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Biogenic Alcohols

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Synthesis of 1-Octanol and 1,1-Dioctyl Ether from Biomass-Derived Platform Chemicals**

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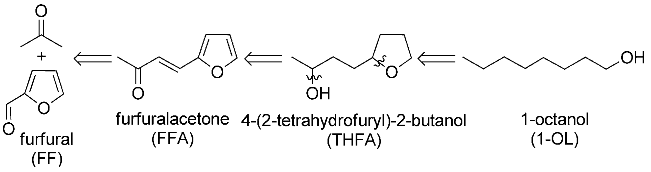
As a consequence of diminishing fossil resources and global endeavors to reduce anthropogenic carbon dioxide emissions, biomass-derived substrates are receiving increasing attention in the effort to establish renewable supply chains for transportation fuels and chemical products.[1] Carbohydrates constitute the largest fraction of biomass feedstock. The conversion of carbohydrates from a set of platform molecules into tailor-made products can be envisaged through selective catalytic transformation steps.[1a,2]

Primary alcohols of medium chain length are very important industrial products, as they are valuable compounds for the production of detergents and surfactants, in perfumery, and as flavors. 1-Octanol is of particular importance and is also used for the synthesis of 1-octene, an important co-monomer for polyethylene. 1-Octanol is predominantly synthesized either by the reaction of ethylene with triethylaluminum (Alfen process) or by oxo synthesis starting from *n*-heptene, which are both petrochemical processes.[3]

Aliphatic alcohols from biomass are accessible by the reduction of fatty acids, but this is commercially exploited almost exclusively for long carbon chains ($\geq C_{12}$).[1a] Carbohydrate-based alcohols are currently limited to short carbon chains ($\leq C_4$) and are obtained through fermentation.[1a,4] In contrast, the formation of alcohols of medium chain length from lignocellulosic platform chemicals is described in only very few cases and is not yet synthetically exploited.[5] 1-Pentanol has been observed as a by-product, for example, in the hydrogenolysis of tetrahydrofurfuryl alcohol and in the selective transformation of levulinic acid into 2-methyltetrahydrofuran.[2,6]

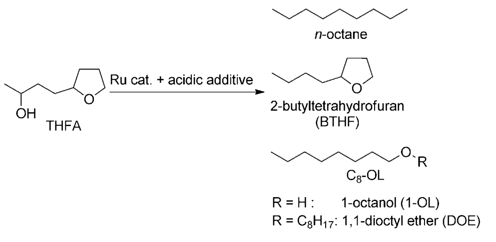
Herein, we describe the highly selective catalytic synthesis of the linear primary C_8 alcohol products 1-octanol and dioctyl ether from the biomass-derived platform molecule furfural[7] and acetone, which is also accessible from carbohydrates,[1c,4] at least in principle. This opens a general strategy for the synthesis of medium-chain-length alcohols from carbohydrate feedstock.

Recently, we proposed the concept of synthetic pathway design for biomass-derived products in analogy to the retrosynthetic analysis used in modern organic synthesis.[2] Scheme 1 shows how 1-octanol can be traced back to furfural and acetone as starting materials using this approach. These compounds are readily converted into furfuralacetone (FFA) by an aldol condensation;[8] FFA can then be hydrogenated to 4-(2-tetrahydrofuryl)-2-butanol (THFA),[9] which might be converted into 1-octanol (1-OL) by selective deoxygenation and ring opening, provided that over-hydrogenation to the alkane can be avoided.[5c,10] Therefore, the challenge in establishing this pathway lies in the development of a selective catalytic system that can give access to 1-octanol from THFA by deoxygenation of the secondary alcohol function coupled with the selective ring-opening of the tetrahydrofuryl ring by hydrogenolysis.



Scheme 1. Retrosynthetic analysis for a pathway to 1-octanol using platform chemicals derived from lingocellulosic feedstock.

Scheme 2 shows the possible products resulting from hydrogenation and dehydration of THFA using a multifunctional catalytic system that provides both transition-metal-based hydrogenation activity and Brønsted acidity.[1d] 2-Butyltetrahydrofuran (BTHF) is obtained by removal of the secondary hydroxy group. BTHF is an interesting molecule in its own right, for example, as a potential fuel additive.[5c,11] Full deoxygenation of THFA leads to *n*-octane.[5c,10a] The targets of the present study are the linear C_8 alcohol products



Scheme 2. Possible C_8 products accessible by catalytic conversion of THFA by dehydration/hydrogenation reactions.

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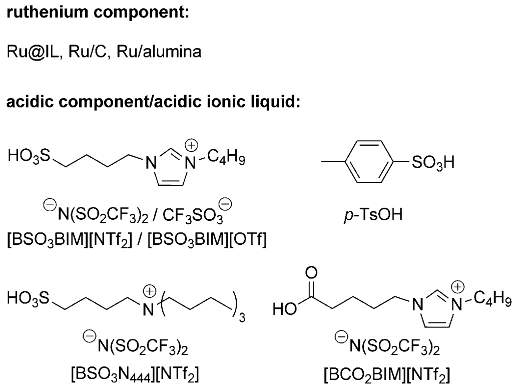
(C_8-OL), which can be directly formed as free 1-octanol (1-OL) by hydrogenolytic ring opening, or as dioctyl ether (DOE) upon reversible etherification.

Scheme 3 gives an overview of the components that were selected for the generation of the catalytic systems in the present study. Ruthenium was introduced as the metal component for hydrogenation because of its proven activity in transformations of FFA, THFA, and related molecules.[2,8,12] Ruthenium nanoparticles stabilized in ionic liquids (Ru@IL) were investigated for this application, along with commercially available heterogeneous catalysts. Brønsted acid additives, including functional ionic liquids (ILs) were chosen to control the acidity required for dehydration.[13] In the first series of experiments, the transformation of THFA under hydrogen with ruthenium nanoparticles (particle size 2–3 nm) was investigated. The nanoparticles were prepared by hydrogenation of $[(cod)Ru(\eta^3\text{-}C_4H_7)_2]$ in the presence of different ILs.[8,13c]



Scheme 3. Metal components and acidic additives, including ionic liquids (ILs), used for the multifunctional catalytic systems.

As seen in Table 1, the Ru@[BCO$_2$BIM][NTf$_2$] catalyst showed no activity in the hydrogenolysis of THFA, indicating that the acidity of the carbonic acid function in the ionic liquid is too weak for the dehydration (Table 1, entry 1). In contrast, the performance of Ru@[BSO$_3$BIM][NTf$_2$] was dominated by the acidity of the SO_3H function, resulting mainly in etherification and isomerization of THFA (entry 2). However, it was possible to reduce the acid-catalyzed side reactions by diluting the Ru@[BSO$_3$BIM][NTf$_2$] catalyst with the inert IL [EMIM][NTf$_2$], which resulted in significant formation of C_8-OL (28 % overall yield of 1-OL and DOE) and high selectivity towards 1-OL (entry 3). Under the same conditions, the use of Ru@[BSO$_3$BIM][OTf] or Ru@[BSO$_3$N$_{444}$][NTf$_2$] resulted in a combination of hydrogenation and acid catalysis that led to a remarkable BTHF yield of up to 75 %, with isomerization and etherification products of THFA as the main side products (entries 4 and 5). Therefore, the system of entry 3 was chosen as first lead structure for further investigation.

Table 1: Hydrogenolysis of THFA with Ru@IL.

Entry	Ionic liquid	Conv. [%]	BTHF [%]	1-OL [%]	DOE [%]	Other[a] [%]
1[b]	[BCO$_2$BIM][NTf$_2$]	0	–	–	–	–
2[b]	[BSO$_3$BIM][NTf$_2$]	>99	5.0	–	–	95
3[c]	[BSO$_3$BIM][NTf$_2$]	>99	66.6	25	2.8	5.6
4[c]	[BSO$_3$BIM][OTf]	>99	69.0	9.7	1.0	21.2
5[c]	[BSO$_3$N$_{444}$][NTf$_2$]	>99	74.4	9.6	3.2	12.8
6[c]	[BSO$_3$N$_{888}$][NTf$_2$]	>99	75.3	3.2	–	21.5

[a] Other = isomers and etherification products of THFA. [b] 120 °C, H_2 (120 bar), 15 h, Ru (0.016 mmol), acidic IL (0.11 mmol), THFA (1.57 mmol). [c] 120 °C, H_2 (120 bar), 15 h, Ru (0.016 mmol), acidic IL (0.11 mmol), THFA (1.57 mmol), [EMIM][NTf$_2$] (2.9 mL).

Monitoring the reaction (Figure 1) revealed that acid-catalyzed self-etherification and isomerization of the substrate also occur with this system and dominate the conversion during the first two hours (Scheme 4). However, the hydrogenolysis of the secondary alcohol group in the side chain of THFA reverses the etherification equilibrium, and the deoxygenation product, BTHF, is accumulated with a maximum of 80 % conversion in the reaction mixture after eight hours. Selective ring opening of the tetrahydrofuryl ring in BTHF then yields 1-OL, which again subsequently undergoes partial etherification under the acidic conditions to

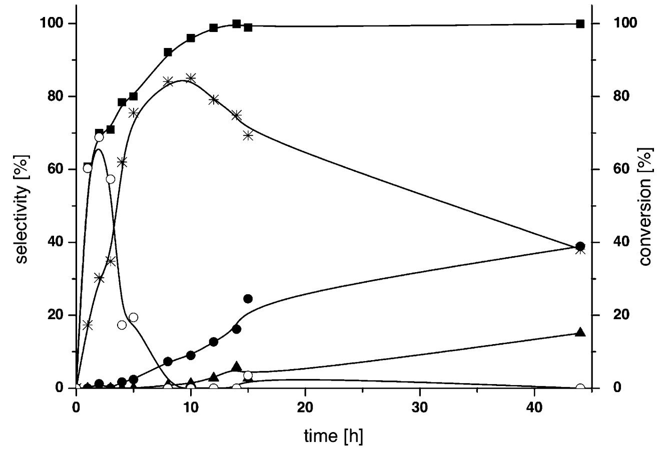
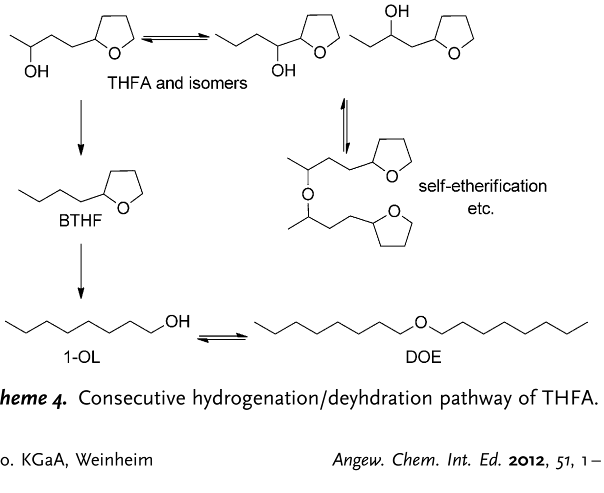


Figure 1. Reaction monitoring of the hydrogenolysis of THFA with Ru@[BSO$_3$BIM][NTf$_2$]. Conversion (—■—), BTHF (—*—), 1-OL (—●—), DOE (—▲—), condensate (—○—). For reaction conditions, see Table 1, entry 3. For structures, see Scheme 4.



Scheme 4. Consecutive hydrogenation/deyhdration pathway of THFA.

produce DOE. Further dehydration to *n*-octane remains insignificant under these conditions, reflecting the greater resistance of the primary alcohol versus secondary alcohols to acid-catalyzed hydrogenolysis.

The monitoring of the hydrogenolysis of THFA allowed elucidation of the complex network of consecutive reactions, which involve uni- and bimolecular transformations of the substrate and product, respectively. Therefore, the reaction parameters of temperature, reaction time, and substrate concentration were selected for further optimization using the simplex algorithm, with the yield of 1-OL as the target value (Figure 2). The parameter limits were set to $T = 120$–$160\,°C$, $t = 10$–25 h and c^0(THFA) = 0.2–0.8 mol L^{-1}, while hydrogen pressure and the substrate-to-catalyst ratio were kept constant.

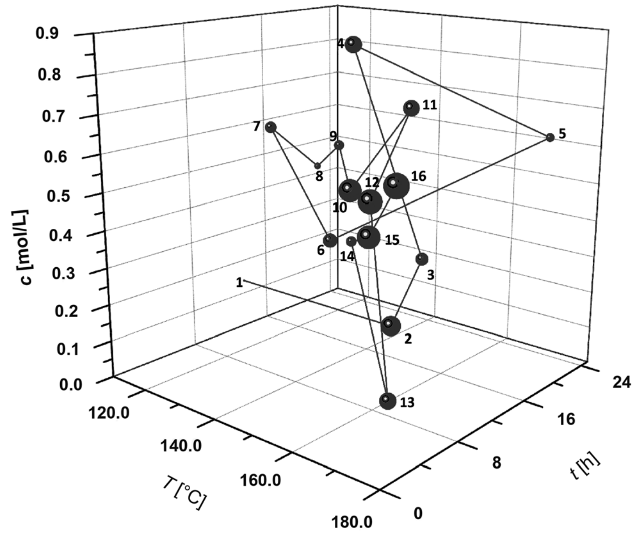


Figure 2. Optimization of reaction conditions for Ru@[BSO$_3$BIM][NTf$_2$] by the simplex algorithm (size of data points correspond to yields of 1-OL).

After 16 iteration steps, the alteration of the command variables reached a stable output within error tolerance. Under the optimized reaction conditions of 150 °C, 15 h, and 0.5 mol L^{-1} substrate concentration, a maximum yield of 45 % 1-OL and an overall C$_8$-OL yield of 71.4 % was obtained. In particular, no over-hydrogenation to *n*-octane was observed.

Using the optimized conditions, a series of combinations of Ru-based catalysts and acidic additives were evaluated for the hydrogenolysis of THFA (Table 2, entries 1–5; see also the Supporting Information). Ru@[N$_{444}$BSO$_3$] gave a slightly higher combined yield for the C$_8$-OL products with a lower 1-OL/DOE-ratio and small amounts of *n*-octane, as compared to the imidazolium ionic liquid (entries 1 and 2). Commercially available Ru/C and Ru/Alox (Alox = aluminum oxide) catalysts also performed well (entries 3 and 4), providing up to 75 % yield of C$_8$-OL with outstanding selectivity for the removal of the secondary hydroxy function. Results varied significantly with the source of the catalysts (see the Supporting Information for details) and the data presented in Table 2 were obtained with Ru/C (5 %) obtained from the supplier abcr. They were found to be reproducible within ± 5.0 % over three independent experiments and varied ± 7.0 % between two different catalyst batches. In combination with *p*-toluenesulfonic acid (*p*-TsOH), a 77 % overall yield of C$_8$-OL was achieved within 15 h, whereby the larger content of DOE and the formation of significant amounts of *n*-octane reflect the higher acidity of the reaction mixture (entry 5).

Once the transformation of THFA into C$_8$-OL had been successfully demonstrated, further development of the synthetic pathway shown in Scheme 1 was attempted. If the reaction sequence was performed in individual steps with intermediate isolation of the products, the cumulative yields of the individual steps (97 %, 98 %, 77 %) resulted in an overall yield of 73 %, based on furfural. A direct one-step conversion of FFA into C$_8$-OL using the multifunctional catalyst systems was not possible, because furfuralacetone (FFA) is very sensitive towards acidic conditions and forms humin-type products in the presence of *p*-TsOH or [BSO$_3$BIM][NTf$_2$].

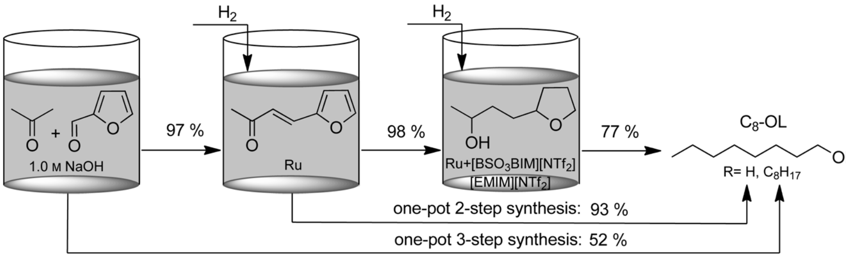
However, a two-step one-pot process could successfully be achieved when the acidic additive was introduced directly into the reaction vessel after full hydrogenation of FFA to THFA (entry 6). After FFA was hydrogenated at 120 °C with H$_2$ (120 bar) for two hours in the presence of Ru/C, the acidic

Table 2: One-pot catalytic synthesis of linear C$_8$ alcohol products (C$_8$-OL) from biomass-derived platform chemicals.[a]

Entry	Substrate	Steps	Catalyst	Additive	BTHF [%]	1-OL [%]	DOE [%]	Octane [%]	Other[b] [%]	C$_8$-OL [%]
1	THFA	1[c]	Ru@[BSO$_3$BIM][NTf$_2$]	–	25.8	44.9	26.1	–	3.2	71.0
2	THFA	1[c]	Ru@[BSO$_3$N$_{444}$][NTf$_2$]	–	11.7	41.5	34.5	2.4	9.9	76.0
3	THFA	1[c]	Ru/C (5 wt % Ru)	[BSO$_3$BIM][NTf$_2$]	47.8	20.5	19.4	–	12.3	39.4
4	THFA	1[c]	Ru/Alox (5 wt % Ru)	[BSO$_3$BIM][NTf$_2$]	23.0	43.6	31.8	–	1.6	75.4
5	THFA	1[c]	Ru/C (5 wt % Ru)	*p*-TsOH	8.7	24.7	51.9	8.5	6.2	76.6
6	FFA	2[d]	Ru/C	[BSO$_3$BIM][NTf$_2$]	5.4	48.8	44.2	–	1.8	93.0
7	FFA	2[d]	Ru/C	*p*-TsOH	2.1	18.1	53.0	16.9	10.8	71.1
8	furfural	3[e]	Ru/C	[BSO$_3$BIM][NTf$_2$]	23.5	32.5	19.8	–	24.2[f]	52.3

[a] Mass distribution of the product mixture after pentane extraction according to GC analysis using *n*-tetradecane as internal standard; > 99 % conversion was observed in all cases. [b] Other = other isomers, mainly 2-propyltetrahydropyran. [c] THFA (1.57 mmol), Ru (0.016 mmol), acidic additive (0.11 mmol) in [EMIM][NTf$_2$] (2.9 mL), 150 °C, H$_2$ (120 bar), 15 h. [d] 1st step: 120 °C, H$_2$ (120 bar), 2 h, neat FFA (1.57 mmol), Ru (0.016 mmol); 2nd step: as in [c], 60 h. [e] 1st step: furfural/acetone 1:10, RT, 15 h, NaOH (50 µL, 1.0 M); 2nd and 3rd step: as in [c] and [d], respectively. [f] Isomers of THFA. Alox = aluminum oxide.

IL [BSO_3BIM][NTf_2] and the [EMIM]-[NTf_2] solvent were added, and the reaction mixture was treated further at 150 °C with H_2 (120 bar) for 45 h to obtain 1-OL and DOE in excellent combined yields of 93 %. Considerable amounts of *n*-octane were formed when *p*-TsOH was used as an acidic additive to Ru/C (entry 7). The ruthenium nanoparticle catalysts could not be used in this procedure, as they were found to be deactivated by agglomeration during the first part of the sequence.



Scheme 5. Integrated multi-step synthesis of linear C_8 alcohol products (C_8-OL) from furfural and acetone as biogenic platform chemicals.

It is even possible to conduct this reaction sequence as a one-pot procedure starting from furfural as a platform chemical (Scheme 5). Furfural was transformed to FFA by an aldol condensation in the presence of excess acetone using sodium hydroxide under standard conditions (see Table 2 for details). After neutralization of the reaction mixture with aqueous HCl and evaporation of acetone, Ru/C was added and the hydrogenation was carried out as above. After 2 h, the acidic IL [BSO_3BIM][NTf_2] and the solvent IL were introduced directly for the final step. The overall yield for C_8-OL was 54 % with a higher 1-OL content, corresponding to a remarkable 33 % yield of the free alcohol. The somewhat lower overall yield can be attributed at least partly to the presence of the salt resulting from the neutralization process. Using a base-catalyzed protocol for the aldol condensation[11] and/or conducting the one-pot procedure in a flow system[14] are possibilities for further development towards a fully integrated reaction sequence.

In summary, we have demonstrated for the first time the selective conversion of tetrahydrofurfurylacetone (THFA) and furfuralacteone (FFA) into 1-octanol and dioctyl ether by dehydration/hydrogenation using a multifunctional catalyst system comprised of a Ru hydrogenation catalyst together with an acidic additive, including functional ionic liquids. Up to 93 % yield of the linear C_8 alcohol products were obtained and the new transformation was integrated into a complete sequence starting from furfural and acetone, which gave a combined yield (of 1-octanol and dioctyl ether) of 73 % overall in a step-wise procedure, and 54 % overall in a one-pot procedure. Using the retrosyntheic approach[2] shown in Scheme 1, other primary alcohols can be readily envisaged to be produced by analogous pathways using the corresponding ketones, $RCOCH_3$. This opens a new general route from biomass-derived platform molecules to medium-chain primary alcohols, again demonstrating the viability of rational pathway design for the exploration of lignocellulosic supply chains.

Experimental Section

All reactions were carried out in a 10 mL stainless-steel high-pressure reactor with a glass inlet. Metal catalysts and ionic liquids were handled under an argon atmosphere. Ru@ILs were freshly prepared before use by suspending [(cod)Ru(η^3-C_4H_7)$_2$] (5.0 mg, 0.016 mmol) in the corresponding ionic liquid (0.11 mmol), followed by hydrogenation at 60 °C with H_2 (60 bar) for two hours. Ru/C (5 wt %, abcr) was activated at 80 °C with H_2 (100 bar) for 10 h prior to use. In a typical hydrogenolysis reaction, 4-(2-tetrahydrofuryl)-2-butanol (THFA; 225.7 mg, 1.57 mmol), 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide (2.9 mL) and the acidic additive (0.11 mmol) were added to the metal catalyst and the reaction mixture was stirred for 15 h at 150 °C with H_2 (120 bar). After carefully venting the reactor, the reaction mixture was extracted with pentane (3 × 20 mL). The colorless solution was concentrated under reduced pressure and the molar composition of the product mixture was analyzed by GC with *n*-tetradecane as an internal standard. Full details of the experimental and analytical procedures are provided in the Supporting Information.

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Keywords: biomass conversion · homogeneous catalysis · hydrogenation · linear alcohols · multifunctional catalysts

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Communications

Biogenic Alcohols

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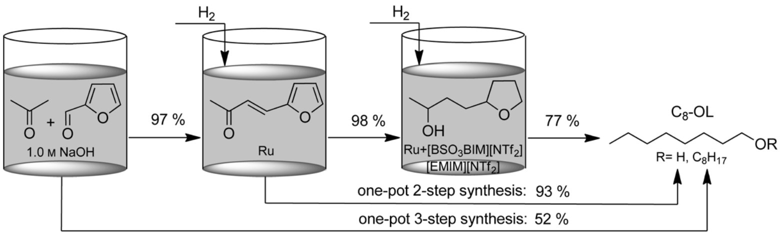
Synthesis of 1-Octanol and 1,1-Dioctyl Ether from Biomass-Derived Platform Chemicals



The happy medium: A new catalytic pathway for the synthesis of the linear primary C_8 alcohol products 1-octanol and dioctyl ether from furfural and acetone has been developed using retrosynthetic analysis. This opens a general strategy for the synthesis of medium-chain-length alcohols from carbohydrate feedstock.