

This document is confidential and is proprietary to the American Chemical Society and its authors. Do not copy or disclose without written permission. If you have received this item in error, notify the sender and delete all copies.

Catalytic Bio-Refining of Ethanol from Wine Waste to Butanol and Higher Alcohols: Modeling the Life Cycle Assessment and Process Design.

Journal:	<i>ACS Sustainable Chemistry & Engineering</i>
Manuscript ID	sc-2018-029596.R1
Manuscript Type:	Article
Date Submitted by the Author:	n/a
Complete List of Authors:	<p>Mazzoni, Rita; University of Bologna, Dipartimento di Chimica Industriale "Toso Montanari"</p> <p>Cesari, Cristiana; Università di Bologna, Dipart. di Chimica Industriale "Toso Montanari"</p> <p>Zanotti, Valerio; Università di Bologna, Dipart. di Chimica Fisica ed Inorganica</p> <p>Lucarelli, Carlo; University of Insubria, Scienza e Alta Tecnologia</p> <p>Tabanelli, Tommaso; Università degli Studi di Bologna Dipartimento di Chimica Industriale Toso Montanari,</p> <p>Puzzo, Francesco; ALMA MATER STUDIORUM Università di Bologna, Dipartimento di Chimica Industriale</p> <p>Passarini, Fabrizio; University of Bologna, Dept. Industrial Chemistry "Toso Montanari"</p> <p>Neri, Esmeralda; Dipartimento di Chimica Industriale "Toso Montanari"</p> <p>Marani, Giovanni; Caviro Distillerie s.r.l.</p> <p>Prati, Rosa; Caviro Distillerie s.r.l.</p> <p>Vigano, Federico; Dipartimento di Energia-Politecnico di Milano</p> <p>Conversano, Antonio; Dipartimento di Energia-Politecnico di Milano</p> <p>Cavani, Fabrizio; University of Bologna, Dip Chimica Indust Materiali</p>



1
2
3 **Catalytic Bio-Refining of Ethanol from Wine Waste to Butanol and Higher Alcohols: Modeling the**
4 **Life Cycle Assessment and Process Design.**
5
6
7
8
9

10 Rita Mazzoni,^{a,*} Cristiana Cesari,^a Valerio Zanotti,^a Carlo Lucarelli,^b Tommaso Tabanelli,^a Francesco
11 Puzzo,^a Fabrizio Passarini,^a Esmeralda Neri,^a Giovanni Marani,^c Rosa Prati,^c Federico Viganò,^{d,e} Antonio
12 Conversano^{d,e} and Fabrizio Cavani^{a,*}
13
14
15
16
17
18

19 ^aDipartimento di Chimica Industriale “Toso Montanari” and Centro Interdipartimentale di Ricerca
20 Industriale – Energia e Ambiente (CIRI-EA), viale Risorgimento, 4 40136 Bologna. ^b Dipartimento di
21 Scienza e Alta Tecnologia – Università dell’Insubria-Como, via Valleggio, 9, 22100 Como. ^c Caviro
22 Distillerie, via Convertite, 8, 48018 Faenza (Ra). ^d LEAP-Laboratorio Energia ed Ambiente Piacenza,
23 via Nino Bixio 27/C, 29121 Piacenza ^eDipartimento di Energia-Politecnico di Milano, Via Lambruschini
24 4, 20156 Milano.
25
26
27
28
29
30
31
32
33
34

35 *E-mail: fabrizio.cavani@unibo.it; rita.mazzoni@unibo.it.
36
37
38
39

40 **Keywords** Bio-ethanol, Guerbet reaction, 1-butanol, homogeneous ruthenium catalyst, advanced
41 biofuel, refining, Life-cycle analysis, engineering assessment.
42
43
44
45
46
47

48 **Abstract**
49

50 Homologation of bio-ethanol to butanol and higher alcohols by means of Guerbet reaction has been
51 performed with a novel ruthenium based bifunctional catalyst under homogeneous conditions in the
52 presence of a basic co-catalyst. Reaction screening demonstrated that the new catalyst shows conversions
53
54
55
56
57
58
59
60

1
2
3 and selectivity comparable with some of ruthenium based bifunctional catalysts recently reported in the
4 literature. The reaction occurs in pure ethanol as well as in ethanol from wine wastes furnished by
5 CAVIRO distillery with up to 46% conversion of ethanol and an overall selectivity to higher alcohols of
6 91% and a minor carbon loss. Based on the laboratory results, an industrialization study has been carried
7 out in order to propose a viable technological solution. The experimental data consistency has been
8 verified and the results have been up-scaled to design a reactor working in a batch or, potentially, semi-
9 batch operation mode. Further analysis of the overall process, together with the introduction of dedicated
10 figures of merit have allowed the estimation of the process performance both in mass and energetic terms,
11 and the outcome has been integrated into a life cycle analysis. Although preliminary, the
12 multidisciplinary approach has converged towards complementary results; more specifically, the
13 adoption of the base co-catalyst NaOEt has showed similar performance in terms of specific alcohols
14 production and energy demand compared to the NaOH case. Moreover this last case proves to be better
15 from an environmental perspective (LCA).
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34

35 **Introduction**

36
37 Bio-ethanol refinery is a very current topic due to environmental issues connected with petrochemical
38 processes and, in order to develop new economic strategies. In particular when it is derived from waste
39 or second generation (non-food) biomass, bio-ethanol is a feedstock with a great potential for both biofuel
40 and biochemical production.¹⁻³ An appealing pathway to upgrade the fuel properties of this bio-derived
41 platform chemical into species with higher energy density and characteristics more similar to
42 conventional fuel is represented by the Guerbet reaction. In principle, this reaction, known for a century,
43 furnishes an ideal mechanism for the catalytic conversion of bio-ethanol into butanol and higher alcohols
44 (both linear and branched). Nevertheless, although the reaction seems simple in theory, it is highly
45 challenging especially for ethanol and particularly concerning the goal of high yields and selectivity.
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 This complication is mainly ascribable to the base-catalyzed aldol condensation of acetaldehyde. This
4
5 reaction is indeed hard to control and can proceed further to complex mixtures of heavy polymers.⁴⁻¹⁰
6
7

8 Starting from this awareness, and looking forward to a route to improve yields and selectivity, the
9
10 approach to Guerbet reaction has been recently widened to homogeneous catalysis. In a recent review by
11
12 Wass et al.¹¹ the “Guerbet renewed” from a homogeneous perspective is described in comparison with
13
14 other approaches, specifically with heterogeneous catalysts. Homogeneous catalytic systems for ethanol
15
16 coupling to yield *n*-butanol are mainly represented by iridium or ruthenium based bifunctional catalysts,
17
18 and more recently by manganese based complexes.^{12,13} More specifically, ruthenium phosphine catalyst
19
20 reported by Wass et al. led to a maximum selectivity of 93% associated with a 20% yield. On the other
21
22 hand, while increasing the yield to 45.8%, selectivity decreases to 84%.¹⁴ The same group reported about
23
24 the use of fermentation broths in order to show some water tolerance of their ruthenium catalysts.¹⁵ The
25
26 same behavior was observed by Tseng et al. who exploited nitrogen ligands based ruthenium
27
28 complexes.¹⁶ Best results up to date in terms of selectivity have been obtained by Jones et al. with a
29
30 tandem catalytic approach that involves iridium and copper or nickel complexes. In this case yield
31
32 reached 37% with an increase in selectivity up to 99%.¹⁷ Employing a ruthenium catalyst with a tridentate
33
34 ligand, the Milstein group firstly introduced in the homogeneous approach the concept of valuable
35
36 mixtures of alcohols, valorizing the formation of hexanol C₆ and octanol C₈.¹⁸
37
38
39
40
41
42

43 Noteworthy, the formation of both linear and branched heavier alcohols can be promoted by highly
44
45 active homogeneous catalysts starting from bio-ethanol. Linear alcohols (from *n*-butanol to *n*-octanol)
46
47 are characterized by an energy density closer to gasoline and can be used directly as a blend in diesel
48
49 engines (with a formulation up to 30% of alcohols in diesel fuel).¹⁹ However, problems can arise from
50
51 the poor lubricating properties of linear alcohols that can dilute the lubricant film on the piston wall, thus
52
53 affecting engine durability.²⁰ For these reasons, branched alcohols (in particular 2-alkyl alcohols, also
54
55
56
57
58
59
60

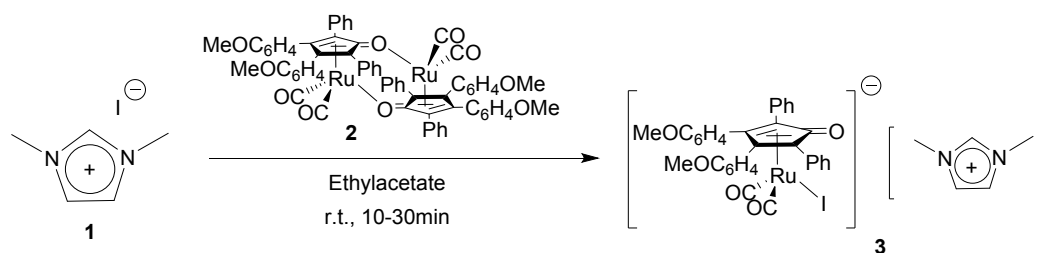
known as Guerbet alcohols), can be added to these blends in order to solve these problems. Indeed, these compounds are already used as lubricants, plasticizer and hydraulic fluids for aircrafts and jet fuels.²¹

The Guerbet reaction represents an alternative pathway to branched alcohols compared to the traditional three-step route: (i) hydroformylation of olefins to aldehydes, (ii) aldol condensation to branched α,β -unsaturated aldehydes, (iii) hydrogenation to 2-alkyl alcohol.²²

Here we describe the catalytic transformation of ethanol from waste into butanol and higher alcohols promoted by a bifunctional ionic ruthenium based homogeneous catalyst active in hydrogenation and dehydrogenation. The reaction occurs without additional solvent in the presence of an inorganic base as condensation co-catalyst. The reaction is barely affected by the presence of water and conditions can be transferred to a real matrix, indeed employing heads and tails from ethanol distillation (supplier: CAVIRO distillery) no significant change in the final reaction mixture is observed. Laboratory results have been integrated with an industrialization study in order to propose a viable technological solution. Furthermore, from data obtained with this latter approach, a quantitative life cycle assessment has been established.

Experimental and methods

Catalyst preparation



Scheme 1 Synthesis of catalyst precursor **3**.

The ruthenium based catalyst precursor was prepared by reacting 1,3-dimethylimidazolium iodide **1** with dicarbonyl(η^4 -3,4-bis(4-methoxyphenyl)-2,5-diphenylcyclopenta-2,4-dienone) ruthenium dimer (**2**)²³

(0.5 eq. vs. imidazolium salt **1**). The reaction mixture was stirred at room temperature until the end of the reaction followed by IR spectroscopy. By precipitation with hexane, a yellow solid was obtained in quantitative yield by filtration and identified as [dicarbonyl- η^4 -3,4-bis(4-methoxyphenyl)-2,5-diphenylcyclopenta-2,4-dienone)halogenide][1-3dimethylimidazolium] ruthenium complex **3** by ^1H -NMR, ^{13}C -NMR and ESI-MS. Complex **3** is stable to air, in organic solvents and in the presence of water.

Catalyst characterization

Catalyst precursor **3** was analyzed by IR (Perkin-Elmer Spectrum Two spectrophotometer), ^1H -NMR, ^{13}C -NMR (Varian Inova 600 (^1H , 599.7; ^{13}C , 150.8 MHz) spectrometers at 298 K; chemical shifts were referenced internally to residual solvent peaks), ESI-MS (Waters Micromass ZQ 4000 with samples dissolved in CH_3CN) and elemental analysis (Thermo-Quest Flash 1112 Series EA instrument). ^1H -NMR (599.7 MHz, CDCl_3): δ 9.91 (s, NCHN), 7.58-6.55 (m, 18H, CH_{aryl}), 7.07 (s, 2H, CH_{im}), 3.75 (s, 6H, NCH₃), 3.70 (s, 6H, -OCH₃). ^{13}C -NMR (150.8 MHz, CDCl_3 , g-HSQC, g-HMBC, DEPT): δ 201.00 (CO), 172.12 (C=O, Cp), 158.40 (-COCH₃), 138.96 (NCHN), 135.21-112.66 (C_{aryl}), 122.55 (CH_{im}), 100.09 ($\text{C}_{2,5}$, Cp), 81.40 ($\text{C}_{3,4}$, Cp), 55.01 (-OCH₃), 36.55 (NCH₃). IR (CH_2Cl_2 , cm^{-1}): 2004, 1944 (ν_{CO}); 1580 ($\nu_{\text{C=O}}$), 1604, 1518 ($\nu_{\text{C=C}}$). ESI-MS (m/z) (+): 97 [M]⁺; (-): 729 [M]⁻. Anal. Calcd (%) for $\text{C}_{38}\text{H}_{33}\text{IN}_2\text{O}_5\text{Ru}$: C, 55.28; H, 4.03; N, 3.39. Found: C, 55.26; H, 4.00; N, 3.41.

General procedure for upgrading of ethanol

In a typical catalytic run, an oven-dried 6mL Schlenk bomb fitted with a Teflon plug valve was charged with the ruthenium catalyst **3** (14mg, 0.0172mmol) and the base (sodium ethoxide (NaOEt) or sodium methoxide (NaOMe) or sodium hydroxide (NaOH), 1.72 mmol). Ethanol (0.5mL, 8.6mmol) was added, under inert atmosphere, to the reaction mixture. The reactor was sealed under inert atmosphere and heated at 150 °C, unless otherwise stated, under stirring for the desired reaction time. The microreactor was then cooled with an ice-water bath and subsequently opened (no release of pressurized gas was observed).

1
2
3 The reaction mixture was diluted by 3 mL of Et₂O and 162uL of THF was added as internal standard.
4
5 The resulting solution was analyzed by Agilent Technologies 7890A GC system using a HP-5 capillary
6
7 column Agilent 190915-413 (30 m x 0.35 mm, thickness 0.25 μm) in order to determine the ethanol
8
9 conversion and product yields. Helium was used as carrier gas with a column flow of 0.909mL/min; the
10
11 injector was maintained at a temperature of 230 °C in the split mode (40:1); total flow was 40.25 mL/min.
12
13 The volume of solution injected was 0.5 μL and the method used was: starting oven temperature is 30°C
14
15 (hold for 11 min) then heated to 270 at 30°C/min (hold for 5 min). Calibrations of all alcohols were
16
17 performed by adding the same amount of THF (internal standard) to the different solutions and plotting
18
19 the ratio A_a/A_s vs mol_a keeping constant the moles of standard. This procedure allows to avoid the
20
21 measure of the total reaction volume obtaining the total amount of moles of analyte.
22
23
24
25
26

27 Compounds were also indentified by GC-MS; in particular we used an Agilent Technologies 6890 GC
28
29 coupled with a mass spectrometer Agilent Technologies 5973 equipped with a non-polar column (5%
30
31 Phenyl - 95% methylsiloxane), 30m x 250 μm x 1.05 μm. Helium was used as carrier gas at a flow rate
32
33 in the column equal to 1ml/min; the injector was maintained at a temperature of 250 °C in the split mode
34
35 (50:1); total flow was 23.9 mL/min. The volume of solution injected was 0.5 μL and the standard
36
37 temperature program was the following: isothermal step at 40 °C for seven minutes, then the ramp of 10
38
39 °C/min until reach 250 °C, final isothermal step for 5 minutes.
40
41
42

43 Light compounds were analyzed by sampling the reactor gaseous stream (once cooled at room
44
45 temperature) by means of both GC-MS and a GC equipped with a TCD.
46

47 The GC-MS was the same as for the liquid phase but the method was changed as follow: the volume
48
49 injected was 0.5 mL and the standard temperature program start at 40 °C (maintained for ten minutes),
50
51 then the ramp of 10 °C/min until reach 220 °C, final isothermal step for 2 minutes.
52
53
54
55
56
57
58
59
60

1
2
3 Hydrogen was detected by means of GC analysis, in particular we used an Agilent Technologies 7890
4 equipped with a thermal conductivity detector (TCD) and a CP Mol Sieves 5A column (25m x 0,53 mm
5 x 50 μ m). Nitrogen was used as carrier gas at a flow rate of 12 mL/min; the injector was maintained at a
6 temperature of 150 °C and the TCD at 250 °C. The volume of solution injected was 0.5 mL and the
7 standard temperature program was the following: isothermal step at 35 °C for 3.5 minutes, then the ramp
8 of 5 °C/min until reach 100 °C, final isothermal step for 5 minutes. The injection of pure reference
9 standards allowed the comparison of retention times in the GC column.
10
11
12
13
14
15
16
17

18 19 **Recycle experiment**

20
21 An oven-dried 6mL Schlenk bomb fitted with a Teflon plug valve was charged with the ruthenium
22 catalyst **3** (14mg, 0.0172mmol) and sodium ethoxide (NaOEt, 122mg, 1.72 mmol). Ethanol (0.5mL,
23 8.6mmol) was added under inert atmosphere. The reactor was sealed under inert atmosphere and the
24 resulting reaction mixture heated, under stirring, at 150 °C for 4h. At the end of the catalytic cycle the
25 microreactor was cooled at room temperature and subsequently connected to the vacuum line. The
26 alcohol mixture was evaporated to dryness then, a new portion of EtOH (0.5mL, 8.6mmol) and NaOEt
27 (122mg, 1.72 mmol) were added under inert atmosphere to the solid residue. The mixture was heated
28 again at 150 °C for 4h. At the end of the second cycle the microreactor was cooled with an ice-water bath
29 and subsequently opened (no release of pressurized gas was observed). THF (162 μ L) was added as
30 internal standard and the reaction mixture was diluted by 3 mL of Et₂O. The resulting solution was
31 analyzed by GC to determine the ethanol conversion and product yields.
32
33
34
35
36
37
38
39
40
41
42
43
44
45

46 47 **Larger scale experiments**

48
49 Catalytic reactions were carried out in a 50mL Schlenk bomb with a Teflon plug valve charged with the
50 ruthenium catalyst **3** (0.2%mol, 142mg, 0.172mmol or 0.1%mol, 71mg, 8.6mmol) and sodium ethoxide
51 (NaOEt, 1.22g, 17.2 mmol). Then ethanol (5mL, 86mmol) was added under inert atmosphere. The reactor
52 was sealed under inert atmosphere and the resulting reaction mixture heated, under stirring, at 150 °C for
53
54
55
56
57
58
59
60

1
2
3 4h. After the reaction run time, the reactor was cooled to room temperature in an ice-water bath. The gas
4
5 phase was analysed collecting 0,250 mL in a gas syringe and injecting to a GC-MS equipped with FID
6
7 and TCD detectors. The solution for GC analysis has been prepared diluting the sample in Et₂O and
8
9 maintaining the same standard (THF) concentration. The sample for the analysis of the resting state of
10
11 the catalyst has been obtained cooling down reaction vessel, filtering off NaOAc, removing alcohol under
12
13 vacuum and analyzing the residual solid by ¹H-NMR, IR, ESI-MS (Figure S7-S9).
14
15

16 17 **Process description**

18
19 The catalytic reaction that has been developed during the present investigation is able to convert the
20
21 residual ethanol fraction generated from the winemaking industry (distillation tails and heads), into
22
23 butanol and higher alcohols in a basic environment. The conceptual design takes into account the
24
25 following most relevant aspects:
26

- 27
28 (i) a catalyst is required for the reaction to happen, hence it needs to be recovered and recycled
29
30 within the process, due to its elevated cost and invested quantity;
31
32 (ii) unreacted ethanol can be separated and recycled back to the reaction feed;
33
34 (iii) butanol needs to be isolated as it might be used for downstream valorization, eg, bio-maleic
35
36 anhydride synthesis²⁴
37
38 (iv) higher alcohols generated during the reaction have market potential. The process flow
39
40 diagram will consider their fractionation, with an impact on the heat balance at plant scale;
41
42 (v) sodium acetate (NaOAc) is a by-product which is synthesized together with the main reaction
43
44 products (butanol and higher alcohols); for its separation, cooling is considered a viable
45
46 strategy in order to obtain a solid precipitate both in anhydrous and hydrated form;
47
48 (vi) during precipitation the NaOAc could drag catalyst and reaction products along with it.
49
50 Hence, the sodium acetate-based solid needs to be flushed;
51
52
53
54
55
56
57
58
59
60

- (vii) in order to effectively treat the solid sodium acetate (rich NaOAc), the solvent selected for flushing should solubilize the least quantity of NaOAc itself, simultaneously recovering useful products and catalyst;

The technological solution proposed has been designed in order to embody the previously mentioned points by envisaging three major units: reaction, separation and fractionation. Special attention has been reserved in selecting the washing solvent that needs to flush the solid NaOAc without dissolving it. With this purpose, an analysis in terms of sodium acetate solubility has been carried out, referring to three conventional solvents commonly adopted in process engineering: water, ethers and ethanol. The research highlights high solubility of sodium acetate in water and ethers, leaving ethanol as the favored component for solid washing (solubility: 2,1g NaOAc/100mL – temperature N/A), with beneficial effects in terms of process compactness due to its usage as a reactant in the reaction chamber. In fact, flushing ethanol, as well as unreacted ethanol and eventual excess ethanol, can be recovered from the fractionation unit and recirculated back to the process feed.

The approach followed during the technical assessment of the overall process starts with an initial evaluation of the experimental results, which have been reviewed with the purpose of drafting the atomic and global mass balance. The uncertainty over the experimental output has been defined in terms of mass percent error over the total reactor inlet stream and the same methodology has been applied to the plant scale scenario.

Once the laboratory experimental information has been reviewed and the product yield has been defined, theoretical process upscaling is carried out and the overall material balance is performed. Carbon stoichiometry has been considered when calculating the product yields, hence, the material balance at plant scale. Nonetheless, catalyst and base consumption have been evaluated starting from the experimental data in terms of moles of reagent consumed per mole of ethanol in the reactor feed-stream (e.g.: $\text{moles}_{\text{catalyst}}/\text{moles}_{\text{EtOH}}$, specific consumption). The laboratory shortfall has been redistributed over

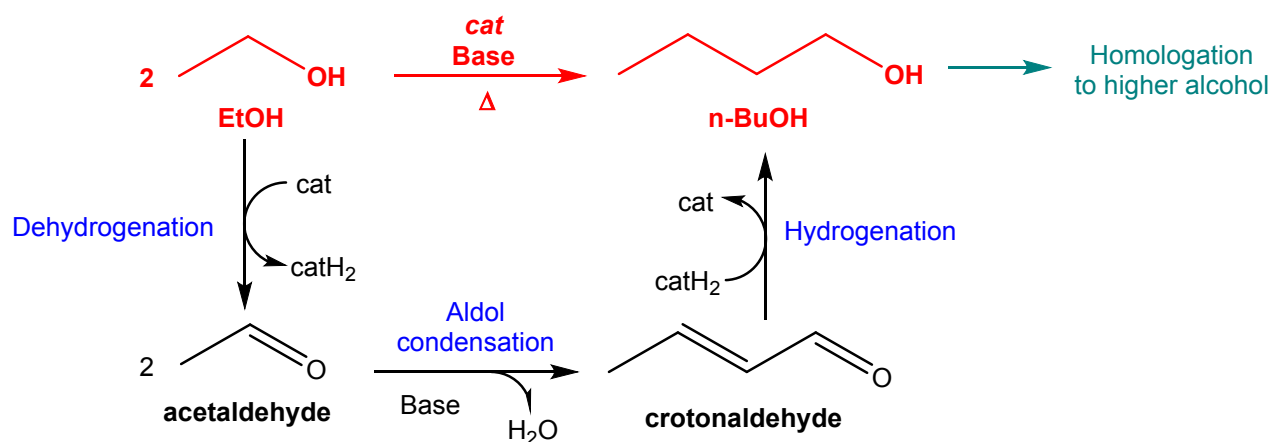
1
2
3 the produced alcohols when defining the mass streams at industrial level thanks to the introduction of a
4 yield amplification factor. The engineering assessment is concluded by defining an early-stage heat
5 balance, which accounts for the major energy consuming units in terms of latent heat, sensible heat and
6 electric power indicatively required, by means of Aspen Plus[®] V9-2016 along with a black-box analysis
7 of the different process units.
8
9

10
11
12 Due to the fact that the experimental campaign has been oriented towards testing the performance of the
13 novel ruthenium-based catalyst by adding sodium hydroxide and sodium ethoxide, the final viability of
14 technological solution has been estimated in both cases by comparing figures of merit such as butanol
15 specific production, alcohols (C4-C10) specific production and energy specific demand.
16
17
18
19
20
21
22
23
24
25

26 **Results and discussion**

27 **Ethanol homologation to higher alcohols promoted by a novel ruthenium based catalyst.**

28
29 The Guerbet mechanism, proposed for homogeneous liquid phase (and most commonly accepted),
30 depicted in Scheme 2 points out that the inherent sustainability of this reaction resides in two principal
31 aspects. Its ability to make null the hydrogen cost, indeed the two equivalents of hydrogen needed in the
32 last step come from the dehydrogenation of ethanol performed by the catalyst in the first step. Moreover,
33 excepting water as the principal by-product the reaction does not need any additional solvent, a good
34 deal for atom economy.
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60



Scheme 2. Proposed mechanism for the Guerbet reaction in homogeneous phase.

On the other hand, the second step of the above mechanism ascribes the C-C bond formation to an aldol condensation step. Although this reaction can be catalysed by both acids and bases, the latter route is generally preferred due to enhanced yields and selectivity toward the desired products. Unfortunately, the base catalysed Cannizzaro reaction can also occur between two acetaldehyde molecules in the presence of water, leading to the formation of one equivalent each of acetic acid and ethanol, in this way the base could be rapidly consumed toward the formation of acetates.

A good catalyst for the transformation of ethanol to saturated higher chain alcohols thus needs to be active in hydrogenation/dehydrogenation and ruthenium cyclopentadienone complexes^{25–28} represent a class of homogenous catalysts, never employed in Guerbet reaction before, which could be good candidates for this reaction. First applying the well known Shvo catalyst²⁵ to ethanol conversion in the presence of a base co-catalyst (entry 1 in Table 1) we obtained very poor results. A conversion of 17% with a dramatic carbon loss of 10% was observed. Similar unsatisfactory results were obtained employing dimer **2** under the same conditions (entry 2).

Thus we synthesized a new catalyst, **3** as previously described in Scheme 1 with a novel ligand combination obtained by treating complex **2**²³ with commercially available imidazolium salt **1**. The reaction is quantitative and complex **3** can be easily purified by precipitation.

The comparison of Ru complex **3** with both Shvo and complex **2** is reported in Table 1. The reactions were performed in ethanol, which acts both as reagent and solvent, in the presence of a basic co-catalyst.

Table 1. Catalysts **Shvo**, **2** and **3** (0,2 mol%) comparison. ^a Basic co-catalyst: NaOEt; ^b Alcohols yield corresponds to the sum of C₄-C₁₀ saturated alcohols.

Entry	Catalyst	Base ^a (mol%)	T (°C)	t (h)	Conv. EtOH (%)	Yield 1- BuOH (C ₄) (%)	Alcohols yield (C ₄ - C ₁₀) (%) ^b	C-loss (%)
1	Shvo	20	150	4	17	4	7	10
2	2	20	150	4	30	8	12	18
3	3	20	150	4	46	32	42	4

As shown in the previous Table, complex **3** shows higher catalytic activity compared to the other Ru complexes, leading to a 46% ethanol conversion toward butanol and higher alcohols with a minor C-loss. This carbon loss can be ascribed to acetaldehyde un-selective decomposition or further conversion to heavy oligomers. It seems clear that depending on the homogeneous complex features, the catalysts have different activity toward de-hydrogenation and hydrogenation, affecting the concentration of acetaldehyde available for side reactions, which increases if de-hydrogenation is favored vs hydrogenation.

After these promising preliminary results, a complete screening of the reaction conditions was performed with catalyst **3** in order to optimize higher alcohols productivity. The catalytic results are summarized in Table 2.

Table 2. Effect of the main reaction parameters (temperature, reaction time and co-catalyst base type) on the conversion and selectivity of the ethanol valorization through the Guerbet reaction. Catalyst: complex **3** (0,2 mol%). Entry 2 was repeated several times to favor comparison of the data. ^a mol% respect to the starting moles of EtOH. ^bAlcohols yield corresponds to the sum of C₄-C₁₀ saturated alcohols.

Entry	Base	Base ^a (mol%)	T (°C)	t (h)	Conv. EtOH (%)	Yield 1- BuOH (C ₄) (%)	Alcohols yield (C ₄ - C ₁₀) (%) ^b	C-loss (%)
1	NaOEt	20	150	0.3	28	16	19	9

2	NaOEt	20	150	4	46	32	42	4
3	NaOEt	20	150	24	63	31	48	15
4	NaOEt	10	150	4	32	19	24	8
2	NaOEt	20	150	4	46	32	42	4
5	NaOEt	40	150	4	75	32	54	21
6	NaOEt	20	80	4	13	<1	<1	>12
7	NaOEt	20	120	4	28	23	26	2
2	NaOEt	20	150	4	46	32	42	4
8	NaOMe	20	150	4	62	25	46	16
9	NaOH	20	150	4	67	26	33	34

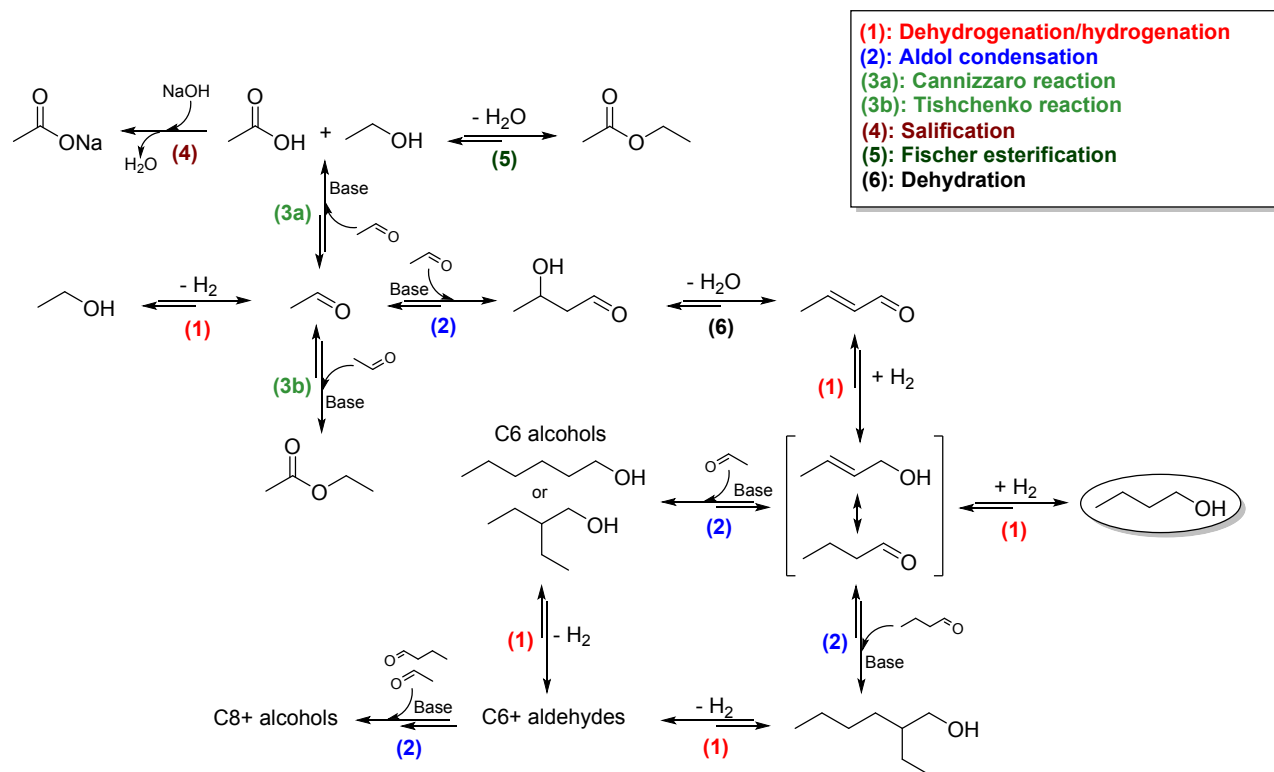
From the results reported in Table 2, the best reaction conditions are as follow (entry 2): a reaction temperature of 150 °C with a reaction time of 4h and NaOEt (20 mol%) as the base co-catalyst allowing for a promising 46% conversion of EtOH with an overall selectivity to higher alcohols of 91%, and selectivity to the main product (*n*-butanol) of 70%, with minor carbon loss (4%). Regarding the turn-over rates a TOF of 317h⁻¹ can be evaluated while considering data in entry 1 (t=20min). Although increasing both reaction time or the amount of base gave a corresponding increase of EtOH conversion and product yields, a consequent increase in the carbon loss due to parasitic oligomerization reactions, drops the selectivity in alcohols from 91 to 76% (entry 3) or to 72% (entry 5). On the other hand, lowering the base percentage (10%, entry 4) leads to minor conversion and a selectivity lower than 80% into the desired products. This could be ascribable to the slowdown of the base-catalyzed aldol condensation step with a consequent non-selective decomposition of the formed acetaldehyde. Moreover, in terms of atom economy the use of a large amount of base in the catalytic mixture actually reduces the efficiency of the system, especially considering that unreacted ethanol can be recovered and recycled. For all these reasons

1
2
3 20 mol% of base was chosen as the best compromise. Quite surprisingly, lowering the temperature (entry
4 6) to 80 °C showed a detrimental effect on the overall process, with almost all the ethanol converted
5
6 wasted in carbon loss. An intermediate temperature 120 °C (entry 7) still gives a lower conversion with
7
8 respect to 150 °C, revealing that the catalyst is already activated toward the Guerbet reaction at this
9
10 temperature.
11
12

13
14 Discussion of the remaining part of Table 2 needs a more detailed analysis of side reactions that can be
15
16 associated with the Guerbet reaction (Scheme 3). Together with dehydrogenation/hydrogenation (1),
17
18 aldol condensation (2) and dehydration (6) which are the main reactions involved in alcohol
19
20 homologation, ethanol and the intermediate acetaldehyde are also prone to undergo 3a, 3b, 4 and 5 side
21
22 reactions. Tishchenko reaction (3b) and Fisher esterification (5) are never observed with catalyst **3** (no
23
24 trace of ethyl acetate was identified in the reaction mixture). On the other hand, Cannizzaro reaction (3a)
25
26 followed by salification (4) represents an Achilles' heel of the reaction, since it consumes the base co-
27
28 catalyst which is transformed into the weak base sodium acetate, as reported for other homogeneous
29
30 Guerbet catalytic mixtures.¹¹⁻¹⁶
31
32

33
34
35 Once the reaction is done we can assume that: if the base co-catalyst employed is NaOEt, it is completely
36
37 transformed in sodium acetate and it can be considered out of the carbon balance,¹¹⁻¹⁶ while if the base
38
39 is NaOH, an equivalent of EtOH is converted to the side product sodium acetate. This base therefore
40
41 gives a contribution to the conversion that can be subtracted from the whole carbon loss and concurrently
42
43 releases an equivalent of water. From a green perspective this can be considered as an *in situ* formation
44
45 of NaOEt from EtOH and NaOH, an easily handled base.
46
47

48
49 Finally, the reaction was performed replacing the base with an acid co-catalyst (20% para *p*-
50
51 toluenesulfonic acid monohydrate) with the aim of avoiding the problems related to the Cannizzaro
52
53 reactions. Under these conditions the catalytic activity of the ruthenium catalyst is quenched and no trace
54
55 of homologated alcohols was detected.
56
57



Scheme 3. Side reactions associated with the Guerbet reaction conditions.

Thus going back to the data analysis in Table 2 we can compare the reaction behavior with respect to different inorganic bases. Conversion, butanol yield, C₄-C₁₀ yield and carbon loss of entry 2,8 and 9 are summarized in Figure 1 for the sake of easy comparison. Replacing NaOEt with NaOMe the reaction leads to a higher conversion but a counterproductive higher carbon loss. It is noteworthy that more odd C number alcohols are detected in this case (see SI, Figure S6) due to methanol that is produced by the acid-base equilibrium between NaOMe and EtOH. Indeed it is rapidly *in-situ* dehydrogenated to formaldehyde (FA). The latter lacks the α -hydrogen required for the aldol condensation but is able to perform a hydroxyalkylation reaction toward the activated position of the products, leading to the formation of odd alcohols and diols. However, FA may also favor the reticulation of the products leading to heavy species undetectable by GC analysis, finally lowering the carbon balance of the overall process. As a result, performing the reaction with NaOH leads to an increased conversion accompanied by an expected increment of the carbon loss (entry 9). Considering that an equivalent of ethanol with respect

to the base (20%) is consumed by the side reaction (3a + 4 in Scheme 3) the carbon loss for the comparison in Figure 1 has been reduced to 14%, still higher with respect to the best conditions obtained with NaOEt (Figure 1). Although water production due to NaOH mediated Cannizzaro reaction seems to be damaging for reaction selectivity to valuable alcohols (70%, considering the above mentioned side reaction assumption), the use of an easily available base is anyway highly desirable.

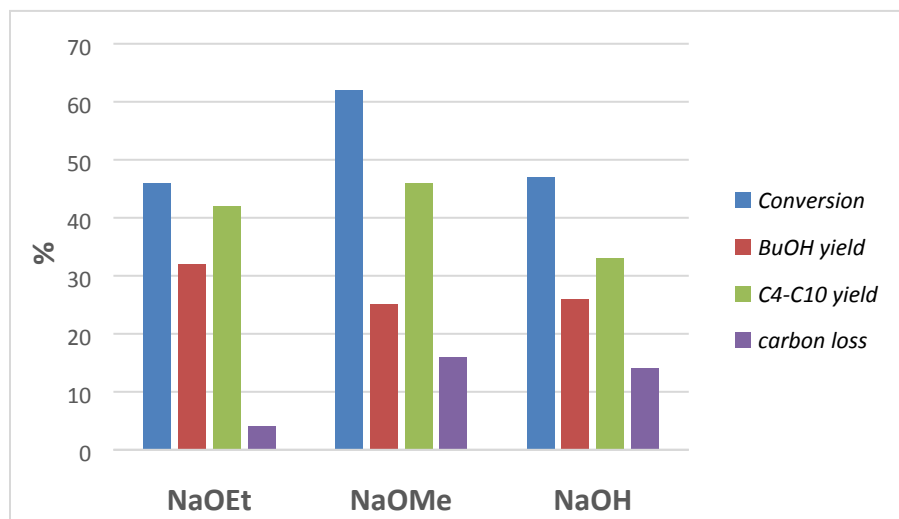


Figure 1. Base screening for the Guerbet reaction promoted by catalyst **3**. Reaction conditions: T = 150°C, autogenous pressure, t = 4h, base = 20 mol%.

A recycle experiment was performed by removing the alcohol mixture at the end of the first cycle under vacuum and adding a new portion of EtOH and NaOEt to the Schlenk bomb to react again under the optimal conditions (150°C for 4 hours). The results (Figure 2) principally demonstrate that catalyst **3** can be recycled keeping a good efficiency. Furthermore, this behavior reinforces the co-catalyst base responsibility in the reaction switch off by means of Cannizzaro reaction. Indeed in the laboratory experiment the alcoholic mixture and residual water have been removed under vacuum, then by adding 20 mol% fresh NaOEt and ethanol to the solid mixture of used catalyst **3** and residual sodium acetate the reaction suddenly restarts. The catalyst **3** does not run out of its activity along the reaction, working with

a TON of 210 within the first cycle, it maintains a similar TON (200) when reused, even though accompanied by a doubled carbon loss and a concurrent partially reduced *n*-butanol yield.

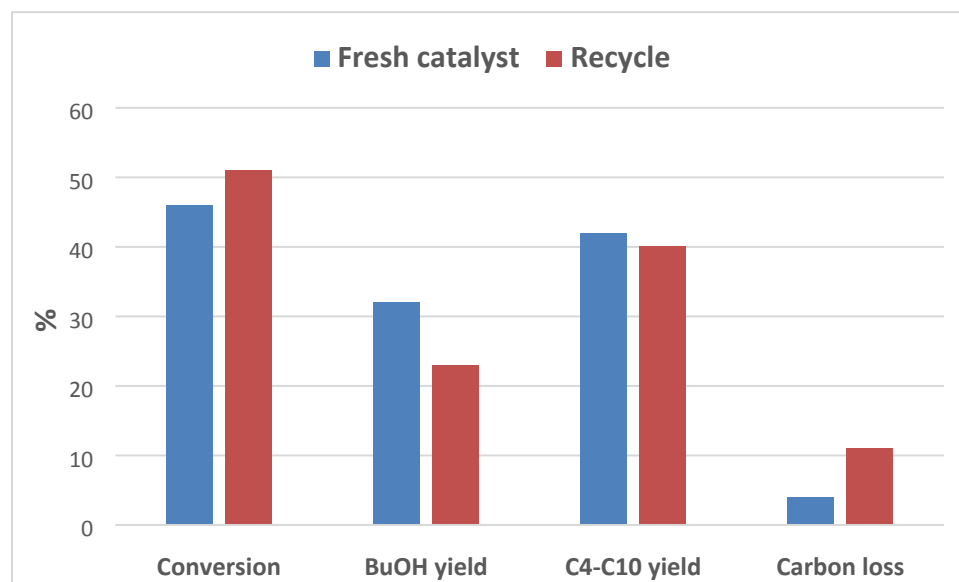


Figure 2. Catalyst **3** recycle. Reaction conditions: T = 150°C, autogenous pressure, t = 4h, base = 20 mol%.

Table 3: Effect of the EtOH starting material on the reaction. ^a EtOH pure: Merck purchaser (code: 24105-1L-M), EtOH CAVIRO: see batch analyses (Figure S1). Catalyst: complex **3** (0,2 mol%). Co-catalyst: NaOEt, 20 mol% respect to EtOH. ^b Alcohols yield corresponds to the sum of C₄-C₁₀ saturated alcohols. ^c EtOH pure from Merck with 5% of water.

Entry	EtOH	T (°C)	t (h)	Conv. EtOH (%)	Yield 1-BuOH (C ₄) (%)	Alcohols yield (C ₄ -C ₁₀) (%) ^b	C-loss (%)
1	EtOH	150	4	46	32	42	4
2	EtOH 95% ^c	150	4	48	29	39	9
3	CAVIRO absolute	150	4	56	33	45	11
4	CAVIRO 95%	150	4	50	25	33	17
5	CAVIRO X	150	4	39	26	28*	11

* Sum of even alcohols.

1
2
3 Table 3 shows that the catalytic mixture can be employed on a real EtOH mixture. Three samples from
4 the Caviro distillery were tested. The first one, being absolute alcohol shows yield in alcohols comparable
5 to pure EtOH supplied by Merck, while in the case of CAVIRO 95% sample (entry 4) a slightly worse,
6 but still satisfactory behavior, is observed probably due to water that affects conversion and inert by-
7 products which increase the carbon loss. Indeed the control experiment (entry 2) in which 5% of water
8 was added to the pure alcohol is in line with the behavior in the real EtOH mixture except for a reduced
9 carbon loss. It is important to underline that in the CAVIRO 95% case several by-products are present in
10 the distillation mixture (see Figure S1 for further details) that make useless alcohol for food purposes.
11 Their role in the bio-refinery process here described not only does not affect the catalytic mixture
12 reactivity that much, but indeed, as in the case of aldehydes, they take part in mixture valorization being
13 intermediate in the Guerbet reaction. Finally the reaction has been performed in a more complex mixture
14 (CAVIRO X; 47% in EtOH) containing a substantial amount of methanol and ethylacetate (entry 5, see
15 Figure S2). In this latter case the conversion has been evaluated only from ethanol to even alcohols. Even
16 though it looks negatively influenced by the matrix the result obtained confirms that the activity of
17 catalyst **3** is maintained even under much more complicated conditions.

37 **Larger scale tests**

38
39 In order to acquire preliminary indications, larger scale tests in 5mL of ethanol (50 mL schlenk bomb)
40 have been carried out and compared with results obtained in the smaller Schlenk bomb as reported in
41 Table 4.
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 4: Effect of the larger scale and of the lower catalyst loading. Reaction conditions: EtOH pure: Merck purchaser (code: 24105-1L-M). Co-catalyst: NaOEt, 20 mol% respect to EtOH. T = 150 °C, t = 4h, autogenous pressure. ^aAlcohols yield corresponds to the sum of C₄-C₁₀ saturated alcohols.

Entry	Cat(mol%)	V _{EtOH} (mL)	Conv. EtOH (%)	Yield 1-BuOH (C ₄) (%)	Alcohols yield (C ₄ -C ₁₀) (%) ^a	C-loss (%)
1	0.2	0.5	46	32	42	4
2	0.2	5	60	32	50	10
3	0.02	0.5	33	15	22	11
4	0.02	5	31	5	8	23

Performing the reaction under the same conditions as the better results obtained in 0,5 mL (entry 1) in an ethanol volume of 5 mL (entry 2), comparable *n*-butanol yield is observed concurrently with an increase of higher alcohol yields. Quite surprisingly, an overpressure has been registered. Analyzing the gas phase by GC-MS and GC-TCD both acetaldehyde and hydrogen can be identified as part of the carbon loss growth, together with the contribution of insoluble oligomers. This reaction mixture was further analyzed: by cooling the vessel at 0°C all the NaOAc was precipitated and filtered off. Once removed the alcohols from the remaining solution, the catalyst resting state was characterized by ¹H-NMR, IR, and ESI-MS techniques. Two principal set of signals reveal the presence of pre-catalyst **3** and of another similar species with analogue NMR pattern (Figure S7) and IR stretching in the terminal CO region (Figure S8). From the ESI-MS spectrum in negative ion (Figure 9), together with the molecular ion of **3** at 729 m/z, it arose a novel species at 646 m/z which could be attributed to a complex in which iodide ligand from **3** is likely substituted by an ethoxy anion. For both the complexes the peak deriving from the CO loss (701 m/z for **3** and 618 m/z for the second species) is also observed.

Lowering the catalyst loading from 0,2 mol% to 0,02 mol% in 0,5 mL EtOH (entry 1 vs entry 3), although a decrease in the overall conversion and yields and an increase of the carbon loss, the catalyst still

maintain a fair efficiency. Even in the latter case a small overpressure has been registered qualitatively revealing hydrogen and acetaldehyde in the gas phase. Finally comparing the catalyst loading (0,2 mol% to 0,02 mol%) in the reaction performed in 5mL of ethanol (entry 2 vs entry 4) a detrimental effect is observed both in yields and carbon loss. As a general consideration the reported preliminary results on the enlargement of the reaction scale are promising in view of a future scale-up (entry 2), on the other hand the reaction behavior with a lower catalyst loading (entry 4) looks to be more affected by the fluid-dynamic of the reactor, limiting the catalyst efficiency in the hydrogenation of the aldol (or other key intermediates) finally favoring the oligomerisation to heavier byproducts.

Technology assessment

Laboratory test results reported for base co-catalysts NaOH (entry 9 in Table 2) and NaOEt (entry 2 in Table 2) have been selected as starting points for process design. Preliminarily to the definition of a suitable block flow diagram, the mass balance has been written and the process has been theoretically up-scaled based on an ethanol load of 1000 kg in batch operation mode.

With reference to the experimental results, the error over the mass balance and the experimental shortfall has been corrected when defining the plant scale scenario via a yield amplification factor applied to the produced alcohols. The outcome is reported in Table 5 and Table 6. This approach provides a closed mass balance needed for subsequent evaluations and representative of a full-size reactor.

Table 5. Mass balance for the base co-catalyst NaOH. Reaction conditions: catalyst **3** (0.2%), T = 150°C, t = 4h, P = autogeneous, NaOH = 20%.

Scale-up parameter: Mass of EtOH [kg]		LAB SCALE				PLANT SCALE		MASS BALANCE [kg]	
Yield Factor [-]						INLET	OUTLET	INLET	OUTLET
		FORMULA	MW	Product Yield	Specific Consumption	Conversion			
		-	kg/kmol	%	kmol/kmol_EtOH(in)	%	kmol	kmol	
	1000								
	1,18								
EtOH		C2H6O	46,07	-	-	66%	21,71	7,32	1000,00 337,35
Catalyst		3	826,00	-	0,002	-	0,04	0,04	35,86 35,86
NaOH		NaOH	40,00	-	0,2	-	4,34	0,00	173,64 0,00
BuOH		C4H10O	74,10	31,28%	-	-	-	3,39	- 251,53

C5	C5H12O	88,15	0,71%	-	-	-	0,06	-	5,44
C6	C6H14O	102,10	6,40%	-	-	-	0,46	-	47,26
C6/7 as C7	C7H16O	116,00	0,33%	-	-	-	0,02	-	2,40
C8	C8H18O	130,23	0,63%	-	-	-	0,03	-	4,42
C8+ as C8	C8H18O	130,23	0,45%	-	-	-	0,02	-	3,22
NaOAc	C2H3NaO2	82,03	20,00%	-	-	-	4,34	-	356,13
Water	H2O	18,00	-	-	-	-	8,00	-	144,00
								1209,49	1187,61
								DELTA MASS [kg]	21,89
								ERROR [kg/kg]	2%

Table 6. Mass balance for the base co-catalyst NaOEt. Reaction conditions: catalyst **3** (0.2%), T = 150°C, t = 4h, P = autogeneous, NaOEt = 20%.

Scale-up parameter: Mass of EtOH [kg]		1000		LAB SCALE			PLANT SCALE		MASS BALANCE [kg]	
Yield Factor [-]		1,06								
	FORMULA	MW	Product Yield	Specific Consumption	Conversion	INLET	OUTLET	INLET	OUTLET	
	-	kg/kmol	%	kmol/kmol_EtOH(in)	%	kmol	kmol			
EtOH	C2H6O	46,07	-	-	46%	21,71	11,77	1000,00	542,17	
Catalyst	3	826,00	-	0,002	-	0,04	0,04	35,86	35,86	
EtONa	C2H5ONa	68,05	-	0,2	-	4,34	0,00	295,42	0,00	
BuOH	C4H10O	74,10	33,20%	-	-	-	3,60	-	267,04	
C5	C5H12O	88,15	0,83%	-	-	-	0,07	-	6,35	
C6	C6H14O	102,10	8,05%	-	-	-	0,58	-	59,44	
C6/7 as C7	C7H16O	116,00	0,35%	-	-	-	0,02	-	2,51	
C8	C8H18O	130,23	1,17%	-	-	-	0,06	-	8,30	
C8+ as C8	C8H18O	130,23	0,88%	-	-	-	0,05	-	6,21	
NaOAc	C2H3NaO2	82,03	20,00%	-	-	-	4,34	-	356,13	
Water	H2O	18,00	-	-	-	-	0,90	-	16,20	
								1331,28	1300,20	
								DELTA MASS [kg]	31,07	
								ERROR [kg/kg]	2%	

In case of base co-catalyst NaOH, an 18% correction (yield amplification factor 1.18 [-]) over the molar yields has been applied in order to compensate for the higher shortfall recorded by the experimental data.

In addition to this, water concentration has been adjusted to close the oxygen balance with a residual

global 2% mass error. When NaOEt is added, the limited shortfall from the laboratory information requires a lower correction (6% amplification – 1.06 [-] yield factor) to deliver the same uncertainty (2% mass error) on the full-scale material balance.

The operation of the reactor can be envisaged in three sequential phases, namely “feeding + cooling”, “flushing + scarping” and “flushing + stirring”, which are described in detail in the paragraphs below.

For the process to be held, a separation section and a fractionation unit are necessary in addition to the reactor. Under the perspective of a semi-batch operation, multiple reactors are required to guarantee an almost continuous feeding of the separation and fractionation units. This would bring higher productivity and possibly lower production costs.

Phase 1: feeding + cooling. In this phase, the reactants are loaded into the reactor, they are heated up to 150 °C, they are kept under stirring while reacting, and they are cooled down once the reaction is completed (4h as from the best case previously selected).

During cooling, NaOAc precipitates towards the reactor walls, dragging useful products and catalyst within the solid phase; the remaining liquid phase is unloaded (Rich Stream-Figure 3) and enters the separation unit where it is heated up to evaporate most of the alcohols that are directed towards a distillation column. At the same time, the remaining catalyst-rich stream is subjected to an additional thermal treatment before being recovered. Phase 1 is represented in Figure 3.

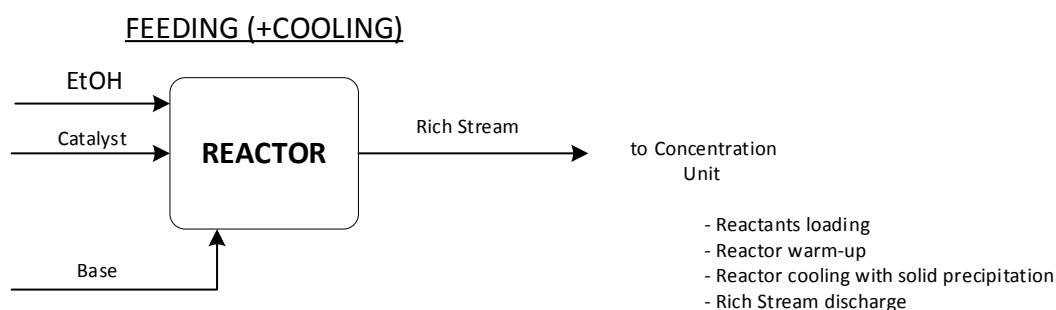


Figure 3. Reactor management in Phase 1: after reactants loading and heating the reaction happens and the reaction chamber is cooled down to allow solid precipitation.

Phase 2: flushing + scraping. At the end of Phase 1, the reactor still contains the solid product, which is rich in alcohols and catalyst. In this phase, a first washing with ethanol is carried out, aiming at recovering such valuable compounds. A scraping-stirrer is moving the rich sodium acetate, exposing it to the flushing process. 300 kg of solvent for this first cleaning step have been assumed, creating a slurry that is separated into a liquid and a solid fraction through filtering (Figure 4). The liquid fraction is sent to the separation unit, undergoing the same treatment as from the Rich Stream of Phase 1, meanwhile the solid fraction is recycled back to the reactor for Phase 3.

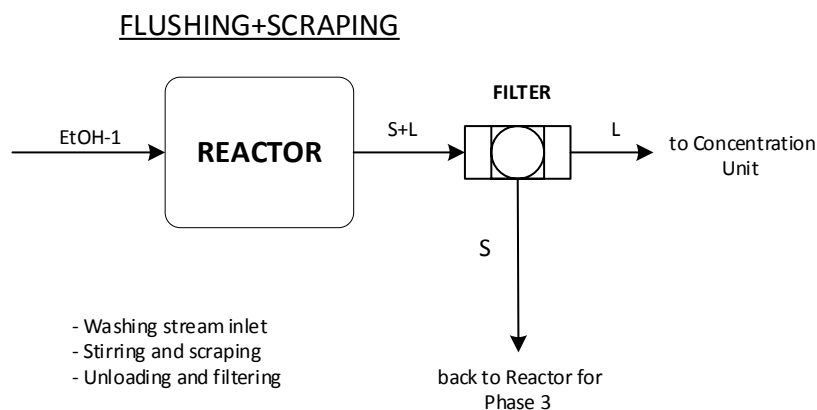
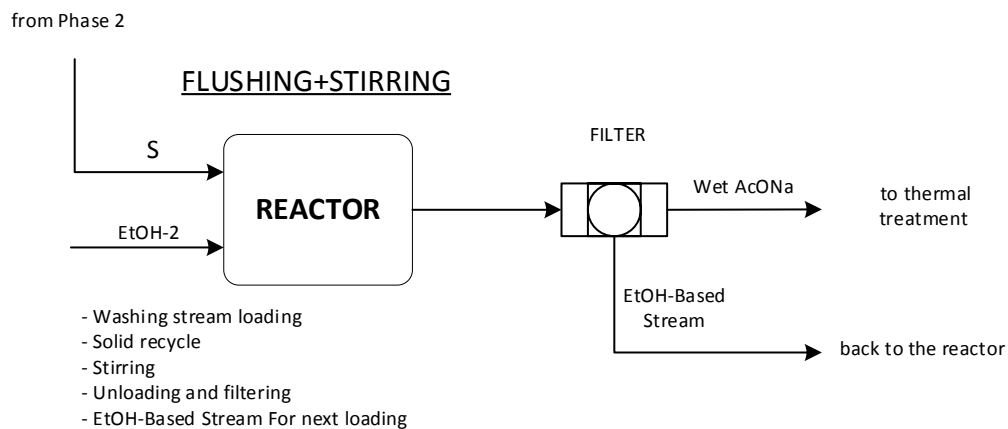


Figure 4. Washing + reactor scraping step (Phase 2) for a better recovery of catalyst and reaction products.

Phase 3: flushing + scraping. Further washing of the reactor under stirring is carried out with 100 kg of ethanol, producing a slurry that is newly filtered to be split into liquid and solid fractions (Phase 3, Figure 5). The liquid fraction, mostly ethanol, is available for the next loading of the reactor. The solid fraction is thermally treated to remove the last alcoholic traces (sent to the fractionation unit) and produce clean NaOAc.



18 **Figure 5.** Reactor during Phase 3. The solid (mainly AcONa) is washed and the ethanol stream is
19 recovered as reactant for a new batch
20
21

22 A comprehensive block flow diagram representing the three phases mentioned above is proposed in
23 Figure 6 where heating, concentration and distillation units are also included.
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

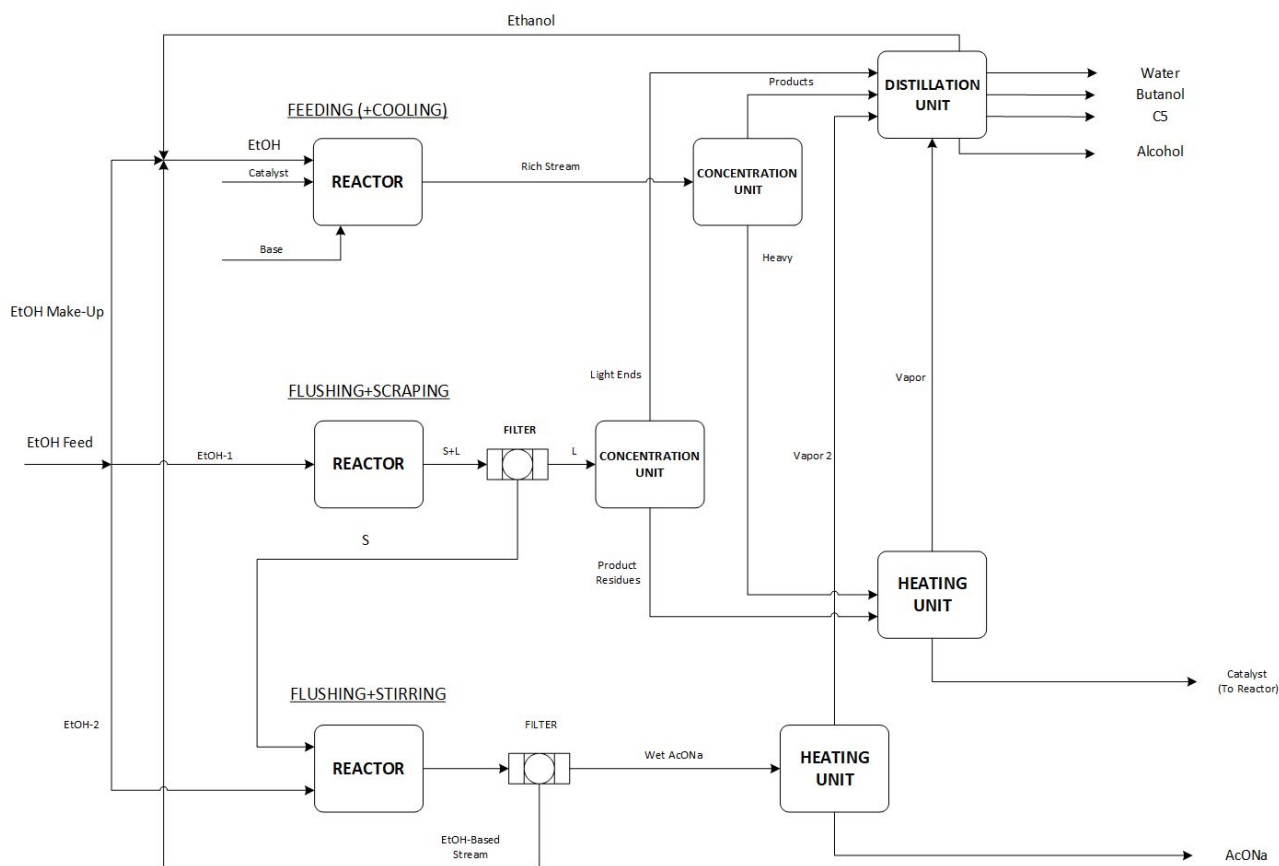


Figure 6. Block flow diagram for the catalytic transformation of EtOH in higher alcohols process. Plant scale process sizing based on $1000 \text{ kg}_{\text{EtOH}}$ reactor load.

Assuming that the reactor material balance at industrial scale is sufficiently representative of the overall process, the global mass balance has been outlined. Particular attention has been given to the recovery and consequent recirculation of ethanol and catalyst employed during batch production at regime; in fact, the global mass balance also accounts for the unreacted ethanol and the washing ethanol separated during the different steps of the process, either via distillation or filtering. It is important to stress that, given the early stage of the investigation, ideal separation and complete catalyst and ethanol recovery have been considered.

A black box analysis of the butanol production process, together with a mass balance over the inlet and outlet ethanol streams have been carried out to estimate the amount of fresh ethanol feed (stream *EtOH*

feed from Figure 6). The results have been used to evaluate the specific butanol and alcohol production and they are reported in Table 7.

Table 7. Global ethanol and alcohols balance, principal figures of merit.

Stream (from Fig. 6)	Description	Flow Rate [kg]	
		Base: NaOH	Base: NaOEt
EtOH-1	Washing ethanol n.1	300,00	300,00
EtOH-2	Washing ethanol n.2	100,00	100,00
Rich Stream-EtOH	Unconverted ethanol in Rich Stream	337,35	542,17
EtOH Make-Up	Makeup ethanol	262,65	57,83
EtOH Feed	Total inlet ethanol: Washing+Feed	662,65	457,83
Total BuOH	Total BuOH produced	251,53	267,04
Total C4-C10	Total Alcohols produced	314,27	349,85
Catalyst		35,86	35,86
Base		173,64	295,42

Figure of Merit	Description	Base: NaOH	Base: NaOEt
		[%]	
Specific BuOH Production	kgBuOH/kgEtOH Tot. Input	37,96%	58,33%
Specific C4+ Production	kgAlcohols/kgEtOH Tot. Input	47,43%	76,41%

Since the washing streams are constant and equal to 300 kg for washing n.1 and 100 kg for washing n.2, the lower conversion attained when NaOEt is employed as a base for the catalytic process implies a higher ethanol stream separated from the distillation unit. This last one is used for the next batch load of the reactor, sensitively reducing the fresh ethanol makeup to be added. Hence, the consumed ethanol is equal to the fresh ethanol reintegrated into the system, higher in case of NaOH. Additionally, lower butanol and total alcohol production are envisaged when NaOH is employed, with the consequence of a lower specific production of alcohols (alcohols produced over ethanol inlet in mass terms) compared to the case with sodium ethoxide. The same behavior is seen when considering the produced butanol

1
2
3 compared to the reacted ethanol (specific butanol production). Given the higher specific butanol and
4 alcohol production, the NaOEt base co-catalyst process seems to be more performing.
5

6
7 Based on the process mass balance, the preliminary plant energy demand has been delivered with the
8 support of Aspen Plus® V9-2016; the simulator has been adopted as a database for the evaluation of
9 sensible and latent heat of the mixture. The starting idea is to calculate the energy demand for distillation
10 by estimating the duty required to vaporizing the alcoholic mixture (reference to Rich Stream – Figure
11 6). In fact, regardless of the splitting and the separation efficiency of the liquid products, they all need to
12 be vaporized and directed to the fractionation unit.
13
14
15
16
17
18
19
20

21 With reference to Table 7, an initial heat duty is required for reagents heating up to 150 °C in order to
22 reach best reaction conditions (reaction unit total heat duty based on alcohols heating). This early-stage
23 evaluation does not account for the heat of reaction since, from preliminary estimations, it is of the order
24 of 1/1000 of the specific heat duty for butanol production.
25
26
27
28
29

30 As already described, the reaction products need to be cooled down for sodium acetate solidification, and
31 successively heated up all over the different pieces of equipment of the separation unit. These last two
32 energy contributions have been considered complementary in a future view of thermal integration
33 through a thermal vector (e.g.: diathermic oil), consequently they do not affect the net plant energy
34 demand. Given the novelty of the process, more details on the energy integration strategy are postponed
35 to further stages of process design.
36
37
38
39
40
41
42
43

44 The last unit is the fractionation section where heating and cooling duty have been estimated by
45 considering a reflux ratio of 1.5 [-] for the distillation columns. The overall cooling duty mainly accounts
46 for the energy demand of the condenser in the fractionation unit, and it has been reported in Table 8 as
47 equivalent electric duty (2% of the total cooling duty). Additional power consumption has been added to
48 the overall plant energy balance for the auxiliaries (e.g.: pumps); the latter has been estimated as 10% of
49 the net heat duty.
50
51
52
53
54
55
56
57
58
59
60

Table 8. Energy Balance

Heat Duty Evaluation	Base: NaOH	Base: NaOEt	Unit
Reaction Unit Total Heat Duty (Reactor Warm-Up)	1130,16	1130,16	MJ
Heat Duty Product Vaporization	1.056,63	973,00	MJ
Heat Duty Washing n.1	303,26	303,26	MJ
Separation Unit Total Heat Duty	1.359,89	1.276,26	MJ
Fractionation Unit Total Heat Duty	2.039,84	1.914,39	MJ
Consumption Summary			
Heat Duty Separation+Fractionation (R=1.5)	3.399,74	3.190,65	MJ
Net Plant Heat Duty	3.170,00	3.044,55	MJ
Total BuOH	251,53	267,04	kg
Total C4-C10	314,27	349,85	kg
Specific heat duty for BuOH	12,60	11,40	MJ/kg_{BuOH}
Specific heat duty for Alcohols	10,09	8,70	MJ/kg_{C4-C10}
Cooling Duty	2.039,84	1.914,39	MJ
Equivalent Cooling Electric Consumption (accounting for removed thermal duty)	40,80	38,29	MJele
Auxiliaries	317,00	304,45	MJele
Total Electric Consumption	357,80	342,74	MJele
Specific Electric Consumption-BuOH	1,42	1,28	Mjele/kg_{BuOH}
Specific Electric Consumption-Alcohols	1,14	0,98	Mjele/kg_{C4-C10}

Although the proposed energy balance is preliminary and based on strong assumptions, it still gives useful insights. In fact, it allows for calculating the process energy requirement per unit product, which is similar for the two bases. Indeed, the higher alcohols production recorded in case of NaOEt base co-catalyst is associated with a lower overall heat duty. Nevertheless, the two process energy requirements per unit product fall within 15% variation. Due to the fact that calculation accuracy is comparable to the variation in the energy outcomes, further evaluations of the process design, together with the adoption of a thermal integration strategy and a better understanding of the distillation unit-energy balance are

1
2
3 necessary before proceeding with a techno-economic assessment, which will deliver a final picture of
4
5 process impact and competitiveness. Moreover, additional experimental activity could also bring positive
6
7 impacts in estimating the mass and energy balance, with shortfall reduction and more accurate atomic
8
9 balance closure that would avoid the introduction of a yield amplification factor.
10
11
12
13

14 **Life cycle assessment**

15
16 Life cycle assessment (LCA) methodology is a standardized approach based on the standard ISO 14040
17
18 series,^{29, 30} used to support design of innovative products and systems. Recent studies have been
19
20 published, regarding the chemical sector, where LCA has been applied to compare conventional
21
22 processes with innovative ones, bio-based or applying principles of Green Chemistry.³¹⁻³³ In the study of
23
24 bio-based chemicals, it is exploited to support decision making and marketing procedures. In fact,
25
26 through a life cycle analysis it is possible to identify environmental criticalities of the innovative reactions
27
28 and to propose valuable alternatives to the traditional routes. For this purpose, generally a cradle-to-gate
29
30 perspective is used, in order to include in the model all the flows from raw material extraction up to the
31
32 synthesis of the chemical.
33
34
35

36
37 Our study is focused on the conversion of waste ethanol coming from distillation heads and tails, and its
38
39 valorization by means of suitable catalysts and reaction conditions for butanol and higher alcohols
40
41 synthesis.
42
43

44
45 This alternative process has been compared, in terms of environmental impact, using SimaPro 8
46
47 (v.8.0.5.13) software and Ecoinvent database.³⁴
48

49
50 For the realization of the scenario of butanol and higher alcohols production from ethanol, all the mass
51
52 and energy flows taken into account for the reaction balances have been calculated by considering the
53
54 synthesis of 1kg of butanol, taken as functional unit (Table 9, 10), comparing two different scenarios:

55
56 - bio-based Butanol production from EtOH, with NaOH;
57
58
59
60

1
2
3 - bio-based Butanol production from EtOH, with NaOEt.
4

5 Since the detailed flows related to catalyst production are unknown, its production has been modeled
6 through the use of the FineChem software tool,³⁵ developed by the ETH Zürich, which allows the
7 estimation of resources consumption and environmental impact based on its molecular structure. The
8 quantity of ruthenium used per unit of catalyst has been added as input of resource.
9

10 Moreover, the co-products of the reaction have been considered as an avoided production of
11 hydrocarbons.
12

13 In collaboration with LEAP research center, an estimation of the energy consumption necessary for the
14 process at industrial scale has been included in the model.
15

16 The environmental impact of the scenarios modelled has been assessed with the use of the
17 IMPACT2002+ analysis method,³⁶ through the expression of the results in terms of damage to climate
18 change, resources, ecosystem quality and human health (Table 11, 12 – Figure 7, 8).
19

20 Preliminary results show a critical issue related to the efficiency of the catalyst, with the necessity of re-
21 using it for many cycles to obtain a relevant environmental advantage.
22

23 The process at laboratory scale that shows the lowest environmental impact results from the use of NaOH;
24 this is mostly due to the lower impact of this chemical compared with NaOEt used in the second route.
25 However, for the reaction with NaOH the results show a high impact for the climate change damage
26 category; at this level no energy recovery for the management of the residues at the end of the reaction
27 has been considered, so it has been taken into account that the non-exploitable products are burned at the
28 end of the reaction with a consequent high amount of carbon dioxide emission (for the reaction that uses
29 NaOH equal to 4.07 kgCO₂/kgBuOH produced).
30

31 Moreover, future endeavors in improving the global process efficiency (reaction yield, catalyst recovery
32 rate, valorization of the co-products), would have positive results related to a lower total impact of the
33 proposed technology.
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 9. Cradle-to-Gate Inventory for the Production of 1 kg of Biobased Butanol from EtOH, reaction with NaOH.

Inventory flow	unit	amount
Input		
NaOH	kg	0.82
Ruthenium	kg	0.15E-01
Output: Avoided Products		
Hydrocarbons	m ³	3.05E-04
Output: Air Emissions		
CO ₂ from catalyst production	kg	2.50
CO ₂ from combustion of residues	kg	4.07
Output: solid residue		
NaOAc	kg	1.69
Output: Water Emissions		
Reaction water	L	1.22
Industrial scale up: energy input		
Specific heat duty	MJ	12.60
Total Electric Consumption	MJ	1.4

Table 10. Cradle-to-Gate Inventory for the Production of 1 kg of Biobased Butanol from EtOH, reaction with NaOEt.

Inventory flow	unit	amount
Input		
NaOEt	kg	1.17
Ruthenium	kg	0.15E-01
Output: Avoided Products		
Hydrocarbons	m ³	3.79E-04
Output: Air Emissions		
CO ₂ from catalyst production	kg	2.50
CO ₂ from combustion of residues	kg	0.26

Output: solid residue		
NaOAc	kg	1.43
Industrial scale up: energy input		
Specific heat duty	MJ	11.4
Total Electric Consumption	MJ	1.28

Table 11. Results from Cradle-to-Gate Analysis in Terms of Characterization Factors per Each Impact Category, lab scale.

Impact category	Unit	Biobased Butanol from EtOH, with NaOH	Biobased Butanol from EtOH, with NaOEt
Carcinogens	kg C ₂ H ₃ Cl eq	0.0174	0.0965
Non-carcinogens	kg C ₂ H ₃ Cl eq	0.022	0.0377
Respiratory inorganics	kg PM _{2.5} eq	0.0018	0.00261
Ionizing radiation	Bq C-14 eq	11	22
Ozone layer depletion	kg CFC-11 eq	5.15E-07	4.85E-07
Respiratory organics	kg C ₂ H ₄ eq	0.000103	0.00253
Aquatic ecotoxicity	kg TEG water	23	62
Terrestrial ecotoxicity	kg TEG soil	22	38
Terrestrial acid/nutri	kg SO ₂ eq	0.0202	0.0365
Land occupation	m ² org.arable	0.0132	0.0281
Aquatic acidification	kg SO ₂ eq	0.00464	0.00935
Aquatic eutrophication	kg PO ₄ P-lim	0.000325	0.00169
Global warming	kg CO ₂ eq	9	6
Non-renewable energy	MJ primary	30	74
Mineral extraction	MJ surplus	0.0542	0.151

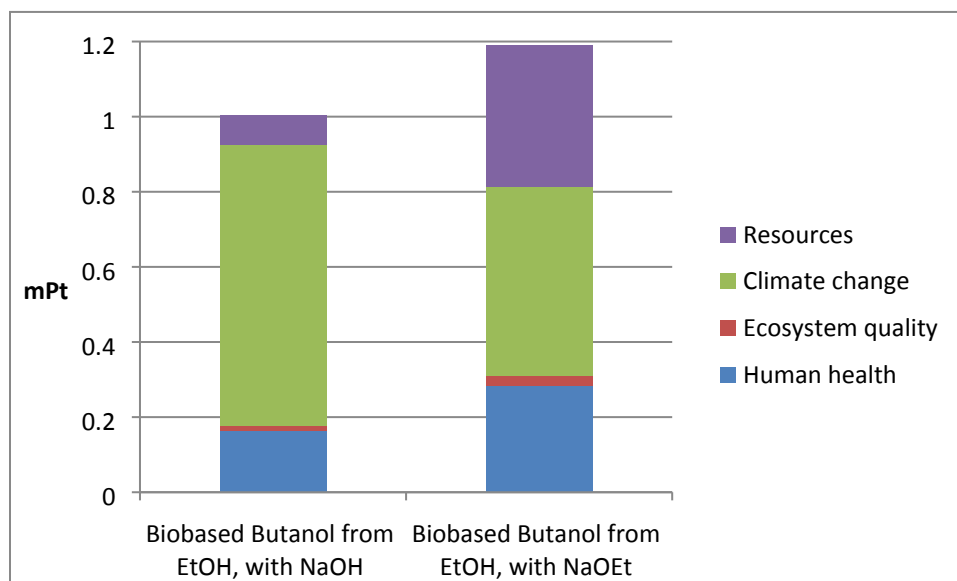


Figure 7. Single score of the two alternative routes, in terms of single score (i.e., cumulative impact), lab scale.

Table 12. Results from Cradle-to-Gate Analysis in Terms of Characterization Factors per Each Impact Category, industrial scale up.

Impact category	unit	Biobased Butanol from EtOH, with NaOH	Biobased Butanol from EtOH, with NaOEt
Carcinogens	kg C ₂ H ₃ Cl eq	0.00883	0.0887
Non-carcinogens	kg C ₂ H ₃ Cl eq	0.0209	0.0367
Respiratory inorganics	kg PM _{2.5} eq	0.00154	0.00237
Ionizing radiation	Bq C-14 eq	10	21
Ozone layer depletion	kg CFC-11 eq	3.69E-07	3.52E-07
Respiratory organics	kg C ₂ H ₄ eq	-9.86E-05	0.00234
Aquatic ecotoxicity	kg TEG water	6	47
Terrestrial ecotoxicity	kg TEG soil	17	34
Terrestrial acid/nutri	kg SO ₂ eq	0.0132	0.0302
Land occupation	m ² org.arable	0.0123	0.0273
Aquatic acidification	kg SO ₂ eq	0.00278	0.00767
Aquatic eutrophication	kg PO ₄ P-lim	2.93E-04	0.00166
Global warming	kg CO ₂ eq	7	5
Non-renewable energy	MJ primary	12	57
Mineral extraction	MJ surplus	0.0515	0.148

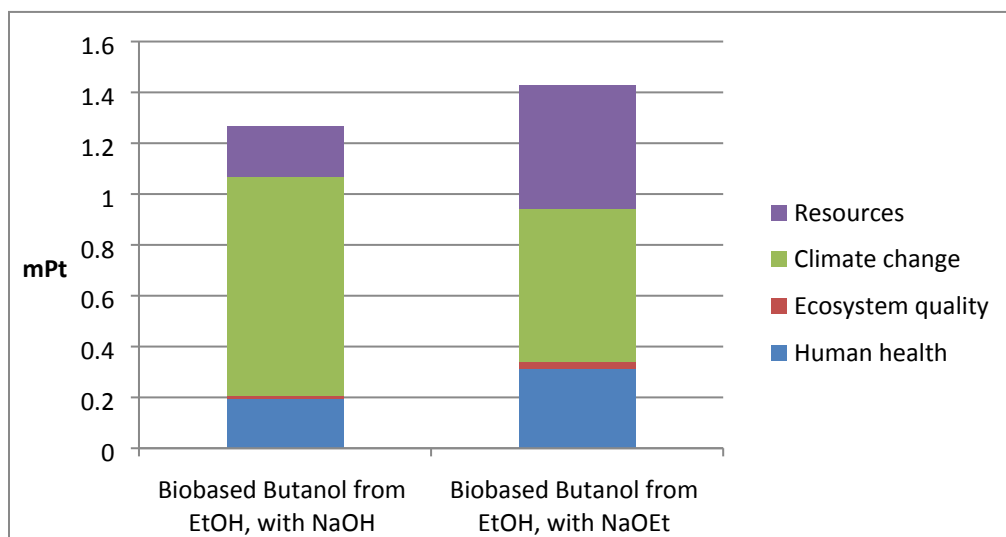


Figure 8. Single score of the two alternative routes, in terms of single score (i.e., cumulative impact), industrial scale up.

Conclusion

A new ionic catalyst combining ruthenium, a non-innocent ligand such as cyclopentadienone and an iodide and containing an imidazolium cation as the counterion was demonstrated to be active in the homologation of ethanol to higher alcohols. Catalyst **3** has been found to have an activity comparable to ruthenium bi-functional catalysts reported in the literature and to be much more active than congeners available from the literature such as **Shvo** and **2** never employed in the Guerbet reaction before.

The reaction screening showed that the base co-catalyst is compulsory in order to activate the catalyst and best reaction conditions were 4 h at 150°C, autogenous pressure and 20% of NaOEt as the base co-catalyst. The reaction requires no additional solvent and performs well both in pure ethanol and in ethanol from wine wastes (CAVIRO distillery). Under the above described conditions an ethanol conversion of 46% is achieved with a selectivity to the main product (*n*-butanol) of 70%, a total sum of selectivity to higher alcohols of 91% and a minor 4% carbon loss. A detrimental effect has been found at lower temperatures and changing reaction time in both directions (20 min-24h). The reaction, performed in a batch mode, is always affected by the Cannizzaro reaction which causes base co-catalyst consumption

1
2
3 toward the formation of sodium acetate. Nevertheless, ruthenium catalyst **3** can be recycled by adding
4
5 new ethanol and base. A slight decrease in efficiency has been observed employing different bases such
6
7 as NaOMe or NaOH. With sodium hydroxide, the increment in carbon loss could be balanced by its high
8
9 availability and ease of handling, thus making the latter base a good candidate for the reaction. Indeed,
10
11 both reaction configurations with NaOEt and NaOH as base co-catalysts have been analyzed by
12
13 technology and life cycle assessments. Preliminary results on reaction scale enlargement show that
14
15 technology and life cycle assessments. Preliminary results on reaction scale enlargement show that
16
17 upscaling the reaction ten times give promising conversion and alcohol yields. With reference to the
18
19 industrialization study, significant assumptions have been made (e.g.: yield amplification factor,
20
21 generated water correction) in order to redistribute the experimental shortfall over the already identified
22
23 products before proceeding with the energy balance. Nevertheless, the early-stage outcome is sufficiently
24
25 representative of the industrial-scale process. It shows higher alcohols production per kg of processed
26
27 ethanol than that obtained from laboratory. Roughly 58% of the ethanol total input is converted into
28
29 butanol [mass base] in case of NaOEt versus only ~37% [mass base] in case of NaOH. The preliminary
30
31 energy analysis gave similar energy consumption per unit product with NaOEt and NaOH, which fall
32
33 within 15% variation (comparable with the accuracy of calculation). This is due to the overall energy
34
35 consumptions being roughly proportional to the respective yields.
36
37

38
39 On the other hand, being a widely available and easily handled species, NaOH represents the base of
40
41 choice from an environmental outlook (LCA), mostly due to the lower impact of the raw material
42
43 production (NaOH) compared with NaOEt. Only with a global assessment of all the flows involved in a
44
45 reaction it is possible to assess the environmental load of a new product. Furthermore, lower impacts
46
47 could be achieved if some improvements of the process efficiency will be carried out, by increasing
48
49 process selectivity and conversion, reusing the catalyst for many times and recovering the co-products
50
51 formed by the reaction.
52
53
54
55
56
57
58
59
60

Supporting Information. Certificate of analysis of EtOH CAVIRO 95% and composition of CAVIRO X real mixtures. ¹H-NMR and ¹³C-NMR and ESI-MS spectra of ruthenium catalyst **3**; GC chromatogram analyses for base co-catalyst comparison; ¹H-NMR, IR and ESI-MS analysis of catalyst resting state.

Author information

Corresponding Author

*E-mail: fabrizio.cavani@unibo.it; rita.mazzoni@unibo.it.

Notes

The authors declare no competing financial interest.

Acknowledgements

We gratefully acknowledge the financial support from Valsovit project (CUP_F72I16000010009) with the contribution of the Emilia Romagna Region through POR FERS 2014-2020 funds (European Regional Development Fund) and the University of Bologna. VZ also acknowledges the PRIN 2015 project from Ministero dell'Università e della Ricerca Scientifica e Tecnologica (20154X9ATP_003).

References

- (1) Angelici, C.; Weckhuysen, B. M.; Bruijninx, P. C. A. Chemocatalytic Conversion of Ethanol into Butadiene and Other Bulk Chemicals. *ChemSusChem* **2013**, *6* (9), 1595–1614.
- (2) Posada, J. A.; Patel, A. D.; Roes, A.; Blok, K.; Faaij, A. P. C.; Patel, M. K. Potential of Bioethanol as a Chemical Building Block for Biorefineries: Preliminary Sustainability Assessment of 12 Bioethanol-Based Products. *Bioresour. Technol.* **2013**, *135*, 490–499.
- (3) Bruijninx, P. C. A.; Weckhuysen, B. M. Shale Gas Revolution: An Opportunity for the Production of Biobased Chemicals? *Angew. Chem. Int. Ed.* **2013**, *52* (46), 11980–11987.
- (4) Kozłowski, J. T.; Davis, R. J. Heterogeneous Catalysts for the Guerbet Coupling of Alcohols. *ACS Catal.* **2013**, *3* (7), 1588–1600.
- (5) Gabriëls, D.; Hernández, W. Y.; 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.* **2015**, *5* (8), 3876–3902.
- (6) Zhang, Q.; Dong, J.; Liu, Y.; Wang, Y.; Cao, Y. Towards a Green Bulk-Scale Biobutanol from

- Bioethanol Upgrading. *J. Energy Chem.* **2016**, *25* (6), 907–910.
- (7) Chierigato, A.; Ochoa, J. V.; 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* **2015**, *8* (2), 377–388.
- (8) Ho, C. R.; Shylesh, S.; Bell, A. T. Mechanism and Kinetics of Ethanol Coupling to Butanol over Hydroxyapatite. *ACS Catal.* **2016**, *6* (2), 939–948.
- (9) Jordison, T. L.; Peereboom, L.; Miller, D. J. Impact of Water on Condensed Phase Ethanol Guerbet Reactions. *Ind. Eng. Chem. Res.* **2016**, *55* (23), 6579–6585.
- (10) Sun, Z.; Vasconcelos, A. C.; Bottari, G.; Stuart, M. C. A.; Bonura, G.; Cannilla, C.; Frusteri, F.; Barta, K. Efficient Catalytic Conversion of Ethanol to 1-Butanol via the Guerbet Reaction over Copper- and Nickel-Doped Porous Solids. *ACS Sustain. Chem. Eng.* **2017**, *5* (2), 1738–1746.
- (11) Aitchison, H.; Wingad, R. L.; Wass, D. F. Homogeneous Ethanol to Butanol Catalysis - Guerbet Renewed. *ACS Catal.* **2016**, *6* (10), 7125–7132.
- (12) Fu, S.; Shao, Z.; Wang, Y.; Liu, Q. Manganese-Catalyzed Upgrading of Ethanol into 1-Butanol. *J. Am. Chem. Soc.* **2017**, *139* (34), 11941–11948.
- (13) Kulkarni, N. V.; Brennessel, W. W.; Jones, W. D. Catalytic Upgrading of Ethanol to N-Butanol via Manganese-Mediated Guerbet Reaction. *ACS Catal.* **2018**, *8* (2), 997–1002.
- (14) 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.* **2013**, *52* (34), 9005–9008.
- (15) Pellow, K. J.; Wingad, R. L.; Wass, D. F. Towards the Upgrading of Fermentation Broths to Advanced Biofuels: A Water Tolerant Catalyst for the Conversion of Ethanol to Isobutanol. *Catal. Sci. Technol.* **2017**, *7* (21), 5128–5134.
- (16) 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.* **2016**, *52* (14), 2901–2904.
- (17) Chakraborty, S.; Piszal, 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.* **2015**, *137* (45), 14264–14267.
- (18) 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.* **2016**, *138* (29), 9077–9080.
- (19) Akhtar, M. K.; Dandapani, H.; Thiel, K.; Jones, P. R. Microbial Production of 1-Octanol: A

- 1
2
3 Naturally Excreted Biofuel with Diesel-like Properties. *Metab. Eng. Commun.* **2015**, *2*, 1–5.
- 4
5 (20) Campos-Fernández, J.; Arnal, J. M.; Gómez, J.; Dorado, M. P. A Comparison of Performance of
6 Higher Alcohols/diesel Fuel Blends in a Diesel Engine. *Appl. Energy* **2012**, *95*, 267–275.
- 7
8 (21) O’Lenick, A. J. Guerbet Chemistry. *J. Surfactants Deterg.* **2001**, *4* (3), 311–315.
- 9
10 (22) Torres, G. M.; Frauenlob, R.; Franke, R.; Börner, A. Production of Alcohols via
11 Hydroformylation. *Catal. Sci. Technol.* **2015**, *5* (1), 34–54.
- 12
13 (23) Blum, Y.; Czarkle, D.; Rahamlm, Y.; Shvo, Y. (Cyclopentadienone)ruthenium Carbonyl
14 Complexes-A New Class of Homogeneous Hydrogenation Catalysts. *Organometallics* **1985**, *4*
15 (8), 1459–1461.
- 16
17 (24) Pavarelli, G.; Velasquez Ochoa, J.; Caldarelli, A.; Puzzo, F.; Cavani, F.; Dubois, J.-L. A New
18 Process for Maleic Anhydride Synthesis from a Renewable Building Block: The Gas-Phase
19 Oxidehydration of Bio-1-butanol. *ChemSusChem* **2015**, *8* (13), 2250–2259.
- 20
21 (25) Conley, B. L.; Pennington-Boggio, M. K.; Boz, E.; Williams, T. J. Discovery , Applications ,
22 and Catalytic Mechanisms of Shvo ’ S Catalyst. *Chem. Rev.* **2010**, *110* (4), 2294–2312.
- 23
24 (26) Cesari, C.; Sambri, L.; Zacchini, S.; Zanotti, V.; Mazzoni, R. Microwave-Assisted Synthesis of
25 Functionalized Shvo-Type Complexes. *Organometallics* **2014**, *33* (11), 2814–2819.
- 26
27 (27) Pasini, T.; Solinas, G.; Zanotti, V.; Albonetti, S.; Cavani, F.; Vaccari, A.; Mazzanti, A.; Ranieri,
28 S.; Mazzoni, R. Substrate and Product Role in the Shvo’s Catalyzed Selective Hydrogenation of
29 the Platform Bio-Based Chemical 5-Hydroxymethylfurfural. *Dalton. Trans.* **2014**, *43* (26),
30 10224–10234.
- 31
32 (28) Cesari, C.; Cingolani, A.; Parise, C.; Zacchini, S.; Zanotti, V.; Cassani, M. C.; Mazzoni, R.
33 Ruthenium Hydroxycyclopentadienyl N-Heterocyclic Carbene Complexes as Transfer
34 Hydrogenation Catalysts. *RSC Adv.* **2015**, *5* (115), 94707–94718.
- 35
36 (29) EN ISO 14040. Environmental Management, Life Cycle Assessment, Principles and Framework;
37 International Organization for Standardization: Geneva, Switzerland, 2006.
- 38
39 (30) EN ISO 14044. Environmental Management, Life Cycle Assessment, Requirements and
40 Guidelines; International Organization for Standardization: Geneva, Switzerland, 2006.
- 41
42 (31) Cespi, D.; Passarini, F.; Neri, E.; Vassura, I.; Ciacci, L.; Cavani, F. Life Cycle Assessment
43 comparison of two ways for acrylonitrile production: the SOHIO process and an alternative route
44 using propane. *J. Cleaner Prod.* **2014**, *69*, 17–25.
- 45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 (32) Cespi, D.; Passarini, F.; Mastragostino, G.; Vassura, I.; Larocca, S.; Iaconi, A.; Chieregato, A.;
4 Dubois, J.-L.; Cavani, F. Glycerol as feedstock in the synthesis of chemicals: A life cycle analysis
5 for acrolein production. *Green Chem.* **2015**, *17*(1), 343-355.
6
7
8 (33) Tripodi, A.; Bahadori, E.; Cespi, D.; Passarini, F.; Cavani, F.; Tabanelli, T.; Rossetti, I.
9 Acetonitrile from Bioethanol Ammoxidation: Process Design from the Grass-Roots and Life
10 Cycle Analysis. *ACS Sustain. Chem. Eng.* **2018**, *6*, 5441-5451.
11
12
13 (34) Wernet, G.; Bauer, C.; Steubing, B.; Reinhard, J.; Moreno-Ruiz, E.; Weidema, B. Theecoinvent
14 database version 3 (part I): overview and methodology, *Int. J. Life Cycle Ass.* **2016**, *21*, 1218-
15 1230.
16
17
18 (35) Finechem Tool. Available online at:
19 <http://www.emeritus.setg.ethz.ch/research/downloads/software---tools/fine-chem.html>.
20
21
22 (36) Jolliet, O.; Margni, M.; Cherles, R.; Humbert, S.; Payet, J.; Rebitzer, G.; Rosenbaum, R. IMPACT
23 2002+: A New Life Cycle Assessment Methodology. *Int. J. Life Cycle Ass.* **2003**, *8* (6), 324-330.
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Synopsis

Catalytic valorization of ethanol from wine waste to higher alcohols by Guerbet reaction: ruthenium based bifunctional catalysis, process design and life cycle assessment.

TOC/graphical abstract

