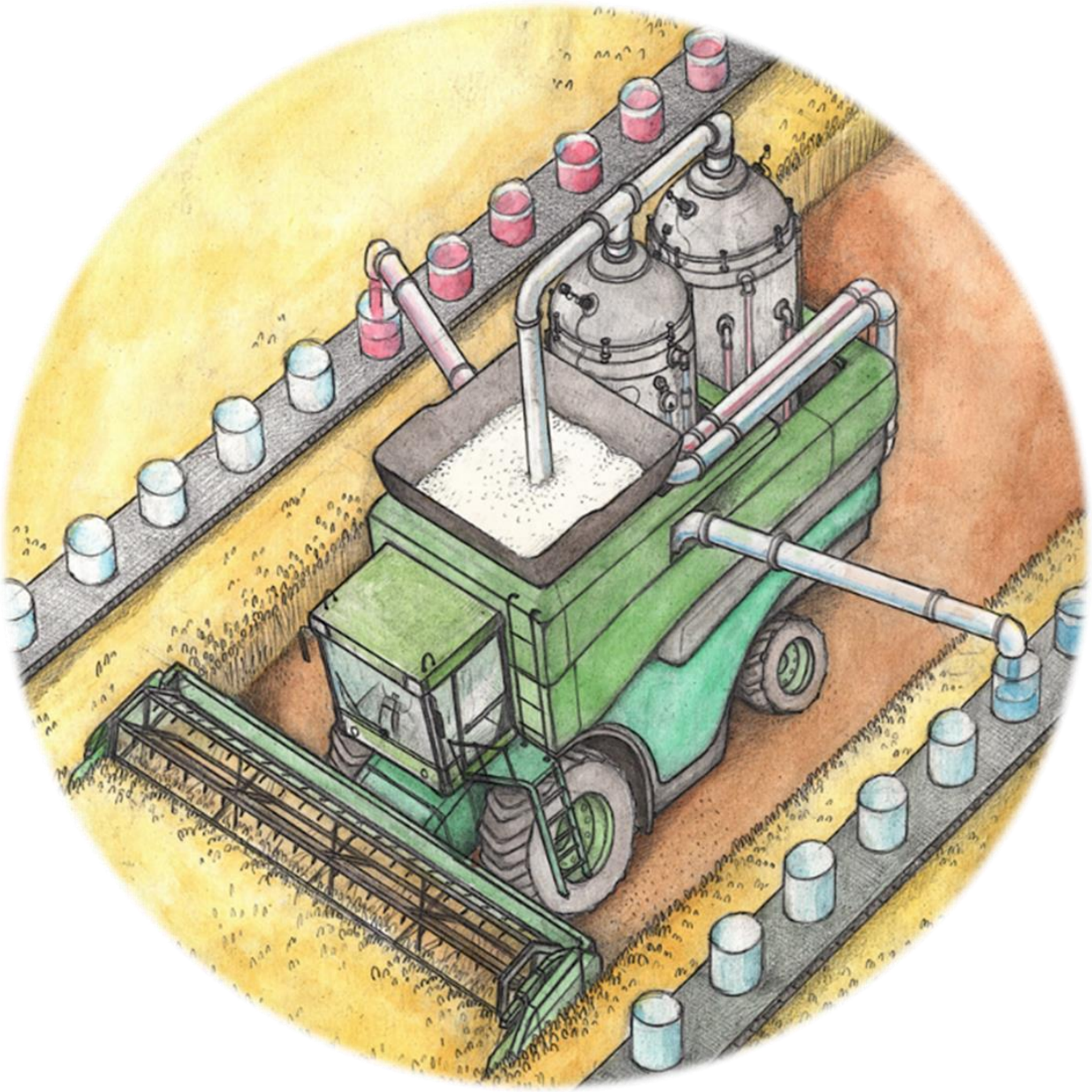
Toward replacing ethylene oxide in a sustainable world: Glycolaldehyde as bio-based C_2 platform molecule

William H. Faveere[†],[a] Sofie Van Praet[†],[a] Benjamin Vermeeren,[a] Kim N.R. Dumoleijn,[b] Kristof Moonen,[b] Esben Taarning,[c] and Bert F. Sels*[a]



Abstract: Nowadays, fossil-based platform molecules such as ethylene and ethylene oxide serve as primary feedstock for the C_2-based chemical industry. However, in search for a more sustainable chemical industry, fossil-based resources may preferentially be replaced by renewable alternatives, provided realistic economic feasibility. This review compares and critically discusses several production routes toward bio-based structural analogs of ethylene oxide and the required adaptations for their implementation in state-of-the-art C_2-based chemical processes. For instance, glycolaldehyde, a structural analog obtainable from carbohydrates via atom-economic retro-aldol, may replace ethylene oxide's leading role. This alternative chemical route may not only accommodate to lower the carbon footprint of conventional chemicals production, but the introduction of a bio-based pathway may also contribute to safer production processes. Where possible, challenges, drawbacks, and prospects are highlighted.

1. Introduction

Today's chemical industry has been built, to a large extent, on the great abundance and high availability of fossil-based resources as raw materials. Currently, 58 % of the crude oil is being used for transportation purposes and 13 % as a feedstock and energy source for the production of petrochemicals. However, a large shift in demand between these sectors is expected, making raw material availability for the chemical industry in the future uncertain.[1,2] Besides recycling and clever product design, a shift to the use of renewable feedstock, such as biomass, is part of the solution towards a circular economy.[3] This trend is reinforced by growing consumer awareness and desire to obtain products with improved environmental footprint.

Hence, the development of new, ecological benign technologies for the production of chemical products is of urge. For commodity chemicals and plastics, the need for an adequate alternative carbon source is requisite not only to create the chemical backbone of these products but also to compensate for the inevitable recycle losses in their circular economy (Scheme 1) and to produce virgin material for those applications where the quality of recycled material is too low.[3]

Ethylene oxide (EO) is a well-established platform molecule in the current chemical industry because of its versatility.[4] EO is produced from ethylene, which is one of the cornerstones of the petrochemical industry. Bio-ethylene has recently gained interest as a possible drop-in feedstock for EO, but at relatively high break-even prices due to the dependence on bio-ethanol as feedstock.[5–11] Less CO_2 is emitted in the production of EO via this route, and some commercial facilities are already operating in Brazil and India, with the largest bio-ethylene producers having a yearly production capacity of 200 Ktonnes.[10]

However, biomass, as the most abundant carbon source on our planet, is already offering such a large variety of functional groups in its chemical structure. For this reason, it seems like an inefficient detour to deconstruct it back to ethylene, before building up functionality again.[12] Furthermore, ethylene does not overcome the disadvantage of EO being dangerous to handle and difficult to transport, which is an additional reason to consider EO as a candidate for substitution. [13]

Over the past decades, several breakthroughs regarding efficient biomass conversion into novel, bio-based components have been reported by the scientific community. [14–17] Nonetheless, on a bulk scale, the properties of these bio-based alternatives will need to be compared to the performance, the production cost, ease of separation, and product specifications of accustomed fossil-based standards. Therefore, such bio-derived routes towards EO over bio ethylene (Figure 1), will not be covered by the scope of this review. Instead, we will focus on structural analogs of EO that can lead to the same or similar products and have the potential to function as a sustainable, difunctional C_2-platform

[a] Dr. W. Faveere, S. Van Praet, B. Vermeeren and Prof. Dr. B. Sels
Centre for Sustainable Catalysis and Engineering
KU Leuven
Celestijnenlaan 200F, 3001 Heverlee, Belgium
E-mail: bert.sels@kuleuven.be
[b] K. Dumoleijn and Dr. K. Moonen
Eastman Chemical Company
Pantserschipstraat 207, 9000 Ghent, Belgium
E-mail: kim.dumoleijn@eastman.com and
kristof.moonen@eastman.com
[c] Dr. E. Taarning
Haldor Topsøe A/S
Nymøllevej 55, 2800 Kgs, Lyngby, Denmark
E-mail: esta@topsoe.dk
[†] These authors contributed equally to this work.
[*] Corresponding author

molecule when implemented in a biorefinery concept. The goal is to cover an identical or even broader range of end-products from these structural analogs in a chemo catalytic manner. First, ethylene oxide will be critically reviewed as C_2 platform molecule. The production, significance, and shortcomings of this significant building block will be discussed. Next, several important EO derived end-products will be highlighted, and recent developments in alternative sustainable, bio-based synthesis routes toward these products will be assessed. Subsequently, the replacement of ethylene oxide by glycolaldehyde as a bio-based C_2 platform molecule will be elucidated conceptually. Finally, a holistic biorefinery model supporting glycolaldehyde as a platform molecule will be formulated.

William Faveere obtained his MSc degree in Bioscience Engineering (Catalytic Technology) at KU Leuven (Belgium) in 2014. He did his master's thesis at the Centre for Surface Chemistry and Catalysis under the supervision of Professor Bert F. Sels, where he studied the adsorption and dynamics in MOF's via NMR spectroscopy. He obtained his PhD degree in the same group where his research focused on amination of bio-based platform molecules.

Sofie Van Praet obtained her MSc degree in Bioscience Engineering (Catalytic Technology) at KU Leuven in 2019. She did her master thesis at the Centre for Surface Chemistry and Catalysis under the guidance of prof. Bert Sels, where she developed an in-depth analysis protocol for branched fatty acids. She is currently doing a PhD in the same group, focussing on the reductive amination of carbohydrates using heterogeneous catalysts.

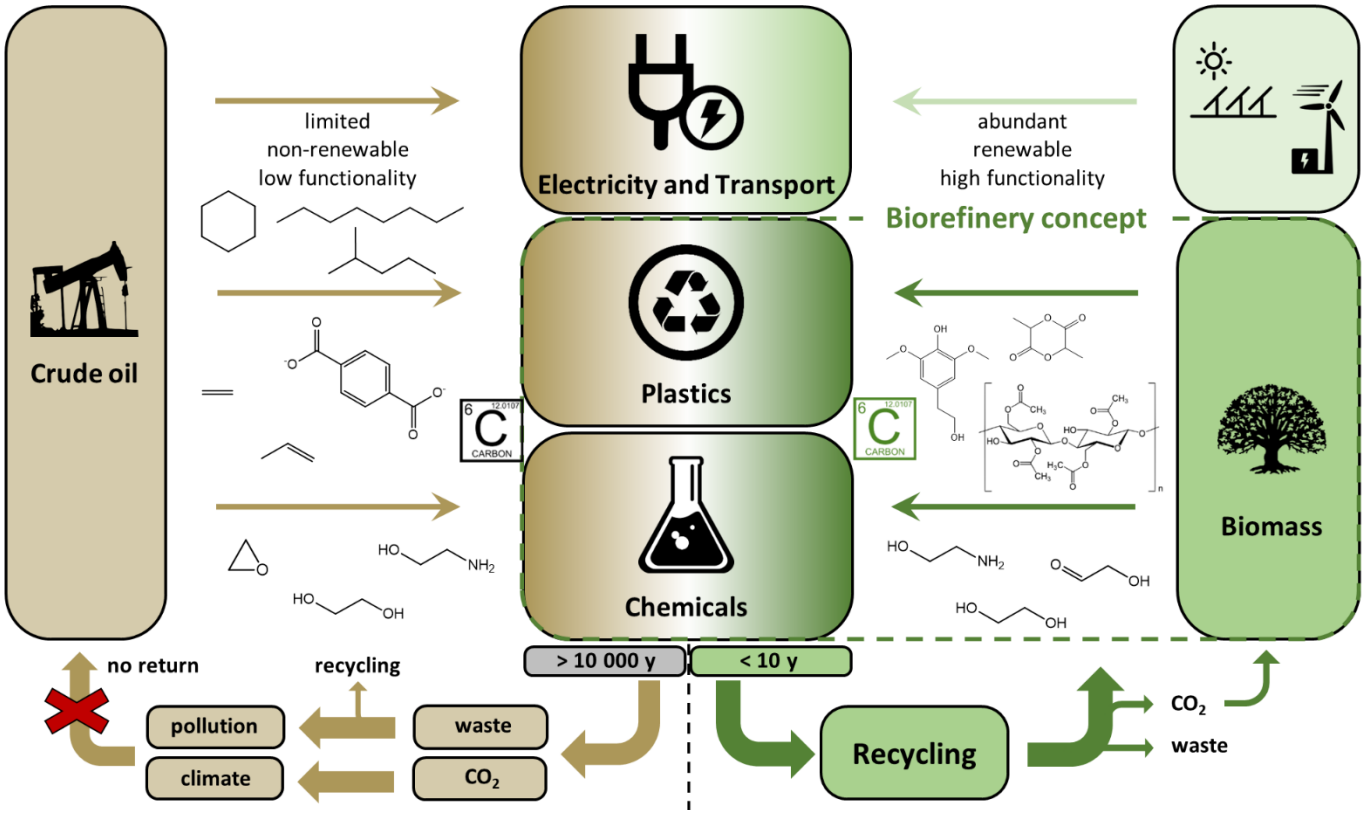
Benjamin Vermeeren obtained his MSc degree in Bioscience Engineering (Catalytic Technology) at KU Leuven in 2019. He did his master thesis at the Centre for Surface Chemistry and Catalysis under the supervision of Professor Bert F. Sels, where he investigated methanolysis as a chemical recycling method for bisguaiacol-based polycarbonates. For his master thesis, he was awarded the INEOS master thesis prize 2019. He is currently doing a PhD in the same group, studying the reductive amination of carbohydrates using heterogeneous catalysis.

Kim Dumoleijn obtained her MSc degree in Industrial Engineering (Chemistry) at KU Leuven in 2011. She then joined Eastman R&D team and is now Senior Research Scientist responsible for several research and development projects in the field of alkyl amine synthesis. She is currently doing a PhD at the University of Ghent in the field of organic chemistry and catalysis.

Kristof Moonen obtained his PhD degree from Ghent University in 2006 in the field of organic chemistry. He then joined Taminco's (currently Eastman) R&D group, where his work focused on amine processes. He is co-author of 18 peer-reviewed papers and has filed 28 patent applications. Currently, he is group leader of Care Chemicals Application Development at Eastman Chemical Company.

Esben Taarning obtained his PhD degree from the Technical University of Denmark in 2009 in the field of organic chemistry and catalysis. He then joined Haldor Topsøe's R&D team and is now R&D Director for Sustainable Chemicals. His work is focused on the development and scale-up of catalytic methods for converting sugars into chemicals. He is the co-author of 55 peer-reviewed papers and has filed 19 patent applications.

Bert F. Sels, full professor at KU Leuven, obtained his PhD degree in 2000 in the field of heterogeneous oxidation catalysis. He was awarded the DSM Chemistry Award in 2000, the Incentive Award by the Belgian Chemical society in 2005, and the Green Chemistry Award in 2015. He is currently director of the Centre for Sustainable Catalysis and Engineering, designing heterogeneous catalysts for future challenges in industrial catalysis. His expertise includes heterogeneous catalysis in biorefineries, design of hierarchical zeolites and carbons, and the spectroscopic and kinetic study of active sites for small molecule activation. He authored 280 peer-reviewed papers and filed 25 patents.



Scheme 1. General outline of the circular bio-economy transitions for energy, chemical industry and the associated to create an environmentally friendly consumer society.

2. Ethylene Oxide as C_2 platform molecule

2.1. Introduction

Ethylene oxide (EO), also known as oxirane, is a cyclic ether and the simplest epoxide.[4] At ambient conditions, EO is a flammable gas with a slightly sweet odor.[13] As a result of its strained ring, EO is highly reactive and can participate in several addition reactions that result in ring-opening. EO is a versatile and valuable building block and is primarily used to manufacture other chemicals, such as building blocks for polyester fibres and plastic packaging film, but can also be directly used to sterilize medical equipment and supplies. Overall, the global ethylene oxide market is projected to reach approximately 32 Mtonnes by the end of 2023, increasing at a compound annual growth rate (CAGR) of 3-4 % per year.[13,18,19]

2.2. Production of Ethylene oxide

Ethylene oxide is generally formed through direct and partial oxidation of ethylene with oxygen in the presence of a silver catalyst.[4] This reaction is exothermic (ΔH = -105 kJ/mol at 250 °C and 1.5 MPa), and the selectivity is usually around 90 %.[20,21] Conversion rates are kept deliberately low (< 10 %) to enable the high selectivity and avoid the complete burn of ethylene and EO to CO_2 as a result of secondary oxidation reactions, which are even more exothermic (-1327 kJ/mol and -1223 kJ/mol, respectively).[4] The CO_2 formed during the reaction, as well as the energy-intensive cooling, compressing, and purification units, are the main contributors to the release of CO_2. On top of the CO_2 released during the manufacturing of its precursor, ethylene, per Mtonne EO produced, 0.2 to 0.3 Mtonnes of additional CO_2 is released. (Figure 1).

Ethylene is one of the most prominent chemical building blocks of the chemical industry, which is largely produced by steam cracking of hydrocarbons (97 %), such as naphtha and ethane, with an annual production of 150 Mtonnes in

2018.[22,23] However, with the formation of 1 to 1.6 Mtonne CO2 per Mtonne ethylene (Figure 1), it is one of the largest contributors to greenhouse gas emission in the petrochemistry.[22] Furthermore, the endothermic hydrocarbon cracking and cryogenic distillation is energy intensive and demand heavy process monitoring due to potential risks such as explosions, fire hazards, etc.

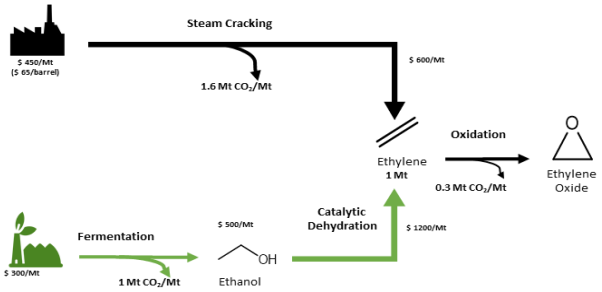


Fig. 1 Overview of the feedstock prices (in 2016) and associated CO_2 emissions (per tonne) for petro- and bio-ethylene routes to ethylene oxide (EO). [4-10,22,23]

2.3. Importance of EO in the chemical industry

Ethylene oxide (EO) is an important platform molecule in the chemical industry.[4] An overview of the essential applications of EO can be found in Figure 2 and will be discussed below.

Ethylene glycol - The majority of EO production (72 %) is dedicated to the synthesis of glycols.[13] They are produced via the hydration of EO and held a capacity of 26 Mtonnes annually in 2018.[13,24,25] The dominant member of the family (90% of EO used in this class) is monoethylene glycol (MEG), with the remaining part being co-produced di-, tri-, tetra-, and polyethylene glycol.[13,24] MEG is generally produced by reacting EO with excess water at 200 °C. Water is recycled while the ethylene glycols are separated by vacuum distillation. This process has been critically reviewed by Yue *et al*.[26] The major applications of MEG are as a raw material for producing polyester fiber and manufacturing polyesters such as poly(ethylene succinate) (PES) and poly(ethylene terephthalate) (PET) or polyurethanes (PU) and in heat transfer liquids, for instance in the automotive industry.[24,26]

Oxidation - Via selective chemical oxidation of MEG, secondary products such as glyoxal and glycolic acid can be obtained.[4] Industrially, glyoxal is produced directly from MEG by oxidation over a Ag or Cu, or multilayer Cu-Ag catalyst in the presence of water and 99 % conversion and 80 % selectivity in a vapor-phase process at 450 °C are reported.[27–30] Glyoxal is commonly used in wood-processing, leather tanning, and pharmaceutical applications.[31–35] Further conversion of glyoxal leads to glycolic acid, which can be used in adhesives and biodegradable polymers as well as in health-care and medicinal products.[36,37] Next to the MEG route, an alternative pathway to glycolic acid has been reported, which relies on the acid-catalyzed reaction of formaldehyde with syngas.[38]

Ethoxylates - A second significant utilization of EO (13 %) comprises the production of so-called ethoxylates via epoxide coupling, to produce polyethoxylated alkylphenols, fatty alcohols, fatty acids, and fatty amines.[4,39] The addition of varying numbers of ethylene oxide molecules to these precursors allows tuning of the polarity and octanol-water partition coefficient of the products and offers a great tool to make surfactants with a wide range of properties. They serve in the formulation of detergents, wetting agents, emulsifiers, and dispersants.[40]

Ethanolamines - Ethylene oxide can react exothermically with aqueous ammonia (NH_3), forming a mixture of primary, secondary, and tertiary ethanolamines.[41] This reaction roughly accounts for 6 % of the EO consumption. The selectivity is merely dependent on the ratio of NH_3 to EO, resulting in a higher monoethanolamine (MEOA) content when an excess of NH_3 is used.[4,41] N-alkyl ethanolamines, such as N,N-dimethylethanolamine (DMAE), are produced similarly using alkyl amines (e.g., dimethylamine; DMA) instead of NH_3. Ethanolamines play an essential role as a precursor or as a final product in applications for CO_2 scrubbing, pharmaceuticals, agrochemicals, fragrances, cosmetics, water treatment, polymers, and detergents.[42–45]

Others - Some other products formed from EO are also worth mentioning. Several glycol ethers (about 4 % of EO), which are commonly used as plasticizers or as solvents in paints or cleaners, are produced by contacting EO with alcohols.[4] Furthermore, ethylene carbonate (2 %) is formed by reacting EO with CO_2.[13] It can be used as a solvent or may be converted to dimethyl carbonate (DMC) by transesterification with methanol forming MEG as a side product.[46]

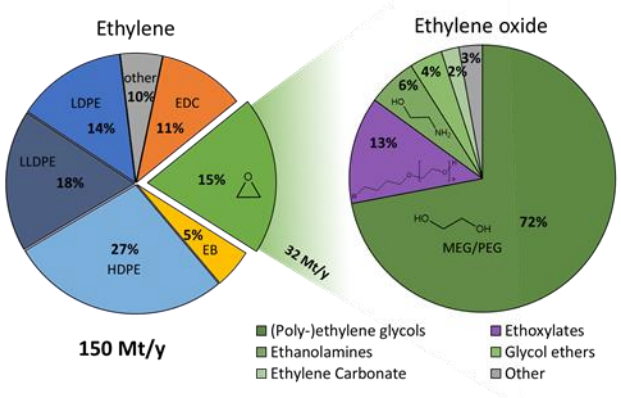


Fig. 2 Applications and market share of Ethylene (150 Mtonnes/y) and Ethylene oxide (32 Mtonnes/y). Green = alternative routes available; purple = No sustainable alternative route currently available. [17,22,24]

2.4. Shortcomings of EO

Besides the large CO_2 emission during the production process of ethylene oxide, safety concerns may be regarded as the second major shortcoming of EO. Due to its highly strained oxirane ring, EO is thermally unstable and highly reactive to other chemicals, including water, which may cause explosions given the exothermic nature of these decomposition reactions. Furthermore, ethylene oxide is very flammable in a wide range of oxygen levels and concentrations.[4,13] Finally, EO is considered carcinogenic, mutagenic, and reprotoxic (CMR) under REACH.[47,48]

Safety and transport of EO are highly regulated, and therefore costly.[49] On-site EO production and utilization are usually preferred and, in the future, may become the only viable option. Nevertheless, even in EO-integrated plants, the intrinsic hazardous properties of EO have led to severe incidents worldwide.[50] For example, in 1962, an EO storage tank ruptured and exploded at the Doe Run Olin Mathieson plant in Brandenburg (Kentucky), due to a failing back-flow of the ammonia reactor into the storage tank, creating a runaway reaction. In the 1980s, EO plants of BASF and BP in Antwerp, Belgium, exploded on different occasions, due to leakages in the insulation packing, which allowed for the formation of polyethylene glycols and local hotspots that initiated disruptive EO decomposition. These examples demonstrate the need for intensive safety measures and reactor design, which comes at a considerable cost.[50]

Recent life cycle assessments (LCA) of EO production demonstrate that the production of EO from fossil-based feedstock produces close to 2 tonnes CO_2 per tonne of EO produced (Figure 1), and therefore contributes significantly to the effect of global warming.[4,22] Moreover, considerable amounts of greenhouse gasses are emitted in the synthesis of EO-derived products. For instance, an estimated 6 kg CO_2 eq. per kg produced PET is emitted, of which 28 % is contributed by MEG production via EO.[51–54] This makes EO manufacturing and utilization a substantial CO_2 contributor to the chemical industry. Considering the growing attention on its safety hazards and the increasing urgency to improve the carbon footprint of the chemical industry, an overview of the state-of-the-art of potentially viable alternatives to EO as a building block is timely.

3. Alternative bio-derived routes for EO applications

The various end-products derived from EO are illustrated in Figure 2. For ethylene glycols, ethanolamines, glycol ethers, and ethylene carbonates, representing about 84 % of the current EO consumption market, alternative synthesis pathways based on structural analogs of EO can be considered. In the case of ethoxylates, however, no robust alternative pathways have been established so far as this chemistry still relies heavily on epoxide coupling.

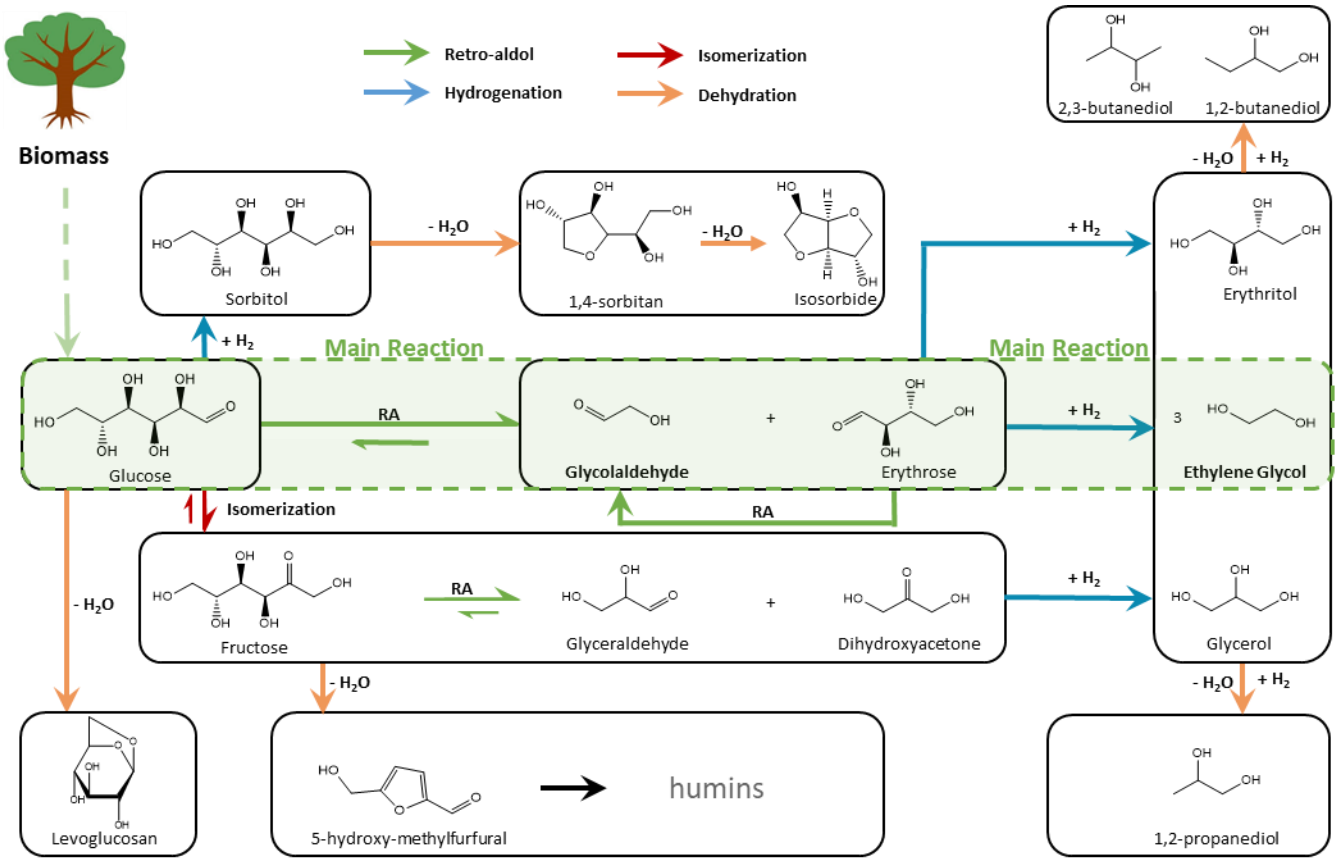
Ethylene glycol - Given that the industrial production of glycols is using 72 % of the available EO, the development of new technologies for biomass conversion to MEG evidently is gaining interest. MEG can be synthesized directly from various bio-feedstock, such as ethanol, glycerol, sorbitol, sugars, and cellulosic biomass. Some excellent and detailed overviews on this subject have recently been provided by Zhang and co-workers.[55,56] They concluded that the route via cellulose and sugar conversion is most favorable concerning MEG yields, and therefore worthwhile to discuss in further detail. Other routes including bio ethylene as a in a drop-in approach and the routes via glycerol and sorbitol that essentially have propylene glycol as a target are less relevant and will therefore not be discussed here.[57–59]

The one-step conversion of cellulose into MEG has been examined in depth. It generally involves catalytic retro-aldol fragmentation of sugars, forming glycolaldehyde (GA) as an *in situ* intermediate. So far, the main hurdle has been the improvement of the efficiency of hydrolyzing cellulose, a recalcitrant complex of carbohydrates, to glucose. The conversion of glucose to MEG occurs through a complex cascade of subsequent and competitive reactions, summarized in scheme 2, making it challenging to obtain high MEG yields. A careful balance of hydrolysis, retro-aldol, hydrogenation, isomerization, and dehydration reactions is of utmost importance to obtain attractive MEG yields. In the best circumstances, MEG is the dominant product with small quantities of 1,2-propylene glycol (1,2-PG), 1,2-butanediol, sorbitol, mannitol, glycerol, etc. as side products. Retro-aldol of glucose to GA competes with its isomerization to fructose, which leads via similar chemistry to C_3 polyol side products.[60–62] Through hydrogenation of GA, preferably fast, MEG is obtained, but the formation of sorbitol from direct glucose hydrogenation is competing here.[56] Hence, such a reaction scheme asks for a fed-batch approach to maintain short glucose contact time and high temperature to stimulate the retro-aldol condensation from an energetic and kinetic point of view.[63] Of all catalysts available, tungsten-based catalysts are the most selective to form MEG from carbohydrates.[56] In this case, tungsten oxide interacts explicitly with the carbohydrate molecule, enabling a formal retro-aldol C-C cleavage. The further conversion of GA to MEG occurs typically in the presence of a Ni or Ru catalyst. For instance, the direct catalytic conversion of cellulose to MEG was first demonstrated by Ji *et al.* in 2008, where a nickel-promoted tungsten carbide catalyst resulted in a yield of 61 % in a one-pot aqueous batch reaction of 30 min at 518 K.[64] The unique role of transition-metal carbides was highlighted, enabling the direct conversion from cellulose to C_2 chemicals with high selectivity without using noble metals.[65] Continued research by Zhang *et al.* pointed out that the yield could be further increased to 75 % by applying different carbon supports with a better pore structure, obtaining a uniform and more disperse particle distribution.[64,66–68] The tungsten crystallites were further investigated, as it was believed to be a heterogeneous catalyst. However, dissolved H_xWO_3 were found to be the main active species responsible for catalyzing the C-C bond cleavage. Tai *et al.* used this tungsten solubility to create binary catalysts of Ru/AC-H_2WO_4 and Raney-Ni-H_2WO_4 to obtain a 60 % MEG yield while the catalyst could be reused up to 30 times.[69–71] It was elucidated that a crucial synergy exists between the WO_x acid sites and metal hydrogenation sites in order to maximize MEG yield.[72]

Particularly, the oxygen vacancies in partially reduced W^{5+} species were reported to be essential to specifically adsorb glucose on the W core with its oxygen atoms, leading to GA and tetroses upon selective cleavage of the C_2-C_3 bond, and ultimately MEG after subsequent hydrogenation over the metal sites.[73,74] Alternatively, recent studies on non-tungsten based catalysts focused on the addition of Sn to the metal catalysts, since this element is known to accelerate glucose to fructose isomerization.[75–77] For instance, Sun *et al.* designed a NiSn alloy catalyst, which improved, besides MEG, also the formation of 1,2-PG.[78] Although the selected examples discussed above highlight the potential of alternative, bio-derived MEG production routes, current lab-scale reactions are usually performed at low substrate concentrations (less than 10 g L^{-1} in water), which hampers industrial upscaling. However, recent progress has been made in this domain. Zhang *et al.* first reported a semi-continuous set-up with glucose feed concentrations up to 50 g L^{-1}.[79] Ooms *et al.* applied a fed-batch system with concentrated (and industrially available) glucose streams (up to 200 g L^{-1}) to simulate the slow release of glucose from cellulose through hydrolysis.[63] With a nickel tungsten carbide catalyst, yields up to 66 % and volume productivities as high as 300 g_{EG} L^{-1} h^{-1} were reported. In addition, their set-up allowed for a fundamental investigation of the reaction mechanism (Scheme 2).

A two-step route from sugars to MEG, as shown in Scheme 2, has also been explored combining hydrous thermolysis, to first form a GA rich oxygenate, with a separate hydrogenation step.[80,81] Liquid phase hydrogenation of the GA-rich thermolytic product with Ru/C at 353 K gave a total MEG yield of 61% over the two steps starting with a 20 wt.% glucose feed.[80] Employing a gas phase hydrogenation using a commercially available Cu/C catalyst at 503 K, resulted in a MEG yield of up to 65% over the two steps.[81]

In order to develop an industrially attractive MEG production process from a biomass feedstock, several constraints should still be tackled: efficient lignocellulosic pre-treatment to fractionate cellulose, minimalization of solvent use by optimal feedstock concentration, higher catalyst stability, and improved MEG separation.[56] For instance, biomass-derived products such as MEG, 1,2-propanediol, and 1,2-butanediol exhibit similar boiling points, and therefore their



Scheme 2. Reaction pathways for the liquid-based conversion of glucose as demonstrated by Ooms et al. over a Nickel-Tungsten Carbide catalyst. Retro-aldol reactions (blue) are the preferred route. Reproduced with permission.[28]

product separation is usually more complicated compared to the conventional petroleum-based MEG production process. In particular, MEG and 1,2-butanediol forms an azeotrope at a molar ratio of 1:1.[82] Zhang and co-workers have therefore investigated a chemical approach based on catalytic dehydration followed by subsequent acid-induced rearrangements to separate MEG from other diols.[82,83] It is based on a different reaction rate of dehydration to aldehydes between MEG and the other diols over strong Brønsted acid catalysts such as H-Beta. This effect is ascribed to the electron-donating effect of the methyl and ethyl groups, which can stabilize carbonium ions in the course of diol dehydration. However, some MEG is still lost in polymerization reactions.

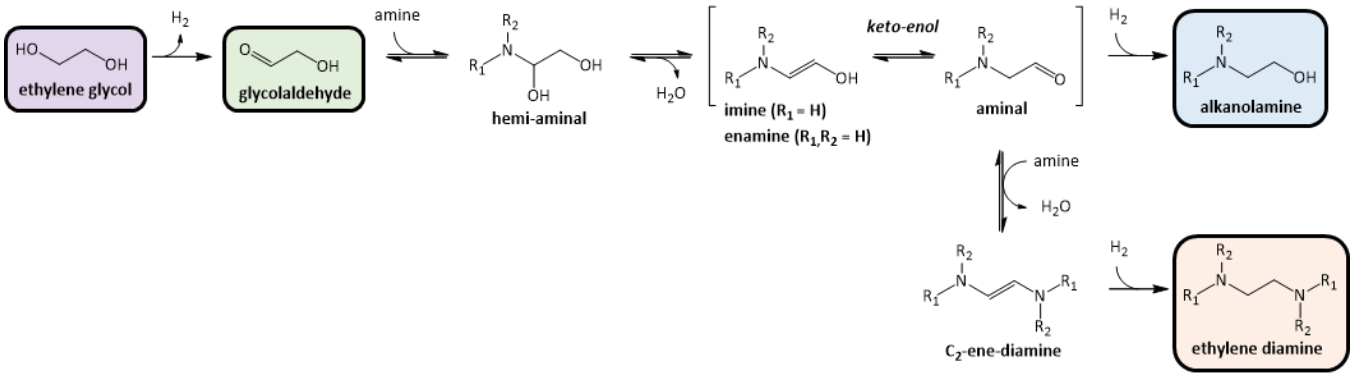
Following the successful demonstration of the chemistry in academic labs, the first bio-MEG pilot-scale approaches are being developed. Avantium, based in The Netherlands, is currently developing a demonstration plant to commercialize a one-step conversion of carbohydrates to MEG. Their Mekong process is a continuous stirred-tank reactor (CSTR) system based on a binary tungsten/hydrogenation catalyst designed to minimize tungsten losses.[84,85] Combined with the fructose to 2,5-furanedicarboxylic acid technology, their overall YXY® process results in the production of fully bio-based polyethylene-furanoate (PEF) bottles with even better material properties than PET.[16,86] These bio-based packaging materials already found their way to consumers, for example, via the bottles of Coca Cola.[87] Other companies, such as Shell, are investigating similar routes, starting from sucrose that is hydrolyzed into a glucose-rich feed for MEG production and a fructose-rich feed towards HMF production.[88,89] A two-step approach, currently being developed by Haldor Topsoe and Braskem is based on hydrous thermolysis of sugars in a fluid bed reactor to GA followed by hydrogenation to MEG.[90]

Many other alternative routes to MEG are available, of which the selective upgrading of C1 chemicals is considered a promising strategy.[24] Current coal-based plants already make use of syngas to produce methanol, that can be converted via subsequent oxidative carbonylation into dimethyl oxalate, which serves as a precursor to MEG.[91,92] However, the use of bio-syngas to ultimately produce building blocks such as methanol and formaldehyde requires gasification of biomass, which destroys its intrinsic functionality. Considering that the gasification of biomass does not

result in optimum exploitation of the bio-based feedstock, and the C1-route by this means does not align with the 12 principles of green chemistry, it is not in the scope of this review.[93,94]
Recent patent literature describes the biological production of ethylene glycol through the fermentation of a carbohydrate source and syngas. Koepke *et al.* observed the production of ethylene glycol from glucose by a genetically engineered microorganism (S. thiotaurini Alanine-Glyoxylate Aminotransferase and P. fluorescens Aldehyde Dehydrogenase in C. autoethanogenum)[95] Furthermore, Pradella *et al.* investigated a fed-batch fermentation in two stages for the production of MEG and acetone through fermentation of a recombinant E.coli strain.[96] The first stage consisted of a growth phase in glucose followed by the second stage, a production phase, in xylose where MEG and acetone where produced. The productivity rate of MEG and acetone were 1.56g $L^{-1}h^{-1}$ and 0.25g $L^{-1}h^{-1}$, respectively.

Oxidation - Availability of bio-MEG can pave the way to bio-based glycolaldehyde and glycolic acid in subsequent oxidation reactions. Berndt *et al.,* for instance, performed the partial oxidation of MEG to glycolic acid on Au/Al_2O_3 catalysts in aqueous solutions, for which the catalytic activity is shown to be primarily determined by gold content and dispersion.[97] Furthermore, Van Haasterecht *et al.* showed that carbon nanotubes containing copper or nickel could convert MEG into glycolic acid under anaerobic aqueous conditions.[98] A selectivity of 96 % at 82 % conversion was reported after 15 hours of reaction at 150 °C, with GA as a reaction intermediate.

Amination - Similarly, alternative pathways have been developed to create alkanolamines from biomass streams. Zhang and co-workers recently reported the synthesis of monoethanolamine (MEOA) from cellulose in a two-step process, a unique approach that combines the acid-catalyzed cellulose hydrolysis with amination in the presence of basic amines.[99,100] Cellulose was converted into GA *via* a retro-aldol process with H_2WO_4 in water at 290 °C in up to 21 % yield. In a second reaction step, the product was further subjected to amination in the presence of ammonia into MEOA (51 %) over a bifunctional Ru/ZrO_2 catalyst at 75 °C and 30 bar of H_2 pressure over 12 hours. The overall MEOA yield

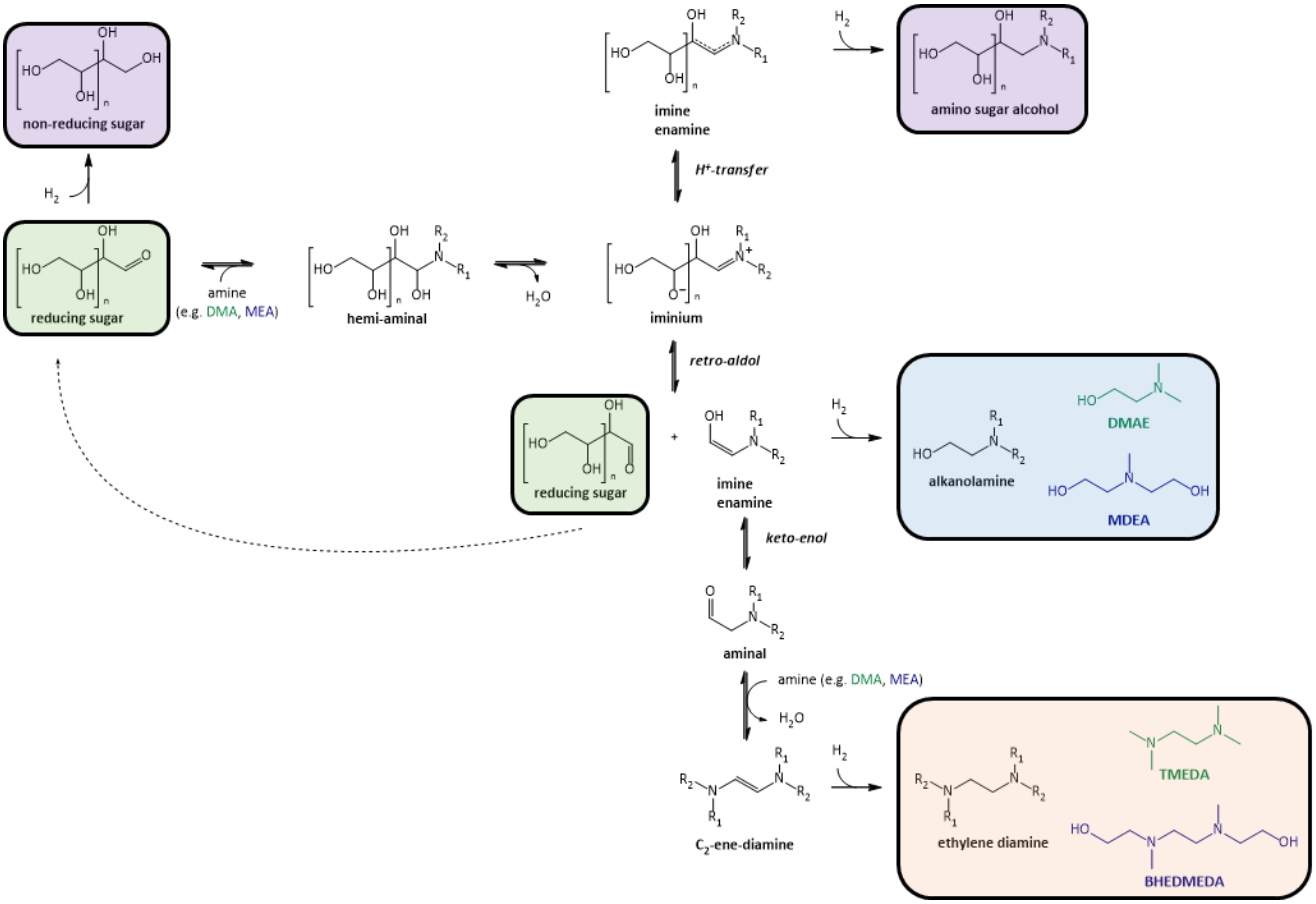


Scheme 3. Reaction pathway for the amination of monoethylene glycol.

from cellulose was 10 %. Catalyst characterization led to the conclusion that Lewis-acidic RuO_2 promotes imine formation from GA, whereas metallic Ru catalyzes the subsequent imine hydrogenation. Recently, Jia *et al.* demonstrated an efficient process for the synthesis of alkanolamines via the direct hydroxyethylation of amines by biomass-derived carbohydrates.[101] Yields up to 87% for the desired alkanolamine could be achieved using xylose and N-methylaniline in the presence of a homogeneous ruthenium catalyst complex. Next to carbohydrate sources, (bio)-MEG can also be utilized directly as a feedstock for amination reactions. A thorough elucidation of the amination mechanism has been conducted by Baiker and co-workers in 1985 (Scheme 3).[102] A continuous fixed-bed reactor at atmospheric pressure was used for the gas-phase amination of MEG with dimethylamine over an Al_2O_3 supported copper catalyst. In this study, the effect of temperature, reactant partial pressure, H_2 partial pressure, and H_2O content was investigated in detail, and GA was observed as an intermediate. The main reaction products were identified as N,N-dimethylethanolamine (DMAE) and N,N,N',N'-tetramethylethylenediamine (TMEDA), with a maximum DMAE selectivity of 74 % (both TMEDA and the enamine intermediate selectivity accounted for 10 %) at a conversion of 94 % at 230 °C. DMAE is mainly used as a building block for flocculants and TMEDA is industrially used as catalyst in the polymerization process of acrylamide gels.[41,103] Interestingly, no net hydrogen is consumed during this process, which indicates a hydrogen-borrowing mechanism, and the excess H_2 is only used to avoid the formation of side-products and catalyst deactivation.

Several patents, based on the research of Baiker and co-workers, were published shortly after. Van Cauwenberge *et al*., for instance, describes the use of a Ru and Co catalyst for the gas-phase amination of MEG with ammonia.[104] Ethylenediamine (EDA) selectivity of 50 % at 43 % conversion at 150-170 °C was reported. Recently, Parvulescu *et al.* described a process for the conversion of MEG to ethylenediamine (EDA) utilizing zeolites with MOR framework structure.[105] At 41% conversion, an EDA selectivity of 8% at 340°C was obtained.

Besides patents, also academic research was conducted in this field. The reductive aminolysis approach was inspired by class-1 aldolase enzymes, Pelckmans *et al*. demonstrated a direct one-pot conversion of glucose to short ethylene



Scheme 4. Reaction pathway for the reductive amination of a reducing sugar (n = 0-2)

diamines involving a consecutive retro-aldol scission of the sugar molecule into the GA intermediate, followed by reductive amination.[106] The presence of an amine led to both a facilitated C-C scission, possible at lower temperatures compared to conventional catalyzed retro-aldol reactions, and the direct stabilization of the reactive GA intermediates through catalytic hydrogenation of the formed imines. The reaction of glucose with dimethylamine in the presence of Ru/C or commercial silica supported 56 wt.% Ni catalysts at 125 °C and 7.5 MPa of H_2 pressure furnished N,N,N',N'-tetramethylethylenediamine (TMEDA) with a yield of 51 %. When the solvent was replaced by N-methylethanolamine (MAE) and an aqueous glucose feed was applied in fed-batch mode, a surprisingly high yield of up to 87 % N, N' -bis(2-hydroxyethyl)-N,N'-dimethylethylenediamine, also denoted as BHEDMEDA, could be achieved (scheme 4). Later, a reaction mechanism for the reductive aminolysis of sugars, based on a combined experimental and theoretical study, was proposed by the same group.[107] It involves hemi-aminal formation between the sugar and the amine, and subsequent dehydration to produce a zwitterionic iminium intermediate, followed by a fast C-C cleavage through intramolecular deprotonation and subsequent hydrogenation of the formed unsaturated amine intermediate. It was proven that to favor the dehydration equilibrium, the water content should be kept to a minimum, while the amine-to-substrate ratio should be kept high to promote the amination equilibrium. When secondary amines are used, the dissociation energy between the αC-βC carbon bond of the intermediate is significantly lowered, which results in a higher selectivity to C_2 amine products (aminolysis route) compared to the formation of amino sugar alcohols (reductive

amination pathway). The reaction mechanism mostly results in high selectivity for ethylene diamines, and not for aminoalcohols, explained as a side-effect of the high amine ratios needed to induce the sugar C-C scission. Another example of an alternative bio-derived route for an EO application has recently been published by Ma *et al.*.[108] This publication elaborates on the continuous production process of taurine from monoethanolamines.
Furthermore, homogeneous catalysts have been developed for the catalytic amination of alcohols under mild conditions. For instance, Schaub *et al.* mention a process for the preparation of alkanolamines from diols by a homogeneous Ru complex in the presence of a solvent.[109] An ethanolamine selectivity of 65 % at 40 % MEG conversion at 135 °C was reported. In addition, Börner *et al.* created a solvent-free process with an iridium-pincer complex and reported yields up to 99 % with MEG and diethylamine.[110]

Carbonates - Starting from MEG, ethylene carbonate can be formed through the reaction with urea using metal oxides as a catalyst.[46] For example, Sun and co-workers reported a yield of 93 % towards ethylene carbonate with zinc oxide as a catalyst after three hours at 150 °C.[111] In the next step, dimethyl carbonate can then be synthesized in high yields via transesterification of ethylene carbonate and methanol.[112] This reaction can be considered an environmentally benign route since CO_2 is utilized. Moreover, the ammonia from urea and MEG are the only byproducts and can be recycled as shuttles or used in other processes.

Glycol ethers - The self-etherification of alcohols, for example, the etherification of ethanol to diethyl ether in the presence of sulphuric acid, is a well-known reaction. The principles of this reaction mechanism are independent of the type of feedstock used and are therefore also valid for bio-derived alcohols such as MEG. For instance, Shi *et al.* and Baimbrigde *et al*. describe the coupling of MEG and lower fatty alcohols in the presence of an acid catalyst.[113,114] Conversions of 90 % are reported with up to 86 % selectivity for the selected glycol ether product. High selectivity is a major advantage over the EO process, where higher separation efforts are needed due to a broader distribution of ether products.

4. Conceptual Biorefinery Platform: Glycolaldehyde as bio-based C_2 platform molecule

In the various bio-derived synthesis routes for C_2 chemistry described in the previous section, MEG often appears as a key intermediate. Hence, one could envision MEG as an alternative, bio-based C_2-platform molecule for EO, capable of being converted into many industrially relevant end-products, such as amines, glycol ethers, and carbonates. However, given the high stability of the alcohol functionality, MEG is considerably less reactive than EO. In comparison to MEG, glycolaldehyde (GA), the typical intermediate in the synthesis of bio-MEG, shows a greater resemblance to EO given the presence of a reactive aldehyde group. Moreover, the step economy can be improved using the intermediate GA as opposed to the final product MEG, since the final hydrogenation step can be avoided. Finally, recent GA production routes have progressed significantly over the years and are catching up to MEG production methods. GA may thus be considered as the true platform chemical potentially replacing EO in an even larger portfolio of commodity and specialty chemicals[32,66,68–72,81,108,109,110], and may form the basis of a novel holistic biorefinery concept.

GA is a remarkable molecule; it is the smallest reducing sugar with both an alcohol and aldehyde functionality. In pure form, it exists at room temperature, in a crystalline dimeric form as 2,5-dihydroxy-1,4-dioxane.[118] Upon melting, the ring partially opens, and a mixture of dimeric and monomeric forms is obtained. In the gas phase, GA exists exclusively in the monomeric form.[119,120] Furthermore, GA is somewhat difficult to handle as the highly reactive aldehyde functionality is prone to many side reactions. The instability or high reactivity of GA in condensed form is originating from its dense functionalization. For instance, α-hydroxy carbonyls can easily be reduced catalytically to alcohols. They are susceptible to aldol condensations and react readily with amines to form an even more labile imine intermediate prone to Maillard reactions[121], caramelization reactions[122], Amadori rearrangements[123] and keto-enol tautomerization[124]. Therefore, GA is often stabilized immediately after production, typically by hydrogenation to MEG.[125] Additionally, the original production route relies on the hydroformylation of formaldehyde with syngas, which has never been used to produce GA on a bulk scale. As a result, GA has found limited use in the chemical industry to date.[126–128] The availability of GA directly from biomass may cause, however, a paradigm shift.
Compared to ethylene and EO, the retro-aldol based production of GA from carbohydrates corresponds better to the 12 principles of green chemistry. Firstly, this route is fully exploiting the functionality of biomass (atom efficiency). Secondly, it would provide the basis for a safer process, with GA being a non-toxic and non-explosive molecule. Studies

on the metabolism of GA are readily ongoing; it is known to have an intraperitoneal-rat LD-50 of 280 mg/kg, *viz*. higher toxicity than caffeine but similar to Aspirin, and it does not bio-accumulate in humans because it is readily metabolized into acetyl coenzyme A.[129–133] These properties stand in sharp contrast to the highly toxic and explosive EO. Finally, it would be interesting to compare both routes in a side-to-side life cycle assessment, which is currently unavailable and may be due to the lack of mature GA technologies. However, as mentioned before, the production of EO and its parent-molecule ethylene comes with significant CO_2 emissions. Many researchers are, therefore, investigating bio-based production routes towards GA, which will be discussed below.

4.1. Developments in bio-based production of glycolaldehyde

Pyrolysis - When biomass is rapidly heated to 500 °C, a pyrolysis-oil is obtained, containing 20 % water and more than 300 oxygenated compounds.[134] The largest fraction of compounds in wood-derived pyrolysis oil comprises acetic acid (3-12 %) and GA (5-13 %), but separation and purification are major hurdles. A process was invented by Stradal and Underwood, which consists of water-based extraction, followed by several vacuum-evaporation and distillation steps to maximize GA yield.[135] De Haan and co-workers investigated these separation processes to obtain a fermentation feedstock for renewable MEG synthesis.[136] A first water treatment could extract 63 % of GA and 88 % of acetic acid present in the pyrolysis oil. After an array of separation and purification steps, an overall GA recovery yield of 17 % could be obtained. A second route via reactive extraction with primary amines was also looked into, where the imine formation and extraction route was promising but also challenging for GA regeneration.[137] An economical process evaluation was made by the same group, where an integrated recovery of acetic acid and GA seemed most suitable due to a combined high recovery and energy recuperation. Starting with 200 Ktonnes of pyrolysis oil with the assumption of 8000 hr/yr operating time, they estimated that 10 Ktonnes of acetic acid and 13 Ktonnes GA could be produced annually in a profitable manner for $600/tonne each.[138] This calculation makes the GA price of the pyrolysis route competitive with the current EO production.

A second major pyrolysis production of GA was demonstrated by Ribeiro *et al.* in a combined hydropyrolysis – hydrodeoxygenation continuous route to produce liquid fuel from biomass.[139] After the hydropyrolysis step, levoglucosan was the major component at 55 wt.% of the liquid product composition, which can be further upgraded to energy-dense products, followed by GA at 5 – 20 wt.% of the liquid as an interesting side-product in light of this review. Although the fast pyrolysis of biomass is a practical method for the production of GA, the heat lability and product composition increase the complexity of the separation process and account for the high operational and investment costs.[140]

Gasification - Similar to the pyrolysis route is the gasification of biomass or biomass waste to syngas, a crucial feedstock for decades for petrochemistry.[93] As already stated, this approach destroys the intrinsic functionality and value of biomass to its bare minimum, which does not accord well to the 12 principles of green chemistry, yet can readily be plugged into our current refineries. Building blocks such as methanol and formaldehyde are then easily obtained.[94]

As mentioned earlier, the current petrochemical route toward GA relies on the homogeneously Rh catalyzed hydroformylation of formaldehyde with syngas under elevated pressure and temperature, with lab-scale yields up to

Method	Advantages	Disadvantages	GA Yield (%)
Pyrolysis	Practical technology	Low selectivity Multi-step separation	17[a] [136]
Gasification (syngas)	Practical technology Implementation in petrorefinery	Expensive catalysts Low C_2 selectivity	35 [147]
Supercritical water	High selectivity Clean technology	Operating conditions	64 [150]

Retro-aldol	High selectivity	Cellulose activation Diol separation	74 [68]
Hydrous Thermolysis	High selectivity High volume feed	Crude feedstock (C_1 + C_3 fragments)	70 [81]

[a] The GA yield mentioned here reflects a recovery yield. The initial GA yield obtained from biomass is around 2%.

Table 1. Advantages and disadvantages of the different technologies to produce GA.

80 % GA.[126–128] However, it is not implemented for bulk production due to the use of an excess of (expensive) ligands and their associated degradation, catalyst recycling, and following purification costs.[141]
A second route starting from formaldehyde is the formose reaction.[142] Since GA has been detected in space, there is much debate over the role formose has played in the origin of life by creating simple sugars and following nucleotides.[142,143] Formation of the first C-C bond is the rate-limiting step in the formose reaction, requiring an induction period and possibly catalyzed by radiation. Once formed, GA acts as auto-catalyst for the further aldol condensation towards C_4 and C_6 sugars in alkaline media.[144] The reaction selectivity towards C_2 products is, therefore, difficult to control.[145,146] Progress has been made by the use of thiazolium salts or N-heterocyclic carbenes as a catalyst, where the active site was sterically or electronically modified to allow C_2 over C_3 selectivity up to 80 % at 40 % conversion.[147,148] Additional efforts have been made to produce GA by means of heterogeneous zeolites.[149] In the presence of NaOH, excellent yields of 100 % GA starting from formaldehyde are obtained with Na-Mordenite. However, the necessity to use almost stoichiometric amounts of NaOH and zeolite makes this route less attractive for industrial implementation.

Supercritical water - The properties of water change considerably when it reaches a supercritical state (T > 647.2 K and P > 22.1 MPa), and parameters such as density and dielectric constant can be varied by manipulating pressure and temperature.[150] Despite the rather demanding process conditions, *viz*. 723 K and 35 MPa, it is one of the few environmentally friendly mediums that can dissolve and decompose cellulose through hydrolysis. Sasaki *et al.* investigated this hydrolysis in sub-supercritical conditions in a continuous set-up without catalyst and found that the supercritical water forms a homogeneous hydrolysis environment that can break up the cellulose crystals.[151] The main reactions that occurred were hydrolysis, retro-aldol condensation, isomerization, and dehydration of the formed sugars and selectivity up to 64 % GA at 99 % conversion was reported.[150] Martinez *et al*. analyzed the influence of reagent concentration on hydrolysis reactions of cellulose and pointed out that increased reaction times, independent of the cellulose concentration, resulted in higher GA yields. [152] Furthermore, through the addition of a flash separation step, the concentration of GA in the liquid stream could be increased to 10%.

Catalytic retro-aldol - This chemical route has been extensively discussed in section 3. Most of the one-pot retro-aldol strategies stabilize the reactive GA intermediate as MEG through metal-catalyzed reduction. However, a multi-pot or continuous approach, could give rise to a versatile production strategy for GA, depending on the subsequent reactions. Semi-continuous or fed-batch approaches have already been investigated by Zhang *et al.* and Ooms *et al.*, demonstrating the viability of concentrated glucose streams usage up to 200 g L^{-1}.[63,79]
An interesting new approach has recently been examined by Xu *et al*.[153] During the retro-aldol conversion of cellulose, the aqueous solvent was replaced by methanol to ease separation afterward, but also reacted with the GA intermediate to form a stable methyl glycolate up to 57 % yield. A tungsten catalyst was used under O_2 atmosphere at 240 °C. This stream of methyl glycolate was then utilized as a feed for hydrogenation reactions over a Cu/SiO_2 catalyst, yielding quantitatively (100 % selectivity) MEG at 200 °C and a subsequent reaction to ethanol (50 % selectivity) at 280 °C. Since the overall ethanol yield of the process was only 30 %, a new catalyst was developed in follow-up research, where a Cu-Pt single-metal alloy increased ethanol selectivity to 70 % with no signs of deactivation after 700 h on-stream.[154] To deal with the safety concerns of a two-step oxidation-hydrogenation, a one-pot process involving tandem catalysis of

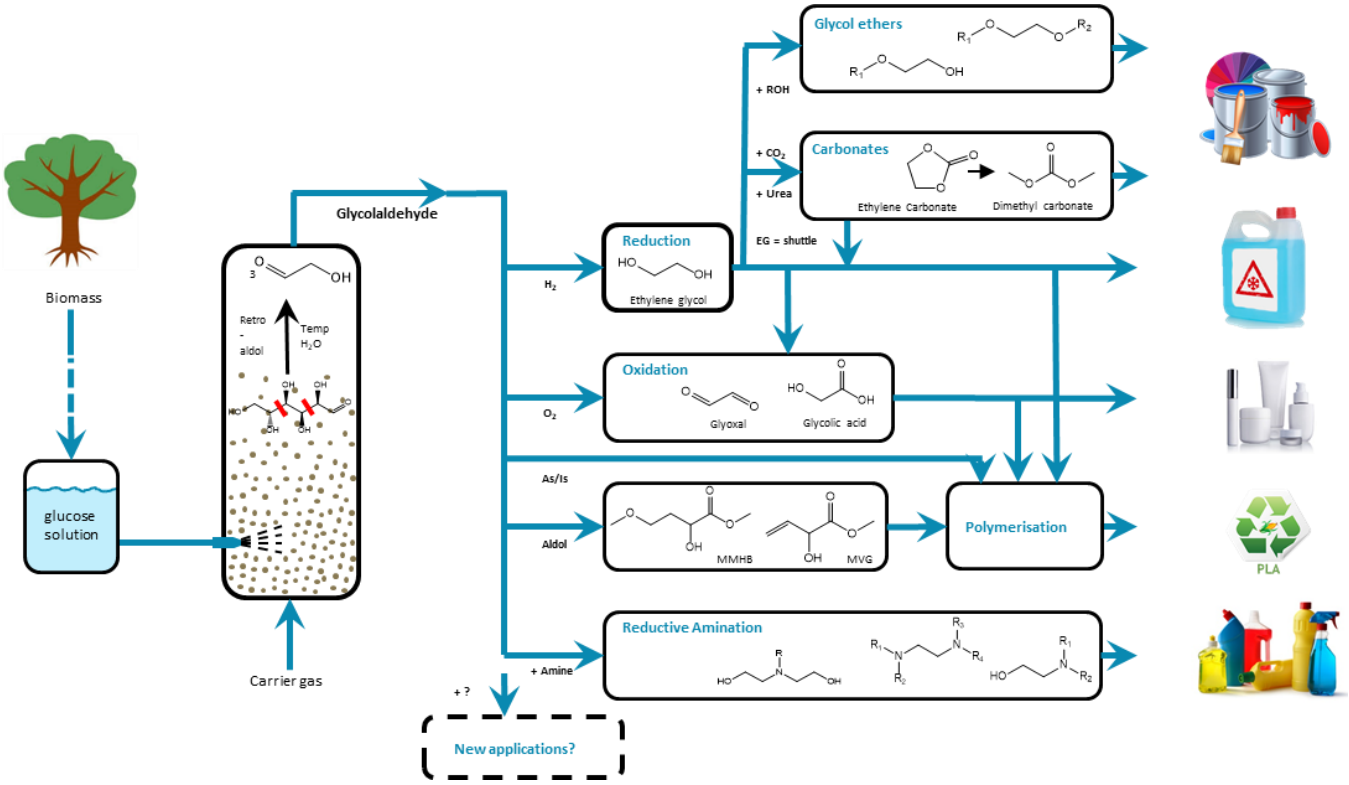
retro-aldol, hydrogenation and hydrogenolysis was developed by the same group. Using an optimized Mo/Pt/WO_x catalyst, ethanol yield reached 43 % with full cellulose conversion at 245 °C and 6 MPa of H_2 with good stability of the catalyst.[155] As an alternative to enzyme-based ethanol production, that still faces economic barriers due to high pre-treatment costs and low efficiency, this chemo catalytic approach demonstrates a promising route that underlines the platform approach of GA, where the methyl glycolate derivative can be utilized for bulk chemicals.[156,157] This approach could, in theory, lead to a 100 % atom-efficient ethanol production in contrast to the 66 % atom-efficiency of current sugar fermentation (i.e., expelling one CO_2 molecule per ethanol produced), given a sustainable carbon-free source of hydrogen can be used in the future.

Hydrous thermolysis - One of the most promising production routes for GA is the hydrous thermolysis of sugars.[158,159] It was invented in 2006 and consists of atomizing an aqueous sugar solution (up to 60 wt.%) into a fluidized sand bed reactor at 500 – 600 °C with a contact time of 0.5 – 2 seconds. The fast pyrolysis can perform fragmentation of sugars with GA yields up to 74 % and feed rates up to 7 kg solution per hour (small scale). More recently, Schandel *et al*. successfully applied this process to a range of sugars, including glucose, fructose, xylose, and sucrose.[160] However, a yield higher than 70% of GA, could only be obtained using glucose as feedstock. No purified GA is obtained, rather a crude feed of which the other fraction consists mainly of C1 fragments such as formaldehyde and C3 fragments such as pyruvaldehyde and acetol. The obtained crude GA feed can be purified by removing formaldehyde traces before being used in the hydrogenation step, yielding MEG.[81,161] Based on the boiling point differences, no difficulties can be expected in the separation of the hydrogenated products. This production route towards MEG is under demonstration by Haldor Topsoe, the so-called MOSAIK process (MOnoSaccharides Industrial Cracker), for the production of sugars-to-biochemicals, in cooperation with Braskem.[90,162] In addition to reduction, they have also shown that the same GA stream is useful for the production of lactic acid derivatives.[163]

4.2. Bulk drop-in applications of GA as a structural analog to EO

Until now, probably because of its limited availability, little attention has been devoted to fully exploit the reactive nature of GA towards a C_2-platform molecule. Currently, GA has only a small application window in the food industry as a browning agent or in flavoring applications.[164] Nevertheless, when available at the proper volume and price, this versatile chemical has several possible bulk applications, of which some will be discussed here (Scheme 5).

Reduction - A detailed overview of the one-pot '*cellulose-to-MEG'* with GA as a key intermediate is already discussed in detail in section 3. Next to these one-pot technologies, systems with a separate hydrogenation step of the GA feed have been explored as well. For instance, Goetz *et al*. describe the hydrogenation of GA with Pd/C at 150 °C in N-methyl pyrrolidine as a solvent.[165] Furthermore, continuous hydrogenation at 160 °C and 35 bar in the presence of a Ru/C catalyst and MEG as a solvent has been described by Jacobson *et al*.[166] Also, homogeneous Ru catalysts are known to catalyze GA hydrogenation.[167,168] Braskem, in cooperation with Haldor Topsoe, plans to utilize its GA-stream obtained via hydrous thermolysis as a feed for reductive reactions.[81,90] In the patent filed, a pyrolysis product is brought into an



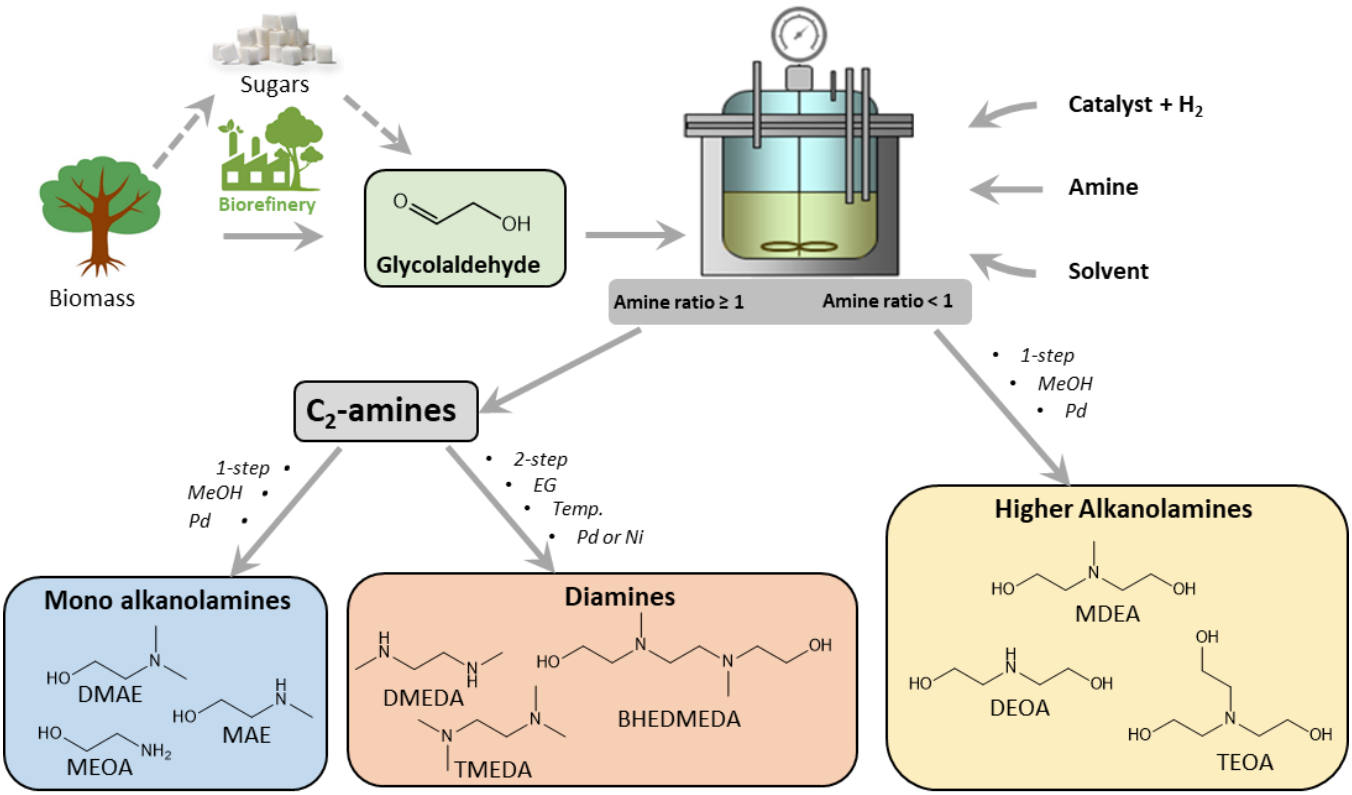
Scheme 5. Holistic model of a glycolaldehyde-based biorefinery for C2-chemistry, based on all proven and currently in-development technologies.

autoclave with a Ru/C as a catalyst and reacted with 90 bar of hydrogen at 80 °C for 6 hours. A yield of 89 % MEG was reported starting from a pyrolysis product feed, where the maximum theoretical MEG yield is determined by the hydrogenation of both glyoxal and GA. On the contrary, a yield of 98 % MEG could be obtained with pure GA solutions.[169]

Oxidation - Applications and synthesis of glyoxal and glycolic acid have been covered earlier in this article when the oxidation of MEG was discussed. The reaction mechanism shows that GA is an important intermediate for glyoxal as well as for glycolic acid, with yields up to 80 % for both components.[28,98] Subsequent work on more direct bio-based processes has confirmed that molybdenum-containing acidic catalysts at 180 °C under an oxygen atmosphere can catalyze the hydrolysis of cellulose, the retro-aldol fragmentation to GA and selectively oxidize GA to glycolic acid.[170,171] A yield of 50 % to glycolic acid has been reported, and despite the laborious recovery of the catalyst, it could be reused up to 9 times.

Polymers - Another interesting product is polyglycolic acid, with versatile applications in packaging and medicinal polymers. Currently, this bio-degradable polymer has two industrial production routes. Polyglycolic acid can be formed by dehydration-polycondensation of glycolic acid or through ring-opening polymerization of its glycolide dimer.[172] Although, the established technologies to produce glycolide are not cost and waste-efficient, the advancement in heterogeneous catalysis and the use of renewable feedstock may increase the market share for glycolide. Recently, Van Wouwe *et al*. developed a facile one-step liquid-phase production of lactide (methyl glycolide), exploiting the shape-selectivity properties of zeolites, potentially accelerating the use of these bio-based plastics in the near future.[173–176] Alternatively, De Clercq *et al*. demonstrated a continuous gas-phase process with a TiO_2-based catalyst to produce the dimers via transesterification of concentrated methyl lactate and methyl glycolate solutions, respectively.[177,178] In addition to the above-mentioned progress, glycolic acid obtained by oxidation of GA might lead to further optimizations of polyglycolic acid production.

Amination - Zhang and co-workers have reported that a Ru/ZrO_2 catalyst can be used for various biomass-derived aldehydes and ketones, resulting in 94 % monoethanolamine (MEOA) and 2 % ethylenediamine (EDA) with aqueous



Scheme 6. Routes towards bio-based alkanolamines and ethylene diamines, as investigated by Faveere *et al.* [184]

ammonia and pure GA as reagents.[99] BASF patented a process for reacting GA with an aminating agent in the presence of H_2, a solvent, and a catalyst.[179] The process was conducted with an ammonia-to-GA molar ratio of 35, THF as inert solvent at 100 °C, and up to 100 bar of H_2 for 8 hours. The maximum reported yields were 82 % of MEOA and 6 % of EDA. This stream of GA-derived amines was used in a subsequent patent where it was employed as the aminating agent to create higher ethanolamines products, with Ni, Co and/or Cu catalysts. At a conversion of 70 %, a selectivity of 88 % triethanolamine (TEOA) was reported.[180]

Faveere *et al*. recently showed the versatility of GA as a substrate of reductive amination reactions.[181] A variety of parameters was investigated, enabling to fine-tune the selectivity between alkanolamines, ethylene diamines, and higher alkanolamines in a one-step process (scheme 6). Furthermore, the authors reported dimethylethanolamine (DMAE) yields of 97 % with a Pd/C catalyst, carried out at 100 °C with 70 bar of H_2 for 1 hour. It was found that protic solvents, preferably methanol, were essential to facilitate the reductive amination by assisting in proton transfers, enhancing the overall reaction kinetics. Some (stable) key-intermediates were detected, such as an oxazolidine derivative, which helped to improve the reaction yields further. The beneficial solvent effect is key in controlling other parameters influencing selectivity, such as the amine-to-substrate ratio. This enables the one-step formation of mono-, di- and tri-alkanolamines such as N-methyldiethanolamine (MDEA, 91 %) with methylamine or triethanolamine (77 %) and ammonia as an aminating agent, respectively. Using the amine-to-substrate ratio to control the formation of primary, secondary, or tertiary amines, is comparable to what is used in the current amination of EO. Nevertheless, reactions with GA intriguingly show higher selectivity towards the higher ethanolamines.[41]

4.3. Novel applications with GA as substrate

Previous sections demonstrated that GA could act as an alternative substrate for some EO derived products and how it could be produced from biomass sources. However, next to drop-in applications, the use of a new platform molecule also offers the opportunity to create new products and processes. Some of them, which are listed below, have already been investigated.

C_2 diamines - Although ethylene diamines can be formed from ethylene oxide, this involves a cumbersome two-step process.[182] In the first stage, monoethanolamine (MEOA) is formed by the reaction of ethylene oxide and ammonia, and the produced MEOA is reductively aminated in a second stage. As a result, the current production of diamines generally avoids the use of ethylene oxide and occurs through the amination of ethylene dichloride (EDC) obtained from ethylene.[183] However, an important disadvantage of this widely practiced industrial route is the stoichiometric production of hydrochloride salts.[182]
Alternatively, the production of C_2-diamines can be conducted starting from GA. Unlike the above-mentioned processes, this novel process can be carried out in one pot without halogenated salts as byproducts, and might eventually replace the current ethylene dichloride-based process. For instance, Faveere *et al*. demonstrated a two-step one-pot approach to obtain ethylene diamines from GA.[181] Methanol as a solvent was shown to further enhance the reductive aminolysis rate by lowering the activation barriers for nucleophilic amine attack and C-C bond scission.
Furthermore, Li *et al*. recently filed a patent describing the rapid two-step synthesis method for bio-based amine compounds. In a first step, formamide derivatives are formed through the reductive amination of aldehyde and ketones by microwave-assisted heating. Subsequently, the formyl group is removed via alcoholysis, resulting in primary aminated compounds.[184]

C_4 building blocks - Plastics are omnipresent in our daily life, but they are very persistent toward degradation. The accumulation of microplastics in the oceans has triggered the search for sustainable and biodegradable polymers such as polyesters.[185] A critical review on the catalytic routes toward bio-based monomers for polyesters has been written by De Clercq *et al*., highlighting GA as a key intermediate in many of the novel processes.[186]
Interestingly, GA and the retro-aldol route from cellulose play an important role in the creation of rare and expensive C_4 sugars (e.g., threose, erythrose, and erythrulose).[187] During the catalytic self-condensation of GA, the difficulty is controlling the selectivity toward tetrose sugars while avoiding subsequent aldol-condensation into hexoses. To address this problem, Tolborg *et al*. used the shape selectivity properties of Sn-MFI zeolite as a catalyst to reach a high C_4 sugar yield of 74%.
In addition to C_4 sugars, the retro-aldol route from cellulose is prominent in the production of bio-based monomers such as lactic acid-like α-hydroxy acids and esters, which will allow engineering of the properties and performance of a new generation of bio-based plastics. When exploring the conversion of carbohydrates to polymer building blocks, some new lactic acid-like polymer building blocks were discovered, such as methyl vinyl glycolate (MVG) and methyl-4-methoxy-2-hydroxybutanoate (MMHB), which are not readily obtainable via conventional routes. Their presence was first observed as co-products in the formation of methyl lactate from sugars in zeolites by Taarning and co-workers, and their formation mechanism was later confirmed by Dusselier *et al.*, opening research towards MVG as a new and diverse platform molecule. [188–190] For instance, new types of diacids can be obtained via metathesis of MVG, with applications in polyamides.[189,191,192] Furthermore, these functional α-hydroxy esters, methyl vinyl glycolate (MVG) and methyl-4-methoxy-2-hydroxybutanoate (MMHB), contain a terminal vinyl or methoxy group respectively, which have the potential to modify and to tune sites in polyesters such as polylactic acid when they are used as (co-)polymerization building blocks.[193] The presence of lactic-acid like molecules was attributed to the presence of tetroses and GA obtained by the retro-aldol reaction of glucose. The reaction starts with the dehydration of the tetrose molecules, in the presence of an Sn-beta zeolite in methanol at 160°C. Subsequently, methanol is added to the terminal aldehyde group, followed by a 1,2-proton shift where the hemiacetal is transformed into the final ester.[190] Additionally, esters can be derived from GA through an aldol condensation with Sn as an efficient catalyst.[190,193–195] As an example, MMHB up to 58 % can be obtained starting from GA when using a homogeneous $SnCl_4{\cdot}5H_2O$ catalyst at 90 °C.[77,193] In contrast, Holm *et al.* reported up to 56 % MVG when Sn-beta was used as a catalyst at 160 °C.[188,194] De Clercq *et al.* and Tolborg *et al.* discovered likely confinement effects, where homogeneous and mesoporous catalysts stimulated the formation of MMHB, whereas microporous catalysts tended to yield MVG at higher temperatures.[187,196]
Applications of new functional α-hydroxy esters are still limited due to their novelty as a plastic monomer. Nevertheless, with the current development of hydrous thermolysis of sugars and the increased research in this field, this route is believed to gain importance in the near future.[158,159,163]
Furthermore, GA can serve as a monomer for renewable thermoplastics. Luebben *et al.* have synthesized a poly(2,5-dihydroxy-1,4-dioxane) by catalytic polymerization of glycolaldehyde dimer, yielding in a polysaccharide-like structure where the GA dimer remains intact.[197,198] The authors anticipate that this plastic could have similar properties to high-density polyethylene (HDPE) if the chain length can be increased from currently 15kDa to over 100kDa.
Additionally, GA can play an important role in the production of biopolymers via its MEG derivative (PES, PET, and PEF).[199]

Drug synthesis – Given the explosive and toxic nature of ethylene oxide, the use of EO in pharmaceutical processes is generally limited to its use as a sterilizing agent.[200] In contrast, the safe handling of GA enables its use as C_2 platform molecule in novel synthesis procedures of drugs. For example, Zhang and co-workers reported the one-step diastereoselective synthesis of bis-tetrahydrofuran alcohol, which serves as an important moiety in synthetic HIV drug candidates.[201] It is based on the cyclization of GA and 2,3-dihydrofuran, in which the GA dimer serves as an electrophile for the catalyzed reaction in the presence of a $MnBr_2$-(S,S)-Ph-phybox ligand complex. Related to this, Xu *et al.* were able to synthesize a variety of 3-(indol-3-yl)-2,3-dihydrofurans from aqueous GA by a $FeCl_3 \cdot 6H_2O$/meglumine catalyst system.[202] Furthermore, the 5-membered oxazolidinic intermediate obtained by Faveere *et al.* shows much resemblance to the nucleoside pentose but with the incorporation of nitrogen.[181] This could potentially serve as a synthetic N-containing nucleoside analog (also called azanucleoside) for the development of new anti-tumour or antiviral drugs.[203,204] Finally, the use of GA is also mentioned in a recently filed patent on small molecule compounds for treating or ameliorating Huntington's disease.[205]

4.4. Applied GA biorefinery concept

Over the past decades, several breakthroughs regarding efficient biomass conversion into novel, bio-based components have been reported by the scientific community. [14–17] The conceptual model for GA as bio-based, C_2-platform molecule starts from monosaccharides, which can be obtained either from sugar-rich crops (e.g., sugarcane) or, more desirably, from the hydrolysis of cellulose as a non-edible feedstock.[206] Lignocellulose accounts for the largest fraction of biomass and is composed of cellulose (35-50 %), hemicellulose (15-35 %), and lignin (15-30 %).[207] Although the production of GA only requires the cellulose fraction, a sustainable biorefinery should maximize the disassembly of the whole feedstock. In this context, it was demonstrated by several research groups that a lignin-first approach is most desirable.[208–214] Lignin contributes significantly to biomass's recalcitrance and, consequently, impedes efficient valorization of the carbohydrates.[208] Therefore, removing the lignin early in the biorefinery is an attractive strategy to facilitate carbohydrate valorization.

5. Summary and Outlook

EO is a versatile and valuable C_2-platform molecule used in the manufacturing of numerous commodity chemicals. However, the established petroleum-based production process towards EO has several drawbacks, such as safety concerns regarding manufacturing and handling (e.g., toxicity, explosions) and high emissions (usually up to 2 kg CO_2 per kg produced product). Therefore, the development of sustainable, bio-derived alternatives for EO is vastly attractive.

Bio-based glycolaldehyde (GA) possesses a unique difunctional reactivity and therefore exhibits excellent potential to be used in the synthesis of chemicals. Considerable research has already been conducted into bio-based GA production processes such as pyrolysis, gasification, supercritical water, catalytic retro-aldol, and hydrous thermolysis. Pyrolysis or gasification of biomass are easily implemented in current refineries, but exhibit relatively low selectivity for GA and partially destroy the intrinsic value of biomass. On the contrary, the use of supercritical water is a clean technology for the fragmentation of biomass into GA, but unfortunately requires demanding process conditions. Recent developments in the retro-aldol approach have shown high selectivity towards GA. In the liquid phase, the reaction mechanism is very complex and results in a range of diols that are difficult to separate by conventional techniques. The MOSAIK process, developed by Haldor Topsoe, is based on the hydrous thermolysis of carbohydrates in the gas phase. At present, this process shows the highest potential for large scale production. Moreover, it has already demonstrated high selectivity and feed volumes, starting from a crude feedstock obtaining 70 % GA and additional C_1-C_3 fragments.
Currently, one of the most interesting GA-derived products is ethylene glycol (MEG), which is a precursor for polyurethanes or (bio-)polyesters such as poly(ethylene succinate) and polyethylene terephthalate and operates as a heat transfer fluid. MEG can also serve as a platform for ethylene carbonate and glycol ethers. In addition, GA has shown to play a major role in oxidation reactions towards glyoxal and glycolic acid and the creation of novel α-hydroxy acids and esters. All these components are bio-based and renewable monomers for bioplastics, with the possibility to be tailored for specific functionalities and applications. It was demonstrated that biomass could be used directly as a feedstock for amination reactions (e.g., the reductive aminolysis of sugars), which yields ethylene diamines, and the

two-step production of MEOA straight from cellulose. However, yield could be increased starting directly from GA as a substrate, unlocked by a solvent effect, and the presence of critical intermediates. Close to quantitative production of ethanolamines via this route has been demonstrated very recently, and different kinds of aminating reagents can readily be used to create a versatile portfolio of alkanolamines, diamines, and higher ethanolamines.
Interestingly, many of the process parameters utilized in the EO-based amination can also be applied to GA, underlining its use as an alternative, bio-based chemical platform for short molecules. An additional feature compared to EO chemistry lies in the creation of new, unexplored applications starting from GA as a building block for polymers or in drug synthesis. Although the unique asymmetric difunctionality of GA contributes to its remarkable reactivity, one must bear mind the obstacles associated with this reactivity. GA can easily be reduced catalytically into alcohols. However, the choice of hydrogenation catalyst is crucial, since GA might 'unzip', resulting in the formation of formaldehyde and hence poisoning the catalyst. Furthermore, GA is susceptible to aldol condensations under particular reaction conditions. In the presence of amines, an imine intermediate is readily formed, which is prone to Maillard reactions, caramelization reactions, Amadori rearrangements, and keto-enol tautomerization. Controlling the reactivity through clever process parameter selection and smart catalysis design will thus be essential in exploiting the full potential of GA as a renewable platform molecule for the C_2-chemistry. Nevertheless, it has already demonstrated its advantages in possible applications.

In conclusion, we propose bio-derived routes based on GA to replace the current EO-based platform models and believe GA can serve a central role in future biorefineries.

Acknowledgements

W.F. thanks the Flemish government for financial support in the Carboleum icon project (Catalisti), Eastman financial support for amine chemistry and the C_2 KULeuven project 2019 for general financial support of the research of B.F.S.. S.V.P acknowledges the Flemish government for their financial support in the A^3 project (Vlaio).

The authors declare no conflict of interest.

W.F and S.V.P contributed equally to this work.

Keywords: Biorefinery • Ethylene Oxide • Glycolaldehyde • Platform molecule • Sustainability

[1] Organization of the Petroleum Exporting Countries, "World oil outlook," can be found under https://www.opec.org/opec_web/static_files_project/media/downloads/publications/WOO_2018.pdf, **2018**.

[2] International Energy Agency, "World Energy Outlook," can be found under https://www.iea.org/reports/world-energy-outlook-2019, **2019**.

[3] Ellen MacArthur Foundation, *Towards the Circular Economy*, **2013**.

[4] H.-J. Arpe, *Industrial Organic Chemistry*, Wiley-VCH, **2010**.

[5] A. Mohsenzadeh, A. Zamani, M. J. Taherzadeh, *ChemBioEng Rev.* **2017**, *4*, 75–91.

[6] M. Yang, X. Tian, F. You, *Ind. Eng. Chem. Res.* **2018**, *57*, 5980–5998.

[7] A. Kang, T. S. Lee, *Bioengineering* **2015**, *2*, 184–203.

[8] K. A. Gray, L. Zhao, M. Emptage, *Curr. Opin. Chem. Biol.* **2006**, *10*, 141–146.

[9] F. W. Bai, W. A. Anderson, M. Moo-Young, *Biotechnol. Adv.* **2008**, *26*, 89–105.

[10] IEA-ETSAP and IRENA, *Production of Bio-Ethylene: Technology Brief*, **2013**.

[11] O. Winter, M. T. Eng, *Hydrocarb. Process.* **1976**, *55*, 125–133.

[12] M. J. Hülsey, H. Yang, N. Yan, *ACS Sustain. Chem. Eng.* **2018**, *6*, 5694–5707.

[13] S. Rebsdat, D. Mayer, in *Ullmann's Encycl. Ind. Chem.*, Wiley-VCH, Weinheim, **2001**, pp. 547–572.

[14] S. F. Koelewijn, C. Cooreman, T. Renders, C. Andecochea Saiz, S. Van Den Bosch, W. Schutyser, W. De Leger, M. Smet, P. Van Puyvelde, H. Witters, et al., *Green Chem.* **2018**, *20*, 1050–1058.

[15] I. Pantelic, B. Cuckovic, in *Alkyl Polyglucosides From Nat. Surfactants to Prospect. Deliv. Syst.*, Elsevier, **2014**, pp. 1–19.

[16] A. J. J. E. Eerhart, A. P. C. Faaij, M. K. Patel, *Energy Environ. Sci.* **2012**, *5*, 6407–6422.

[17] Y. Liao, S. F. Koelewijn, G. van den Bossche, J. van Aelst, S. van den Bosch, T. Renders, K. Navare, T. Nicolaï, K. van Aelst, M. Maesen, et al., *Science* **2020**, *367*, 1385–1390.

[18] ReportBuyer, "Global and China Ethylene Oxide (EO) Industry report, 2017-2021," can be found under https://www.prnewswire.com/news-releases/global-and-china-ethylene-oxide-eo-industry-report-2017-2021-300493113.html, **2017**.

[19] IHS Markit, "Ethylene Oxide," can be found under https://ihsmarkit.com/products/ethylene-oxide-chemical-economics-handbook.html, **2019**.

[20] T. E. Lefort, *Process for the Production of Ethylene Oxide*, **1931**, US1998878 A.

[21] J. Jovanovic, T. M. Nisbet, T. J. Olthof, M. J. F. M. Verhaak, *Process for the Production of Ethylene Oxide*, **2012**, US9139544 B2.

[22] H. Zimmermann, R. Walzl, in *Ullmann's Encycl. Ind. Chem.*, Wiley-VCH, Weinheim, **2009**, pp. 465–529.

[23] Nexant, "Ethylene Technology Report," can be found under https://www.nexantsubscriptions.com/reports/ethylene-2018-program, **2018**.

[24] S. Rebsdat, D. Mayer, in *Ullmann's Encycl. Ind. Chem.*, Wiley-VCH, Weinheim, **2012**, pp. 532–544.

[25] European Commission, *From the Sugar Platform to Biofuels and Biochemicals*, **2015**.

[26] H. Yue, Y. Zhao, X. Ma, J. Gong, *Chem. Soc. Rev.* **2012**, *41*, 4218–4244.

[27] O. V Vodyankina, L. N. Kurina, G. A. Izatulina, *React. Kinet. Catal. Lett.* **1998**, *64*, 103–107.

[28] J. B. Trecek, G. L. Wiesner, *Vapor Phase Oxidation Process for Glyoxal*, **1981**, US4258216 A.

[29] V. S. Shmotin, A. S. Knyazev, A. I. Titkov, A. N. Salanov, O. V. Vodyankina, L. N. Kurina, *Russ. J. Appl. Chem.* **2006**, *79*, 1458–1462.

[30] O. V. Magaev, A. S. Knyazev, O. V. Vodyankina, N. V. Dorofeeva, A. N. Salanov, A. I. Boronin, *Appl. Catal. A Gen.* **2008**, *344*, 142–149.

[31] A. Ballerini, A. Despres, A. Pizzi, *Holz als Roh - und Werkst.* **2005**, *63*, 477–478.

[32] G. Mattioda, B. Metivier, J. P. Guette, *Chemtech* **1983**, *13*, 478–481.

[33] V. R. Chumbhale, P. A. Awasarkar, *Appl. Catal. A Gen.* **2001**, *205*, 109–115.

[34] A. N. Pestryakov, V. V. Lunin, A. N. Devochkin, L. A. Petrov, N. E. Bogdanchikova, V. P. Petranovskii, *Appl. Catal. A Gen.* **2002**, *227*, 125–130.

[35] M. A. Salaev, A. A. Krejker, O. V. Magaev, V. S. Malkov, A. S. Knyazev, E. S. Borisova, V. M. Khanaev, O. V. Vodyankina, L. N. Kurina, *Chem. Eng. J.* **2011**, *172*, 399–409.

[36] K. A. Athanasiou, G. G. Niederauer, C. M. Agrawal, *Biomaterials* **1996**, *17*, 93–102.

[37] Y. Yamamoto, K. Uede, N. Yonei, A. Kishioka, T. Ohtani, F. Furukawa, *J. Dermatol.* **2006**, *33*, 16–22.

[38] K. Miltenberger, in *Ullmann's Encycl. Ind. Chem.*, Wiley-VCH, Weinheim, **2000**, pp. 481–492.

[39] K. Kosswig, in *Ullmann's Encycl. Ind. Chem.*, Wiley-VCH, Weinheim, **2000**, pp. 431–501.

[40] E. Smulders, E. Sung, in *Ullmann's Encycl. Ind. Chem.*, Wiley-VCH, Weinheim, **2011**, pp. 394–449.

[41] M. Frauenkron, J.-P. Melder, G. Ruider, R. Rossbacher, H. Höke, in *Ullmann's Encycl. Ind. Chem.*, Wiley-VCH, Weinheim, **2001**, pp. 405–528.

[42] R. Idem, M. Wilson, P. Tontiwachwuthikul, A. Chakma, A. Veawab, A. Aroonwilas, D. Gelowitz, *Ind. Eng. Chem. Res.* **2006**, *45*, 2414–2420.

[43] B. Han, T. Geng, Y. Jiang, H. Ju, *J. Surfactants Deterg.* **2015**, *18*, 91–95.

[44] K. D. Bremecker, J. L. Natonski, A. C. Eachus, *Int. J. Cosmet. Sci.* **1991**, *13*, 235–247.

[45] A. Calignano, G. La Rana, D. Piomelli, *Eur. J. Pharmacol.* **2001**, *419*, 191–198.

[46] H.-J. Buysch, in *Ullmann's Encycl. Ind. Chem.*, Weinheim, **2000**, pp. 45–62.

[47] A. Kolman, M. Chovanec, S. Osterman-Golkar, *Rev. Mutat. Res.* **2002**, *512*, 173–194.

[48] D. W. Lachenmeier, in *Side Eff. Drugs Annu.*, Elsevier B.V., **2018**, pp. 273–279.

[49] R. Bubbico, G. Dore, B. Mazzarotta, *J. Loss Prev. Process Ind.* **1998**, *11*, 49–54.

[50] J.-L. Gustin, *Loss Prev. Bull.* **2001**, *157*, 11–18.

[51] M. Ghanta, T. Ruddy, D. Fahey, D. Busch, B. Subramaniam, *Ind. Eng. Chem. Res.* **2013**, *52*, 18–29.

[52] M. Ghanta, D. Fahey, B. Subramaniam, *Appl. Petrochemical Res.* **2014**, *4*, 167–179.

[53] L. Chen, R. E. O. Pelton, T. M. Smith, *J. Clean. Prod.* **2016**, *137*, 667–676.

[54] P. P. Van Uytvanck, B. Hallmark, G. Haire, P. J. Marshall, J. S. Dennis, *ACS Sustain. Chem. Eng.* **2014**, *2*, 1098–1105.

[55] J. Pang, M. Zheng, R. Sun, A. Wang, X. Wang, T. Zhang, *Green Chem.* **2016**, *18*, 342–359.

[56] M. Zheng, J. Pang, R. Sun, A. Wang, T. Zhang, *ACS Catal.* **2017**, *7*, 1939–1954.

[57] A. Y. Yin, X. Y. Guo, W. L. Dai, K. N. Fan, *Green Chem.* **2009**, *11*, 1514–1516.

[58] J. Wang, S. Shen, B. Li, H. Lin, Y. Yuan, *Chem. Lett.* **2009**, *38*, 572–573.

[59] P. B. Smith, in *ACS Symp. Ser.*, **2012**, pp. 183–196.

[60] J. Zhang, B. Hou, A. Wang, Z. Li, H. Wang, T. Zhang, *AIChE J.* **2015**, *61*, 224–238.

[61] C. Luo, S. Wang, H. Liu, *Angew. Chemie - Int. Ed.* **2007**, *46*, 7636–7639.

[62] W. Anutrasakda, K. Eiamsantipaisarn, D. Jiraroj, A. Phasuk, T. Tuntulani, H. Liu, D. N. Tungasmita, *Catalysts* **2019**, *9*, 1–16.

[63] R. Ooms, M. Dusselier, J. A. Geboers, B. Op De Beeck, R. Verhaeven, E. Gobechiya, J. A. Martens, A. Redl, B. F. Sels, *Green Chem.* **2014**, *16*, 695–707.

[64] N. Ji, T. Zhang, M. Zheng, A. Wang, H. Wang, X. Wang, J. G. Chen, *Angew. Chemie - Int. Ed.* **2008**, *47*, 8510–8513.

[65] J. Pang, J. Sun, M. Zheng, H. Li, Y. Wang, T. Zhang, *Appl. Catal. B Environ.* **2019**, *254*, 510–522.

[66] N. Ji, M. Zheng, Y. Huang, A. Wang, T. Zhang, in *ACS Natl. Meet. B. Abstr.*, **2011**, pp. 77–85.

[67] Y. Zhang, A. Wang, T. Zhang, *Chem. Commun.* **2010**, *46*, 862–864.

[68] M. Y. Zheng, A. Q. Wang, N. Ji, J. F. Pang, X. D. Wang, T. Zhang, *ChemSusChem* **2010**, *3*, 63–66.

[69] Z. Tai, J. Zhang, A. Wang, M. Zheng, T. Zhang, *Chem. Commun.* **2012**, *48*, 7052–7054.

[70] Y. Liu, C. Luo, H. Liu, *Angew. Chemie - Int. Ed.* **2012**, *51*, 3249–3253.

[71] Z. Tai, J. Zhang, A. Wang, J. Pang, M. Zheng, T. Zhang, *ChemSusChem* **2013**, *6*, 652–658.

[72] Y. Liu, Y. Liu, Y. Zhang, *Appl. Catal. B Environ.* **2019**, *242*, 100–108.

[73] M. S. Hamdy, M. A. Eissa, S. M. A. S. Keshk, *Green Chem.* **2017**, *19*, 5144–5151.

[74] J. Chai, S. Zhu, Y. Cen, J. Guo, J. Wang, W. Fan, *RSC Adv.* **2017**, *7*, 8567–8574.

[75] R. Gounder, M. E. Davis, *J. Catal.* **2013**, *308*, 176–188.

[76] R. Bermejo-Deval, M. Orazov, R. Gounder, S. J. Hwang, M. E. Davis, *ACS Catal.* **2014**, *4*, 2288–2297.

[77] J. Dijkmans, D. Gabriëls, M. Dusselier, F. De Clippel, P. Vanelderen, K. Houthoofd, A. Malfliet, Y. Pontikes, B. F. Sels, *Green Chem.* **2013**, *15*, 2777–2785.

[78] R. Sun, M. Zheng, J. Pang, X. Liu, J. Wang, X. Pan, A. Wang, X. Wang, T. Zhang, *ACS Catal.* **2016**, *6*, 191–201.

[79] G. Zhao, M. Zheng, J. Zhang, A. Wang, T. Zhang, *Ind. Eng. Chem. Res.* **2013**, *52*, 9566–9572.

[80] C. M. Osmundsen, E. Taarning, M. S. Holm, *Process for the Preparation of Ethylene Glycol from Sugars*, **2018**, US9926247 B2.

[81] C. Marup Osmundsen, E. Taarning, M. B. Larsen, *Process for the Preparation of Ethylene Glycol from Sugars*, **2017**, US20190010103 A1.

[82] S. Ai, M. Zheng, Y. Jiang, J. Pang, C. Wang, A. Wang, X. Wang, T. Zhang, *Chem. Eng. J.* **2018**, *335*, 530–538.

[83] S. Ai, M. Zheng, Y. Jiang, X. Yang, X. Li, J. Pang, J. Sebastian, W. Li, A. Wang, X. Wang, et al., *AIChE J.* **2017**, *63*, 4032–4042.

[84] J. C. Van Der Waal, G. J. M. Gruter, *Continuous Process for Preparing Ethylene Glycol from a Carbohydrate Source*, **2016**, WO2016114661 A1.

[85] J. C. Van Der Waal, *Process for Preparing Ethylene Glycol from a Carbohydrate*, **2018**, WO2016114658 A1.

[86] Avantium, “PEF Products and applications,” can be found under https://www.avantium.com/technologies/yxy/, **2020**.

[87] Coca-Cola, “Plantbottle technology,” can be found under https://www.coca-cola.eu/news/sharing-plantbottle-technology-with-the-world/, **2020**.

[88] J. P. A. M. J. G. Lange, P. Huizenga, *Process for the Preparation of Monoethylene Glycol*, **2016**, US20160096789 A1.

[89] D. Muthusamy, P. Huizenga, V. Q. Nguyen, *Method for the Production of Glycols from a Carbohydrate Feed*, **2017**, WO2017070067 A1.

[90] A. H. Tullo, *Chem. Eng. News* **2017**, *95*, 10.

[91] C. Zhang, D. Wang, B. Dai, *Catalysts* **2017**, *7*, 122.

[92] S. Zhang, Q. Liu, G. Fan, F. Li, *Catal. Letters* **2012**, *142*, 1121–1127.

[93] A. Molino, S. Chianese, D. Musmarra, *J. Energy Chem.* **2016**, *25*, 10–25.

[94] A. M. Bahmanpour, A. Hoadley, A. Tanksale, *Rev. Chem. Eng.* **2014**, *30*, 583–604.

[95] M. Koepke, R. Jensen, *Microorganisms and Methods for the Biological Production of Ethylene Glycol*, **2019**, US20190185888 A1.

[96] J. Geraldo Da Cruz Pradella, A. Fernanda Beraldi Zeidler, A. Karina Bramnilla Costa, *Methods for the Co-Production of Ethylene Glycol and Three Carbon Compounds*, **2019**, US20190276858 A1.

[97] H. Berndt, I. Pitsch, S. Evert, K. Struve, M. M. Pohl, J. Radnik, A. Martin, *Appl. Catal. A Gen.* **2003**, *244*, 169–179.

[98] T. Van Haasterecht, T. W. Van Deelen, K. P. De Jong, J. H. Bitter, *Catal. Sci. Technol.* **2014**, *4*, 2353–2366.

[99] G. Liang, A. Wang, L. Li, G. Xu, N. Yan, T. Zhang, *Angew. Chemie - Int. Ed.* **2017**, *56*, 3050–3054.

[100] A. Wang, G. Liang, T. Zhang, *Method for Preparing Ethanolamine and Diamine by Glycolaldehyde Reductive Amination*, **2017**, CN107011194 A.

[101] L. Jia, M. Makha, C. X. Du, Z. J. Quan, X. C. Wang, Y. Li, *Green Chem.* **2019**, *21*, 3127–3132.

[102] J. Runeberg, A. Baiker, J. Kijenski, *Appl. Catal.* **1985**, *17*, 309–319.

[103] P. Sepulveda, J. G. P. Binner, *Chem. Mater.* **2001**, *13*, 4065–4070.

[104] G. van Cauwenberghe, J.-P. Melder, B. Willem Hoffer, T. Krug, K. Pickenäcker, F.-F. Pape, E. Schwab, *Method for Producing Ethylene Amines and Ethanol Amines by the Hydrogenating Amination of Monoethylene Glycol and Ammonia in the Presence of a Catalyst*, **2009**, US7700806 B2.

[105] A.-N. Parvulescu, A. Gordillo, M. K. Schroeter, J.-P. Melder, J. Bechtel, T. Heidemann, S. A. Schunk, U. Müller, *Process for*

the Conversion of Ethylene Glycol to Ethylenediamine Employing a Zeolite Catalyst, **2019**, US20190308929 A1.

[106] M. Pelckmans, W. Vermandel, F. Van Waes, K. Moonen, B. F. Sels, *Angew. Chemie - Int. Ed.* **2017**, *56*, 14540–14544.

[107] M. Pelckmans, T. Mihaylov, W. Faveere, J. Poissonnier, F. Van Waes, K. Moonen, G. B. Marin, J. W. Thybaut, K. Pierloot, B. F. Sels, *ACS Catal.* **2018**, *8*, 4201–4212.

[108] C. Ma, D. Butler, V. Milligan, B. A. Hammann, H. Luo, J. Brazdil, D. Liu, R. V. Chaudhari, B. Subramaniam, *Ind. Eng. Chem. Res.* **2020**, DOI 10.1021/acs.iecr.0c02277.

[109] T. Schaub, B. Buschhaus, K. Brinks, M. Schelwies, R. Paciello, J.-P. Melder, M. Merger, *Process for Preparing Alkanolamines by Homogeneously Catalyzed Alcohol Amination*, **2014**, US9193666 B2.

[110] N. Andrushko, V. Andrushko, P. Roose, K. Moonen, A. Börner, *ChemCatChem* **2010**, *2*, 640–643.

[111] Q. Li, W. Zhang, N. Zhao, W. Wei, Y. Sun, *Catal. Today* **2006**, *115*, 111–116.

[112] B. M. Bhanage, S. I. Fujita, Y. Ikushima, M. Arai, *Green Chem.* **2003**, *5*, 429–432.

[113] L. Shi, Y. Ni, W. Zhu, Y. Liu, H. Liu, Z. Liu, *Method for Directly Preparing Glycol Dimethyl Ether and Co-Producing Ethylene Glycol from Ethylene Glycol Monomethyl Ether*, **2018**, EP3330246 B1.

[114] C. L. Baimbridge, P. V. Bolomey, J. D. Love, *Method for Producing Glycol Ethers*, **2004**, US6730815 B2.

[115] C. Lamy, E. M. Belgsir, J. M. Léger, *J. Appl. Electrochem.* **2001**, *31*, 799–809.

[116] B. Wieland, J. P. Lancaster, C. S. Hoaglund, P. Holota, W. J. Tornquist, *Langmuir* **1996**, *12*, 2594–2601.

[117] A. Serov, C. Kwak, *Appl. Catal. B Environ.* **2010**, *97*, 1–12.

[118] Y. Kobayashi, H. Takahara, H. Takahashi, K. Higasi, *J. Mol. Struct.* **1976**, *32*, 235–246.

[119] V. A. Yaylayan, S. Harty-Majors, A. A. Ismail, *Carbohydr. Res.* **1998**, *309*, 31–38.

[120] J. Kua, M. M. Galloway, K. D. Millage, J. E. Avila, D. O. De Haan, *J. Phys. Chem. A* **2013**, *117*, 2997–3008.

[121] H. Nursten, *The Maillard Reaction: Chemistry, Biochemistry and Implications*, Royal Society Of Chemistry, Cambridge, **2005**.

[122] L. W. Kroh, *Food Chem.* **1994**, *51*, 341–416.

[123] J. E. Hodge, *Adv. Carbohydr. Chem.* **1955**, *10*, 169–205.

[124] P. Pérez, A. Toro-Labbé, *Theor. Chem. Acc.* **2001**, *105*, 422–430.

[125] M. Dusselier, M. Mascal, B. F. Sels, in *Sel. Catal. Renew. Feed. Chem.* (Ed.: K.M. Nicholas), Springer International Publishing, Heidelberg, **2014**, pp. 1–40.

[126] S. R. Auvil, P. L. Mills, *Improvements in Glycol Aldehyde Process*, **1984**, EP0129530 A3.

[127] K. Q. Almeida Lenero, E. Drent, R. Van Ginkel, R. I. Pugh, *Process of Preparing Glycolaldehyde*, **2005**, US7449607 B2.

[128] T. A. Puckette, T. J. Devon, *Process for the Production of Glycolaldehyde*, **2007**, US20080081931 A1.

[129] M. J. Murphy, D. A. Dunbar, L. S. Kaminsky, *Toxicol. Appl. Pharmacol.* **1983**, *71*, 84–92.

[130] M. Gallo, R. Amonette, C. Lauber, R. L. Sinsabaugh, D. R. Zak, *Microb. Ecol.* **2004**, *48*, 218–229.

[131] I. Magneron, A. Mellouki, G. Le Bras, G. K. Moortgat, A. Horowitz, K. Wirtz, *J. Phys. Chem. A* **2005**, *109*, 4552–4561.

[132] R. Lorenzi, M. E. Andrades, R. C. Bortolin, R. Nagai, F. Dal-Pizzol, J. C. F. Moreira, *Diabetes Res. Clin. Pract.* **2010**, *89*, 262–267.

[133] R. Lorenzi, M. E. Andrades, R. C. Bortolin, R. Nagai, F. Dal-Pizzol, J. C. F. Moreira, *Cardiovasc. Toxicol.* **2010**, *10*, 244–249.

[134] A. V Bridgwater, *Int. J. Glob. Energy Issues* **2007**, *27*, 160–203.

[135] J. A. Stradal, G. L. Underwood, *Process for Producing Hydroxyacetaldehyde*, **1991**, WO1991014379 A1.

[136] C. R. Vitasari, G. W. Meindersma, A. B. de Haan, *Green Chem.* **2012**, *14*, 321–325.

[137] C. R. Vitasari, G. W. Meindersma, A. B. De Haan, *Sep. Purif. Technol.* **2012**, *95*, 103–108.

[138] A. B. de Haan, G. W. Meindersma, J. Nijenstein, C. Vitasari, in *Third Nord. Wood Biorefinery Conf.*, **2011**, pp. 63–68.

[139] V. K. Venkatakrishnan, J. C. Degenstein, A. D. Smeltz, W. N. Delgass, R. Agrawal, F. H. Ribeiro, *Green Chem.* **2014**, *16*, 792–802.

[140] J. A. Stradal, G. L. Underwood, *Process for Producing Hydroxyacetaldehyde*, **1993**, US5252188 A.

[141] Y.-S. Liu, *Process for Removing Degradation Acids from Hydroformylation Reactions*, **2010**, US8513468 B2.

[142] J. K. Jørgensen, C. Favre, S. E. Bisschop, T. L. Bourke, E. F. Van Dishoeck, M. Schmalzl, *Astrophys. J. Lett.* **2012**, *757*, L4.

[143] A. Coutens, M. V. Persson, J. K. Jørgensen, S. F. Wampfler, J. M. Lykke, *Astron. Astrophys.* **2015**, *576*, A5.

[144] G. Cassone, J. Sponer, J. E. Sponer, F. Pietrucci, A. M. Saitta, F. Saija, *Chem. Commun.* **2018**, *54*, 3211–3214.

[145] I. V. Delidovich, a. N. Simonov, O. P. Pestunova, V. N. Parmon, *Kinet. Catal.* **2009**, *50*, 297–303.

[146] I. V. Delidovich, A. N. Simonov, O. P. Taran, V. N. Parmon, *ChemSusChem* **2014**, *7*, 1833–1846.

[147] A. J. Vetter, M. E. Janka, J. R. Zoeller, *Coupling of Formaldehyde to Glycolaldehyde Using N-Heterocyclic Carbene Catalysts*, **2009**, US7498469 B1.

[148] E. Gehrer, W. Harder, K. Ebel, J.-P. Melder, J. H. Teles, *Catalytic Preparation of Formaldehyde Condensates*, **1994**, US5298668 A.

[149] A. H. Weiss, *Glycolaldehyde or Ethylene Glycol from Formaldehyde*, **1980**, US4238418 A.

[150] M. Sasaki, K. Goto, K. Tajima, T. Adschiri, K. Arai, *Green Chem.* **2002**, *4*, 285–287.

[151] M. Sasaki, Z. Fang, Y. Fukushima, T. Adschiri, K. Arai, *Ind. Eng. Chem. Res.* **2000**, *39*, 2883–2890.

[152] C. M. Martínez, D. A. Cantero, M. D. Bermejo, M. J. Cocero, *Cellulose* **2015**, *22*, 2231–2243.

[153] G. Xu, A. Wang, J. Pang, X. Zhao, J. Xu, N. Lei, J. Wang, M. Zheng, J. Yin, T. Zhang, *ChemSusChem* **2017**, *10*, 1390–1394.

[154] C. Yang, Z. Miao, F. Zhang, L. Li, Y. Liu, A. Wang, T. Zhang, *Green Chem.* **2018**, *20*, 2142–2150.

[155] M. Yang, H. Qi, F. Liu, Y. Ren, X. Pan, L. Zhang, X. Liu, H. Wang, J. Pang, M. Zheng, et al., *Joule* **2019**, *3*, 1937–1948.

[156] R. M. Wahlström, A. Suurnäkki, *Green Chem.* **2015**, *17*, 694–714.

[157] M. E. Himmel, S. Y. Ding, D. K. Johnson, W. S. Adney, M. R. Nimlos, J. W. Brady, T. D. Foust, *Science* **2007**, *315*, 804–807.

[158] P. A. Majerski, J. K. Piskorz, D. S. A. G. Radlein, *Production of Glycolaldehyde by Hydrous Thermolysis of Sugars*, **2006**, US7094932 B2.

[159] E. Taarning, M. S. Holm, *Process for Preparing Ketene in the Presence of a Fluidized Bed Material with a Surface Area up to 600M2/G*, **2014**, WO2014131764 A1.

[160] C. B. Schandel, M. Høj, C. M. Osmundsen, A. D. Jensen, E. Taarning, *ChemSusChem* **2020**, *13*, 688–692.

[161] E. Taarning, *Process for Removing Formaldehyde from a Composition Comprising Glycolaldehyde*, **2014**, US9796649B2.

[162] Haldor Topsoe, “Braskem and Haldor Topsoe start up demo unit for developing renewable MEG,” can be found under https://blog.topsoe.com/braskem-and-haldor-topsoe-start-up-demo-unit-for-developing-renewable-meg, **2019**.

[163] M. S. Holm, Z. I. Sadaba, S. Tolborg, C. Marup Osmundsen, E. Taarning, *Process for the Conversion of Sugars to Lactic Acid and 2-Hydroxy-3-Butenoic Acid or Esters Thereof Comprising a Metall-Silicate Material and a Metal Ion*, **2015**, US9573123 B2.

[164] T. Hofmann, W. Bors, K. Stettmaier, *J. Agric. Food Chem.* **1999**, *47*, 379–390.

[165] R. W. Goetz, *Glycol Aldehyde and Ethylene Glycol Processes*, **1980**, US4200765 A.

[166] S. E. Jacobson, C. F. Chueh, *Process for the Production of Ethylene Glycol through the Hydroformylation of Glycol Aldehyde*, **1985**, US4496781 A.

[167] L. C. Costa, *Catalytic Hydrogenation of Glycolaldehyde to Produce Ethylene Glycol*, **1982**, US4321414A.

[168] L. C. Costa, *Process for Producing Ethylene Glycol via Catalytic Hydrogenation of Glycolaldehyde*, **1982**, US4317946 A.

[169] M. S. Holm, E. Taarning, *Process for the Preparation of Ethylene Glycol from Sugars*, **2016**, WO2016001169 A1.

[170] Y. Han, J. Zhang, X. Liu, *Molybdenum-Containing Acidic Catalysts to Convert Cellulosic Biomass to Glycolic Acid*, **2014**, US8846974 B2.

[171] J. Zhang, X. Liu, M. Sun, X. Ma, Y. Han, *ACS Catal.* **2012**, *2*, 1698–1702.

[172] K. Yamane, Y. Kawakami, *Glycolide Production Process, and Glycolic Acid Oligomer for Glycolide Production*, **2007**, US7235673 B2.

[173] R. Hagen, A. B. Verweij, U. Mühlbauer, J. Schulze, W. Tietz, K.-D. Göhler, *Process for Preparing a Mixture of Lactide Derivatives*, **2009**, EP2321294 A2.

[174] P. P. Upare, J. S. Chang, I. T. Hwang, D. W. Hwang, *Korean J. Chem. Eng.* **2019**, *36*, 203–209.

[175] M. Dusselier, P. Van Wouwe, A. Dewaele, P. A. Jacobs, B. F. Sels, *Science* **2015**, *349*, 78–80.

[176] P. VanWouwe, M. Dusselier, E. Vanleeuw, B. Sels, *ChemSusChem* **2016**, *9*, 907–921.

[177] R. De Clercq, M. Dusselier, E. Makshina, B. F. Sels, *Angew. Chemie - Int. Ed.* **2018**, *57*, 3074–3078.

[178] R. De Clercq, E. Makshina, B. F. Sels, M. Dusselier, *ChemCatChem* **2018**, *10*, 5649–5655.

[179] W. Mägerlein, J.-P. Melder, J. Pastre, J. Eberhardt, T. Krug, M. Kreitschmann, *Reaction of Glycolaldehyde with an Aminating Agent*, **2012**, US8772548 B2.

[180] W. Mägerlein, J.-P. Melder, J. Pastre, J. Eberhardt, T. Krug, M. Kreitschmann, *Method for Preparing Higher Ethanolamines*, **2014**, US8742174 B2.

[181] W. Faveere, T. Mihaylov, M. Pelckmans, K. Moonen, F. Gillis-D'hamers, R. Bosschaerts, K. Pierloot, B. F. Sels, *ACS Catal.* **2020**, *10*, 391–404.

[182] S. Sridhar, R. G. Carter, in *Kirk-Othmer Encycl. Chem. Technol.*, **2001**, pp. 485–519.

[183] M. Rossberg, W. Lendle, G. Pfleiderer, A. Tögel, E.-L. Dreher, E. Langer, H. Rassaert, P. Kleinschmidt, H. Strack, R. Cook, et al., in *Ullmann's Encycl. Ind. Chem.*, Wiley-VCH, Weinheim, **2006**, pp. 1–186.

[184] H. Li, Z. Fang, R. L. Smith, *Rapid Synthesis Method for Biomass-Based Amine Compound*, **2020**, WO2020029846 A1.

[185] K. L. Law, R. C. Thompson, *Science* **2014**, *345*, 144–145.

[186] R. De Clercq, M. Dusselier, B. F. Sels, *Green Chem.* **2017**, *19*, 5012–5040.

[187] S. Tolborg, S. Meier, S. Saravanamurugan, P. Fristrup, E. Taarning, I. Sádaba, *ChemSusChem* **2016**, *9*, 3022.

[188] M. S. Holm, S. Saravanamurugan, E. Taarning, *Science* **2010**, *328*, 602–605.

[189] A. Sølvhøj, E. Taarning, R. Madsen, *Green Chem.* **2016**, *18*, 5448–5455.

[190] M. Dusselier, P. Van Wouwe, F. de Clippel, J. Dijkmans, D. W. Gammon, B. F. Sels, *ChemCatChem* **2013**, *5*, 569–575.

[191] A. Dewaele, L. Meerten, L. Verbelen, S. Eyley, W. Thielemans, P. Van Puyvelde, M. Dusselier, B. Sels, *ACS Sustain. Chem. Eng.* **2016**, *4*, 5943–5952.

[192] E. Taarning, A. B. Sølvhøj, *New Adipate-Type Compounds and a Process of Preparing It*, **2017**, WO2017191282 A1.

[193] M. Dusselier, P. Van Wouwe, S. De Smet, R. De Clercq, L. Verbelen, P. Van Puyvelde, F. E. Du Prez, B. F. Sels, *ACS Catal.* **2013**, *3*, 1786–1800.

[194] M. S. Holm, Y. J. Pagán-Torres, S. Saravanamurugan, A. Riisager, J. A. Dumesic, E. Taarning, *Green Chem.* **2012**, *14*, 702–706.

[195] S. Van De Vyver, C. Odermatt, K. Romero, T. Prasomsri, Y. Román-Leshkov, *ACS Catal.* **2015**, *5*, 972–977.

[196] R. De Clercq, M. Dusselier, J. Dijkmans, R. I. Iacobescu, Y. Pontikes, B. F. Sels, *ACS Catal.* **2015**, *5*, 5803–5811.

[197] S. D. Luebben, J. W. Raebiger, *ACS Symp. Ser.* **2015**, *1192*, 305–328.

[198] S. D. Luebben, J. W. Raebiger, A. J. Skaggs, *Renewable Polymer and Method of Making*, **2015**, US9040635 B1.

[199] M. Barletta, A. Cicci, *Stud. Surf. Sci. Catal.* **2019**, *179*, 231–242.

[200] G. C. C. Mendes, T. R. S. Brandão, C. L. M. Silva, *Am. J. Infect. Control* **2007**, *35*, 574–581.

[201] W. L. Canoy, B. E. Cooley, J. A. Corona, T. C. Lovelace, A. Millar, A. M. Weber, S. Xie, Y. Zhang, *Org. Lett.* **2008**, *10*, 1103–1106.

[202] J. Xu, W. Huang, R. Bai, Y. Queneau, F. Jérôme, Y. Gu, *Green Chem.* **2019**, *21*, 2061–2069.

[203] J. Du, C. K. Chu, *Nucleosides and Nucleotides* **1998**, *17*, 1–13.

[204] D. Hernández, A. Boto, *European J. Org. Chem.* **2014**, *2014*, 2201–2220.

[205] N. Zhang, S. Babu, S. J. Barraza, A. Bhattacharyya, G. Chen, G. M. Karp, A. J. Kassick, A. R. A. Mazzotti, M. Woll, W. Yan, *Heteroaryl Compounds for Treating Huntington's Disease*, **2020**, WO2020005877 A1.

[206] M. Pelckmans, T. Renders, S. Van De Vyver, B. F. Sels, *Green Chem.* **2017**, *19*, 5303–5331.

[207] W. Schutyser, T. Renders, S. Van Den Bosch, S. F. Koelewijn, G. T. Beckham, B. F. Sels, *Chem. Soc. Rev.* **2018**, *47*, 852–908.

[208] T. Renders, S. Van Den Bosch, S. F. Koelewijn, W. Schutyser, B. F. Sels, *Energy Environ. Sci.* **2017**, *10*, 1551–1557.

[209] T. Renders, G. Van Den Bossche, T. Vangeel, K. Van Aelst, B. Sels, *Curr. Opin. Biotechnol.* **2019**, *56*, 193–201.

[210] Y. Huang, Y. Duan, S. Qiu, M. Wang, C. Ju, H. Cao, Y. Fang, T. Tan, *Sustain. Energy Fuels* **2018**, *2*, 637–647.

[211] L. Shuai, M. T. Amiri, Y. M. Questell-Santiago, F. Héroguel, Y. Li, H. Kim, R. Meilan, C. Chapple, J. Ralph, J. S. Luterbacher, *Science* **2016**, *354*, 329–333.

[212] R. Rinaldi, R. Jastrzebski, M. T. Clough, J. Ralph, M. Kennema, P. C. A. Bruijnincx, B. M. Weckhuysen, *Angew. Chemie - Int. Ed.* **2016**, *55*, 8164–8215.

[213] A. J. Ragauskas, G. T. Beckham, M. J. Biddy, R. Chandra, F. Chen, M. F. Davis, B. H. Davison, R. A. Dixon, P. Gilna, M. Keller, et al., *Science* **2014**, *344*.

[214] M. V. Galkin, J. S. M. Samec, *ChemSusChem* **2016**, *9*, 1544–1558.