Molecular Catalysed Guerbet Reaction: Moving to the Larger and the Greener through LCA and Scale Up Simulation Approaches.

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Keywords

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Abstract

Efficient homologation of bio-ethanol can be performed under mild conditions exploiting a catalytic system based of a ruthenium molecular catalyst, benzoquinone and a base as a co-catalysts. Conversions and selectivity can be tuned by changing the head space of the reactor. On this basis, preliminary design of a full-scale process has been developed based on the experimental results. The process has been characterized with specific energy and performance indicators per unit of produced butanol, which have been used as input for the life cycle assessment analysis. The LCA was applied

as scientific methodology to address potential burdens of the baseline configuration, 3X catalytic cycles, electricity from Italian grid and heat from natural gas. Hotspots were identified according to a multi-impact approach method (ReCiPe 2016). The usage of dedicated lignocellulosic biomass as a source of EtOH, the synthesis of the catalytic system and the energy requirements were addressed as the major contributors. Thus, further sensitivity scenarios were created. The best configuration was identified in the use of waste biomasses and in an integrated cogeneration unit. In addition, enabling the recovery of the catalytic system up to five cycles to scenario shows a reduction in the impacts higher than 50% for the categories of global warming potential, -41% for the mineral resource scarcity and around -16% for the fine particulate matter formation. The results were also confirmed by an uncertainty analysis with the Monte Carlo method, which demonstrated the major environmental sustainability of the Guerbet route compared to the oxo synthesis from propylene.

1. Introduction

The zero-emission policy for the sales of new vehicles by 2035 supported by the European Parliament this year underlines the urgency to reduce fossil fuels exploitation and CO_2 emissions.[1,2] The strategy furnishes a combination of different approaches depending on the field of application and the Guerbet reaction constitutes an ideal pathway for ethanol homologation, since Guerbet alcohols are both suitable for biofuel application[3,4,5] and possess excellent lubricant properties (required for example in hydraulic fluids, cosmetic emollients and surfactants).[6]

This reaction would represent a valuable alternative from an ecological transition point of view in comparison with the established OXO[7] and ABE[8] processes to produce butanol. The Guerbet reaction is nowadays used by Sasol to upgrade C_6-C_{16} alcohols, yielding longer analogues which are commercialized as surfactants and solubilizers for paints, inks and coatings, for cosmetic application, as lubricants and emulsifiers for the textile and metal sectors.[9] The semi-continuous technology patented by the German company is designed to yield high-purity alcohols without expensive and
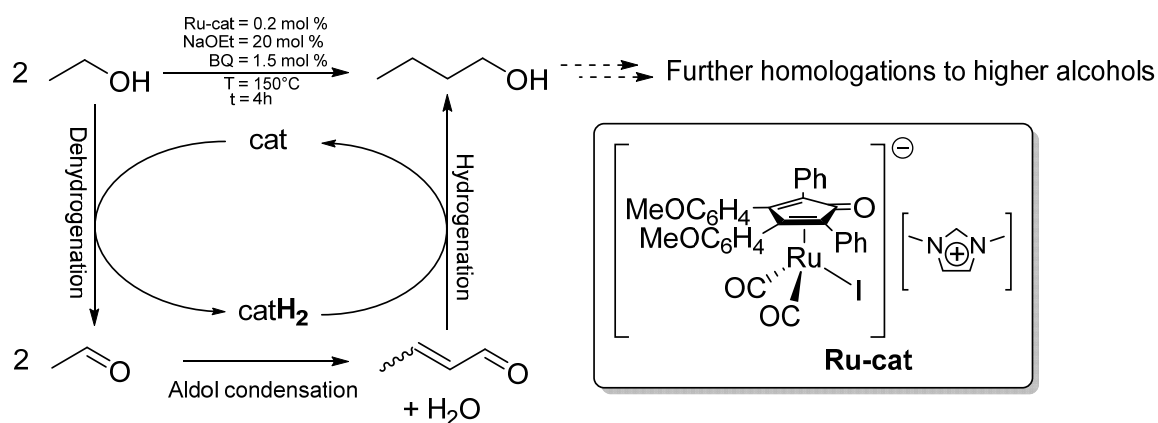
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wasteful washing and purification steps. It consists of a reactive distillation allowing for an optimal separation of the product mixture from the alkaline and/or metal-containing catalyst and possible byproducts.[10]

Due to the plurality of reactions involved and to prevent the formation of unwanted side products, such as ethers, esters, olefins and paraffins[11] in heterogeneous catalysis and acetate salts in homogeneous systems,[12] the conditions employed and, above all, the catalyst properties need to be finely tuned. These catalytic systems are often suitable due to multifunctionality: i) hydrogenation/dehydrogenation ability and ii) the presence of acidic/basic sites or co-catalysts to promote the aldol condensation step. It is important to underline that, although the reported mechanism is supported by many studies,[13,14,15,16] alternative pathways involving direct ethanol self-condensation or condensation with a molecule of acetaldehyde have also been proposed,[17,18,19,20] thus the exact mechanism is likely to be dependent on the catalyst and the reaction conditions.

When catalyzed by heterogeneous systems, the Guerbet reaction involves adjacent Lewis acid-basic site pairs acting synergistically to achieve Guerbet reactivity,[21] even though strong basic sites are fundamental.[15]

The drawbacks of the heterogeneously catalysed Guerbet reaction are the requirement of high temperatures (> 250 °C), and the difficulty to achieve both high conversion and selectivity. To get round these concerns, homogeneous catalytic systems have been designed and widely studied in the last two decades starting from the pioneering work with ruthenium phosphine catalysts[22] by Wass et al. in 2016 who introduced the idea of "Guerbet renewed" as a new perspective: homogeneous catalysis.[23] Several approaches employ iridium, ruthenium and manganese bifunctional catalysts which require milder reaction conditions with a larger control on yields and selectivity in comparison to the heterogeneous counterpart. [24, 25, 26, 27, 28, 29] First drawbacks for the still most efficient ruthenium complexes were documented by Wass et al. in 2013[21] and confirmed by Szymczak[30] as the inverse correlation between butanol yield and selectivity. Jones and co-workers were later able to keep a 99%

butanol selectivity up to 37% yield employing a tandem catalytic approach exploiting iridium, copper or nickel complexes.[31] At the same time Milstein group enlarged the homogeneous Guerbet reaction catalysed by ruthenium catalyst with a tridentate ligand, to the co-valorization of higher alcohols.[32] The current interest in this reaction and its drawbacks have also been highlighted by Liauw and co-workers, who went into details on the reasons for the failure in alcohol homologation of a another bifunctional ruthenium catalyst.[33] Exploring real matrix derived feedstocks, Wass and co-workers demonstrated some water tolerance in the transformation of fermentation broths (first-generation biomass) into iso-butanol.[34] In this context, part of our group recently reported a phosphine-free ionic ruthenium cyclopentadienone complex for the production of second-generation alcohol mixtures bio-ethanol derived from wine waste.[12] An impressive boost in conversion and alcohol yields was obtained by implementing the catalytic system with a benzoquinone as a co-catalyst (Scheme 1), improving the selectivity toward >C_6 alcohols. The new system reaches the most promising performances in terms of EtOH conversion and alcohols yield reported so far.[12,35]

Scheme 1. Guerbet reaction conditions from our previous work.[12]

Although the reaction would well fit in a context of circular economy in the wine production chain, a step forward to reach applicability is compulsory. In this work, the experimental design of the process has been deepened with a study on the influence of dead volume ratios.

Based on the available information, the present work provides a perspective of future industrial applications of the technology, with and insight on its related environmental impacts. This has been carried out with a preliminary conceptual design of a full-scale process and the evaluation of mass and energy balance. The calculation of energy and performance indicators resulting from the aforementioned technology assessment have been the input to a Life Cycle Analysis (LCA). The LCA has been applied to the full-scale process in order to estimate the potential burdens of the process and set the basis for future improvements. LCA represents a well-established methodology for assessing bio-based sector. Several studies were already published to investigate different aspects on the argument. However, one of the most questionable and challenging issue is the carbon neutrality of chemicals from biomasses. Thanks to the CO_2 sequestration during plants growth, bio-chemicals impact on climate change is too often considered equal to zero. However, in a recent publication Zuiderveen and co-workers[36] have demonstrated that none among the emerging bio-based products investigated (86) reached such neutrality, even if impacts on climate change are in general lower than the same substances from fossil. Therefore, there is the necessity to investigate the impacts of bio-products by considering a holistic approach able to go beyond the concept of carbon footprint.[37] A multi impacts assessment is in fact recommended by literature.[38,39,40] For this reason, we applied the LCA methodology to investigate the Guerbet reaction, partly already study so far.[41,42]

2. Materials and methods

2.1 Materials

Diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled before use and stored in round flasks containing pre-dried molecular sieves. Ethanol (EtOH) and other solvents not previously listed were used without additional purification.

[**Ru-cat**] was prepared as previously reported.[42, 43] p-benzoquinone [**BQ**] (Alfa Aesar) was purified by column chromatography (stationary phase: silica gel, eluent: CH_2Cl_2).

2.3 General procedure for upgrading of EtOH with co-catalyst

The catalytic runs were carried out in oven-dried Schlenk bombs fitted with a Teflon plug valve having different internal volumes (7.5-13.4-53.8 mL). The reactor was loaded with the ruthenium catalyst **Ru-cat** (0.2 mol%), the base (NaOEt, 20 mol%) and BQ (1.5 mol%). Finally, ethanol was added under inert atmosphere in different volumes from 0.5 to 1 mL. The Schlenk bomb was sealed under inert atmosphere and heated at 150 °C, under magnetic stirring for 4 hours. After cooling with a cold-water bath, the microreactor was opened and then hydrogen was detected by means of an Agilent Technologies 7890A GC equipped with a thermal conductivity detector (TCD) and a HP-molesieve column (30m x 0.53 mm x 50 μm). Nitrogen was used as carrier gas at a flow rate of 3 mL/min; the injector was maintained in split mode 5:1 at a temperature of 150 °C and the TCD at 150 °C. The volume of gas injected was 0.04 mL and the standard temperature program was a single isothermal step at 50 °C for 5 minutes. Reaction mixture was diluted 1:9 with Et_2O. THF (150 μL) was added as internal standard. Ethanol conversion and product yields were determined by injecting the resulting solution (1 μL) into an Agilent Technologies 7890A GC system using a HP-5 capillary column Agilent 190915-413 (30 m x 0.35 mm, thickness 0.25 μm). Helium was used as carrier gas with a column flow of 0.909mL/min; the injector was kept at a temperature of 230 °C in split mode (40:1); total flow was 40.25 mL/min. The method used was: starting oven temperature 30°C (hold for 11 min), ramp to 270 at 30°C/min (held for 5 min). All products were calibrated. THF (150 μL) was added to different solutions of alcohols at increasing concentration and the ratio A_a/A_s vs mol_a was plotted (mol_s = constant). This way the measure of the total reaction volume can be avoided.

After a catalytic run in the best conditions (Entry 4, Table 1), the end reaction mixture was completely dried on vacuum, then dissolved in D_2O and analysed by ^1HNMR spectroscopy (Figure S7). DMSO

(99.97%, VWR) was added in equimolar amounts to the initial sodium ethoxide (3.42 mmol) and used as internal standard to quantify the amounts of water-soluble species.

2.4 Engineering assessments

The engineering assessment has consisted in two main steps: (i) evaluation of the outcomes from the experimental campaign and (ii) preliminary design of a full-scale process. Experimental results reported in Section 3 have been analysed evaluating atomic balance: missing carbon has been expressed in terms of carbon loss related to ethanol, while the error in oxygen mass balance has been corrected tuning the amount of produced water.

Based on the analysis of the data collected during the experimental campaign, the performance of the catalytic reactor has been extrapolated and expressed in terms of product yields, ethanol conversion and specific consumption of reagents, catalyst and co-catalyst. Thus, a conceptual design of a process at industrial scale has been carried out, on which mass and energy balances have been drawn. Thermodynamic properties have been taken using Aspen Properties® v10.[44] Results have been provided in terms of specific quantities with respect to produced butanol.

2.4 LCA: inventory, database and software

LCA framework and standardization

Life Cycle Assessment (LCA) is among the most preferred descriptive and quantitative modelling methodologies for overarching estimation of the potential environmental impacts associated with a product-system (i.e., substance/material, compound, system, service, etc.). According to ISO standards 14040-14044 (ISO 2006a; ISO 2006b),[45,46] the LCA framework consists of four conceptual phases: i) goal and scope definition, ii) life cycle inventory (LCI), iii) life cycle impact assessment (LCIA) and iv) interpretation. During the first stage, the object of the study is defined by determining the system boundaries and the functional unit (FU). The former consists of the

identification of the phases of the product life cycle that characterize the analysis (i.e., cradle to grave

or cradle to gate) and which function is described by the FU, a measurable and scalable reference

flow used to normalize the inventories and to run comparisons. In the LCI, the data collection occurs

through dedicated checklists. Primary data are generally collected from experiments and measures;

secondary and tertiary information are also used to fill all the background processes (e.g., electricity

mix). Data quality assessment is also performed to guarantee reliability, completeness, geographical,

technological, and temporal correlation. During the third stage, the impact assessment takes place.

LCIA applies the environmental mechanisms and characterization models to relate the LCI results to

the selected category indicators for a quantitative estimate of the environmental impacts, including

(but not limited to) climate change, water depletion, cumulative energy demand. The robustness of

the models created can be tested through sensitivity simulations and an uncertainty analysis. Finally,

during interpretation the practitioners can evaluate the results obtained and use them to support the

decision making.

System boundaries

In this study, a cradle to gate perspective was applied (Figure S1): from the raw material extraction

and transformation into EtOH (upstream) up to the plant gate (core) for the synthesis of 340.2 kg of

bio-BuOH (FU). The cradle to gate perspective is common for chemical products given the variability

of the downstream processes (i.e., several applications and consequent different end of life scenarios).

As depicted in Figure S1 the model includes all the process needs obtained from the engineering

simulation - production of the NaOEt (auxiliary), electricity, heat and the catalytic system (catalyst +

co-catalyst) - as well as all the co-products recovery (e.g., NaOAc, alcohols mixture and H_2) and the

treatments of waste (e.g., spent catalysts sent to incineration). All the input flows in Figure S1 (white

blocks) takes into account all the upstream flows, i.e., the resources consumption and impacts related

to that specific substance/energy carrier until its usage within the model including transportation up

to the production plant (core). In the case some molecules were not available in the selected database

they were simulated according to the stoichiometric equation. This is the case of NaOEt that was

created using the mass balance deriving from the reaction $CH_3COOH + NaOH \rightarrow CH_3COONa +$

H_2O. The figure highlights all the output flows from the core, such as the main product (bio-ButOH,

blue dotted), the spent catalytic system (sent to thermal incineration, see sub-heading below) and the

co-products (NaOAc, alcohols mixture and H_2, in light orange). Multifunctionality was treated

considering a consequential approach for these by-products that under our-own control. As detailed

in the Baseline scenario sub-heading, the model takes into account the avoided impacts (dashed green)

from the recovery of NaOAc, alcohols mixture and H_2 that could be used/sold directly from the plant

manager. Full LCI is reported in ESI (see Table S1 and Table S2). Ecoinvent database (v.3.9)[47] was

used to fill the background information, by selecting the market scenarios (to include impacts from

average transportation distances) and the allocation at the point of substitution (APOS) unit models.

Geographical boundaries were settled in Italy and RER processes were used, if available. Despite the

fact the consequential (CONS) approach was used for our by-products we decided to adopt the APOS

model to have more conservative results (i.e., potentially higher burdens). In fact, the application of

a CONS approach on the entire supply chains would allow more benefits from potential substitution

of material/energy within the entire supply chain. However, there is no assurance the consequential

approach is really respected along the chain, since we have no direct control on it, we proceed with a

more conservative way.

Catalytic system

The whole catalytic synthesis was simulated from the roots by following the recipe at laboratory

scale. The stoichiometric reactions were adopted to recreate mass balances for each step (balanced

reaction taken from Reaxys®)[48] involved in the production of the final active system

($C_{38}H_{33}N_2O_5RuI$). Several stages of simulation were necessary to fill data gap, since no precursors

exist in the database. To our knowledge, this approach is proposed for the first time in literature. In

fact, due to the lack of information on retrosynthesis (corporate knowhow), several LCA studies

which involve the use of catalysts only focus on the metal amount consumed calculated from the system stoichiometry.[49,50,51] Energy consumption for the production of the catalytic system was excluded, due to the differences between laboratory and industrial scale. All the steps are reported in the ESI (Table S3). The baseline scenario assumes that the catalytic system (catalyst + co-catalyst) is used for three cycles before being sent to the hazardous waste incinerator for treatment (*Hazardous waste, for incineration {Europe without Switzerland}| market for hazardous waste, for incineration | APOS, U*).

Baseline scenario

The baseline model, *Scenario 3X_2° EtOH dedicated biomass (baseline)*, includes the Italian electricity mix (*Electricity, medium voltage {IT}| market for | APOS, U*) and second-generation bio-EtOH to feed the plant. Wood chips from responsible management sources (i.e., FSC® - The Forest Stewardship Council®)[52] were used as a primary raw material for the production of the alcohol (*Ethanol, without water, in 95% solution state, from fermentation {CH}| ethanol production from wood | APOS, U*). As stated above, the scenario includes the benefits from the recovery of the by-products. Hydrogen flow (2.1 kmol) is sent to the boiler with 100% efficiency for the production of 1014 MJ. This way, the system avoids the requested volume of natural gas able to generate the same energetic amount (28 m^3, assuming 37 MJ/m^3).[53] The model also integrates the recovery of the alcoholic mixture (C6:C8:C10), that could be used as a valuable substitute for synthetic lubricant oil in 1:1 ratio (*Lubricating oil {RER}| production | APOS, U*), and of trihydrated NaOAc sold in replacement of the virgin salt (*_Sodium acetate {GLO}| sodium acetate production | APOS, U*).

Sensitivity analyses

In addition, two further scenarios were created to test the model sensitivity: the *Scenario 3X_2° EtOH waste biomass* and the *Scenario 5X_2° EtOH waste biomass_COGEN*. The former differs from the baseline only for the usage of waste lignocellulosic biomasses. The latter considers the reuse of the catalytic system for two more cycles and the co-production of electricity and heat in a cogeneration

plant within the biorefinery boundaries (*Electricity, high voltage {IT}| heat and power co-generation, wood chips, 6667 kW, state-of-the-art 2014 | APOS, U* and *Heat, district or industrial, other than natural gas {IT}| heat and power co-generation, wood chips, 6667 kW, state-of-the-art 2014 | APOS, U*).

Uncertainty analysis

Finally, an uncertainty analysis with the Monte Carlo method was performed. Data pedigree matrix was used to calculate uncertainty ranges for LCI data concerning reagents, catalyst, energy input, emissions and waste streams. A lognormal statistical distribution, with a 95% confidence interval and an iterative calculation number of 1,000 simulations, was applied. Results from the analysis were used to compare the scores achieved by the three bio-BuOH routes with the traditional oxo synthesis from oil, i.e., the hydro-formylation of propene (*1-butanol {RER}| hydroformylation of propylene | APOS, U*), the most prominent worldwide.[54] The reason why we performed the comparison with the fossil-based route for ButOH is related to the importance of the oxo synthesis, the main pathway worldwide[55] that replaced the traditional fermentative process ABE (acetone-butanol-ethanol). Starting from 1950s, ABE process progressively declined and then disappeared in favour of the fossil pathway.[56] In fact, the aim of the analysis was to verify the environmental sustainability of the Guerbet-based bio-ButOH respect to the traditional route, a more consolidated synthesis also thanks to the usage of abundant and cheaper reagents (propylene, carbon monoxide and hydrogen). Further comparison with alternative fuels or lubricants were not taken into account since their use may also depends on the technology adopted and/or the final application/sector.

SimaPro (v.9.5)[57] was adopted as simulation software to run the LCIA, by selecting the ReCiPe 2016 method (v.1.08).[58] It allows the assessment of 18 impact categories at midpoint level (Global warming = GWP; Stratospheric ozone depletion = SOD; Ionizing radiation = IR; Ozone formation, Human health = OZ_HH; Fine particulate matter formation = FPM; Ozone formation, Terrestrial ecosystems = OZ_TE; Terrestrial acidification = TA; Freshwater eutrophication = FWEu; Marine

eutrophication = Meu; Terrestrial ecotoxicity = TEc; Freshwater ecotoxicity = FEc; Marine ecotoxicity = MEc; Human carcinogenic toxicity = HCT; Human non-carcinogenic toxicity = HNCT; Land use = LU; Mineral resource scarcity = MRS; Fossil resource scarcity = FRS; Water consumption = WC), which represents the problem-oriented results. In addition, the method allows the grouping into 3 damage-oriented to receptors (endpoint) and, eventually, the weighting into single score.

3. Results and discussion

*3.1 The influence of headspace on the Guerbet reaction catalysed by **Ru-cat/BQ/NaOEt** system.*

The experimental study on the Guerbet reaction selected as a benchmark for this study was carried out by running several catalytic runs while changing the amount of ethanol added and/or the reactor volume. The results, reported in Table 1, were sorted by the ratio between the volume occupied by the liquid and the total reactor volume (V_{liq}/V_r).

Table 1. Experimental results regarding the Guerbet reaction performances variation over the headspace. Conditions: **Ru-cat** 0.2 mol% , NaOEt 20 mol%, **BQ** 1.5 mol%, T = 150°C, t = 4h ; *under H_2 atmosphere.

Entry	V liq (ml)	Vr (ml)	V_{liq}/V_r (%)	Conv. EtOH (%)	BuOH yield (sel.) %	C_6-C_{10} yield (sel.) %	H_2 yield (%)	C-loss (%)	g BuOH/g Ru/time (h^{-1})	g C_6-C_{10}/g Ru/time (h^{-1})
1	0.5	53.8	0.9	76.0	27.4 (36)	26.1 (34)	24.4	22.5	12.5	10.7
2	0.5	13.4	3.7	77.3	33.8 (44)	30.6 (40)	16.7	12.9	15.5	8.1
3	0.5	7.5	6.7	71.3	38.6 (54)	27.2 (38)	9.2	5.6	17.7	7.3
4	1	7.5	13.3	63.2	41.0 (65)	20.3 (32)	9.7	1.9	18.8	5.5
5[a]	1	7.5	13.3	52.1	38.5 (74)	10.9 (21)	9.3[b]	2.8	17.7	4.5

[a] under H_2 atmosphere (1 bar), [b] hydrogen yield has been obtained as measuredH_2 - initialH_2

The product distribution also depicted in Figure 1 shows that by increasing the volume occupation of the liquid in the vessel a sensitive improving on the reaction efficiency is observed. Indeed, although the conversion slightly decreases, alcohol yields and selectivity are improved, and the carbon loss

almost disappears at 13.3% occupation (entry 4). Furthermore, the reduced headspace volume promotes the selectivity toward butanol up to 65% under the best conditions (entry 4). On the other hand, lowering the volume occupation still in the presence of a low carbon loss (entry 4 occupation, 13.3% vs. entry 3, 6.7%) increases the selectivity in higher alcohols (C_6-C_{10}). The productivity is also reported as grams of product obtained per gram of ruthenium used for a single catalytic run (Table 1, last column). By decreasing the headspace, the productivity towards butanol increases while that for higher alcohols decreases, following the same trend reported for the selectivity.
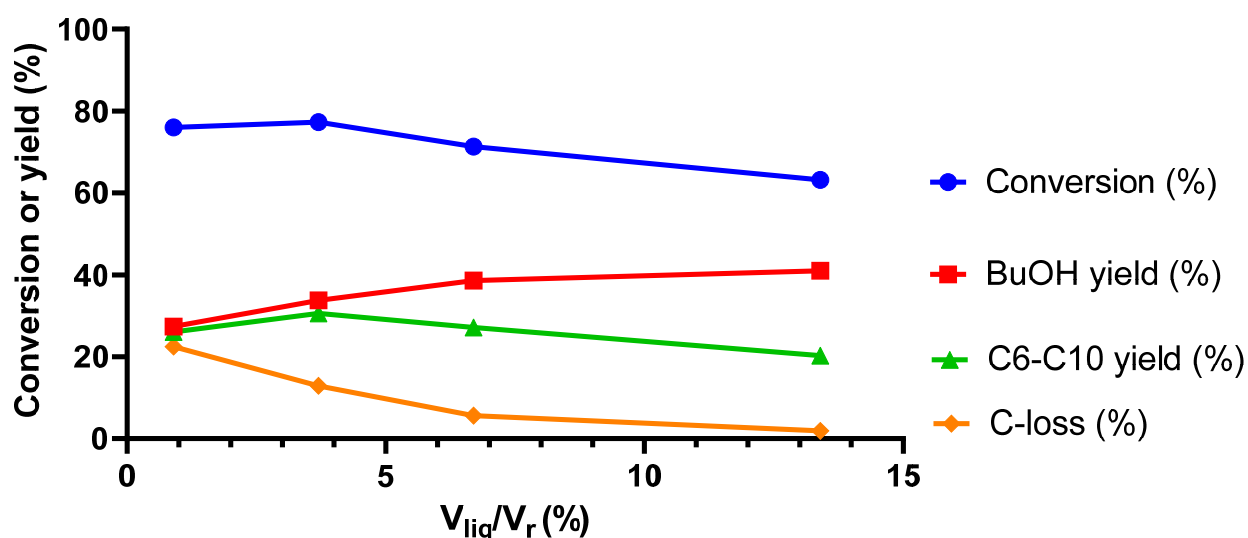

Figure 1. Effect of the headspace variation on the reaction performances. Conditions: Ru-cat 0.2 mol% , NaOEt 20 mol%, BQ 1.5 mol%, T = 150°C, t = 4h.

The data reported in Table 1 are summarized in Figure 1, showing that selectivity can be finely tuned by varying the reactor sizing.

An interesting effect of the volume occupation was also observed for the production of hydrogen, a side reaction,[12] monitored via GC-TCD analysis of the reactor headspace as reported in Table 1. Indeed, H_2 yields in Table 1 suggest that its side-production is discouraged when the headspace in the vessel is decreased, also positively affecting the carbon loss. Unless for the lower liquid occupation (entry 1) where hydrogen production is in line with the carbon loss, a difference in some points excess of H_2 yield vs. carbon loss can be observed while lowering the headspace (entry 2-4).

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This unusual behaviour is in line with what previously observed,[12] and can be explained taking into consideration some hydrogen that could come from the co-catalyst NaOEt in the presence of water from condensation. This can be accounted separately by the ethanol carbon balance, in a parasite reaction that consumes the base co-catalyst, namely NaOEt + H_2O that leads to NaOAc + $2H_2$ as reported by Beller and co-workers for ruthenium pincer catalysts exploited for H_2 production from EtOH in water under basic (OH^-) conditions.[59]

In order to complete the balance of the two principal reactions involved in the system, it is also important to recall that the primary side reaction that affects the homogeneous Guerbet process is the Cannizzaro reaction, which turns off the reaction by quantitatively convert the co-catalytic base NaOEt (20 mol%) in acetates as previously stated.[23, 34, 12]

Operating at the best conditions (Entry 4, Table 1), the water-soluble fraction was collected and analysed through ^{1}H-NMR spectroscopy using DMSO as internal standard. The spectrum (Figure S7) shows the presence of sodium acetate while only traces of sodium butanoate were found. Sodium acetate was quantified in 3,42 mmol, corresponding to the amount of NaOEt employed as co-catalyst, confirming that the reaction is switched off by the quantitative transformation of sodium ethoxide into sodium acetate by means of the Cannizzaro reaction.

Since all the NaOEt is side transformed in sodium acetate, this can be considered apart from the ethanol carbon balance. Thus C-loss reported in Table 1, only refers to the transformation of ethanol. Since no intermediates are found in the GC solution analyses, the C-loss is attributable to heavy insoluble compounds, which, as previously reported for the liquid phase Guerbet reaction, arise from the polymerization of acetaldehyde to insoluble polymers or from further homologation of alcohol toward insoluble polymers as well..[23]

Interestingly, performing the reaction under H_2 atmosphere (under the best conditions, 13.3% of volume occupation, entry 4) an higher selectivity in butanol can be obtained (75%) (entry 5, Table1).

Although the conversion is lower and the hydrogen production seems to be slightly affected by the initial hydrogen, the overall productivity of the reaction on butanol yield is similar.

Overall, the positive effect of an increased volume occupation benefits the selectivity of the process toward the production of butanol, reducing the side production of hydrogen and other species that fall within the C-loss. Driven by these experimental results, an engineering assessment on a possible industrial design of the process and a subsequent LCA analysis are reported in this work.

3.2 Engineering assessment

The evaluation of the experimental results reported in Table 1 and Figure 1 **Errore. L'origine riferimento non è stata trovata.** shows higher ethanol conversions and butanol yields together with a decrease in carbon losses when increasing volume occupation. Taking into account the limited dead volume in industrial reactors, this trend has been extrapolated up to 16% volume occupation, identifying the specific indicators reported in Table 2 and assumed as a basis for the preliminary design of the full-scale reactor. The assumption on the performance of the full-scale reactor with respect to the volume occupation is close to the experimental results recorded at the maximum investigated volume occupation, equal to 13.3%.

Table 2: Assumptions on the performance of the full-scale catalytic reactor based on extrapolation of experimental results.

Species	Yield [%]	Specific Consumption [mol/molEtOH$_{in}$]	Conversion [%]
EtOH (C2)	-		60.0
Catalyst (Ru-cat)	-	0.002	
p-Benzoquinone (co-catalyst)	-	0.015	
NaOEt (base)	-	0.208	
Butanol (BuOH)	42.3		
Hexanol (C6)	12.0		
Octanol (C8)	5.8		
Decanol (C10)	1.9		

The mass balance of the full-scale reactor with reference to a processed amount of 1000 kg of ethanol is reported in Table 3 and it is affected by an absolute deviation in the order of 0.2%w.

Table 3: Mass balance of the full-scale reactor.

Species	Formula	MW [kg/kmol]	Reactor Inlet [kg]	Reactor Outlet [kg]
EtOH	C_2H_6O	46.07	1000.0	400.0
Catalyst (Ru-cat)	-	826.00	35.9	35.9
p-Benzoquinone (co-catalyst)	$C_6H_4O_2$	108.10	35.2	35.2
NaOEt (base)	C_2H_5ONa	68.05	307.7	0.0
BuOH	$C_4H_{10}O$	74.12		340.2
C6	$C_6H_{14}O$	102.16		88.4
C8	$C_8H_{18}O$	130.23		40.7
C10	$C_{10}H_{22}O$	158.28		13.1
Hydrogen	H_2	2.02		4.2
Carbon losses (EtOH)	C_2H_6O	46.07		0.0
NaOAc (by-product)	$C_2H_3NaO_2$	82.03		371.0
Water	H_2O	18.00		47.7

In order to evaluate mass and energy balance characteristic of the novel butanol production process, a conceptual design of a full-scale facility has been conceived and represented in Figure 2. The process operates in a semi-batch mode and it is divided into three main sections: (i) reaction unit (reactor R-01 and related accumulation tank TK-01); (ii) post treatment unit (vessel V-01, filter F-01 and associated tank TK-02); (iii) fractionation section (evaporators E-01, E-02 and the two distillation columns C-01 and C-02). The fed ethanol, catalyst, co-catalyst and the base enter the reaction unit where chemical reaction occurs. R-01 is a batch stirred reactor operating at 150°C for 4h and it is associated to a blanketing system avoiding contact between the catalyst and the atmosphere. The products accumulated in TK-01 are conveyed towards the post-treatment unit where temperature is lowered down to 25°C to allow precipitation of Sodium Acetate within V-01, still operating in batch mode. Catalyst washing also occurs within vessel V-01 with a dedicated stream of ethanol. After washing, unloaded products from V-01 enter a filter where sodium acetate is separated from the rest of the mixture still containing the catalyst, which is highly soluble in ethanol. Moreover, products are recirculated within vessel V-01 to assure proper washing operations. After adequate recirculation and NaOAc recovery, products are processed in the continuous fractionation section. Coupling of the upstream discontinuous process and the continuous fractionation unit is possible due to vessel TK-02

being operated as buffer. Within the fractionation section, evaporator E-01 and column C-01 operated at atmospheric pressure have the purpose of separating hydrogen and ethanol from the catalyst and heavier products. E-02 and C-02 operate under vacuum, limiting the maximum temperature to avoid catalyst degradation. E-02 has the purpose of recovering the catalyst as tail product. C-02 has the purpose of separating product-grade butanol from heavier alcohols. Recovered ethanol is fully reused within the process, representing 40% of the reactor input, thus limiting ethanol consumption.

Figure 2: Conceptual design of the novel catalytic butanol production process.

Table 4 reports specific energy consumption and performance indicators with reference to 1kg of produced butanol. Most of the energy consumption is due to the heat duty required from reboilers and condensers used in the fractionation unit. Electric consumption for heat rejection and other auxiliaries has been estimated as 10% of the hot heat duty.

Table 4: Main mass and energy balances of the novel full-scale process, expressed per kgBuOH.

Specific Figures	Value	Unit
Catalyst	0.11	kg/kgBuOH
Co-catalyst	0.10	kg/kgBuOH
NaOEt consumption	0.90	kg/kgBuOH
EtOH consumption	1.76	kg/kgBuOH
AlOH production	0.42	kg/kgBuOH
NaOAc production	1.09	kg/kgBuOH
Electricity consumption	1.41	MJ_{el}/kgBuOH
Heat consumption	12.15	MJ_{th}/kgBuOH

3.2 LCA: impact assessment results, sensitivity and uncertainty analysis

Figure 1 and Table S4 collect results at midpoint level for the baseline pathway (*Scenario 3X dedicated biomass*), obtained from the analysis of the model created using indicators from Table 4 together with all the background information for the synthesis of the catalytic system, the energy requirements and the production of chemicals. Red-shade bars (above the zero) represent the potential burdens; on the contrary, the green ones show all the benefits derived from the material and energy recovery processes. As depicted, the chemicals input to the system (EtOH and NaOEt) produce the greater contribution among the entire set of categories, ranging from 20% to 98%. In the case of the alcohol, the use of dedicated sources deriving from sustainable management (*Wood chips, wet, measured as dry mass {CH}| market for | APOS, U*) has impacts far from being considered negligible, in particular for the categories LU (98% contribution), HCT (47%), FRS (36%), GWP (29%), Meu (20%) and FPM (18%). On the other hand, the NaOEt production chain affects the impact categories mostly due to the production processes of EtOH (12-67%) and NaOH (18-55%). A contribution analysis of the NaOEt supply chain is depicted in Figure S2.

Energy requirements (electricity from the grid and heat from natural gas) affect mostly GWP (17%) and FRS (17%), both considered combustion-related categories, as well as FWEu (19%). The latter due to the usage of hard coal in thermoelectric plant (50% contribution).

The results obtained for the metal catalytic system reflect the highest contribution for the MRS (79%). At the same time, it also has non-negligible influence on other categories besides that mentioned above, often considered the most consolidated for the metal catalytic systems. Among these, HCT (41%), Fec (16%) and FWEu (17%) are those mostly affected. The reason is explained in Figure S3, where a substance contribution analysis reveals that the supply chain of the Ruthenium dimer compound generates higher impacts for the Fec and HCT; on the contrary the 1,3-dimethylimidazolim iodide (imidazolium salt) contributes mostly the FWEu. A further contribution in Figure S4 has

revealed that the burdens of the catalyst (Ru) and co-catalyst (p-benzoquinone) are balanced among the entire set of categories considered. The former predominates in FWEu, Meu, Fec, HCT and MRS; the latter mostly on TEC.

Since the main contributors to the overall impacts are found to be the chemicals input to the model, the energy requirements and the catalytic system production, a sensitivity analysis was carried. In the first case, the employment of waste lignocellulosic biomass was assumed in replacement of wood chips from FSC® (*Scenario 3X waste biomass*). Results at midpoint level, collected in Figure S5 and Table S5, are quite similar to the scores of the baseline except for the LU category, for which a stronger difference was denoted. In fact, the process for the waste lignocellulosic biomass differs from the former just in terms of soil occupation, since no fertilizers are used for the forest growth. An impressive reduction of -1.12E+03 m^2a crop eq./FU was found. This finding confirms the importance of including LU category when the bio-based sector is under study, as recently reported in literature.[60] The further sensitivity analysis (*Scenario 5X waste biomass COGEN*) takes the benefits of using the catalytic system for 5 cycles together with those deriving from the usage of a cogeneration plant for the coproduction of heat and electricity. Results are reported in Table S6 and Figure 2. The graph shows how the contribution of the fossil fuels used in energy on the GWP and FRS categories is almost gone due to the use of renewable biomasses, despite the contribution of the heat generation on PMF, HCT and HNCT increased drastically as a consequence of the airborne emissions deriving from the combustion. A similar trend is observed for the LU, due to the usage of wood chips from dedicated sources (*Wood chips, wet, measured as dry mass {Europe without Switzerland}| market for | APOS, U*). The sensitivity also reflects the importance of enhancing the catalyst recyclability to raise the environmental sustainability of the entire reaction. Moving from 3 up to 5 cycles considerably decreases the contribution on the selected categories. For this reason, a further comparison was performed to counterpose the impacts of the three bio-based scenarios described. Five impact categories were selected (GWP, PMF, LU, MRS and FRS) since the most predominant after

weighting at endpoint level (damage-oriented). Results in Figure S6 classify the *Scenario 5X waste biomass COGEN* as the most favourable for three categories out of four. Compared to the baseline, the reduction achieved is higher than 50% in the case of GWP, -41% for the MRS and around -16% for the FMP. On the contrary, benefits derived from energy and material recoveries on FRS are nine times greater thanks to a lower exploitation of the fossil resources due to the cogeneration plant. The *Scenario 3X waste biomass* results in having lower repercussions in terms of LU, given the usage of non-dedicated timber for the EtOH production and energy generation.

Finally, in order to verify the model robustness, a Monte Carlo analysis was performed by comparing the three bio-based pathways with the traditional route based on propylene hydroformylation. The latter was simulated with the ecoinvent default process *1-butanol {RER}| hydroformylation of propylene | APOS, U*. The comparison was repeated for 1,000 runs after having estimated the range of uncertainty with the pedigree matrix. Results, reported in Figure 3, classify the Guerbet process as a more competitive alternative to the fossil-based for three categories out of five (GWP, PMF and FRS). The lower material and energy demand, as well as the integrated system of the biorefinery, seems to reward the bio-based routes, even if wood chips from dedicated timber are used and the catalyst is not recycled for more than three cycles. Scores on LU achieve comparable values only in the case of a null usage of the cogeneration technology (i.e., *Scenario 3X waste biomass*). Finally, the results on MRS are not easy to commensurate since the fossil-based process seems to not include any metal consumption for the catalyst generally used in the oxo synthesis.[61] A detailed analysis reveals how the main contributor is, in fact, the infrastructure. Nonetheless, less than 7.5 catalytic cycles are necessary to reach the same score for the MRS category, which is far from technically unfeasible.
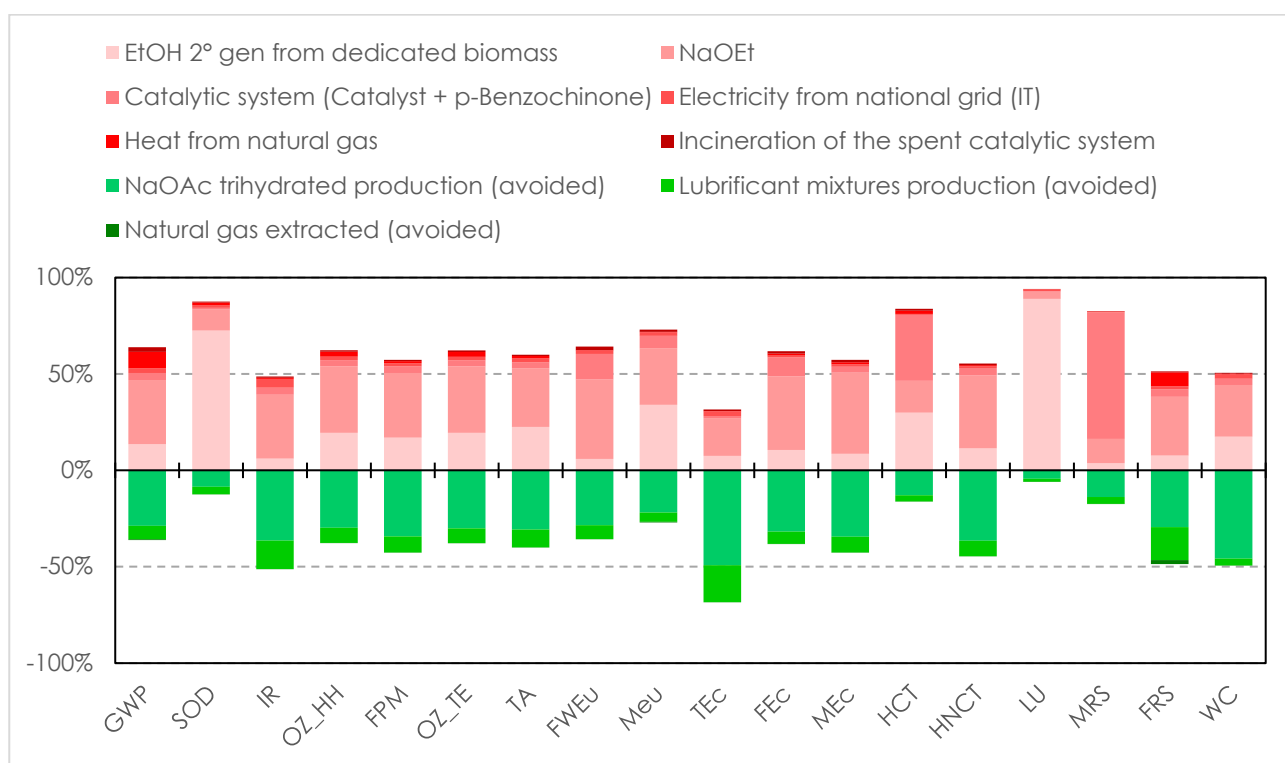
Figure 1 LCIA Scenario 3X dedicated biomass (baseline) at midpoint H, using ReCiPe 2016 method (v.1.08).

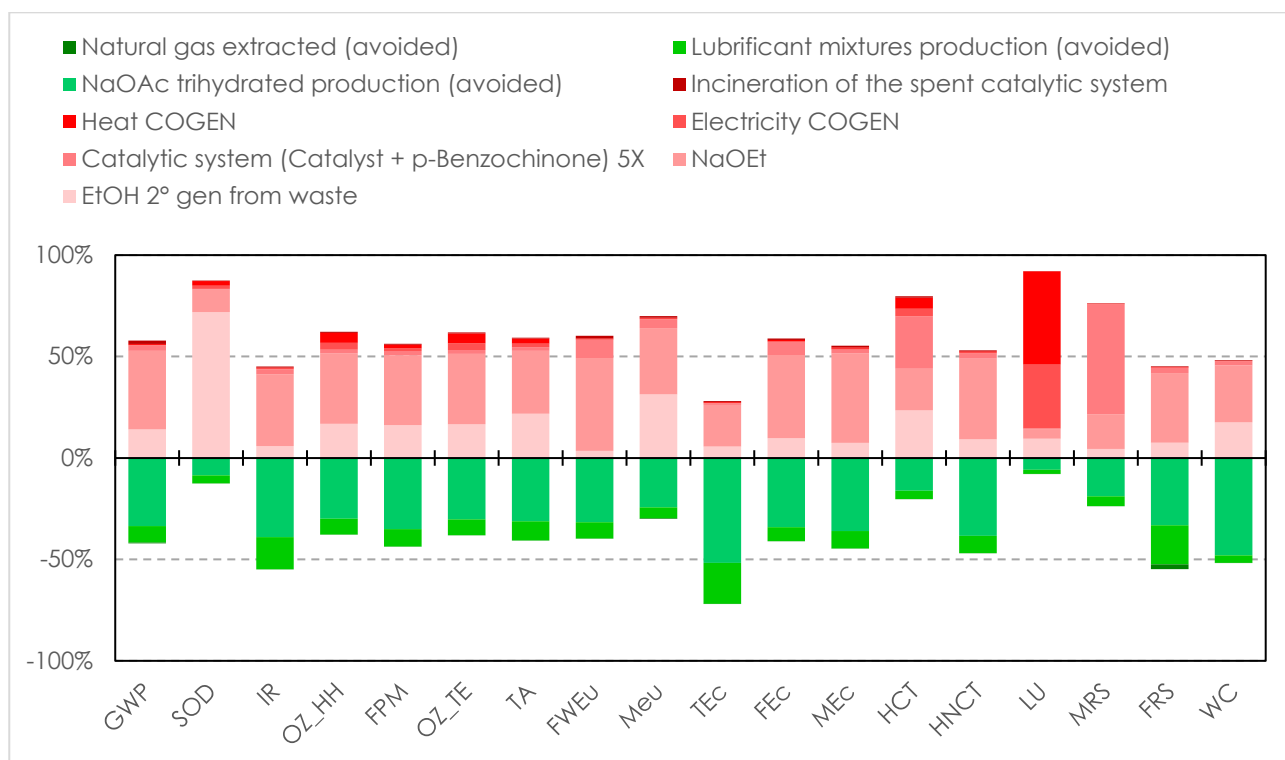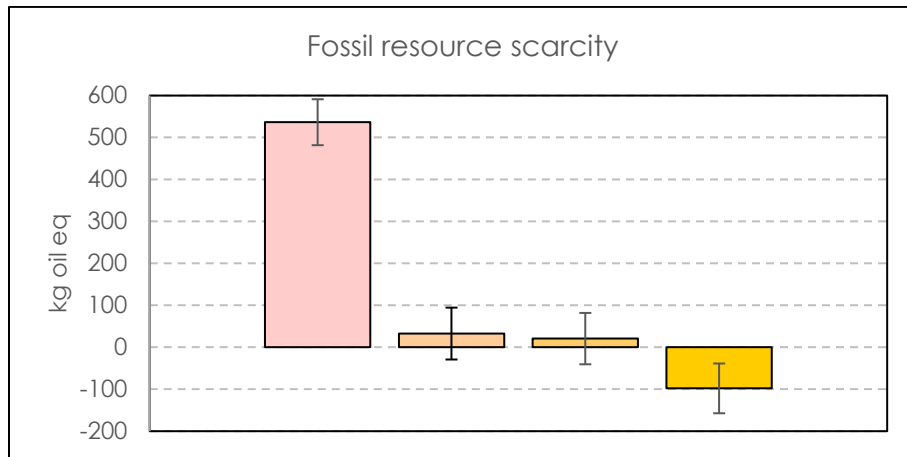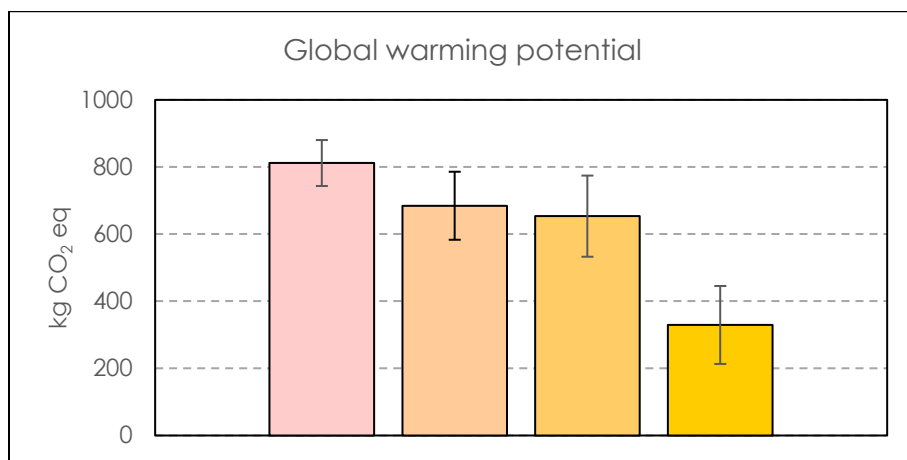Legend for the impact categories reported in the next caption.

Figure 2 LCIA Scenario 5X waste biomass COGEN at midpoint H, using ReCiPe 2016 method (v.1.08). FEc = Freshwater ecotoxicity; FPM = Fine particulate matter formation; FRS = Fossil resource scarcity; FWEu = Freshwater eutrophication; GWP = Global warming potential; HCT = Human carcinogenic toxicity; HNCT = Human non-carcinogenic toxicity; IR = Ionizing radiation; LU = Land use; MEc = Marine ecotoxicity; Meu = Marine eutrophication; MRS = Mineral resource scarcity; OZ_HH = Ozone formation, Human health; OZ_TE = Ozone formation, Terrestrial ecosystems; SOD = Stratospheric ozone depletion; TA = Terrestrial acidification; TEc = Terrestrial ecotoxicity; WC = Water consumption.
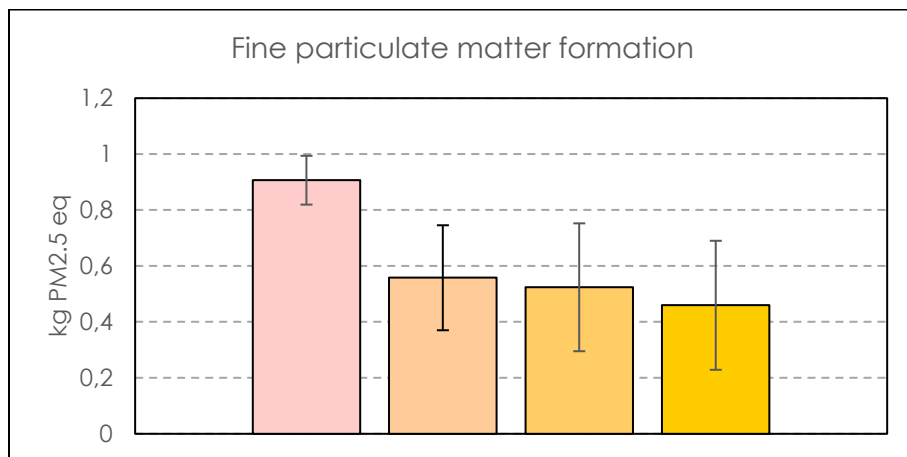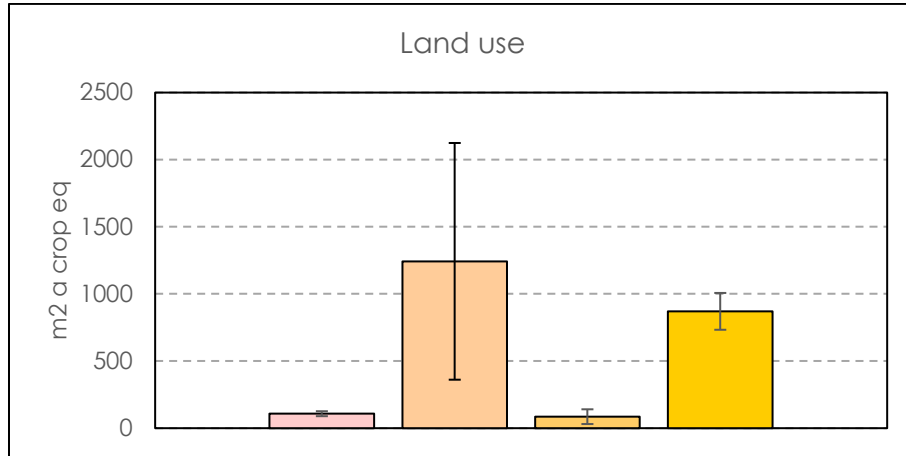
a)

Fossil resource scarcity

b)

Global warming potential

c)

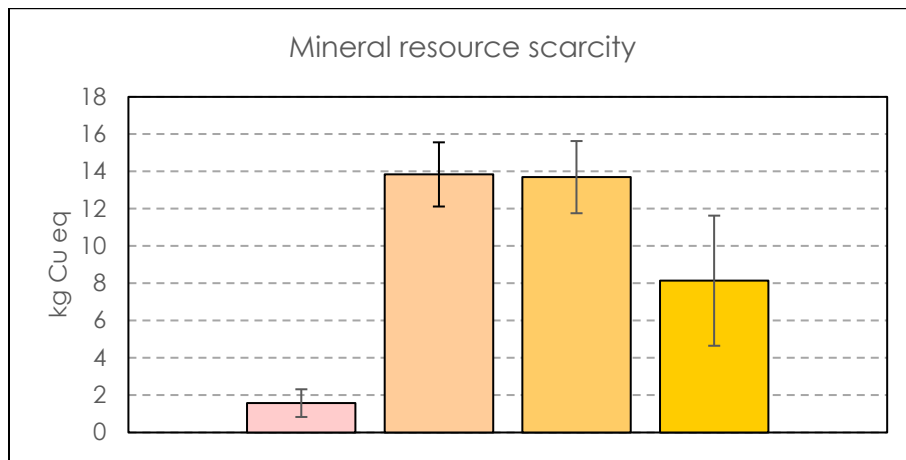Fine particulate matter formation

d)

e)

Figure 3 Uncertainty analysis of the scenarios at midpoint H/A using ReCiPe 2016 method (v.1.08). Monte Carlo simulation (1,000 runs). ☐ BuOH from propylene (fossil), ☐ Scenario 3X (baseline), ☐ Scenario 3X (waste biomass) and ☐ Scenario 5X COGEN.

4. Conclusions

The homogeneous triad **Ru-cat/BQ/NaOEt** performs better when decreasing the headspace of the reactor. The positive effect of an increased volume occupation benefits the selectivity in butanol which arose from 36% at $V_{liq}/V_r = 0.9\%$ to 65% at $V_{liq}/V_r = 13.3\%$. It also reduce the side products both in the gas phase (hydrogen yield concurrently decrease from 24.4% to 9.2%) and in heavy species (C-loss is indeed halved). The catalytic system at the lab scale is thus sensitively improved by reducing the head space and these can be assumed as the best conditions for the **Ru-cat/BQ/NaOEt** system for the Guerbet reaction. Driven by these experimental results, a conceptual design of the process has been carried out. Even if only preliminary, the engineering evaluations may be deemed representative of the novel process at industrial scale. The catalytic process requires a basic environment (i.e., consumption of 0.90 kgNaOEt/kgBuOH) to produce butanol and 0.42 kgAlOH/kgBuOH of higher alcohols, with an electric and thermal consumption of 1.41 MJ$_e$/kgBuOH and 12.15 MJ$_{th}$/kgBuOH respectively. The results from engineering simulation have been also used to carry out a LCA analysis of the entire system considering the production of 340.2 kg of BuOH as FU. Several configurations were studied to verify the contribution of the catalyst recycling (from 3 up to 5 cycles) and of different energy sources (traditional electricity mix vs cogeneration from wood chips). The life cycle study was used as a screening methodology for addressing the environmental sustainability of the innovation proposed at an early design stage. Its application in R&D to support ecodesign strategies represents one the key factors in the chemical sector to guide upscaling. In this study we verified the competitiveness of the Guerbet route compared to the traditional fossil-based pathways, laying the groundwork for a future industrialization. Nonetheless, the study is affected by some limitations, such as the absence of upscaled energetic data for the catalytic system assembly. Therefore, given the fact we have identified the non-negligible contribution of the catalytic system on the whole impact, further studies will be focused to increase the knowledge and return a more comprehensive review on such aspect.

Acknowledgements

Supporting Information.

Supporting Information are available at …

Abbreviations

BuOH	Butanol
AlOH	Higher alcohols
ESI	Electronic supporting information
EtOH	Ethanol
NaOEt	Sodium ethoxyde
NaOAc	Sodium acetate
Cn	alcohol containing n carbon atoms
Conv.	Conversion
C-loss	Carbon loss
BQ	p-benzoquinone
FEc	Freshwater ecotoxicity
FPM	Fine particulate matter formation
FRS	Fossil resource scarcity
FU	Functional unit
FWEu	Freshwater eutrophication
GWP	Global warming potential
HCT	Human carcinogenic toxicity
HNCT	Human non-carcinogenic toxicity
IR	Ionizing radiation
ISO	International Organisation for Standardisation
LCA	Life cycle assessment

LCI	Life Cycle Inventory
LCIA	life cycle impact assessment
LU	Land use
MEc	Marine ecotoxicity
Meu	Marine eutrophication
MRS	Mineral resource scarcity
MW	Molecular weight
NaOAc	Sodium acetate
OZ_HH	Ozone formation, Human health
OZ_TE	Ozone formation, Terrestrial ecosystems
SOD	Stratospheric ozone depletion
TA	Terrestrial acidification
TEc	Terrestrial ecotoxicity
WC	Water consumption

References

[1]   https://www.europarl.europa.eu/news/en/headlines/society/20180920STO14027/reducing-car-emissions-new-co2-targets-for-cars-and-vans-explained;

[2] https://www.europarl.europa.eu/news/en/headlines/economy/20221019STO44572/eu-ban-on-sale-of-new-petrol-and-diesel-cars-from-2035-explained)

[3]Akhtar M. K., Dandapani H., Thiel K., Jones P. R. Microbial production of 1-octanol: A naturally excreted biofuel with diesel-like properties, Metab. Eng. Commun. 2 (2015) 1–52. DOI: 10.1016/j.meteno.2014.11.001

[4]Harvey B. G., Meylemans H. A. The role of butanol in the development of sustainable fuel technologies, Chem. Technol. Biotechnol. 86 (2011) 2-9. https://doi.org/10.1002/jctb.2540

[5]Yang C., Meng. Z. Y. Bimolecular Condensation of Ethanol to 1-Butanol Catalyzed by Alkali Cation Zeolites, J. Catal. 142 (1993) 37-44. https://doi.org/10.1006/jcat.1993.1187

[6]Gabriëls D., Yesid Hernández W., Sels B., Van Der Voort P., Verberckmoes A. Review of catalytic systems and thermodynamics for the Guerbet condensation reaction and challenges for biomass valorization, Catal. Sci. Technol., 5 (2015) 3876-3902. DOI: 10.1039/C5CY00359H

[7] Zhang B., Peña Fuentes D., Börner A. Hydroformylation, ChemTexts 8 (2022) 2. https://doi.org/10.1007/s40828-021-00154-x

[8] Veza I., Said M. F. M., Latiff Z. A. Progress of acetone-butanol-ethanol (ABE) as biofuel in gasoline and diesel engine: A review, Fuel Proc. Technol. 196 (2019) 106179. https://doi.org/10.1016/j.fuproc.2019.106179

[9] https://www.sasolguerbet.com/about-us/; https://www.sasolguerbet.com/fileadmin/user_upload/0280.SAS-BR-Isofol_WEB.pdf

[10] Scherf E., Letsch H –J., Schroeder C., Herrmann A. T. Method for producing metal-free Guerbet alcohols, Patent US6419797B1 (2002) assigned to Sasol Germany GMBH.

[11] Petrolini D. D., Eagan N., Ball M. R., Burt S. P., Hermans I., Huber G. W., Dumesic J. A., Martins L. Ethanol condensation at elevated pressure over copper on AlMgO and AlCaO porous mixed-oxide supports, Catal. Sci. Technol. 9 (2019) 2032-2042. DOI: 10.1039/C9CY00316A

[12] Cesari C., Gagliardi A., Messori A., Monti N., Zanotti V., Zacchini S., Rivalta I., Calcagno F., Lucarelli C., Tabanelli T., Cavani F., Mazzoni R. Boosting the guerbet reaction: A cooperative catalytic system for the efficient bio-ethanol refinery to second-generation biofuels, J. Catal. 405 (2022) 47-59. https://doi.org/10.1016/j.jcat.2021.11.027

[13] Hanspal S., Young Z. D., Shou H., Davis R. J. Multiproduct Steady-State Isotopic Transient Kinetic Analysis of the Ethanol Coupling Reaction over Hydroxyapatite and Magnesia, ACS Catal. 5 (2015) 1737–1746. https://doi.org/10.1021/cs502023g

[14] Moteki T., Flaherty D. W. Mechanistic Insight to C–C Bond Formation and Predictive Models for Cascade Reactions among Alcohols on Ca- and Sr-Hydroxyapatites, ACS Catal. 6 (2016) 4170–4183. https://doi.org/10.1021/acscatal.6b00556

[15] Ho C. R., Shylesh S., Bell A. T. Mechanism and Kinetics of Ethanol Coupling to Butanol over Hydroxyapatite, ACS Catal. 6 (2016) 939–948. https://doi.org/10.1021/acscatal.5b02672

[16] León M., Díaz E., Ordóñez S. Ethanol catalytic condensation over Mg–Al mixed oxides derived from hydrotalcites, Catal. Today 164 (2011) 436-442. https://doi.org/10.1016/j.cattod.2010.10.003

[17] Scalbert J., Thibault-Starzyka F., Jacquot R., Morvan D., Meunier F. Ethanol condensation to butanol at high temperatures over a basic heterogeneous catalyst: How relevant is acetaldehyde self-aldolization? J. Catal. 311 (2014) 28-32. https://doi.org/10.1016/j.jcat.2013.11.004

[18] Chieregato A., Velasquez Ochoa J., Bandinelli C., Fornasari G., Cavani F., Mella M. On the Chemistry of Ethanol on Basic Oxides: Revising Mechanisms and Intermediates in the Lebedev and Guerbet reactions, ChemsusChem 8 (2015) 377-388. https://doi.org/10.1002/cssc.201402632

[19] Scheid A. J., Barbosa-Coutinho E., Schwaab M., Salau N. P. G. Mechanism and Kinetic Modeling of Ethanol Conversion to 1-Butanol over Mg and Al Oxide Derived from Hydrotalcites, Ind. Eng. Chem. Res. 58 (2019) 12981–12995. https://doi.org/10.1021/acs.iecr.9b01491

[20] Ndou A. S., Plint N., Coville N. J. Dimerisation of ethanol to butanol over solid-base catalysts, Appl. Catal. A: Gen. 251 (2003) 337-345. https://doi.org/10.1016/S0926-860X(03)00363-6

[21] Carvalho D. L., de Avillez R. R., Rodrigues M. T., Borges L. E. P., Appel L. G. Mg and Al mixed oxides and the synthesis of n-butanol from ethanol, Appl. Cat. A: General, 415–416 (2012) 96-100. https://doi.org/10.1016/j.apcata.2011.12.009

[22] Dowson G. R. M., Haddow M. F., Lee J., Wingad R. L., Wass D. F., Catalytic Conversion of Ethanol into an Advanced Biofuel: Unprecedented Selectivity for n-Butanol, Angew. Chem. Int. Ed. 52 (2013) 9005 –9008. https://doi.org/10.1002/anie.201303723

[23] Aitchison H., Wingad R. L., Wass D. F., Homogeneous Ethanol to Butanol Catalysis - Guerbet Renewed, ACS Catal. 6 (2016) 7125–7132. https://doi.org/10.1021/acscatal.6b01883

[24] Messori A., Gagliardi A., Cesari C., Calcagno F., Tabanelli T., Cavani F., Mazzoni R. Advances in the homogeneous catalyzed alcohols homologation: The mild side of the Guerbet reaction. A mini-review, Catal. Today, 2023, https://doi.org/10.1016/j.cattod.2023.01.010

[25] S. Fu, Z. Shao, Y. Wang, Q. Liu, Manganese-Catalyzed Upgrading of Ethanol into 1-Butanol, J. Am. Chem. Soc. 139 (2017) 11941–11948. https://doi.org/10.1021/jacs.7b05939

[26] Kulkarni N. V., Brennessel W. W., Jones W. D. Catalytic Upgrading of Ethanol to N-Butanol via Manganese-Mediated Guerbet Reaction, ACS Catal. 8 (2018) 997–1002. https://doi.org/10.1021/acscatal.7b03653

[27] Liu Y., Shao Z., Wang Y., Xu L., Yu Z., Liu Q. Manganese Catalyzed Selective Upgrading of Ethanol with Methanol into Isobutanol, ChemSusChem 12 (2019) 3069 – 3072. https://doi.org/10.1002/cssc.201802689

[28] Rawat K. S., Mandal S. C., Bhauriyal P., Garg P., Pathak B., Catalytic upgrading of ethanol to n-butanol using an aliphatic Mn–PNP complex: theoretical insights into reaction mechanisms and product selectivity, Catal. Sci. Technol. 9 (2019) 2794–2805. DOI: 10.1039/C9CY00501C

[29] King A. M., Sparkes H. A., Wingad R. L., Wass D. F. Manganese Diphosphine and Phosphinoamine Complex-es Are Effective Catalysts for the Production of Biofuel Alcohols via the Guerbet Reaction, Organometallics 39 (2020) 3873−3878. https://doi.org/10.1021/acs.organomet.0c00588

[30] Tseng K.-N. T., Lin S., Kampf J. W., Szymczak N. K. Upgrading Ethanol to 1-Butanol with a Homogeneous Air-Stable Ruthenium Catalyst, Chem. Commun. 52 (2016) 2901–2904. DOI: 10.1039/C5CC09913G

[31] Chakraborty S., Piszel P. E., Hayes C. E., Baker R. T., Jones W. D. Highly Selective Formation of N-Butanol from Ethanol through the Guerbet Process: A Tandem Catalytic Approach, J. Am. Chem. Soc. 137 (2015) 14264–14267. https://doi.org/10.1021/jacs.5b10257

[32] Xie Y., Ben-David Y., Shimon L. J. W., Milstein D. Highly Efficient Process for Production of Biofuel from Ethanol Catalyzed by Ruthenium Pincer Complexes, J. Am. Chem. Soc. 138 (2016) 9077–9080. https://doi.org/10.1021/jacs.6b05433

[33] Ohligschlager A., van Staalduinen N., Cormann C., Muhlhans J., Wurm J., Liauw M. A. The Guerbet Reaction Network – a Ball-in-a-Maze-Game or: Why Ru-MACHO-BH is Poor in Coupling two Ethanol to n-Butanol, Chemistry—Methods 1 (2021) 181 –191. https://doi.org/10.1002/cmtd.202000056

[34] Pellow K. J., Wingad R. L., Wass D. F. Towards the Up-grading of Fermentation Broths to Advanced Biofuels: A Water Tolerant Catalyst for the Conversion of Ethanol to Isobutanol, Catal. Sci. Technol. 7 (2017) 5128–5134. DOI: 10.1039/C7CY01553D

[35] Cavani F., Zanotti V., Mazzoni R., Lucarelli C., Cesari C., Tabanelli T., Puzzo F. Improved process for the transformation of primary aliphatic alcohols into higher aliphatic alcohols, patent WO2019193079 (A1) (2019) assigned to the University of Bologna.

[36] Zuiderveen E., Kuipers K., Caldeira C., Hanssen S., van der Hulst M., de Jonge M., Vlysidis A., van Zelm R., Sala S., Huijbregts M. The potential of emerging bio-based products to reduce environmental impacts. Preprint (2022) available at https://www.researchsquare.com/article/rs-1816061/v1 (accessed 04 August 2023) https://doi.org/10.21203/rs.3.rs-1816061/v1

[37] International Organization for Standardization (ISO) (2018) 14067:2018, Greenhouse Gases—Carbon Footprint of Products—Requirements and Guidelines for Quantification. Geneva, Switzerland: ISO.

[38] Ögmundarson Ó., Herrgård M.J., Förster J., Hauschild M.Z., Fantke P. Addressing environmental sustainability of biochemicals. Nat. Sustain. 3 (2020) 167–174. https://doi.org/10.1038/s41893-019-0442-8

[39] European Committee for Standardization (CEN) (2015) EN 16760:2015, Bio-Based Products—Life Cycle Assessment. European Committee for Standardisation. Brussels, Belgium: CEN.

[40] Arfelli F., Maria Pizzone D., Cespi D., Ciacci L., Ciriminna R., Salvatore Calabrò P., Pagliaro M., Mauriello F., Passarini F. Prospective life cycle assessment for the full valorization of anchovy fillet

leftovers: The LimoFish process. Waste Manage. 168 (2023) 156–166. https://doi.org/10.1016/j.wasman.2023.06.002

[41] Patel A.D., Telalović S., Bitter J.H., Worrell E., Patel M. K. Analysis of sustainability metrics and application to the catalytic production of higher alcohols from ethanol. Catal. Today 239 (2015) 56-79. https://doi.org/10.1016/j.cattod.2014.03.070

[42] Mazzoni R., Cesari C., Zanotti V., Lucarelli C., Tabanelli T., Puzzo F., Passarini F., Neri E., Marani G., Prati R., Viganò F., Conversano S., Cavani F. Catalytic Biorefining of Ethanol from Wine Waste to Butanol and Higher Alcohols: Modeling the Life Cycle Assessment and Process Design. ACS Sustain. Chem. Eng. 7 (2019) 224–237. https://doi.org/10.1021/acssuschemeng.8b02959

[43] Cesari C., Cingolani A., Teti M., Messori A., Zacchini S., Zanotti V., Mazzoni R. Imidazolium Salts of Ruthenium Anionic Cyclopentadienone Complexes: Ion pair for bifunctional catalysis in ionic liquids, Eur. J. Inorg. Chem. 11-12 (2020) 1114-1122. https://doi.org/10.1002/ejic.201900993

[44] https://www.aspentech.com/en;; https://www.aspentech.com/en/products/engineering/aspen-plus

[45] International Organization for Standardization (ISO) (2006a) 14040:2006/Amd 1:2020, Environmental Management—Life Cycle Assessment—Principles and Framework. Geneva, Switzerland: ISO.

[46] International Organization for Standardization (ISO) (2006b) 14044:2006 Amd 1:2017 + Amd 2:2020 Environmental management — Life cycle assessment — Requirements and guidelines — Amendment 1. Geneva, Switzerland: ISO.

[47] Ecoinvent Centre (formerly Swiss Centre for Life Cycle Inventories), Ecoinvent v.3.9 Database, 2023.

[48] Reaxys®. Available at: https://www.reaxys.com (accessed on 30 January 2024)

[49] Cespi D., Passarini F., Neri E., Vassura I., Ciacci L., Cavani F. Life Cycle Assessment comparison of two ways for acrylonitrile production: the SOHIO process and an alternative route using propane, J. Clean. Prod. 69 (2014) 17–25. https://doi.org/10.1016/j.jclepro.2014.01.057

[50] Cespi D., Passarini F., Cavani F., Neri E., Vassura I. Comparison of Different Chemical Processes from a Life Cycle Perspective, Chem. Eng. Trans. 36 (2014) 169–174. DOI: 10.3303/CET1436029

[51] Cucciniello R., Cespi D., Riccardi M., Neri E., Passarini F., Pulselli F. M. Maleic anhydride from bio-based 1-butanol and furfural: a life cycle assessment at pilot scale, Green Chem. (2023) Accepted Manuscript. DOI: 10.1039/D2GC03707F

[52] The Forest Stewardship Council® (FSC®). Available at: https://connect.fsc.org/fsc-public-certificate-search (accessed on 30 January 2024)

[53] The Engineering ToolBox. Available at: https://www.engineeringtoolbox.com/fuels-higher-calorific-values-d_169.html (accessed on 30 January 2024).

[54] Uyttebroek M., Van Hecke W., Vanbroekhoven K. Sustainability metrics of 1-butanol. Catal. Today 239 (2015) 7–10.

[55] Hahn H.D., Dämbkes G., Rupprich N., Bahl H., Frey G.D. Butanols. In: Ullmann's encyclopedia of industrial chemistry. 2013, Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim.10.1002/14356007.a04_463.pub3

[56] Nexant Inc. (2008) Topical report. Biobutanol: The next big biofuel. Available at: https://www.nexanteca.com/reports/biobutanol-next-big-biofuel (accessed 04 August 2023)

[57] PRé Consultants. SimaPro v.9.5. Amersfoort, Netherland 2023.

[58] Huijbregts M. A. J., Steinmann Z. J. N., Elshout P. M. F., Stam G., Verones F., Vieira M. D. M., Hollander A., Zijp M., van Zelm R. (2017) ReCiPe 2016 – A harmonized life cycle impact assessment method at midpoint and endpoint level, National Institute for Public Health and the Environment (RIVM), Netherlands.

[59] Sponholz P., Mellmann D., Cordes C., Alsabeh P.G., Li B., Li Y., Nielsen M., Junge H., Dixneuf P., Beller M. Efficient and Selective Hydrogen Generation from Bioethanol using Ruthenium Pincer-type Complexes, ChemSusChem 7 (9) (2014) 2419–2422. https://doi.org/10.1002/cssc.201402426

[60] Cespi D. Bio-Based Chemicals from Dedicated or Waste Biomasses: Life Cycle Assessment for Evaluating the Impacts on Land. Sustain. Chem. 4 (2023) 184-196. https://doi.org/10.3390/suschem4020014

[61] Zhang B., Fuentes D. P., Börner A. Hydroformylation. ChemTexts 8 (2022) 2-27. https://doi.org/10.1007/s40828-021-00154-x