Electronic Supplementary Material (ESI) for Green Chemistry.

Supplementary Information

Reviving electrocatalytic reductive amination: A sustainable route from biogenic levulinic acid to 1,5-dimethyl-2-pyrrolidone

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Contents

1 Additional results

1.1 Influence of the amine structure

Due to the differing results for sterically different ketonic substrates, an impact of the steric hindrance of the amine was expected as well. The reductive amination of acetone with methylamine and ethylamine was already investigated by Smirnov *et al.*[1] In this work, very similar results were obtained (Figure S1).

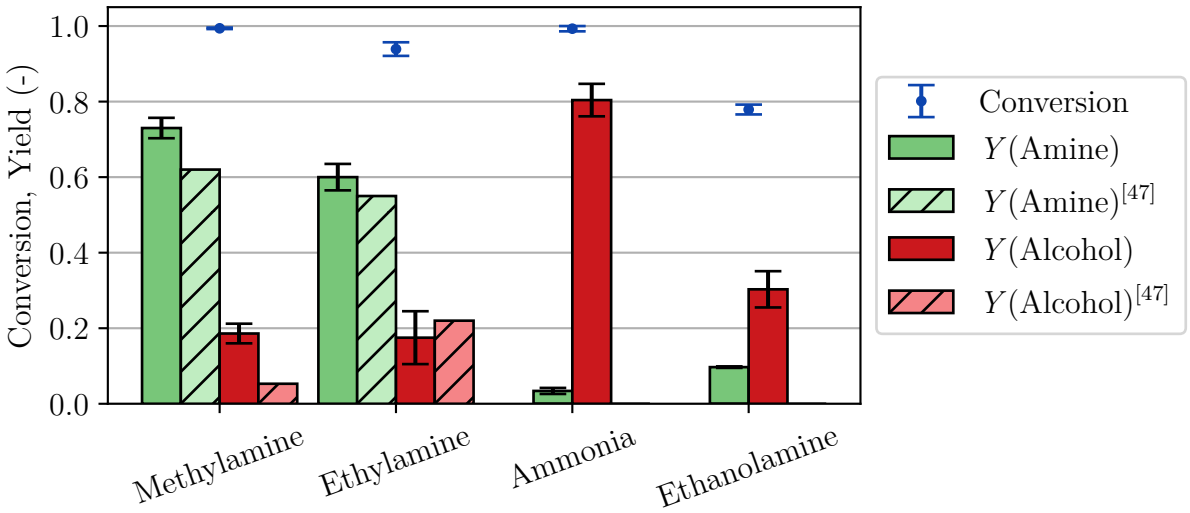
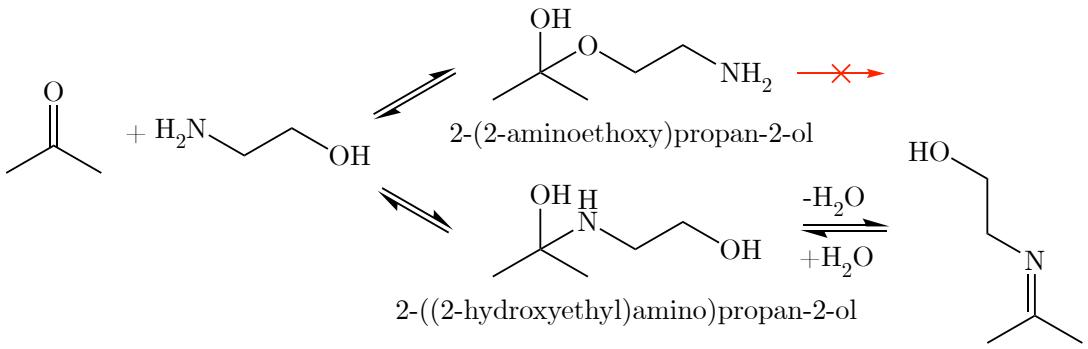


Figure S1: Conversion and yields Y of the electrocatalytic reductive amination of acetone with different amines compared to the results of Smirnov *et al.*[1] Conditions: Pb electrodes, 0.04 A cm^{-2}, 2.4 mol L^{-1} ketone in 0.5 M KH_2PO_4, acetone to amine ratio: 1:1.2, pH = 12, one faraday equivalent, 283 K.

The slightly lower yields of the secondary amine in literature can be due to the size or geometry of the setup as mentioned above. Again elongation of the carbon chain leads to a lower yield for N-ethylisopropylamine (60(4) %) than for N-methylisopropylamine (73(3) %) which can be explained by the imine yields of 59 % (methylamine) and 42 % (ethylamine) before electrolysis.
Additionally, the performances of ammonia and ethanolamine were investigated as they are interesting amination agents for industrial applications leading to primary and highly functionalized amines. Using 25 % aqueous ammonia, only 3(1) % of the aminated product

were obtained. The reaction mainly yielded isopropanol (80(4) %). This is due to no observable imine formation in the reaction solution before electrolysis.
In order to enhance the imine formation another system was adapted from literature. Meza-León *et al.*[2] used ammonium chloride in combination with sodium bicarbonate to form an imine from acetone. Usage of this imine without further purification is reported in the second step of their reaction forming calyxamines. They detected the formation by a phase separation which was also observed in this reproduction of their experiment. However, investigations with NMR spectroscopy could not proof the imine formation, only acetone was visible. Deploying the separated phase in electrolysis showed again almost no aminated product but isopropanol. It is likely that reducing the imine in electrolysis is challenging due to its instability. The imine formation can take place but it decomposes to acetone as soon as its exposed to the electrolyte solution or a NMR solvent.
Using ethanolamine, 9.7(2) % of the secondary amine and 30(5) % isopropanol were obtained. The carbon balance of this reaction is around 81(4) % and thus 5 to 10 % lower than for the other amines. NMR spectra show the formation of another substrate before electrolysis (section 3.2). A nucleophilic attack of the hydroxy group instead of the amine group may lead to the formation of 2-(2-aminoethoxy)propan-2-ol (Scheme S1). This inhibits the reduction of imine and ketone and leads to the lower conversion of 78(1) % and lower yields of this reaction.



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Scheme S1: Mechanism of the imine formation of acetone with ethanolamine and possible side reaction.

2 Experimental

2.1 Electrolysis batch experiments

Electrolysis experiments were performed in custom-built cells. They consist of a stacking construction of two modules with cylindrical recesses (r = 1 cm, h = 1 cm) in square manufactured parts. They are completed by a module for cooling and are screwed and fixed by plates from both sides. The modules are separated by two electrodes and a Nafion®N-324 membrane (0.15 mm thick, Teflon fabric reinforced) (Figure S2). The electrode surface of each electrode amounts to 3 cm^2. The distance between the electrodes is 2 cm and each compartment holds a volume of 3 mL. The thickness of the electrodes varied for the different materials: Pb (0.5 mm), Cu (1 mm), Ag (1 mm), Cd (0.5 mm), Zn (0.5 mm), Sn (0.5 mm), Ni (0.01 mm). Pb, Cu and Ni electrodes were commercial samples from the mechanical workshop, Ag (99.9 %), Cd (99.99 %), Zn (99.99 %), and Sn (99.8 %) were purchased from chempure. A *BASETech BT-305* power unit or the *Metrohm Autolab PGSTAT 302N* potentiostat ensured a constant current density.

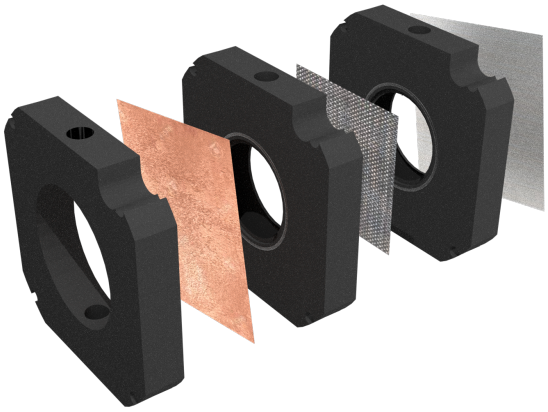

Figure S2: Electrochemical setup for batch electrolysis from left to right with cooling module, cathode, cathode compartment, membrane, anode compartment, and anode.

Prior to starting the experiment, the electrodes were mechanically polished by wet sanding with 900 followed by 2000 grit in order to remove organic residues and metal oxides. After assembling, the anodic compartment was filled with 2.5 mL aqueous H_3PO_4 (25 %). 2.5 mL reaction solution for the cathodic chamber consisted of 6 mmol ketone, 7.2 mmol

amine, electrolyte, solvent and concentrated KOH in order to set the pH value to 12. The solution was cooled down to 275 K in the refrigerator before injection. The cathode was continuously cooled with ice water in the *Julabo MC-4* thermal control unit. The resulting temperature of the reaction solution was approximately 283 K preventing the evaporation of volatile substrates such as acetone and methylamine. The complete setup is depicted in Figure S3.

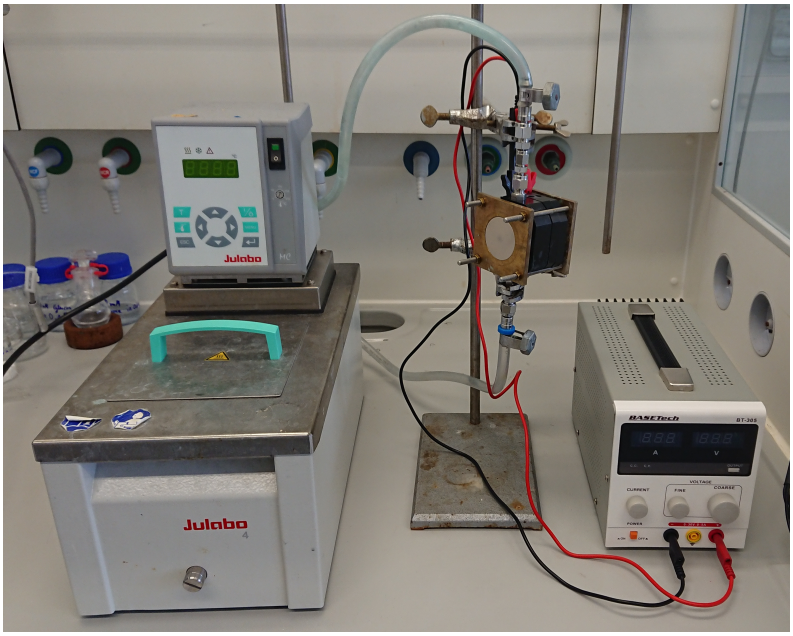

Figure S3: Electrochemical setup for batch electrolysis including cell, thermal control unit, and power unit.

2.2 Microwave experiments

The reaction solution was heated in a microwave after electrolysis of levulinic acid in order to obtain 1,5-dimethylpyrrolidin-2-one. Therefore, it was filled in a 10 mL vial. The heating process contained a one minute temperature ramp to 473 K, holding this temperature for 10 minutes, and then cooling to room temperature for around 5 minutes (*Monowave 450* device from *Anton Paar*). Pressure in the vial rised to around 20 bar during this process.

2.3 Purification of the product solution

1,5-Dimethyl-2-pyrrolidone was extracted from the product solution with dichloromethane. The separated organic layer was washed with aqueous NaCl solution, dried over anhydrous $MgSO_4$, and filtered. The dichloromethane was removed under reduced pressure to obtain the desired product. This procedure was based on Smirnov's[1] method. No further steps were necessary after filtration as visibile in the NMR spectrum of the purified 1,5-dimethyl-2-pyrrolidone in Figure S11.

2.4 Nuclear magnetic resonance spectroscopy

Reaction solutions before and after electrolysis were qualitatively and quantitatively analyzed by NMR spectroscopy. All ^{1}H, ^{13}C, HSQC, and HMBC spectra were measured at room temperature with a *Bruker Avance* spectrometer (^{1}H: 400 MHz, ^{13}C: 100 MHz). The solvent was DMSO-d_6 and trioxane was used as the internal standard.
Before spectroscopy, a defined mass of the solution (150 mg) was mixed with 0.6 mL DMSO-d_6 and 15 mg trioxane. Precipitated electrolyte was removed by using a *CHROMAFIL Xtra PA* syringe filter (25 mm, 0.45 μm). Intermediates and products were identified using ^{13}C and 2D-NMR and then quantified by ^{1}H-NMR spectroscopy comparing the integrals of the peaks concerning the products, intermediates, and the internal standard. Zerofilling, phase, and baseline were corrected manually. Processed spectra can be found in section 3.2. The chemical shift δ is expressed in ppm and all coupling constants (J) are stated in Hz.

2.5 Chemicals: Origin and purity

The origin and purity of the chemicals used in this work are listed in Table S1 below. They were used without further purification.

Table S1: Origin and purity of the experimentally used chemicals.

Substance	Supplier	Purity (%)
Acetic acid	Chemsolute	99.5
Acetone	Roth	99.5
Acetonitrile	Roth	99.8
2-Butanone	Sigma-Aldrich	99.7
Cyclopentanone	Fluka	99
Dimethylsulfoxide-d_6	Sigma-Aldrich	99.8
Levulinic acid	Sigma-Aldrich	98
Methanol	Chemsolute	99.8
Methylamine solution (40 %)	Merk	-
Monopotassium phosphate	Fluka	99
2-Pentanone	Sigma-Aldrich	99.5
3-Pentanone	Alfa Aesar	99
Phosphoric acid (88 %)	Merck	-
Potassium hydroxide	Chemsolute	85
Sodium hydroxide	Fluka	97
Sulfuric acid	Merck	80
1,3,5-Trioxane	Sigma-Aldrich	99

3 NMR spectroscopy

3.1 Basic equation for calculations

In the following, an assigned ^{1}H-NMR spectra of each product solution is depicted. The integrated signals were used to quantify the substances according to Equation 3.1.

$$n_{\mathrm{Sub}} = \frac{\nu_{\mathrm{Std}} \cdot A_{\mathrm{Sub}} \cdot m_{\mathrm{Std}} \cdot m_{\mathrm{Ges}}}{\nu_{\mathrm{Sub}} \cdot A_{\mathrm{Std}} \cdot M_{\mathrm{Std}} \cdot m_{\mathrm{NMR}}} \tag{3.1}$$

n_{Sub}: molar amount of substrate in reaction solution (mol)
$\nu_{\mathrm{Sub/Std}}$: number of hydrogen atoms of the substrate/standard assigned to the peak (-)
$A_{\mathrm{Sub/Std}}$: integral of the substrate/ standard peak (-)
$m_{\mathrm{NMR/Std}}$: mass of the sample in NMR tube/ of the standard (g)
m_{Ges}: total mass of the substrate solution in electrolysis cell (g)

3.2 N-Methylisopropylamine

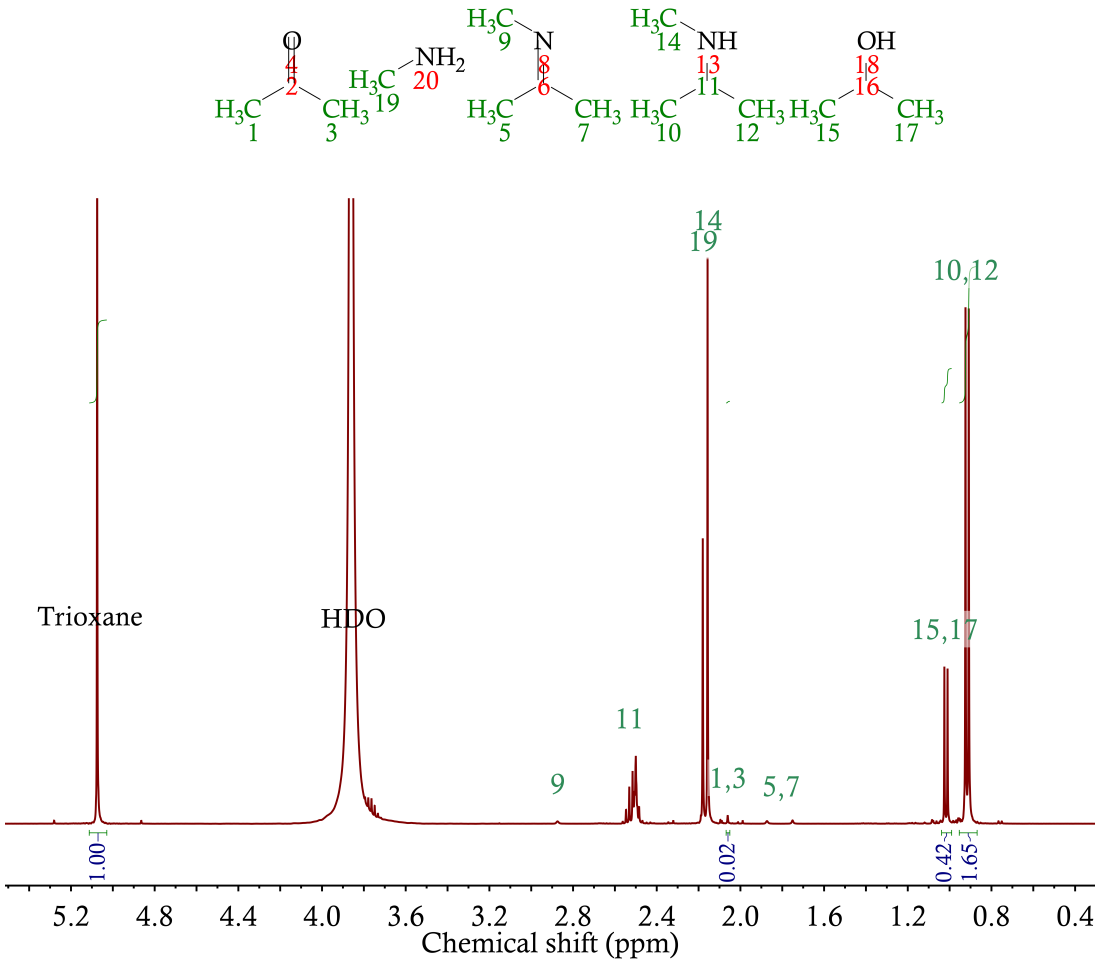

Figure S4: NMR spectrum of the reaction solution of acetone with methylamine after electrolysis.
N-Methylisopropylamine: ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.57 - 2.43 (m, 1H), 2.16 (s, 3H), 0.92 (d, J = 6.3 Hz, 6H)
Isopropanol: ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.81 - 3.73 (m, 1H), 1.02 (d, J = 6.1 Hz, 6H).

3.3 N-Methylbutan-2-amine

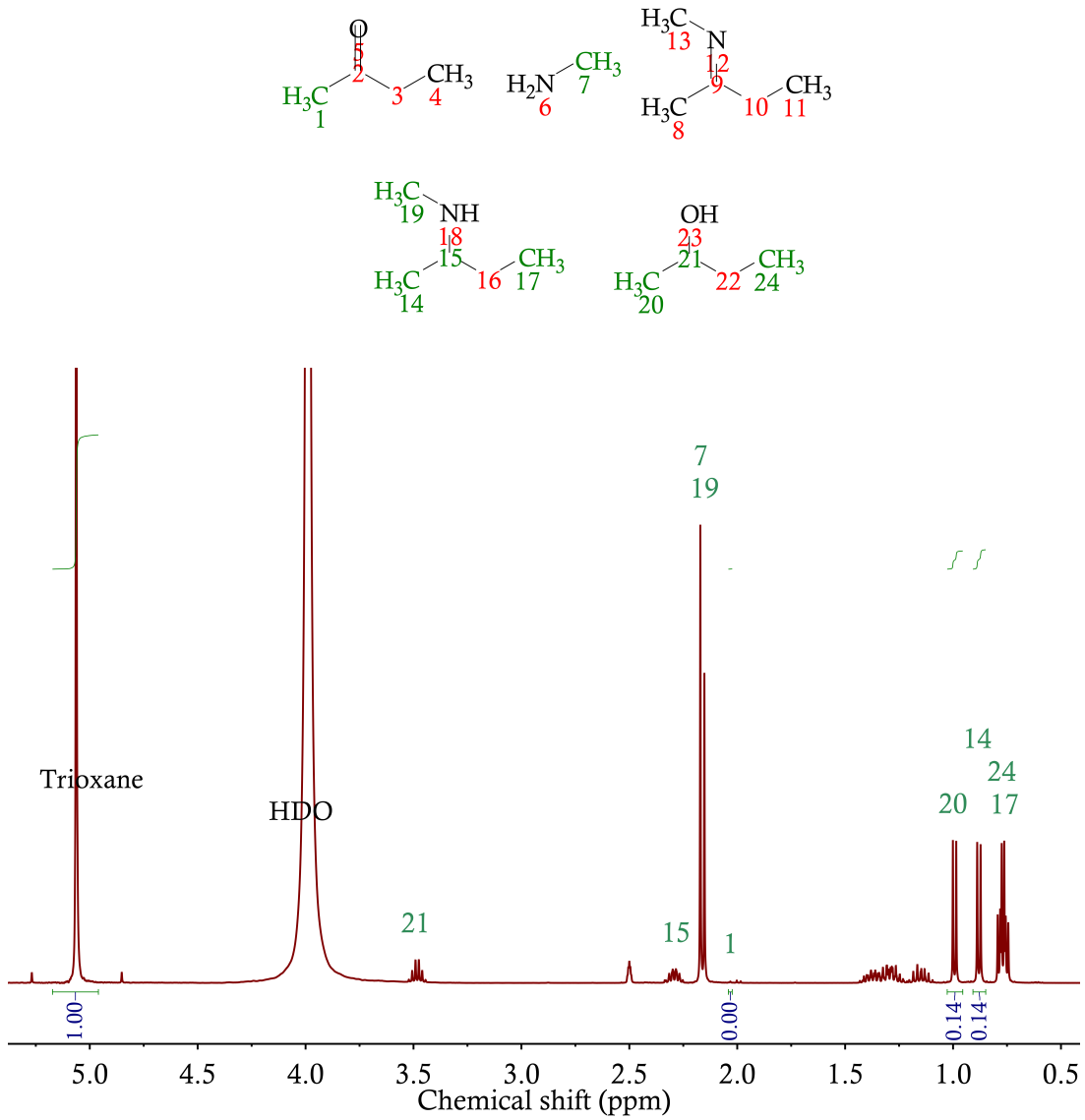

Figure S5: NMR spectrum of the reaction solution of butanone with methylamine after electrolysis.
N-Methylbutan-2-amine: ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.35 - 2.23 (m, 1H), 2.15 (s, 3H), 0.88 (d, J = 6.3 Hz, 3H)
2-Butanol: ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.48 - 3.51 (m, 1H), 0.99 (d, J = 6.2 Hz, 3H).

3.4 N-Methylpentan-2-amine

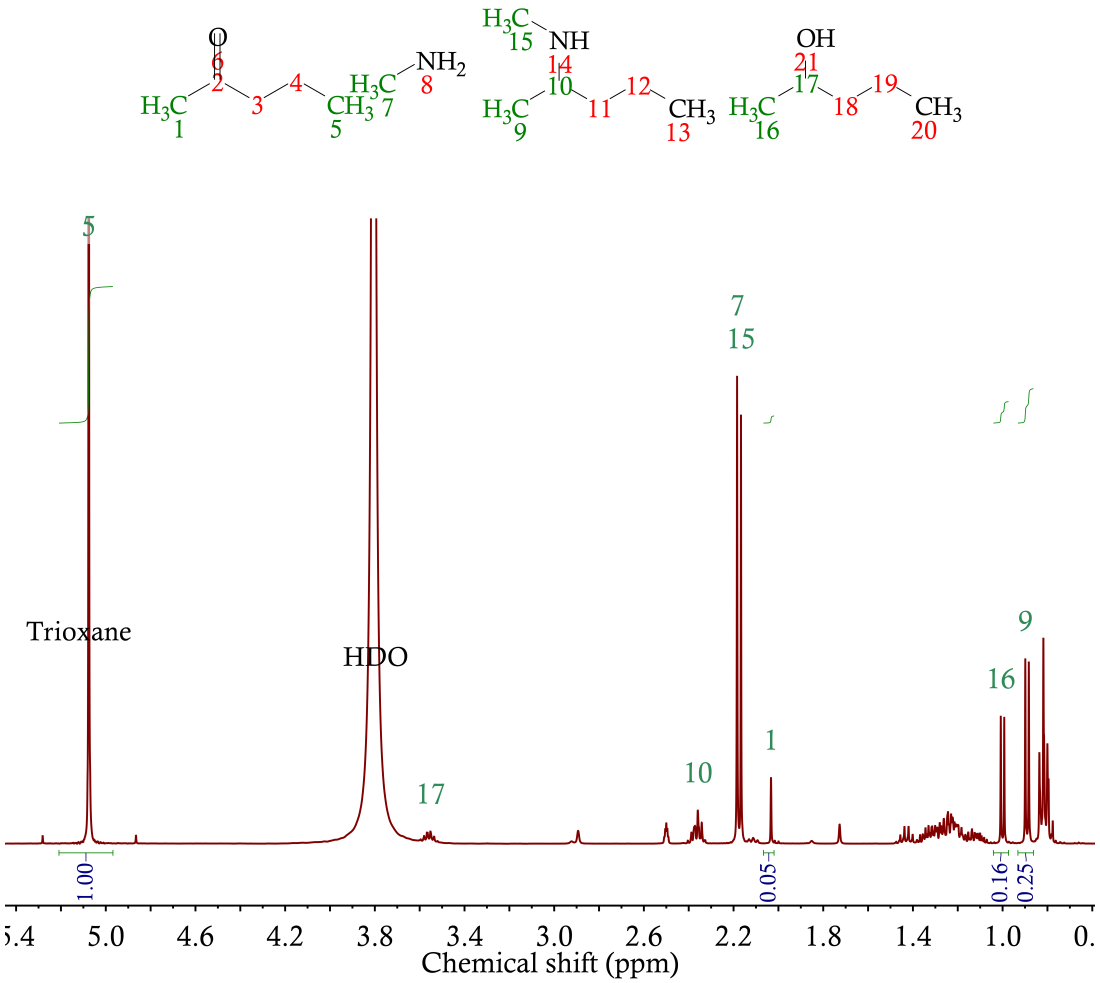

Figure S6: NMR spectrum of the reaction solution of 2-pentanone with methylamine after electrolysis.
N-Methylpentan-2-amine: ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.37 (m, 1H), 0.89 (d, J = 6.3 Hz, 3H)
2-Pentanol: ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.62 - 3.49 (m, 1H), 1.00 (d, J = 6.2 Hz, 3H).

3.5 N-Methylpentan-3-amine

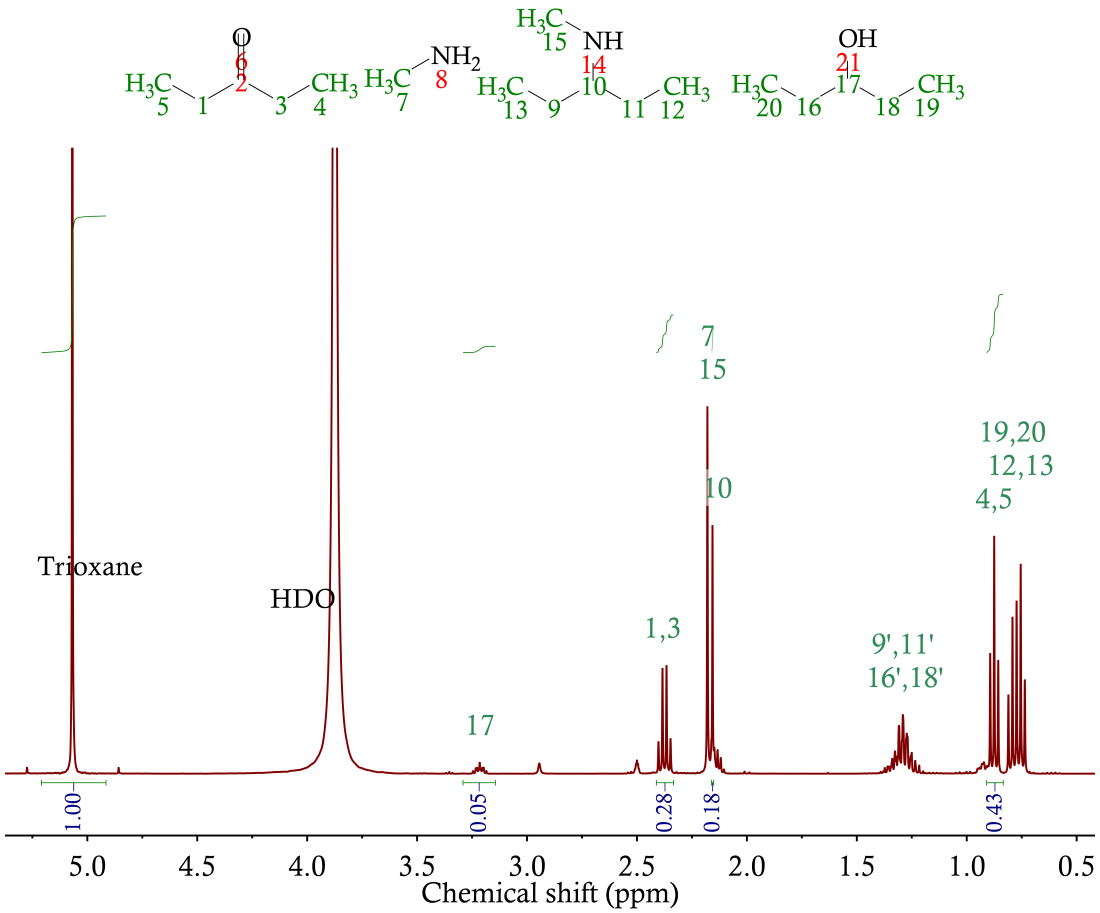

Figure S7: NMR spectrum of the reaction solution of 3-pentanone with methylamine after electrolysis.
N-Methylpentan-3-amine: ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.16 (s, 3H), 2.17 - 2.08 (m, 1H), 1.38 - 1.20 (m, 4H), 0.75 (t, J = 7.5 Hz, 6H)
3-Pentanol: ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.27 - 3.16 (m, 1H), 1.37 - 1.21 (m, 4H), 0.80 (t, J = 7.4 Hz, 6H).

3.6 N-Methylcyclopentanamine

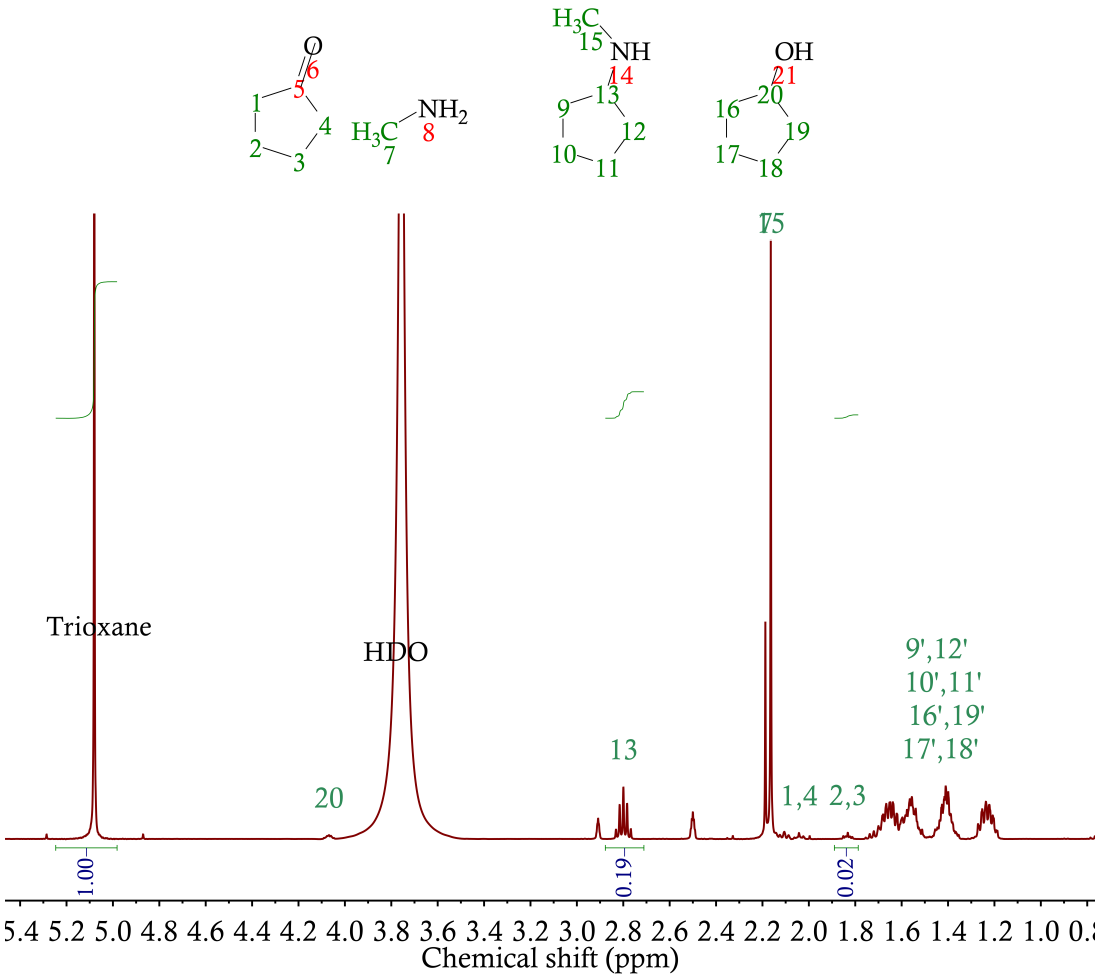

Figure S8: NMR spectrum of the reaction solution of cyclopentanone with methylamine after electrolysis.
N-Methylcyclopentanamine: ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.80 (p, J = 6.4 Hz, 1H), 2.16 (s, 3H)
Cyclopentanol: ^{1}H NMR (400 MHz, DMSO-d_6) δ 4.11 - 4.02 (m, 1H).

3.7 4-(Methylamino)-pentanoic acid

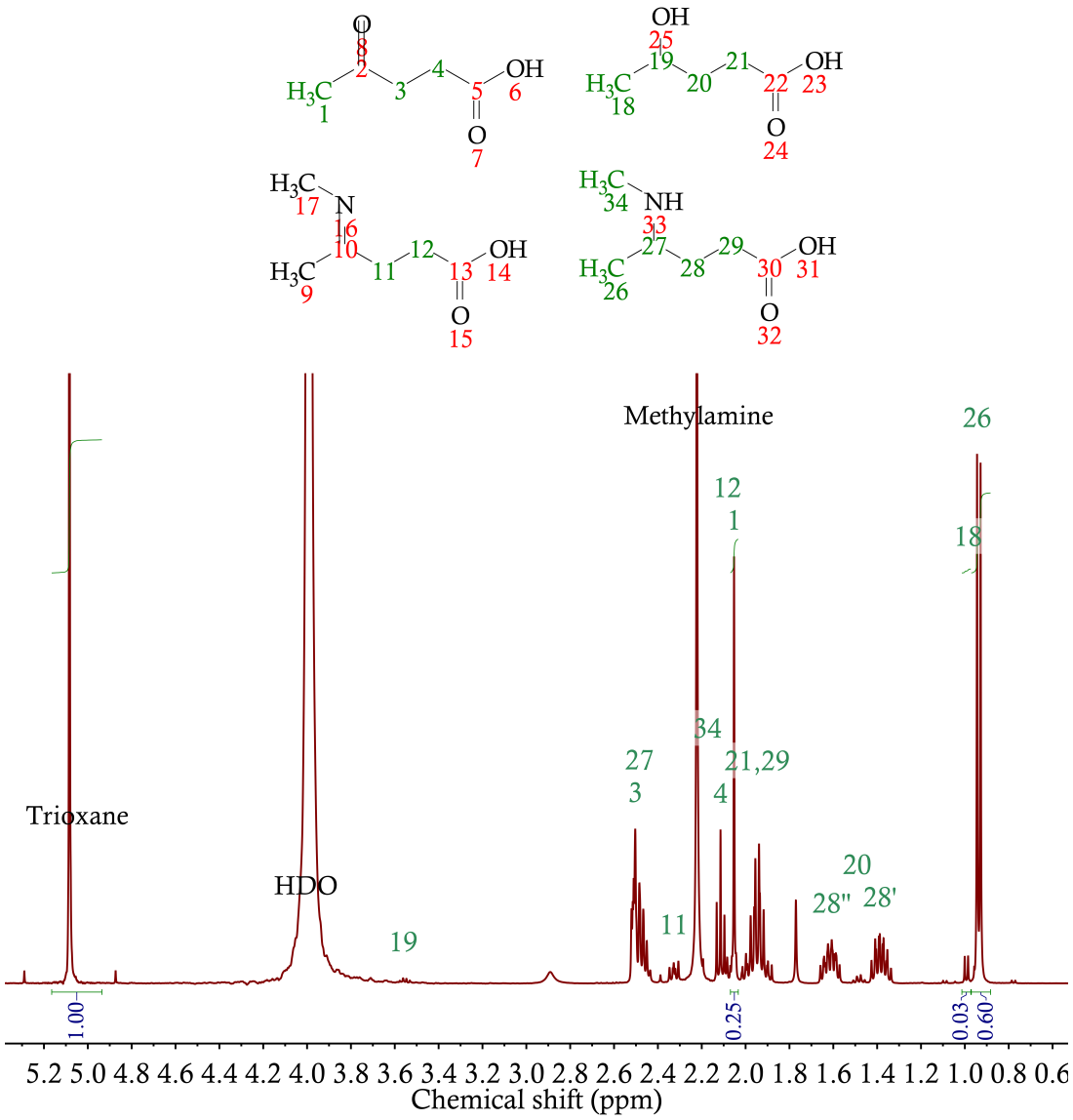

Figure S9: NMR spectrum of the reaction solution of levulinic acid with methylamine after electrolysis.
4-(Methylamino)-pentanoic acid: ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.53 - 2.41 (m, 1H), 1.95 - 1.82 (m, 2H), 1.65 - 1.31 (m, 2H), 0.93 (d, J = 6.2 Hz, 3H)
4-Hydroxypentanoic acid: ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.61 - 3.50 (m, 1H), 1.95 - 1.82 (m, 2H), 1.55 - 1.38 (m, 2H), 0.99 (d, J = 6.2 Hz, 3H).

3.8 1,5-Dimethyl-2-pyrrolidone

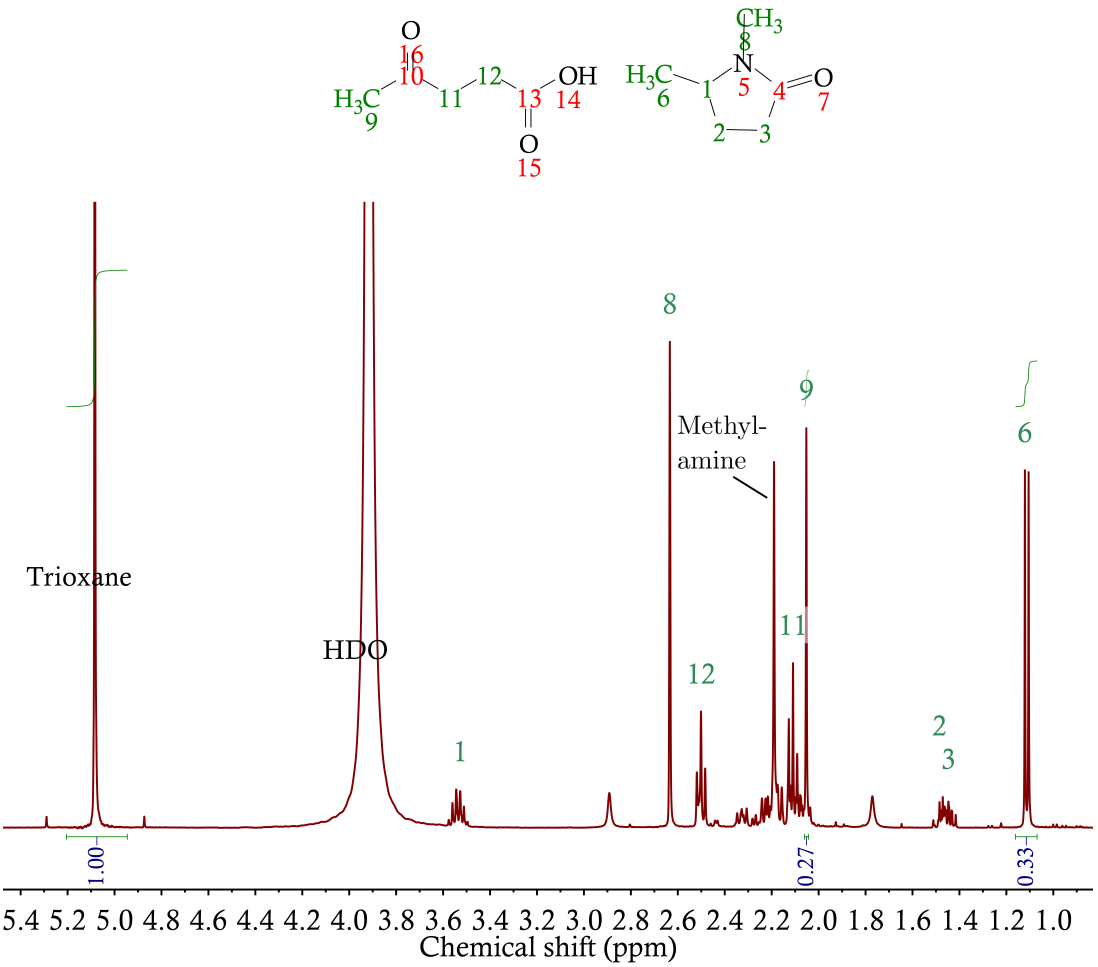

Figure S10: NMR spectrum of the reaction solution of levulinic acid with methylamine after electrolysis and heating.
1,5-Dimethyl-2-pyrrolidone: ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.54 (m, 1H), 2.63 (s, 3H), 1.53 - 1.39 (m, 4H), 1.11 (d, J = 6.3 Hz, 3H).

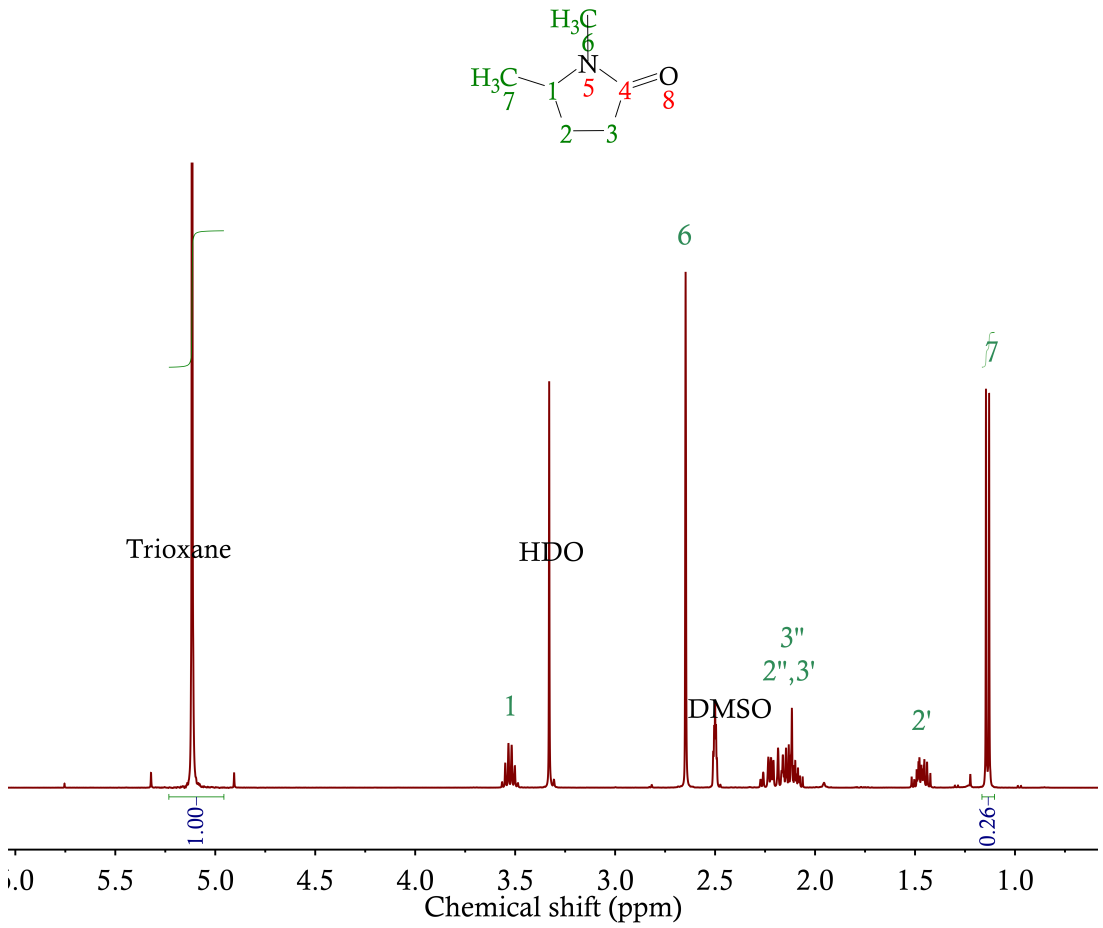

Figure S11: NMR spectrum of purified 1,5-dimethyl-2-pyrrolidone.
1,5-Dimethyl-2-pyrrolidone: ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.53 (h, J = 6.3 Hz, 1H), 2.66 (s, 3H), 2.32 - 2.04 (m, 3H), 1.63 - 1.36 (m, 1H), 1.15 (d, J = 6.3 Hz, 3H).

Bibliography

[1] Y. D. Smirnov, A. P. Tomilov, *Zhurnal Organicheskoi Khimii* **1992**, *28*, 51–58.

[2] R. L. Meza-León, A. D. García, F. Sartillo-Piscil, L. Quintero, M. S. Rivadeneyra, S. Cruz-Gregorio, *Tetrahedron Letters* **2013**, *54*, 6852–6854.