Heterogeneous & Homogeneous & Bio- & Nano-

CHEMCATCHEM

CATALYSIS

Accepted Article

Title: Catalytic Gas-Phase Cyclization of Glycolate Esters: a Novel Route Toward Glycolide-Based Bioplastics

Authors: Rik De Clercq, Ekaterina Makshina, Bert F Sels, and Michiel Dusselier

To be cited as: *ChemCatChem* 10.1002/cctc.201801469

Link to VoR: http://dx.doi.org/10.1002/cctc.201801469

A Journal of

ChemPubSoc Europe

WILEY-VCH

www.chemcatchem.org

WILEY-VCH

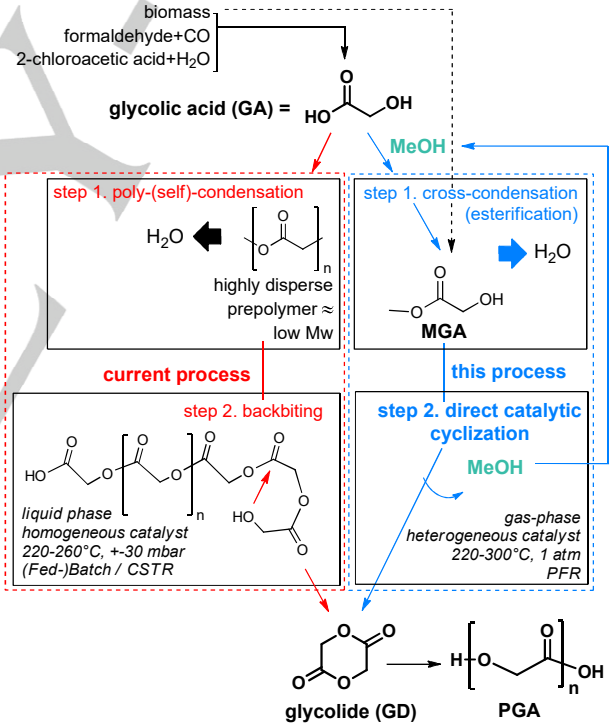
FULL PAPER

Catalytic Gas-Phase Cyclization of Glycolate Esters: a Novel Route Toward Glycolide-Based Bioplastics

Dr. Rik De Clercq, Dr. Ekaterina Makshina, Prof. Dr. Bert F. Sels, Prof. Dr. Michiel Dusselier*

Abstract: A catalytic process to produce glycolide, the cyclic dimer of glycolic acid (GA), is proposed. Glycolide is the key building block of the biodegradable plastic polyglycolic acid. Instead of the current industrial two-step route, which involves the polycondensation of GA and a subsequent backbiting reaction, a new route based on the gas-phase transesterification of methyl glycolate (MGA) over a fixed catalyst bed is presented. With specific supported TiO_2 catalysts, a high glycolide selectivity of 75-78% can be achieved at the thermodynamically-limited equilibrium conversion of MGA (54% at 300 °C, 5.6 vol% MGA, 1 atm). The absence of solvent and the continuous nature of the process should allow for easy product separation and recycling of unconverted esters, while the few side-products, i.e. linear alkyl glycolate dimers and trimers seem recoverable via methanolysis. The reaction is compared to the cyclization of other α-hydroxy esters, such as methyl lactate to lactide, over the same catalysts, in terms of kinetics and thermodynamics. The absence of a methyl substitution on the α-carbon seems to lead to faster cyclization kinetics of MGA when compared to methyl lactate or the double-substituted methyl-2-hydroxy-isobutyrate. Contrarily, glycolide production is less favored thermodynamically compared to lactide. The absence of glycolide decomposition at temperatures up to 300 °C however allows to increase equilibrium conversion by taking the endergonic reaction to higher temperatures.

Polyglycolic acid (PGA) is a crystalline biodegradable polyester built from glycolic acid (GA). PGA has applications in medicine – related to its biocompatibility (tissue engineering, sutures, release of bioactive agents);[1-2] in certain packaging applications – related to its gas-barrier properties (e.g. as intermediate layer in PET bottles, or, films) as well as in tools for oil production.[3] GA is the smallest α-hydroxy-acid[4] and its linear polymer is the simplest structural example of an aliphatic polyester (Scheme 1). Aside from polyesters, GA can be used as such, e.g. in skincare and cleaning products or as an auxiliary in textile printing and leather treating. GA is mainly made through the carbonylation of formaldehyde or trioxane; via the hydrolysis of 2-chloroacetic acid or; via electrolytic reduction of oxalic acid.[5] Alternatively, fermentation of carbohydrates can also lead to GA,[6] while recent biomass-based chemocatalytic routes have also been reported.[4, 7] For example, starting from glyoxal (found in pyrolysis bio-oil), Dapsens et al. made GA and its esters by using Lewis acidic zeolite catalysts.[8] Starting from cellulose, Zhang et al. showed 49% of GA yield using heteromolybdic acids with oxygen,[9] while Huang et al. proceeded via the oxidation of short polyols with Pt/C catalysts.[10] A direct acid-catalyzed conversion of cellulose in methanol in presence of Sn triflate also produced methyl glycolate (MGA) as side-product next to other esters[11], while recent work demonstrated the use of hexoses as bio-derived source for MGA.[12] This work fits in the broader context of deriving polymers, and polyesters specifically, from sugar-based biomass.[7, 13]



Scheme 1. Synthesis of glycolide and PGA from GA: the current scheme involving a polymerization-backbiting approach (red) from GA vs. the new proposed process (blue) via the catalytic cyclization of MGA in gas-phase. If GA is used, an easy esterification step is needed, but in case MGA is produced directly (e.g. some biomass routes in alcoholic solvent), a one-step glycolate-to-glycolide saves a process step and unit operations.

In order to produce quality PGA with control over dispersity, the cyclic dimer of GA, i.e. glycolide (GD), is needed (Scheme 1). GD can be polymerized via ring-opening polymerization to attain high-molecular weights, and the molecule also allows easy access to co-polymers with other α-hydroxyacids (e.g., lactic acid) through

[*] Dr. R. De Clercq, Dr. E. Makshina, Prof. B. F. Sels, Prof. M. Dusselier*
Centre for Surface Chemistry and Catalysis, KU Leuven
Celestijnenlaan 200F, 3001 Heverlee
E-mail: michiel.dusselier@kuleuven.be

Supporting information for this article is given via a link at the end of the document

their respective cyclic dimers (e.g., lactide[14-17]) or with lactones.[18-20] The state of the art synthesis of GD, from the free acid, runs via a two-step process, starting with a pre-polymerization of an aqueous GA solution via condensation by distilling off the water. Then, the formed oligomers are usually dissolved in a high-boiling solvent, sometimes in the presence of a catalyst. A backbiting reaction then converts the prepolymer into cyclic adducts, which are continuously removed by distillation (red square, Scheme 1).[21-23] Both consecutive reactors/steps require high temperatures (220-260 °C), low pressures (as low as 3 mbar) and have to run for multiple hours to achieve satisfactory yields of the prepolymer and glycolide. Unfortunately, as this conventional process is almost exclusively described in patent literature, it is difficult to find representative numbers in terms of GD yields as the focus usually lies on GD production rates and purity. Nevertheless, one patent discloses that the prepolymerization step yields about 50 wt% of PGA oligomers after heating an aqueous GA solution at 170-200 °C for 2 hours under 1 atm, followed by reducing the pressure to 5 mbar and continuing the condensation reaction for 2 more hours at 200 °C.[33] The subsequent backbiting reaction yielded about 60 wt% of distilled GD after 5 h at 260 °C under 3-8 mbar of pressure. GD distillation rates of 10-30 g h^{-1} have been reported.[33-35] GD yields can likely be increased by continuing the backbiting reaction for longer times, as there are no thermodynamic limitations since the product is continuously removed. Still, up to 20 wt% of the prepolymers is lost as side-products during the backbiting step.[35] Clearly, the necessity of high boiling solvents, high temperatures, low pressures and long reaction times are severe disadvantages to the conventional GD production process. Moreover, the GD production capacity through this process seems to be limited by the distillation rate of GD from the high-boiling solvent, rather than the actual production rate.

Therefore, we present a new gas-phase catalytic approach capable of producing GD with 75 - 80 % of selectivity directly from the methyl ester of GA. This approach resembles the novel catalytic process very recently reported for lactide synthesis, from alkyl lactate esters, by our group.[24] The here-proposed vapor-phase GD route aligns well with existing unit operations in the chemical industry as well as with recent direct synthesis routes toward esters of GA, including MGA.[8, 11-12] Moreover, this process does not require near-vacuum pressures, solvents or long reaction times, opposed to the conventional route.

Results and Discussion

In our recent work we discovered the excellent catalytic activity of certain silica-supported Ti-catalysts for the ring-closing trans-esterification of methyl lactate into lactide, the cyclic precursor to polylactic acid plastics.[24, 25] Here, we expand the scope of this catalytic vapor-phase process and demonstrate, in our knowledge for the first time, that a new route to GD is feasible, taking into account remarkable differences in reactivity and thermodynamics. The process relies on vaporizing undiluted MGA in an inert gas stream (N_2) and sending the gas mixture over a fixed catalyst bed

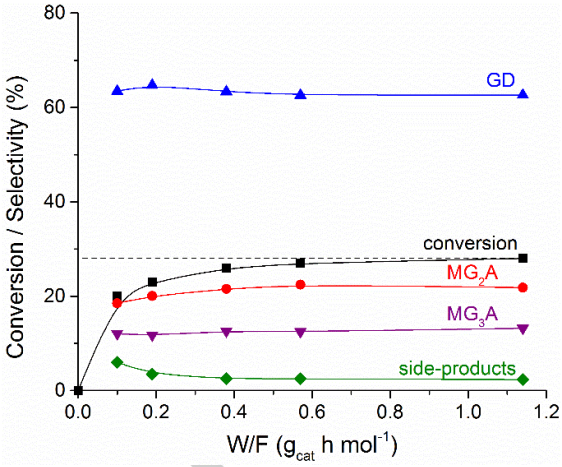


Figure 1. Kinetic plot of the gas-phase transesterification of MGA to GD using a 5 wt% TiO_2/SiO_2 catalyst. Conditions: 5.6 vol% MGA in N_2, T = 220 °C, WHSV = 4.4 – 53.2 h^{-1}. For a similar plot using a 0.4 wt% catalyst plot, see Fig. S1.

in a plug flow reactor (for calculations on ideal plug flow behaviour, see Note S1 in the Supporting Information). An exploratory set of experiments at 220 °C, presented in Figure 1 as conversion/selectivity *vs.* contact time, shows that the catalytic transesterification of MGA in the gas-phase very swiftly reaches equilibrium (at the reaction conditions used) at approximately 30% MGA conversion, where the selectivity of GD amounts to 63% using a 5 wt% TiO_2/SiO_2 catalyst (Fig. 1). Linear dimers (MG_2A) and trimers (MG_3A), formed with 22 and 13% selectivity respectively, are the main byproducts. With only 2% selectivity, nearly no other (unidentified) side products are formed. In similar conditions, methyl lactate (MLA) was found to have a higher equilibrium conversion of about 50%,[24] while another striking difference in the glycolate experiments here is the formation of trimers, which were not observed for the cyclization of MLA. A control experiment without catalyst failed to convert MGA at 220 °C. In order to better understand and exploit the differences between lactate and glycolate transesterification chemistry in the gas-phase, kinetic experiments were conducted with both α-hydroxy ester substrates. The TiO_2 loading of the TiO_2/SiO_2 catalyst was reduced from 5 wt% (as in Fig. 1) to 0.4 wt% (see Table S1 for physicochemical catalyst characterization, or our earlier work,[25] for more detailed data of these two catalysts), to slow down the MGA transesterification (Full kinetic plot in Figure S1), allowing for a more accurate kinetic assessment. Still, the turnover frequency (TOF, h^{-1}) of the Ti sites on the catalyst's surface (0.4 wt% of TiO_2 is below the monolayer coverage limit of TiO_2 on SiO_2 surfaces[26-28]) was more than five times higher for MGA than MLA, *viz.* 614 *vs.* 116 h^{-1}, respectively under similar reaction conditions (Fig. 2A). This demonstrates the higher reactivity of MGA for this Ti-catalyzed gas-phase cyclization transesterification. Reactions at different temperatures allowed to estimate apparent activation energies (E_a, Fig. 2B) for ester conversion, leading to a slightly lower value, 37 *vs.* 48 kJ.mol^{-1}, for MGA compared to MLA respectively. The value for MGA sheds doubt on the rate-determining step of the process (e.g. chemisorption, reaction, or desorption). The MLA value is in line

10.1002/cctc.201801469

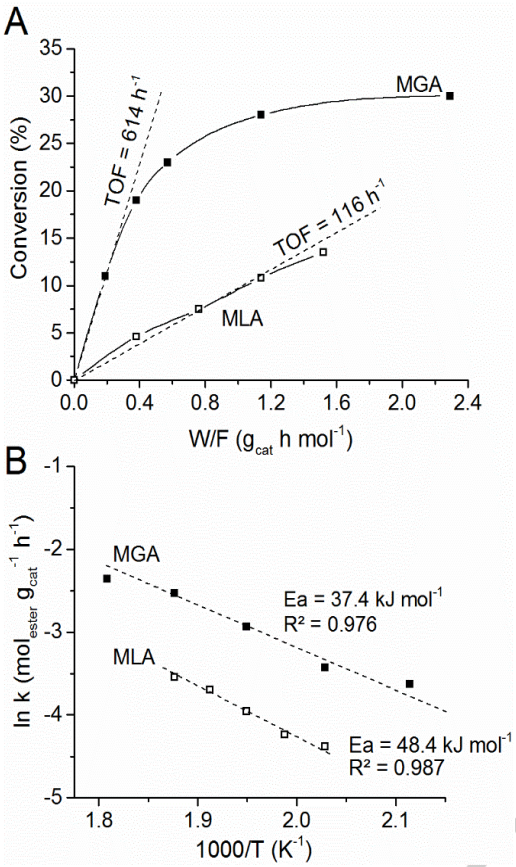


Figure 2. A) Comparison of TOF in the initial kinetic region of the conversion of MGA or MLA with a 0.4 wt% TiO_2/SiO_2 catalyst (5.6% ester in N_2, 220°C). B) Arrhenius plot for the transesterification of MGA and MLA with a TiO_2/SiO_2 catalyst (0.4 and 1 wt% TiO_2 loading for MGA and MLA respectively. This comparison is reasonable given that the E_a for MLA transesterification was shown to be relatively constant over a broad range of TiO_2-loadings.[24] Reaction conditions for conversion of (i) MLA: 5.7 % L-MLA in N_2, 220-260 °C, WHSV = 15.5 h^{-1} and (ii) MGA: 5.6 % MGA in N_2, 200-280 °C, WHSV= 26.6 h^{-1}.

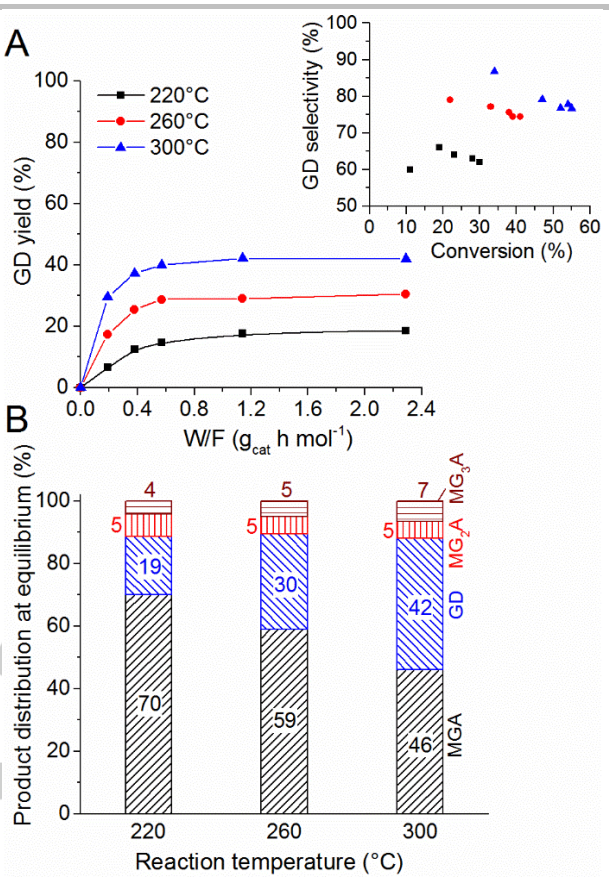


Figure 3. A) Influence of reaction temperature on GD yield, reaction kinetics and corresponding conversion-selectivity plot (inset) (5.6% MGA in N_2, 220-300°C, 0.4 wt% TiO_2/SiO_2 catalyst). B) Influence of reaction temperature on the product distribution of MGA species at equilibrium (5.6% MGA in N_2, 220-300°C, W/F = 2.3 g_{cat} h mol^{-1}, 0.4 wt% TiO_2/SiO_2 catalyst).

with those previously documented for the production of lactide from MLA (around 52-56 kJ.mol^{-1}, calculated on LD formation instead of ester conversion).[24] Despite the quite mediocre value for the apparent E_a for MGA conversion, reactions at higher temperatures have significant benefit in terms of GD formation. Higher reaction temperatures not only increase the equilibrium conversion of MGA (e.g. from 30 to 54% at 220 and 300 °C resp., see Fig. S2), but concomitantly increase the GD selectivity, potentially via differences in apparent E_a of GD vs. MG_2A and MG_3A formation or their thermodynamics. Combined, increasing temperatures thus leads to much higher GD yields (Figure 3A, and inset). Surprisingly, no degradation of GD occurred at higher reaction temperatures. This is in sharp contrast to the conversion of MLA, where the decarbonylation of LD or MLA itself[29-30] with formation of acetaldehyde was observed at reaction temperatures above 220 °C.[24] Because additional methyl groups are lacking on the 6-membered ring of GD, or on the α-carbon of MGA, no decarbonylation to acetaldehyde can take place. Other possible volatile co-products such as formaldehyde were not observed. Higher reaction temperatures can thus be used to obtain a product distribution substantially richer in GD at equilibrium conversion (Fig. 3B), indicating the overall reaction to be endothermic and reversible. At 300 °C, the desired GD yield surpasses 40%, *e.g.* at W/F values of 0.5 g_{cat} h mol^{-1} and close to 80% GD selectivity can be obtained (Fig. 3A).

At lower, non-equilibrium conversions, maximal GD selectivity of 86% can be achieved (blue triangles in selectivity-conversion inset in Fig. 3A). The main side-products, linear dimeric (MG_2A) and trimeric (MG_3A) GA esters, should have distinct boiling points and given separation from GD and MGA, can either be ring-closed (transesterification) in a recycle run (only for MG_2A) or subjected to (acid/base-catalyzed) methanolysis to recuperate to MGA.

We experimentally calculated values for the equilibrium constant of the gas phase reaction, K_p - while ignoring linear dimer or trimer formation for simplicity - based on:

$$K_p = \frac{\left(\frac{P_{GD}}{P^\circ}\right)\left(\frac{P_{MeOH}}{P^\circ}\right)^2}{\left(\frac{P_{MGA}}{P^\circ}\right)^2}$$

The partial pressure of each compound in the above formula was calculated from their corresponding molar fraction (assuming ideal gas law and thus the use of partial pressure instead of fugacity) in the vapor phase at equilibrium multiplied by the reaction pressure of 1 atm. Each partial pressure in K_p needs to be divided by a reference p° of 1 atm, to render K_p unitless. Using K_p and the following relation, $\Delta_r G$, the Gibbs free energy of reaction, can be estimated at a given temperature:

$$K_p = e^{\frac{-\Delta_r G}{RT}}$$

The equilibrium distribution of the vapor-phase with molar fractions at different reaction temperatures and thereof calculated K_p and $\Delta_r G$ values are found in Table 1.

Table 1. Composition of the vapor phase at equilibrium conversion (see Fig. 3B) at different T and corresponding equilibrium constant K_p and free energy, under the assumption that linear dimers and trimers are not formed.[a]

T (°C)	Molar fraction % in vapor phase at equilibrium					K_p ; $\Delta_r G$ (kJ mol^{-1})
	N_2	MGA	o-xyl	GD	MeOH	
220	93.4	4.0	0.2	0.8	1.6	1.4*10^{-3} ; 27.1
260	93.1	3.3	0.2	1.1	2.3	5.5*10^{-3} ; 23.0
300	92.7	2.5	0.2	1.5	3.0	2.3*10^{-2} ; 18.0

[a] 5.6% MGA in N_2, WHSV = 2.2 h^{-1}

The value at 220 °C, i.e. 27.1 kJ mol^{-1} can be compared with the value for MLA at the same temperature and ester concentration, *viz.* 18.7 kJ mol^{-1} (calculated from data in ref.[24]). This points out that cyclization via transesterification on the preferably isolated titanium sites[24, 25] is more spontaneous (thermodynamically favorable) for MLA than MGA, although both are endergonic ($\Delta_r G$ > 0). At higher temperatures, the GD forming reaction becomes more spontaneous, e.g. at 300 °C with a $\Delta_r G$ of 18 kJ mol^{-1}. Comparing the free energy for lactide formation is not possible at such high temperatures due to extensive LD-consuming side-reactions occurring during MLA conversion above 260 °C.[1] The data from Table 1 can also lead to a van 't Hoff plot using the natural logarithm of K_p (Fig. 4). This plot allows estimating the standard enthalpy and entropy (25 °C) of the gas-phase reaction based on the assumption that both are constant in the investigated T-range. The analysis confirms that the transesterification is quite endothermic ($\Delta_r H°$ ca. 83 kJ mol^{-1}), and that the reaction is favored in terms of entropy, with a $\Delta_r S°$ of about 113 J K^{-1} mol^{-1}.

The entropic gain likely derives from the fact that three gas-phase molecules (GD and two methanol) are created from two starting reagent molecules. The standard Gibbs free energy $\Delta_r G°$ of the gas-phase reaction at 298 K can thus be calculated from these values of $\Delta_r H°$ and $\Delta_r S°$ and mounts to 49.2 kJ.mol^{-1}. An exergonic reaction ($\Delta_r G$ < 0) is only to be expected at temperatures above 735 K or 462 °C. Our experimental values were compared to standard Gibbs free energies and enthalpies of reaction

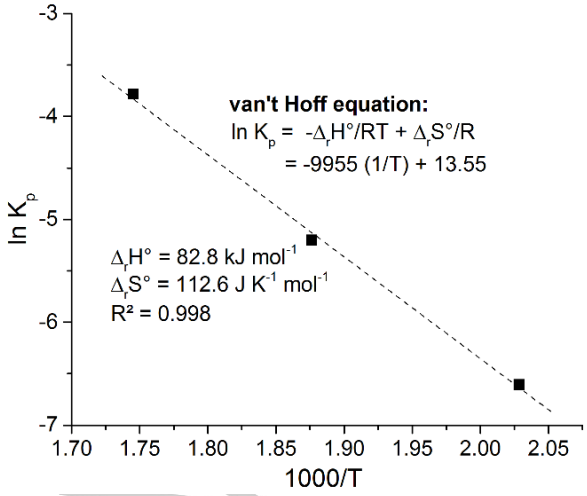
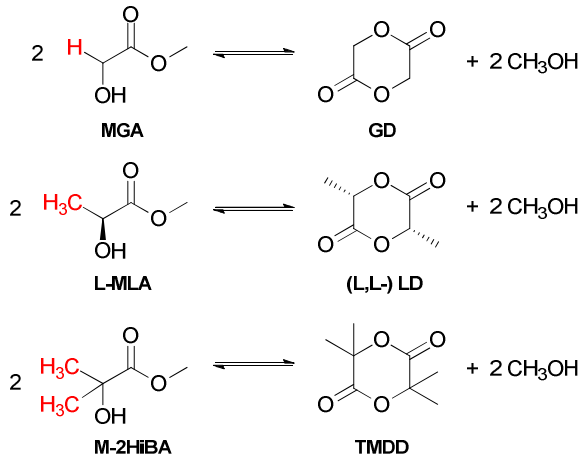


Figure 4. van 't Hoff plot for the conversion of MGA to GD based on the data in Table 1.

(subscript $\Delta_{r\text{-}f}X°$) calculated via energies of formation of the relevant components in the gas phase ($\Delta_f G°$, $\Delta_f H°$, $S°$ resp.) as found in databases or publications (see Table S2).[31-32] The thus calculated $\Delta_{r\text{-}f}H°$ value of 89.3 kJ mol^{-1} is in good agreement with our experimental measurements, while the $\Delta_{r\text{-}f}G°$ of 70.9 kJ mol^{-1} is a bit off (vs. measured 49.2 kJ mol^{-1}). This can either be due to inaccuracies in database computational values for $\Delta_f G°$ or S° of specific compounds (notably, for MGA, experimentally verified data is lacking), or, due to errors in our assumptions, i.e. the standard entropy of reaction being constant in function of T and/or the exclusion of ca. 20% of (MG_2A and MG_3A) side-products from the equilibrium calculations.

Mechanistically, the overall slower reaction with MLA compared to MGA (Fig. 2A, even though thermodynamics are more in favor of MLA cyclisation than MGA) could be due to the methyl substitution on the α-carbon, somewhat hindering the formation of cyclic ester (sterically or electronically). For MLA, the reaction to LD was assumed to run via the intermediate formation of its linear ester dimer (ML_2A), with strong indications that the latter's formation, and not the final cyclization, is the rate-limiting step.[24] For MGA, since we do not understand the rate-determining step (vide supra), care must be taken to interpret these differences. In order to gain some insight, the catalytic cyclization of methyl-2-hydroxy isobutyrate (M-2HiBA) to its corresponding cyclic ester 3,3,6,6-tetramethyl-1,4-dioxane-2,5-dione (TMDD), was studied and compared to the production of GD and LD (Scheme 2). The $\Delta_{r\text{-}f}H°$ and $\Delta_{r\text{-}f}G°$ of TMDD formation via this route, respectively estimated at 105.8 kJ mol^{-1} and 77.8 kJ mol^{-1}, confirms its similar endothermic and endergonic nature (Table S2). Contrary to MGA and MLA, the transesterification of M-2HiBA, having two methyl groups on the α-carbon, towards its cyclic ester TMDD (identified by GC-MS, Figure S3) is far more difficult. At 220 °C, nearly no M-2HiBA is converted using a 5 wt% TiO_2/SiO_2 catalyst, even at extended contact times (Figure 5A). At higher reaction temperatures, M-2HiBA conversion increases swiftly, though the selectivity towards TMDD drops significantly (Figure 5B). Instead,

a fraction of M-2HiBA dehydrates to methyl methacrylate, in addition to the formation of a volatile co-product, which was likely methyl isopropyl ether according to GC-MS analysis (Figures S4 and S5). The formation mechanism of methyl isopropyl ether is outside the scope of this work, but a decarboxylation reaction of M-2HiBA could be possible (Figure S6). Seemingly, the methyl substituents on the α-carbon reduce the reactivity of the esters for the gas-phase catalytic cyclization over TiO_2/SiO_2 catalysts, giving the following order in reactivity: MGA > MLA > M-2HiBA, but also induce a lowering of the thermal stability of the cyclic ester. While converting MGA and MLA rapidly leads to their cyclic esters GD and LD, nearly no cyclic ester can be made of M-2HiBA.



Scheme 2. Synthesis of 1,4-dioxane-2,5-dione (GD); 3,6-dimethyl-1,4-dioxane-2,5-dione (LD) and 3,3,6,6-tetramethyl-1,4-dioxane-2,5-dione (TMDD) from their respective methyl α-hydroxy esters by gas-phase transesterification.

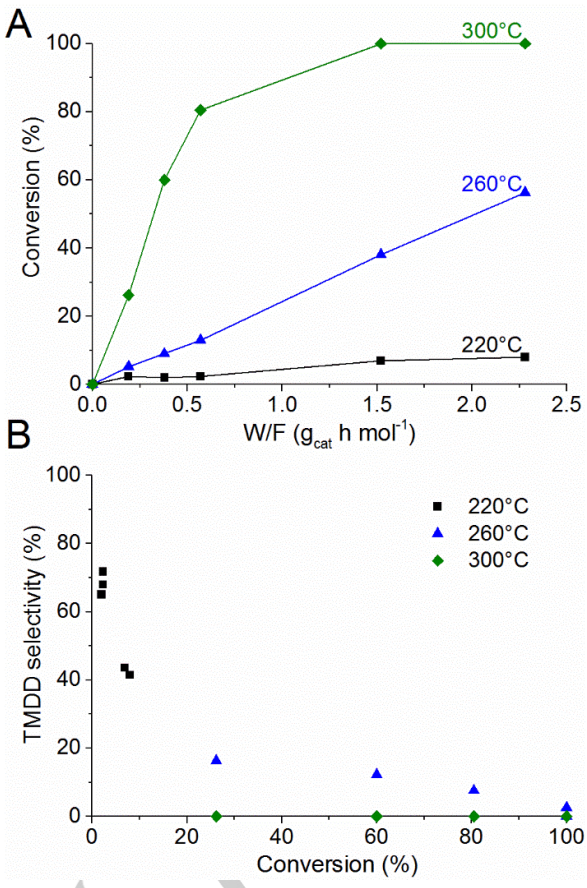


Figure 5. A) Kinetic plots of the conversion of M-2HiBA to TMDD at different reaction temperatures and B) corresponding conversion-selectivity plot with a 5 wt% TiO_2/SiO_2 catalyst. Reaction conditions: 5.7 % M-2HiBA in N_2, T = 220-300 °C, WHSV = 2.9 – 35.2 h^{-1}.

Conclusions

A new and selective gas-phase process to obtain glycolide – a valuable monomer for polyester bioplastics – is proposed, using specific TiO_2/SiO_2 catalysts identified and characterized in earlier work.[1, 25] The direct cyclization of methyl glycolate via transesterification allows selective glycolide formation at elevated temperatures. Compared to methyl lactate cyclization to lactide, precursor to the commercial bioplastic polylactic acid, the formation of glycolide is up to 6 times faster. This likely derives from the lack of steric or electronic effects imposed by additional methyl groups on the α-carbon, as corroborated by kinetic experiments with other α-OH ester substrates such as methyl-2-hydroxy-isobutyrate. Despite faster kinetics, the cyclization of methyl glycolate is thermodynamically less preferred, as one deals with larger $\Delta_r G$ values, in comparison to the cyclization of MLA. Hence, equilibrium conversions are lower for MGA than for MLA at 220 °C (± 30 vs 50 % conversion resp. at a 5.6 vol% ester concentration in N_2). However, compared to lactide the higher thermal stability of glycolide and/or methyl glycolate shows limited decarbonylation, enabling operation at higher reaction temperature, pushing not only the rate but also the thermodynamic equilibrium to the cyclic products. This way, at 300 °C, thermodynamic equilibrium is achieved at 54% MGA conversion, yielding 42% of glycolide with a selectivity up to 78%. The highest selectivity of 86% was measured at conversions below equilibrium. The other products are mainly linear methyl glycolate dimers and trimers, which should be easily separable from GD and valued from there or recycled into MGA.

Experimental Section

Materials: Supported TiO_2/SiO_2 catalysts (5 and 0.4 wt% TiO_2 loading) were prepared by incipient wetness impregnation of an amorphous, large-pore SiO_2-gel (Alfa Aesar, 287 m^2 g^{-1}, pore volume 0.91 cm^3 g^{-1}) with a suitable amount of Ti-isopropoxide dissolved in 2-propanol. For more detailed information, see our references containing identical catalyst samples (preparation and characterization) as used here[1, 25]. Basic characterization included N_2-physisorption on a Micromeritics Instruments Tristar 3000 at -196 °C, for BET and pore volume (t-plot, desorption) and elemental analysis on an Ultima ICP-AES, after acid digestion in aqua regia and HF. Methyl glycolate (>98%) and methyl-2-hydroxy isobutyrate (>99.5%) were purchased from TCI Europe, while methyl lactate (97%) and o-xylene were obtained from Acros Ogranics. **Catalytic reactions**

with methyl glycolate, methyl-2-hydroxyisobutyrate and methyl lactate were performed in a custom-built plug-flow fixed-bed reactor equipped with 6 parallel quartz reactors (length 480 mm, inner diameter of 4 mm) that can be operated one at a time. The quartz reactors were filled with 10-300 mg of catalyst (sieved fraction 250-500 µm), supported by quartz wool. If less than 300 mg was used, the catalyst bed was diluted with quartz pellets (125-250 µm) in order to get a total catalyst bed weight of 300 mg. Before reaction, the catalysts were pretreated for 1 hour (heating rate: 7 °C min^{-1}) at 300 °C under a N_2 flow of 20 ml min^{-1}. After this pretreatment, the reactor passively cooled down to the desired reaction temperature. Feed solutions typically consisted of 95 vol% α-hydroxy ester and 5 vol% o-xylene (non-interfering internal standard, similar boiling point). The solution was fed to an evaporation chamber held at 210°C with a Waters 515 HPLC pump (typically 0.004-0.006 ml min^{-1}, depending on the used ester), and mixed there with a N_2 flow (typically 20 ml min^{-1}) yielding a molar composition of 5.6/0.2/94.2 of the gas mixture (α-hydroxy ester/o-xylene/N_2). Changes in molar composition of the vapor fraction (e.g. higher concentration of esters) were realized by simultaneously changing the feed mixture and N_2 to ensure the same total molar amount of gas was used. The diluted feed gas was then passed to the reactor (220-300 °C) and over the catalyst bed. After the reaction, a make-up N_2-stream (ca. 30 ml min^{-1}) was added to dilute the products prior to analysis. Then, the gas was passed to the on-line GC for analysis. Transfer lines to and from the reactor tube were heated at 210 °C. **Analysis**: Effluent gases were analyzed by an on-line GC (HP 6890 Series) equipped with an Agilent CP-Sil-24CB capillary column and FID detector using the following temperature program: 80 °C for 3 minutes, heating to 280 °C (20 °C min^{-1}) and then isothermal for 1 minute. Product yields were calculated with o-xylene as internal standard, taking into account response factors for each compound as determined via calibration curves with commercial standards if available. All data points were taken after 2 hours on stream. Response factors of components that are not commercially available (e.g. TMDD or any of the linear dimers) were estimated based on the response factors of known, similar compounds such as lactide, glycolide and methanol. Conversion, selectivity, yield, weight hourly space velocity (WHSV), turnover frequency (TOF) and a measure for residence time (weight catalyst over mole gaseous feed, W/F) were calculated as follows:

$$\text{Conversion} = \frac{\text{moles of MLA converted}}{\text{initial amount of MLA}} (\%)$$

$$\text{Selectivity} = \frac{\text{moles of product} * \text{moles of MLA incorporated in product}}{\text{moles of MLA converted}} (\%)$$

Yield = conversion x selectivity (%)

$$\text{WHSV} = \frac{\text{mass of MLA fed to reactor}}{\text{catalyst mass} * \text{hour}} (h^{-1})$$

$$\text{TOF} = \frac{\text{moles of MLA converted}}{\text{moles of Ti on catalyst} * \text{hour}} (h^{-1})$$

$$\text{W/F} = \frac{catalyst\ mass * hour}{total\ moles\ of\ gas} (g_{cat}\ h\ mol^{-1})$$

Acknowledgements

R.D.C. acknowledges IWT (Agency for Innovation by Science and Technology, project number 131404) for financial support. M.D. thanks Research Foundation - Flanders (FWO) for funding and KU Leuven BOF for his appointment to Research Professor. E.M., B.F.S and M.D. thank the Industrial Research Fund (IOF, grant ZKC8139). A patent application was filed for this process.

Keywords: glycolide • bioplastics • transesterification • sustainable chemistry • supported catalysts

[1] P. A. Gunatillake, R. Adhikari, *Eur Cell Mater* **2003**, *5*, 1-16.
[2] L. S. Nair, C. T. Laurencin, *Prog. Polym. Sci.* **2007**, *32*, 762-798.
[3] K. Yamane, H. Sato, Y. Ichikawa, K. Sunagawa, Y. Shigaki, *Polym. J.* **2014**, *46*, 769.
[4] M. Dusselier, B. F. Sels, in *Selective Catalysis for Renewable Feedstocks and Chemicals, Topics in Current Chemistry, Vol. 353* (Ed.: K. M. Nicholas), Springer International Publishing, **2014**, pp. 85-125.
[5] K. Miltenberger, in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, **2000**.
[6] O. M. Koivistoinen, J. Kuivanen, D. Barth, H. Turkia, J.-P. Pitkänen, M. Penttilä, P. Richard, *Microbial Cell Factories* **2013**, *12*, 82-82.
[7] R. De Clercq, M. Dusselier, B. F. Sels, *Green Chem.* **2017**, *19*, 5012-5040.
[8] P. Y. Dapsens, C. Mondelli, B. T. Kusema, R. Verel, J. Perez-Ramirez, *Green Chem.* **2014**, *16*, 1176-1186.
[9] J. Zhang, X. Liu, M. Sun, X. Ma, Y. Han, *ACS Catal.* **2012**, *2*, 1698-1702.
[10] Z. Huang, F. Li, B. Chen, F. Xue, Y. Yuan, G. Chen, G. Yuan, *Green Chem.* **2011**, *13*, 3414-3422.
[11] M. Dusselier, R. De Clercq, R. Cornelis, B. F. Sels, *Catal. Today* **2017**, *279, Part 2*, 339-344.
[12] L. Feng, G. Li, Y. Yan, W. Hou, Y. Zhang, Y. Tang, *RSC Advances* **2018**, *8*, 30163-30170.
[13] G. L. Gregory, E. M. López-Vidal, A. Buchard, *Chem. Commun.* **2017**, *53*, 2198-2217.
[14] P. Van Wouwe, M. Dusselier, E. Vanleeuw, B. Sels, *ChemSusChem* **2016**, *9*, 907-921.
[15] W. W. Gerhardt, D. E. Noga, K. I. Hardcastle, A. J. Garcia, D. M. Collard, M. Weck, *Biomacromolecules* **2006**, *7*, 1735-1742.
[16] M. Dusselier, P. Van Wouwe, A. Dewaele, P. A. Jacobs, B. F. Sels, *Science* **2015**, *349*, 78-80.
[17] P. P. Upare, Y. K. Hwang, J.-S. Chang, D. W. Hwang, *Ind. Eng. Chem. Res.* **2012**, *51*, 4837-4842.
[18] O. Dechy-Cabaret, B. Martin-Vaca, D. Bourissou, *Chem. Rev.* **2004**, *104*, 6147-6176.
[19] S. Inkinen, M. Hakkarainen, A.-C. Albertsson, A. Sodergard, *Biomacromolecules* **2011**, *12*, 523-532.
[20] R. Auras, L.-T. Lim, S. E. M. Selke, H. Tsuji, Editors, *Poly(Lactic Acid): Synthesis, Structures, Properties, Processing, And Applications*, John Wiley & Sons, Inc., **2010.**
[21] R. Hagen, Patent EP2559725A1, **2011.**
[22] S. Suzuki, K. Yamane, T. Ono, K. Sunagawa, Patent EP2377858, **2008**.
[23] C. A. Thayer, H. E. Bellis, US Patent 5374743, **1994.**
[24] R. De Clercq, M. Dusselier, E. Makshina, B. F. Sels, *Angew. Chem. Int. Ed.* **2018**, *57*, 3074-3078.
[25] R. De Clercq, M. Dusselier, C. Poleunis, D. P. Debecker, L. Giebeler, S. Oswald, E. Makshina, B. F. Sels, *ACS Catal.* **2018**, *8*, 8130-8139.
[26] M. Cozzolino, M. Di Serio, R. Tesser, E. Santacesaria, *Appl. Catal., A* **2007**, *325*, 256-262.
[27] A. Muñoz-Paez, G. Munuera, in *Stud. Surf. Sci. Catal., Vol. 63* (Eds.: G. Poncelet, P. A. Jacobs, P. Grange, B. Delmon), Elsevier, **1991**, pp. 627-636.
[28] X. Gao, S. R. Bare, J. L. G. Fierro, M. A. Banares, I. E. Wachs, *The Journal of Physical Chemistry B* **1998**, *102*, 5653-5666.
[29] B. M. Murphy, M. P. Letterio, B. Xu, *ACS Catal.* **2016**, *6*, 5117-5131.
[30] B. M. Murphy, M. P. Letterio, B. Xu, *J. Catal.* **2016**, *339*, 21-30.

[31] W. V. Steele, R. D. Chirico, S. E. Knipmeyer, A. Nguyen, N. K. Smith, *J. Chem. Eng. Data* **1996**, *41*, 1285-1302.

[32] V. N. Emel'yanenko, S. P. Verevkin, E. N. Stepurko, G. N. Roganov, M. K. Georgieva, *Russ. J. Phys. Chem. A* **2010**, *84*, 1301-1308.

[33] K. Yamane, Y. Kawakami, US Patent 2004/0122240A1, **2004**.

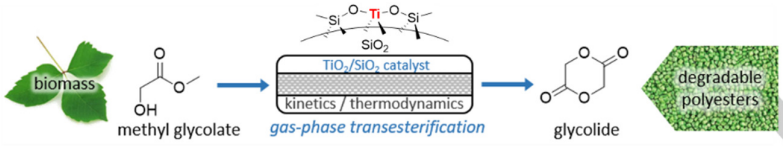
[34] S. Suzuki, K. Yamane, M. Kagoshima, M. Kikuchi, US Patent 2012/0289713 A1, **2012**.

[35] K. Yamane, Y. Ikeyama, US Patent 2016/0002197A1, **2016.**

10.1002/cctc.201801469

WILEY-VCH

FULL PAPER



A novel process to produce glycolide, the cyclic dimer of glycolic acid, is proposed, via gas-phase transesterification of methyl glycolate. Glycolide is the key building block of the biodegradable plastic polyglycolic acid.

*De Clercq R., Makshina E., Sels, B.F., Dusselier M.**

Page No. – Page No.

Catalytic Gas-Phase Cyclization of Glycolate Esters: a Novel Route Toward Glycolide-Based Bioplastics