



Advances in the homogeneous catalyzed alcohols homologation: The mild side of the Guerbet reaction. A mini-review

Alessandro Messori^{a,b,1}, Anna Gagliardi^{a,b,1}, Cristiana Cesari^{a,b}, Francesco Calcagno^{a,b}, Tommaso Tabanelli^{a,b,c}, Fabrizio Cavani^{a,b,c}, Rita Mazzoni^{a,b,c,*}

^a Department of Industrial Chemistry "Toso Montanari", viale Risorgimento, 4, 40136 Bologna, Italy

^b Center for Chemical Catalysis – C, University of Bologna, viale Risorgimento 4, 40136 Bologna, Italy

^c Interdepartmental Centre for Industrial Research, Renewable Sources Environment, Sea, Energy (CIRI-FRAME), viale Risorgimento, 4, 40136 Bologna, Italy

ARTICLE INFO

Keywords:

Bio-ethanol
Bio-refinery
Homogeneous catalysis
Ruthenium complexes
Manganese complexes

ABSTRACT

The Guerbet reaction would be an optimal solution for bio-ethanol refinery by homologation and it substantially requires the development of active and highly selective catalysts. Although heterogeneous catalysis remains more desirable, homogeneous Guerbet catalytic systems are nowadays acknowledged as challenging proposals for high selectivity and conversion under mild reaction conditions. Several molecular bi-functional catalysts, based on ruthenium, iridium and manganese complexes bearing different ligands such as phosphine, bidentate bisphosphine (P-P) and phosphamine (P-N), pincer (N-N-N), (P-N-P) and cyclopentadienone, are active in the co-presence of a base, which is essential in all the cases for the condensation reaction. This mini-review is aimed to describe the state of the art, with incremental steps forward to understand the role of the catalytic systems and the reaction conditions on conversion and selectivity. While showing different efficiency, mutable behavior by minimal change in the ligand scaffold, variation in water tolerance and only one example of recyclability, metal catalysts are found to be similar in terms of proposed mechanisms. The influence of additives and capability to maintain activity in fermentation broth and bio-ethanol from wine value chain to second generation bio-fuel are also discussed. Although not yet completely rationalized, experimental and theoretical mechanistic investigations pave the way for the design of more stable and efficient catalysts toward improved applicability.

1. Introduction

The necessity to reduce fossil fuels exploitation and CO₂ emissions has become urgent, as reflected by the zero-emission policy for the sales of new vehicles by 2035 supported by the European Parliament this year. [1] The strategy envisions a combination of different approaches depending on the field of application. While battery-powered vehicles have been advised for private transport, synthetic fuels have been recognized as the best alternative for ships, planes, heavy duty vehicles and, generally speaking, for all vehicles that run on long distances and

require high autonomy, endurance and/or power. Bioethanol, constituting 67% of all biofuels (including biodiesel and HVO, namely Hydrotreated Vegetable Oil) produced worldwide in 2021, [2] is the most used renewable fuel in road transport. It has been estimated that high-level ethanol blends reduce life cycle greenhouse gases emissions by 40% on average. [3] However, the use of ethanol fuel presents some drawbacks due to its lower energy density compared to gasoline and its corrosivity to standard infrastructure, leading to the requirement of specifically designed engines installed on flexible fuel vehicles (FFVs). On the other hand, butanol and higher alcohols could be employed in

Abbreviations: HVO, Hydrotreated Vegetable Oil; FFV, flexible fuel vehicles; NHOC, net heat of combustion; PNNL, Pacific Northwest National Laboratory; KO^tBu, Potassium tert-butoxide; NaO^tBu, Sodium tert-butoxide; LiO^tBu, Lithium tert-butoxide; NaOAc, Sodium acetate; NaOH, Sodium hydroxide; KOH, Potassium hydroxide; Dppm, 1,1-bis(diphenylphosphino)-methane; bpi, 1,3-bis(2-pyridylimino)isoindolate; P₄-^tBu, phosphazene; LCA, Life cycle assessment; BQ, Benzoquinone; TON, turn over number; TOF, turn over frequency; Tp', tris(3,5-dimethyl-pyrazolyl)borate; ¹Pr, 1,3-bis(2,6-diisopropyl-phenyl)-1,3-dihydro-2H-imidazol-2-ylidene; IR, Infrared spectroscopy; PEG, polyethylene glycol; MeOH, methanol; EtOH, ethanol; iBuOH, isobutanol; DFT, density functional theory; FES, free energy surface; CPCM, conductor-like polarizable continuum model.

* Corresponding author at: Department of Industrial Chemistry "Toso Montanari", viale Risorgimento, 4, 40136 Bologna, Italy.

E-mail address: rita.mazzoni@unibo.it (R. Mazzoni).

¹ Alessandro Messori and Anna Gagliardi contributed equally to this paper.

<https://doi.org/10.1016/j.cattod.2023.01.010>

Received 16 December 2022; Received in revised form 9 January 2023; Accepted 12 January 2023

Available online 20 January 2023

0920-5861/© 2023 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

standard engines without modifications and have shown the potential to be blended with diesel fuel. [4] Interestingly, n-butanol is noncorrosive, only slightly soluble in water, and its net heat of combustion (NHOC), is higher compared to ethanol (26.8 MJ/L vs 21.1 MJ/L) and roughly 83% compared to fossil gasoline (32.3 MJ/L). [5,6] In this regard, the Guerbet reaction constitutes an ideal pathway for ethanol homologation. The reaction, overall resembling a simple condensation with the release of a water molecule, is often suggested to occur along three sequential steps (Scheme 1). First, the reactants are dehydrogenated to the corresponding aldehydes. Two aldehydes, which can derive from the same alcohol or from two different alcohols, undergo aldol condensation followed by dehydration, yielding an unsaturated aldehyde characterized by the sum of the carbon atoms of the starting molecules. Hydrogenation of such intermediate leads to the final higher alcohol. The catalyst properties and the conditions employed need to be wisely tuned to allow for the plurality of reactions involved, at the same time discouraging the formation of unwanted side products, such as ethers, esters, olefins and paraffins [7] in heterogeneous catalysis and acetate salts in homogeneous systems. [8].

Accordingly, a variety of Guerbet-active materials has been developed over time and employed in both homogeneous and heterogeneous catalysis. These catalytic systems are often characterized by multifunctionality, which is given by the combination of i) hydrogenation/dehydrogenation ability and ii) the presence of acidic/basic sites to promote the aldol condensation step, the dehydration of the aldol or, more in general, modulate the strength of adsorption/interaction of reagents and intermediates. It must be noted that although the reported mechanism is supported by many studies, [9–12] alternative pathways involving direct ethanol self-condensation or condensation with a molecule of acetaldehyde have also been proposed, [13–16] showing that the exact mechanism is indeed dependent on the catalyst and the reaction conditions.

The Guerbet reaction has been known since the end of the nineteenth century, when its inventor Marcel Guerbet reported the first example of direct alcohol coupling to heavier analogues. At that time and for many years, the interest around the Guerbet reaction was mild and mostly limited to academia, since higher alcohols could be produced via cheaper processes from fossil feedstocks, even though a few patents describing catalysts and processes for the production of Guerbet alcohols were issued since the 1930s. [17] However, with the introduction of the concept of biorefinery towards the end of the twentieth century, this transformation was revived and regained increasing interest due to its potentiality to offer a fossil-free pathway for the manufacture of valuable products. Guerbet alcohols are in fact typically branched in the β -position and possess excellent lubricant properties which make them suitable as hydraulic fluids, cosmetic emollients, surfactants, as well as

for advanced biofuels application.

Although the core of this mini-review will be dedicated to the description on advances in the development of catalysts for the Guerbet reaction from an homogeneous perspective, that actually is still in its infancy, authors believe that an introduction on the current scenario of heterogeneous counterpart is mandatory, as well as useful, to do a critical analysis on the eventual applicability of the “mild side” of the Guerbet reaction.

In 2014 Abengoa, a former Spanish multinational company active in sustainable technology, infrastructures, green energy and water sectors, was looking forward to enriching its business strategies with a Guerbet-based alcohol upgrading process. In a series of patents and applications filed by the company between 2012 and 2014, the inventors claimed the intellectual property over the gas-phase, continuous flow transformation of C_1 - C_3 alcohols into C_3 - C_{15} analogues using Guerbet-active mixed metal oxides deriving from thermal decomposition of hydrotalcites. These catalysts were characterized by the presence of trivalent gallium and other components such as bivalent alkaline earth or transition metals, trivalent metals including Al and La, and noble metals with a preference for Pd. [18] In fact, gallium-containing oxides are known in literature to effectively promote the dehydrogenation of light alcohols in the gas phase. [19–21] A good fraction of the documents was focused on the production of 1-butanol from ethanol, which was favored by the co-feeding of acetaldehyde and hydrogen allowing for up to 70% butanol selectivity at 35% yield or up to 95% selectivity at 15% yield. [22].

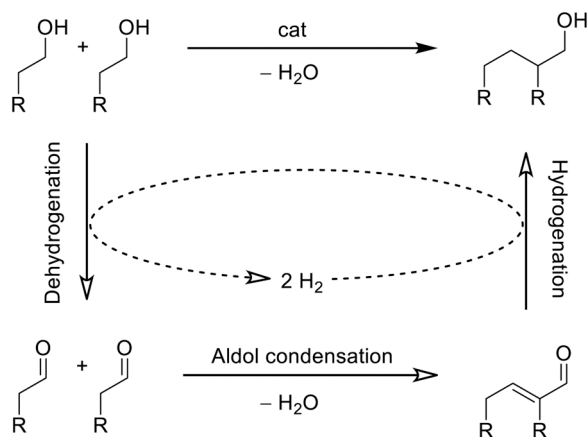
Abengoa's strategy relied on heterogeneous catalysis, which can be economically convenient due to the facility of separation of the final products and the versatility of the catalysts. These are usually relatively easy to synthesize, can tolerate a wide range of conditions and can be readily regenerated and recycled. A relevant feature of Abengoa's approach resided in the commitment to second-generation ethanol from lignocellulosic biomass and agricultural residues, [23] which was an ambitious plan considering the competitiveness of the established OXO [24] and ABE [25] processes to produce butanol. However, the pioneer industrial facility for the commercial deployment of Guerbet bioalcohols from second generation ethanol was never erected due to financial issues that eventually brought the company to bankruptcy.

In 2019, Catalyxx acquired the worldwide exclusive license of Abengoa's technologies for catalyst formulation, uses, and production process to convert ethanol into longer chain alcohols including n-butanol, n-hexanol, n-octanol, n-decanol and 2-ethylhexanol, [26] and is now looking for interested parties for licensing.

The Guerbet reaction is also used by Sasol to upgrade C_6 - C_{16} alcohols to β -alkylated C_{12} - C_{32} analogues, which are then commercialized in pure cuts or in blends for cosmetic application, as lubricants and emulsifiers for the textile and metal sectors, as surfactants and solubilizers for paints, inks and coatings. [27] The semi-continuous technology patented by the German company 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, in order to yield high-purity alcohols without expensive and wasteful washing and purification steps. [28] Oxidation to carboxylic acids [29, 30] and further esterification with the same Guerbet alcohols [31] enables the company to achieve an assorted portfolio of branched oxygenates.

While these realities represent industrial milestones in the history of the Guerbet reaction, parallel advances in academic and patent literature have been proceeding abreast. In fact, boosting catalytic activity and selectivity by improving the catalyst properties and the attempt to solve process development and environmental issues have been a key priority across all strategies relying on gas-phase and liquid-phase heterogeneous catalysis.

Hydrotalcite-derived Mg-Al mixed oxide catalysts, analogous to those patented by Abengoa, have been reported and keep receiving great interest due to their high surface area, structural stability, non-toxicity,



Scheme 1. Simplified Guerbet reaction proposed mechanism for primary alcohols.

and tunable acid-base properties. [12,32] In fact, it was demonstrated that the reaction mechanism involves adjacent Lewis acid-basic site pairs acting synergistically to achieve Guerbet reactivity, [33] even though strong basic sites are fundamental. [12] Systematic studies have also been conducted to explore the influence of the reaction parameters, including temperature, pressure, space velocity and hydrogen co-feeding, [34] on the catalytic activity of these materials. Cu emerged as a good non-noble metal candidate to incorporate in the Mg-Al framework with the purpose of enhancing catalytic activity and higher alcohols selectivity in continuous, gas-phase systems [7,35] as well as in liquid phase, batch conditions. [36] The Battelle Memorial Institute, operating agency of the Pacific Northwest National Laboratory (PNNL) which is also working on ethanol conversion to jet fuel, [37] has claimed a method for alcohol upgrading including a Guerbet step on a similar CuO-MgO-Al₂O₃ catalyst formulation. [38] Copper hydroxalicates have also been further functionalized with other metals such as nickel, [39] indium and palladium [40] with good results.

Copper was also employed to functionalize MgO and MnO basic oxides to help the hydrogenation/dehydrogenation steps of the reaction. [41] In fact, MgO has been widely used as a reference for catalytic activity, due to its superior performance in ethanol coupling to 1-butanol, [16,42,43] and other recent functionalization examples include the support of Pd/MgO on high surface area graphite. [44].

On the other hand, the excellent activity and selectivity displayed by hydroxyapatites Ca₁₀(PO₄)₆(OH)₂ paved the way for further studies on the role of phosphates, [43] the substitution of calcium, [45] and the functionalization with transition metals such as copper while introducing hydrogen in the feed. [46].

Other successful approaches include the employment of Cu/CeO₂ with high surface area, [47] Cu/CeO₂ supported on activated carbon, [48] and transition metals supported on (La-doped) alumina, [49–51] as well as alternative reaction conditions involving microwave heating. [52].

The drawbacks of heterogeneous catalysis applied to the Guerbet reaction, as it is often the case, are the requirement of temperatures above 250 °C (often above 300 °C), and the difficulty to simultaneously achieve high conversion and selectivity. To circumvent these concerns, homogeneous catalytic systems have been designed in the last two decades, as will be reviewed in this work. Notorious troublesome inconveniences of homogeneous catalysis, such as the catalyst stability, the necessity of a high amount of a base co-catalyst and the challenging separation of catalysts and by-products from the valuable alcohols, will be discussed together with other lights and shadows that make the molecular approach prone but still not suitable for industrial application.

2. The mild side of the Guerbet reaction

Up to date, only a few overviews report on the homogeneously catalysed Guerbet reaction by transition metal complexes. The first, published by Wass et al. in 2016, summarized the necessity to extend the subject from an exquisite heterogeneous approach, to a homogeneous alcohol homologation perspective with particular emphasis on butanol yield and selectivity. [53] We direct the reader to that review for details on the very first steps in the field that involved iridium and rhodium complexes, coadiuvated by suitable phosphine ligands albeit towards low conversions and selectivities. [54–57] The same year, a similar approach was given by Wang and Cao, [58] and two years later by Ni and co-workers. [59] Since then, a flourishing literature both focusing on the design of more efficient catalytic systems and highlighting the need of more defined mechanistic insights, significantly improved the state of the art. Considerable attention was kept on the most promising ruthenium based bifunctional complexes, extending the reaction scope to the valorisation of the comprehensive range of Guerbet alcohols (not only butanol but also linear and branched C₆-C₁₀ alcohols). Furthermore, first examples on the use of first row transition metal complexes

for alcohol homologation opened a new challenging chapter towards greener process development and catalyst cost reduction. This review is aimed to rationalize the steps forward in the field with special consideration to criticisms and proposed solutions for the design of process conditions and the tuning of metal-based hydrogenation/dehydrogenation catalyst by changing the structural features of ligands on transition metal complexes.

2.1. Ruthenium complexes

Taking inspiration from the hydrogen borrowing activity demonstrated by several bifunctional ruthenium complexes over the years, [60–65] this latter became the second raw metal of choice for the homogeneous Guerbet process development since 2010, when the first patent on the exploitation of group VIII-X phosphine supported metal complexes for the conversion of ethanol to n-butanol was filed. [66].

2.1.1. Ruthenium catalysts with phosphine ligands

The Mitsubishi Chemical Corporation claimed in 2010 [66] about selected examples of ruthenium catalysts/base co-catalyst systems suitable for the homologation of ethanol to n-butanol revealing [RuCl₂(PPh₃)₃] (0.5 mol%) with an excess of triphenylphosphine (3.5 mol%), potassium tertbutoxide as a base co-catalyst (KO^tBu 3.5 mol%) under hydrogen pressure (20 atm) at 180 °C for 3 h as the best conditions at that time. This system was able to reach 21% yield in n-butanol with 93% selectivity. The reaction was tested both in solvent (o-xylene) and in neat substrate.

Lately, in 2013 Wass and co-workers introduced the use of bidentate phosphines ligands with the dimeric [RuCl₂(η⁶-p-cymene)]₂ as the ruthenium catalyst precursor. [67] Excellent performance for that time had been obtained with the preformed complexes [RuCl(η⁶-p-cymene)(L)]Cl (best with L = 1,1-bis(diphenylphosphino)-methane (dppm) 0.1 mol%, cat 0.04 mol%, base NaOEt 5 mol%, yield 21%, n-butanol selectivity 94%, T = 150 °C, time 4 h) in that neither hydrogen pressure nor hydrogen acceptor such as 1,7-octadiene were needed anymore to run the reaction. An increased quantity of phosphine ligands improved conversion (over 40%) but lowered the speed of the reaction and the selectivity on n-butanol (< 85%). At a preliminary glance it was already clear that the ruthenium complex played somehow a role also in the aldol condensation preventing the spontaneously fast base catalysed condensation of acetaldehyde.

An interesting improvement in conversion (up to 31%), selectivity (>90%) and water tolerance was then achieved by the same group [68] combining [RuCl₂(η⁶-p-cymene)]₂ with mixed chelating ligands such as phosphineamine with increased σ-donor properties. As a further insight in the ruthenium catalyst behaviour, hydride species such as [RuH(η⁶-p-cymene)(L)]⁺ were observed with ionization mass spectrometry (ESI-MS) and NMR spectroscopy.

These pioneering results, being also patented with BP Biofuels UK, [69] paved the way for a larger exploration on variously decorated ruthenium complexes for the homogeneous homologation of ethanol to butanol and higher alcohols.

2.1.2. Ruthenium catalysts with pincer ligands

Another family of suitable bifunctional complexes for the conversion of ethanol to butanol is represented by trischelate pincers as ancillary ligands. The first example was communicated in 2016 by Szymczak and co-workers that reported on the activity of N-N-N pyridylimino isonolate ruthenium complexes (Fig. 1). Both the hydride catalyst **1** and the chloride precursors **2-H**, **2-OMe**, **2-Cl** were found suitable for alcohol upgrading. [70] Reaction conditions screening on **2-H** demonstrated that the performances of this kind of catalysts, although leading to a not outstanding yield in butanol (best results: 27% with a selectivity of 83%, cat loading 0.1 mol%, NaOEt 5 mol%, 150 °C, 2 h), is not affected by the presence of oxygen. Catalyst deactivation can be controlled by an excess of phosphine ligand (one equivalent of PPh₃) in

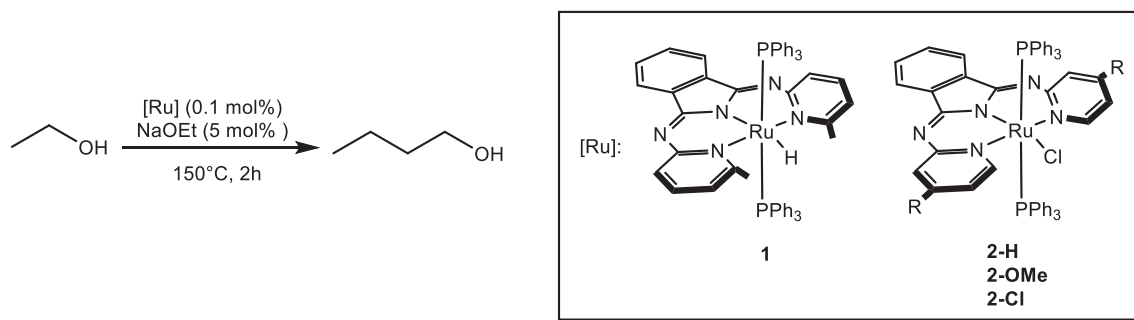


Fig. 1. Ru(II) catalysts decorated with N-N-N tridentate pincer ligands employed in the Guerbet reaction by the group of Szymczak. [70].

order to limit its dissociation (ethanol conversion 49%, butanol selectivity 84%). Starting the reaction with a mixture of ethanol/butanol (80%/20%) shed light on the catalyst trend toward the formation of longer chain alcohols than butanol (Fig. 1).

During the same year, hydride containing bifunctional catalysts bearing P-N-P as pincer ancillary ligands (Fig. 2) were reported by Milstein and co-workers, to be very effective for this transformation under similar conditions. [71] Screening of different ligands candidate the acridine-based system **3** as the best one leading to very high TON (higher than 18000) at low catalyst loading (0.001 mol%), although good conversions (73%) were affordable only at a 0.02 mol% concentration of the catalyst.

For the first time Milstein underlined the importance of alcohols higher than butanol for the production of bio-fuels, introducing C₆ and C₈ linear and branched alcohol as valuable products as well. The lower selectivity in butanol (36% at 73% conversion) became thus counterbalanced by the fact that higher alcohols, previously considered as side products, were recognized to have their share in the bio-fuel value chain. Reactivity studies on the resting state of the reaction, where a hydrido dicarbonyl dearomatized P-N-P complex was identified, allowed to draw a preliminary mechanistic study that suggests dearomatization as the activation process for the metal based catalyst.

Very recently Stephenson, Szymczak and co-workers also reported on a pathway exploiting ethanol homologation to higher alcohols, which is catalysed by their pincer N-N-N complexes in a tandem alkylation strategy for C-C bond forming reaction with nucleophiles for functionalization of fine chemical with Guerbet alcohols. [72].

From the Guerbet reaction point of view, the design of a new ligand scaffold ClRu(5-Mebpi)(PPh₃)₂ (bpi = 1,3-bis(2-pyridylimino)isindolate) **4** improved the catalyst efficiency for producing biofuels up to 65% (Ru cat 0.2 mol%, PPh₃ 0.2 mol%, NaO^tBu 40 mol%, mesitylene (0.5 mL), 150 °C, 2 h) in valuable alcohol mixtures leading to the highest TON (155890) (yield 11%, **4** loading 0.0001% mol%, PPh₃ 0.0001 mol%, NaO^tBu 40 mol%, mesitylene (0.5 mL), 150 °C, 168 h) and TOF (12690 h⁻¹, 2 h, 2.5% yield) for a homogeneous catalyst up to date. Changes in steric encumbrance and electronic demand of the ligand (Fig. 3 **4** alcohols yield 65%, **5** yield 28%, **6** yield 52%) lead to trends which, although hard to rationalize, confirm that simple perturbations to the N-N-N ligand can impart significant differences in catalytic activity. Stability studies stated **4** as the slower in degradation. Cyclic voltammetry experiments provided an indication on the electronic difference between the 3- (**4**) and 4- (**6**) substituted ligands with an E_{1/2} value 70 mV more negative for **4**.

These results underline the importance of both the rational design of ligands and the fine tuning of reaction conditions in order to reduce competitive reactions that can intercept aldehydes towards Cannizzaro [73] or Tishchenko [74] products (Scheme 2) such as acetates which can be monitored, as also previously suggested for other ligand scaffold (vide infra), [75] by means of NMR techniques. Best conditions were reached employing an inert co-solvent (mesitylene) with NaO^tBu as the base of choice for a reproducible mass balance. Although not desirable for applications 40 mol% of base loading provided the highest conversion.

An interesting screening on the influence of alkali metals on the

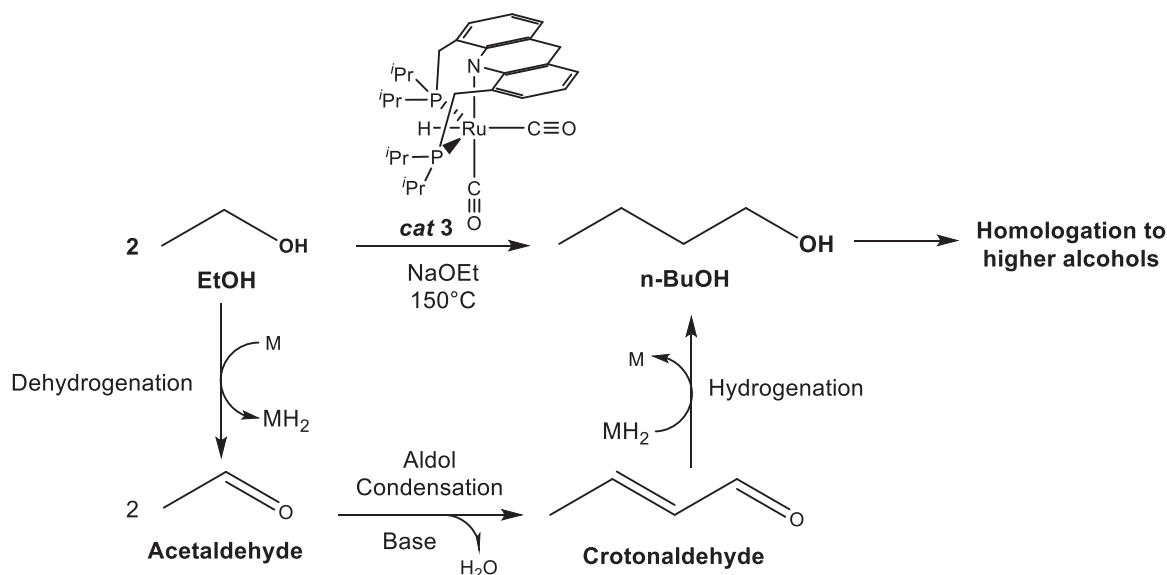


Fig. 2. Pincer type complexes exploited in ethanol homologation by Milstein group [71] and proposed ideal mechanism accounting the formation of higher alcohol under liquid homogeneous conditions.

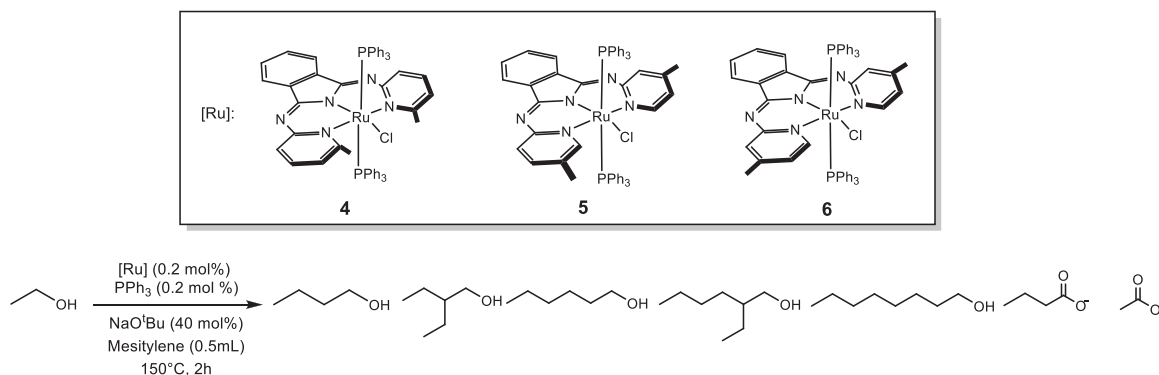
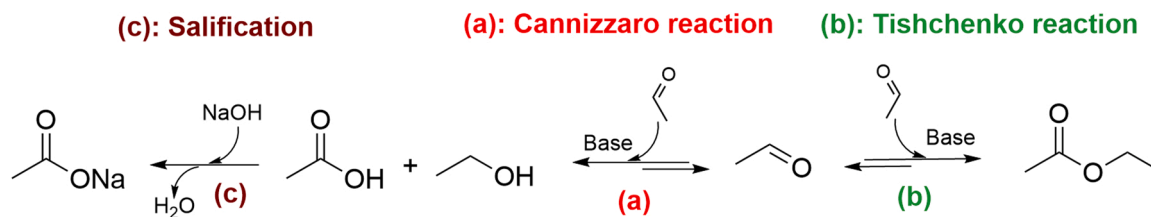


Fig. 3. Ruthenium complexes 4, 5 and 6 bearing N-N-N pincer ligands employed by Stephenson and Szymczak [72] for the study of steric and electronic effects on the Guerbet reaction.



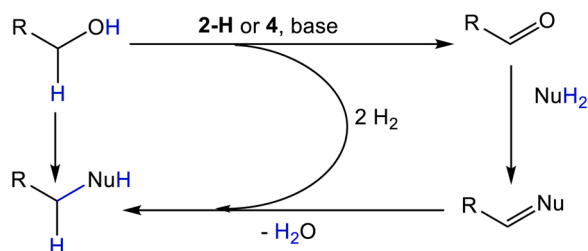
Scheme 2. Side reactions associated with the Guerbet reaction conditions in homogeneous phase.

parasite Cannizzaro reaction revealed that increasing their dimension (from NaO^tBu vs KO^tBu , 20 mol%) led to higher yields in carboxylated salts (from 6% to 16%), with a further detrimental effect when increasing the base quantity of KO^tBu up to 40% (46%). The addition of 40 mol% of 18-crown-6 as a sequestering agent for the alkali metal cation reduced the loss of ethanol to only 5% even though with a lower yield (46%) if compared with NaO^tBu (58%). On the other way around LiO^tBu did not form carboxylate salts, but provided lower Guerbet activity (33% yield). Further experiments with organic superbases (phosphazene $\text{P}_4\text{-}^t\text{Bu}$, 40 mol%) performed in the presence of LiBARF_{24} ($\text{ArF}_{24} = 3,5\text{-trifluoromethylphenyl}$), NaBARF_{24} and KBARF_{24} salts confirmed the trend, suggesting a correlation between the alkali metal acidity and reactivity.

Employing the optimized Guerbet conditions, the reaction was thus combined in the sequential Guerbet-alkylation strategy for the functionalization of several carbon pronucleophiles such as fluorene, nitriles and ketones (Scheme 3). While this approach deserves to be underlined as an interesting development towards possible applications of Guerbet alcohols in fine chemistry, we redirect the reader to the relative reference [72] for further details to avoid deviating from the topic of this minireview.

2.1.3. Ruthenium catalysts with a cyclopentadienone ligand

The first example of a phosphine-free ruthenium system emerged in 2019 by Mazzoni, Cavani and co-workers [75] when an ionic carbonyl



Scheme 3. General reaction for ethanol upgrading via tandem Guerbet-alkylation reaction. Nu = fluorene, nitriles and ketones. [72].

cyclopentadienone complex, counterbalanced by a dimethylimidazolium salt (7 in Fig. 4), appeared to be competitive with available homogeneous Guerbet catalysts (46% conversion of ethanol and 91% overall selectivity to $\text{C}_4\text{-C}_{10}$ higher alcohols under the following conditions: cat loading, 0.2 mol%; NaOEt , 20 mol%; temperature, 150 °C; reaction time, 4 h). Cyclopentadienone based ruthenium pre-catalysts were selected, since they are known to be active in hydrogenation and dehydrogenation reactions. [76–84] Although low, the carbon loss (4%) could be ascribed to acetaldehyde unselective decomposition or further conversion to heavy oligomers.

The same group lately performed a rationalization of the catalyst behaviour changing the counteranion (8–10 in Fig. 4), which put further accent on the delicate equilibrium between ligand scaffold, metal environment and reactivity in the Guerbet catalytic cycle. [8].

With both a theoretical and an experimental approach pre-catalyst behaviour was correlated as follows: i) the close H-bond interaction of the carbonyl group of cyclopentadienone cycle with N-CH-N proton of 7 and 9 is likely improving the structural stability of the tight ion pairs, along with their corresponding hydride species; ii) the acidity of the N-CH-N proton in imidazolium salt is not prone to be deprotonated by the buffer EtOH/NaOEt ; iii) from an electronic point of view, best pre-catalyst 7 activated hydride showed the strongest hydrogen bond and the highest hydride donor ability, which was likely to accelerate reduction and conversely decelerate the dehydrogenation step favouring the Guerbet reaction.

Worth noting, bioethanol refinery, especially when it is derived from waste or second generation (non-food) biomass, has a great potential for both biofuel and biochemicals production. With the reaction barely affected by the presence of water, conditions were transferred to a real matrix. Upon testing catalyst 7 on ethanol from wine value chain waste (head and tails of ethanol distillation supplied by CAVIRO distillery), no significant change in the final reaction mixture was observed.

Concurrently to the usual side reaction that consumes the base co-catalyst producing acetates as in previously described homogeneous Guerbet systems, molecular H_2 was also stockpiled in the headspace. This behaviour resembles that reported by Beller and co-workers for H_2 production from EtOH in water under basic conditions (proposed

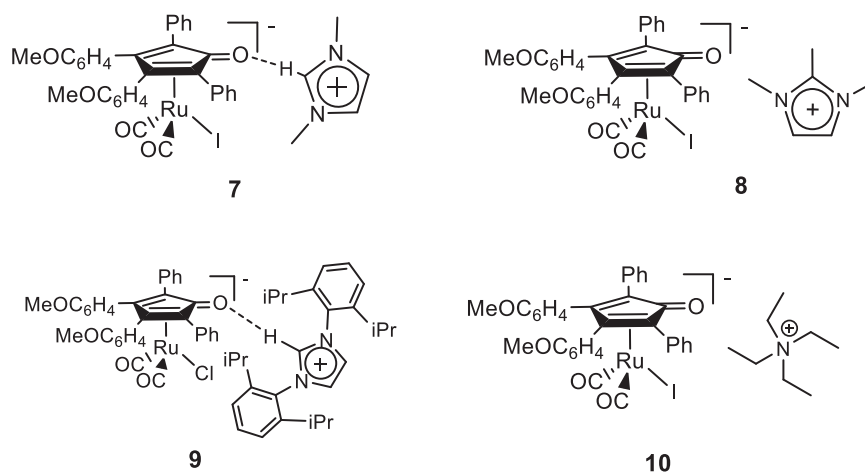


Fig. 4. Anionic bis-carbonyl cyclopentadienone ruthenium pre-catalysts 7, [75] 8, 9 and 10 tested by Mazzoni and Cavani [8] to check the influence on counter-cations on the Guerbet reaction.

reaction: $\text{NaOEt} + \text{H}_2\text{O}$ that leads to $\text{NaOAc} + 2 \text{H}_2$. [85] Catalyst 7 worked with a not outstanding turn over number (around 200, calculated on catalyst loading of 0.2 mol% and at maximum conversion), but it was prone to be recycled. Larger scale test (10 times ethanol feedstock) led to a comparable n-butanol yield with an increase of higher alcohols yield. When performing the reaction with NaOH, the production of a higher concentration of water favoured the Cannizzaro reaction, partially affecting the overall efficiency of the reaction. However, NaOH represents a more easily handled base compared to NaOEt. For this reason, it was also analysed, in parallel to NaOEt, along the first and unique (although preliminary) up to date multidisciplinary approach consisting of an industrialization study and a Life Cycle Analysis (LCA)

implemented for a homogeneous Guerbet process simulation.

Once the experimental data consistency was verified, the theoretical upscale to an ethanol load of 1000 kg resulted in the design of a reactor working in batch or, potentially, semibatch operation mode. The operation of the reactor can be envisaged in three sequential phases, namely “feeding + cooling”, “flushing + scarping” and “flushing + stirring”. For the process to be held, a separation section and a fractionation unit are necessary in addition to the reactor (Fig. 5). Multiple reactors are required to guarantee an almost continuous feeding of the separation and fractionation units (considering the perspective of a semibatch operation). This would bring higher productivity and possibly lower production costs.

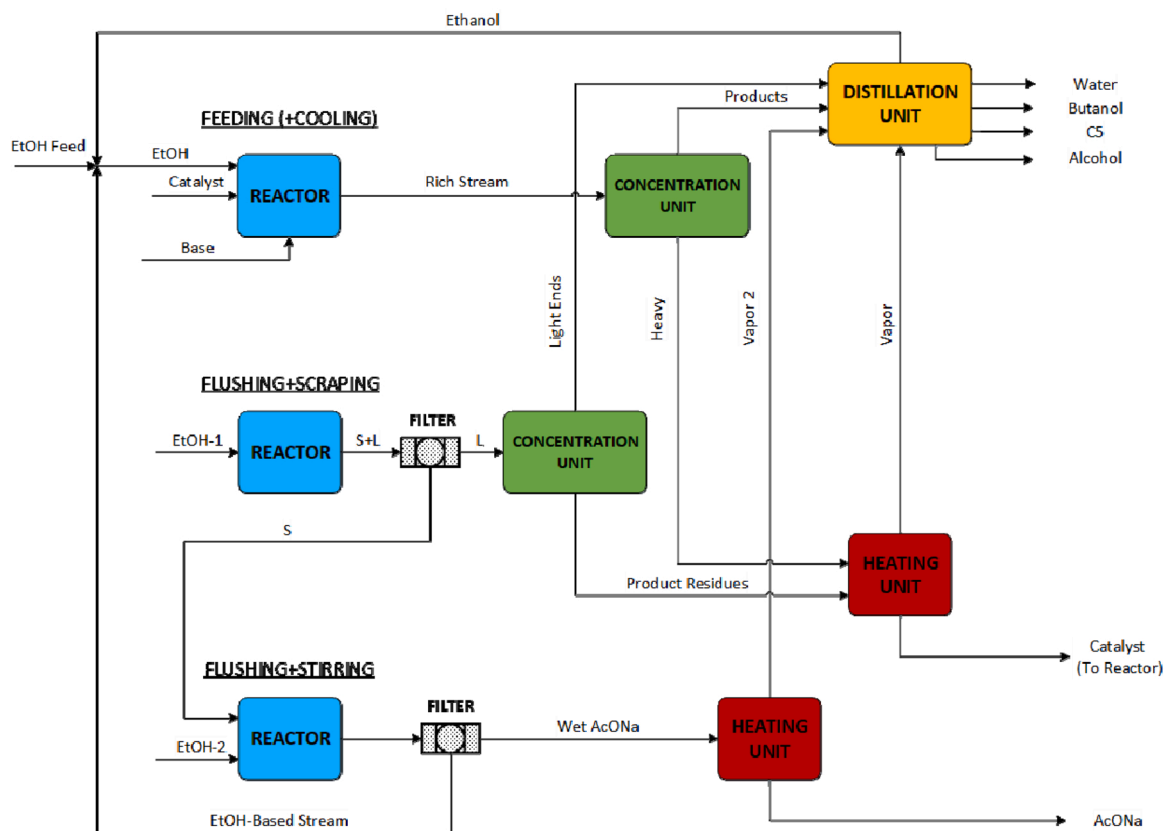


Fig. 5. Block flow diagram for the catalytic transformation of EtOH in higher alcohols process representing the theoretical upscale of the Guerbet reaction catalysed by 7. Plant scale process sizing based on 1000 Kg_{EtOH} . [75].

As a general remark, butanol and total alcohol production were calculated. When NaOH was employed, the process led to a lower specific production of alcohols (alcohols produced over ethanol inlet in mass terms) compared to the case with NaOEt. Plant energy demand was based on the process mass balance and delivered with the support of Aspen Plus V9–2016. The preliminary proposed energy mass balance was based on strong assumptions (e.g., yield, amplification factor, generated water correction), in order to redistribute the experimental shortcoming over the already identified products before proceeding with the energy balance. Nevertheless, the preliminary outcome is adequately representative of the industrial-scale process showing higher alcohols production per kg of processed ethanol than that obtained from the laboratory. Roughly 58% of the total input of ethanol is converted into butanol [mass base] in the case of NaOEt, while only ~37% [mass base] in the case of NaOH. The preliminary energy analysis gave similar energy consumption per unit product for the two bases.

For LCA calculations the reaction balance considered the synthesis of 1 kg of butanol. Although still presenting concerns regarding the need to recycle the catalyst several times to obtain relevant environmental advantages, the preliminary analysis of the process at laboratory scale showed that a lower environmental impact is linked to the use of NaOH, which is ascribed to the lower impact of this chemical compared that of NaOEt.

Although the reaction would well fit in a context of circular economy for the wine production chain, LCA and engineering assessments suggested that the process needed to be improved in terms of efficiency to become suitable for industrial application.

Conversion and selectivity of the above-described catalytic system have been more recently remarkably boosted by the addition of p-benzoquinone (BQ) as co-catalysts.[8,86] The 7/BQ/NaOEt catalytic triad (Fig. 6) led to a highly competitive conversion of 78% and alcohols yield 75% (cat loading 0,2 mol%, BQ 1,5 mol%, NaOEt 20 mol%, 24 h, 150 °C).

Moreover, the addition of BQ avoided hydrogen evolution as a side reaction and made the system more tolerant to water than the sole 7.

Upon a further increase of the NaOEt loading (40 mol%, reaction time 4 h) conversion reached 88% (0.2% mol ruthenium catalyst loading, 1.5% mol benzoquinone loading), while butanol and higher alcohols were produced in yields up to 85% (overall selectivity 97%). The catalytic system can be recycled. In general, the reaction screening resembles the behaviour of 7/base system alone with an increment of ca. 20% of ethanol conversion and maintaining the selectivity. Nevertheless, BQ addition favours the formation of alcohols higher than C₄, with a yield in butanol close to 40%. The Cannizzaro reaction still consumes the base, remaining an Achilles' heel of the reaction. The best TON of 670 was reached with 7 (0.1 mol%) / BQ (0.5 mol%) / NaOEt 20 mol%. From a circular economy perspective in wine and distillates production chain, the cooperative 7/BQ/NaOEt catalytic process can be transferred to a real bio-ethanol feedstock even in the presence of significant amounts of water and with no significant change in the product distribution.

2.1.4. Ruthenium complexes with bidentate nitrogen ligands for Guerbet reaction in water

The sole example of N-N chelating ligand scaffold, other than the claiming reported in Wass patent with BP Northamerica, [87] has been employed by Jones et al. for the transformation of ethanol in butanol in an aqueous medium [88] that simulates a fermentation broth mixture typically composed of 90% water and 10% ethanol. [89] Phenanthroline based iridium catalysts were previously found active by Mu and co-workers (2014) for ethanol homologation in aqueous medium, [90] achieving 26% yield in butanol and 8% yield in higher alcohols (52% conversion of ethanol) with an equimolar addition of KOH and NaOAc at 150 °C. Feng et al. also developed a less successful aqueous Guerbet system. [91] The catalyst employed by Jones, [(p-cymene)Ru(6,6'-dihydroxybipy)Cl]Cl ([Ru(bipyOH)]) with a 2,2-bipyridine ligand scaffold (11 in Fig. 7), was known in the literature to perform transfer hydrogenations in aqueous media. [92] Although leading to not yet promising results (28% maximum yield in butanol with 57% selectivity - [Ru(bipyOH)] loading 2 mol%, KO^tBu 60 mol%), it is worth noting that the Guerbet reaction here was run for the first time at a temperature as low as 80 °C.

The feedstock ratio of 90:10 found in fermentation broth is also tolerated, although with a decrease in butanol yield (20%) and selectivity (48%). Screening of reaction conditions allowed to demonstrate that the lower reactivity in diluted solutions is attributable to lower ethanol concentration rather than catalyst degradation. The effect of different alkali metals performing the reaction reflects the behaviour previously described for N-N-N pincer catalysts in neat ethanol (paragraph 2.1.2). Weaker bases such as sodium acetate or sodium phenoxide did not show any formation of alcohols or dehydrogenation products, as expected. Organic amine bases were also not productive for catalysis. Interestingly no acetates, that are common by-products in the homogeneous catalysed Guerbet reaction, are produced under Jones conditions. The possibility to improve the catalytic system efficiency by reducing the purification steps (e.g. distillation) of fermentation broth would be a step forward towards the development of valuable processes.

2.2. First row complexes

Prior to 2015, all homogeneous catalytic systems used in the Guerbet reaction were based on noble metals (mainly ruthenium and iridium). To address better economic and environmental sustainability, the move to first row transition metals was firstly explored by Baker and Jones in 2015. [93] They developed a catalytic tandem system combining Fujita and Yamaguchi's Cp^{*}Ir[(2-OH-6-phenyl)pyridine]Cl (12), [94] able to dehydrogenate primary alcohols, and two basic transition metal complexes as alternative to classic inorganic bases: [Tp⁺Ni(μ-OH)]₂ (Tp⁺: tris(3,5-dimethyl-pyrazolyl)borate) (13) and [(IPr)CuOH] (14) (IPr: 1,3-bis(2,6-diisopropyl-phenyl)-1,3-dihydro-2 H-imidazol-2-ylidene). The authors emphasized how inorganic bases, particularly NaOEt, are quite inefficient in achieving high-rate acetaldehyde coupling, lowering the reaction selectivity in butanol. To shift selectivity toward short chain

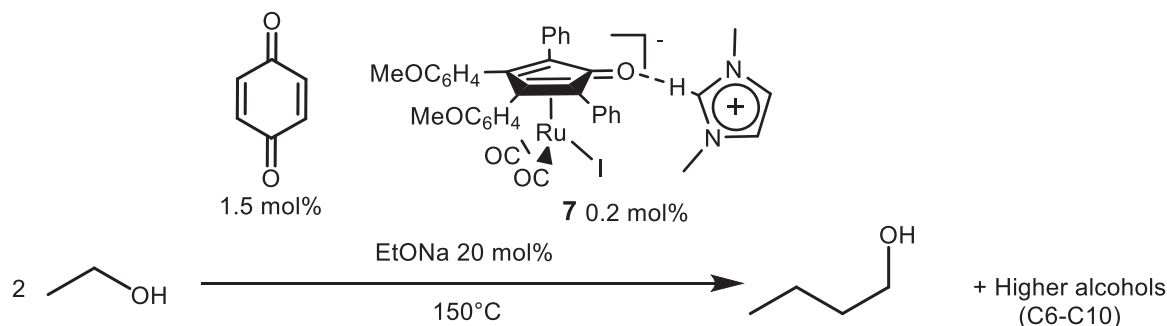


Fig. 6. Guerbet reaction boosted by the catalytic triad 7/BQ/NaOEt, best reaction conditions. [8].

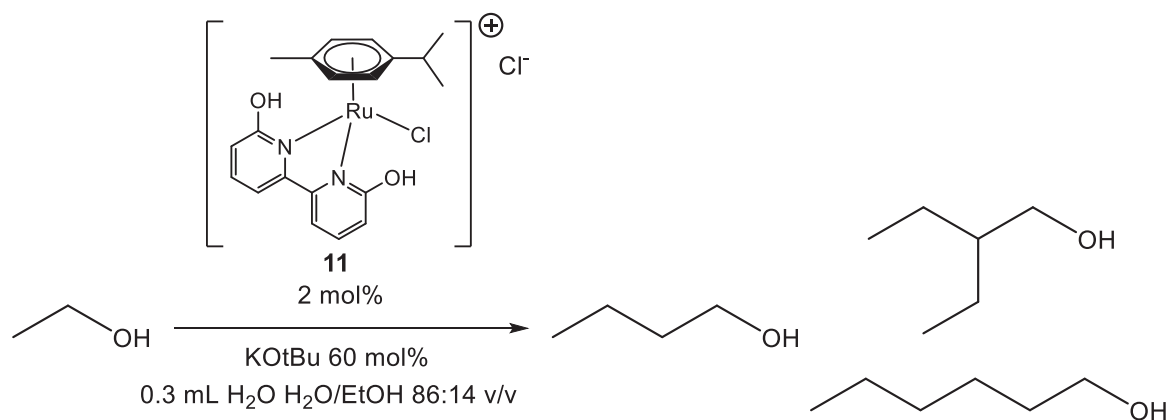


Fig. 7. Guerbet reaction in aqueous phase at 80 °C catalyzed by N,N water soluble complex **11**, best reaction conditions. Yield in 1-hexanol 7%; yield in 2-ethylbutanol 3%.[\[88\]](#).

aldehyde condensation, highly basic and bulky nickel and copper complexes were studied to catalyse aldol condensation steps ([Fig. 8](#)).

The catalytic tandem system was tested on ethanol homologation at 150 °C for 24 h using an iridium catalytic loading of 0.2 mol% and 5 mol% of basic nickel or copper complex. The reaction proceeded achieving moderate ethanol conversions (37% for nickel and 32% for copper) with good yields in butanol (34% for nickel and 28% for copper). Authors claimed a 99% butanol selectivity in both reactions considering butanol as the only traceable product.

Analysis on aldol condensation of acetaldehyde showed how with the classic inorganic base KOH low yields of crotonaldehyde were displayed (23% after 24 h at 150 °C), while basic nickel and copper complexes afforded a complete conversion at the same conditions and no C₈ aldol condensation products were detected. These experiments confirmed how these two metallic bulky systems inhibited C₄ coupling and control experiments in hydrogen atmosphere suggested no involvement in hydrogenation step of the catalytic cycle. Iridium complex **12** was only responsible for the hydrogenation/dehydrogenation of substrates and co-participation of the copper complex in catalyst activation was demonstrated by NMR experiments.

The first breakthrough in a homogeneous catalytic system entirely based on a first-row transition metal was reported by Liu in 2017. [\[95\]](#) A series of manganese (I) pincer P-N-P and N-N-P complexes ([Fig. 9](#)) was screened using a loading of 0.01 mol% and NaOEt (6 mol%) at 160 °C for 24 h. Among the others, manganese catalysts **15** and **16** were the most active in the reaction with a TON of 972 (9.7% ethanol conversion with 6.8% butanol yield).

The cyclohexyl homologues **17** and **18** displayed similar activities. Authors suggested that the catalytically active species undergo the release of an halide (**15** and **17**) or a carbonyl (**16** and **18**) ligand towards the formation of a dicarbonyl complex. The product mixture contain alcohols from C₄ to C₁₂ and sodium acetate originated by

Cannizzaro and Tischchenko side reactions, as reported for all the molecular catalyst/base co-catalyst systems discussed along the review.

Thermal stability given by the pincer scaffold guaranteed the achievement of a TON of 114120 after 7 days of reaction (11.2% ethanol conversion, 9.8% butanol yield at 160 °C with a catalytic loading of 0.0001% mol of catalyst mixture - **I** in [Fig. 9](#)).

Screening on the catalyst mixture **I** showed little influence on catalytic performances of using a base chosen amongst NaOEt (9.7% conversion, 6.8% butanol yield), NaOtBu (8.5% conversion, 6.1% butanol yield), NaOH (8.1% conversion, 5.8% butanol yield) and KOH (9.7% conversion, 6.4% butanol yield). However, in the case of NaOAc (1.7% conversion, 1.7% butanol yield), mechanistic studies revealed how acetate tends to coordinate to the active site of manganese creating a stable irreversible complex, which inhibits catalytic activity.

Water influence was also tested: 10 ppm added to the reaction mixture lowered the overall performances (7.6% ethanol conversion and 4.8% butanol yield) and authors demonstrated that water is engaging the manganese complex in an off-cycle equilibrium. Moreover, the presence of the N-H moiety on the catalyst demonstrated to be essential for an efficient aldehyde hydrogenation. Increasing the hydrogen pressure (given by an addition of ethanol or H₂) favoured the hydrogenation of intermediates, limiting oligomer formation by acetaldehyde or crotonaldehyde.

Interestingly, experimental mechanistic studies on catalyst activation showed the interconversion of the complex into different activated species that led to a hypothetical catalytic cycle ([Fig. 10](#)).

The same complex **15** was lately studied by the Jones group [\[96\]](#) under harsher conditions (150 °C, 24 h, 25 mol% KOH, 0.5 mol% catalyst), which reported 30% ethanol conversion, 11% butanol yield, 3% yield of higher alcohols (C₆-C₈) and 16% of carbon loss. Considering the low cost of the metal, these performances start to be competitive with ruthenium based systems. The missing ethanol was related to the

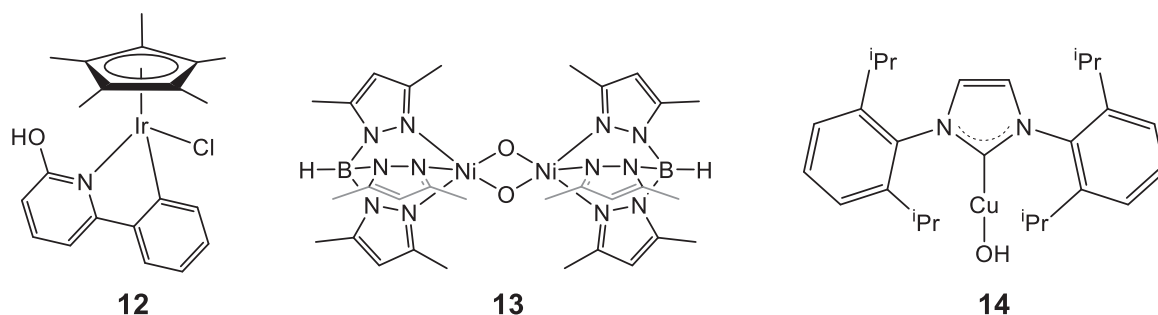


Fig. 8. Transition metal complexes employed in the catalytic tandem systems **12**, **13** and **12**, **14** developed by Baker and Jones exploiting **13** or **14** as the co-catalytic bases. [\[94\]](#).

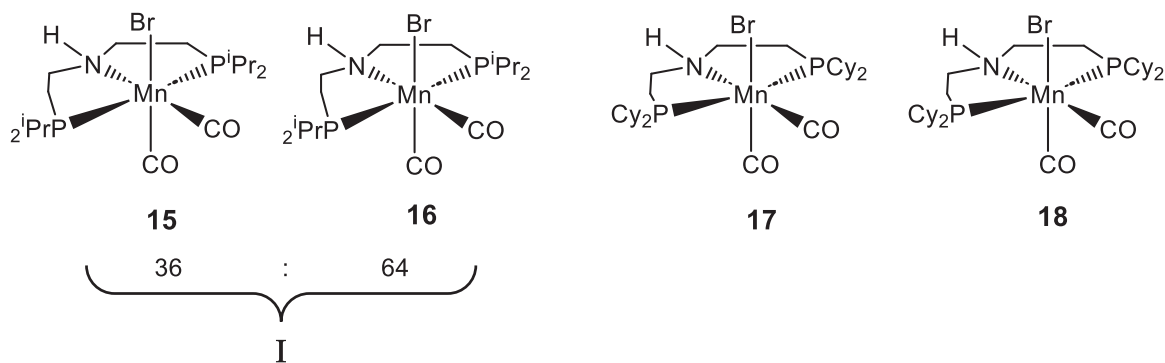


Fig. 9. P-N-P pincer manganese complexes **15-18** active in the homologation of ethanol to butanol and higher alcohols. [95].

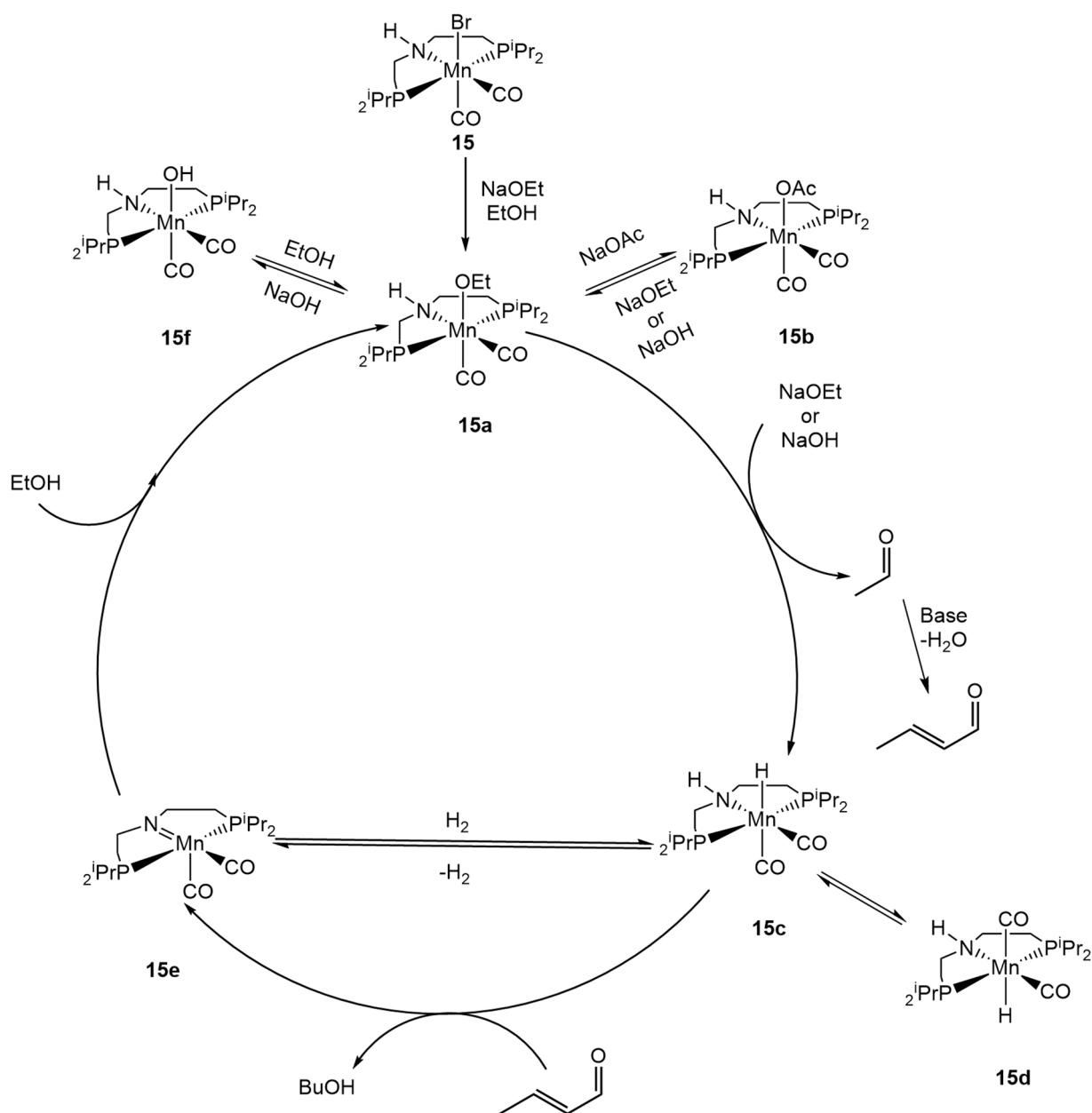


Fig. 10. Catalytic reaction mechanism proposed by Liu [95] for a manganese complex bearing a P-N-P ligand (**15**) as pre-catalyst.

expected co-production of sodium acetate and H₂ release was observed in the head of the reactor. Authors explored different bases to catalyse aldol condensation and many catalyst/base ratios to improve selectivity finding that NaOEt (25 mol%) with a catalyst loading of 0.5% was the best combination (62% ethanol conversion, 30% BuOH yield, 10% C₆-C₈ alcohols yield at 24 h). Reactivity studies on the catalyst confirmed that **15** can react with the base, creating an activated complex **15e** (Fig. 11).

The base, then, keeps the catalyst active during the reaction. The amine proton is also playing a crucial role, but the authors did not exclude an alternative minor secondary activation path not involving it.

Finally, to study steric and electronic influence of the ligand, a series of complexes employing different substituents on phosphorus atoms of the pincer scaffold were tested in catalysis. As in the previous paper, bulky ligands dramatically lowered catalytic activity, while electronic effects seemed to play a key role in the activity of the system.

In 2020, Wass et al. [97] reported on the most recent application of a first-row transition metal in the Guerbet reaction. Two manganese diphosphine and phosphinoamine complexes **19** and **20** were tested on ethanol homologation to butanol after they demonstrated to be active in the formation of isobutanol from ethanol and methanol (Fig. 12).

Complex **20** revealed to be moderately active, reaching a TON of 100 after 90 h of reaction with a catalytic loading of 0.05 mol% at 150 °C with 10 mol% NaOEt. A 15.5% ethanol conversion was observed with 4.8% butanol yield and 0.34% of C₆ alcohols yield. Complex **19** however, showed little activity reaching only 0.73% conversion in the same conditions due to lower stability. Indeed, complex **19** upon addition of the base is subjected to a detrimental partial ligand redistribution to a monochelated complex.

First row transition metals are still extremely poorly explored in this process. Anyway the promising results reported pave the way for their future development. Limiting side reactions, promoting aldol condensation and catalyst stability seem to be the pivotal points that research need to focus on to address cheaper and more sustainable catalysts.

2.3. Mechanistic investigation

2.3.1. The theoretical approach

In the last two decades, density functional theory (DFT) calculations have been demonstrated to be reliable and crucial tools to unravel complicated reaction mechanisms, especially if paired with kinetic simulations. [98] However, theoretical approaches find their maximum potential when simulations are performed in synergy with experiments. [99].

As discussed in the previous sections, the mechanism of the Guerbet reaction usually involves two catalytic species: a dehydrogenation/hydrogenation catalyst and an acid/base catalyst that cooperate to homologate alcoholic substrates. As simple in theory as challenging in practice, the reaction mechanism is still far from being extensively disclosed. Wass and co-workers in 2016 claimed that answering questions regarding mechanism could pave the way for rational catalyst design. [53] Regarding theoretical investigations, at the best of our knowledge only one work was published about mechanistic insights via DFT calculations for the Guerbet reaction in homogeneous phase. [100] In 2019

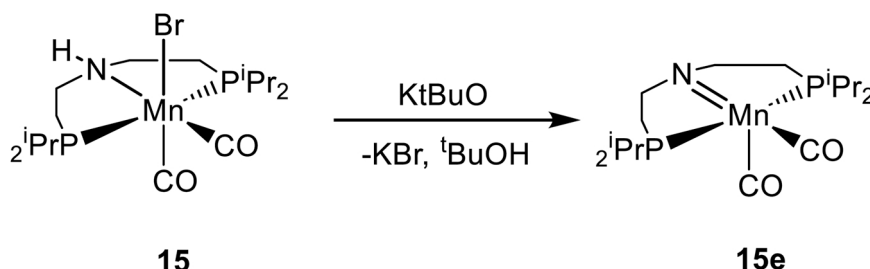


Fig. 11. Reactivity of complex **15** with KtBuO proposed as the pre-catalyst activation pathway. [96].

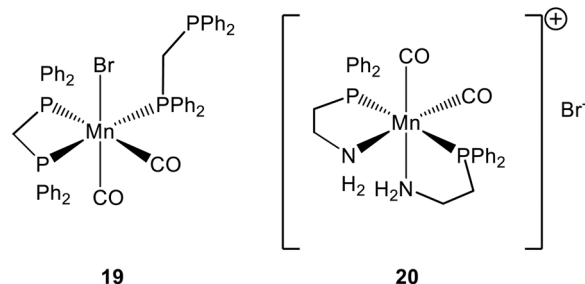


Fig. 12. Bischelated P-P and P-N manganese complexes **19** and **20** reported by Wass^[97] as suitable pre-catalysts for the Guerbet reaction.

Pathak and co-workers characterized the reaction mechanism of the catalytic upgrading of ethanol to 1-butanol in the presence of an aliphatic Mn-P-N-P-Br complex and sodium ethoxide (previously described in paragraph 2.2) [95,96] using DFT calculations. [100] The authors computed the free energy surface (FES) of the reaction using the golden standard B3LYP functional [101–104] and the 6–311++G(d,p) [105–107] basis set for all the atoms, except for Mn for which the LANL2D basis set [108,109] was employed. Thermal and solvent (modeled as conductor-like polarizable continuum model, CPCM, for THF) [110,111] corrections were considered as well as D3 dispersion corrections. [112] Pathak and co-workers confirmed that the reaction mechanism follows i) dehydrogenation of ethanol to acetaldehyde, ii) aldol condensation to crotonaldehyde, and iii) its hydrogenation to 1-butanol, as already proposed for the Mn-PNP-Br catalyst by Liu et al. [95] Thanks to the computational insights, the authors established that steps i) and iii) are catalyzed by the Mn complex as a bifunctional catalyst since the metal centre cooperates with the N-site for proton/hydride borrowing (species **15e**, Fig. 10), while step ii) is base catalyzed by NaOEt. The theoretical investigation also provided insights into selectivity distribution and validations of experimental observations. Liu et al. experimentally isolated a stable adduct between the Mn-P-N-P catalyst and NaOEt (species **15a**, Fig. 10), [95] which also Pathak and co-workers computationally observed and claimed as the resting state of the process, due to its high stability in energy. [100] DFT calculation also confirmed that butanol is the favoured intermediate of step iii) rather than crotyl alcohol, which is produced as well, but hardly reduced to 1-butanol. [95,100] Insights regarding the selectivity issue between 1-butanol and C₆ alcohols were possible thanks to a direct comparison between the FESs of the aldol condensation pathways with acetaldehyde or crotonaldehyde as starting materials. The latter leads to a FES which is higher in energy, making C₆ products kinetically disfavoured and increasing the selectivity of the process to 1-butanol. The authors also carried out microkinetic simulations of a simplified mechanism starting from DFT outcomes, showing the effect of changing some of the factors governing the reaction, such as temperature or concentration of ethanol, over yield and selectivity.

The paper of Pathak and co-workers is a good example of the potential of DFT calculations in exploiting challenging chemical pathways. [100] We hope that new theoretical works about the Guerbet reaction

will be published, especially putting the accent on the potential of a combined experimental/computational approach to disclose the reasons behind the behaviours of many of the catalysts reported in literature. Such an approach is promising to tackle the problem of designing new and more efficient ways to carry out the Guerbet reaction.

2.3.2. Experimental and modeling approaches

First and unique, up to date, experimental and simulation synergic approach aimed to gain insight into the kinetic behaviour of the Guerbet reaction network, was reported in 2021 by Liauw and co-workers. [113] They also proposed a reason for the uneffective catalytic activity of Ru-MACHO-BH, a bifunctional ruthenium catalyst expected to work since useful for hydrogen borrowing. [114] This systematic approach exploited time-resolved concentration profiles determined with in-situ infrared spectroscopy (IR) to depict kinetic with the help of chemometrics models for aldol condensation (base KO^tBu) and ethyl acetate saponification (subsystems 3 and 4 in Scheme 4). Redox subsystems 1 and 2, consist in several steps involving redox catalytic species (deriving from Ru-MACHO-BH pre-catalyst), [115–118] that are not detectable under process conditions. The related kinetic model is created from activation barriers of DFT calculations found in the literature, [119–121] adapting barrier heights to reproduce the experimental concentration profiles. Kinetic models were then integrated into a microkinetic model of the entire network of the homogeneous Guerbet reaction with MatLab.

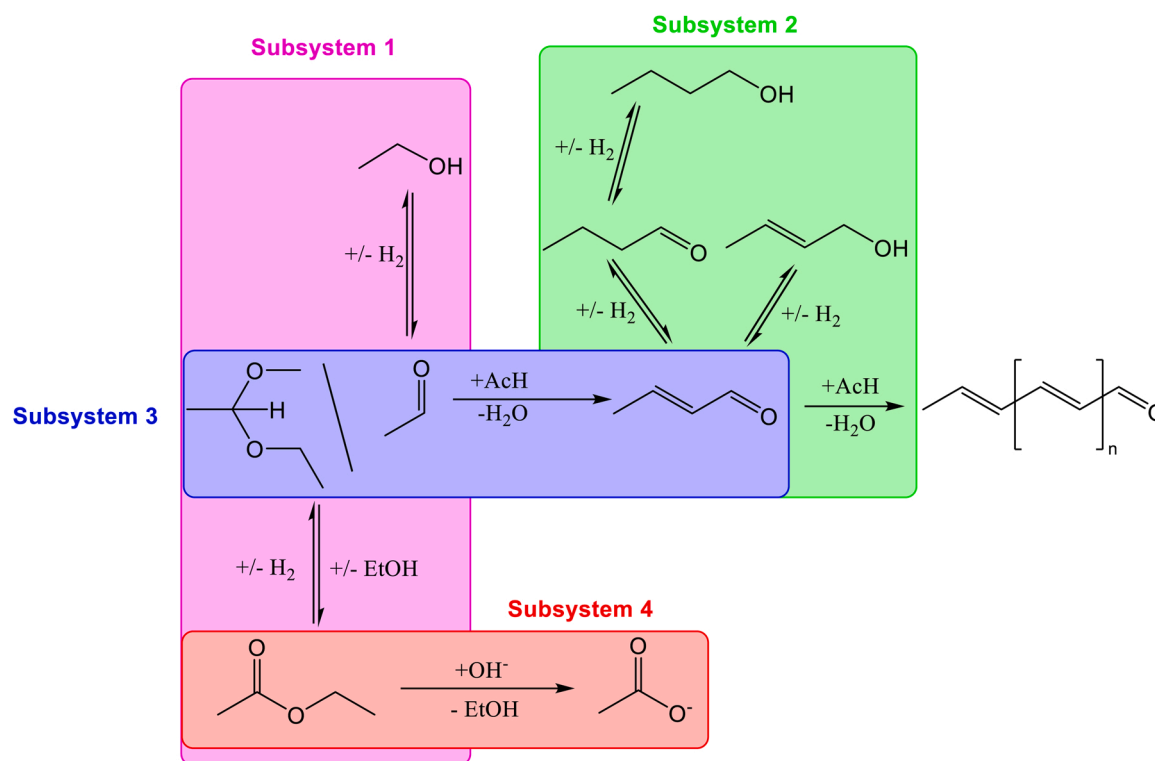
As generally defined in previous descriptions, the Guerbet reaction from ethanol to higher alcohols in homogeneous liquid systems is influenced by catalyst, base concentrations, water production, temperature and (hydrogen) pressure. The main side reactions are the polymerization of acetaldehyde to heavy components and the formation of acetates (also ethylacetate as an intermediate) that consumes the base. All these parameters were screened from experimental tests through simulation toward the conclusion that no parameter variation could lead to high butanol yields if Ru-MACHO was used as redox catalyst. The

additional benefit of the microkinetic simulation thus consists of understanding the reason why the catalyst fails in the reaction. This knowledge could help to identify critical properties of a successful redox catalyst for the Guerbet reaction. The main problem is that the saponification reaction proceeds with the increment of water. This problem should be solved with water tolerant catalysts, which are likely to have a higher activation barrier for dehydrogenation (ethanol to acetaldehyde) if compared with Ru-MACHO. However, this hypothesis still cannot be confirmed by further simulation probably due to overestimated rate coefficients of aldol condensation and the absence of uncatalyzed Cannizzaro reaction in the model. Nevertheless, this information about a role of high activation barrier for dehydrogenation is an important descriptor of a good Guerbet redox catalyst and may be used for the design of new Guerbet homogeneous catalysts.

Another important experimental study on the role of reaction parameters and on how bifunctional homogeneous ruthenium catalysts performs was proposed by the group of Guironnet in 2022. [122] Indeed, one of the Szymczak catalysts, namely 2-H, was employed in a flow reactor, with the principal aim to shed light on the self condensation reaction mechanism and to increase the knowledge on the design of stable and better performing catalytic systems suitable for industrial application. In fact, although a positive effect of homogeneously catalysed Guerbet reaction on selectivity is well established, currently the fundamentals of this selectivity are not yet fully understood.

Usually, homogeneous Guerbet catalysts are employed in closed batch reactors at 120–150 °C and these conditions, together with the fact that reactants can be found both in the liquid and in the vapor phase, make kinetic studies difficult. In the work by Guironnet, the authors took advantage of the steady-state kinetic analysis usually employed for heterogeneous catalysts in flow systems [10,11].

In a specifically designed continuous stirred-tank reactor (CSTR) (Fig. 13), the vapor-liquid equilibrium was exploited in order to maintain the homogeneous catalyst concentration at a constant value. Taking inspiration from industrial processes that use homogeneous catalysts in



Scheme 4. Assumed Guerbet reaction network. Subsystems: 1. The redox system of C2-substances (ethanol, acetaldehyde/1-ethoxyethanol and ethyl acetate); 2. the redox system of C4-substances (crotonaldehyde, crotyl alcohol, butanal, butanol), 3. the aldol condensation of acetaldehyde and 4. the saponification of ethyl acetate. [113].

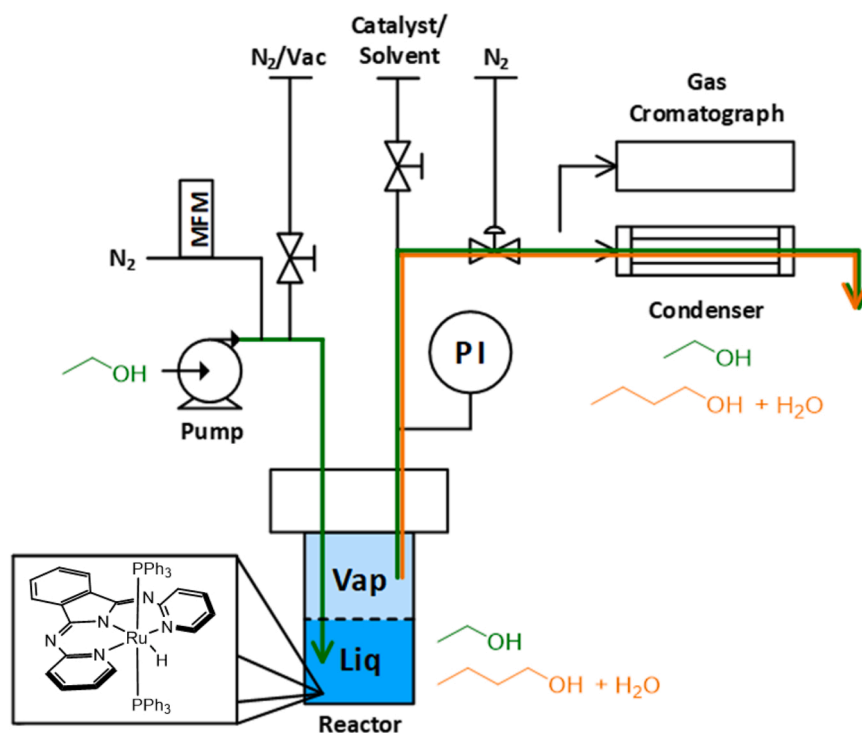


Fig. 13. Schematic for continuous stirred-tank reactor designed by the group of Guironnet [122] to study the Guerbet reaction catalysed by a ruthenium molecular complex (2-H) under flow conditions.

continuous flow reactors (e.g. Ruhrchemie/Rhone-Poulenc, Monsanto/Cativa processes and Shell higher olefin) [123–125] the catalyst was dissolved in a non-volatile solvent (the best was defined as a low

molecular weight polyethylene glycol (PEG) MW = 500 g mol⁻¹), while the volatile substrates were fed continuously. The key reaction steps were investigated independently measuring the composition of the

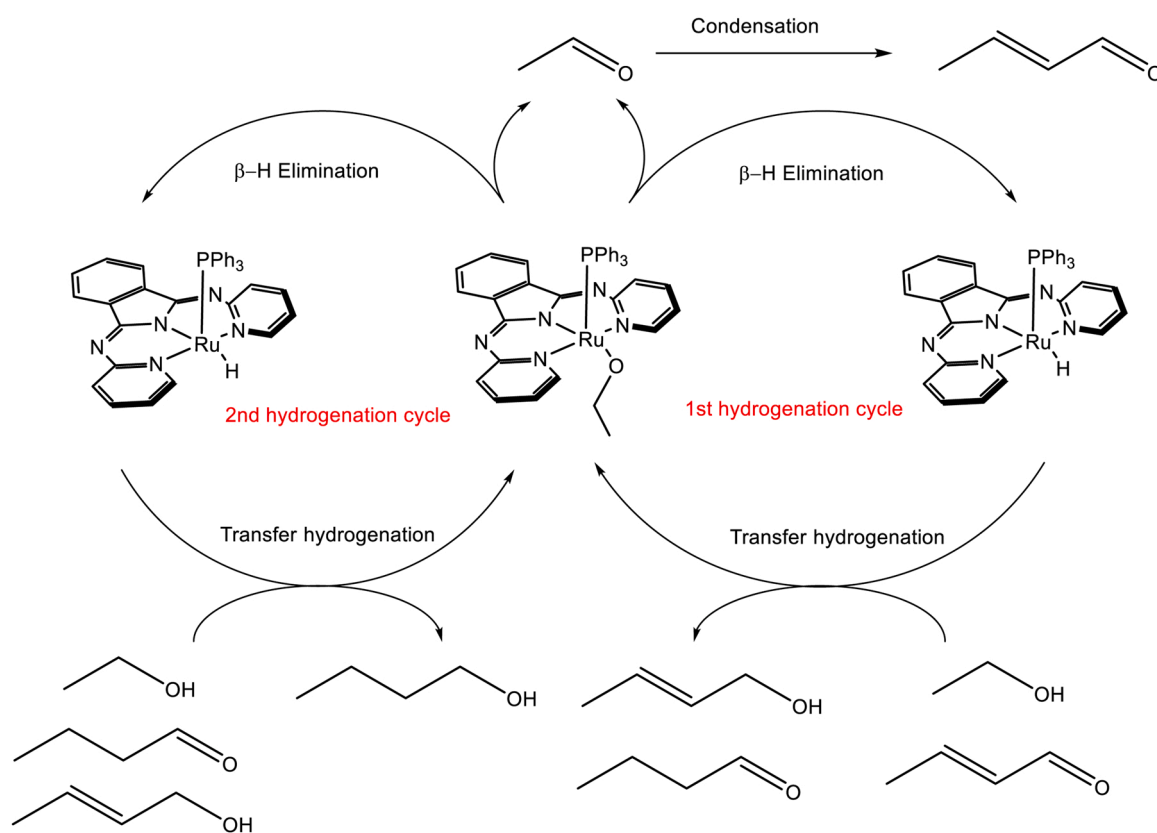


Fig. 14. Guerbet mechanism proposed by author for 2-H to proceed via transfer hydrogenation. [122].

vapor outlet stream from the reactor by on-line gas chromatography. The flow reactor setup allowed to analyze the catalyst activity under quasi-steady-state conditions without altering its chemical structure.

Reaction condition screening highlighted the absence of mass transfer limitations: the rate of mass transfer was rapid in comparison to the Guerbet reaction; thus the concentration of ethanol was constant throughout the liquid phase. No mass transfer effects were detectable between the liquid phase and the headspace. More in general, from a mechanistic perspective, the authors established what summarized in the following, under their standard operating conditions (PEG 5.33 mL, NaOEt 386 mM, **2-H** 0.66 mM, N₂ 8.4 mL min⁻¹, EtOH 1.25 μL min⁻¹, Pressure 16 psi, Residence time 35 s, Temperature 120 °C, acetaldehyde, butanol, 2-ethyl-butanol, and hexanol as major products exiting the reactor) and considering that ethanol conversion for flow coupling was kept below 5 mol% to ensure quasi-steady-state kinetics:

- **2-H** did not exhibit any selectivity for 1-butanol from ethanol coupling, which was confirmed by comparing experimental ($C_4/C_6 = 4$) product distribution with a prediction calculated using a random step-growth condensation model based on Flory's equal reactivity principle [126] ($C_4/C_6 = 40$) at equal conversion (2.5 mol%);
- hydrogenation was fast compared to aldol condensation and **2-H** operated through a hydrogen-transfer pathway, with β-hydride elimination as the rate limiting step defined by the absence of unsaturated C₄ intermediates. The assumptions of a very high speed for the hydrogenation step could be, indeed further underlined considering the short residence time and the low substrate concentrations. On these basis, a reaction mechanism involving two cycles was proposed: one for the monounsaturated and one for the diunsaturated product (Fig. 14).
- the formation of acetates, attributable to Cannizzaro disproportionation reaction (as expected) and characterized by low volatility, was accounted for the lack of gas-phase mass balance and detected in control experiments in batch reaction;
- the authors eventually established that molecular hydrogen, while potentially formed during the reaction, does not participate in the hydrogenation reaction.

2.4. Co-condensation of ethanol and methanol to isobutanol

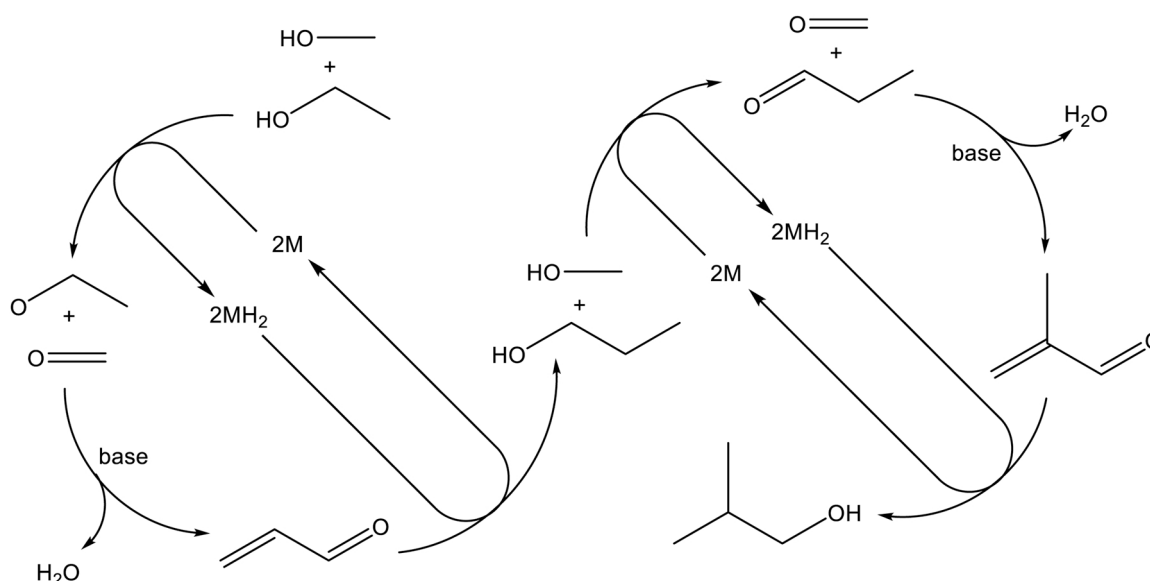
Within the framework of ethanol upgrading to advanced biofuel, in addition to butanol and higher chain alcohols, a renewed interest in the

production of isobutanol has been growing in recent years. The great interest in isobutanol stems from its superior fuel properties, such as a higher energy density and octane number, over n-butanol, making the branched isomer an ideal gasoline additive. [53] A borrowed hydrogen process via adapted Guerbet-type mechanism provides a potential route for the synthesis of isobutanol using ethanol and methanol as substrates.

The co-condensation reaction of ethanol and methanol (easily available feedstock) was firstly investigated by heterogeneous catalysis employing metal oxides (MgO, ZnO, CaO, ZrO₂), [127] heterogeneous Copper-based catalysts, [128] MgO impregnated on carbon support, [129] and immobilized Iridium catalysts [130] which allow to reach high conversion but with low selectivity, using high reaction temperature and high catalyst loading. Very recently, a series of homogeneous catalysts have been tested in order to obtain an enhanced selectivity under milder operative conditions. The proposed mechanism via Guerbet process for the formation of isobutanol involves two linked cycles, each comprising dehydrogenation, aldol coupling and hydrogenation steps. At first, equimolar amounts of methanol and ethanol form one equivalent of n-propanol which subsequently reacts with a second molecule of methanol to produce isobutanol and two equivalents of water as the only by-product (Scheme 5). [53].

Avoiding alcohol homocoupling is fundamental in order to favour higher selectivity towards isobutanol. For this reason, the co-condensation reaction is usually performed in excess of methanol, facilitating higher conversion of ethanol (the limiting reagent), and high concentration of base co-catalyst, which does not affect the selectivity due to the difficult dehydrogenation of isobutanol. The only product usually detected in very low amount is propanol which is an intermediate of the catalytic process.

Ruthenium complexes with bis-chelate diphosphine and mixed P-N donor ligands (Fig. 14) proved to be effective under the following conditions: molar ratio of methanol/ethanol 14.4:1, yields up to 75% with 99.8% selectivity at 180 °C for 20 h. They were the first homogenous catalysts for the conversion of ethanol/methanol mixtures to isobutanol. [131] The chelated diphosphine (Dppm), with a small bite angle, was confirmed as the most successful diphosphine ligand. A large excess of base (200 mol% of NaOMe vs ethanol) is required to maintain the efficiency of the system. The catalyst performs well also with sodium hydroxide and wet ethanol, maintaining good conversion and yields at shorter reaction times (yield 74% and selectivity 96%). On the other hand, P-N ligands were less active, needing a longer reaction time to obtain similar selectivity. Lowering the temperature or the amount of



Scheme 5. Proposed mechanism for the co-condensation of ethanol and methanol via Guerbet chemistry.[53].

base proved to be detrimental for the catalytic system. Moreover, the recycling tests confirmed the fundamental role of the base co-catalyst; this observation, together with the detected presence of propanol as an intermediate and reaction studies in labeled $^{13}\text{C}_3\text{OH}$, allowed to frame the reaction into a Guerbet-type mechanism.

In subsequent years, Wass et al. deepened the study of the upgrading of MeOH/EtOH mixtures to isobutanol through the Guerbet process with particular attention to Ru pre-catalyst water tolerance, which is an essential feature to extend the catalyst life in a hydrated environment without the need to perform an expensive and energy-intensive drying step. In fact, water produced during the reaction adds up to the pre-existing water content in the alcoholic feedstock. [132] In this case the study was also extended to P-N-P tridentate ligand (**23** in Fig. 15). Under the standard conditions (methanol to ethanol molar ratio of 14.4:1, catalyst loading of 0.1 mol%, NaOMe base as co-catalyst with loading of 200 mol%, reaction temperature of 180 °C), the latter showed a similar catalytic activity to the phosphinoamine based Ru catalyst in terms of yield and selectivity, confirming *trans*-[RuCl₂(dppm)₂] (**21**) as the most efficient pre-catalyst. This is even more marked using NaOH as base and when some water is added to the system. Actually, the use of NaOH as base in presence of water led to a small increase in isobutanol yield (71%) keeping high selectivity (97%); this could be explained by the fact that water is able to convert sodium methoxide to methanol and sodium hydroxide. Conversely, this is detrimental in the case of P-N and P-N-P ligands due to the easy formation of a substantial amount of solid side-products (consisting of sodium formate, carbonate and acetate) that affect negatively the yield and selectivity in the Guerbet products. By adding a large amount of water (molar ratio of methanol:ethanol:water of 14.4:1:16.2) to the system comprising the pre-catalyst **20**, an isobutanol yield of 36% at high selectivity (78%) was obtained, confirming the high water tolerance of this catalyst. Finally, the stability of the catalytic system was also confirmed by the authors using commercial alcoholic drinks as ethanol sources.

Inspired by Wass' work, Mansell et al. investigated the influence of the bidentate 2-phosphinophosphinine ligand on the catalytic activity of ruthenium complexes in hydrogen borrowing reactions. [133] However, under the same Guerbet operating conditions, these pre-catalysts were less active, providing an isobutanol yield of 38% with 88% selectivity. Conversely, a similar behaviour to P-N donor ligands was observed by increasing the reaction time to 20 h: 50% in isobutanol yield with 96% selectivity versus 51% yield with 90% selectivity.

As already outlined for ethanol homologation, in order to improve the sustainability of the Guerbet process, the replacement of expensive noble-metal catalysts with first-row base metals has received an increased attention in recent years, proving to be a great challenge. In 2017 Liu et al. reported the first homogeneous non-noble-metal catalyst for the direct homologation of ethanol to n-butanol. [95] Furthermore, the catalytic activity of a series of manganese (I) pincer P-N-P catalyst (**15** in Fig. 11) were evaluated by Liu et al. also in the upgrading of ethanol with methanol into isobutanol. [134].

The catalytic reaction, composed of ethanol (1 mL), methanol (10.4 mL), Mn catalyst (0.05 mol% based on ethanol), and NaOMe (350 mol% based on ethanol) was performed at 160 °C for 16 h leading to an isobutanol yield of 28% with 80% selectivity. A notable TON value of 9233 was further achieved with pincer P-N-P Mn-catalyst **15** by increasing the reaction temperature to 200 °C for 48 h with a very low

catalyst loading.

In 2020 also Wass and co-workers turned their attention to the first-row transition metal complexes as an alternative to noble-metals. Inspired by the pioneering work of Liu et al. on Mn-pincer P-N-P complexes, they synthesized a variety of manganese bis-chelated complexes (e.g. **19** and **20** in Fig. 2), in order to evaluate the influence of the surrounding ligands on the catalytic activity in the co-condensation of ethanol and methanol to isobutanol via Guerbet-type process. [97].

A longer reaction time is needed (90 h) under the reaction conditions previously employed for similar ruthenium complexes [67,68] (EtOH/MeOH 1:14.4, catalyst loading 0.1 mol%, NaOMe 200 mol%, 160 °C). The trend of the catalytic activity of the differently substituted Mn-complexes resembles that of the ruthenium congeners, confirming dppm-based ligand the most effective for isobutanol production (iBuOH yield 11%, 69% selectivity). This behaviour suggests a ligand-assisted mechanism which is still under investigation by the group.

Comparing the performance of bis-chelated Mn complexes with the pincer P-N-P Mn-catalyst, this latter resulted more active at lower running times (10% isobutanol yield in 4 h) with a very high ethanol conversion (78%). This data indicates significant solid by-product formation identified by NMR analysis mainly as sodium formate probably derived from Cannizzaro-type reaction with methanol.

The same considerations done for ethanol homologation can be transferred to the Mn-catalyzed transformation of ethanol and methanol into isobutanol. Quite harsh conditions and poor conversion still affect this family of catalysts, which on the other hand show, in some cases, promising stability. Although challenging, it is worth the risk to keep designing new molecular catalysts based on first-row transition metals for the Guerbet reaction, as a highly recommended evolution from both an economic and an environmental point of view.

3. Summary and outlooks

The Guerbet reaction, especially when applied to bio-ethanol refining by homologation, is an intriguing and win over reaction. Its mechanism is as elaborate, due to the requirement of multitasking catalytic systems, as (in principle) elegant, thanks to the high atom economy.

However, an industrial scale-up of second-generation biofuels-production processes from bio-ethanol waste-derived feedstocks is still thwarted by several critical technological issues and bottleneck steps. Indeed, one of the main abilities that prevents this reaction from becoming cost effective is the low efficiency in selectivity and conversion.

Although research in heterogeneous catalysis is still flourishing and in promising evolution in this field, the historical successful experience in the homogeneously catalyzed OXO reactions, selectively driven by rhodium complexes, led several researchers to look at the Guerbet process also on a homogeneous perspective.

Several molecular bi-functional complexes, based on ruthenium, iridium and lately manganese, mainly selected for their ability in hydrogen borrowing reactions, revealed their efficiency in ethanol homologation in the liquid phase.

Several ligands such as phosphine, bidentate bisphosphine (P-P) and phosphamine (P-N), pincer (N-N-N), (P-N-P) and cyclopentadienone, in ruthenium complexes with catalytic loading in a range of 0.02–0.5 mol

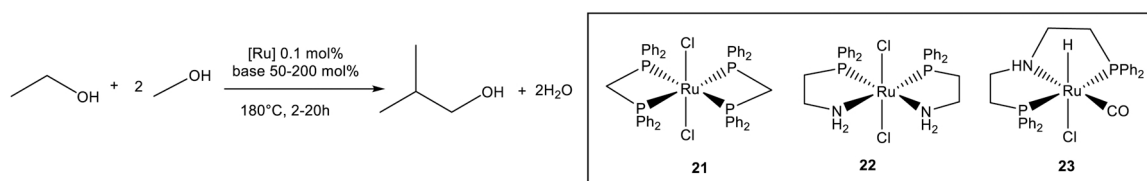


Fig. 15. P-P, P-N and P-N-P chelating complexes **21**, **22** and **23** exploited by Wass [131] for the cross-condensation of ethanol and methanol to iso-butanol.

%, are effective in promoting the reaction with a general inversion in butanol selectivity while increasing the conversion. Anyway, when considering the valorization of butanol and higher alcohols (up to C₁₀) as bio-fuel, conversion exceeds 50% with high selectivity.

Combining ruthenium cyclopentadienone catalyst **7** with benzoquinone as a co-catalyst improves the conversion by more than 20%, maintaining the overall selectivity in higher alcohols (C₄-C₁₀) higher than 95%.

Some of the catalysts were water tolerant (**7**, **11**, **21**) and were found effective in the transformation of real mixtures, such as fermentation broths and bio-ethanol from wine industry waste, into alcohol blends which are, in principle, readily available as second generation bio-fuel.

Although the results are much improved, thus becoming very competitive with the heterogenous counterparts, some important issues need to be highlighted and remain still unsolved for all the systems studied:

- i) a base co-catalyst in high mol% (>20%) is needed;
- ii) the base is lost during the reaction due to Cannizzaro side reaction, which produces acetates as wastes;
- iii) TON (the higher calculated for less efficient catalytic loading at very low conversion for long time reaction) and TOF are far from being cost effective;
- iv) recyclability, stated for ruthenium cyclopentadienone **7** and relative catalytic systems (**7**/BQ) run effectively for few cycles. LCA and engineering scale-up studies, although interesting, since they were employed for the first time in homogeneous Guerbet reaction, assessed the need to recycle the catalysts many more times in order to have in hand a process applicable from both a cost and an environmental point of view.

Interestingly, in all the reported cases, a substantial sensitivity to minimal changes in ligand environment, both in terms of steric encumbrance and electronic behavior, highlights the huge importance of fine tuning in the design of novel complexes for this application.

Several bases were applied to reduce the co-catalyst impact to the reaction. This is a difficult problem to resolve, but the authors believe that there is still room for co-catalysts investigation.

An essential purpose to gain efficiency in homogeneous catalysts for the Guerbet reaction is to increase the effort in mechanistic insight, which is currently led by experimental approaches. A nice correlation between in situ characterization and theoretical simulations found application in understanding the reason for the failure in alcohol homologation of some hydrogen borrowing catalysts. Another group screened the reaction conditions with an innovative reaction design in flow chemistry. Working at low conversion with an N-N-N pincer ruthenium catalyst supported on PEG allowed to obtain further information on reaction and catalyst behavior. Quite surprisingly, only one example of DFT calculation was reported for the mechanism study.

The homogeneous approach to the Guerbet reaction is still a matter of challenging research. Main problems to be solved regard the base co-catalyst, the metal-based catalyst stability and recyclability.

Further development would be necessary for mechanistic investigation in order to help the design of more efficient and stable catalysts, simplifying the experimental (trial and error) approach.

Nevertheless, studies on molecular metal based catalysts stability are currently underdeveloped. Indeed, they deserve more experimental effort in order to identify, as an example, the form of the catalyst in the resting states. The principal aim, in authors' opinion, should be at first to understand if their final form is irretrievably deactivated or not. In the latter case the design of a strategy for the stabilization of the molecular active form of the catalyst, or the regeneration of the pre-catalyst, could lead to systems suitable for multiple recycling. With this as a compulsory condition in order to imagine an industrial development.

On the other hand, catalyst immobilization toward the formation of a more stable and easily recoverable solid would be desirable in order to

improve the applicability of molecular or hybrid catalysts to liquid phase Guerbet reaction. Within this field, unless the Van der Waals' weak interactions on PEG employed to study the reaction under flow conditions, no literature is available. More stable and better recyclable systems could be developed exploiting ionic or covalent bonded functionalized metal complexes on suitable solid supports. Furthermore, support environment itself could favour the stability improvement and, in the best scenario, it could also be non-innocent in the reaction performances. In order to move to real application, it remains the mandatory need of a supported molecular catalyst that is active or reactivable in its final stable or stabilized by regeneration form.

Credit author statement

All author have contributed to the literature research, to the discussion and to the writing. In particular Anna Gagliardi, Tommaso Tabanelli and Fabrizio Cavani for the introducing overview on heterogeneous catalysis; Alessandro Messori, Cristiana Cesari and Rita Mazzoni for the central description of advances in homogeneous catalysis; Francesco Calcagno for the DFT calculations.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data Availability

No data was used for the research described in the article.

Acknowledgements

We gratefully acknowledge the University of Bologna.

References

- [1] a) <https://www.europarl.europa.eu/news/en/headlines/society/20180920STO14027/reducing-car-emissions-new-co2-targets-for-cars-and-vans-explained>; b) <https://www.europarl.europa.eu/news/en/headlines/economy/20221019STO44572/eu-ban-on-sale-of-new-petrol-and-diesel-cars-from-2035-explained>.
- [2] <https://www.iea.org/data-and-statistics/charts/global-biofuel-production-in-2019-and-forecast-to-2025>.
- [3] [https://afdc.energy.gov/vehicles/flexible_fuel_emissions.html#:~:text=Carbon%20dioxide%20\(CO2\)%20released,conventional%20vehicles%20per%20mile%20traveled;Life-Cycle%20Greenhouse%20Gas%20Emission%20Reductions%20of%20Ethanol%20with%20the%20GREET%20Model](https://afdc.energy.gov/vehicles/flexible_fuel_emissions.html#:~:text=Carbon%20dioxide%20(CO2)%20released,conventional%20vehicles%20per%20mile%20traveled;Life-Cycle%20Greenhouse%20Gas%20Emission%20Reductions%20of%20Ethanol%20with%20the%20GREET%20Model).
- [4] M.K. Akhtar, H. Dandapani, K. Thiel, P.R. Jones, Microbial production of 1-octanol: a naturally excreted biofuel with diesel-like properties, *Metab. Eng. Commun.* 2 (2015) 1–52.
- [5] B.G. Harvey, H.A. Meylemans, The role of butanol in the development of sustainable fuel technologies, *Chem. Technol. Biotechnol.* 86 (2011) 2–9.
- [6] C. Yang, Z.Y. Meng, Bimolecular condensation of ethanol to 1-butanol catalyzed by alkali cation zeolites, *J. Catal.* 142 (1993) 37–44.
- [7] D.D. Petrolini, N. Eagan, M.R. Ball, S.P. Burt, I. Hermans, G.W. Huber, J. A. Dumesic, L. Martins, Ethanol condensation at elevated pressure over copper on AlMgO and AlCaO porous mixed-oxide supports, *Catal. Sci. Technol.* 9 (2019) 2032–2042.
- [8] C. Cesari, A. Gagliardi, A. Messori, N. Monti, V. Zanotti, S. Zacchini, I. Rivalta, F. Calcagno, C. Lucarelli, T. Tabanelli, F. Cavani, R. Mazzoni, Boosting the guerbet reaction: a cooperative catalytic system for the efficient bio-ethanol refinery to second-generation biofuels, *J. Catal.* 405 (2022) 47–59.
- [9] S. Hanspal, Z.D. Young, H. Shou, R.J. Davis, Multiproduct steady-state isotopic transient kinetic analysis of the ethanol coupling reaction over hydroxyapatite and magnesia, *ACS Catal.* 5 (2015) 1737–1746.
- [10] T. Moteki, D.W. Flaherty, 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.
- [11] C.R. Ho, S. Shylesh, A.T. Bell, Mechanism and kinetics of ethanol coupling to butanol over hydroxyapatite, *ACS Catal.* 6 (2016) 939–948.
- [12] M. León, E. Díaz, S. Ordóñez, Ethanol catalytic condensation over Mg–Al mixed oxides derived from hydrotalcites, *Catal. Today* 164 (2011) 436–442.
- [13] J. Scalbert, F. Thibault-Starzyka, R. Jacquot, D. Morvan, F. Meunier, Ethanol condensation to butanol at high temperatures over a basic heterogeneous

- catalyst: How relevant is acetaldehyde self-aldolization? *J. Catal.* 311 (2014) 28–32.
- [14] A. Chiericato, J. Velasquez Ochoa, C. Bandinelli, G. Fornasari, F. Cavani, M. Mella, On the chemistry of ethanol on basic oxides: revising mechanisms and intermediates in the Lebedev and Guerbet reactions, *ChemSusChem* 8 (2015) 377–388.
- [15] A.J. Scheide, E. Barbosa-Coutinho, M. Schwaab, N.P.G. Salau, 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.
- [16] A.S. Ndou, N. Plint, N.J. Coville, Dimerisation of ethanol to butanol over solid-base catalysts, *Appl. Catal. A: Gen.* 251 (2003) 337–345.
- [17] D. Gabriëls, W. Yesid Hernández, B. Sels, P. Van Der Voort, A. Verberckmoes, Review of catalytic systems and thermodynamics for the Guerbet condensation reaction and challenges for biomass valorization, *Catal. Sci. Technol.* 5 (2015) 3876–3902.
- [18] A.R. Arjona, J.L. Sanz Yague, A. Corma Canos, M.E. Domine, Catalyst for the production of higher alcohols. Patent WO2014001595A1 (2014) assigned to Abengoa bioenergía nuevas tecnologías SA.
- [19] J. De Maron, M. Eberle, F. Cavani, F. Basile, N. Dimitratos, P.J. Maireles-Torres, E. Rodríguez-Castellón, T. Tabanelli, Continuous-flow methyl methacrylate synthesis over gallium-based bifunctional catalysts, *ACS Sust. Chem. Eng.* 9 (2021) 1790–1803.
- [20] L. Izzo, T. Tabanelli, F. Cavani, P. Blair Vásquez, C. Lucarelli, M. Mella, The competition between dehydrogenation and dehydration reactions for primary and secondary alcohols over gallia: unravelling the effects of molecular and electronic structure via a two-pronged theoretical/experimental approach, *Catal. Sci. Technol.* 10 (2020) 3433–3449.
- [21] T. Tabanelli, S. Cocchi, B. Gumina, L. Izzo, M. Mella, S. Passeri, F. Cavani, C. Lucarelli, J. Schütz, W. Bonarath, T. Netscher, Mg/Ga mixed-oxide catalysts for phenol methylation: Outstanding performance in 2,4,6-trimethylphenol synthesis with co-feeding of water, *Appl. Catal. A Gen.* 552 (2018) 86–97.
- [22] J.L. Sanz Yague, J.D. Martínez Perez, Y. Pena Gomez C.M. Reyes Valle, M.R. Sanchez, Process for the preparation of higher alcohols from lower alcohols by guerbet condensation, patent (2015) WO2015097285A1 assigned to Abengoa Bioenergía Nuevas Tecnologías S.A.
- [23] <https://www.ieabioenergy.com/wp-content/uploads/2015/02/IX2-Chartartegui-Abengoa-2nd-generation.pdf>.
- [24] B. Zhang, D. Peña Fuentes, A. Börner, Hydroformylation, *ChemTexts*, 2022, p. 2.
- [25] I. Veza, M.F.M. Said, Z.A. Latif, Progress of acetone-butanol-ethanol (ABE) as biofuel in gasoline and diesel engine: a review, *Fuel Process. Technol.* 196 (2019), 106179.
- [26] <https://www.catalyxxinc.com/>.
- [27] <https://www.sasolguerbet.com/about-us/>; https://www.sasolguerbet.com/fileadmin/user_upload/0280.SAS-BR-Isosol_WEB.pdf.
- [28] E. Scherf, H. –J. Letsch, C. Schroeder, A.T. Herrmann Method for producing metal-free Guerbet alcohols. Patent US6419797B1 (2002) assigned to Sasol Germany GMBH.
- [29] A.T. Herrmann, H. Ziehe, D. Schaefer, E.-O. Toensen, C. Schroeder Production of Guerbet acids comprises reaction of a Guerbet alcohol in the presence of a dehydrogenation catalyst to form a Guerbet aldehyde followed by oxidation with oxygen or an oxygen-containing gas. Patent DE10232458A1 (2003) assigned to Sasol Germany GMBH.
- [30] <https://www.sasolguerbet.com/guerbet-alcohols-and-derivatives/isocarb/>.
- [31] <https://www.sasolguerbet.com/guerbet-alcohols-and-derivatives/guerbet-esters/>.
- [32] X. Wu, G. Fang, Y. Tong, D. Jiang, Z. Liang, W. Leng, L. Liu, P. Tu, H. Wang, J. Ni, X. Li, Catalytic upgrading of ethanol to n-butanol: progress in catalyst development, *ChemSusChem* 11 (2018) 71–85.
- [33] D.L. Carvalho, R.R. de Avillez, M.T. Rodrigues, L.E.P. Borges, L.G. Appel, Mg and Al mixed oxides and the synthesis of n-butanol from ethanol applied catalysis a: general 415–416 (2012) 96–100.
- [34] M.A. Portillo Crespo, F. Vidal-Barrero, L. Azancot, T. Ramírez Reina, M. Campoy, Insights on guerbet reaction: production of biobutanol from bioethanol over a Mg–Al spinel catalyst, *Front. Chem.* 10 (2022), 945596.
- [35] M.F. Guo, M.J. Gray, H. Job, C. Alvarez-Vasco, S. Subramaniam, X. Zhang, L. Kovarik, V. Murugesan, S. Phillips, K.K. Ramasamy, Uncovering the active sites and demonstrating stable catalyst for the cost-effective conversion of ethanol to 1-butanol, *Green. Chem.* 23 (2021) 8030–8039.
- [36] P. Benito, A. Vaccari, C. Antonetti, D. Licursi, N. Schiarioli, E. Rodríguez-Castellón, A.M. Raspolli, Galletti Tunable copper-hydrotalcite derived mixed oxides for sustainable ethanol condensation to n-butanol in liquid phase, *J. Clean. Prod.* 209 (2019) 1614–1623.
- [37] R.A. Dagle; M.V. Dagle, Single-reactor conversion of ethanol to 1-/2-butenes. Patent US20200165176A1 (2020) assigned to Battelle Memorial Institute.
- [38] K.K. Ramasamy, M.F. GUO; M.J. Gray, S. Subramaniam Method of converting ethanol to higher alcohols. Patent US10745330B2 (2020) assigned to Battelle Memorial Institute.
- [39] Y.H. Willinton, K. De Vlieger, P. Van Der Voort, A. Verberckmoes, Ni–Cu hydrotalcite-derived mixed oxides as highly selective and stable catalysts for the synthesis of β -branched bioalcohols by the Guerbet reaction, *ChemSusChem* 9 (2016) 3196–3205.
- [40] O. Micali Perrone, F. Lobefaro, M. Aresta, F. Nocito, M. Boscolo, A. Dibenedetto, Butanol synthesis from ethanol over CuMgAl mixed oxides modified with palladium (II) and indium (III), *Fuel Process. Technol.* 177 (2018) 353–357.
- [41] C. Lopez-Olmos, M.V. Morales, A. Guerrero-Ruiz, I. Rodríguez-Ramos, Continuous catalytic condensation of ethanol into 1-butanol: the role of metallic oxides (M = MgO, BaO, ZnO, and MnO) in Cu-M/graphite catalysts, *Ind. Eng. Chem. Res.* 59 (2020) 16626–16636.
- [42] K.K. Ramasamy, M. Gray, H. Job, C. Smith, Y. Wang, Tunable catalytic properties of bi-functional mixed oxides in ethanol conversion to high value compounds, *Catal. Today* 269 (2016) 82–87.
- [43] S. Hanspal, Z.D. Young, J.T. Prillaman, R.J. Davis, Influence of surface acid and base sites on the Guerbet coupling of ethanol to butanol over metal phosphate catalysts, *J. Catal.* 352 (2017) 182–190.
- [44] C. López-Olmos, M. Virtudes Morales, A. Guerrero-Ruiz, C. Ramirez-Barria, E. Asedegbega-Nieto, I. Rodríguez-Ramos, Continuous gas-phase condensation of bioethanol to 1-butanol over bifunctional Pd/Mg and Pd/Mg–carbon catalysts, *ChemSusChem* 11 (2018) 3502–3511.
- [45] L. Silvester, J.-F. Lamonier, C. Lamonier, M. Capron, R.-N. Vannier, A.-S. Mamede, F. Dumeignil, Guerbet reaction over strontium-substituted hydroxyapatite catalysts prepared at various (Ca+Sr)/P ratios, *ChemCatChem* 9 (2017) 2250–2261.
- [46] D. Jiang, G. Fang, Y. Tong, X. Wu, Y. Wang, D. Hong, W. Leng, Z. Liang, P. Tu, L. Liu, K. Xu, J. Ni, X. Li, Multifunctional Pd@UiO-66 catalysts for continuous catalytic upgrading of ethanol to n-butanol, *ACS Catal.* 8 (2018) 11973–11978.
- [47] J.H. Earley, R.A. Bourne, M.J. Watson, M. Poliakoff Continuous catalytic upgrading of ethanol to n-butanol and >C4 products over Cu/CeO2 catalysts in supercritical CO2. *Green Chem.* 17 (2015) 3018–3025.
- [48] D. Jiang, X. Wu, J. Mao, J. Ni, X. Li, Continuous catalytic upgrading of ethanol to n-butanol over Cu–CeO₂/AC catalysts, *Chem. Commun.* 52 (2016) 13749–13752.
- [49] J. He, X. Li, J. Kou, T. Tao, X. Shen, D. Jiang, L. Lina, X. Lia, Catalytic upgrading of ethanol to higher alcohols over nickel-modified Cu–La₂O₃/Al₂O₃ catalysts, *Catal. Sci. Technol.* (2022), <https://doi.org/10.1039/d2cy01554d>.
- [50] A.V. Chistyakov, S.A. Nikolaev, P.A. Zharova, M.V. Tsodikov, F. Manentic, Linear α -alcohols production from supercritical ethanol over Cu/Al₂O₃ catalyst, *Energy* 166 (2019) 569–576.
- [51] I. Nezam, J. Zak, D.J. Miller, Condensed-phase ethanol conversion to higher alcohols over bimetallic catalysts, *Ind. Eng. Chem. Res.* 59 (2020) 13906–13915, 31.
- [52] S. Marx, B. Ndabab, Rapid microwave-assisted liquid phase conversion of bio-ethanol to n-butanol over a heterogeneous catalyst, *Biofuels* 12 (2021) 861–868.
- [53] H. Aitchison, R.L. Wingad, D.F. Wass, Homogeneous ethanol to butanol catalysis-guerbet renewed, *ACS Catal.* 6 (2016) 7125–7132.
- [54] G. Gregorio, G.F. Pregaglia, R. Ugo, Condensation of alcohols catalysed by tertiary phosphine transition metal complexes, *J. Organomet. Chem.* 37 (1972) 385–387.
- [55] K. Koda, T. Matsu-ura, Y. Obora, Y. Ishii, Y. Guerbet, Reaction of ethanol to n-butanol catalyzed by iridium complexes, *Chem. Lett.* 38 (2009) 838–839, 38.
- [56] T. Matsu-ura, S. Sakaguchi, Y. Obora, Y. Ishii, Guerbet reaction of primary alcohols leading to beta-alkylated dimer alcohols catalyzed by iridium complexes, *J. Org. Chem.* 71 (2006) 8306–8308.
- [57] G. Xu, T. Lammens, T., Q. Liu, X. Wang, L. Dong, A. Caiazzo, N. Ashraf, J. Guan, X. Mu, *Green Chem.* 16 (2014) 3971–3977.
- [58] Q. Zhang, J. Dong, Y. Liu, Y. Wang, Y. Cao, Towards a green bulk-scale biobutanol from bioethanol upgrading, *J. Ener. Chem.* 25 (2016) 907–910.
- [59] X. Wu, G. Fang, Y. Tong, D. Jiang, Z. Liang, W. Leng, L. Liu, P. Tu, H. Wang, J. Ni, X. Li, Catalytic upgrading of ethanol to n-butanol: progress in catalyst development, *ChemSusChem* 11 (2018) 71–85.
- [60] M.H.S.A. Hamid, P.A. Slatford, J.M. Williams, Borrowing hydrogen in the activation of alcohols, *J. Adv. Synth. Catal.* 349 (2007) 1555–1575.
- [61] G.E. Dobreiner, R.H. Crabtree, Dehydrogenation as a substrate-activating strategy in homogeneous transition-metal catalysis, *Chem. Rev.* 110 (2010) 681.
- [62] A.C. Marr, Organometallic hydrogen transfer and dehydrogenation catalysts for the conversion of bio-renewable alcohols, *Catal. Sci. Technol.* 2 (2012) 279–287.
- [63] Y. Obora, Recent advances in α -alkylation reactions using alcohols with hydrogen borrowing methodologies, *ACS Catal.* 4 (2014) 3972–3981.
- [64] B.G. Reed-Berendt, D.E. Latham, M.B. Dambatta, L.C. Morrill, Borrowing hydrogen for organic synthesis, *ACS Cent. Sci.* 7 (2021) 570–585.
- [65] L.M. Kabadwal, S. Bera, D. Banerjee, Recent advances in sustainable organic transformations using methanol: expanding the scope of hydrogen-borrowing catalysis, *Org. Chem. Front.* 8 (2021) 7077–7096.
- [66] Y. Tanaka, M. Utsumomiya, Process of producing alcohol. Patent US20100298613A1, (2010) assigned to Mitsubishi Chemical Corporation.
- [67] G.R.M. Dowson, M.F. Haddow, J. Lee, R.L. Wingad, D.F. Wass, Catalytic conversion of ethanol into an advanced biofuel: unprecedented selectivity for n-butanol, *Angew. Chem. Int. Ed.* 52 (2013) 9005–9008.
- [68] R.L. Wingad, P.J. Gates, S.T.G. Street, D.F. Wass, Catalytic conversion of ethanol to n-butanol using ruthenium P–N ligand complexes, *ACS Catal.* 5 (2015) 5822–5826.
- [69] U.K.D. Wass, F. Duncan, F.G.R.M. Dowson, Conversion of alcohols Patent US20130116481 (2013) assigned to BP Biofuels.
- [70] K.-N.T. Tseng, S. Lin, J.W. Kampf, N.K.N.K. Szymczak, Upgrading ethanol to 1-butanol with a homogeneous air-stable ruthenium catalyst, *Chem. Commun.* 52 (2016) 2901–2904.
- [71] Y. Xie, Y. Ben-David, L.J.W. Shimon, D. Milstein, Highly efficient process for production of biofuel from ethanol catalyzed by ruthenium pincer complexes, *J. Am. Chem. Soc.* 138 (2016) 9077–9080, 138.
- [72] A.M. Davies, Z.-Y. Li, C.R.J. Stephenson, N.K. Szymczak, Valorization of ethanol: ruthenium-catalyzed guerbet and sequential functionalization processes, *ACS Catal.* 12 (2022) 6729–6736.
- [73] S.Ueber Cannizzaro, den der Benzoësäure entsprechenden Alkohol, *Justus Liebigs Ann. Chem.* 88 (1853) 129–130.

- [74] L. Kurti, B. Czako, *Strategic Applications of Named Reactions in Organic Synthesis*, Elsevier Academic Press, Burlington, MA, 2005, p. 456.
- [75] R. Mazzoni, C. Cesari, V. Zanotti, C. Lucarelli, T. Tabanelli, F. Puzzo, F. Passarini, E. Neri, G. Marani, R. Prati, F. Viganò, A. Conversano, F. Cavani, 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.
- [76] B.L. Conley, M.K. Pennington-Boggio, E. Boz, T. Williams, Discovery, applications, and catalytic mechanisms of shvo's catalyst, *Chem. Rev.* 110 (2010) 2294–2312.
- [77] C. Cesari, S. Conti, S. Zacchini, V. Zanotti, M.C. Cassani, R. Mazzoni, Sterically driven synthesis of ruthenium and ruthenium–silver N-heterocyclic carbene complexes, *Dalton Trans.* 43 (2014) 17240–17243.
- [78] C. Cesari, A. Cingolani, M. Teti, A. Messori, S. Zacchini, V. Zanotti, R. Mazzoni, Imidazolium salts of ruthenium anionic cyclopentadienone complexes: ion pair for bi-functional catalysis in ionic liquids, *Eur. J. Inorg. Chem.* (2020) 1114–1122.
- [79] C. Cesari, L. Sambri, S. Zacchini, V. Zanotti, R. Mazzoni, Microwave-assisted synthesis of functionalized shvo-type complexes, *Organometallics* 33 (2014) 2814–2819.
- [80] T. Pasini, G. Solinas, V. Zanotti, S. Albonetti, F. Cavani, A. Vaccari, A. Mazzanti, S. Ranieri, R. Mazzoni, Substrate and product role in the shvo's catalyzed selective hydrogenation of the platform bio-based chemical 5-hydroxymethylfurfural, *Dalton Trans.* 43 (2014) 10224–10234.
- [81] C. Cesari, A. Cingolani, C. Parise, S. Zacchini, V. Zanotti, M.C. Cassani, R. Mazzoni, Ruthenium hydroxycyclopentadienyl N-heterocyclic carbene complexes as transfer hydrogenation catalysts, *RSC Adv.* 5 (2015) 94707–94718.
- [82] C. Cesari, R. Mazzoni, H. Müller-Bunz, M. Albrecht, Ruthenium (0) complexes with triazolylidene spectator ligands: Oxidative activation for (de) hydrogenation catalysis, *J. Organomet. Chem.* 793 (2015) 256–262.
- [83] C. Cesari, R. Mazzoni, E. Matteucci, A. Baschieri, L. Sambri, M. Mella, A. Tagliabue, F.L. Basile, C. Lucarelli, Hydrogen transfer activation via stabilization of coordinatively vacant sites: tuning long-range p-system electronic interaction between Ru(0) and NHC pendents, *Organometallics* 38 (2019) 1041–1051.
- [84] C. Cesari, R. Conti, A. Cingolani, V. Zanotti, M.C. Cassani, L. Rigamonti, R. Mazzoni, Synthesis and reactivity of poly(propyleneimine) dendrimers functionalized with cyclopentadienone N heterocyclic-carbene ruthenium (0) complexes, *Catalysts* 10 (2020) 264.
- [85] P. Sponholz, D. Mellmann, C. Cordes, P.G. Alsabeh, B. Li, Y. Li, M. Nielsen, H. Junge, P. Dixneuf, M. Beller, Efficient and selective hydrogen generation from bioethanol using ruthenium pincer-type complexes, *ChemSusChem* 7 (2014) 2419–2422.
- [86] F. Cavani, V. Zanotti, R. Mazzoni, C. Lucarelli, C. Cesari, T. Tabanelli, F. Puzzo, Improved process for the transformation of primary aliphatic alcohols into higher aliphatic alcohols, patent WO2019193079 (A1) (2019) assigned to the University of Bologna.
- [87] D.F. Wass Catalytic conversion of alcohols. Patent WO201531561 (2015) assigned to BP Northamerica.
- [88] T.A. DiBenedetto, W.D. Jones Upgrading of Ethanol to n-Butanol via a Ruthenium Catalyst in Aqueous Solution, *Organometallics* 40 (2021) 1884–1888.
- [89] C.H. Christensen, B. Jørgensen, J. Rass-Hansen, K. Egeblad, R. Madsen, S. K. Klitgaard, S.M. Hansen, M.R. Hansen, H.C. Andersen, A. Riisager, Formation of acetic acid by aqueous-phase oxidation of ethanol with air in the presence of a heterogeneous gold catalyst, *Angew. Chem. Int. Ed.* 45 (2006) 4648–4651.
- [90] G. Xu, T. Lammens, Q. Liu, X. Wang, L. Dong, A. Caiazza, N. Ashraf, J. Guan, X. Mu, Direct self-condensation of bio-alcohols in the aqueous phase, *Green. Chem.* 16 (2014) 3971–3977.
- [91] X. Zhang, Z. Liu, X. Xu, H. Yue, G. Tian, S. Feng, Hydrothermal synthesis of 1-butanol from ethanol catalyzed with commercial cobalt powder, *ACS Sust. Chem. Eng.* 1 (2013) 1493–1497.
- [92] I. Nieto, M.S. Livings, J.B. Sacchi, L.E. Reuther, M. Zeller, E.T. Papish, Transfer hydrogenation in water via a ruthenium catalyst with OH groups near the metal center on a bipy scaffold, *Organometallics* 30 (2011) 6339–6342.
- [93] S. Chakraborty, P.E. Piszal, C.E. Hayes, R.T. Baker, W.D. Jones, Highly selective formation of n-butanol from ethanol through the guerbet process: a tandem catalytic approach, *J. Am. Chem. Soc.* 137 (2015) 14264–14267.
- [94] K.-I. Fujita, T. Yoshida, Y. Imori, R. Yamaguchi, Dehydrogenative oxidation of primary and secondary alcohols catalyzed by a Cp*Ir complex having a functional C,N-chelate ligand, *Org. Lett.* 13 (2011) 2278–2281.
- [95] A. Fu, Z. Shao, Y. Wang, Q. Liu, Manganese-catalyzed upgrading of ethanol into 1-butanol, *J. Am. Chem. Soc.* 139 (2017) 11941–11948.
- [96] V.N. Kulkarni, W.W. Brennessel, W.D. Jones, Catalytic upgrading of ethanol to n-butanol via manganese-mediated guerbet reaction, *ACS Catal.* 8 (2018) 997–1002.
- [97] A.M. King, H. A. Sparkes, R.L. Wingad, D.F. Wass, Manganese diphosphine and phosphinoamine complexes are effective catalysts for the production of biofuel alcohols via the guerbet reaction, *Organometallics* 39 (2020) 3873–3878.
- [98] M. Kalek, F. Himo, Mechanism and selectivity of cooperatively catalyzed meyer–schuster rearrangement/Tsuji–trost allylic substitution. evaluation of synergistic catalysis by means of combined DFT and kinetics simulations, *J. Am. Chem. Soc.* 139 (2017) 10250–10266.
- [99] F. Planas, M. Costantini, M. Montesinos-Magraner, F. Himo, A. Mendoza, Combined experimental and computational study of ruthenium n-hydroxyphthalimido-yl carbenes in alkene cyclopropanation reactions, *ACS Catal.* 11 (2021) 10950–10963.
- [100] K.S. Rawat, S.C. Mandal, P. Bhauriyal, P. Garg, B. Pathak, 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.
- [101] A.D. Becke, A new mixing of Hartree–Fock and local density-functional theories, *J. Chem. Phys.* 98 (1993) 1372–1377.
- [102] A.D. Becke, Density-functional exchange-energy approximation with correct asymptotic behavior, *Phys. Rev. A* 38 (1988) 3098–3100.
- [103] C. Lee, W. Yang, R.G. Parr, Development of the Colle–Salvetti correlation-energy formula into a functional of the electron density, *Phys. Rev. B* 37 (1988) 785–789.
- [104] A.D. Becke, Density-functional thermochemistry. III. The role of exact exchange, *J. Chem. Phys.* 98 (1993) 5648–5652.
- [105] W.J. Hehre, R. Ditchfield, J.A. Pople, Self-consistent molecular orbital methods. XII. Further extensions of gaussian-type basis sets for use in molecular orbital studies, *Org. Mol. J. Chem. Phys.* 56 (1972) 2257–2261.
- [106] P.C. Hariharan, J.A. Pople, The influence of polarization functions on molecular orbital hydrogenation energies, *Theor. Chim. Acta* 28 (1973) 213–222.
- [107] R. Krishnan, J.S. Binkley, R. Seeger, J.A. Pople, Self-consistent molecular orbital methods. XX. A basis set for correlated wave functions, *J. Chem. Phys.* 72 (1980) 650–654.
- [108] P.J. Hay, W.R. Wadt, Ab initio effective core potentials for molecular calculations. Potentials for the transition metal atoms Sc to Hg, *J. Chem. Phys.* 82 (1985) 270–283.
- [109] P.J. Hay, W.R. Wadt, Ab initio effective core potentials for molecular calculations. Potentials for K to Au including the outermost core orbitals, *J. Chem. Phys.* 82 (1985) 299–310.
- [110] V. Barone, M. Cossi, Quantum calculation of molecular energies and energy gradients in solution by a conductor solvent model, *J. Phys. Chem. A* 102 (1998) 1995–2001.
- [111] M. Cossi, N. Rega, G. Scalmani, V. Barone, Energies, structures, and electronic properties of molecules in solution with the C-PCM solvation model, *J. Comput. Chem.* 24 (2003) 669–681.
- [112] S. Grimme, J. Antony, S. Ehrlich, H. Krieg, A consistent and accurate ab initio parametrization of density functional dispersion correction (DFT-D) for the 94 elements H–Pu, *J. Chem. Phys.* 132 (2010), 154104.
- [113] A. Ohlrigschläger, N. van Staalduinen, C. Cormann, J. Mühlhans, J. Wurm, M. A. Liauw, 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.
- [114] A. Anaby, M. Schelwies, J. Schwaben, F. Rominger, A.S.K. Hashmi, T. Schaub, *Organometallics* 37 (2018) 2193–2201.
- [115] W. Kuriyama, T. Matsumoto, O. Ogata, Y. Ino, K. Aoki, S. Tanaka, K. Ishida, T. Kobayashi, N. Sayo, T. Saito, Catalytic hydrogenation of esters. Development of an efficient catalyst and processes for synthesizing (R)-1,2-Propanediol And 2-(l-menthoxy)ethanol, *Org. Process Res. Dev.* 16 (2012) 166–171.
- [116] E. Alberico, A.J.J. Lennox, L.K. Vogt, H. Jiao, W. Baumann, H.-J. Drexler, M. Nielsen, A. Spannenberg, M.P. Checinski, H. Junge, M. Beller, Unravelling the mechanism of basic aqueous methanol dehydrogenation catalyzed by Ru–PNP pincer complexes, *J. Am. Chem. Soc.* 138 (2016) 14890–14904.
- [117] A. Kaithal, M. Schmitz, M. Hölscher, W. Leitner, Ruthenium(II)-catalyzed β -methylation of alcohols using methanol as C1 source, *ChemCatChem* 11 (2019) 5287–5291.
- [118] A. Kaithal, M. Schmitz, M. Hölscher, W. Leitner, On the mechanism of the ruthenium-catalyzed β -methylation of alcohols with methanol, *ChemCatChem* 12 (2020) 781–787.
- [119] R.A. Farrar-Tobar, Z. Wei, H. Jiao, S. Hinze, J.G. de Vries, Selective base-free transfer hydrogenation of α,β -unsaturated carbonyl compounds using iPrOH or EtOH as hydrogen source, *Chem. A Eur. J.* 24 (2018) 2725–2734.
- [120] X. Chen, Y. Jing, X. Yang, Unexpected direct hydride transfer mechanism for the hydrogenation of ethyl acetate to ethanol catalyzed by SNS pincer ruthenium complexes, *Chem. A Eur. J.* 22 (2016) 1950–1957.
- [121] J. Neumann, C. Bornschein, H. Jiao, K. Junge, M. Beller, Hydrogenation of aliphatic and aromatic nitriles using a defined ruthenium PNP Pincer catalyst, *Eur. J. Org. Chem.* (2015) 5944–5948.
- [122] N.M. Wang, S. Dillon, D. Guironnet, Mechanistic investigations on a homogeneous ruthenium Guerbet catalyst in a flow reactor, *React. Chem. Eng.* 7 (2022) 711–718.
- [123] W. Keim, Oligomerization of ethylene to 1-olefins: discovery and development of the shell higher olefin process (SHOP), *Angew. Chem. Int. Ed.* 52 (2013) 12492–12496.
- [124] C.W. Kohlpaintner, R.W. Fischer, B. Cornils, Aqueous biphasic catalysis: ruthenium/rhodium-poulenc oxo process, *Appl. Catal., A* 221 (2001) 219–225.
- [125] G.J. Sunley, D.J. Watson, High productivity methanol carbonylation catalysis using iridium. the cativatmprocess for the manufacture of acetic acid, *Catal. Today* 58 (2000) 293–307.
- [126] P.J. Flory, Fundamental principles of condensation polymerization, *Chem. Rev.* 39 (1946) 137.
- [127] W. Ueda, T. Kuwabara, T. Ohshida, Y. Morikawa, A low-pressure guerbet reaction over magnesium oxide catalyst, *J. Chem. Soc., Chem. Commun.* 22 (1990) 1558–1559.
- [128] C. Carlini, M. Di Girolamo, A. Macinai, M. Marchionna, M. Noviello, A. Maria, R. Galletti, G. Sbrana, Selective synthesis of isobutanol by means of the Guerbet reaction: Part 2. Reaction of methanol/ethanol and methanol/ethanol/n-propanol mixtures over copper based/MeONa catalytic systems, *J. Mol. Catal. A Chem.* 200 (2003) 137–146.

- [129] E.S. Olson, R.K. Sharma, T.R. Atlich, Higher-alcohols biorefinery: improvement of catalyst for ethanol conversion, *Appl. Biochem. Biotechnol.* 113 – 116 (2004) 913–932.
- [130] Q. Liu, G. Xu, X. Wang, X. Mu, Selective upgrading of ethanol with methanol in water for the production of improved biofuel—*isobutanol*, *Green. Chem.* 18 (2016) 2811–2818.
- [131] R.L. Wingad, E.J.E. Bergström, M. Everett, K.J. Pellow, D.F. Wass, Catalytic conversion of methanol/ethanol to *isobutanol* – a highly selective route to an advanced biofuel, *Chem. Commun.* 52 (2016) 5202–5204.
- [132] K.J. Pellow, R.L. Wingad, D.F. Wass, Towards the upgrading of fermentation broths to advanced biofuels: a water tolerant catalyst for the conversion of ethanol to *isobutanol*, *Catal. Sci. Technol.* 7 (2017) 5128–5134.
- [133] R.J. Newland, M.F. Wyatt, R.L. Wingad, S.M. Mansell, A ruthenium(II) bis (phosphinophosphinine) complex as a precatalyst for transfer-hydrogenation and hydrogen-borrowing reactions, *Dalton Trans.* 46 (2017) 6172–6176.
- [134] Y. Liu, Z. Shao, Y. Wang, L. Xu, Z. Yu, Q. Liu, Manganese-catalyzed selective upgrading of ethanol with methanol into *isobutanol*, *ChemSusChem* 12 (2019) 3069–3072.