 mL). After 24 h under stirring and heating at 80 °C, the reaction mixture was allowed to cool to room temperature and a solution of HCl 2N in Et$_2$O (2 equiv) was then added dropwise. The mixture was stirred for 5 min and the formed precipitate was filtered. The solid was washed several times with Et$_2$O and dried to afford the desired products 5b-7b as hydrochloride salts.

**Reduction of methyl esters 8a-10a in 1,2,3-TMP with V(O)(OiPr)$_3$ in association with TMDS:**

In a sealed tube under an inert atmosphere of argon was added a magnetic stirring bar, followed by a solution of ester 8a - 10a (8 mmol) in 1,2,3-TMP (4 mL, [2 M]). Next, V(O)(OiPr)$_3$ (1 mol%, 0.08 mmol, 0.019 mL) and TMDS (2 equiv., 16 mmol, 2.8 mL) were added. The reaction mixture was stirred at 100 °C for 24 h. Thereafter, THF (10 mL) and TBAF (1 M in THF, 1 equiv., 8 mL) were added and the mixture was stirred for 2 h. The organic phase was recovered with dichloromethane and washed with water, dried with MgSO$_4$, and the solvents were removed under reduced pressure. The crude product was purified by column chromatography on silica gel (cyclohexane/ethyl acetate, 99:1~9:1) to yield alcohols 8b - 10b.

**Reduction of carboxylic acids 11a and 12a in 1,2,3-TMP with InBr$_3$ in association with TMDS:**

In a sealed tube under an inert atmosphere of argon was added a magnetic stirring bar, followed by a solution of carboxylic acid 11a or 12a (5 mmol) in 1,2,3-TMP (5 mL, [1 M]). Next, InBr$_3$ (1 mol%, 0.05 mmol, 17.7 mg) was added. TMDS (2 equiv. 10 mmol, 1.77 mL) was then added carefully and slowly (formation of bubbles) over several minutes. The reaction mixture was then stirred at 60 °C for 24 h. The solvent was evaporated under reduced pressure and the crude material was purified by column chromatography on silica gel (cyclohexane/ethyl acetate, 99:1~9:1) to afford alcohol 11b or 12b.

**General procedure for the reduction of nitriles 3a, 4a and 13a-17a with Cu(OTf)$_2$ in association with TMDS:**

In a sealed tube under an inert atmosphere of argon was added a magnetic stirring bar, followed by a solution of nitrile 3a, 4a, 12a-16a (2 mmol) in 1,2,3-TMP (2 mL, [1 M]) and Cu(OTf)$_2$ (10 mol%, 72 mg). Next, TMDS (2 equiv., 4 mmol, 0.71 mL) were carefully added and the reaction mixture was then stirred at 100 °C for 24 h before being allowed to cool to room temperature. A solution of HCl 2N in Et$_2$O...
(2 equiv) was then added dropwise. The mixture was stirred for 5 min and the formed precipitate was filtered. The solid was washed several times with Et₂O and dried to afford desired products \textbf{13b-19b} as hydrochloride salts.
Preparation of 1,2,3-TMP: GC of the reaction crude, before purification:

KOH (3.3 eq.)
DMS (1.7 eq.)
TBAHS 10 mol%

r.t., 48 h
Conversion > 99%

Selectivity > 96%

GC of pure products:

1,2,3-trimethoxypropane
RT = 7.49 min.

1,3-dimethoxypropan-2-ol
RT = 7.09 min.
2,3-dimethoxypropan-1-ol
RT = 7.66 min.

3-methoxypropan-1,2-diol
RT = 7.58 min.

Glycerol
RT = 9.62 min.
Short description of toxicological tests of 1,2,3-TMP (OECD guidelines)

**OECD, OECD guideline for the testing of chemicals, Acute Oral Toxicity – Acute Toxic Class Method (423) (table 1, entry 2).**

Acute toxicities studies were carried out to evaluate the toxicity of 1,2,3-TMP when being exposed in large quantities at a time. Acute oral toxicity tests were performed on rats in order to evaluate the toxicity of 1,2,3-TMP when it is swallowed. The Median Lethal Dose (LD$_{50}$) value, which is the dose required to kill half the rats, was determined. Complete procedure available on


**OECD, OECD guideline for the testing of chemicals, Acute Dermal Toxicity (402) (table 1, entry 3).**

This test provided information on health hazard likely to arise from a short-term exposure 1,2,3-TMP by the dermal route. Complete procedure available on

http://www.oecdbookshop.org/oecd/display.asp?K=5LMQCR2K7PTL&lang=FR&sort=sort_date%2Fd&stem=true&sf1=Title&st1=402&sf3=SubjectCode&sp1=not&st4=E4%2Bor%2BE5%2Bor%2BP5&sf4=SubVersionCode&ds=402%3B+Tous+les+th%8mes%3B+%&m=1&dc=2&plang=en (accessed on 3 June 2013).

**OECD, OECD guideline for the testing of chemicals, Acute Dermal Irritation/Corrosion (404) (table 1, entry 4).**

This test provided information on health hazard likely to arise from exposure to 1,2,3-TMP by dermal application. Rabbits were used for this test to see if there is any irritation and corrosion. Complete procedure available on

http://www.oecdbookshop.org/oecd/display.asp?K=5LMQCR2K7PNP&lang=FR&plang=en&sort=sort_date%2Fd&stem=true&sf1=Title&st1=404&sf3=SubjectCode&sp1=not&st4=E4%2Bor%2BE5%2Bor%2BP5&sf4=SubVersionCode&ds=404%3B+Tous+les+th%8mes%3B+%&m=1&dc=2 (accessed on 3 June 2013).
OECD, *OECD guideline for the testing of chemicals, Acute Eye Irritation/Corrosion (405)* (table 1, entry 5).

This test provided information on health hazard likely to arise from exposure to 1,2,3-TMP by application on the eye. Rabbits were used for this test. 1,2,3-TMP was applied in a single dose in the conjunctival sac of one eye of each animal. The other eye, which remained untreated, served as a control. Complete procedure available on

http://www.oecdbookshop.org/oecd/display.asp?K=5K91HSNVQHXP&lang=FR&plang=en&sort=sort_date%2Fd&stem=true&sf1=Title&st1=405&sf3=SubjectCode&sp1=not&st4=E4%2Bor%2BE5%2Bor%2BP5&sf4=SubVersionCode&ds=405%3B+Tous+les+th%8mes%3B+%26+m=1&dc=4 (accessed on 3 June 2013).

OECD, *OECD guideline for the testing of chemicals, Skin Sensitization: Local Lymph Node Assay (429)* (table 1, entry 6).

Local Lymph Node Assay (LLNA) is a test performed on mices. It measures the proliferative response of the lymph node cells from the draining auricular lymph node, after application of 1,2,3-TMP. As explained on OECD website, “This proliferation is proportional to the dose applied and provides a measurement of sensitization. The method described is based on the use of radioactive labelling to measure cell proliferation.” Complete procedure available on

http://www.oecdbookshop.org/oecd/display.asp?K=5LMQCR2K61XN&lang=FR&plang=en&sort=sort_date%2Fd&stem=true&sf1=Title&st1=429&sf3=SubjectCode&sp1=not&st4=E4%2Bor%2BE5%2Bor%2BP5&sf4=SubVersionCode&ds=429%3B+Tous+les+th%8mes%3B+%26+m=1&dc=2 (accessed on 3 June 2013).

OECD, *OECD guideline for the testing of chemicals, Bacterial Reverse Mutation Test (471)* (Ames Test, table 1, entry 7).

This test was performed to predict mutagenicity and thus carcinogenicity of 1,2,3-TMP. Suspensions of bacterial cells as *Salmonella typhimurium* and *Escherichia coli* were exposed to 1,2,3-TMP in the
presence and in the absence of an exogenous metabolic activation system. Complete procedure available on

http://www.oecdbookshop.org/oecd/display.asp?K=5LMQCR2K7MG0&lang=FR&plang=en&sort=sort_date%2Fd&stem=true&sf1>Title&st1=471&sf3=SubjectCode&sp1=not&st4=E4%2Bor%2BE5%2Bor%2BP5&sf4=SubVersionCode&ds=471%3B+Tous+les+th%E8mes%3B+&m=1&dc=2 (accessed on 3 June 2013).

OECD, OECD guideline for the testing of chemicals, Ready Biodegradability (301) (table 1, entry 8).

The biodegradability of 1,2,3-TMP in an aerobic aqueous medium was measured with the CO₂ evolution test (test B). A solution of 1,2,3-TMP in a mineral medium was incubated or inoculated. After 28 days, degradation was measured by CO₂ production compared to a reference without 1,2,3-TMP. Complete procedure available on

http://www.oecdbookshop.org/oecd/display.asp?K=5LMQCR2K7QM0&lang=FR&plang=en&sort=sort_date%2Fd&stem=true&sf1>Title&st1=301&sf3=SubjectCode&sp1=not&st4=E4%2Bor%2BE5%2Bor%2BP5&sf4=SubVersionCode&ds=301%3B+Tous+les+th%E8mes%3B+&m=1&dc=2 (accessed on 3 June 2013).

OECD, OECD guideline for the testing of chemicals, Freshwater Alga and Cyanobacteria, Growth Inhibition Test (201) (table 1, entry 9).

This test was performed to determine the effects of 1,2,3-TMP on the growth of freshwater microalgae and/or cyanobacteria. Exponentially growing test organisms were exposed to 1,2,3-TMP in batch cultures over a period of 72 hours. Several concentration of 1,2,3-TMP were studied and the limit test corresponds to one dose level of 0.1 g/L (maximum dose). The concentration of 1,2,3-TMP bringing 50% inhibition of growth rate (E₅₀) after 72 h was determined. Complete procedure available on

http://www.oecdbookshop.org/oecd/display.asp?K=5LMQCR2K7S5H&lang=FR&plang=en&sort=sort_date%2Fd&stem=true&sf1>Title&st1=201&sf3=SubjectCode&sp1=not&st4=E4%2Bor%2BE5%2Bor%2BP5&sf4=SubVersionCode&ds=201%3B+Tous+les+th%E8mes%3B+&m=1&dc=2 (accessed on 3 June 2013).
OECD, *OECD guideline for the testing of chemicals, Daphnia sp., Acute Immobilisation Test (202)* (table 1, entry 10).

This test described the acute toxicity of 1,2,3-TMP towards daphnids, which were exposed to 1,2,3-TMP for 48 h. The immobilization of daphnids was recorded at 24 h and 48 h and compared to a control experiment without 1,2,3-TMP. Several concentration of 1,2,3-TMP were studied and the limit test corresponds to one dose level of 0.1 g/L (maximum dose). The concentration estimated to immobilize 50% of the daphnids (EC$_{50}$) was determined after 48 h. Complete procedure available on


OECD, *OECD guideline for the testing of chemicals. Fish, Acute Toxicity Test (203)* (table 1, entry 11).

This test described the acute toxicity of 1,2,3-TMP towards fish, which were exposed to 1,2,3-TMP 96 h. Mortalities were recorded at 24 h, 48 h, 72 h and 96 h and the concentrations which kill 50 per cent of the fish (LC$_{50}$) were determined. Several concentration of 1,2,3-TMP were studied and the limit test corresponds to one dose level of 0.1 g/L (maximum dose). Complete procedure available on

http://www.oecdbookshop.org/oecd/display.asp?K=5LMQCR2K7RZT&lang=FR&plang=en&sort=sort_date%2Fd&stem=true&sf1=Title&st1=203&sf3=SubjectCode&sp1=not&st4=E4%2Bor%2BE5%2Bor%2BP5&sf4=SubVersionCode&ds=203%3B+Tous+les+th%E8mes%3B+&m=1&dc=2 (accessed on 3 June 2013).
Catalyst and hydride source screening for the reduction of benzonitrile 13a

Table S1. Catalyst and hydride source screening for the reduction of benzonitrile 13a.

<table>
<thead>
<tr>
<th>Entry</th>
<th>[M] 20 mol%</th>
<th>Si-H 8 equiv.</th>
<th>Solvent [0.5 M]</th>
<th>Conv. (%)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CoCl₂</td>
<td>PMHS</td>
<td>Toluene</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>Co(acac)₂</td>
<td>PMHS</td>
<td>Toluene</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>Co(OAc)₂</td>
<td>PMHS</td>
<td>Toluene</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>Co₂(CO)₈</td>
<td>PMHS</td>
<td>Toluene</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>Pd(OAc)₂</td>
<td>PMHS</td>
<td>Toluene</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>NiCl₂(PPh₃)₂</td>
<td>PMHS</td>
<td>Toluene</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>Ni(acac)₂</td>
<td>PMHS</td>
<td>Toluene</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>Ni(acac)₂</td>
<td>PMHS</td>
<td>2-MeTHF</td>
<td>&gt; 90</td>
</tr>
<tr>
<td>9</td>
<td>Cu(OTf)₂</td>
<td>PMHS</td>
<td>Toluene</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>Cu(OTf)₂</td>
<td>PMHS</td>
<td>2-MeTHF</td>
<td>&gt; 95</td>
</tr>
<tr>
<td>11</td>
<td>Cu(OTf)₂</td>
<td>TMDS</td>
<td>1,2,3-TMP</td>
<td>&gt; 99</td>
</tr>
<tr>
<td>12</td>
<td>Cu(OAc)₂</td>
<td>TMDS</td>
<td>2-MeTHF</td>
<td>0</td>
</tr>
<tr>
<td>13</td>
<td>Cu(acac)₂</td>
<td>TMDS</td>
<td>2-MeTHF</td>
<td>0</td>
</tr>
<tr>
<td>14</td>
<td>Fe(OTf)₂</td>
<td>TMDS</td>
<td>2-MeTHF</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>Bi(OTf)₃</td>
<td>TMDS</td>
<td>2-MeTHF</td>
<td>0</td>
</tr>
</tbody>
</table>

aConversions were determined by ¹H NMR spectroscopy.
\(^1\)H NMR spectra of the reduction of 4-hydroxybenzylamine in 2-MeTHF and 1,2,3-TMP

in 2-MeTHF after acidic treatment and evaporation of solvents (300 MHz, MeOD):

in 1,2,3-TMP after acidic treatment and evaporation of solvents (300 MHz, MeOD):
1,2,3-triméthoxypropane [20637-49-4]

\[
\begin{array}{c}
O \\
\text{O} \\
\text{O}
\end{array}
\]

Colorless liquid; \(^1\)H NMR: \(\delta = 3.37\) (s, 6H, CH\(_3\)), 3.42-3.52 (m, 8H, CH\(_3\), CH, CH\(_2\)); \(^{13}\)C NMR: \(\delta = 57.6\) (CH\(_3\)), 59.0 (CH\(_3\)), 72.0 (CH\(_2\)), 78.9 (CH); IR (ATR): \(\nu_{\text{max}} = 2981, 2888, 2815, 1452, 1192, 1107, 961, 834\) cm\(^{-1}\); GC-MS: RT = 4.12 min. \(m/z\) (intensity %) = 102 (48) [M - CH\(_3\)OH]\(^{+}\), 89 (100), 71 (16), 59 (92), 45 (46); HRMS-ESI: \(m/z\) [MNa]\(^{+}\) calcd for C\(_6\)H\(_{14}\)NaO\(_3\): 157.0835 found: 157.0831.

Benzyl alcohol [CAS 100-51-6] (1b)

\[
\begin{array}{c}
\text{O} \\
\text{H}
\end{array}
\]

Colorless liquid; \(^1\)H NMR: \(\delta = 1.84\) (br, 1H, OH), 4.69 (s, 2H, CH\(_2\)), 7.26-7.39 (m, 5H, 5×CH\(_{\text{arom}}\)); \(^{13}\)C NMR: \(\delta = 65.1\) (CH\(_2\)), 127.0 (2×CH\(_{\text{arom}}\)), 127.6 (CH\(_{\text{arom}}\)), 128.5 (2×CH\(_{\text{arom}}\)), 140.9 (C\(_q\)); IR (ATR): \(\nu_{\text{max}} = 3310, 3030, 2930, 1498, 1450, 1205, 910, 804, 729\) cm\(^{-1}\); GC-MS: RT = 5.32 min. \(m/z\) (intensity %) = 108 (72) [M]\(^{+}\), 137 (31), 79 (100), 77 (62).

(2-methoxyphenyl)methanol [CAS 612-16-8] (2b)

\[
\begin{array}{c}
\text{O} \\
\text{H}
\end{array}
\]

White solid; \(^1\)H NMR: \(\delta = 2.30\) (t, \(J = 6.5\) Hz, 1H, OH), 3.87 (s, 3H, CH\(_3\)), 4.69 (d, \(J = 6.1\) Hz, 2H, CH\(_2\)), 6.88-6.97 (m, 2H, 2×CH\(_{\text{arom}}\)), 7.26-7.29 (m, 2H, 2×CH\(_{\text{arom}}\)); \(^{13}\)C NMR: \(\delta = 55.1\) (CH\(_3\)), 61.5 (CH\(_2\)), 110.1 (CH\(_{\text{arom}}\)), 120.5 (CH\(_{\text{arom}}\)), 128.5 (CH\(_{\text{arom}}\)), 128.7 (CH\(_{\text{arom}}\)), 129.1 (C\(_q\)), 157.2 (C\(_q\)); IR (ATR): \(\nu_{\text{max}} = 3346, 2938, 2936, 1601, 1589, 1491, 1462, 1238, 1027, 750\) cm\(^{-1}\); GC-MS: RT = 7.95 min. \(m/z\) (intensity %) = 138 (100) [M]\(^{+}\), 121 (24), 105 (70), 91 (38), 77 (58), 65 (18), 51 (16).

4-phenylbutylamine [CAS 13214-66-9] (3b)

\[
\begin{array}{c}
\text{CH}_{\text{3}} \text{NH}_{2}
\end{array}
\]

Yellow gel; \(^1\)H NMR (400 MHz, MeOD): \(\delta = 1.63-1.71\) (m, 4H, 2×CH\(_2\)), 2.64 (t, \(J = 6.0\) Hz, 2H, CH\(_2\)), 3.94-3.97 (m, 2H, CH\(_2\)), 4.88 (t, \(J = 6.4\) Hz, 2H, CH\(_2\)), 5.23 (s, 1H, H\(_{\text{am}}\)), 7.26-7.29 (m, 2H, 2×CH\(_{\text{arom}}\)), 7.30-7.34 (m, 3H, 3×CH\(_{\text{arom}}\)); \(^{13}\)C NMR: \(\delta = 15.3\) (CH\(_{\text{3}}\)), 27.3 (CH\(_{\text{2}}\)), 31.7 (CH\(_{\text{2}}\)), 42.6 (CH\(_{\text{2}}\)), 47.9 (CH\(_{\text{2}}\)), 128.4 (CH\(_{\text{arom}}\)), 128.6 (CH\(_{\text{arom}}\)), 128.8 (CH\(_{\text{arom}}\)), 128.9 (CH\(_{\text{arom}}\)), 149.5 (C\(_q\)), 157.0 (C\(_q\)); IR (ATR): \(\nu_{\text{max}} = 3345, 2928, 2865, 2119, 1607, 1412, 1231, 1019\) cm\(^{-1}\); GC-MS: RT = 8.36 min. \(m/z\) (intensity %) = 186 (26) [M]\(^{+}\), 145 (58), 139 (100), 107 (2), 93 (16), 81 (25).
2.87 (t, J = 6.0 Hz, 2H, CH₂), 7.13-7.27 (m, 5H, 5×CH₃); ¹³C NMR (100 MHz, MeOD): δ = 28.9 (CH₂), 29.4 (CH₂), 36.2 (CH₂), 40.9 (CH₂), 126.9 (CH₃), 129.4 (2×CH₃), 129.4 (2×CH₃), 143.0 (C₆); IR (ATR): νmax = 3200, 2973, 2916, 1497, 1453, 1029, 745, 697 cm⁻¹; GC-MS: RT = 8.76 min. m/z (intensity %) = 149 (42) [M⁺], 132 (18), 117 (10), 104 (44), 91 (68), 77 (16), 65 (36), 51 (14), 45 (100).

2-naphthalenemethanamine [CAS 2018-90-8] (4b)⁴

White solid, Mp = 55-57 °C; ¹H NMR (400 MHz, MeOD): δ = 3.94 (s, 2H, CH₂), 7.42-7.47 (m, 3H, 3×CH₃), 7.76-7.83 (m, 4H, 4×CH₃); ¹³C NMR (100 MHz, MeOD): δ = 46.8 (CH₂), 126.5 (CH₃), 126.6 (CH₃), 127.0 (CH₃), 127.1 (CH₃), 128.6 (CH₃), 128.7 (CH₃), 129.2 (CH₃), 134.1 (C₆), 135.1 (C₆), 140.9 (C₆); IR (ATR): νmax = 3246, 2957, 1596, 1459, 1364, 815, 738 cm⁻¹; GC-MS: RT = 11.08 min. m/z (intensity %) = 157 (80) [M⁺], 156 (100), 141 (14), 129 (58), 115 (14), 102 (6), 77 (16), 63 (8), 51 (6).

4-chloroaniline hydrochloride [CAS 20265-96-7] (5b)⁵

Brown solid, Mp = 193-194 °C; ¹H NMR (MeOD): δ = 7.39 (d, J = 8.7 Hz, 2H, 2×CH₃), 7.57 (d, J = 8.5 Hz, 2H, 2×CH₃); ¹³C NMR (MeOD): δ = 126.1 (2×CH₃), 130.0 (C₆), 131.4 (2×CH₃), 135.4 (C₆); IR (ATR): νmax = 2804, 2602, 2554, 1489, 1093, 1015, 819 cm⁻¹; MS-EI: m/z (intensity %): 129 (34) [M+H]+, 127 (100) [M⁺], 100 (8), 92 (15), 65 (17).

aniline hydrochloride [CAS 142-04-1] (6b)⁵

Brown solid, Mp = 189-191 °C; ¹H NMR (MeOD): δ = 7.38 (d, J = 8.3 Hz, 2H, 2×CH₃), 7.51-7.59 (m, 3H, 3×CH₃); ¹³C NMR (MeOD): δ = 124.0 (2×CH₃), 130.0 (CH₃), 131.2 (2×CH₃), 131.4 (C₆); IR (ATR): νmax = 2813, 2570, 1490, 1463, 740, 686 cm⁻¹; MS-EI: m/z (intensity %): 93 (100) [M⁺], 66
4-cyanoaniline hydrochloride [CAS 2570-98-1] (7b)

Light brown solid, Mp = 168 °C; $^1$H NMR (MeOD): $\delta$ = 7.10 (d, $J = 8.3$ Hz, 2H, 2×CH$_{arom}$), 7.63 (d, $J = 8.3$ Hz, 2H, 2×CH$_{arom}$); $^{13}$C NMR (MeOD): $\delta = 111.4$ (C$q$), 124.3 (2×CH$_{arom}$), 135.2 (2×CH$_{arom}$), 137.8 (C$q$); IR (ATR): $\nu_{max}$ = 2800, 2545, 2236, 1607, 1574, 1553, 1107, 1067, 835 cm$^{-1}$; MS-EI: m/z (intensity %): 118 (100) [M]$^+$, 91 (60).

octadecan-1-ol [CAS 112-92-5] (8b)

White solid, Mp = 57-58 °C; $^1$H NMR: $\delta = 0.87$ (t, $J = 6.7$ Hz, 3H, CH$_3$), 1.20-1.40 (m, 30H, 15×CH$_2$), 1.53-1.58 (m, 2H, CH$_2$), 3.63 (t, $J = 6.6$ Hz, 2H, CH$_2$); $^{13}$C NMR: $\delta = 14.2$ (CH$_3$), 22.8 (CH$_2$), 25.9 (CH$_2$), 29.5 (CH$_2$), 29.6 (CH$_2$), 29.8 (CH$_2$), 29.8 (CH$_2$), 32.1 (CH$_2$), 32.9 (CH$_2$), 63.2 (CH$_2$); IR (ATR): $\nu_{max}$ = 3292, 2956, 2916, 2848, 1472, 1462, 1262, 1061, 730, 719 cm$^{-1}$; GC-MS: RT = 14.31 min. m/z (intensity %) = 252 (2) [M-H$_2$O]$^+$, 224 (4), 182 (2), 168 (4), 153 (5), 139 (6), 125 (22), 111 (46), 97 (76), 83 (100), 69 (76), 55 (95), 43 (64).

4-methylbenzyl alcohol [CAS 589-18-4] (9b)

White solid, Mp = 64 °C; $^1$H NMR: $\delta = 1.62$ (br, 1H, OH), 2.36 (s, 3H, CH$_3$), 4.65 (s, 2H, CH$_2$), 7.17 (d, $J = 7.9$ Hz, 2H, 2×CH$_{arom}$), 7.26 (d, $J = 8.0$ Hz, 2H, 2×CH$_{arom}$); $^{13}$C NMR: $\delta = 21.2$ (CH$_3$), 65.0 (CH$_2$), 127.1 (2×CH$_{arom}$), 129.2 (2×CH$_{arom}$), 137.2 (C$q$), 138.0 (C$q$); IR (ATR): $\nu_{max}$ = 3350, 2920, 1518, 1453, 1444, 1340, 1207, 1027, 1011, 802 cm$^{-1}$; GC-MS: RT = 6.38 min. m/z (intensity %) = 122 (100) [M]$^+$, 121 (20), 107 (100) [M – CH$_3$]$^+$, 93 (34), 91 (60) [M – CH$_2$OH]$^+$, 79 (72), 77 (32).
4-methoxybenzyl alcohol [CAS 105-13-5] (10b)\(^4\)

Colorless oil; \(^1\)H NMR: \(\delta = 1.66\) (br, 1H, OH), 3.81 (s, 3H, CH\(_3\)), 4.62 (s, 2H, CH\(_2\)), 6.89 (d, \(J = 8.7\) Hz, 2H, 2\(\times\)CH\(_{\text{arom}}\)), 7.29 (d, \(J = 8.3\) Hz, 2H, 2\(\times\)CH\(_{\text{arom}}\)); \(^{13}\)C NMR: \(\delta = 55.4\) (CH\(_3\)), 64.9 (CH\(_2\)), 114.0 (2\(\times\)CH\(_{\text{arom}}\), 128.7 (2\(\times\)CH\(_{\text{arom}}\), 133.2 (C\(_q\), 159.2 (C\(_q\)); IR (ATR): \(\nu_{\text{max}} = 3335, 2935, 2850, 1609, 1511, 1244, 1171, 1032, 1001, 813\) cm\(^{-1}\); GC-MS: RT = 7.89 min. \(m/z\) (intensity \%) = 138 (100) [M]\(^+\), 137 (29), 109 (40), 107 (10) [M – CH\(_2\)OH]\(^+\), 77 (9).

8-bromo-1-octanol [CAS 50816-19-8] (11b)\(^7\)

Colorless oil; \(^1\)H NMR: \(\delta = 1.31\) (m, 6H, 3\(\times\)CH\(_2\)), 1.41-1.50 (m, 2H, CH\(_2\)), 1.51-1.60 (m, 3H, CH\(_2\), OH), 1.81-1.90 (m, 2H, CH\(_2\)), 3.40 (t, \(J = 6.9\) Hz, 2H, CH\(_2\)), 3.65 (t, \(J = 6.7\) Hz, 2H, CH\(_2\)); \(^{13}\)C NMR: \(\delta = 25.9\) (CH\(_2\)), 28.2 (CH\(_2\)), 28.9 (CH\(_2\)), 29.4 (CH\(_2\)), 32.6 (CH\(_2\)), 32.9 (CH\(_2\)), 34.0 (CH\(_2\)), 62.3 (CH\(_2\)); IR (ATR): \(\nu_{\text{max}} = 3342, 2940, 2852, 1465, 1258, 1025, 870, 720\) cm\(^{-1}\); GC-MS: RT = 7.52 min. \(m/z\) (intensity \%) = 208 (2) [M]\(^+\), 162 (20), 148 (15), 135 (4), 111 (23), 83 (40), 69 (94), 55 (100), 41 (58).

2-(4-methoxyphenyl)ethanol [CAS 702-23-8] (12b)\(^6\)

Colorless oil; \(^1\)H NMR: \(\delta = 1.51\) (br, 1H, OH), 2.82 (t, \(J = 6.5\) Hz, 2H, CH\(_2\)), 3.80 (s, 3H, CH\(_3\)), 3.83 (t, \(J = 6.5\) Hz, 2H, CH\(_2\)), 6.86 (d, \(J = 8.7\) Hz, 2H, 2\(\times\)CH\(_{\text{arom}}\)), 7.15 (d, \(J = 8.7\) Hz, 2H, 2\(\times\)CH\(_{\text{arom}}\)); \(^{13}\)C NMR: \(\delta = 38.4\) (CH\(_2\)), 55.3 (CH\(_3\)), 63.9 (CH\(_2\)), 114.1 (2\(\times\)CH\(_{\text{arom}}\), 130.1 (2\(\times\)CH\(_{\text{arom}}\), 130.6 (C\(_q\), 158.4 (C\(_q\)); IR (ATR): \(\nu_{\text{max}} = 3402, 2956, 2849, 1610, 1509, 1242, 1170, 1020, 807\) cm\(^{-1}\); MS-ESI: \(m/z\) [MH]\(^+\) found: 153.1.

Benzylamine hydrochloride [CAS 3287-99-8] (benzylamine CAS 100-46-9) (13b)\(^8\)\(^9\)

---

S17
Yellow solid, Mp > 240 °C; $^1$H NMR (MeOD): $\delta$ = 4.11 (s, 2H, CH$_2$), 7.42-7.47 (m, 5H, 5×CH$_{arom}$); $^{13}$C NMR (MeOD): $\delta$ = 45.4 (CH$_2$), 130.8 (4×CH$_{arom}$), 130.9 (CH$_{arom}$), 135.1 (C$_q$); IR (ATR): $\nu_{max}$ = 3344, 2966, 2879, 2689, 2573, 1595, 1477, 1467, 1382, 1215, 1058 745, 693 cm$^{-1}$; MS-ESI: m/z [M-Cl]$^+$ found: 107.9.

4-methylbenzylamine hydrochloride [CAS 26177-45-7] (14b)$^{10}$

![Structure](image)

Yellow solid, Mp > 185 °C; $^1$H NMR (400 MHz, MeOD): $\delta$ = 2.37 (s, 3H, CH$_3$), 4.08 (s, 2H, CH$_2$), 7.27 (d, $J$ = 7.8 Hz, 2H, 2×CH$_{arom}$), 7.35 (d, $J$ = 8.0 Hz, 2H, 2×CH$_{arom}$); $^{13}$C NMR (100 MHz, MeOD): $\delta$ = 22.1 (CH$_3$), 45.0 (CH$_2$), 130.9 (2×CH$_{arom}$), 131.7 (2×CH$_{arom}$), 132.3 (C$_q$), 141.3 (C$_q$); IR (ATR): $\nu_{max}$ = 3309, 3094, 2917, 1621, 1592, 1515, 1381, 1245, 971, 813, 669 cm$^{-1}$; MS-ESI: m/z [MH-Cl]$^+$ found: 123.8.

4-methoxybenzylamine hydrochloride [CAS 17061-61-9] (15b)$^{10}$

![Structure](image)

Yellow-orange solid, Mp > 220 °C; $^1$H NMR (MeOD): $\delta$ = 3.84 (s, 3H, CH$_3$), 4.07 (s, 2H, CH$_2$), 7.01 (d, $J$ = 8.7 Hz, 2H, 2×CH$_{arom}$), 7.41 (d, $J$ = 8.5 Hz, 2H, 2×CH$_{arom}$); $^{13}$C NMR (MeOD): $\delta$ = 44.8 (CH$_2$), 56.7 (CH$_3$), 116.3 (2×CH$_{arom}$), 127.1 (C$_q$), 132.6 (2×CH$_{arom}$), 162.2 (C$_q$); IR (ATR): $\nu_{max}$ = 3320, 3093, 2950, 2785, 2600, 1615, 1498, 1379, 1244, 1191, 1019, 829, 640 cm$^{-1}$; MS-ESI: m/z [M-Cl]$^+$ found: 138.1.

4-chlorobenzylamine hydrochloride [CAS 42365-43-5] (16b)$^{10}$

![Structure](image)

White solid, Mp > 194 °C; $^1$H NMR (400 MHz, MeOD): $\delta$ = 4.12 (s, 2H, CH$_2$), 7.46-7.50 (m, 4H, 4×CH$_{arom}$); $^{13}$C NMR (100 MHz, MeOD): $\delta$ = 44.6 (CH$_2$), 131.1 (2×CH$_{arom}$), 132.8 (2×CH$_{arom}$), 134.0 (C$_q$), 137.0 (C$_q$); IR (ATR): $\nu_{max}$ = 3313, 3095, 2944, 2790, 2731, 2599, 1567, 1491, 1381, 1214, 1095,
1019, 827, 640 cm\(^{-1}\); MS-ESI: \(m/z [M-Cl]^+\) found: 141.9.

### 4-hydroxybenzylamine hydrochloride [CAS 1004-23-5] (17b)

![4-hydroxybenzylamine](image)

Green solid, Mp > 190 °C; \(^1\)H NMR (300 MHz, MeOD): \(\delta = 3.98\) (s, 2H, CH\(_2\)), 6.81 (d, \(J = 8.3\) Hz, 2H, 2×CH\(_{arom}\)), 7.25 (d, \(J = 8.3\) Hz, 2H, 2×CH\(_{arom}\)); \(^{13}\)C NMR (100 MHz, MeOD): \(\delta = 44.5\) (CH\(_2\)), 116.8 (2×CH\(_{arom}\)), 124.9 (C\(_q\)), 131.8 (2×CH\(_{arom}\)), 159.3 (C\(_q\)); IR (ATR): \(\nu_{max} = 3269, 3134, 2974, 2554, 1613, 1517, 1472, 1449, 1383, 1214, 1085, 825, 617\) cm\(^{-1}\); MS-ESI: \(m/z [M-Cl]^+\) found: 123.8.

### 4-phenylbutylamine hydrochloride [CAS 30684-06-1] (18b)

![4-phenylbutylamine](image)

Yellow solid, Mp = 157-161 °C; \(^1\)H NMR (300 MHz, MeOD): \(\delta = 1.60-1.70\) (m, 4H, 2×CH\(_2\)), 2.67 (t, \(J = 6.4\) Hz, 2H, CH\(_2\)), 2.92 (t, \(J = 7.0\) Hz, 2H, CH\(_2\)), 7.12-7.28 (m, 5H, 5×CH\(_{arom}\)); \(^{13}\)C NMR (100 MHz, MeOD): \(\delta = 28.1\) (CH\(_2\)), 29.3 (CH\(_2\)), 36.2 (CH\(_2\)), 40.8 (CH\(_2\)), 126.9 (CH\(_{arom}\)), 129.4 (2×CH\(_{arom}\)), 129.5 (2×CH\(_{arom}\)), 142.8 (C\(_q\)); IR (ATR): \(\nu_{max} = 3108, 2973, 2916, 2757, 2618, 2518, 1605, 1497, 1395, 745, 696\) cm\(^{-1}\); MS-ESI: \(m/z [M-Cl]^+\) found: 150.0.

### (2-Naphthylmethyl)amine hydrochloride [CAS 2241-98-7] (19b)

![2-Naphthylmethylamine](image)

Beige solid, Mp > 240 °C; \(^1\)H NMR (400 MHz, MeOD): \(\delta = 4.31\) (m, 2H, CH\(_2\)), 7.55-7.59 (m, 3H, 3×CH\(_{arom}\)), 7.92-8.00 (m, 4H, 4×CH\(_{arom}\)); IR (ATR): \(\nu_{max} = 3250, 3054, 2915, 2766, 2737, 2612, 1575, 1508, 1441, 1408, 1126, 995, 863, 826, 738\) cm\(^{-1}\); MS-ESI: \(m/z [M-Cl]^+\) found: 157.9.
1,2,3-Trimethoxypropane [20637-49-4]
Benzyl alcohol [CAS 100-51-6] (1b)
(2-methoxyphenyl)methanol [CAS 612-16-8] (2b)

<table>
<thead>
<tr>
<th>(ppm)</th>
<th>180</th>
<th>170</th>
<th>160</th>
<th>150</th>
<th>140</th>
<th>130</th>
<th>120</th>
<th>110</th>
<th>100</th>
<th>90</th>
<th>80</th>
<th>70</th>
<th>60</th>
<th>50</th>
<th>40</th>
<th>30</th>
<th>20</th>
<th>10</th>
</tr>
</thead>
</table>

Electronic Supplementary Material (ESI) for Green Chemistry
This journal is © The Royal Society of Chemistry 2013
4-phenylbutylamine [CAS 13214-66-9] (3b)
naphthalen-2-ylmethanamine [CAS 2018-90-8] (4b)
4-chloroaniline hydrochloride [CAS 20265-96-7] (5b)
aniline hydrochloride [CAS 142-04-1] (6b)
4-cyanoaniline hydrochloride [CAS 2570-98-1] (7b)
octadecan-1-ol [CAS 112-92-5] (8b)
4-methylbenzyl alcohol [CAS 589-18-4] (9b)
4-methoxybenzyl alcohol [CAS 105-13-5] (10b)

![Chemical structure of 4-methoxybenzyl alcohol](image)

Electronic Supplementary Material (ESI) for Green Chemistry
This journal is © The Royal Society of Chemistry 2013
4-methoxybenzyl alcohol [CAS 50816-19-8] (11b)
2-(4-methoxyphenyl)ethanol [CAS 702-23-8] (12b)
Benzylamine hydrochloride [CAS 3287-99-8] (benzylamine CAS 100-46-9) (13b)
4-methylbenzylamine hydrochloride [CAS 26177-45-7] (14b)
4-methoxybenzylamine hydrochloride [CAS 17061-61-9] (15b)
4-chlorobenzylamine hydrochloride [CAS 42365-43-5] (16b)
4-hydroxybenzylamine hydrochloride [CAS 1004-23-5] (17b)
4-phenylbutylamine hydrochloride [CAS 30684-06-1] (18b)
(2-Naphthylmethyl)amine hydrochloride [CAS 2241-98-7] (19b)

Electronic Supplementary Material (ESI) for Green Chemistry
This journal is © The Royal Society of Chemistry 2013
References


