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ARTICLE

# A versatile biobased continuous flow strategy for the production of 3-butene-1,2-diol and vinyl ethylene carbonate from erythritol

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A versatile, tunable and robust continuous flow procedure for the deoxydehydration (DODH) of biobased erythritol toward 3-butene-1,2-diol is described. The procedure relies on specific assets of multistep continuous flow processing. Detailed mechanistic and computational studies on erythritol show that either 3-butene-1,2-diol or butadiene are obtained in high selectivity and yield on demand, as a function of the DODH reagent/substrate ratio and of the process parameters. Short reaction times (1-15 min) at high temperature (225-275 °C) and moderate pressure are reported. 3-Butene-1,2-diol is then further converted downstream into its corresponding carbonate, *i.e.* 4-vinyl-1,3-dioxolan-2-one (vinyl ethylene carbonate), an important industrial building block. The carbonation step uses a supported organocatalyst, and could be directly concatenated to the first DODH step. This unprecedented procedure also relies on a unique combination of on- and off-line analytical protocols for reaction monitoring and product quantification, and offers a biobased strategy toward important industrial building blocks otherwise petrosourced.

## Introduction

The deoxydehydration (DODH) reaction is a classical procedure for the conversion of vicinal diols into olefins.[1-5] In the actual context of transitioning from petrobased to biobased chemical processes, the DODH reaction on biobased polyols attracts considerable attention.[6-16] One of the most privileged biobased polyol for DODH processes is glycerol (**1**), leading to fundamental chemical building blocks such as allyl alcohol (**2**), acrolein or acrylic acid.[7,11,14,16,17]

Most DODH procedures require a metal catalyst, typically rhenium-, molybdenum- and vanadium-based, often in the presence of a sacrificial reductant such as triphenylphospine, octanol or hydrogen (Figure 1a).[8] Alternative metal-free DODH procedures typically require a large excess of formic acid (**FA**) or triethylorthoformate (**TEOF**, Figure 1b).[11,15,16] Our group recently reported a robust process for the metal- and solvent-free DODH of glycerol using the unique assets of continuous flow processing and the reactivity of hybrid *O,O,O*-orthoesters **3**.[11] Quick exposure (1-6 min) to high temperature (250 °C) under continuous flow conditions gave high yield of **2** (up to 97%), and the DODH reaction proceeded extremely well with only one equivalent of **TEOF** and a catalytic amount of **FA** (Figure 1b).

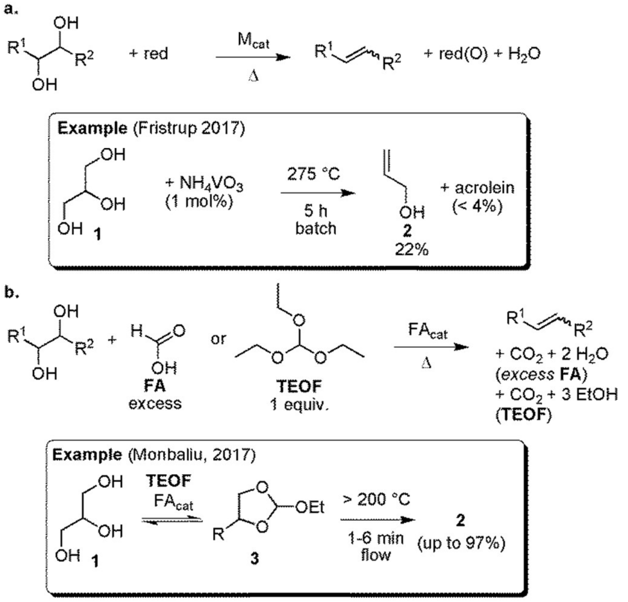

**Fig. 1** (a) Metal-catalyzed DODH[13] and (b) metal-free DODH on vicinal diols.[11]

Much less is reported on the DODH of other low value biobased polyols, although it would expand significantly the range of fundamental industrial building blocks obtained from non-fossil resources.[15,16,18] Substituted olefins, conjugated olefins, and aromatic compounds are potentially accessible from biobased polyols. Among biobased polyols, erythritol (**4**), a C4-polyol widely accessible through yeast or fungal fermentation of glucose or through the decarboxylation of pentoses, has a promising forecast in biorefineries.[18]

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Electronic Supplementary Information (ESI) available: details of the microfluidic setup, components, experimental procedures, in- and off-line analysis and computations. See DOI: 10.1039/x0xx00000x

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The DODH of **4** was scarcely reported in the literature, and typically relied either on Re/V-catalyzed or metal-free strategies with long reaction times (up to 100 h, Figure 2a). Butadiene (**5**) remained the privileged target so far, although other high valued added industrial building blocks are also accessible. 2,5-Dihydrofuran (**6a**), 3-butene-1,2-diol (**7a**) and (*E*,*Z*)-2-butene-1,4-diol ((*E*,*Z*)-7**b**) were often reported as trace compounds or, in some instances, major impurities. One of the earliest reports dates back to 1996 with Andrews' seminal work on the Re-catalyzed DODH of **4**.[19] Upon optimization, the authors reported up to 80% of **5** after 28 h at 135 °C in chlorobenzene with $PPh_3$ as reductant. Other minor side-products included **7a** and (*Z*)-**7b**.

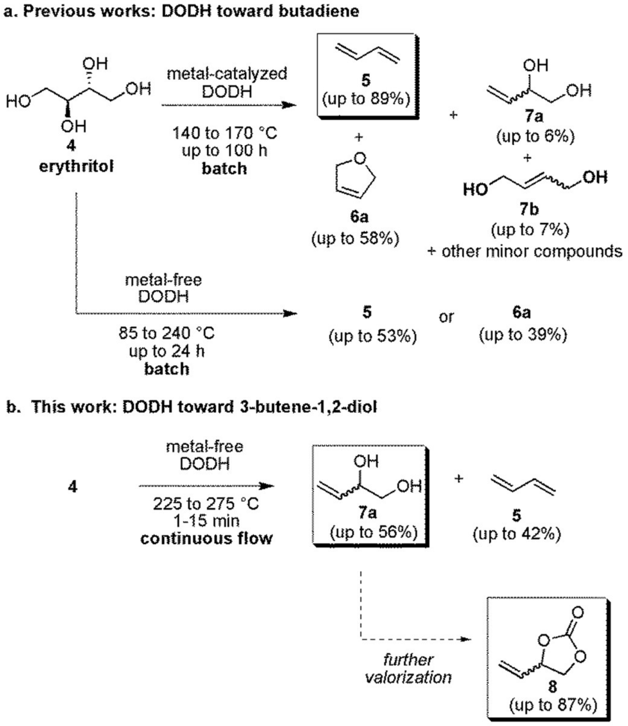

**Fig. 2** (a) Previously reported procedures for the DODH of erythritol toward butadiene and other important industrial building blocks; (b) This work: metal-free DODH of erythritol toward 3-butene-1,2-diol, and other important industrial building blocks.

In a series of papers, Toste reported an efficient methyltrioxorhenium (MTO) process for the DODH of **4** under anaerobic conditions that provided **5** in 89% yield within 1.5 h of reaction at 170 °C in octanol. The procedure was also amenable to xylitol, glucose and other polyols.[20,21] Abu-Omar reported a MTO-catalyzed DODH procedure in heptanol at 165 °C. The authors reported 58% yield in **6a** and but-2-enal (**6b**) was detected as a minor by-product.[22,23] Gebbink used a 2,4-tri(*tert*-butyl)cyclopentadienyl trioxorhenium catalyst for the DODH of **4**, and demonstrated that the distribution of products depends on the reaction conditions. Butadiene (**5**) was obtained in 67% yield after 1.5 h at 170 °C in octanol. 2,5-Dihydrofuran (**6a**), **7a** and (*Z*)-**7b** were obtained in variable amounts not exceeding 7%.[24] Nicholas and colleagues reported a Re-catalyzed DODH on **4** giving **5** in 14-60%, **6a** in 2-14% and (*Z*)-**7b** in 5-7% after 100 h of reaction at 150 – 160 °C.[25] The authors next studied a MTO-process amenable to other polyols that used hydroaromatic reductants. Erythritol (**4**) gave **5** in 43% yield after 24 h at 150 °C in 1-butanol with indoline as reductant.[26] Tomishige developed a ceria-supported Re-catalyst doped with Au nanoparticles. The catalyst was utilized on **4**, and very high yield in **5** were obtained after 60 h at 140 °C under ~80 bar of pressure. The main by-products were **7a** and (*E*)-**7b**, accounting for 8% in total.[27] De Vos reported a Mo-catalyzed DODH procedure on various diols; with erythritol, butadiene and 2,5-dihydrofuran were obtained in up to 3% (200 °C in mesitylene, 2 h) and 15% (200 °C in octanol, 18 h), respectively.[28]

A metal-free DODH procedure on biobased polyols such as **4** was first reported by Ellman using anaerobic conditions and an excess of **FA**. The procedure was optimized on simple diols and glycerol (**1**), and next attempted on **4**. 2,5-Dihydrofuran (**6a**) was obtained in 39% yield after about 24 h at 210 – 240 °C.[15] The authors then extended the procedure to quinic and shikimic acids at 225 °C in sulfolane, thus providing biobased benzoic acid.[16] A similar procedure was described for the DODH of xylitol toward 1,3-pentadiene.[29] Another paper also reported the conversion of **4** toward **5** using a tosylation/elimination sequence (~53% overall yield).[30]

We describe herein the development of a versatile metal-free DODH procedure for upgrading erythritol (**4**) under intensified continuous flow conditions (Figure 1b). The procedure relies on specific assets of multistep continuous flow processing.[31] This process is unique since it reports for the first time the production of high value-added 3-butene-1,2-diol (**7a**) in good yield. The procedure is versatile and convenient, and, unlike procedures of the prior Art, a simple adjustment of the DODH reagent/substrate ratio, as well of the reaction medium enables to shift the selectivity toward other valuable chemicals, such as butadiene (**5**), 2,5-dihydrofuran (**6a**) and but-2-enal (**6b**). Unprecedented short reaction times (1-15 min) at high temperature (225-275 °C) and moderate pressure (6.9 bar) are reported. The reaction output critically depends on the nature of the reaction medium: the formation of 3-butene-1,2-diol (**7a**) and butadiene (**5**) is favored in DMSO, while in [EMIM][ES], anhydroerythritol (**anh-4**), 2,5-dihydrofuran (**6a**) and but-2-enal (**6b**) become the major products. Computations and mechanistic investigations on model compounds give insight on product filiation. Eventually, 3-butene-1,2-diol (**7a**) is converted in high yield and selectivity into 4-vinyl-1,3-dioxolan-2-one (vinyl ethylene carbonate, **8**) using an organocatalyzed continuous flow process (Figure 1b). The procedure includes a unique combination of on- and off-line analytical procedure for reaction monitoring and product quantification, and offers a biobased strategy toward important industrial building blocks otherwise petrosourced.

## Experimental section

### General information

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The DODH reactor effluent was sampled at steady state and analyzed off-line by $^1H$ NMR, by GC/MS or by GC/FID. $^1H$ NMR was conducted on a 400 MHz Bruker Avance spectrometer in $d_6$-acetone or in $d_4$-methanol with mesitylene as an internal standard (Supporting Information). The chemical shifts are reported in ppm relative to TMS as internal standard or to solvent residual peak. Gas chromatography coupled with ion trap mass spectrometry (GC/MS) was performed on the volatile fraction of the reactor effluent collected in air-tight sealed vials. Headspace-Solid Phase Micro Extraction technique (HS-SPME) with Carboxen-PDMS fibers (Supelco, PA, US) was carried out for the analysis of the volatile fraction (Supporting Information). Some components of the liquid fraction (residual erythritol and anhydroerythritol) were analysed after derivatization. Gas Chromatography was performed with a Trace-GC 2000 (Thermo-Scientific, Waltham, MA, USA). Mass spectrometric detection was performed with a PolarisQ ion-trap (Thermo-Scientific, Waltham, MA, USA). Gas chromatography coupled with flame ionization detection (GC/FID) was performed to monitor the carbonation reaction of 3-butene-1,2-diol. External calibration curves established with pure commercial compounds were used to calculate conversions and yields. Selectivity is defined as the ratio between the yield and the conversion. On-line reaction monitoring was carried out by IR spectrometry, using a FlowIR$^{TM}$ from Mettler-Toledo (Supporting Information). Glycerol, erythritol, formic acid (FA), triethyl orthoformate (**TEOF**), 3-butene-1,2-diol, (*E*)-and (*Z*)-2-butene-1,4-diol, 2,5-dihydrofuran, but-2-enal, furan, anhydroerythritol, butadiene, *cis*- and *trans*-cyclohexane-1,2-diol, dimethyl sulfoxide (DMSO), 1-ethyl-3-methylimidazolium ethyl sulfate ([EMIM][ES]), EMIM acetate ([EMIM][Ac]), EMIM trifluoroacetate ([EMIM][TFA]), EMIM dicyanamide ([EMIM][DCA]), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), polymer-supported DBU (PS-DBU), dimethyl carbonate (DMC) and vinyl ethylene carbonate were obtained from commercial sources, and used as received.

### Experimental setup

The reactor for the DODH reaction (Figures 3 and 10) featured a modular continuous flow assembly consisting of plug-and-play thermoregulated stainless-steel (SS) coils (1.58 mm outer diameter, 500 µm internal diameter) equipped with SS connectors, ferrules and unions (Valco). Feed solutions were handled with ThalesNano Micro HPLC pumps, equipped with 316 SS parts and check valves (IDEX/Upchurch Scientific), or with high force Chemyx Fusion 6000 syringe pumps equipped with SS syringes and Dupont Kalrez O-rings. Downstream pressure was regulated with a spring-loaded backpressure regulator (6.9 bar, IDEX/Upchurch Scientific) embedded in a SS holder. Feed and collections lines consisted of PEEK tubing (1.58 mm outer diameter, 750 µm internal diameter) equipped with PEEK/ETFE connectors and ferrules (IDEX/Upchurch Scientific).

The reactor for the homogeneous carbonation reaction (Figure 8) was constructed from high purity PFA capillary coil (1/16” outer diameter, 750 µm internal diameter) equipped with Super Flangeless nuts and ferrules. The reactor for the heterogeneous carbonation reaction (Figures 9 and 10) featured a modular continuous flow assembly consisting of plug-and-play thermoregulated stainless-steel (SS) coils (1.58 mm outer diameter, 500 µm internal diameter) equipped with SS connectors, ferrules and unions (Valco), and a SS packed-bed column (10 cm × 7 mm o.d. × 3.5 mm i.d.). Feed and collections lines consisted of PEEK tubing (1.58 mm outer diameter, 750 µm internal diameter) equipped with PEEK/ETFE connectors and ferrules (IDEX/Upchurch Scientific). Feed solutions were handled with ThalesNano Micro HPLC pumps, equipped with 316 SS parts and check valves (IDEX/Upchurch Scientific), or with high force Chemyx Fusion 6000 syringe pumps equipped with SS syringes and Dupont Kalrez O-rings. Downstream pressure was regulated with a dome-type backpressure regulator (11 bar, Zaiput Flow Technologies). An on-line IR spectrometer was inserted downstream to enable real-time reaction monitoring.

### Computational study

Computations were performed at the MP2/6-31+G** level of theory with the Gaussian 09 package of programs (Revision D.01).[32] Computations were run with implicit solvent (PCM, $\varepsilon$ = 46.826, DMSO). Stationary points were optimized with gradient techniques using very tight optimization convergence criteria. Transition states were localized using the Newton-Raphson algorithm, and the nature of the stationary points was determined by analysis of the Hessian matrix. Activation and reaction energies were obtained from the thermochemical calculations (298.15 K, 1 atm). Intrinsic reaction coordinate (IRC) calculations were performed on each transition state.

### Typical runs

**DODH on erythritol (4) toward butadiene (5).** A feed solution (500 mL total volume) of erythritol (**4**) was prepared by mixing **4** (2.4 M in DMSO), 2 equiv. of triethyl orthoformate, 0.1 equiv. of formic acid in DMSO, and connected to a HPLC pump set at 0.2 mL min$^{-1}$. The reaction mixture was reacted for 6 min at 225 °C under 6.9 bar of counter-pressure (Figure 3). The outlet of the reaction coil was connected to a cooling SS capillary loop (2 min residence time). The reactor effluent was collected and analyzed (42% yield in butadiene, see Figures 4-6).

**DODH on erythritol (4) toward 3-butene-1,2-diol (7a).** A feed solution (500 mL total volume) of erythritol (**4**) was prepared by mixing **4** (2.4 M in DMSO), 1 equiv. of triethyl orthoformate, 0.1 equiv. of formic acid in DMSO, and connected to a HPLC pump set at 1.25 mL min$^{-1}$. The reaction mixture was reacted for 1 min at 250 °C under 6.9 bar of counter-pressure (Figure 3). The outlet of the reaction coil was connected to a cooling SS capillary loop (2 min residence time). The reactor effluent was collected and analyzed (56% yield in 3-butene-1,2-diol, see Figures 4-6).

**DODH on erythritol (4) toward 2,5-dihydrofuran (6a).** A feed solution (500 mL total volume) of erythritol (**4**) was prepared by mixing **4** (3.1 M in [EMIM][ES]), 1 equiv. of triethyl orthoformate, 0.1 equiv. of formic acid in [EMIM][ES], and loaded in a syringe

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pump set at 80 µL min$^{-1}$. The reaction mixture was reacted for 15 min at 275 °C under 6.9 bar of counter-pressure (Figure 3). The outlet of the reaction coil was connected to a cooling SS capillary loop (2 min residence time). The reactor effluent was collected and analyzed (23% yield in 2,5-dihydrofuran, see Figures 4-6).

**DODH on erythritol (4) toward but-2-enal (6b).** A feed solution (500 mL total volume) of erythritol (**4**) was prepared by mixing **4** (3.1 M in [EMIM][ES]), 2 equiv. of triethyl orthoformate, 0.1 equiv. of formic acid in [EMIM][ES], and loaded in a syringe pump set at 80 µL min$^{-1}$. The reaction mixture was reacted for 15 min at 275 °C under 6.9 bar of counter-pressure (Figure 3). The outlet of the reaction coil was connected to a cooling SS capillary loop (2 min residence time). The reactor effluent was collected and analyzed (35% yield in but-2-enal, see Figures 4-6).

**Preparation of 4-vinyl-1,3-dioxolan-2-one (vinyl ethylene carbonate, 8) from 3-butene-1,2-diol (7a) under homogeneous conditions**. The syringe pump used to deliver neat 3-butene-1,2-diol (**7a**) was set to 31.2 µL min$^{-1}$ (1 equiv.) and the syringe pump used to deliver the 0.0791 M solution of DBU in DMC was set to 93.8 µL min$^{-1}$ (2 mol% DBU, 3 equiv. DMC). Both streams were mixed in a PEEK T-mixer using Super Flangeless nuts and ferrules. The homogeneous mixture entered a PFA capillary coil (1/16" o.d., 1/32" i.d., 0.5 mL internal volume) heated at 160 °C. The outlet of the capillary coil reactor was connected to a dome-type back-pressure regulator set at 11 bar (Figure 8). After equilibration, the reactor effluent was collected, quenched with saturated aqueous $NH_4Cl$, diluted with EtOH, and analyzed by GC/FID (69% yield in vinyl ethylene carbonate, see Table 2).

**Preparation of 4-vinyl-1,3-dioxolan-2-one (vinyl ethylene carbonate, 8) from 3-butene-1,2-diol (7a) with polymer-supported DBU**. The HPLC pump used to deliver the solution of 3-butene-1,2-diol (**7a**) in DMSO was set at 0.1 mL min$^{-1}$ (1 equiv.) and the HPLC pump used to deliver neat DMC was set at 0.04 mL min$^{-1}$ (3 equiv.). Both streams were mixed in a PEEK T-mixer using Super Flangeless nuts and ferrules. The mixture was preheated in a SS coil (1.58 mm o.d., 500 µm i.d., 0.65 mL internal volume), and then reacted in a SS column (10 cm × 7 mm o.d. × 3.5 mm i.d.), both heated at 160 °C. The SS column was loaded with 200 mg of PS-DBU (1.5-2.5 mmol g$^{-1}$ loading) dispersed with 1 g of glass beads (425-600 µm). A dome-type back-pressure regulator was connected downstream the reactor and set at 11 bar (Figure 9). After equilibration, the reactor effluent was collected, diluted with EtOH and analyzed by GC/FID (87% yield in vinyl ethylene carbonate, see Figure 9).

**Preparation of 4-vinyl-1,3-dioxolan-2-one (vinyl ethylene carbonate, 8) from erythritol (4).** A feed solution (500 mL total volume) of erythritol (**4**) was prepared by mixing **4** (2.4 M in DMSO), 1 equiv. of triethyl orthoformate, 0.1 equiv. of formic acid in DMSO, and connected to a HPLC pump set at 1.25 mL min$^{-1}$. The reaction mixture was reacted for 1 min at 250 °C under 6.9 bar of counter-pressure (Figure 10). The outlet of the reaction coil was connected to a cooling SS capillary loop (2 min residence time). The effluent of the DODH reactor was collected in a surge under sonication, and utilized without additional treatment for the preparation of vinyl ethylene carbonate (**8**). The crude effluent of the DODH reactor was delivered with an HPLC pump set at 0.1 mL min$^{-1}$ (1 equiv. of **7a**). Neat DMC was delivered with an HPLC pump set at 0.4 mL min$^{-1}$ (5.5 equiv.) and both streams were mixed in a PEEK T-mixer using Super Flangeless nuts and ferrules. The mixture was preheated in a SS coil (1.58 mm o.d., 500 µm i.d., 0.65 mL internal volume), and then reacted in a SS column (10 cm × 7 mm o.d. × 3.5 mm i.d.), both heated at 160 °C. The SS column was loaded with 200 mg of PS-DBU (1.5-2.5 mmol g$^{-1}$ loading) dispersed with 1 g of glass beads (425-600 µm). The reactor effluents were conveyed through an on-line IR spectrometer for reaction monitoring. A dome-type back-pressure regulator was connected downstream and set at 11 bar. The reactor effluents were sampled, diluted with EtOH and analyzed by GC/FID to complement IR data.

## Results

Unlike glycerol (**1**), erythritol (**4**) and other biobased polyols are solids. The strategy envisioned for the continuous flow DODH of **1** reported previously was therefore not directly transposable to other biobased substrates.[11] The first challenge was to identify a suitable solvent that would enable straightforward implementation under flow conditions while keeping the environmental footprint acceptable. The solvent of choice had to meet important selection criteria: (a) it must ensure high solubility of the substrates (> 1 M) for high throughput, (b) it must to be thermally (for short exposure times at > 200 °C) and chemically stable and (c) it must ideally be considered as a green solvent, or it must at least have a low toxicity profile. Additionally, its viscosity (typ. $\eta$ = << 1 N s m$^{-2}$ at 22 °C) must not preclude simple and straightforward pumping for long operation times. With these important criteria in mind, we screened a large variety of solvents including lower alcohols, DMSO, sulfolane, propylene carbonate, acetic acid and ionic liquids based on the ethyl methylimidazolium cation (EMIM) ([EMIM][Ac], [EMIM][TFA], [EMIM][DCA] and [EMIM][ES]). Although most of these solvents met the low viscosity requirement and at least two of the selection criteria above-mentioned, only DMSO, [EMIM][DCA] and [EMIM][ES] gave full satisfaction. For instance, erythritol **4** was soluble up to 7 M in DMSO in the presence of **TEOF** (2 equiv.) and **FA** (10 mol%), without affecting processability under continuous flow conditions.

The next step was to assess the DODH on a model compound in the above-selected solvents. We selected **1**, since its DODH reaction toward allyl alcohol (**2**) was a well-understood process, and performed the reaction under continuous flow conditions with 1 equiv. of **TEOF** and 10 mol% of **FA** as catalyst. The concentration of **1** in the feed was set at 2.4 M and 3.1 M in DMSO and [EMIM][ES], respectively, and the reaction proceeded as expected (74 and 72% yield, 97 and >93% selectivity, respectively). The reaction failed in [EMIM][DCA] (no conversion). With a refined selection of solvents, the optimization of the DODH on **4** commenced with a thorough screening of process parameters including temperature, pressure, residence time, reagent ratio and solvent nature (Figure 3). The overall progress of the reaction was monitored off-line, and the results indicated that the no

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reaction occurred below 175 °C, and that significant DODH occurred between 225 and 275 °C. The reactor effluent was collected at steady state, and processed for analysis. The volatile fraction (b.p. < 70 °C, including butadiene, 2,5-dihydrofuran and furan) was collected in air-tight sealed vials downstream through automated valves, and was analyzed by by HS-SPME/GC-MS. The liquid fraction (b.p. > 70 °C, including 3-butene-1,2-diol, 2-butene-1,4-diol, anhydroerythritol and but-2-enal) was collected after cooling and analyzed by high-field $^1$H NMR or GC/MS after derivatization (Supporting Information).

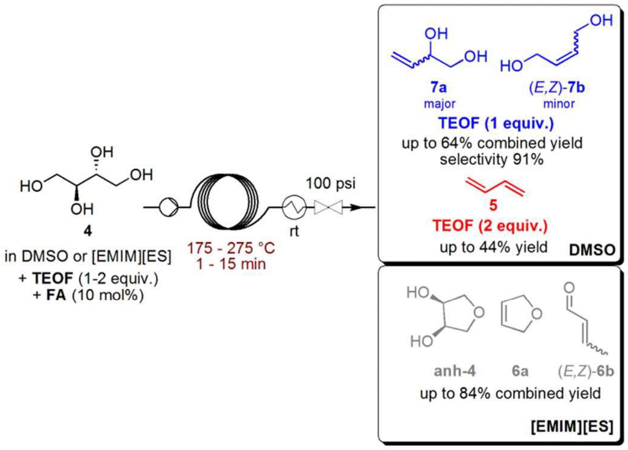

**Fig. 3** Simplified setup for the DODH of erythritol (**4**) under continuous flow conditions (major products are shown).

The first results were collected at 6 min of residence time with 1 or 2 equiv. of **TEOF** with increasing process temperatures (Figure 4) in DMSO. The production of butadiene (**5**) increased with the excess of **TEOF**, and reached a maximum at 225 °C with about 42%, and then decreased. Under these conditions, the volatile fraction contained almost exclusively **5**; 2,5-dihydrofuran (**6a**) and furan (**6c**) were barely detected (Supporting Information).

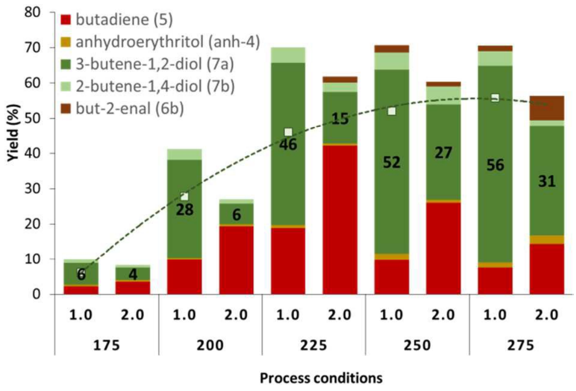

**Fig. 4** Composition of the reactor effluent (volatile and liquid fractions, yield in %) for 6 min of residence time using 1 or 2 equiv. of **TEOF** at temperatures ranging from 175 to 275 °C in DMSO. The dotted line summarizes the evolution of the yield for 3-butene-1,2-diol (**7a**) with 1 equiv. of **TEOF**. The X axis shows relative amount or **TEOF** (1 or 2 equiv.) and temperature (175 - 275 °C).

With a stoichiometric amount of **TEOF**, the amount of 3-butene-1,2-diol (**7a**) increased progressively and plateaued at 275 °C with 56% yield (Figure 4). 2-Butene-1,4-diol (**7b**) remained below 6%, with a maximum at 275 °C with 1 equiv. of **TEOF**. Anhydroerythritol (**anh-4**) reached a maximum of 2% at 275 °C with 2 equiv. of **TEOF**. At higher temperature, significant charring occurred, and solid material accumulated in the reactor, giving inconsistent results and hence clogging the reactor. The conversion, determined by GC/MS from the residual amount of **4** after derivatization of the crude reactor effluent increased up to 90% at 275 °C with 1 equiv. **TEOF**, while the conversion was complete with 2 equiv. **TEOF** (Supporting Information).

Further optimization was considered with the residence time and the amount of **TEOF** (Figure 5). Two additional residence times were considered, namely, 1 and 15 min at 225, 250 and 275 °C with 1 or 2 equiv. **TEOF**. For the 225 - 275 °C range of temperature, it is clear that the amount of diene **5** correlated with the excess of **TEOF**. A maximum of 42% yield in butadiene was obtained at 250 °C with 2 equiv. of **TEOF** and the longest residence time (15 min). Butadiene (**5**) appears as a competitive side-product for the production of 3-butene-1,2-diol (**7a**), and the best condition for reducing its formation involved quick exposure (1 min) of **4** at high temperature (250 or 275 °C) in the presence of 1 equiv. of **TEOF**. Under such conditions, the yield of **5** remained under 10%, and the yield of **7a** reached up to 56%. Isomeric 2-butene-1,4-diol (**7b**) was formed in 1-6%, with the largest amounts being formed with 1 equiv. of **TEOF**.

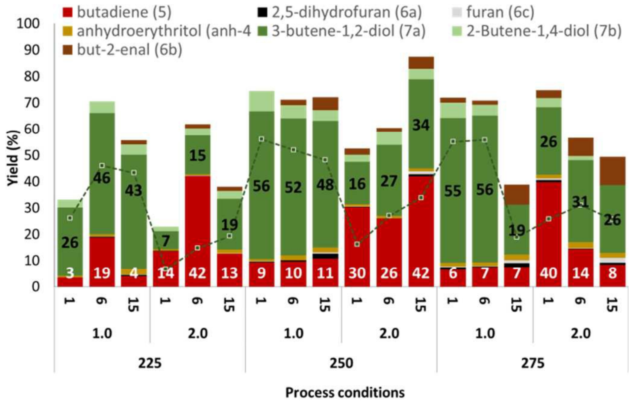

**Fig. 5** Composition of the reactor effluent (volatile and liquid fractions, yield in %) for residence times ranging from 1 to 15 min, using 1 or 2 equiv. of **TEOF** at temperatures ranging from 225 to 275 °C in DMSO. The dotted line summarizes the evolution of the yield for 3-butene-1,2-diol (**7a**). Yields are given for butadiene (**5**, white) and for 3-butene-1,2-diol (**7a**, black). The X axis shows the process conditions: residence time (1, 6, 15 min), relative amount or **TEOF** (1 or 2 equiv.) and temperature (225, 250 and 275 °C) in DMSO.

The formation of but-2-enal (**6b**) became significant at 250 °C. The residence time had also an impact on its formation, reaching a maximum of 11% at 275 °C with 2 equiv. of **TEOF** within 15 min of residence time (1.8% within 1 min of

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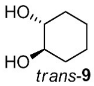
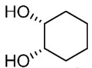
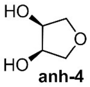
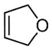
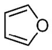
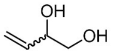
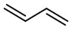
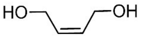
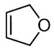
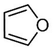
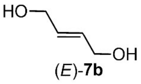
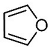
**Table 1.** DODH under continuous flow conditions on model substrates (1 equiv. **TEOF**, 10 mol% **FA**, 250 °C, 100 psi)

| Entry | Substrate | Product(s) (%) |
|---|---|---|
| 1[a] |  *trans*-**9** | no DODH products |
| 2[a] |  *cis*-**9** |  (61)<br>**10** |
| 3[b] |  **anh-4** |  (62)  (1)<br>**6a** **6c** |
| 4[a,c] |  **7a** |  (18)<br>**5** |
| 5[a] |  (*Z*)-**7b** |  (1)  (1)<br>**6a** **6c** |
| 6[a,c] |  (*E*)-**7b** |  (34)  (3)<br>**6b** (50:50 *E*/*Z*) **6c** |

[a] in DMSO, 1 min; [b] in [EMIM][ES], 6 min; [c] the corresponding formates were detected in 5-8%

residence time). Anydroerythritol (**anh-4**) was detected in 1-2%, irrespective of the process conditions. A larger excess of **TEOF** (3 equiv.) did not improve the selectivity or the yield. Concentrations up to 7 M in DMSO were achievable, but it significantly affected the reaction, and the yield dropped to 13% and 16% for **7a** and **5**, respectively (15% and 42%, respectively, with 2.4 M in DMSO).

Analysis of the volatile fraction (Fig. 6) indicates that 2,5-dihydrofuran (**6a**) and furan (**6c**) are not produced below 225 °C in significant amounts (> 1%). Generally, the relative amount of **6a** and **6c** increases with the residence time and with the temperature. At 225 and 250 °C with 2 equiv. of **TEOF**, the volatile fraction mostly contains **5**, while at 275 °C, the relative amount of **6a** and **6c** increases (3% combined yield).

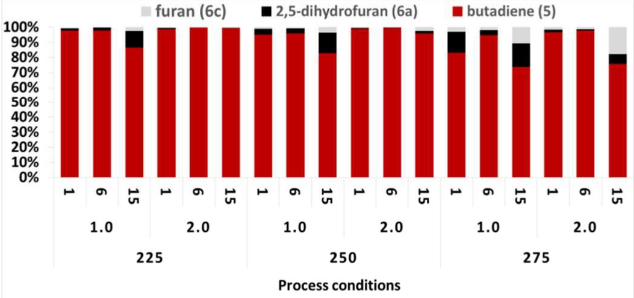


**Fig. 6** Fractional composition of the volatile effluent (relative amounts in %). The X axis shows the process conditions: residence time (1, 6, 15 min), relative amount of **TEOF** (1 or 2 equiv.) and temperature (225, 250 and 275 °C) in DMSO.

When the DODH reaction was attempted on **4** in [EMIM][ES] (3.1 M) within the 175 – 275 °C range, the product profile changed drastically. 3-Butene-1,2-diol (**7a**) or 2-butene-1,4-diol (**7b**) were not anymore detected, irrespective of the temperature and residence time. The production of diene **5** was suppressed for all experiments with 1 equiv. of **TEOF**, although its production increased linearly from 225 °C with 2 equiv. of **TEOF** to reach 25% yield at 275 °C with a residence time of 15 min. In [EMIM][ES], it turned out that the main products of the process included anhydroerythritol (**anh-4**, up to 27%), 2,5-dihydrofuran (**6a**, up to 23%) and but-2-enal (**6b**, up to 35%). The amount of **6a** increased linearly with 1 or 2 equiv. **TEOF** from 225 to 275 °C with 15 min of residence time, although the yield was much higher with 1 equiv. **TEOF** (23%) (Supporting Information). Larger amounts of **6b** were observed from 200 °C with 2 equiv. of **TEOF** and the longest residence time (15 min).

To further understand product filiations, several control experiments were carried out both in DMSO and [EMIM][ES] with model substrates including commercial *cis*- and *trans*-cyclohexanediol, anhydroerytritol (**anh-4**), 3-butene-1,2-diol (**7a**), as well as *E*- and *Z*-2-butene-1,4-diol (*E*,*Z*-**7b**) under DODH conditions (Table 1). A preliminary requirement for vicinal diols to undergo DODH is a relative *cis* configuration. It is thus expected, as confirmed by computations at the MP2 level of theory (see below) that anhydroerythritol (**anh-4**) forms 2,5-dihydrofuran (**6a**) under such conditions, while anhydrothreitol does not. Cyclohexanediol (*cis*- and *trans*-**9**) was utilized as a model compound. Under DODH conditions (1 min, 250 °C), cyclohexene (**10**) was not formed starting from *trans*-**9**, while 61% of **10** was observed from *cis*-**9** under the same conditions, in agreement with previously reported data.[2,3,15]

Compound **anh-4** gave **6a** in 57-62% in DMSO and [EMIM][ES], respectively, and furan (**6c**) was observed (1%) in both cases within 6 min at 250 °C. Compound **anh-4** is obtained from **4** by an acid-catalyzed cyclodehydration, which appears to be favored in [EMIM][ES]. Further aromatization proceeds at high temperature, leading to **6c**. The direct cyclodehydration of (*Z*)-2-butene-1,4-diol ((*Z*)-**7b**) toward **6a** was reported in the presence of Re-based catalysts,[26] although it is less likely to occur under our conditions. Control experiments on **7a**, (*Z*)-**7b** *and* (*E*)-**7b** further completed the picture. Under DODH conditions (250 °C, 1 min, 1 equiv. of **TEOF**), **7a** gave up to 18% of diene **5**, and less than 5% of its formate esters. (*Z*)-**7b** only gave very low amounts of diene **5** (1%), **6a** (2%) and the corresponding mono- and diformates (7%). Under the same conditions, diol (*E*)-**7b** gave 34% of but-2-enal (**6b**, 50:50 *E*/*Z*), and 3% of furan (**6c**), while **5** was not detected. These results clearly emphasize that the formation of **5** under these conditions proceeds mostly through a 1,2-DODH process from **7a**, and thus excludes the involvement of 1,4-DODH process from (*E*,*Z*)-**7b**.[18]

Based upon our preliminary reports on the mechanism of DODH on glycerol and derivatives, computations at the MP2/6-31+G** level were carried out to gain further insight on the selectivity and mechanism of the reaction. We assumed that hybrid orthoesters of type **3a** from erythritol (**4**) behave

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similarly than those derived from **1,** and form transient dioxolidin-2-ylidene carbenoid species under the reported conditions. Such carbenoid species next undergo a concerted fragmentation with concomitant $CO_2$ extrusion and formation of an alkene (Figure 7, Supporting Information). The formation of hybrid orthoesters **3a** from polyols and alkylorthoformates in the presence of an acid catalyst is a dynamic and complex process[33] that is simplified here for rationalizing the DODH reaction. The experimental selectivity of the reaction can be correlated with the calculated activation parameters for the corresponding transition states. As a reference, we started first with the DODH of **1** in DMSO, yielding allyl alcohol (**2**) and $CO_2$, which gave a Gibbs free activation energy ($\Delta G^{\neq}$) of 10.7 kcal $mol^{-1}$. The DODH on *cis*-**9** proceeded with $\Delta G^{\neq}$ of 11.1 kcal $mol^{-1}$, while on *trans*-**9**, $CO_2$ extrusion costed an additional 30.5 kcal $mol^{-1}$ to form alkene **10**. The calculated $\Delta G^{\neq}$ for **anh-4** was of 11.6 kcal $mol^{-1}$, and no transition state structures were isolable for its *trans* isomer.

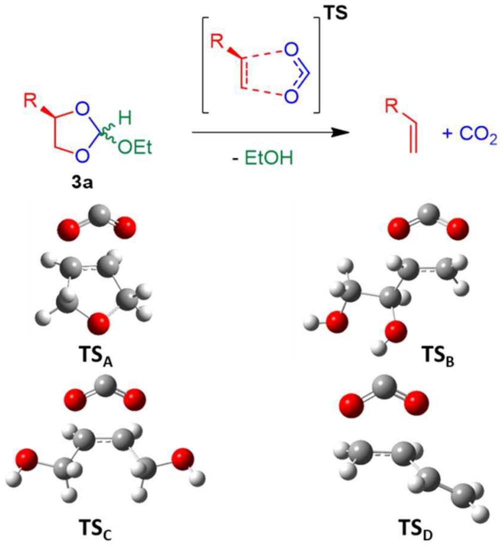
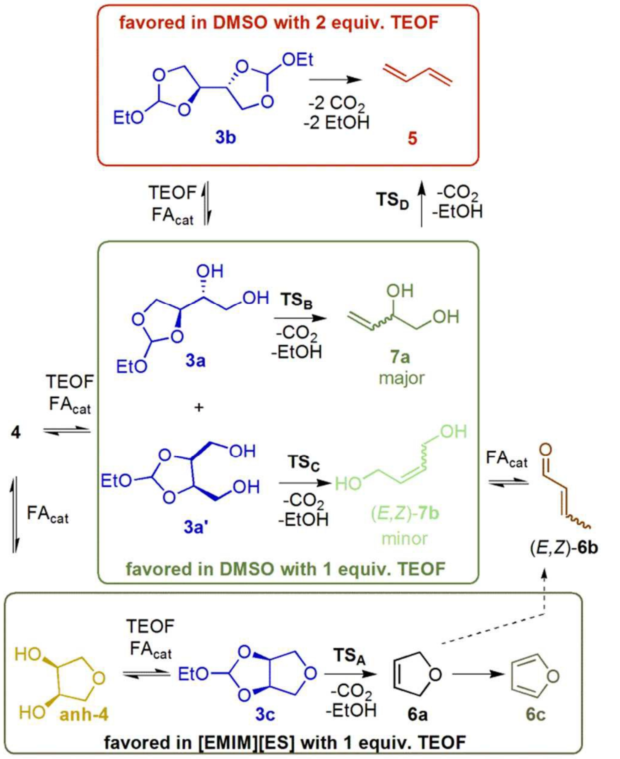


**Fig. 7** Structures of representative transition states **TS$_{A-D}$** involved in the formation of 2,5-dihydrofuran (**TS$_A$**, from anhydroerythritol), 3-butene-1,2-diol (**TS$_B$**, from erythritol), *cis*-2-butene-1,4-diol (**TS$_C$**, from erythritol) and butadiene (**TS$_D$**, from 3-butene-1,2-diol) through thermal extrusion of EtOH and $CO_2$ from the corresponding hybrid ethyl orthoesters **3**.

These results therefore confirm the requirement for vicinal diols to be locked in a relative *cis* configuration. Starting now from **4**, from which two isomeric hybrid orthoesters **3a,a'**, and hence two isomeric dioxolidin-2-ylidene carbenoids, are likely to form (Supporting Information), thus yielding either **7a** or (*Z*)-**7b**. The formation of diol **7a** is associated with a free energy of activation of 10.2 kcal $mol^{-1}$, while the formation of (*Z*)-**7b** through an isomeric TS is less favorable with a $\Delta\Delta G^{\neq}$ = 3.1 kcal $mol^{-1}$. These results emphasize that the selectivity might be rationalized by the $\Delta\Delta G^{\neq}$ between the two isomeric pathways leading to **7a** or (*Z*)-**7b** through $CO_2$ extrusion, thus explaining the slower formation of the internal olefin (*Z*)-**7b**.[26] An additional DODH on apical olefin **7a** leading to the formation of diene **5** comes with a significantly lower $\Delta G^{\neq}$ (7.8 kcal $mol^{-1}$) that reflects the emergence of a stereoelectronic effect further stabilizing the corresponding TS structure.

A clear filiation of the major products observed upon DODH of **4** arose from these considerations (Scheme 1). In DMSO, the output of the DODH on **4** depends essentially, at the optimum temperature of 250 °C, on the excess of **TEOF** and of the reaction medium: with 1 equiv. **TEOF**, apical diol **7a** is the main product, while with 2 equiv. **TEOF**, the formation of diene **5** becomes significant. The formation of aldehyde **6b** at 250 °C in DMSO is most likely related to a catalytic dehydration of internal diol (*E*)-**7b**.[34] Diol (*E*)-**7b** is formed as a minor product at high temperature experiments in DMSO, most likely through an isomerization of (*Z*)-**7b**. Although it is difficult to exclude the contribution of hybrid bisorthoester **3b** to the formation of **5**, it is clear that the emergence of favorable stereoelectronic effects in **TS$_D$** would contribute significantly to the formation of diene **5** from apical diol **7a**. In [EMIM][ES], the acid-catalyzed cyclodehydration of **4** toward **anh-4** becomes competitive.[18] Compound **anh-4** next reacts with **TEOF** at high temperature to yield **6a** upon DODH, rather than **7a,b** or **5**. It is worth mentioning that isomeric 2,3-dihydrofuran was never observed during these experiments. The formation of aldehyde **6b** was reported upon metal-catalyzed DODH on erythritol, although its formation remained below 10%.[22] Here, the formation of much larger amounts of **6b** in [EMIM][ES] is most likely related to the thermal isomerisation of **6a**, rather than the catalytic dehydration of diol (*E*)-**7b** since the latter was not detected under these conditions.[34]



**Scheme 1** Rationalization of the filiation between the various DODH products. Only major products were considered.

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Next, we envisioned the direct preparation of 4-vinyl-1,3-dioxolan-2-one (**8**, vinyl ethylene carbonate) from crude 3-butene-1,2-diol (**7a**) under continuous flow conditions. Carbonate **8** is an important commodity chemical that has numerous applications, notably for the synthesis of polymers[35-37] and as additive in Li-ion batteries.[38,39] It is typically manufactured by the addition of $CO_2$ to 1,3-butadiene monoxide. The methodology was first patented in 1950,[40] but still stimulates considerable research efforts.[41-44] However, this route raises safety and environmental concerns as 1,3-butadiene monoxide is toxic, unstable and exclusively petrobased. An emerging alternative route consists in the transesterification involving dialkyl carbonates with apical diol **7a**. Literature data regarding such transesterification is scarce, and only one patent reported a catalytic process using 1.5-3.1 wt% of NaOMe and 2 equiv. of dimethyl carbonate (DMC).[45] Procedures for the carbonation of glycerol in the presence of organocatalysts are increasingly reported.[46,47] Based upon our expertise, we developed an organocatalyzed transesterification under continuous flow conditions.[48]

Scouting of reaction conditions started with commercial **7a** and DMC in the presence of DBU as an organocatalyst under neat conditions. Both homogeneous and polymer-supported DBU were assessed for the organocatalytic carbonation of **7a**. In a representative homogeneous experiment, neat DMC (containing DBU) and **7a** were mixed through a static mixer, and further reacted in a heated capillary coil reactor under 11 bar of counter-pressure, to enable superheated conditions in DMC (Figure 8). DMC and **7a** formed directly a homogeneous solution. Process parameters such as temperature, residence time, catalyst loading and DMC/**7a** molar ratio were thoroughly assessed (Table 2 and Supporting Information for full details of the optimization).

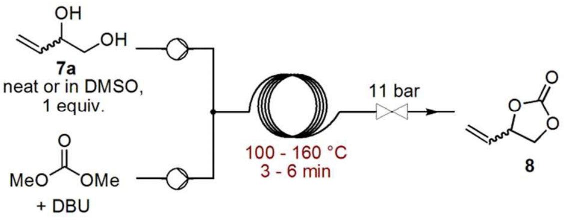

**Fig. 8** Simplified continuous-flow setup for the homogeneous carbonation of commercial 3-butene-1,2 diol.

Increasing the temperature from 100 to 160 °C with 2 mol% of DBU and 2 equiv. of DMC drastically improved the conversion from 23 to 70%. The selectivity toward **8** was barely affected and decreased from 84 to 80% (entries 1-4). When the residence time was changed from 3 to 4 min, the conversion was slightly improved up to 77% and the selectivity was not affected (81%). A further increase in residence time did not improve the overall yield (entries 4-6). Decreasing the catalytic loading down to 1 mol% affected the conversion, which dropped to 52%. The conversion plateaued at 80% while increasing the amount of organocatalyst to 3 or 4 mol%. At elevated DBU loading (4 mol%), the selectivity however dropped to 73%, and an extensive amount of gas was observed downstream the BPR (entries 5, 7-9), most likely as a consequence of the decarboxylation of **8** toward 1,3-butadiene monoxide.

**Table 2.** Process optimization for the homogeneous continuous flow carbonation of purified 3-butene-1,2-diol.

| Entry | Residence time (min) | T (°C) | DMC (equiv.) | DBU [a] (mol%) | Conv. [b] (%) | Selec. [b] (%) |
|---|---|---|---|---|---|---|
| 1[c] | 3 | 100 | 2 | 2 | 23 | 84 |
| 2[c] | 3 | 120 | 2 | 2 | 31 | 83 |
| 3[c] | 3 | 140 | 2 | 2 | 44 | 81 |
| 4[c] | 3 | 160 | 2 | 2 | 70 | 80 |
| 5[c] | 4 | 160 | 2 | 2 | 77 | 81 |
| 6[c] | 6 | 160 | 2 | 2 | 83 | 76 |
| 7[c] | 4 | 160 | 2 | 1 | 52 | 78 |
| 8[c] | 4 | 160 | 2 | 3 | 80 | 80 |
| 9[c] | 4 | 160 | 2 | 4 | 80 | 73 |
| 10[c] | 4 | 160 | 3 | 2 | 86 | 80 |
| 11[c] | 4 | 160 | 3.5 | 2 | 87 | 79 |
| 12[d] | 4 | 160 | 3 | 2 | 95 | 80 |

[a] The loading of organocatalyst is relative to the number of moles of 3-butene-1,2-diol. [b] Conversion and yield were determined by GC-FID. [c] 3-Butene-1,2-diol was pumped as a neat solution. [d] 3-Butene-1,2-diol was pumped as a 1.5 M solution in DMSO.

Tuning of the DMC/**7a** molar ratio in the 2-3.5 range indicated that 3 equiv. of DMC gave the best results, with 86% conversion and a 80% selectivity toward **8** (entries 5, 10-11). The impact of DMSO on the reaction was then evaluated, before attempting full concatenation from erythritol. To mimic the effluent of the DODH reactor that provided **7a** in 56% yield (Figure 4), a solution of purified **7a** in DMSO was reacted with neat DMC (containing DBU). The optimized process parameters established here above (160 °C, 4 min, 2 mol% DBU and 3 equiv. of DMC) were utilized. The results indicated that DMSO had a positive impact on the conversion (95%), while the selectivity remained unchanged (Table 2, entries 11-12). To maximize cost-efficiency and ease downstream purification, polymer-supported DBU was assessed as heterogeneous catalyst. The previous continuous flow setup was adapted for hosting a packed-bed column and a preheating loop at 160 °C for the substrates (Figure 9a). Similar process conditions were utilized (**7a** in DMSO, 3 equiv. of neat DMC, 160 °C, 11 bar). The packed-bed column was filled with a mixture of glass beads (425-600 µm) and polystyrene-supported DBU (PS-DBU). Increasing the Weight Hourly Space Velocity (WHSV, Figure 9b) from 3.96 to 13.88 $h^{-1}$ affected the conversion, which decreased from 92 to 67%, while the selectivity remained steady (90-95%).

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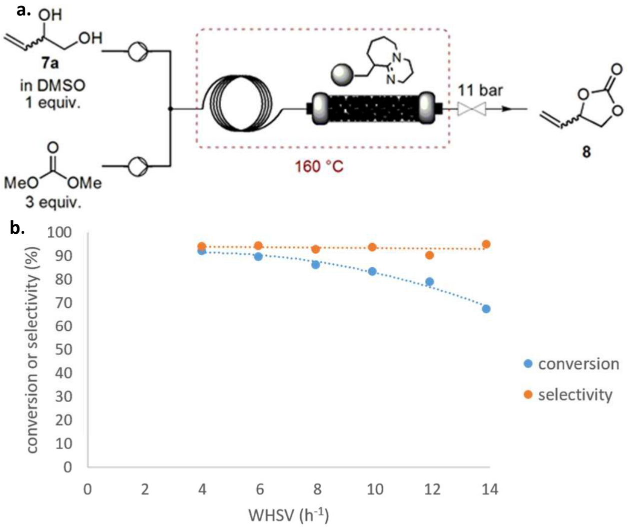

**Fig. 9** (a) Simplified continuous flow setup for the heterogeneous carbonation of commercial **7a**; (b) Evolution of the conversion and selectivity (off-line GC/FID) as a function of the WHSV for the heterogeneous carbonation of commercial **7a**. The WHSV is defined as the mass of **7a** fed per hour and per mass of PS-DBU.

Full concatenation of the DODH and carbonation steps was then performed from **4** (Figure 10). The crude effluent from the DODH reactor was collected, degassed, and further reacted with DMC over PS-DBU without any additional treatment or purification step. By comparison to the experiments with commercial **7a**, the conversion was slightly affected, most likely a consequence of the presence of impurities competing with the active sites of the heterogeneous catalyst. For instance, at a WHSV of 2.14 $h^{-1}$ and with 5.5 equiv. of DMC, the conversion of crude **7a** was 73%, while it was 79% at a WHSV of 11.89 $h^{-1}$ and with 3 equiv. of DMC for commercial **7a** (Figure 9). However, the selectivity (97%) toward carbonate **8** remained unaffected.

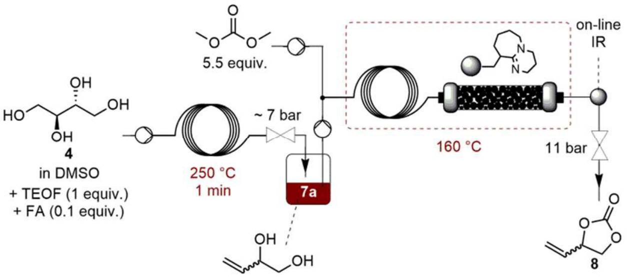

**Fig. 10** Simplified concatenated flow process combining the DODH on erythritol under the best conditions to maximize the production of 3-butene-1,2-diol and its subsequent heterogeneous organocatalyzed carbonation toward vinyl ethylene carbonate. The WHSV of 3-butene-1,2-diol over PS-DBU is 2.14 $h^{-1}$.

The unique profile of the reagents and products enabled on-line reaction monitoring using IR spectroscopy. The carbonation of diol **7a** with DMC ($\nu_{C=O}$ at 1750 $cm^{-1}$) toward carbonate **8** ($\nu_{C=O}$ at 1810 $cm^{-1}$) was monitored through the evolution of the main characteristic vibration bands. Figure 11a illustrates the evolution of the transcarbonation reaction of **7a** as a function of the temperature (25-160 °C). On-line conversion of **4** to **8** was obtained by combining on-line IR qualitative information and off-line quantitative GC/FID (Figure 11b). The concatenated continuous flow setup was operated for 24 h to assess catalyst stability over time upon processing crude **7a**. The concentration in vinyl ethylene carbonate remained quite stable over the first 10 h of operation, but decreased drastically as TOS increased. Samples were collected for off-line quantitative GC analysis, which indicated that the conversion of 3-butene-1,2-diol was in the 65-73% range over the first 10 h, but then dropped to 28% after 24 h (Supporting Information). However, the selectivity was unaffected by the operation time (90-99%). Catalyst deactivation was rationalized by the presence of impurities from the DODH, such as traces of formic acid and/or dissolved $CO_2$, which would poison the basic sites of the heterogeneous catalyst.

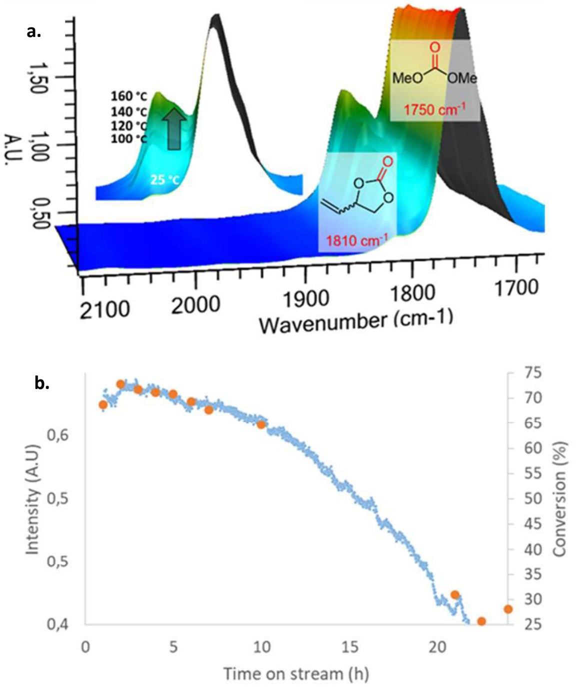

**Fig. 11a.** On-line IR reaction monitoring showing characteristic vibration bands of interest ($\nu_{C=O}$ at 1810 $cm^{-1}$ and $\nu_{C=O}$ at 1750 $cm^{-1}$) for the carbonation of neat **7a** with DMC with homogeneous DBU at various temperatures (11 bar; reaction parameters are described in Table 2, entries 1-4). The upper insert illustrates the relative increase in carbonate **8** from 25 to 160 °C. **b.** On-line reaction monitoring showing the decrease of the conversion toward carbonate **8** by combining on-line IR qualitative monitoring (blue series, relative intensity of the 1810 $cm^{-1}$ band) and off-line quantitative GC/FID (orange dots, GC conversion of **7a**). The reaction was monitored over 24 h of continuous operation. Reaction parameters are described in Figure 10.

## Conclusion

This work illustrates a versatile and robust continuous flow procedure for the deoxydehydration (DODH) of biobased

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erythritol toward 3-butene-1,2-diol, and its further carbonation toward vinyl ethylene carbonate. The procedure relies on advanced continuous flow techniques and the combination of on- and off-line analytics. Computational and mechanistic investigations provide insights on the various products formed and their filiation, enabling a fine tuning of the reaction parameters to push the conversion of erythritol toward 3-butene-1,2-diol up to 56% yield. This procedure is unique since (a) 3-butene-1,2-diol is obtained in amounts of preparative interest from a biobased resource and (b) unprecedented short reactions times are reported (1 min). Process conditions can be easily tuned to form other valuable industrial building blocks such as butadiene, 2,5-dihydrofuran and but-2-enal. In addition, this work provides a simple, selective and effective carbonation procedure from 3-butene-1,2-diol toward vinyl ethylene carbonate. The procedure accommodates either homogeneous or heterogeneous organocatalysts, and is amenable to crude 3-butene-1,2-diol. Both steps are directly concatenable after degassing of crude 3-butene-1,2-diol.

## Acknowledgments

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## Notes and *references*

1 O. Kamm and C. S. Marvel, *Org. Synth.*, 1921, **1**, 15.
2 G. Crank and F. W. Eastwood, *Aust. J. Chem.*, 1964, **17**, 1385–1391.
3 G. Crank and F. W. Eastwood, *Aust. J. Chem.*, 1964, **17**, 1392–1398.
4 E. Block, 2005. Olefin Synthesis by Deoxygenation of Vicinal Diols. Organic Reactions. 30:2:457–566
5 C. Boucher-Jacobs, K. M. Nicholas, *Top. Curr. Chem.*, 2014, **353**, 163–184.
6 T. Wang, S. Liu, M. Tamura, Y. Nakagawa, N. Hiyoshi and K. Tomishige, *Green Chem.*, 2018, DOI: 10.1039/C8GC00574E
7 Y. Nakagawa, S. Tazawa, T. Wang, M. Tamura, N. Hiyoshi, K. Okumura and K. Tomishige, *ACS Catal.*, 2018, **8**, 584–595.
8 A. R. Petersen and P. Fristrup, *Chem. Eur. J.*, 2017, **23**, 10235–10243.
9 R. Sun, M. Zheng, X. Li, J. Pang, A.-Q. Wang, X. Wang and T. Zhang, *Green Chem.*, 2017, **19**, 638–642.
10 D. S. Morris, K. Van Rees, M. Curcio, M. Cokoja, F. E. Kühn, F. Duarte and J. B. Love, *Catal. Sci. Technol.*, 2017, **7**, 5644–5649.
11 N. N. Tshibalonza and J.-C. M. Monbaliu, *Green Chem.*, 2017, **19**, 3006–3013.
12 M. Kim and H. Lee, *ACS Sustain. Chem. Eng.*, 2017, **5**, 11371–11376.
13 A. R. Peetersen, L. B. Nielsen, J. R. Dethlefsen and P. Fristrup, *ChemCatChem*, 2017, **10**, 769–778.
14 J. R. Dethlefsen and P. Fristrup, *ChemSusChem*, 2015, **8**, 767–775.
15 E. Arceo, P. Marsden, R. G. Bergman and J. A. Ellman, *Chem. Commun.*, 2009, 3357–3359.
16 E. Arceo, J. A. Ellman and R. G. Bergman, *ChemSusChem*, 2010, **3**, 811–813.
17 D. Sun, Y. Yamada, S. Sato and W. Ueda, *Green Chem.*, 2017, **19**, 3186–3213.
18 E. V. Makshina, M. Dusselier, W. Janssens, J. Degrève, P. A. Jacobs and B. F. Sels, *Chem. Soc. Rev.*, 2014, **43**, 7917–7953.
19 G. K. Cook and M. A. Andrews, *J. Am. Chem. Soc.*, 1996, **118**, 9448–9449.
20 M. Shiramizu and F. D. Toste, *Angew. Chem. Int. Ed.*, 2012, **51**, 8082–8086.
21 M. Shiramizu and F. D. Toste, *Angew. Chem. Int. Ed.*, 2013, **52**, 12905–12909.
22 J. Yi, S. Liu and M. M. Abu-Omar, *ChemSusChem*, 2012, **5**, 1401–1404.
23 S. Liu, A. Senocak, J. L. Smeltz, L. Yang, B. Wegenhart, J. Yi, H. I. Kenttämaa, E. A. Ison and M. M. Abu-Omar, *Organometallics*, 2013, **32**, 3210–3219.
24 S. Raju, J. T. B. H. Jastrzebski, M. Lutz and R. J. M. Klein Gebbink, *ChemSusChem*, 2013, **6**, 1673–1680.
25 I. Ahmad, G. Chapman and K. M. Nicholas, *Organometallics*, 2011, **30**, 2810–2818.
26 C. Boucher-Jacobs and K. M. Nicholas, *Organometallics*, 2015, **34**, 1985–1990.
27 S. Tazawa, N. Ota, M. Tamura, Y. Nakagawa, K. Okumura and K. Tomishige, *ACS Catal.*, 2016, **6**, 6393–6397.
28 M. Stalpaert and D. De Vos, *ACS Sustainable Chem. Eng.*, 2018, doi: 10.1021/acssuschemeng.8b02532.
29 R. Sun, M. Zheng, X. Li, J. Pang, A. Wang, X. Wang and T. Zhang, *Green Chem.*, 2017, **19**, 638–642.
30 B. Sivaraman, S. S. Badle and V. Rangaswamy, *ChemistrySelect*, 2016, **1**, 4630–4632.
31 R. Gérardy, N. Emmanuel, T. Toupy, V. E. Kassin, N. N. Tshibalonza, M. Schmitz and J. C. M. Monbaliu, *Eur. J. Org. Chem.*, 2018, 2301–2351.
32 Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, and D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.
33 R.-C. Brachvogel and M. von Delius, *Chem. Sci.*, 2015, **6**, 1399–1403.
34 H. B. Singh, G. E. Klinzing and J. Coull, *Ind. Eng. Chem. Prod. Res. Dev.*, 1973, **12**, 184–189.
35 A. K. Diallo, L. Annunziata, S. Fouquay, G. Michaud, F. Simon, J. M. Brusson, S. M. Guillaume and J. F. Carpentier, *Polym. Chem.*, 2014, **5**, 2583–2591.
36 V. Sabatini, S. Gazzotti, H. Farina, S. Camazzola and M. A. Ortenzi, *ChemistrySelect*, 2017, **2**, 10748–10753.
37 A. Duval and L. Avérous, *ChemSusChem*, 2017, **10**, 1813–1822.
38 B. Li, Y. Wang, H. Lin, J. Liu, L. Xing, M. Xu and W. Li, *Electrochim. Acta*, 2014, **141**, 263–270.
39 C. Forestier, P. Jankowski, A. Wizner, C. Davoisne, G. Gachot, L. Sannier, S. Grugeon, P. Johansson, M. Armand and S. Laruelle, *J. Power Sources*, 2017, **345**, 212–220.
40 W. W. Prichard, US Patent 1950/2511942A
41 J. A. Kozak, J. Wu, X. Su, F. Simeon, T. A. Hatton and T. F. Jamison, *J. Am. Chem. Soc.*, 2013, **135**, 18497–18501.
42 T. Werner, N. Tenhumberg and H. Büttner, *ChemCatChem*, 2014, **6**, 3493–3500.

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DOI: 10.1039/C8GC02468E

43 S. Arayachukiat, C. Kongtes, A. Barthel, S. V. C. Vummaleti, A. Poater, S. Wannakao, L. Cavallo and V. D'Elia, *ACS Sustain. Chem. Eng.*, 2017, **5**, 6392–6397.

44 J. Steinbauer and T. Werner, *ChemSusChem*, 2017, **10**, 3025–3029.

45 I.-S. Yeo, B.-W. Woo, S.-W. Yoon, J.-H Lee, S.-H. Park, N.-J. Jang, US Patent 2010/0048918

46 D. O. Nogueira, S. P. De Souza, R. A. C. Leão, L. S. M. Miranda and R. O. M. A. De Souza, *RSC Adv.*, 2015, **5**, 20945–20950.

47 G. Fioranic, A. Perosa and M. Selva, *Green Chem.*, 2018, **20**, 288-232.

48 L. Di Marco, M. Hans, L. Delaude and J. C. M. Monbaliu, *Chem. Eur. J.*, 2016, **22**, 4508–4514.

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DOI: 10.1039/C8GC02468E

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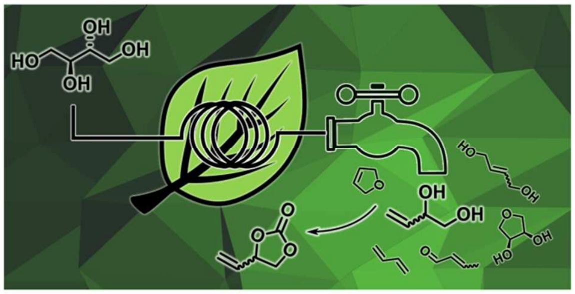

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