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Catalytic transesterification routes to novel vinyl glycolate derivatives of polyhydric alcohols

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Abstract

Methyl vinyl glycolate (methyl 2-hydroxybut-3-enoate, MVG) has recently become obtainable from Sn catalysed cascade reactions of mono- and disaccharides. The chemical structure of MVG present several options for chemical transformations and has great potential as a renewable platform chemical for industrial added-value compounds within *e.g.* polymer chemistry. Herein, we report a catalytic benign transesterification method for the synthesis of MVG ester derivatives of trimethylolpropane (TMP) and pentaerythritol (PE). The secondary alcohol group of MVG greatly complicates the reaction and requires a highly selective catalyst to push the reaction towards high conversion while avoiding polymerization. Thus, a range of different catalytic systems, e.g. *Candida Antarctica Lipase B* (CALB), Brønsted bases/acids, salicylic aldehyde as well as Lewis acids were evaluated for the reaction. Despite the challenges this leads to unique derivatives of TMP and PE with an additional chemical handle compared to classic derivatives like the methacrylate and mercaptopropionate.

Keywords

Methyl vinyl glycolate, transesterification, trimethylolpropane, *Candida Antarctica Lipase B*, tin(II) chloride

1. Introduction

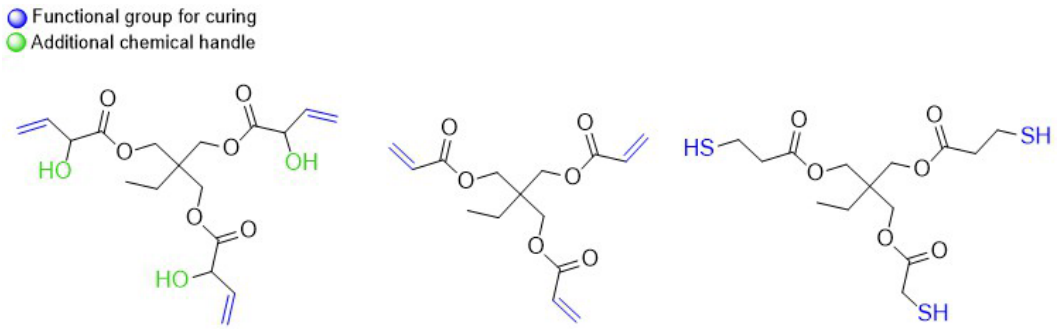
The progressing depletion of fossil fuels and increasing environmental concern demands design and development of novel bio-sustainable materials and chemicals. Currently, hemi-cellulose and sugar crops provide great potential as sustainable carbon sources. The ample functionality of biomass-derived sugars permits the synthesis of unique high functionality platform chemicals such as lactic acid, 5-hydroxymethylfurfural, trans-2,5-dihydroxy-3-pentenoic acid methyl ester (DPM) and levulinic acid [1]. Unlike biofuels, these novel chemicals find application within niche markets and represent high-margin low-volume products [2].

Methyl vinyl glycolate (MVG) is another very interesting molecule within this type of renewable platform chemicals. Despite MVGs small molecular structure, it possesses multiple functionalities (hydroxyl, vinyl and ester) enabling a range of chemical modifications. Formation of MVG was discovered by Holm, Saravanamurugan and Taarning [3] during examination of chemocatalytic (rather than fermentation) routes for the synthesis of lactic acid derivatives from C6 sugars. The MVG was rationalized to form *via* an initial retro-aldol reaction, which was supported by employing C4 sugar substrates where high yields, up to 55%, were obtained with Lewis acidic tin-based catalysts. This route of formation was confirmed in a mechanistic study by Dusselier et al. [4].

Applications with MVG are so far relatively uncharted, however, its high functionality makes it interesting as a platform chemical, e.g. within polymer chemistry for the creation of unique materials. In this context, Sølvhøj, Taarning and Madsen [5] investigated both homo- and cross-metathesis reactions of MVG. Moreover, Dusselier et al. have studied the copolymerization of MVG and lactic acid, where an initial hydrolysis of MVG seemed to be necessary for the polymerization process [6]. Likewise, initial hydrolysis was also required when the homo-metathesis product (dimethyl-2,5-dihydroxy-3-

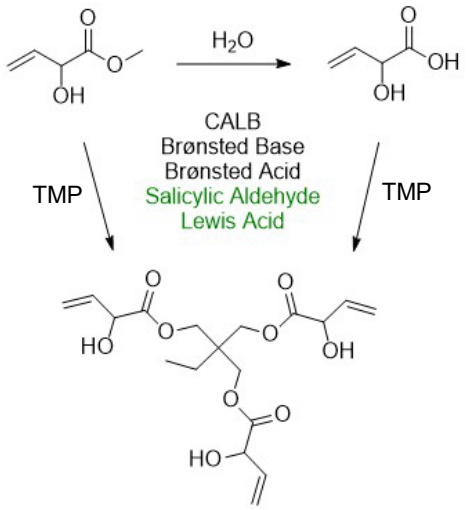
hexenedioate) of MVG was investigated as a cross-linking agent within poly lactic acid (PLA) systems [7]. Despite these promising initial studies, new applications with MVG must be further developed to allow the compound to become industrially relevant [8]. Hence, as part of our interest in synthesis of bio-based chemicals [9] and design of new coating materials [10], we therefore set out to further develop the chemistry of MVG. Herein, we present the first direct transesterification of MVG for the synthesis of a new class of polyhydric alcohols derivatives; vinyl glycolic functionalized polyhydric alcohols.

MVG can be envisaged as propitious for a novel class of polyhydric alcohol derivatives with advanced functionalities. Typical polyhydric alcohol derivatives like trimethylolpropane (TMP) ester derivatives of tris(3-mercaptopropionate) and triacrylate find use within coating chemistry [11]. These classical derivatives only possess one functional group per branch, which upon curing, is lost. The secondary alcohol group of MVG introduces an additional chemical handle, where further chemical transformations are possible (Scheme 1). The ability to perform such manipulations is potentially highly valuable, as it provides opportunities for property fine-tuning. Accordingly, we anticipate MVG derivatives to find possible use in both coating systems, adhesives or as additives in formulations requiring a hydrophilic surface as well as in applications where functionalization of the hydroxyl groups provide specialized polymer properties.



Scheme 1. Structures of the TMP derivatives TMP-VG (left), TMP-acrylate (center) and TMP-mercaptopropionate (right).

The synthesis of esters of TMP, and other polyols, are generally straightforward and prepared *via* a simple esterification process, albeit harsh conditions are necessary. Thus, typically is high temperature as well as reduced pressure along with abundant excess of the corresponding carboxylic acid required to achieve high yields [12][13]. These conditions are, unfortunately, unsuited when utilizing MVG as the secondary alcohol group may induce polymerization, which is further promoted with MVG in large excess. Furthermore, is it considerably more attractive to perform the reaction under stoichiometric conditions. MVG is surprisingly volatile despite its high boiling point ($T_b \sim 160$ °C), and this is probably the reason why previous studies have hydrolyzed MVG to vinyl glycolic acid (VGA) prior to polymerization [6][7]. This further complicates the reaction, as high conversions are dependent on by-product removal. Thus, the synthesis of branched MVG esters is highly dependent on an efficient chemoselective catalyst. In this study, catalytic systems for the synthesis of MVG derivatives of TMP and pentaerythritol (PE) through direct transesterification or esterification have been investigated (Scheme 2). Although the study evolves around the transesterification of MVG and polyhydric alcohols, the findings are transferable to other transesterifications systems where the hydroxyl group of α-hydroxy acid esters evoke complications.



Scheme 2. Catalytic routes to the TMP-VG derivative.

2. Experimental

2.1. Materials

MVG was kindly donated by Haldor Topsøe A/S, *Candida Antarctica Lipase B* (CALB) was kindly donated by Novozymes A/S and ethoxy-PE (Polyol4290) and ethoxy-TMP (Polyol3380) were kindly donated by Perstorp. All other solvents, reagents and materials were obtained commercially and used without further purification unless otherwise stated. Dry toluene and DMSO were obtained by a PureSolv™ MD-7 Solvent Purification System from Innovative Technology with Al_2O_3 as stationary phase. Vacuum of about 10 mbar was generated with an oil pump (without a manometer), and applied for the equilibrium esterification/transesterification reactions to facilitate byproduct and water removal. Anhydrous propanol and t-butanol was obtained by storing over activated 4 Å molecular sieves at least 24 h prior to use, according to standard laboratory procedure [14].

2.2. Methods

NMR spectroscopy was performed on a Bruker Ascend spectrometer with a Prodigy cryoprobe operating at 400 MHz for ^{1}H NMR and 101 MHz for ^{13}C NMR. HSQC and HMBC analysis where conducted for structure validation when ^{1}H and ^{13}C NMR proved insufficient. All NMR spectra were recorded with d^{6}-DMSO as solvent. Chemical shifts (δ) are reported in ppm downfield from TMS (δ = 0 ppm) using solvent resonance as the internal standard (^{1}H: 2.51 ppm, ^{13}C: 39.52 ppm). First order coupling constants (*J*) are reported in Hz when applicable. Multiplicities are reported as singlet (s), doublet (d), triplet (t), quartet (q) doublet of doublets (dd), doublet of triplets (dt) and multiplets (m).

Infrared spectra were recorded on a Bruker alpha-P FT-IR spectrometer with 4 cm^{-1} resolution. Peaks are reported as strong intensity (s), medium intensity (m), weak intensity (w) and broad peaks (b).

2.3. Syntheses

102 ***Vinyl glycolic acid (VGA)***

103 A 10 mL round bottom flask was charged with MVG (4 mmol), CALB (50 mg) and 5 mL distilled water. The
104 mixture was then magnetically stirred with a stirring bar at 60 °C for 18 h (TLC indicated the reaction was
105 finished), where after the enzymes were removed by filtration followed by the water by rotary
106 evaporation yielding a yellowish liquid in quantitative yields. ^{1}H NMR (400 MHz, d^{6}-DMSO) δ/ppm: 5.94
107 (ddd, *J* = 17.2, 10.4, 4.9 Hz, 1H, *H*C-OH), 5.36 (dd, *J* = 17.3, 1.9 Hz, 1H, *H*CH), 5.16 (dt, *J* = 10.5, 1.9 Hz, 1H,
108 HC*H*), 4.51 (dt, *J* = 5.0, 1.9 Hz, 1H, C*H*). ^{13}C NMR (101 MHz, d^{6}-DMSO) δ/ppm: 174 (*C*OO), 137 (*C*H), 116
109 (H*C*H) and 71.5 (H*C*-OH). FTIR ν/cm^{-1}: 2500- 3392 (s,b O-H stretch), 1718 (s, C=O stretch), 1642 (w, C=C
110 stretch), 1211 (m, C-O stretch), 1138 (m, C-O stretch), 1071 (m, C-O stretch), 990 cm^{-1} (w, C=C-H oop).

111 ***Ethoxylated PE/TMP (ethoxy-PE/ethoxy-TMP)***

112 A 10 mL round bottom flask was charged with MVG (4 mmol) and ethoxy-PE (Polyol 4290, 0.25 mmol) or
113 ethoxy-TMP (Polyol3380, 0.25 mmol), CALB (50 mg) and 5 mL anhydrous toluene. A tube with activated 4
114 Å molecular sieves was positioned on the flask, and the flask filled with N_2 gas after two vacuum cycles.
115 Subsequently, the mixture was magnetically stirring with a stirring bar for 70 h (^{1}H NMR indicated the
116 reaction was finished by the peak appearing at 4.2 ppm). After reaction, the enzymes were removed by
117 filtration (by addition of acetone) and the toluene removed by rotary evaporation (40 °C, 50 mbar) to
118 obtain a transparent yellowish oil. Yield MVG-ethoxy-PE 83% (^{13}C NMR relative to ethoxy-PE). Yield MVG-
119 ethoxy-TMP 80% (^{1}H NMR relative to ethoxy-TMG).

120 ***TMP-VG***

121 ***Method using VGA and tin(II) chloride:*** VGA (4 mmol), TMP (1 mmol) and $SnCl_2 \cdot 2H_2O$ (10 mg) was
122 magnetically stirred in a 5 mL round bottom flask at 60 °C under vacuum for 40 h (^{1}H NMR indicated the
123 reaction was finished by the peak appearing at 4.05 ppm). Yield 87.5% (^{13}C NMR relative to TMP).

124 ***Method using MVG and tin(II) chloride:*** MVG (8 mmol), TMP (1 mmol) and $SnCl_2 \cdot 2H_2O$ (10 mg, 1 mmol)
125 was added to a 5 mL round bottom flask and the mixture magnetically stirred in closed system at 120 °C
126 for 18 h (^{1}H NMR indicated the reaction was finished by the peak appearing at 4.05 ppm). Conversion 65%
127 (^{13}C NMR relative to TMP).

128 ***Method using salicylic aldehyde:*** A 5 mL round bottom flask was charged with VGA (2 mmol), TMP (0.25
129 mmol), salicylic aldehyde (0.2 mmol) and 1 mL anhydrous toluene. The solution was purged with N_2 and
130 subsequently magnetically stirred at 100 °C for 14 h (^{1}H NMR indicated full TMP conversion by the peak
131 disappearing at 3.35 ppm). Yield 100% (^{13}C NMR relative to TMP).

132 The products were purified by flash column chromatography with ethyl acetate:heptane (1:1) as eluent.
133 ^{1}H NMR (400 MHz, d^6-DMSO) δ/ppm 5.98-5.83 (m, *3.5 H*, C*H*), 5.75 (d, *J* = 6.1 Hz, *2H,* O*H*) ,5.56-5.45 (m,
134 *1H, CH-oligomer)* 5.37 (dt, *J* = 17.2, 1.8 Hz, 3H, *H*CH), 5.19 (dt, *J* = 10.4, 1.6 Hz, , *3H,* HC*H*), 4.7 (m, 0.5 H,
135 *H*C-OH, oligomer), 4.6 (m, 0.5 H, *H*C-OH), 4.09-3.97 (m, *6H* C(C*H*$_2$O-)$_3$), 1.41 (q, *J* = 7.6 Hz, *2H* CC*H*$_2$CH$_3$) and
136 0.84-0.78 (m, *3H,* CCH$_2$C*H*$_3$). ^{13}C NMR (101 MHz, d^6-DMSO) δ/ppm 172.38 (*C*OO), 136.14 (H*C*), 116.72
137 (H*C*H), 71.47 (H*C*-OH), 64.09 (C(*C*H$_2$O-)$_3$), 41.27 (quaternary carbon), 22.73 (C*C*H$_2$CH$_3$), 7.66 (C*H*$_3$). FTIR
138 ν/cm^{-1}: 3373 (m,w O-H stretch), 2969 (w, C-H stretch of sp^3 carbon), 1735 (s, C=O stretch of ester), 1644
139 (w, C=C stretch of vinyl), 1464 (w, CH$_2$ bend), 1387 (w,CH$_3$ bend), 1190 (s, C-O stretch), 1135 (s, C-O stretch),
140 1088 (s, C-O stretch), 987 (s, =C-H oop of vinyl), 932 (s, =C-H oop of vinyl).

141 ***Transesterification of MVG with TMP using Lewis acids***

142 20 mL glass tubes were charged with TMP (0.5 mmol), MVG (4 mmol) and a metal chloride (0.02 mmol).
143 The glass tubes were evacuated to vacuum and positioned in a Carousel 12 Plus Reaction Station™ that
144 was preheated to 120 °C and stirred. During reaction (12 h), the tubes were shortly removed from the
145 carousel every 4 h to take small samples (~0.05 mL) by a syringe, which were added directly to d^6-DMSO
146 in NMR tubes and stored in a fridge prior to analysis. Samples from reaction with $FeCl_2$ and $YbCl_3$ were
147 filtered prior to analysis to avoid severe signal broadening from metal ions.

148 ***Transesterification of MVG with TMP/PE using tin(II) chloride***

149 Typically 10 mL round bottom flask was charged with MVG (12 mmol), TMP/PE (1.5 mmol), $SnCl_2 \cdot 2H_2O$
150 (15 mg, 1.5 mmol) and evacuated to vacuum, where after it was placed in an oil bath at 120 °C with
151 magnetically stirring. During reaction, aliquots of the reaction mixture (~0.05 mL) were periodically
152 syringed, and added to d^6-DMSO in NMR tubes. All samples were stored in a fridge prior to NMR analysis.

153 ## 3. Results and Discussion

154 ### 3.1. Analytic method for transesterification reactions

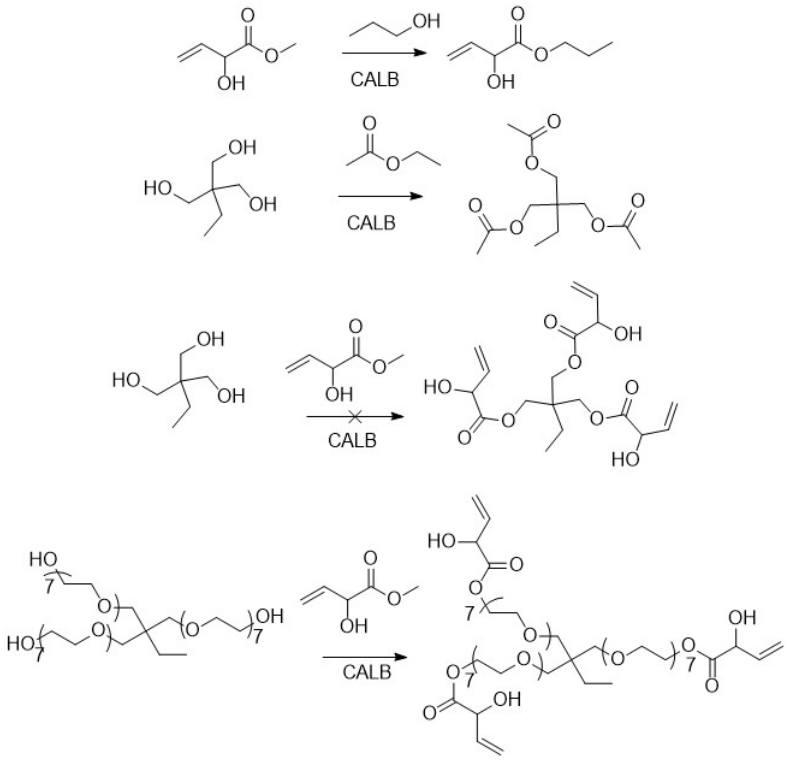
155 In order to evaluate the transesterification reactions comprehensibly, a reliable method for determination
156 of conversion as well as the degree of acylation and oligomerization was necessary. Such analysis is not
157 common practice within these types of reactions, however it was noticed that acylation moves the
158 chemical shift of the quaternary carbon in ^{13}C NMR sufficiently upfield to identify each individual species.
159 Through comparison between standard and quantitative ^{13}C NMR it was found that standard ^{13}C NMR was
160 adequate, both for the determination of conversion and acylation degree based on integration of the
161 quaternary carbons. By conducting HSQC and HMBC experiments, it was found that the degree of
162 polymerization could be determined by ^{1}H NMR (see SI for detailed description).

163 **3.2. *Candida Antarctica Lipase B* (CALB) catalyzed transesterification**

164 The transesterification of MVG and TMP/PE requires high chemoselectivity, especially for primary alcohols
165 over secondary alcohols. Enzymes have emerged as sustainable catalysts with high regio- and
166 enantioselectivity and *Candida Antarctica Lipase B* (CALB) has been extensively studied for the selective
167 acylation of sugars with high selectivity reported towards the acylation of primary hydroxyl groups
168 [15,[16], while it also tolerates other functional groups such as vinyl or acrylic double bonds [17].
169 Moreover, secondary alcohols in the α-position to the acyl donor are generally not reactive in CALB-
170 catalyzed acylations [18],[19]. CALB is further known to catalyze the acylation of polyols and the
171 transesterification of α-hydroxy acids, thus potentially making it an ideal catalyst for the present study
172 [20],[21].

173 When carrying out the CALB catalyzed transesterification between MVG and TMP or PE low product yield
174 was observed (Table 1, entry 1). However, CALB was able to catalyze the transesterification between propanol
175 and MVG (result not shown), thereby proving that CALB was able to catalyze the transesterification with MVG
176 as acyl donor and it is also known to catalyze the acylation of glycerol and pentaerythritol in preparation of
177 branched molecules [22],[23]. Accordingly, it was rationalized that CALBs inability to catalyze the
178 transesterification between MVG and TMP/PE was due to steric constrains within the active center of the
179 enzyme. We hypothesized that by extending the length of the polyol branches the individual branches could
180 enter the active site of the enzyme while the rest of molecule stays outside. Thus, the hydroxyl groups become
181 more available for the enzyme despite the molecule becomes more sterically demanding at the core. When
182 changing the polyols to the analogous ethoxylated adducts, up to 80% transesterification yields were obtained
183 using just a 4 times molar excess of MVG in toluene (Table 1, entries 2 and 4). This supports the hypothesis
184 that steric properties is a main issue for the reaction with polyols like TMP and PE. The ethoxylation further
185 reduces the polarity and changes the physical state of the substrate (oils rather than solids) allowing for
186 conducting the reaction in bulk. Unfortunately, when carrying out the reaction in bulk MVG (15-fold excess) no

conversion was observed (Table 1, entry 3), indicating that MVG inactivates the enzyme as is common with highly solvating molecules like DMSO and DMF [24]. This effect combined with the high viscosity of ethoxylated polyols and low reaction temperatures makes CALB unsuitable for carrying out this reaction without solvents. Surprisingly, a small degree of oligomerization was observed despite CALB - according to the literature [18],[21] - cannot polymerize α-hydroxy acids.



Scheme 3. CALB transesterification reactions of MVG.

3.3. Brønsted base/acid catalyzed transesterification

Homogeneous base catalysis is superior in the transesterifications reactions of biodiesel [25]. However, bases are generally highly sensitive towards acid and water impurities, and the applied MVG contained VGA impurities (~3.3% determined by ^{1}H NMR). As MVG is also reported to dimerize with equimolar

198 amounts of base, it was not surprising that the transesterification of MVG with propanol did not proceed
199 with 5 mol% KOH.

200 Transesterification of, e.g. biodiesel, is also widely applied using homogeneous acid catalysis due to
201 the robustness of acids against typical impurities (acid and water) [25]. In line with this, sulfuric acid
202 actively catalyzed the transesterification between MVG and propanol (Table 1, entry 5), but unfortunately
203 also produced copious amounts of unwanted byproducts in high yields making the system useless.

204 **3.4. Salicylic aldehyde catalyzed (trans)esterification**

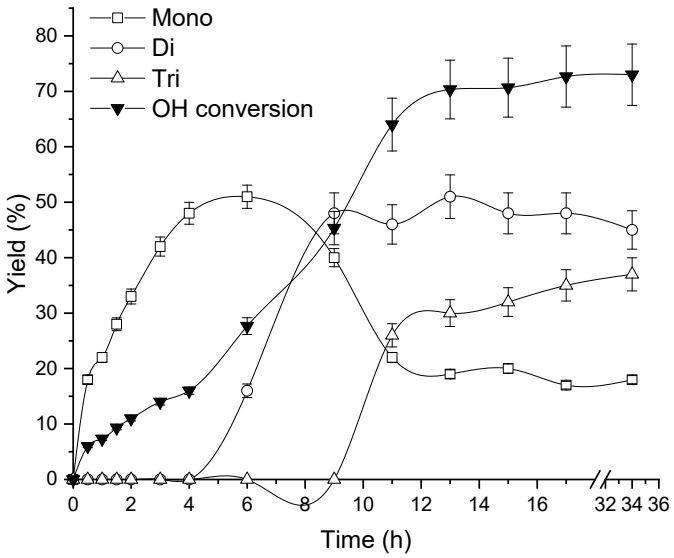
205 Outside of the typical transesterification catalysts, salicylic aldehyde has been found to irreversibly
206 catalyze the esterification process of α-hydroxy acids [26]. Salicylic aldehyde proved very efficient in
207 catalyzing the esterification process between VGA and TMP resulting in quantitative yield with only 2.66
208 times VGA excess (Table 1, entry 6). This is quite impressive as esterification reactions are typically carried
209 out with more than 10-fold excess of one of the substrates and removal of the produced byproducts to
210 obtain high conversions [27]. Unfortunately, salicylic aldehyde could not catalyze the process with MVG
211 as acyl donor, deeming it necessary to carry out a hydrolysis step to VGA before its eventual use. Although
212 the hydrolysis step potentially is easy to do also in a larger (industrial) setting, it would probably be
213 undesirable as it also introduces an accompanying energy consuming purification step.

214 **3.5. Lewis acid catalyzed transesterification**

215 ***Tin(II) chloride***

216 We hypothesized that tin(II) chloride would be a good Lewis acid catalyst for this reaction as tin(II)
217 compounds are known to be efficient Lewis acid catalysts for transesterification and esterification
218 reactions and, as previously mentioned, co-polymerization of lactic acid and VGA was achieved using tin(II)

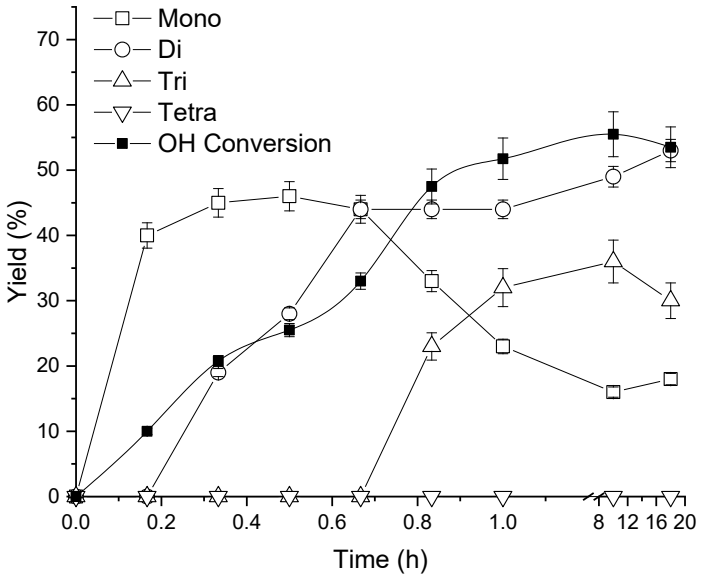
219 chloride [6],[27],[28]. When $SnCl_2 \cdot 2H_2O$ was used as catalyst for the esterification of MVG in the present
220 study, the reaction was also found to proceed quite selectively under benign conditions reaching full
221 conversion with equimolar amount of VGA and PE (based on OH groups) at 60 °C with vacuum in 43 h
222 (Table 1, entry 8), while higher temperatures led to undesired evaporation of VGA. Similarly, was the
223 triacylated TMP derivative also successfully synthesized (Table 1, entry 9). On the other hand, in the
224 transesterification MVG proved too volatile to carry out the direct transesterification under those
225 conditions (60 °C, vacuum), and only 45% conversion was reached after 74 h without the applied vacuum.
226 However, by increasing the reaction temperature to 120 °C it proved possible, in the closed system, to
227 significantly increase the rate of the transesterification, while maintaining limited oligomerization and
228 MVG evaporation, and obtain 75% conversion within 13 h with just a 2.66-fold molar excess of MVG to
229 TMP (Table 1, entries 13 and 1 and Figure 1). Despite the reaction being solvent free, the reaction rate
230 appeared to be independent of the conversion as well as the acylation degree. Moreover, oligomerization
231 occurred only in miniscule amounts with average degree of polymerization (DP) below 1.3 and DP of
232 oligomerized MVG units stabilizing around 2, indicating that 20% of the MVG molecules had dimerized.



234 **Figure 1.** Product distribution plot of mono-, di- and triacylated TMP in the transesterification of MVG and
235 TMP in closed system with tin(II) chloride as catalyst. Reaction conditions: 1.5 mol% $SnCl_2 \cdot 2H_2O$, 2.66 MVG
236 to TMP ratio (based on OH-groups), 120 ^oC.

237 Surprisingly, when carrying out the analogous tin(II) catalyzed transesterification reaction with PE the
238 OH conversion reaches a plateau after approximately just 1 h albeit at a conversion of only about 50%
239 (Figure 2). Similarly, the reaction rate did apparently not change as function of conversion nor did the
240 acylation degree and oligomerization was negligible. In order to obtain higher conversion, vacuum-heat
241 cycles was attempted where evaporation of MVG was avoided by cooling the reaction mixture to room
242 temperature before applying vacuum for 2 h followed by 2 h stirring at 120 ^oC. The two first cycles
243 increased the conversion approximately 10% per cycle, but oligomerization increased simultaneously thus
244 providing a lower overall yield.

245 The rapid reaction kinetics of PE compared to TMP was unexpected considering the similarity of the
246 molecules. The difference could possibly be a coordinative effect originating from the fourth hydroxyl
247 group of PE, however, since the reaction rate was not dependent of the acylation degree (which should
248 markedly affect the coordinative properties), the observed reactivity difference could be related to
249 properties such as, e.g. solubility and viscosity (i.e. diffusion).



251 **Figure 2.** Product distribution plot of mono-, di-, tri- and tetraacylated PE in the transesterification of MVG and

252 PE in closed system with tin(II) chloride as catalyst. Reaction conditions: 1.5 mol% $SnCl_2 \cdot 2H_2O$, 2.66 MVG to PE

253 ratio (based on OH-groups), 120 °C.

254

255

256

257

Table 1 Esterification/transesterification of VGA/MVG with polyols using different catalyst systems at optimized conditions

Entry	Alcohol	Acyl donor	Acyl donor: alcohol ratio (mol/mol)	Catalyst	Solvent	Time (h)	Temp (°C)	Yield (%)	TON (mol/mol)	DP_{avg}[a]	DP[b]
1	TMP	MVG	6.66:1	CALB[c]	t-butanol	65	60	2	1[g]	1.78	2.27
2	Ethoxy-TMP	MVG	4:1	CALB[c]	Toluene	20	80	82	41[g]	1.42	2.43
3	Ethoxy-TMP	MVG	15:1	CALB[c]	-	24	80	0	0	N/A	1.00
4	Ethoxy-PE	MVG	4:1	CALB[c]	Toluene	18	80	83	42[g]	1.27	2.21
5	Propanol	MVG	1:10	H_2SO_4[d]	-	18	60	>99*	5	N/A	1.00
6	TMP	VGA	2.6:1	Salicylic Aldehyde[e]	Toluene	14	100	>99	10	1.64	2.71
7	TMP	VGA	1:1	Salicylic Aldehyde[e]	Toluene	24	100	75	8	1.20	2.00
8	PE	VGA	1:1	$SnCl_2{\cdot}2H_2O$[f]	-	40	60	90	60	1.46	2.53
9	TMP	VGA	1.3:1	$SnCl_2{\cdot}2H_2O$[f]	-	40	60	>99	66	1.24	2.22
10	PE	MVG	2.66:1	$SnCl_2{\cdot}2H_2O$[f]	-	2	120	55	37	1.13	2.00
11	TMP	MVG	2.66:1	$SnCl_2{\cdot}2H_2O$[f]	-	13	120	75	50	2.00	2.02
12	TMP	MVG	1.33:1	$SnCl_2{\cdot}2H_2O$[f]	-	70	60	45	30	N/A	N/A
13	TMP	MVG	5.33:1	$SnCl_2{\cdot}2H_2O$[f]	-	70	60	73	49	1.13	3.34

[a] DP_{avg}: Degree of polymerization including unreacted (with regard to MVG homo condensation) MVG. [b] DP: Degree of polymerization excluding unreacted (with regard to MVG homo condensation) MVG. [c] 50 mg CALB. [d] One drop, i.e. about 0.01 mL. [e] 10 mol%. [f] 1.5 mol%. [g] Turn over number given as mmol/100 mg catalyst, as the catalyst loadings by supplier was not provided in mol/g. *: Conversion rather than yield and a range of unidentified side products. Data based on NMR spectra, see SI Figures S24-S46

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259

Alternative metal chlorides

The good performance of tin(II) chloride for the transesterification of MVG and TMP, without forming notable side products, prompted us to investigate other Lewis acidic metal chloride catalysts for the reaction. Based on the good results of tin(II) chloride, the more acidic tin(IV) chloride was examined despite it not being a typical transesterification catalyst [29], while aluminium(III) chloride, zinc(II) chloride and ytterbium(III) chloride was selected as they are more common Lewis acids. Chromium(III) chloride are in rare and specific cases an efficient transesterification catalyst [30],[31], whereas iron(II) chloride was chosen to have an untypical transesterification catalyst in the study. The ^{13}C NMR signal pattern in the δ 40-46 ppm range was characteristic for the MVG-TMP product mixture obtained in the tin catalyzed reactions (Figure 3), and allowed to estimate the conversions for the other metal chlorides. The additional signals at δ 159-164 ppm were indicate of the byproducts.

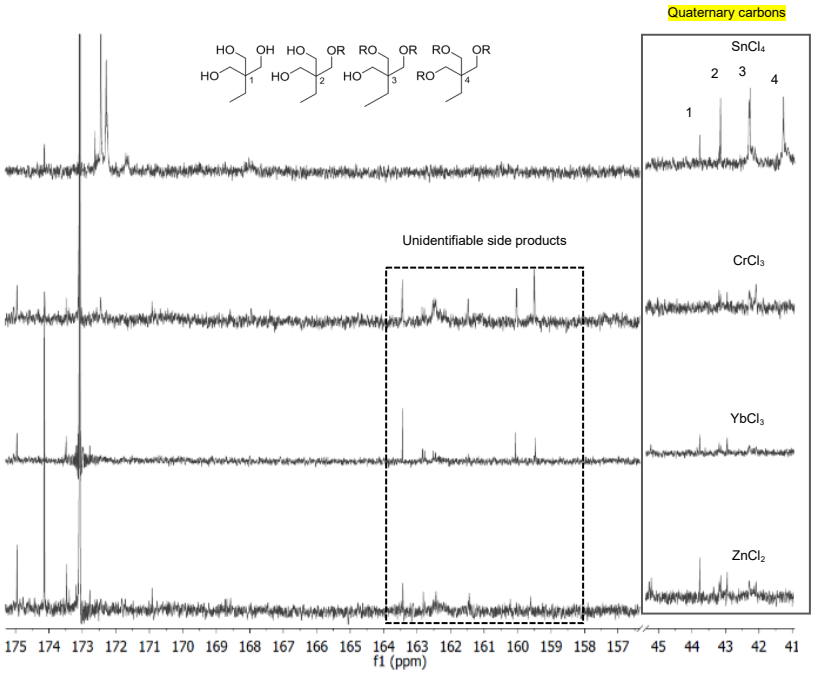

Figure 3. ^{13}C NMR spectra of the products after transesterification between MVG and TMP in closed system with various metal chloride catalysts. Reaction conditions: 1.33 mol% metal chloride, 2.66 MVG to TMP ratio (based on OH-groups), 120 °C, 12 h.

As summarized in Figure 4, most of the catalysts based on alternative metals than tin yielded only moderate conversions in the reaction as well as a range of byproducts (unidentified), as also found for H_2SO_4 (see above) though even more prominent. The lower catalytic activity observed for these catalysts, including the strong Lewis acid aluminum(III) chloride which performed quite poor, could be related to their limited solubility as only the tin halides efficiently dissolved in the TMP/MVG media under the applied reaction conditions. Thus, unfortunately the difference in solubility complicated the direct comparison between activity and acidity. Nevertheless, it was evident that tin chlorides was superior for this reaction. Notably, tin(IV) chloride was apparently found to be significantly more active than tin(II) chloride for the reaction allowing it to reach a final product yield of ~75% within 4-8 h instead of 12 h. This could be correlated to tin(IV) being a stronger Lewis acid and harder metal species than tin(II), thereby facilitating reaction with the oxygen-rich substrates. Interestingly, similar superior reactivity of tin(IV)/tin(II) salts have also previously been found in formation of α-hydroxy acids from tetroses [4]. The superior performance of the tin chlorides was partly ascribed to their complete dissolution in the reaction mixture (see above). Thus, if presence of tin chloride is undesired in the product a filtration through silica with an appropriate solvent would be necessary. However, this would make reusability of the catalyst cumbersome and a further development of the process could therefore instead target investigation of a suitable heterogeneous tin catalyst, where catalyst recycling is easy by simple filtration.

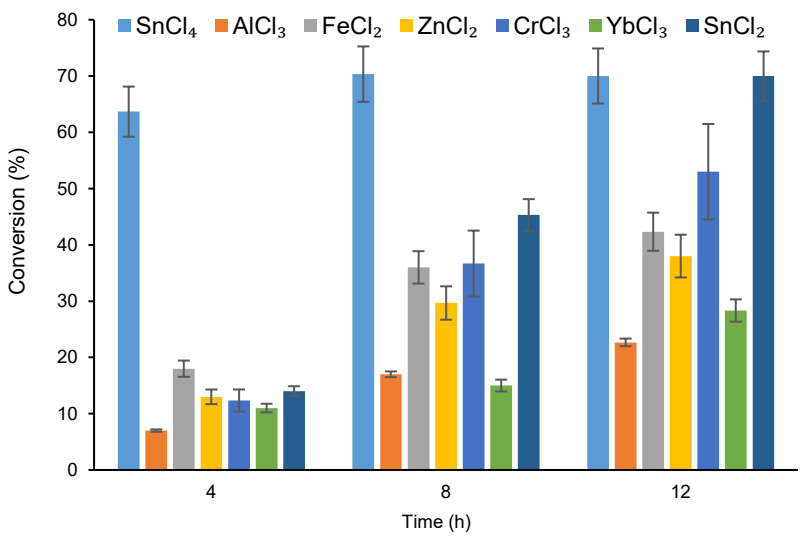

Figure 4. Yields from the transesterification of TMP and MVG with various metal chlorides in closed system. Reaction conditions: 1.33 mol% catalyst, 2.66 MVG to TMP ratio (based on OH-groups), 120 °C.

4. Conclusions

A catalytic and benign method for the synthesis of a unique class of polyhydric derivatives - with multiple functionalities - based on the novel bio-based molecule MVG were successfully developed. Salicylic aldehyde catalyzed the esterification process to provide the triacylated VG derivative of TMP in excellent yield with negligible oligomerization from VGA. Tin chlorides efficiently catalyzed the direct transesterification process from MVG, whereas other Lewis acidic metal chlorides provided low activity and selectivity. Furthermore, CALB was found to catalyze the transesterification process with ethoxylated polyols, albeit high MVG concentrations inactivated the enzyme. Overall, the reported work demonstrates that novel MVG derivatives of polyols can be synthesized with negligible oligomerization under benign and solvent free conditions with low MVG excess by use of catalysts with tin(IV) chloride being superior. The new MVG derivatives with a secondary hydroxyl group could possibly find use in coating systems,

adhesives or as additives, where a hydrophilic surface is required or the hydroxyl groups functionalized to comply with other specialized polymer properties.

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Conflict of interest

The authors declare that they have no conflict of interest.

References

[1] Elliot SG, Andersen C, Tolborg S, Meier S, Sádaba I, Daugaard AE, Taarning E (2017) RSC Adv. 7: 985–996.

[2] Bozell JJ, Petersen GR (2010) Green Chem. 12: 539–554.

[3] Holm MS, Saravanamurugan S, Taarning E (2010) Science 328: 602–605.

[4] Dusselier M, Van Wouwe P, deClippel F, Dijkmans J, Gammon DW, Sels BF (2013) ChemCatChem 5: 569–575.

[5] Sølvhøj A, Taarning E, Madsen R (2016) Green Chem. 18: 5448–5455.

[6] Dusselier M, Van Wouwe P, De Smet S, De Clercq R, Verbelen L, Van Puyvelde P, Du Prez FE, Sels BF (2013) ACS Catal. 3: 1786–1800.

[7] Dewaele A, Meerten L, Verbelen L, Eyley S, Thielemans W, Van Puyvelde P, Dusselier M, Sels B (2016) ACS Sustainable Chem. Eng. 4: 5943–5952.

[8] https://info.topsoe.com/biochemicals (Topsoe MOSAIK™ solution), accessed April 28,2020.

[9] Li H, Zhao W, Saravanamurugan S, Dai W, He J, Meier S, Yang S, Riisager A (2018) Commun. Chem. 1:32,

1-11.

[10] Nameer S, Larsen DB, Duus JØ, Daugaard AE, Johansson M (2018) ACS Sustainable Chem. Eng. 6: 9442-9450.

[11] Günduz G, Chemistry, Materials and Properties of Surface Coatings, DEStech Publications, Inc, 215AD, 2016.

[12] Panchal TM, Patel A, Chauhan DD, Thomas M, Patel JV (2017) Renew. Sustain. Energy Rev. 70: 65–70.

[13] Wolfang P, Hauer B, Haring D, Dietsche F (2006) Enzymatic Synthesis of Polyol Acrylates, US20060030013A1.

[14] Amerigo WL, Chai C (2009) Purification of Laboratory Chemicals, 6. ed, Elsevier.

[15] Haraldsson GG, Gudmundsson, BÖ, Almarsson Ö (1995) Tetrahedron 51: 941–952.

[16] Kulshrestha, AS, Gao W, Gross RA (2005) Macromolecules 38: 3193–3204.

[17] Hoffmann C, Stuparu MC, Daugaard A, Khan A (2015) J. Polym. Sci. Part A Polym. Chem. 53: 745–749.

[18] Anderson EM, Larsson KM, Kirk O (1998) Biocatal. Biotransformation 16: 181–204.

[19] Li G, Yao D, Zong M (2008) Eur. Polym. J. 44: 1123–1129.

[20] Cavalcanti EDC, Aguieiras ÉCG, da Silva PR, Duarte JG, Cipolatti EP, Fernandez-Lafuente R, da Silva JAC, Freire DMG (2018) Fuel 215: 705–713.

[21] From M, Adlercreutz P, Mattiasson B (1997) Biotechnol Lett. 19: 315–317.

[22] Happe M, Kouadio M, Treanor C, Sawall JP, Fornage A, Sugnaux M, Fischer F (2014) J. Mol. Catal. B Enzym. 109: 40–46.

[23] Nguyen HD, Löf D, Hvilsted S, Daugaard AE (2016) Polymers 8: 363.

[24] Nott K, Brognaux A, Richard G, Laurent P, Favrelle A, Jérôme C, Blecker C, Wathelet JP, Paquot M, Deleu M (2012) Prep. Biochem. Biotechnol. 42: 348-363.

[25] Lam MK, Lee KT, Mohamed AR (2010) Biotechnol. Adv. 28: 500–518.

[26] Weng SS, Li HC, Yang TM (2013) RSC Adv. 3: 1976–1986.

[27] Ferreira AB, Lemos Cardoso A, da Silva JM (2012) ISRN Renew. Energy 2012: 1–13.

[28] Casas A, Ramos MJ, Rodríguez JF, Pérez Á (2013) Fuel Process. Technol. 106: 321–325.

[29] Patel Y, George J, Pillai SM, Munshi P (2009) Green Chem. 11: 1056-1060.

[30] Cao J, Qi B, Liu J, Shang Y, Liu H, Wang W, Lv J, Chen Z, Zhang H, Zhou X (2016) RSC Adv. 26: 21612–21616.

[31] Reddy CR, Iyengar P, Nagendrappa G, Prakash BSJ (2005) J. Mol. Catal. A Chem. 229: 31–37.