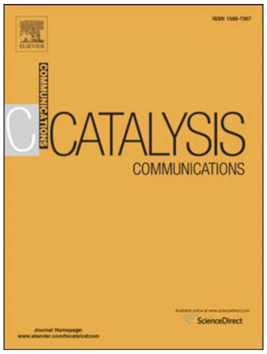

Indium(III) Triflate Promoted Synthesis of Alkyl Levulinates from Furyl Alcohols and Furyl Aldehydes

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Indium(III) Triflate Promoted Synthesis of Alkyl Levulinates from Furyl Alcohols and Furyl Aldehydes

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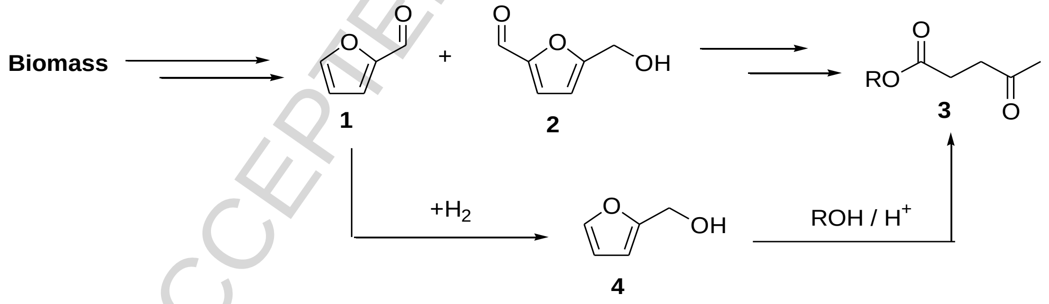
KEYWORDS: biomass valorization· indium(III) triflate · homogeneous catalysis · furan alcoholysis · alkyl levulinate esters

ABSTRACT: A facile protocol for the alcoholysis of furfuryl alcohol into levulinate esters has been developed employing low catalyst loadings of indium(III) triflate. This method provides a rapid and efficient route for the synthesis of these useful materials. The alcoholysis reactions of 5-hydroxymethylfurfural (HMF), furfural and furfural dimethylacetal were also investigated under these reaction conditions.

1. Introduction

The growing demand for fossil fuel resources comes at a time of diminishing reserves of these non-renewable resources and an increasing awareness of the influence of greenhouse gases on global climate change. These factors have led to considerable interest in alternative strategies for energy production which have reduced environmental impact. Biomass valorization, in particular, has attracted considerable interest as a sustainable and renewable source of both energy and feedstock chemicals for the chemical industry [1,2]. Initial developments in this area relied on the use of starch and vegetable oils, however, these resources are valued food commodities and thus subsequent interest has considered lignocellulose residues, sustainably sourced from agriculture and forestry activities, as a promising low cost and abundant alternative [3-5]. One of the most advanced and commercially viable lignocellulosic-fractionating technologies currently developed is the Biofine Process, which involves the acid catalyzed hydrolysis of polysaccharides to their monomeric constituents, which are then in turn converted to furfural **1**, levulinic acid and formic acid via 5-hydroxymethyl furfural (HMF) **2** [6]. While routes for the subsequent conversion of levulinic acid into a wide range of fuel additives, such as levulinate esters **3** and chemical intermediates are well established [7,8], similar routes for the valorization of furfural are less well explored.



Scheme 1. Conversion of carbohydrates into alkyl levulinic esters.

Recent developments have demonstrated that furfural can also be converted into levulinate esters but must initially be converted to furfuryl alcohol **4** by hydrogenation prior to hydrolysis. This is an attractive process, since it provides a route for the conversion of furfural, produced as a minor by-product in biomass hydrolysis, into an additional source of levulinate products (Scheme 1) [9]. These hydrolysis processes typically employ mineral acids which can be expensive due to their highly corrosive nature which requires specialist materials for reactor construction [9,10]. This has led to the development of protocols that employ heterogeneous materials, such as zeolites and solid acid catalysts, as promoters which has alleviated some of these issues [11,12]. As part of an ongoing programme to develop new catalysts and novel reaction processes [13-17], we were interested in the potential application of water-tolerant Lewis acid catalysts as promoters of furan alcoholysis reactions. Of particular interest to us has been the development of protocols employing indium(III) salts, and in particular indium(III) triflate ($In(OTf)_3$), which have emerged as highly flexible, non-toxic and chemoselective catalysts in synthetic chemistry. The recent disclosure by Sun on the indium(III) chloride-mediated hydrolysis of monosaccharides to levulinic acid prompted us disclose our current studies in this area [18].

2. Experimental

2.1 Materials

Commercially available materials were used as received except for furfural which was purified by distillation under reduced pressure prior to use.

2.2 Product Analysis and Quantification

Reaction mixtures were analyzed by GC-MS using a Varian 450GC equipped with a Varian CP-8410 autoinjector and Varian 300MS. Chromatography was carried out using a VF-5ms capillary column (30m, 0.25mm i.d. and 0.25μm) and a gradient temperature profile with an initial temperature of 50 °C for 3 minutes rising to 280 °C at a rate of 20 °C/minute. Products were identified using the NIST library or by comparison with authentic standards in full scan mode. Levulinate ester quantification was achieved either in full scan mode or using selective ion monitoring (SIM) of the extracted *m/z* 99 ion chromatographs. The alkyl levulinate was quantified using a calibration curve generated by dilution of a standard butyl levulinate solution using the instrument response in either full scan mode or at *m/z* 99. Where necessary, the analytical samples were diluted to fall within the calibration curve concentration range, and were analyzed in duplicate.

2.3 Typical procedure for the alcoholysis of furfuryl alcohol in 1-butanol

Indium triflate (28 mg, 0.05 mmol, 1 mol%) was added to a solution of furfuryl alcohol (490 mg, 5 mmol) in 1-butanol (20 mL) and the mixture heated to reflux and stirred for 1.5 hours. Upon completion of the reaction, the excess alcohol was removed and the residue purified by chromatography (hexane) to give n-butyl levulinate **3d** as a light orange oil; ν_{max} (film)/cm^{-1} (neat) = 1732, 1359, 1310, 1159, 1069, 1027,; ^{1}H NMR ($CDCl_3$; 400 MHz) δ = 4.05 (2H, t, *J* = 7 Hz), 2.75 (2H, t, *J* = 7 Hz), 2.55 (2H, t, *J* = 7 Hz), 2.20 (3H, s), 1.60 (2H, pent, *J* = 7 Hz), 1.35 (2H, hex, *J* = 7 Hz), 0.95 (3H, t, *J* = 7 Hz); ^{13}C NMR ($CDCl_3$; 100 MHz) δ = 206.6, 172.7, 64.5, 38.0, 30.6, 29.7, 28.1, 19.1, 13.7; MS (EI) *m/z* 172.

2.4 Typical procedure for the alcoholysis of HMF in 1-butanol

Indium triflate (21 mg, 0.037 mmol, 5 mol%) was added to a solution of 5-hydroxymethylfurfal (94 mg, 0.75 mmol) in 1-butanol (20 mL) and water (27 mg, 1.50 mmol), and the mixture heated to reflux and stirred for 4 hour. At this time the reaction was cooled to room temperature and an additional portion of indium triflate (4 mg, 1 mol%) was added. The reaction was heated to reflux and stirred for an additional two hours and the conversion to **3d** determined by quantitative GC-MS analysis.

2.5 Typical procedure for the alcoholysis of furfural in 1-butanol

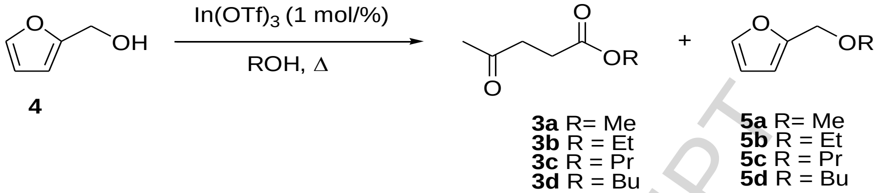
Indium triflate (14 mg, 0.025 mmol, 5 mol%) was added to a solution of furfural (48 mg, 0.50 mmol) in 1-butanol (10 mL) and the mixture heated to reflux and stirred for 1 hour. At this time the reaction was cooled to room temperature and an additional portion of indium triflate (14 mg, 0.025 mmol, 5 mol%) was added. The reaction was heated to reflux and stirred for an additional two hours and the conversion to **3d** determined by quantitative GC-MS analysis.

3. Results and Discussion

3.1 Catalytic Activity of Indium(III) Triflate

Our initial studies considered the alcoholysis reactions of furfuryl alcohol **4** to the corresponding alkyl levulinate esters in a range of alcohol solvents. Previous studies have demonstrated that reactions employing low boiling point alcohols, such as methanol and ethanol, proceed slowly giving low yields of the corresponding alkyl levulinate esters, unless enclosed pressurized reactors which allow the use of high temperatures are employed [11,12]. In line with these previous reports, only low conversions of furfuryl alcohol to **3a** and **3b** were observed when low catalyst loadings were employed (Table 1, entries 1 and 2). GC-MS analysis of these reactions did demonstrate, however, the efficient conversion of furfuryl alcohol to the corresponding intermediate ethers. Previously, this transformation has been shown to only occur at elevated temperatures [12], and demonstrates the high efficiency of In(OTf)$_3$ in etherification reactions [19]. In the case of ethanol, extending the reaction time, and increasing the quantity of catalyst provided significantly improved conversions to **3b**. Further improvements were achieved by adding the catalyst to the reaction in two separate portions, and under these optimized reaction conditions, moderate conversions of **3b** were achieved at comparatively low reaction temperatures (Table 1, entry 3).

Table 1. In$(OTf)_3$ mediated alcoholysis of furfuryl alcohol.[a]

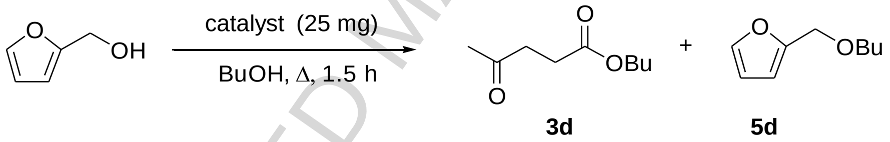


Entry	Alcohol	Time (h)	Temperature (^oC)	Catalyst (mol %)	Yield 3 (%)[a]
1	MeOH	1	65	1	<5
2	EtOH	1	78	1	10
3	EtOH	12	78	10	52
4	PrOH	1	97	1	34
5	PrOH	3	97	1	83
6	BuOH	1.5	118	1	92

[a] Experimental conditions: indium triflate (1 mol%) was added to a solution of **4** (5 mmol) in 1-butanol (20 mL) and heated to reflux for 1.5 hours.
[b] Determined by quantitative GC-MS analysis.

Gratifyingly, the use of higher boiling solvents which allow for higher reaction temperatures, such as 1-propanol, led to a rapid reaction with high yields of **3c** being achieved after only 3 hours even when low catalyst loadings were employed (entry 5). Reactions employing 1-butanol were even more rapid, and gave near quantitative yields of butyl levulinate **3d** in short reaction times, typically less than 1.5 hours (entry 6). In both of these cases, formation of the corresponding intermediate furyl ether product was again rapid, suggesting that it is the subsequent temperature dependant ring-opening reaction which is rate limiting. In these reactions it is noteworthy that only trace quantities of the symmetrical alkyl ether by-products, produced from the alkyl alcohol, were detected by GC-MS analysis. The production of levulinate esters from furfuryl alcohol with minimal generation of the corresponding alkyl ether by-product is highly desirable, as it improves the economic potential of the process. As expected, reactions containing no catalyst gave no conversion of the starting material to ether or alcoholysis products, demonstrating the high catalytic activity of In$(OTf)_3$ in these reactions. We next turned our attention to catalyst recovery and recycling using the alcoholysis reaction in 1-butanol. In line with previous reports [20], the catalyst can be recovered from these reactions by aqueous extraction of the reaction mixture and subsequent drying which produced a catalyst which exhibited comparable activity to the fresh material (see Supplementary Information). Finally, to demonstrate the efficiency of In(OTf)$_3$ in the alcoholysis reaction of furfuryl alcohol, we undertook a series of experiments employing a small range of heterogeneous catalysts under our standard reaction conditions (Table 2).

Table 2. Heterogeneous catalyzed alcoholysis reactions of furfuryl alcohol.[a]



Entry	Catalyst[b]	BET Surface Area (m^2g^{-1})[c]	Pore Width (nm)[e]	Acidity (μmol g^{-1})[f]	Yield 3d (%)[g]
1	ZSM-5-(30)	405	0.82	1450	13
2	Zeolite Y-(5)	763	1.11	300	<5
3	Al-13-(2.34)	614	2.44	440	<5
4	Al-13-(3.18)	980	3.18	530	15
5	Amberlyst™-15	45[d]	24[d]	4600[d]	95

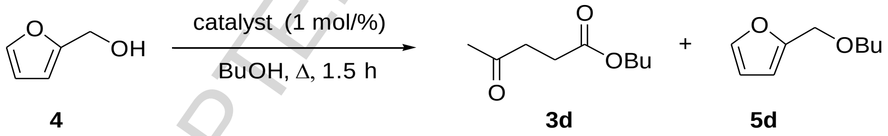
[a] Experimental conditions: the catalyst (25 mg) was added to a solution of **4** (1 mmol) in 1-butanol (4 mL) and heated to reflux for 1.5 hours.
[b] All aluminosilicate catalysts were stored at 120 °C for 12 hours prior to use.
[c] Obtained by the Brunauer–Emmett–Teller (BET) method.
[d] Literature value: see reference [21].
[e] Determined by the non-linear density function theory (NLDFT) method.
[f] Determined by temperature programmed desorption (TPD) analysis.
[g] Determined by quantitative GC-MS analysis.

Reactions employing both microporous (entries 1 and 2) and mesoporous aluminosilicate [14-17] materials (entries 3 and 4) gave the expected low yields of **3d** in line with previous literature reports, where longer reaction times are typically required for generation of significant quantities of the levulinate ester product [11,21,22]. Reactions employing the highly acidic cation exchange resin Amberlyst^{TM}-15 (entry 5) proceeded rapidly as expected to give an excellent yield of **3d** which were comparable to our In(OTf)$_3$ catalyst, although in this case, significant quantities of the symmetrical alkyl ether by-product were observed [22].

3.2 Catalytic Activity of Metal Triflates

With the potential of this approach established, we carried out a study to identify whether other commercially available metal triflates or In(III) salts are effective promoters of furfuryl alcohol alcoholysis (Table 3).

Table 3. Metal triflate-mediated furfuryl alcohol alcoholysis reactions.[a]



Entry	Catalyst	Yield 3d (%)[b]
1	In(OTf)$_3$	92
2	InBr$_3$	<5
3	Cu(OTf)$_2$	66
4	Yb(OTf)$_3$	27
5	Gd(OTf)$_3$	12

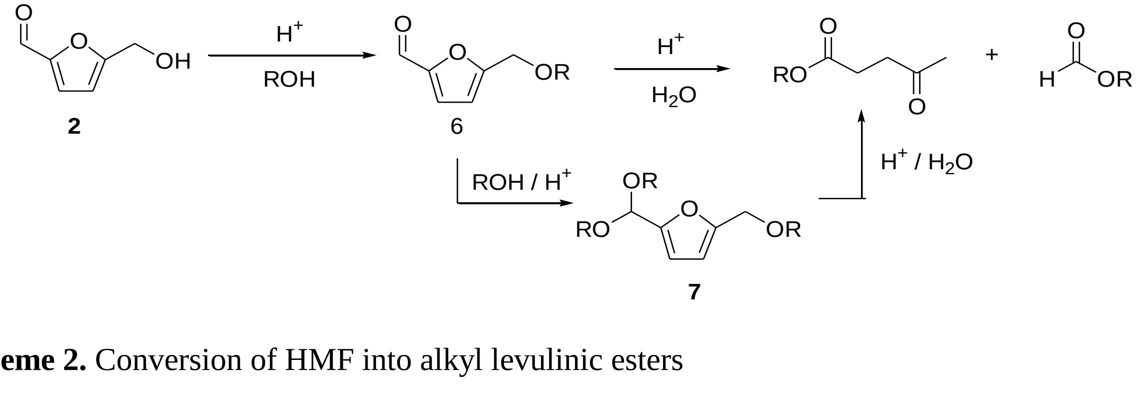
[a] Experimental conditions: the catalyst (1 mol%) was added to a solution of **4** (5 mmol) in 1-butanol (20 mL) and heated to reflux for 1.5 hours.

[b] Determined by quantitative GC-MS analysis.

Interestingly, the alcoholysis of furfuryl alcohol in 1-butanol employing indium(III) tribromide (InBr$_3$) as catalyst gave no conversion to butyl levulinate, with the starting alcohol being recovered in near quantitative yield (entry 2). Subtle counterion effects have previously been observed in indium-mediated processes, which are thought to be due to coordination effects which manifest themselves either in a variation in the activity or selectivity of the catalyst, and suggests that the physical properties of the counterion are of critical importance [23]. All of the triflate catalysts studied generated **3d** under the reaction conditions, however, only copper(II) triflate ($Cu(OTf)_2$) showed significant activity, generating moderate yields of butyl levulinate (entry 3). As expected, gadolinium(III) triflate ($Gd(OTf)_3$) was less active than ytterbium(III) triflate ($Yb(OTf)_3$) producing low yields of the ester product (entry 5). GC-MS analysis of these crude reaction mixtures did, however, indicated that all of the catalysts studied were effective in generating the intermediate alkyl ether suggesting that these catalyst are less efficient in promoting the subsequent ring-opening reaction.

3.3 Alcoholysis Reactions of 5-Hydroxymethylfurfural

We next turned our attention to the alcoholysis reactions of HMF, an important platform chemicals for the synthesis of a range of polymer building blocks and biofuels, and another highly attractive substrate for levulinate ester production given its potential for sustainable generation from biomass sources (Scheme 2) [3,8]. The alcoholysis reaction proceeds through initial formation of the corresponding HMF ether **6**, which undergoes acid catalyzed ring-opening to generate the levulinate product and eqimolar quantities of butyl formate [8,22,24].



Scheme 2. Conversion of HMF into alkyl levulinic esters

Under our standard conditions, employing low catalyst loadings in 1-butanol at reflux temperatures, the alcoholysis reaction proceeded more slowly than the corresponding reaction with furfuryl alcohol, and extended reaction times were required to achieve moderate conversions. An added drawback of employing these extended reaction times was the generation of both polymeric products, and increased quantities of the dibutyl ether by-product. We therefore undertook a study with the goal of determining optimal catalyst loadings in order to reduce reaction times and so limit the generation of degradation products.

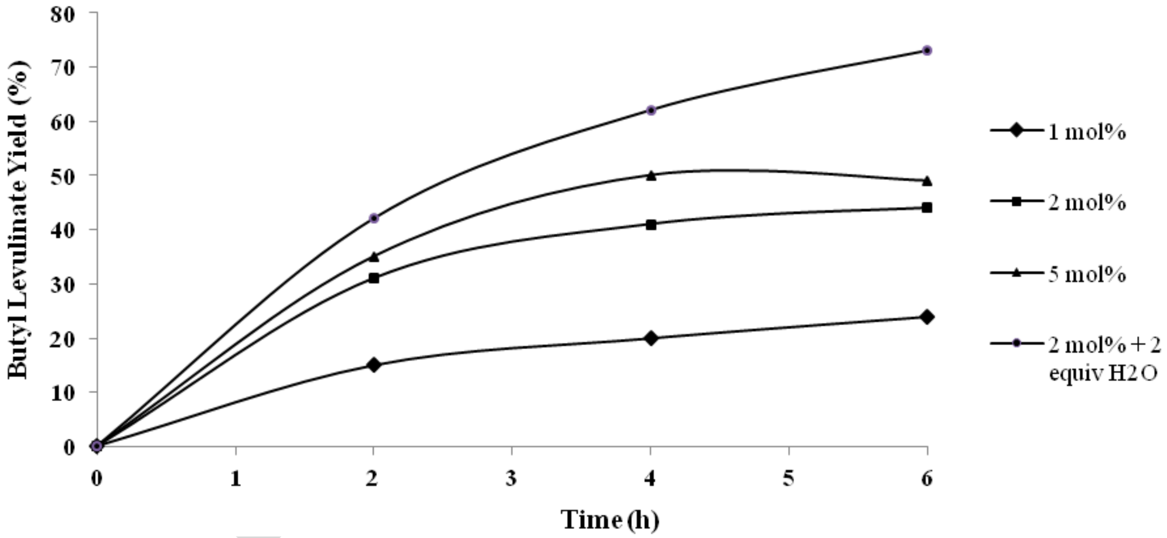


Fig. 1. Influence of catalyst loading on butyl levulinate formation from In(OTf)$_3$ catalyzed HMF alcoholysis reactions in 1-butanol

Product formation increased with increasing quantities of catalyst, however, the generation of **3d** slowed over the course of the reaction (Figure 1). Further extending reaction times led to no tangible improvement in overall conversion, and indeed led to increased generation of degradation products. Furthermore, in reactions employing higher catalyst loadings, significant quantities (~20%), of the acetal product, 5-(dibutoxymethyl)-2-furanbutanol **7** (R =

OBu) were identified by GC-MS analysis. Acetal products derived from HMF have been identified as possible intermediates in the formation of levulinate esters from both biomass sources and HMF [8,22,24-26], although the precise role of these intermediates is currently unclear. The formation of this product could be suppressed by adding two equivalents of water to the reaction mixture which led to significantly improved overall conversions to **3d** by minimizing the generation of the acetal product. The addition of additional quantities of water has also previously been demonstrated to be highly beneficial in the alcoholysis reaction of furfuryl alcohol in 1-butanol, where it has been proposed to accelerate the ring-opening reaction of the intermediate ether [12]. In addition to the formation of **3d** and 5-(dibutoxymethyl)-2-furanbutanol **7**, quantities of both of the expected hydrolysis products butyl formate and formal dibutyl acetal were identified by GC-MS analysis of the crude reaction mixture. In line with previous reports, no levulinic acid formation was observed in these reactions.

3.4 Alcoholysis Reactions of Furfural

Finally, we investigated the alcoholysis reactions of furfural, a substrate which has to date attracted considerably less attention than furfuryl alcohol or HMF for direct levulinate ester formation, presumably due to its much greater resistance to alcoholysis. Given that acetal products have been observed in a number of protocols for levulinate ester formation, we were intrigued as to the precise role of acetal products in furan alcoholysis reactions, particularly if their efficient in situ generation could circumvent either the reduced reactivity of substrates such as furfural or their tendency to undergo acid catalyzed polymerization, and hence lead to the development of more efficient alcoholysis protocols. We have previously demonstrated that In(OTf)$_3$, is a highly efficient catalyst for the formation of both cyclic and acyclic acetals [27-29], and the development of such a tandem protocol would be highly attractive, given the recent interest in this area [30-34].

Our studies initially considered the alcoholysis of furfural in 1-butanol employing 1 mol/% of In(OTf)$_3$ at reflux temperatures. Encouragingly, low conversions to butyl levulinate were achieved under these conditions if extended reaction times were employed, however, extensive humin and polymer formation were also observed over the time course of the reaction (Figure 2).

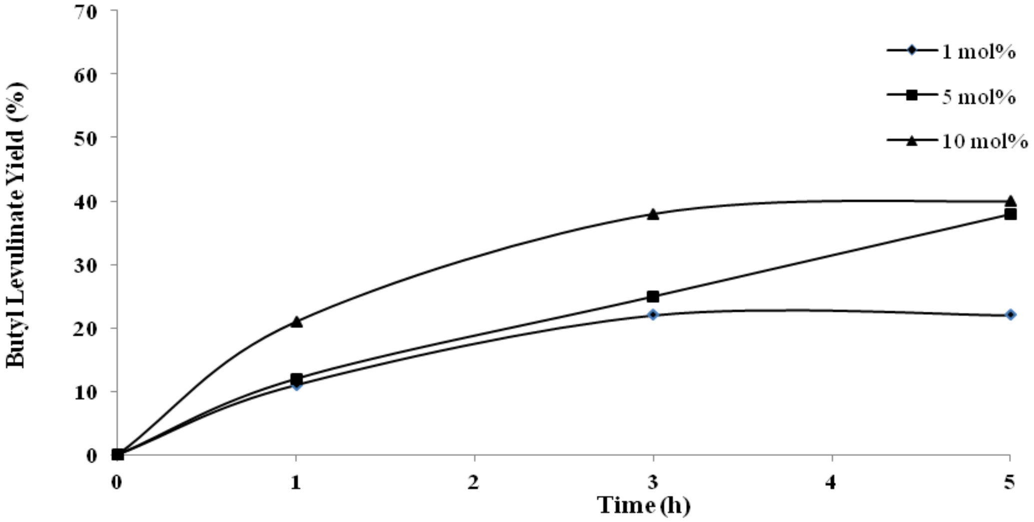
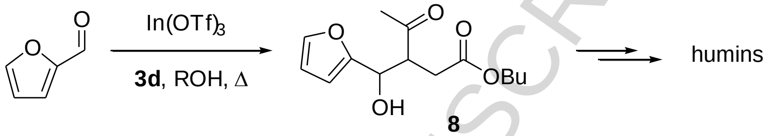


Fig. 2. Influence of catalyst loading on butyl levulinate formation from In(OTf)$_3$ catalyzed furfural alcoholysis reactions in 1-butanol

Increasing the quantity of catalyst to 5 mol% or 10 mol% led to very rapid consumption of the furfural starting material, but did not lead to increased quantities of **3d**, with similar conversions to those obtained with lower catalyst loadings being observed. This may suggest that once formed, **3d** is consumed by competing side-reactions in addition to polymer and humin formation. It is noteworthy that indium(III) salts have been demonstrated to be highly efficient promoters of a range of carbon-carbon bond forming reactions through the formation of enol intermediates [35]. A reaction sequence in which **3d**, once generated, is consumed by enol formation followed by aldol reaction with furfural to give **8,** followed by subsequent humin formation can be envisaged [8] (Scheme 3).



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Scheme 3. Aldol reaction of furfural and butyl levulinate

This reaction pathway would not only explain the moderate conversions to **3d** but would also explain the consumption of the aldehyde starting material. Significantly, small quantities (~5%) of both the aldol product **8** and the corresponding α,β−unsaturated ester produced by elimination were identified by GC-MS analysis of the crude reaction mixtures. No significant aldol products derived from the self-condensation of **3d** were detected, however, and indeed, GC-MS analysis of test reactions involving **3d** in the presence of $In(OTf)_3$ in 1-butanol gave no identifiable aldol products. Conversions to **3d** are also limited by the inherent instability of furfural in the presence of Lewis acid catalysts, and indeed, heating this material in non-alcoholic solvents, such as toluene, in the presence of the $In(OTf)_3$ led to significant formation of insoluble polymeric material.

In addition to aldol and polymeric products, reactions employing high catalyst loadings led to the production of significant quantities (~ 15%) of a product identified by GC-MS analysis as 2-furancarboxaldehyde dibutyl acetal. This product was present in the early stages of the reaction and persisted over the time course of the reaction. To determine whether formation of **3d** proceeded through this acetal intermediate, we investigated the alcoholysis reactions employing

2-furancarboxaldehyde dimethyl acetal as the starting material. As expected, this substrate underwent very rapid transacetalization under the reaction conditions to produce the corresponding dibutyl acetal product [28,29]. This material, however, proved to be resistant to alcoholysis under the lower reaction temperatures employed in this study, with only trace quantities of **3d** being produced in these reactions.

4. Conclusions

In conclusion, we have demonstrated that low loadings of In(OTf)$_3$ efficiently catalyze the alcoholysis reactions of furfuryl alcohol to produce alkyl levulinate esters in short reaction times. The protocol employs a commercially available, water tolerant catalyst, and does not require time consuming and complicated work-up procedures frequently associated with the use of mineral acids. Furthermore, this catalyst also catalyzes the efficient alcoholysis reactions of HMF, although higher catalyst loadings are required to achieve high conversions for this transformation. In the case of alcoholysis reactions of furfural, extensive degradation of the starting material and aldol reactions of the alkyl levulinate ester product and acetalization of the furfural starting material have been identified as potential competing reactions which further limit conversions. Studies are currently under way to demonstrate the potential of this catalyst in the transformations of raw biomass sources, and to develop indium containing materials which can function as heterogeneous catalysts for the alcoholysis reactions.

Supporting Information.

General methods, catalyst recycling data, product characterization and GC-MS product profiles.

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References

[1] J. N. Chheda, G. W. Huber, J. A. Dumesic, Angew Chem. Int. Ed. 46 (2007) 7164–7183.

[2] B. Katryniok, S. Paul, V. Bellière-Baca, P. Rey, F. Dumeignil, Green Chem. 12 (2010) 2079–2098.

[3] G. W. Huber, S. Iborra, A. Corma, Chem. Rev. 106 (2006) 4044–4098.

[4] T. R. Carlson, T. P. Vispute, G.W. Huber, ChemSusChem 1 (2008) 397–400.

[5] J.-P. Lange, in Catalysis for Renewables: From Feedstock to Energy Production, ed. G. Centi and R. A. van Santen, Wiley-VCH, Weinheim, 2007, pp. 21–51.

[6] D. J. Hayes, S. Fitzpatrick, M. H. B. Hayes, J. R. H. Ross, in Biorefineries-Indusrtial Processes and Products: Status Quo and Future Directions, ed. B. Kamm, P. R. Gruber and M. Kamm, Wiley-VCH, Weinheim, 2008, 139–164.

[7] S. Dutta, S. De, B. Saha, M. I. Alam, Catal. Sci. Technol. 2 (2012) 2025–2036.

[8] M. J. Climent, A. Corma, S. Iborra, Green Chem. 16 (2014) 516–547.

[9] J.-P. Lange, E. van der Heide, J. V. Buijtenen, R. Price, ChemSusChem 5 (2012) 150–166.

[10] D. W. Rackemann, W. O. S. Doherty, Biofuels. Bioprod. Bioref. 5 (2011) 198–214.

[11] J.-P. Lange, W. D. Van De Graaf, R. J. Haan, ChemSusChem 2 (2009) 437–441.

[12] Z. Zhang, K. Dong, Z. Zhao, ChemSusChem 4 (2011) 112–118.

[13] B. M. Smith, E. J. Skellam, S. J. Oxley, A. E. Graham, Org. Biomol. Chem. 5 (2007) 1979–1982.

[14] T. M. Kubczyk, S. M. Williams, J. R. Kean, T. E. Davies, S. H. Taylor, A. E Graham, Green Chem. 13 (2011) 2320–2325.

[15] T. E Davies, J. R. Kean, D. C. Apperley, S. H. Taylor, A. E. Graham, ACS Sus. Chem. & Eng. 2 (2014) 860–866.

[16] M. W. C. Robinson, A. M. Davies, I. Mabbett, T. E. Davies, D. C. Apperley, S. H. Taylor, A. E. Graham, J. Mol. Catal. A: Chem. 329 (2010) 57–63.

[17] M. W. C. Robinson, A. M. Davies, I. Mabbett, D. C. Apperley, S. H Taylor, A. E. Graham, J. Mol. Catal. A: Chem. 314 (2009) 10–14.

[18] Y. Shen, J. Sun, Y. Yi, B. Wang, R. Sun, J. Mol. Catal. A: Chem. DOI 10.1016/j.molcata.2014.07.007.

[19] For the use of indium(III) trichloride in etherification reactions see: G. Bhaskar, M. Solomon, G. Babu, D. Muralidharan, P. T. Perumal, Ind. J. Chem. 49B (2010) 795–801.

[20] R. Ghosh, S. Maiti, A. Chackraborty, R. Halder, J. Mol. Catal. A: Chem. 215 (2004) 49–53.

[21] P. Neves, S. Lima, M. Pillinger, S. M. Rocha, J. Rocha, A. A. Valente, Catalysis Today 218–219 (2013) 76–84.

[22] P. Lanzafame, D. M. Temi, S. Perathoner, G. Centi, A. Macario, A. Aloise, G. Giodarno Catalysis Today 175 (2011) 435–441.

[23] C. G. Frost, J. P. Hartley, D. Griffin, Tetrahedron Lett. 43 (2002) 4789–4791.

[24] X. Hu, C.-Z. Li, Green Chem. 113 (2011) 1676–1679.

[25] J. Chen, G. Zhao, L. Chen, RSC Adv. 4 (2014) 4194–4202.

[26] M. Balakrishnan, E. R. Sacia, A. T. Bell, Green Chem. 14 (2012) 1626–1634.

[27] B. M. Smith, A. E. Graham, Tetrahedron Lett. 48 (2007) 4891–4894.

[28] B. M. Smith, T. M. Kubczyk, A. E. Graham, Tetrahedron 68 (2012) 7775–7781.

[29] B. M. Smith, A. E. Graham, A. E. Tetrahedron Lett. 52 (2011) 6281–6283.

[30] L. F. Tietze, Chem. Rev. 96 (1996) 115–136.

[31] D. J. Phillips, K. S. Pillinger, L. Wei, A. E. Taylor, A. E.; Graham, Tetrahedron 63 (2007) 10528–10533.

[32] M. C. Bagley, V. Lin, D. J. Phillips, A. E. Graham, Tetrahedron Lett. 50 (2009) 6823–6825.

[33] G. H. Harris, A. E. Graham, Tetrahedron Lett. 51 (2010) 6890–6892.

[34] D. J. Phillips, A. E. Graham, Synlett 2008 649–652.

[35] A. Dandia, A. K. Jain, S. Sharma, Tetrahedron Lett. 53 (2012) 5270–5274.

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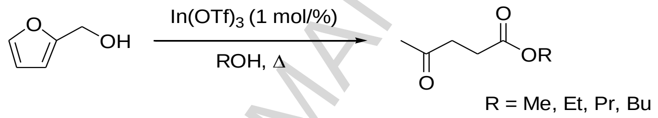

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Indium(III) triflate catalyses the alcoholysis of a range of furyl substrates in alcoholic solvents to produce the corresponding levulinate esters.

Indium(III) Triflate Promoted Synthesis of Alkyl Levulinates from Furyl Alcohols and Furyl Aldehydes

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Highlights

- Low loadings of In(OTf)$_3$ catalyse alcoholysis reactions of furfuryl alcohol.
- HMF alcoholysis reactions proceed efficiently under higher In(OTf)$_3$ loadings.
- Moderate yields of butyl levulinate are also achieved from furfural.
- The catalyst can be recycled without a significant decrease in catalytic activity.