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PAPER

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A tunable precious metal-free system for selective oxidative esterification of biobased 5-(hydroxymethyl)furfural†

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Oxidative esterification of biomass-derived 5-(hydroxymethyl) furfural (HMF) and furfural and their derivatives has been performed using a simple MnO_2/NaCN system. The developed method allows the selective one-pot transformation of HMF to dimethyl furan-2,5-dicarboxylate (FDME) in 83% isolated yield without the formation of a free acid. Simplification of FDME production provides the missing link for manufacturing sustainable value-added materials from biomass. Addition of water to the oxidative system allows fine-tuning of reaction selectivity to obtain the previously difficult-to-access pure methyl 5-(hydroxylmethyl) furan-2-carboxylate in one step directly from the unprotected HMF without chromatographic separation.

Introduction

Biomass processing is one of the most rapidly developing branches of green chemistry, sustainable development and engineering.[1–7] Due to the huge abundance of renewable carbohydrates in nature, cellulose and other sugars appear to be the most promising sources of organic carbon for the chemical industry.[8–13] This is the key reason why compounds which can be easily prepared from carbohydrates (HMF, furfural, levulinic acid *etc.*) have been included in the list of platform-chemicals of the chemical industry of the future.[14–17] Nowadays the production of carbohydrate-based chemicals has reached the industrial level and continues to increase.[18] At the same time, the search for selective and convenient chemical transformations of biobased substances to value-added compounds remains a challenge of general importance.[19–23] The oxidation of the side-groups in HMF is one of the most intensively studied aspects of its chemistry[21] and a number of precious-metal-based catalytic systems have been developed.[24–29] The importance of 2,5-furandicarboxylic acid (FDCA)[30] is clearly justified since it is a biomass-based analog of the oil-based terephtalic acid and therefore a precursor for the green

equivalent of the most common synthetic polyester, polyethylene terephthalate (PET, Fig. 1).[31–33]

In the vast majority of cases, PET synthesis starts from dimethyl 2,5-furandicarboxylate (furan dicarboxylic methyl ester, FDME) instead of a free acid, since methanol is more volatile than water and can be easily separated in the course of polycondensation. Therefore, direct synthesis of FDME from HMF is a cutting-edge process that is in high demand, since such transformation will shorten the technological pathway and increase its cost-efficiency (Fig. 1). Moreover, the formation of FDCA usually proceeds under strongly basic conditions and acidification of the obtained FDCA salt leads to the formation of superstoichiometric amounts of inorganic salt as a byproduct, which is undesirable from the environmental point of view.

There are two main types of oxidative processes: catalytic oxidation with molecular oxygen and oxidation with stoichio-
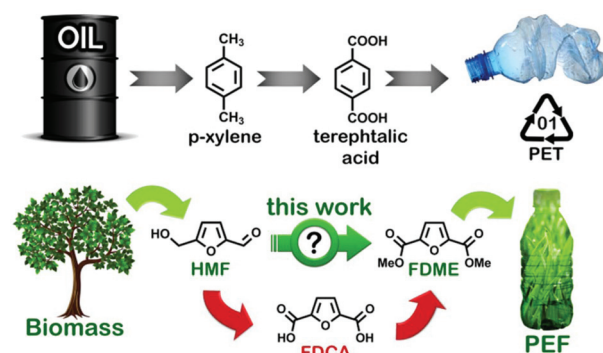
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Fig. 1 Comparison of polyester production by means of oil and biomass processing.

metric oxidants.[21] On the one hand, oxidation with molecular oxygen is attractive since oxygen is a cheap and easily available oxidant. On the other hand, the requirement of high oxygen pressure is a critical drawback from the practical point of view, because it implies the use of specific equipment and extremely increased safety precautions.[34] Utilization of molecular oxygen carriers is significantly more safe, especially when introducing the biomass oxidation steps into pre-existing frameworks of chemical production. In this work we present cyanide-promoted oxidative esterification of HMF and other biomass-based furanic compounds using MnO_2 as a recyclable oxygen carrier.[35–39] The developed oxidation system allows one-pot oxidative esterification of HMF to FDME and other esters. It allows the neat preparation of esters of the poorly affordable 5-hydroxymethyl-2-furancarboxylic acid (HMFCA, Fig. 2). Importantly, in the present study the common commercially available MnO_2 is used as an oxygen carrier instead of applying the highly expensive precious-metal-based catalytic systems.

Results and discussion

As stated above, one of the key prospective routes of HMF application is its transformation to FDME, which is a precursor of various biomass-based polyesters. Among the known methods of oxidative esterification of aldehydes, the NaCN/MnO_2/MeOH/AcOH oxidative process (known as Corey–Gilman–Ganem oxidation[40]) seems to be the most promising because of the utilization of a cheap oxidant and simple reaction conditions. The classical reaction protocol, which requires extremely high loadings of MnO_2 (20 equiv.) and NaCN (5 equiv.), leads to the formation of FDME in just a moderate yield of 42%.

In the first part of our study, we optimized reaction conditions and decreased the loading of NaCN and MnO_2 by more than 10 times. The dependence of product distribution on the quantity of the oxidant is shown in Fig. 3. At a decreased MnO_2 loading (2 equiv.), MHMFC **3a** formed as a major
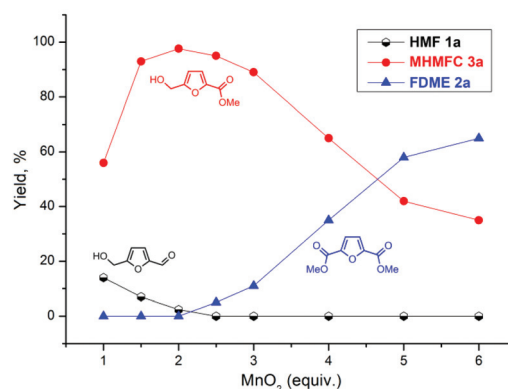

Fig. 3 Oxidative esterification of HMF to MHMFC and FDME.

product with excellent selectivity. Upon increasing the quantity of MnO_2, the product distribution changed, with FDME **2a** becoming a major product. Even at a high oxidant loading (20 equiv.), MHMFC was still produced in a significant amount. To overcome the formation of MHMFC, we introduced 2,5-diformylfuran (DFF) in the oxidative esterification process (Fig. 4), which allowed us to achieve 97% yield of FDME. To increase the yield of FDME during HMF oxidation, we therefore decided to pre-oxidize HMF to DFF. Pre-oxidation can be easily done using the interaction of HMF with MnO_2 in the absence of cyanide. In this one-pot protocol, an 83% isolated yield of FDME **2a** was achieved. The developed procedure was tested on the scope of alcohols using both protocols: starting from HMF with pre-oxidation or starting from DFF in a one-step manner (Table 1).

The corresponding diesters **2a–f** were obtained in good yields for various alcohols. Amazingly, even the easily oxidizable benzyl (entry 5, Table 1) and allyl (entry 6, Table 1) alcohols gave satisfactory results in this reaction. In the case of allyl alcohols, the reaction was slow enough to allow the isolation of the intermediate monoallyl ester **2f′** (see the ESI† for details). In the cases of *tert*-butanol and phenol (entries 7 and 8, Table 1), no formation of esters was detected. This fact can be explained by the low activity of these alcohols associated
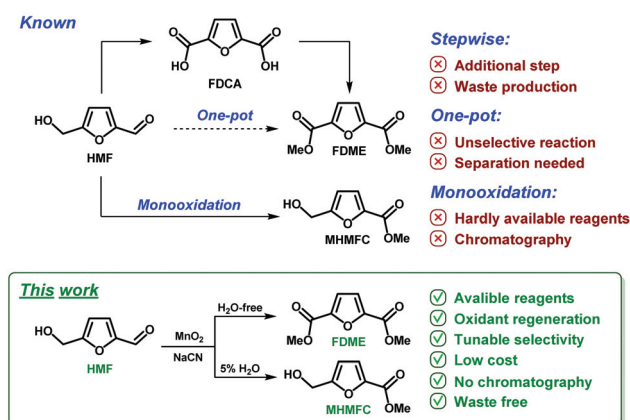

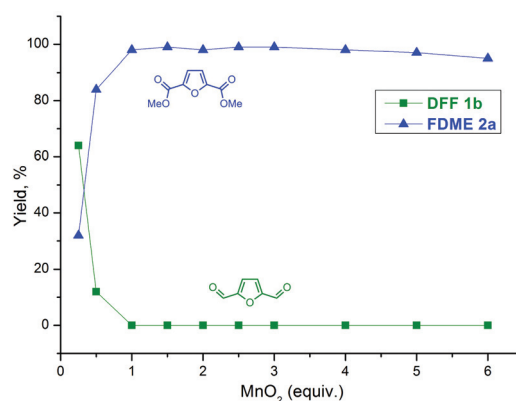Fig. 2 Different pathways of oxidative esterification of HMF.

Fig. 4 Selective oxidative esterification of DFF to FDME.

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Table 1 Interaction of HMF and DFF with various alcohols under the CN-promoted oxidative esterification conditions[a]

Entry	ROH	Product	Yield[b] from HMF, %	Yield[b] from DFF, %
1	MeOH	**2a**	83	97
2	EtOH	**2b**	61	84
3	n-PrOH	**2c**	54	69
4	i-PrOH	**2d**	27	38
5	BnOH[c]	**2e**	49	61
6	AllylOH[c]	**2f**	33	48
7	t-BuOH	—	—	—
8	PhOH	—	—	—

[a] Reaction conditions are shown in Table S1. [b] Isolated yields are reported. [c] CH_2Cl_2 was used as an additional solvent.

with the steric hindrance in *tert*-butanol and delocalization of the oxygen electron pair in phenol. As the next step of our study, we attempted to involve various HMF derivatives and related compounds in oxidative esterification (Table 2). In the

Table 2 Oxidative esterification of biomass-derived furfurals[a]

Entry	Substrate	Product	Yield[b], %
1	**1b**	**2a**	97
2	**4**	**5**	89
3	**6**	**7**	76
4	**1c**	**3c**	83
5	**1e**	**3e**	52
6	**1d**	**3d**	61
7	**1f**	**3f**	42
8	**1g**	**3g**	95
9	**8**	**9**	98

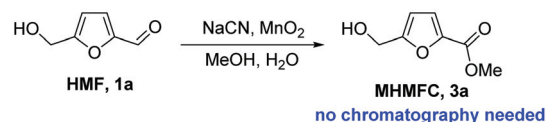[a] Reaction conditions are shown in Table S1. [b] Isolated yields are reported.

majority of cases, good yields of the ester were achieved. Remarkably, 5-formyl-2-furancarboxylic acid **1f** (FFCA) was easily transformed into a monoester of FDCA in a moderate yield by using the described procedure (entry 7, Table 2); this result is hardly achievable by other methods. *p*-Anisaldehyde **8** (entry 9, Table 2) was also subjected to oxidative esterification. The corresponding methyl ester was produced in a nearly quantitative yield, which indicates that the described procedure can be successfully applied to non-furanic aromatic aldehydes as well.

As the next step of our study, we optimized the reaction conditions for selective preparation of MHMFC **3a**, a methyl ester, which is difficult to access directly from HMF. The main obstacles were the oxidation of HMF to DFF and the overoxidation of MHMFC. To solve these problems, we decided to add some water (5 vol%) to the reaction medium to regulate the oxidative activity of MnO_2. Fortunately, this approach proved to be effective and MHMFC **3a** was obtained in pure form in a moderate yield without chromatographic separation; it was isolated by simple extraction (Scheme 1). The method is highly suitable for lab-scale synthesis of MHMFC and further investigation of its chemistry; the straightforward isolation procedure is crucial for synthetic applications.[41] It is important to note that in this case we obtain an ester rather than a free acid; the former is much more stable during storage.

On the basis of the unraveled Corey–Gilman–Ganem reaction mechanism[42] we have proposed two possible pathways of HMF oxidative esterification (Scheme 2). In the first step, HMF can show two alternative types of reactivity: cyanohydrine formation and oxidation to DFF. According to the obtained results, we can conclude that the oxidation of the cyanohydrine moiety to acylcyanide occurs faster than the oxidation of the hydroxymethyl group. Addition of water diminishes the oxidative activity of MnO_2, making pathway 2 (Scheme 2) less favorable and thus switching the selectivity towards the formation of MHMFC. Alternatively, pre-oxidation of HMF to DFF makes pathway 1 impossible, and the selective formation of FDME (pathway 2, Scheme 2) is observed.

An important part of our study is concerned with the regeneration of MnO_2. After the reaction, MnO_2 was filtered off, washed with water and methanol, and then dried in an oven at 180 °C in air. The obtained solid was reintroduced in oxidative esterification and showed activity comparable to the activity of the starting material. After 7 recycles of MnO_2 no considerable changes in product yield were observed (see Table S2†).

The structure of MnO_2 prior to the reaction, after the reaction and after the regeneration was examined by scanning electron microscopy (Fig. 5). The results indicate that the size of

Scheme 1 Synthesis of MHMFC under modified conditions.

3466 | *Green Chem.*, 2019, **21**, 3464–3468

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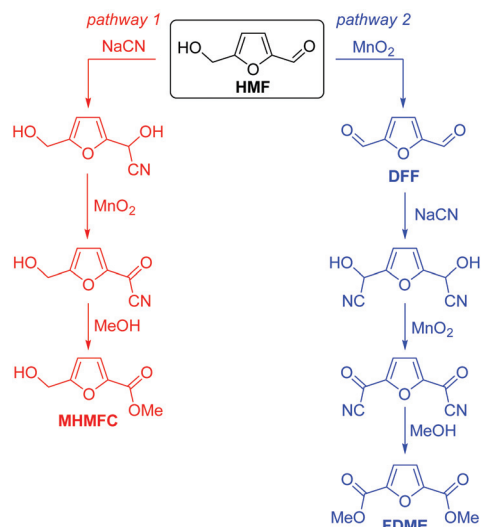
Scheme 2 Possible mechanistic pathways of the oxidative esterification of HMF.
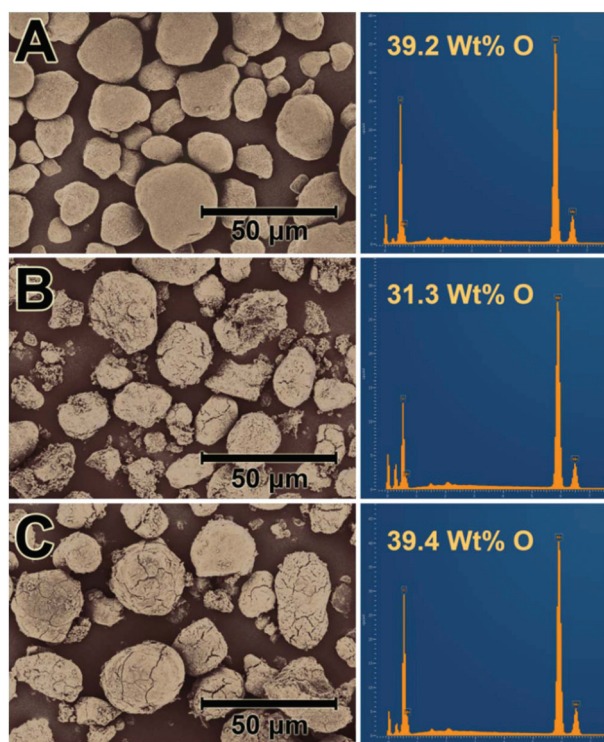

Fig. 5 FE-SEM microimages of MnO_2 and the corresponding EDX spectra: (A) prior to the reaction; (B) after the reaction; (C) after drying at 180 °C.

the particles and morphology of the surface do not undergo significant changes. EDX analysis of the MnO_2 surface shows that the oxygen content is decreased by approximately 8 wt% after the reaction (Fig. 5B), which can be explained by partial reduction of Mn(IV) to Mn(II); after the regeneration, the amount of oxygen returns to the initial value.

Sodium cyanide, which is used in the described reaction as a promoter, is a very cheap and available reagent, especially in comparison with other reagents known to mediate similar transformations. Production of NaCN for industrial purposes exceeds 1 million metric tons annually; efficient procedures of cyanide utilization and detoxification are well developed and include thermal hydrolysis, oxidation and microbiological degradation.[43,44] The handling, usage and complete life-cycle assessment of NaCN-based industrial technologies are a well-developed area, where toxicity and waste contamination issues are thoroughly regarded and resolved.[45] Environmental factors for the described oxidative esterification procedure were roughly estimated (see the ESI†). The obtained values (EF = 0.1–3) correspond to the high performance process suitable for the production of bulk chemicals.[46]

Conclusions

In summary, we have shown that NaCN-promoted oxidative esterification of biobased furfurals can be readily achieved with MnO_2 as a recoverable oxygen carrier. The suggested system makes it possible to obtain the highly valuable FDME directly from HMF without the formation and isolation of FDCA. Various alcohols and HMF derivatives were successfully tested in this reaction; good yields of the corresponding esters confirmed the general applicability of the method. Addition of water allows fine tuning of the chemical activity of the studied oxidation system, enabling access to methyl esters of HMFCA in pure form without chromatographic separation.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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