MINIREVIEW

Review of catalytic systems and thermodynamics for the Guerbet condensation reaction and challenges for biomass valorization

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The Guerbet condensation reaction is an alcohol coupling reaction that has been known for more than a century. Because of the increasing availability of bio-based alcohol feedstock, this reaction is of growing importance and interest in terms of value chains of renewable chemical and biofuel production. Due to the specific branching pattern of the alcohol products, the Guerbet reaction has many interesting applications. In comparison to their linear isomers, branched-chain Guerbet alcohols have extremely low melting points and excellent fluidity. This review provides thermodynamic insights and unravels the various mechanistic steps involved. A comprehensive overview of the homogeneous, heterogeneous and combined homogeneous and heterogeneous catalytic systems described in published reports and patents is also given. Technological considerations, challenges and perspectives for the Guerbet chemistry are discussed.

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1. General introduction

1.1 Guerbet reaction

The Guerbet reaction, as described in 1899 in the French journal *Comptes Rendus*,[1] was named after its inventor Marcel Guerbet. The reaction is a condensation reaction of two alcohols to the final 'Guerbet' alcohol with the release of water, as shown in Scheme 1. A primary or secondary alcohol with a
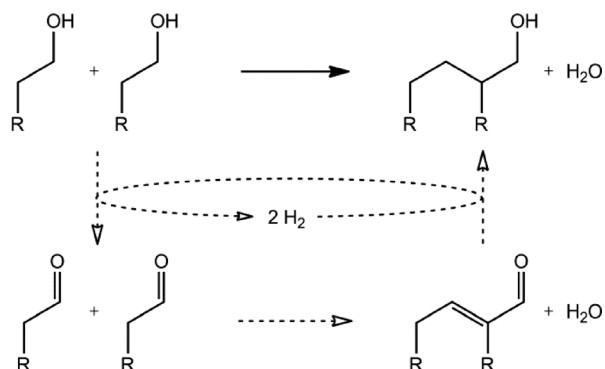

Dries Gabriëls

Dries Gabriëls obtained his MSc in Engineering (Catalytic Technology) at the Center for Surface Chemistry and Catalysis at KU Leuven in 2013. His master's thesis was performed under the guidance of Prof. B. Sels and dealt with the synthesis of heteroatomic zeolites and their application to acid catalysis in biomass reactions. Currently, he is doing his PhD thesis investigating heterogeneous catalysts for the valorization of bio-alcohols by means of Guerbet condensation.

Willinton Yesid Hernández

Willinton Y. Hernández studied Chemistry at the National University of Colombia. He obtained his PhD in Chemistry at the University of Seville in Spain (2010) by working on the design of heterogeneous catalysts for the preferential oxidation of CO in the presence of hydrogen. After a post-doctoral period at the University of Lyon-IRCELYON (Lyon, France, from 2010 to 2013) and the ICIQ (Tarragona, Spain, from 2013 to 2014) working on automotive depollution systems and the water oxidation reaction, he joined the COMOC research group at Ghent University (Belgium). His current research is mostly focused on the valorization of bio-alcohols by the Guerbet reaction.

Scheme 1 Schematic representation of the Guerbet reaction for primary alcohols.

methylene group adjacent to the hydroxylated carbon atom may be condensed with the same (self-condensation) or another alcohol (cross-condensation) resulting in a heavier and often branched alcohol containing the sum of the carbon atoms of the reactants. The rather complex Guerbet reaction requires the use of a catalytic system that exhibits at the same time acidic, basic and dehydrogenation/hydrogenation properties. A plurality of reactions is involved, thus the process is particularly sensitive and less predictable. Appropriate selection of reaction conditions and well-thought development of the catalytic system are of utmost importance as both the proportion and strength of each different site need to be adequately tuned in order to maximize the yield of the target alcohols. This raises the question whether multifunctional catalysts should be developed, or whether the reaction should be executed in a multistage process using different catalysts, each of them bearing one catalytic function and isolated in different reactor types.

In addition to higher alcohols formed by condensation processes (self and/or cross-condensation ones), side reactions result in the formation of other compounds, such as esters and carboxylic acids, or salts thereof. Next to lowering the process efficiency, these unwanted products often poison the catalytic system. It is therefore desirable to minimize the formation of such by-products.

The investigation of Guerbet alcohols and their use in various fields is attractive due to the important advantages that such alcohols have, as compared to their corresponding linear isomers:[2,3]

1. Branched Guerbet alcohols have a much lower melting point than their linear counterparts. They are used not only for the synthesis of functional liquids that have to remain fluid at very low temperatures, like some lubricants or hydraulic fluids for aircrafts, but also for their application as jet fuel.

Prof. Bert F. Sels obtained his PhD in 2000 at KU Leuven by working on oxidation chemistry, followed by a post-doc at BASF until 2002 and post-doc for 3 years at the National Science Foundation. He became an assistant professor in 2003, teaching courses on analytical chemistry and heterogeneous catalysis. He is a full professor of the Faculty of Bioengineering Sciences at Leuven since 2012. He has published 205 papers and 19 patents, and is a recipient of numerous awards including the DSM Chemistry and ISGC Green Chemistry awards. His current research explores heterogeneous catalysis for renewables conversion and its integration into bio-refinery concepts.

Bert Sels

Pascal Van Der Voort is a full professor at Ghent University and the director of the research group COMOC that he founded in 2007. The group consists of 5 post-docs, 15 PhD students, 3 technicians and typically 10 master students. His research interests are mainly in the field of porous materials, including MOFs, COFs, PMOs, oxides and carbons for applications in chromatography, microelectronics, urban mining, catalysis and adsorption. He teaches general chemistry, solid state chemistry, nanoporous materials and heterogeneous catalysis in several faculties of Ghent University. He has 172 papers indexed in the web of science and holds several patents.

Pascal Van Der Voort

An Verberckmoes obtained her MSc in Bio-engineering (Chemistry) in 1994, her PhD in 1998 (KU Leuven) and then joined the R&D Center of ExxonMobil working in the area of catalyst and process development which resulted in 17 patents. In 2008, she went to University College Ghent and became an assistant professor in 2011. Since 2013, she has been an assistant professor at Ghent University. She now teaches courses on organic chemistry and spectroscopy at the Faculty of Engineering and Architecture. She co-heads the INCAT research group. Her current research focuses on the synthesis optimization, scale-up and testing of heterogeneous catalysts.

An Verberckmoes

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2. Cosmetic emollients made with Guerbet alcohols show good oxygen permeability due to branching of the alcohols. This is an essential property for skin applications. Moreover, since the alcohols are completely saturated, they exhibit excellent oxidation and color stability and do not become rancid.

3. Because of branching, they are less viscous than their linear equivalents, which is a desired property for surfactants in a number of detergent formulations where a low temperature is desired.

4. Finally, due to the unique position of the branches, Guerbet alcohols are more biodegradable than synthetic branched alcohols, especially when the branches are made up of an even number of carbon atoms.

During the last three decades, numerous catalytic systems have been studied and proposed to promote the conversion and selectivity of the Guerbet reaction, most of them based on homogeneous and homogeneous/heterogeneous systems. A new driver to study and exploit the Guerbet reaction is the potential valorization of bio-based oxygenates. Nowadays, the availability of renewable alcohols is readily increasing, exposing new opportunities for the Guerbet chemistry.

1.2 Biomass sources of Guerbet alcohols

Branched alcohols are often produced in a three-step process involving hydroformylation of olefins to aldehydes, aldol condensation to branched α,β-unsaturated aldehydes and subsequent hydrogenation to 2-alkyl alcohols.[4–6] The Guerbet condensation of alcohols is an alternative one-step process for the production of these 2-alkyl alcohols, also referred to as Guerbet alcohols. This reaction is of growing importance in biomass conversion processes as it provides an efficient way for the upgrading of smaller alcohols to heavier branched-chain alcohols with a unique branching pattern.[2,7] Many renewable carbon sources are excellent feedstock for the production of alcohols. Moreover, the utilization of biomass waste would make particular merit due to its scale, availability, low cost and minimal impact on food production. Bio-derived alcohols (and aldehydes) are becoming more important because of their growing industrial availability. In a recent study, the renewable chemicals market was estimated to reach US$ 84.8 billion in 2018 from about US$ 57 billion in 2013, with (bio)alcohols currently making up for the largest segment.[8] Their renewable and environmentally benign characteristics promote the development of new processes for the generation and utilization of bio-alcohols.[9]

Biochemical routes to bio-alcohols. In a short time, ethanol has become one of the most prominent sources of bio-based carbon for the production of fuels and chemicals and due to its potential as a renewable fuel, its production is still expected to increase.[10] Bioethanol is usually produced *via* fermentation of carbohydrates such as starch and sugars (first generation ethanol).[11,12] In order to be truly sustainable, the production of chemicals and fuels from biomass should not compete with food production. Therefore, much research focuses on the development of more efficient technologies from low-cost and non-food biomass sources. Promising results are reported for the production of ethanol from cellulosic (second generation) and algal (third generation) feedstocks.[13–19] Next to carbohydrates, syngas can also be fermented into alcohols.[20–25] Syngas is a mixture containing mainly CO, CO_2, H_2 and H_2O that is obtained by gasification of coal or biomass, *e.g.* the thermochemical process in which the carbon source reacts with air or oxygen.[20] This allows for the utilization of a wider range of biomass types including low-cost organic waste without the need for specific fractionation.[26] The production of ethanol through syngas fermentation is already available as a commercial process, for instance in the INEOS Bio process.[23,27]

Next to ethanol, higher alcohols containing 3 to 5 carbon atoms are also formed during fermentation. This mixture is often referred to as 'fusel oil' due to the oily consistency of the heavier compound fraction obtained after distillation.[28,29] Generally, these fusel alcohols are considered waste compounds in the production of bioethanol and are often burnt to fuel the distillation columns. However, due to their potential as renewable fuels and feedstock for the synthesis of heavier oxygenates, interest for these higher alcohols is growing. Optimization of the production and valorization of these higher alcohols is currently under investigation. Biochemical production of *n*-butanol and other fusel alcohols can be increased through metabolic engineering[30,31] and adapted reactor design.[32] The alcohols can be used for esterification[33] or Guerbet-type condensation reactions.[34–36]

Chemocatalytic routes to bio-alcohols. Methanol is industrially produced from syngas by hydrogenation of CO using a copper–zinc oxide catalyst.[20,37] Several papers also describe the chemocatalytic conversion of syngas into ethanol and higher alcohols.[20,38–42] Three different pathways from syngas to ethanol are reported: direct selective hydrogenation of CO over a solid catalyst, homologation of methanol which involves reductive carbonylation on a redox catalyst, or a classical methanol synthesis reaction followed by carbonylation to acetic acid and subsequent hydrogenation to ethanol. Although carbonylation of methanol to ethanol is a promising step (TCX Technology by Celanese[43]), none of these routes have been practiced commercially. Selective production of higher alcohols is generally reported on Rh based catalysts,[44–46] but utilization of cheaper bimetallic catalysts has been also shown to form higher alcohols.[42,47–49] Whereas most research focuses on the production of C_2–C_6 alcohols, recent publications also report the conversion of syngas into long-chain alcohols containing up to 22 carbon atoms.[50–52] Though these catalytic developments show promising results, the commercial synthesis of ethanol and higher alcohols from syngas is currently challenging due to low yield and selectivity.

Next to biochemical pathways, smaller alcohols can also be produced from bio-based platform chemicals such as levulinic acid. Levulinic acid can be synthesized through acid catalysis of carbohydrate feedstocks such as lignocellulose.[53,54] Next, levulinic acid can be hydrogenated, typically leading to formation of γ-valerolactone and 2-methyltetrahydrofuran,

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but higher H_2-pressures also lead to production of C_4 and C_5 alcohols like 1-pentanol, 2-pentanol, 1,4-pentanediol and 2-butanol.[55,56] The yields of both levulinic acid production and its conversion to pentanols are currently limiting its industrial applicability.[54–56]

The bioavailability of C_6 alcohols is currently limited. Whereas fusel oil from fermentation contains fractions of C_3, C_4 and C_5 alcohols, it is not a viable source of hexanols. On the other hand, the lightest fraction of plant-derived fatty alcohols is typically made up of C_8 and C_{10} alcohols. Two recent publications report the chemocatalytic conversion of cellulosic biomass to hexane and hexanols.[57,58] These hexanols are identified as intermediates in the reaction pathway to hexane, with n-hexanol being the most stable isomer. Thus, careful tuning of reaction conditions and catalyst composition can facilitate the selective formation of n-hexanol and other C_6 alcohols, opening up an interesting route to bio-based hexanol.

Longer alcohols with more than 6 carbon atoms, also called fatty alcohols, are usually obtained directly from natural fats and oils or from fatty acids and esters. The oils are first extracted from plants and converted to fatty alcohols by catalytic hydrogenation.[38,59] Smaller fatty alcohols ($C_{8–16}$) are typically obtained from coconut and palm oils, while longer alcohols ($C_{18–22}$) are produced from rapeseed and soybean oils, amongst others.[60] Recent developments also report metabolic engineering as a tool for the microbial production of fatty alcohols, acids or esters.[61–63] Typically, sugars are used as the primary feedstock, but through metabolic engineering, it is also possible to express enzymes that enable the conversion of less convenient carbohydrate sources such as hemicellulose.[62]

In the MixAlco process,[64] a wide range of biodegradable materials is anaerobically digested by a mixture of microorganisms, which produce short carboxylic acids from the feed. The carboxylic acids are continuously neutralized to their corresponding salts, thermally converted to ketones and subsequently hydrogenated to produce a mixture of secondary alcohols containing up to 13 carbon atoms.

Bio-based Guerbet alcohols. Due to the growing availability of short bio-alcohols such as ethanol, there has been increasing and renewed interest for the Guerbet condensation reaction. Many publications focus on the Guerbet self-condensation of ethanol for the production of n-butanol and higher alcohols.[65–78] Just like ethanol, n-butanol can be used as a renewable fuel, yet in comparison with ethanol, it has a higher energy density, a lower volatility and a lower propensity to absorb water. Methanol on the other hand lacks a second carbon atom and cannot self-condensate by Guerbet condensation. It is therefore often applied in the Guerbet reaction with ethanol or n-propanol for the production of isobutanol, a product which can be processed to isobutene and methyl-$tert$-butyl ether.[79–85] The latter is often used as a fuel additive to increase octane numbers.[86] Butanol can also serve as a source of C_4-olefins. Butenes, obtained by dehydration of butanol, can be transformed into higher-value molecules such as 1,3-butadiene,[87] aromatics,[88] or biofuels.[89]

Higher alcohols such as n-butanol can also be upgraded to more valuable oxygenates. For instance, the Guerbet self-condensation of n-butanol produces 2-ethylhexanol (2EH), industrially the most important compound in the group of "plasticizer alcohols".[5,90–92] It is mostly applied in the synthesis of polymer additives, $e.g.$ as a phthalate ester in PVC applications, giving the polymer improved flexibility and durability. However, the branched alcohol also has numerous other applications as a solvent and an emollient, or in fragrances and flavors.[93] Compared to the industrial synthesis process, in which propene is hydroformulated to butyraldehyde, followed by aldol condensation and subsequent hydrogenation, the Guerbet condensation of n-butanol provides a renewable pathway for the production of 2EH and other "plasticizer alcohols" from higher alcohols.[5]

As for aldehydes and ketones produced in biomass conversion (Fig. 1), they can either first be hydrogenated to alcohols or be coupled directly by aldol condensation, thereby skipping the first dehydrogenation step of the Guerbet reaction cascade. This allows for the direct upgrading of mixed feedstocks such as ABE (acetone, n-butanol and ethanol) fermentation mixtures[34–36] or MixAlco[64] product streams without the need for intermediate hydrogenation steps. Integration of fermentation and chemocatalytic conversion can be easily achieved, $e.g.$ by continuous extraction.[35,36] Condensation of these oxygenate mixtures over Guerbet-type catalysts can produce mixed biofuels with increased energy density, lower water absorption propensity and lower volatility. Due to the higher rate of acetone alkylation compared to Guerbet condensation, the main products from ABE condensation are aliphatic ketones containing up to 11 carbons.[34,35] Substitution of isopropanol for acetone results in more reduced oxygenates, but because of lower concentration of acetone in the reaction mixture, reduced oxygenates with C_{12+} are also produced due to Guerbet condensation of the reagent alcohols.[36] Careful selection of the reagent mixture allows the production of various bio-fuels or specialty chemicals to be more controllable.
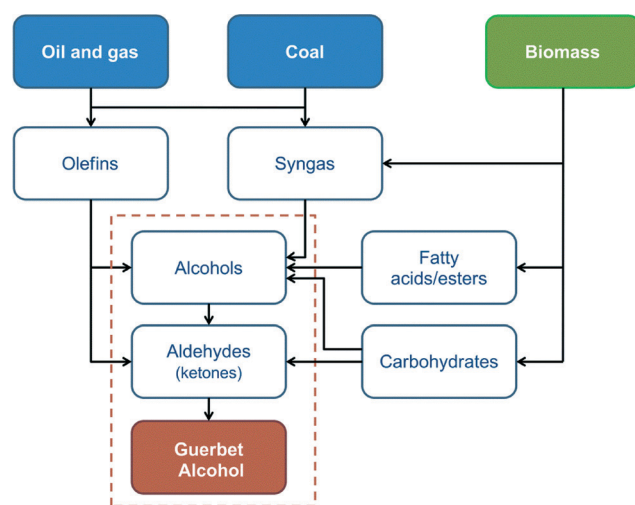

Fig. 1 Overview of oil and gas, coal and biomass sources for the production of Guerbet alcohols.

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Guerbet products of heavier fatty alcohols have a unique branching pattern which in comparison with their linear isomers leads to extremely low melting points and excellent fluidity. This facilitates further processing of these alcohols, but also causes them to be excellent renewable feedstocks for applications such as "cold wash" detergents, low temperature lubricants and hydraulic fluids. They can also be used for the production of plasticizers and waxes, and as emulsifiers, emollients and thickening agents in food or cosmetic applications. Due to the fact that they are completely saturated, these Guerbet alcohols have excellent thermal and oxidative stability, hence outstanding color permanence.[2]

2. Focus of the review

This review is aimed at describing the thermodynamic considerations and reaction mechanisms in the Guerbet condensation reaction, including their implications for catalyst development and reactor design. Equilibrium compositions in the intermediate reaction steps are calculated at atmospheric pressure using *n*-butanol as a model compound. Schematic representations of the different Guerbet reaction steps and a comprehensive scheme of by-product formation routes are assembled. Furthermore, an overview of the different catalyst types and reaction conditions is provided and discussed. In the patent and open literature, different families of catalysts and catalytic systems that show promising activity have been identified. These catalytic systems can be divided into three main families: (i) homogeneous systems, (ii) mixed systems in which a homogeneous base is combined together with a heterogeneous transition metal catalyst, and (iii) purely heterogeneous systems. This review is aimed at providing a detailed overview of such catalytic systems, the variety of possible reagents from very low (*e.g.* ethanol, propanol, *etc.*) to high boiling alcohols (*e.g.* fatty alcohols) and the very different process conditions depending on the type of starting alcohol. Technological considerations, challenges and future perspectives are discussed.

3. Thermodynamics and mechanisms

3.1 Reaction mechanisms and thermodynamic considerations

Coupling of alcohols has been investigated under a wide range of conditions with various types of catalysts, both in liquid and in vapor phase. Although different reaction mechanisms have been proposed, it is most commonly accepted that C–C bond formation occurs *via* an aldolization step. Hence, the Guerbet condensation reaction includes four different reaction steps; the alcohol is first dehydrogenated after which carbonyl compounds are coupled by aldol addition and subsequent dehydration and finally they are hydrogenated to saturated alcohols. A schematic representation of the different reaction steps in the Guerbet reaction with *n*-butanol as the model substrate is shown in Scheme 2.
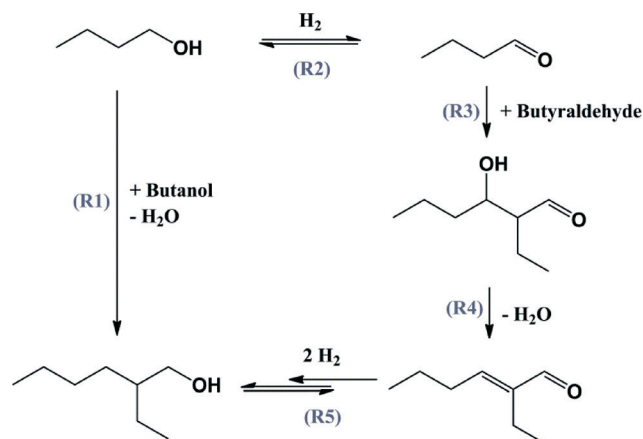
Scheme 2 Schematic representation of the reaction steps in the Guerbet reaction with *n*-butanol as the model substrate. R1, net Guerbet reaction; R2, dehydrogenation; R3, aldol addition; R4, dehydration; R5, hydrogenation.

This mechanism involving aldolization is supported by several arguments. Intermediate products of the pathway are often observed[92,94–98] and can be reduced to the product alcohol under the same conditions.[70,96] The conditions applied in the Guerbet reaction are suitable for aldol condensation.[94,97,99] Moreover, addition of C[13]-labeled ethanal to the reaction mixture of ethanol resulted in a high amount of C[13]-containing Guerbet products[94] and the rate of product formation was found to be proportional to the concentrations of the aldehyde.[94,97,100] Finally, at least one of both reacting alcohols requires an α-methylene group in order to undergo Guerbet condensation, a requisite for the formation of the aldol condensation product, which cannot form should both alcohols lack an α-hydrogen atom.[98] Together with the specific α-alkyl branching of Guerbet alcohols, these findings support an aldol-type coupling mechanism.

An Ellingham-type plot in Fig. 2 displays the change in the Gibbs free energy ΔG for temperatures between 150 and 550 °C. Next to the global reaction (Scheme 2, R1), the different steps of dehydrogenation (R2), aldol condensation (R3–4) and hydrogenation (R5) are shown. Note that the calculations were performed in Aspen Plus® software for pure compounds at atmospheric pressure, in their real state and not in their standard state.[87] The Gibbs free energy change (ΔG) for the direct conversion of *n*-butanol to 2-ethylhexanol is negative for the whole range of temperatures considered, therefore the reaction is favorable at 150–550 °C.

The intermediate reaction steps show different behaviors. For the dehydrogenation of *n*-butanol (R2), ΔG is positive below 300 °C, showing its endothermic behavior. The opposite is true for the hydrogenation step (R5) where ΔG increases with increasing temperature, becoming positive at temperatures higher than 300 °C. The aldol condensation reaction (R3–4) on the other hand shows a slightly negative ΔG for the whole range of temperatures. It is therefore favorable at all temperatures, yet the reaction is limited by thermodynamic equilibrium. Though the different reaction steps
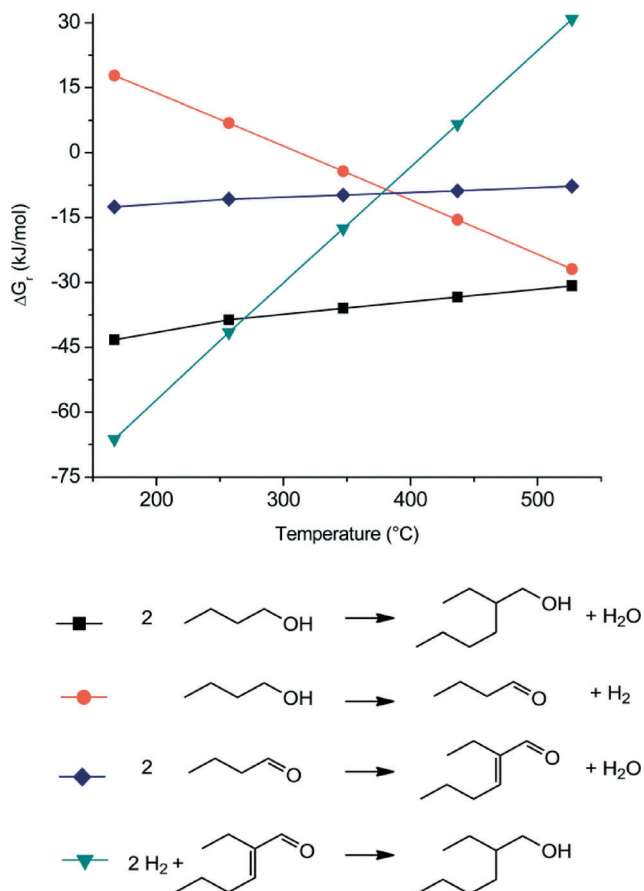
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Fig. 2 Calculated thermodynamic data for the Guerbet condensation of *n*-butanol. Δ*G* values of the global reaction (R1), intermediate dehydrogenation (R2), aldol condensation (R3–4) and hydrogenation (R5) steps are plotted. The calculations were performed with Aspen Plus® software for pure components at a pressure of 1 atm. Δ*G* is calculated in the real state, thus is different from Δ*G*^{0}.

require different temperatures, the net reaction of *n*-butanol to 2-ethylhexanol is favorable at all temperatures studied. The choice of temperature should therefore be determined by kinetic factors, in order to catalytically adapt the different reaction steps and optimize the yield of the Guerbet alcohol.

Fig. 3 shows the equilibrium compositions of the Guerbet reaction and the considered intermediate steps at different temperatures. The data were calculated for pure reagent feeds or stoichiometric mixtures at a pressure of 1 atm, using the equilibrium based reactor (REquil) in Aspen Plus® software. *n*-Butanol was used as a model substrate for the Guerbet condensation reaction due to the commercial importance of its Guerbet product and because the software database contained most of the intermediates required for the calculations. Fig. 3A shows the equilibrium composition for the net reaction of *n*-butanol (BuOH) to 2-ethylhexanol (Scheme 2, R1). An almost complete conversion of BuOH can be obtained for temperatures below 350 °C, while at higher temperatures, a minor fraction of BuOH (<5 mol%) remains unreacted. Riittonen *et al.*[68] reported a theoretical maximum conversion of 98.5% for the condensation of ethanol to *n*-butanol at

250 °C and 70 bar, and Olcese and Bettahar[101] calculated a thermodynamically favorable equilibrium for the Guerbet reaction of ethanol both in vapor and in liquid phase.

The first step in the generally accepted reaction pathway is the dehydrogenation of the reagent alcohol to the corresponding aldehyde or ketone (Scheme 2, R2). The equilibrium compositions are shown in Fig. 3C. As alcohol dehydrogenation is an endothermic reaction, it is thermodynamically favored at higher temperatures; temperatures higher than 400 °C are required to obtain near full conversion of *n*-butanol. As one reagent is converted into two products, a decrease in partial pressure of the alcohol will shift the equilibrium towards the aldehyde. The dehydrogenation reaction is often identified as the rate limiting step, in particular when lower temperatures[100] or higher hydrogen partial pressures[81,92] are applied, for instance with low boiling point alcohols in liquid phase reactions. Kinetically, the conversion of the feed alcohol into an aldehyde will be promoted by consumption of the aldehyde in the subsequent reaction steps. Depending on the catalytic system, the produced hydrogen can either be liberated into the reaction medium or remain adsorbed on the catalyst. Liberation of molecular hydrogen can facilitate the first dehydrogenation step, but could complicate the reduction of unsaturated aldol condensation products. Yet, when hydrogen is too strongly adsorbed on the catalyst, transfer of H atoms into the carbon skeleton might become complicated.[101] Many catalytic systems include a transition metal compound to facilitate the (de)hydrogenation steps at lower temperatures. Catalytic systems without transition metals require much higher temperatures for alcohol coupling due to the higher activation energy of dehydrogenation.[65,69,75,80,96,102,103] Next to the different reaction mechanisms proposed (*vide infra*), dehydrogenation on these catalysts is often proposed to occur by transfer hydrogenation mechanisms like the Meerwein–Ponndorf–Verley reaction (MPV),[104] in which the hydrogen from the reagent alcohol is directly transferred to the unsaturated aldol product. It was shown by Gines and Iglesia[94] that addition of copper to a K–Mg$_5$CeO$_x$ catalyst resulted in much higher incorporation of deuterium in both reactants and products when the reaction was carried out in the presence of D$_2$. Product mixtures obtained with copper-free catalysts contained significantly less deuterium atoms. It is therefore unlikely for purely basic materials to use gas phase H$_2$ as a source for the hydrogenation of condensation products. These observations rather support the importance of a hydride transfer mechanism on materials free of transition metals. Hydride transfer can be realized by either formation of adsorbed proton and hydride ions[73] (borrowing-hydrogen principle, Scheme 3A) or a direct hydrogen-transfer mechanism involving a hydride shift[105] (Scheme 3B) as in the case of the MPV reaction.

In the next step (Scheme 2, R3), butyraldehyde is transformed *via* aldolization into 2-ethyl-3-hydroxyhexanal and subsequently dehydrated (Scheme 2, R4) to 2-ethyl-2-hexenal, the coupled α,β-unsaturated aldehyde. Aldol reactions are catalyzed by basic, acidic or amphoteric catalysts and occur
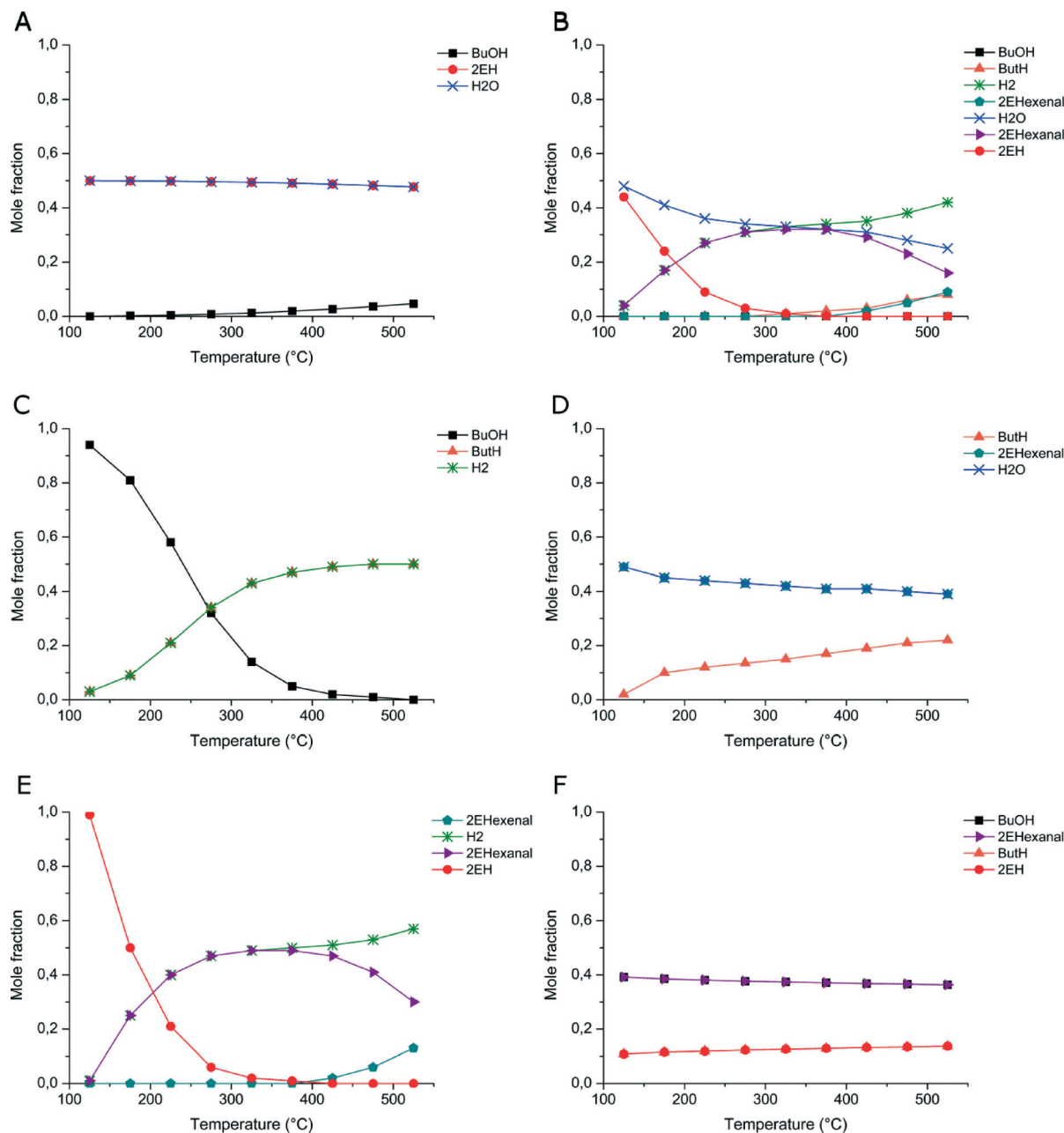
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Fig. 3 Equilibrium compositions calculated for: A) the overall Guerbet condensation of *n*-butanol, reaction (R1); B) the Guerbet condensation of *n*-butanol taking into account the different reaction steps generally considered, reaction (R2)–(R5); C) the dehydrogenation of *n*-butanol to butyraldehyde, reaction (R2); D) the aldol condensation of butyraldehyde to 2-ethyl-2-hexenal, reaction (R3) + (R4); E) the hydrogenation of 2-ethyl-2-hexenal, reaction (R5); F) the MPV reaction of *n*-butanol with 2-ethylhexanal to butyraldehyde and 2-ethyl-1-hexanol with a molar ratio of 1 : 1. The calculations were performed in Aspen Plus® software using the equilibrium based reactor (REquil), COMMON process type, NTRL base model and assuming a pressure of 1 atmosphere. Reactions (R1)–(R5) are in line with Scheme 2. (BuOH = *n*-butanol; ButH = butyraldehyde; 2EHexenal = 2-ethyl-2-hexenal; 2EHexanal = 2-ethylhexanal; 2EH = 2-ethyl-1-hexanol).

through the formation of an enol or an enolate. By nucleophilic attack on another carbonyl compound, a C–C bond is formed at the α-carbon of the enolized carbonyl. This first aldol addition step is thermodynamically unfavorable, but the subsequent dehydration to the α,β-unsaturated aldehyde is highly favorable and drives the reaction, contributing to a suitable equilibrium of the aldol condensation.[87] Consequently, aldol addition products are generally not observed

in the condensation of light alcohols under atmospheric conditions.[7,106–109] For liquid phase reactions, hence at increased pressure, the detrimental effect of water on conversion and selectivity is often reported.[36,68,110–112] Although this is generally caused by a deactivating effect on the catalyst, water could also influence the thermodynamic equilibrium of the aldol condensation. It might slow down the desired reaction pathway, thereby leaving intermediate aldehydes
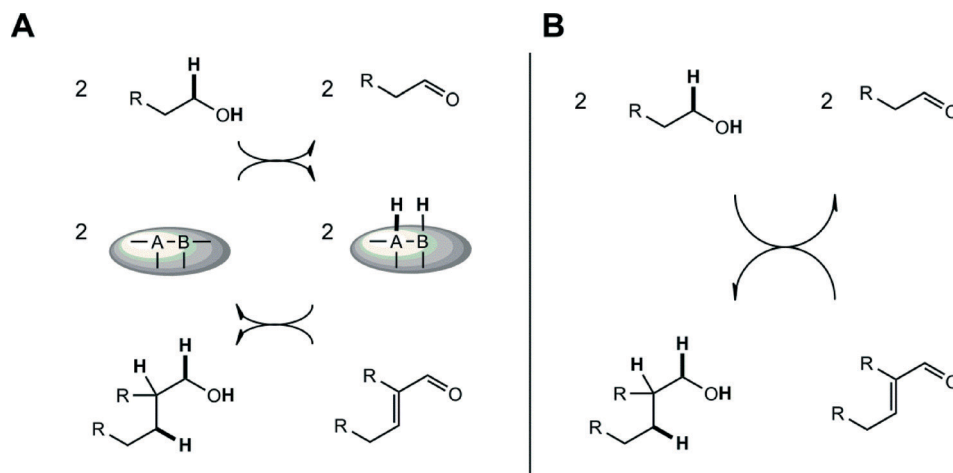
Scheme 3 A) Hydrogen-borrowing transfer (de)hydrogenation based on the intermediate formation of adsorbed protons and hydride ions; B) transfer (de)hydrogenation based on a direct hydride shift.

unreacted and available for other, undesired parallel reactions. The equilibrium compositions of the aldol condensation step were calculated at different temperatures and are shown in Fig. 3D. At a temperature of 150 °C, the conversion of butyraldehyde is almost complete. In contrast to dehydrogenation, aldol condensation is slightly exothermic, hence the conversion of the reagent declines when the temperature is increased. Therefore, under conditions when dehydrogenation is more favorable, *e.g.* high temperatures and lower partial pressures, the rate limiting step is often found to be aldol condensation.[2]

The final steps in the sequence are two hydrogenation steps (Scheme 2, R5) to convert the α,β-unsaturated aldehyde into a completely saturated 2-alkyl-alcohol, *viz.* 2-ethyl-2-hexanol. The equilibrium compositions are shown in Fig. 3E. Parallel to the first dehydrogenation step where lower temperatures limit the release of hydrogen from the alcohol, lower temperatures now favor the incorporation of hydrogen into the α,β-unsaturated aldehyde. Hydrogenation of the unsaturated aldehyde is an exothermic reaction, thus requiring mild temperatures for a favorable equilibrium. 2-Ethyl-hexanol is the main compound only at temperatures below 200 °C. At higher temperatures, the equilibrium is shifted to the aldehyde function and at temperatures above 400 °C, also hydrogenation of the C═C bond becomes incomplete. The Meerwein–Ponndorf–Verley (MPV) reduction in which the coupled aldehyde is hydrogenated by direct transfer of a hydrogen molecule obtained from *n*-butanol was also calculated for 2-ethylhexanal and *n*-butanol. The results are shown in Fig. 3F. Although the equilibrium conversion of the MPV reaction is low (about 13% conversion), kinetically the reaction could play an important role in the overall network.

By combining all these intermediate steps simultaneously in the calculation (Scheme 2, R2–5), the equilibrium compositions shown in Fig. 3B were obtained. At temperatures up to 350 °C, a total conversion to coupled oxygenates is achieved. For temperatures higher than 350 °C, the thermodynamic

equilibrium includes small fractions of butyraldehyde. Remarkably, when the dehydrogenation and hydrogenation reaction steps are carried out at 1 atm, the partial pressure of H_2 is insufficient for the total reduction of the aldol products. At temperatures as low as 200 °C, 2-ethylhexanal is the major carbon compound and at temperatures higher than 400 °C, small fractions of unreduced 2-ethylhexenal are produced. From a thermodynamic perspective, at reaction temperatures higher than 125 °C, an increase in H_2 partial pressure is required for the complete hydrogenation of the intermediates to the desired Guerbet alcohols. An equivalent deduction was made by Meunier *et al.*[113] from thermodynamic calculations for the ethanol condensation reaction, supporting the other reaction pathways for the Guerbet condensation of ethanol.[71,95,113]

More direct condensation mechanisms have been proposed for the Guerbet reaction of ethanol to *n*-butanol on basic heterogeneous catalysts. The main reaction route is suggested to occur by direct coupling of two alcohol molecules with dehydration through the elimination of the hydroxyl of one alcohol molecule and the hydrogen attached to the α-carbon of the second one (Scheme 4, R6). Direct condensation of an alcohol with its corresponding aldehyde (Scheme 4, R7) or with its enol form (Scheme 4, R8) is reported as a minor reaction pathway.[67,71]

The direct condensation route involving two ethanol molecules was first proposed by Yang and Meng[75] and supported by Ndou *et al.*[67] because the addition of intermediate products from the aldol pathway did not seem to increase the production of *n*-butanol from ethanol. However, factors such as the difference in the amount of available hydrogen or surface adsorption of aldol intermediates were not taken into account. Di Cosimo *et al.*[95] stated that the hydrogen pressure was insufficient to hydrogenate butyraldehyde under the applied conditions and Scalbert *et al.*[71] noticed that under the conditions applied (400 °C), the experimentally obtained reaction quotient of butanol from acetaldehyde was several
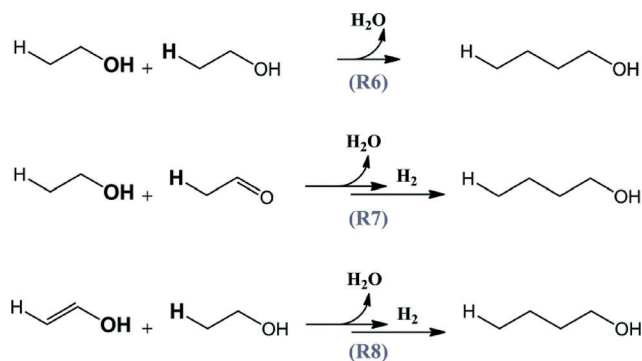
Scheme 4 Schematic representation of the direct condensation mechanisms for ethanol condensation. R6, main mechanism; R7 and R8, minor mechanisms proposed for the direct condensation.

orders of magnitude higher than the theoretical thermodynamic equilibrium for aldol condensation. The same group also argues the limited hydrogenation activity of metal-free basic catalysts.[113]

In a recent paper by Chieregato et al.,[114] the direct condensation mechanism was further supported by kinetic experiments in combination with in situ infrared spectroscopy (DRIFTS), MS and DFT calculations. Based on their findings, the authors assume the formation of a carbanion on the MgO surface. This carbanion can attack another ethanol molecule with elimination of water, resulting in the formation of n-butanol (analogous to Scheme 4, R6). On the other hand, the carbanion can also react with an aldehyde molecule producing either crotyl alcohol or 3-buten-1-ol. According to the authors, these alkenols will preferably dehydrate to 1,3-butadiene or rearrange into 3-buten-2-ol, but are not considered intermediates for n-butanol formation.

Note that these direct mechanisms have been so far only suggested for the specific Guerbet condensation of ethanol to n-butanol on purely basic heterogeneous catalysts (MgO,[67,114] hydroxyapatite,[71] and RbLi-X[75]) and at relatively high temperatures (350–450 °C). Although valid arguments are provided for this direct coupling mechanism under these conditions, the aldol condensation pathway is considered to be the main reaction mechanism at lower temperatures and on metal-containing catalysts, even by the same authors.[113] Moreover, publications on the direct coupling mechanism focus exclusively on ethanol. So far, no other alcohols have been reported to show evidence for the direct condensation mechanism. It would be interesting to see whether other alcohols, for instance n-propanol, behave similarly to ethanol and whether the direct condensation mechanism can account for the highly specific 2-alkyl branching pattern of Guerbet alcohols. So far, only one publication[67] has reported the use of higher alcohols (n-propanol) under these conditions and the authors, who argued for direct coupling mechanisms in an earlier publication,[99] completely support the aldol condensation pathway.

The selective formation of 2-alkyl alcohols can easily be accounted for by the aldol condensation mechanism. The possibility of other mechanisms occurring at higher temperatures
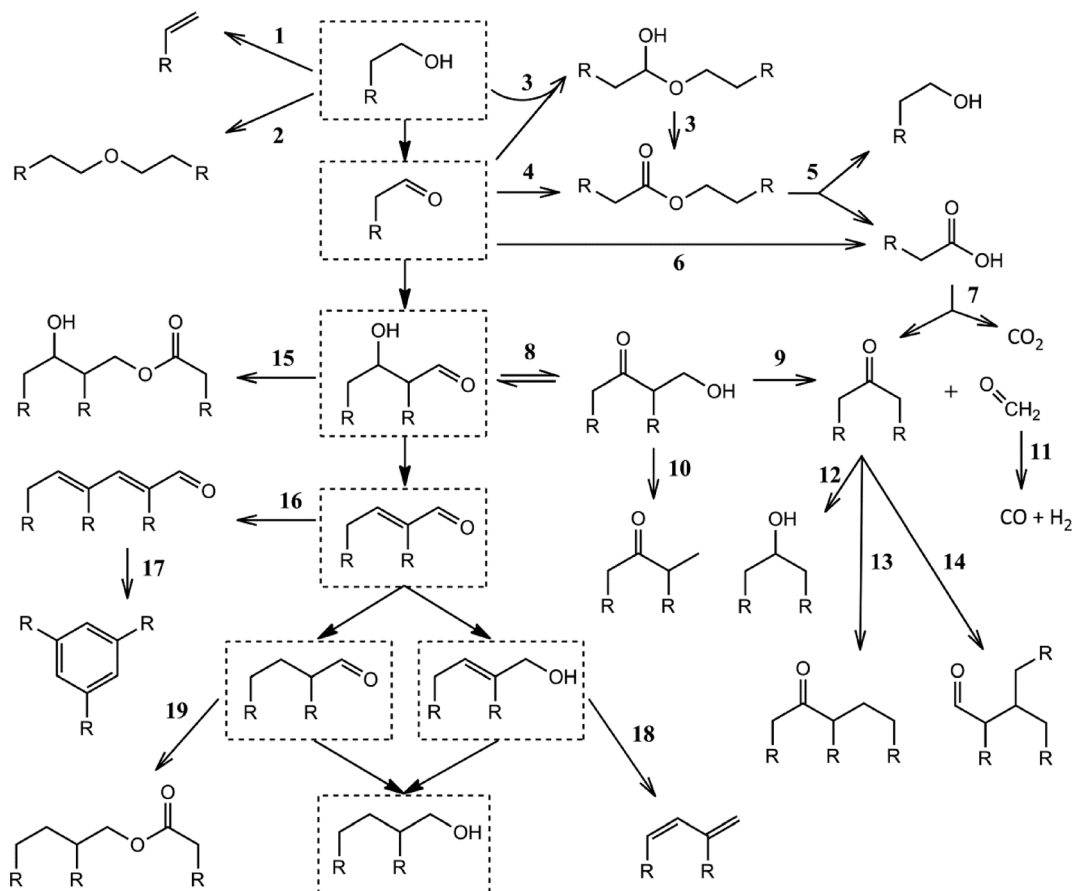
(>350 °C) is not excluded, but as this review is aimed at providing a general overview of the Guerbet chemistry, the aldol condensation pathway is considered to be the main mechanism.

3.2 By-product formation

The Guerbet condensation reaction typically generates several by-products. Their formation has been studied thoroughly,[66,95,108,109,115,116] and many by-products are explained by further reaction of intermediates in the aldol condensation pathway.[106,107,117] The most common side reactions include dehydration to olefins or ethers, esterification, oxidation to carboxylic acids and further aldol condensation to heavier compounds. An overview of the most important by-products is shown in Scheme 5.

Direct dehydration of reagent alcohols results in olefins (Scheme 5, reaction 1) or ethers (Scheme 5, reaction 2), but dehydration can also occur from coupled intermediates such as α,β-unsaturated alcohol compounds (Scheme 5, reaction 18). This is often the case in ethanol condensation and generates 1,3-butadiene, of which the formation mechanism has been studied extensively since 1933.[87,114,118–120] Dehydration usually occurs on acid sites. Studies of Guerbet condensation with catalysts having acid–base bifunctionality show that dehydration rates are higher on more acidic materials, whereas dehydrogenation is favorable over basic sites. The effect is clearly visible when materials with tunable acid–base functionality are used, such as Mg/Al mixed oxides,[72,95,115] hydroxyapatites,[121] Mg/Zr mixed oxides[103] and Na-doped ZrO₂.[69] Materials containing more and stronger acid sites facilitate undesirable dehydration reactions.

Another frequently reported side-reaction is ester formation. It is generally considered to occur by Tishchenko- or Cannizzaro-type reactions.[95,106–109] In the Tishchenko reaction, alkoxide species react with aldehydes to form esters via a hydride shift.[122,123] The Cannizzaro reaction[124] on the other hand involves the reduction of an alkanal to the corresponding alcohol simultaneously occurring with the oxidation of an aldehyde to the corresponding carboxylic acid. However, the Cannizzaro reaction typically occurs when non-enolizable aldehydes are reacted, which is not the case for Guerbet condensation. Whether the Cannizzaro reaction plays a role in acid and ester formation is not clear. As suggested by some authors,[108,125,126] hemiacetals can be formed by reaction of an alcohol with an aldehyde. Followed by dehydrogenation, this hemiacetal is subsequently converted to a more stable ester (Scheme 5, reaction 3).[125,126] Esterification mainly occurs after condensation of the aldehyde corresponding to the reagent alcohol (Scheme 5, reaction 4) but can also occur from the coupled aldehyde (Scheme 5, reaction 19) or directly after aldol addition (Scheme 5, reaction 15). The latter reaction, also called the aldol–Tishchenko reaction, produces a trimeric glycol ester.[117] Due to the fast dehydration of the aldol addition product, this compound is generally not observed in vapor phase reactions.

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Scheme 5 Scheme of by-product formation routes. Reaction numbers are referred to in section 3.2.

Hydrolysis of these esters results in the formation of the alcohol and a carboxylic acid (Scheme 5, reaction 5). Also, direct oxidation of the aldehyde or alcohol in the presence of water, base and metal catalyst results in carboxylic acid formation (Scheme 5, reaction 6).[127,128] Subsequently, the formed carboxylic acids can also condensate into ketones with liberation of CO_2 (Scheme 5, reaction 7).[106,107,129,130] As Guerbet condensation reactions are base-catalyzed, the formation of acids and CO_2 is detrimental due to poisoning of the catalytic system. Shen *et al.*[107] showed that MgO and SrO based catalysts in the vapor phase aldol condensation of butyraldehyde were deactivated with increasing amounts of butanoic acid. Similarly, Gangadharan *et al.*[106] noticed a more severe deactivation due to an increase in propionic acid during the aldol condensation of propanal over $Ce_xZr_{1-x}O_2$.

Ketones can also be derived from the aldol addition product. An intramolecular hydride shift isomerizes this aldol to the keto form (Scheme 5, reaction 8) which is then subsequently decomposed by retro-aldol reaction into formaldehyde and the ketone (Scheme 5, reaction 9). Dehydration and hydrogenation of the aldol isomer (Scheme 5, reaction 10) generates a branched ketone. Under the applied conditions, secondary alcohols are considered to be produced by hydrogenation of the formed ketones (Scheme 5, reaction 12).[95,108]

Heavier by-products are the result of further condensation reactions. Ketones (Scheme 5, reaction 13 and 14) and aldehydes (Scheme 5, reaction 16) can form higher boiling compounds through further aldol condensation reactions. The trimeric conjugated 2,4-dienal molecule can undergo a cyclization reaction to form aromatic structures (Scheme 5, reaction 17). Benzene and alkyl-substituted aryl compounds are therefore often observed in Guerbet and aldol condensation reactions.[66,106,107] Further condensation to heavier products is identified as a main factor for catalyst deactivation, especially in vapor phase reactions.[67] The acid–base properties of the catalyst should be carefully balanced in order to prevent by-product formation and catalyst deactivation. Rapid back donation of the adsorbed proton to the product is required to allow its desorption, which is one of the factors elucidating the success of amphoteric materials. An increase in stability can also be achieved by addition of a transition metal compound. Reduction of the unsaturated intermediates of the aldol-condensation pathway prevents further condensation reactions and facilitates desorption of the preferred product.[109]

The formation of the most important by-products in Guerbet condensation was investigated by calculation of the equilibrium compositions at different temperatures. Similar to the previous calculations, data were calculated for pure

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reagent feeds at a pressure of 1 atm using the equilibrium based reactor (REquil) in Aspen Plus® software. *n*-Butanol was used as a model substrate for the Guerbet condensation reaction. When esterification was considered as a possible reaction, the equilibrium compositions shown in Fig. 4A were obtained. Although formation of the ester is thermodynamically possible at the whole temperature range, butylbutyrate is only present in small amounts, about 5 mol% of the product mixture with a maximum at 350 °C.

Contrary to esterification, a complete selectivity to olefins was calculated for the whole temperature range when dehydration reactions were considered. The results are shown in Fig. 4B. At lower temperatures, prior to dehydration, the formation of the Guerbet alcohol still occurs, whereas at higher temperatures, the reagent *n*-butanol is completely dehydrated to 1-butene. No ether formation was observed. From a kinetic point of view, prevention of dehydration reactions in Guerbet condensation is of utmost importance. Dehydration is generally catalyzed by Brønsted acid sites. Hence, fine-tuning of the acid–base properties is a key factor in the development of selective and active catalytic systems for Guerbet condensation.

4. Catalyst development and reaction conditions

4.1 Homogeneous base

In 1899, Marcel Guerbet reported the condensation of primary alcohols upon heating in the presence of their sodium alkoxides.[1] Ever since, many different catalytic systems and reaction conditions have been applied in the patent and open literature. Originally, metallic sodium was used as a precursor, which in the presence of alcohols is converted into sodium alkoxides, but the expensive and reactive sodium metal is difficult to handle and is often replaced with cheaper technical-grade alkali hydroxides. Water removal is regularly applied to increase both conversion and selectivity.

Very few references report the direct condensation of alcohols using solely basic catalysis. In these cases, either high temperatures or carbonyl promoters are required together with extensive water removal. In one of the first reports described in the open literature, Sulzbacher[131] reported the self-condensation of cetyl alcohol (C_{16}) to obtain the respective branched molecule 2-tetradecyl-octadecyl alcohol (C_{32}) only by adding the sodium metal to the melted alcohol and keeping a reaction temperature of 300 °C. The main side products identified were the dimer ketone and unsaturated C_{32} molecules. The last ones appeared mostly at short reaction times, *i.e.* 30 minutes. The same author reported the use of technical-grade potassium hydroxide together with boric anhydride or alkyl borate.[131,132] A decent conversion of 79% was obtained with potassium hydroxide and the recovery of reaction products was easy since no carboxylic acid nor a ketone was formed. Similarly, Gast *et al.*[133] successfully used the combination of potassium hydroxide and boron compounds for the Guerbet reaction of unsaturated fatty alcohols such as alcohols derived from soybean and linseed oil. After reaction at 300 °C for 3 to 4 hours, both alcohols yield a mixture of condensed alcohols with average molecular weights of 720–860 Da. Only small amounts of ethers, esters, or carbonyl compounds were present in the final product from either alcohol. Alkali hydroxides were also used without boron compounds in the temperature range of 200–300 °C.[134] The use of less than 3 mol% strong alkali hydroxides (KOH, NaOH) resulted in selectivities up to 91% when water was continuously removed by azeotropic distillation. The maximum yield obtained in the patent is 64%. Increasing the amount of the KOH catalyst is beneficial for the reaction rate, but is accompanied by formation of more unwanted by-products.

An objective of Miller and Bennett was to effect the Guerbet reaction without the use of an added alkali metal or alkali metal hydroxide.[135] By combining catalytic amounts of phosphates with CaO as a water absorbent, some examples show low amounts of acid or ester by-products. From the
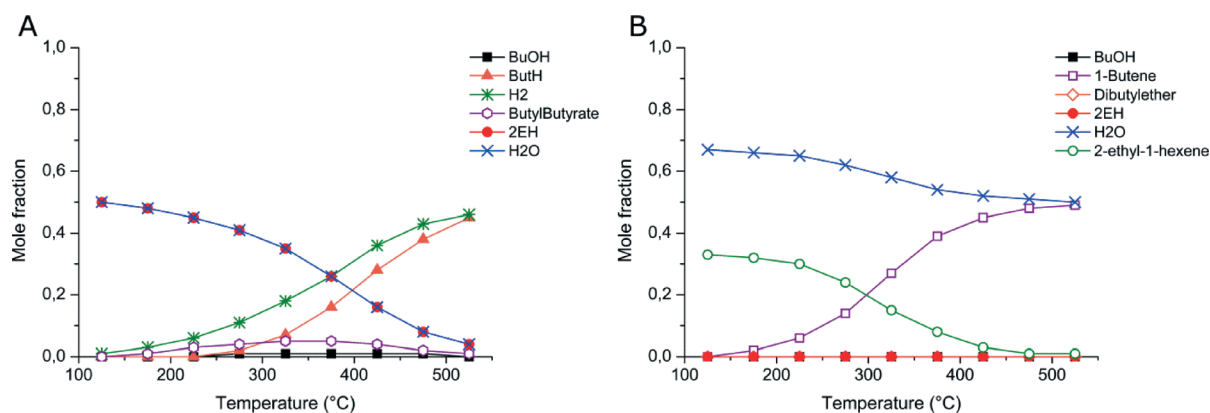

Fig. 4 Equilibrium compositions calculated for the Guerbet condensation of *n*-butanol in case the following side reactions are allowed: A) esterification to butylbutyrate; B) dehydration of *n*-butanol to 1-butene and dibutyl ether and dehydration of 2EH to 2-ethyl-1-hexene. The calculations were performed in Aspen Plus® software using the equilibrium based reactor (REquil), COMMON process type, NTRL base model and assuming a pressure of 1 atmosphere. (BuOH = *n*-butanol; ButH = butyraldehyde; 2EH = 2-ethyl-1-hexanol).

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phosphates used, the *ortho*- and pyro-phosphates are preferred as poly- and meta-phosphates are too acidic.

Dehydrogenation is generally considered to be the rate determining step in liquid phase reactions, explaining the high reaction temperatures (300 °C) in the references just discussed. While the majority of catalytic systems presented further make use of a transition metal compound as a dehydrogenation catalyst, a few relatively recent inventions are based upon the discovery that unsaturated reagents promote the reaction rate. Young *et al.*[136] used mixtures of the reagent alcohol together with aldehydes, both saturated or unsaturated, or allyl alcohols. With a metal alkoxide as the sole catalyst, suitable yields (53%) could be obtained at temperatures as low as 100–220 °C. Eliminating the need for a transition metal at these temperatures is a substantial advantage. According to the patent, the reaction mechanism occurs as illustrated in Scheme 6.
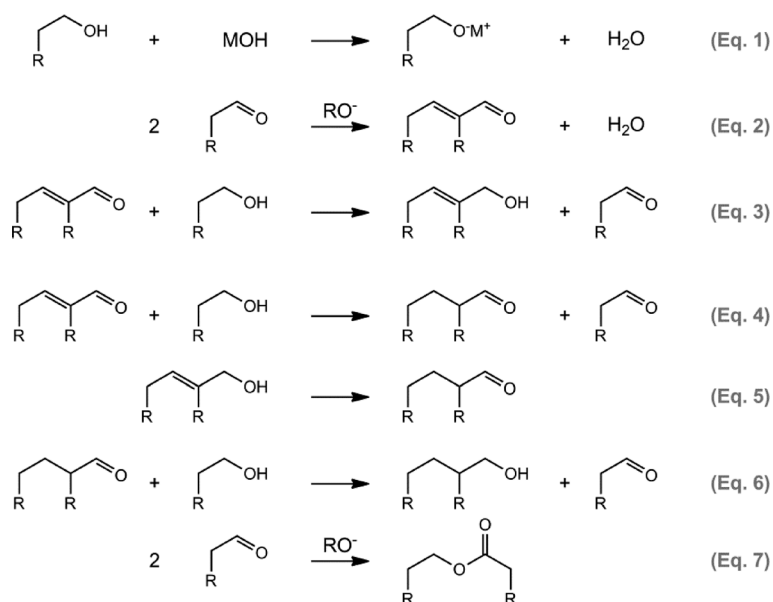
Alkoxide catalysis reduces the unsaturated dimer aldehyde either to the allyl dimer alcohol (Scheme 6, eqn (3)) or to the saturated dimer aldehyde (Scheme 6, eqn (4)), while it produces a new monomer aldehyde. Further, isomerization of the allyl dimer alcohol to the saturated dimer aldehyde (Scheme 6, eqn (5)) is also catalyzed by the alkoxide, which essentially acts as a hydrogen transfer catalyst, next to its typical activity for aldol condensation.

More recently, Waykole and co-workers[137] have prepared Guerbet alcohols by self-condensation of linear fatty alcohols ranging from *n*-octanol to *n*-dodecanol. Instead of a transition metal catalyst, heptanal was added to the reaction medium functioning as a carbonyl promoter. The reaction was performed at the reflux temperature of the corresponding alcohol (as low as 195 °C for *n*-octanol) in the presence of 3 mol% KOH. The water produced was removed by azeotropic distillation using a Dean-Stark apparatus. C_{16}, C_{20} and C_{24}

Guerbet alcohols were obtained with around 70% conversion after 9, 6 and 4 hours, respectively. The concentration of the Guerbet alcohols in the final reaction mixture was over 70 wt% in the case of the C_{16} and C_{20} products and 64 wt% for the C_{24} products.

4.1.1 Homogeneous base and homogeneous transition metal. Next to the base compound, most catalytic systems make use of metal compounds to accelerate the dehydrogenation and hydrogenation steps in the Guerbet pathway. Many combinations of strong alkali hydroxides with homogeneous transition metals have been patented: ferric ions,[138] Pd(II) alkyl carboxylates,[139] organic silver[140] and zinc compounds,[141] metals of the platinum series,[142] and Cr(III), Mn(II), Fe(II), Pb(II), and Co(II) salts.[143] The patent by Cull *et al.*[138] illustrates the empirical nature of catalyzing the reaction, wherein 0.1–0.5 wt% ionic promoters, in particular ferric ions, speed up the condensation process by three folds in the presence of NaOH, almost without affecting the selectivity. Closely related materials, such as ferrous ions, were found ineffective or insufficiently effective.

When, in the presence of an alkali metal catalyst, certain palladium compounds are used as the sole co-catalysts, a significantly improved reaction rate may be obtained. For example, only 5 ppm $PdCl_2$ can decrease the time from 7.25 h to 30 minutes.[139] In a recent patent of BP Biofuels, group VIII transition metal ions (Fe, Ru, and Os) with phosphine ligands are being used in combination with a base.[144] Catalyst compositions described herein can be obtained under the conditions of lower hydrogen partial pressure. In the example, the conversion process is carried out at a hydrogen partial pressure of less than one bar, in contrast to the patent by Mitsubishi[145] where higher hydrogen partial pressures are used with phosphines of metals from group VIII to X.

Scheme 6 Reaction steps in the Guerbet condensation mechanism according to Young *et al.*[136]

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Homogeneous transition metal catalysts were also studied by Gregorio *et al.*[146] They employed several phosphine complexes (Rh, Ru, Ir, Pt, Pd and Au) for the self-condensation of *n*-butanol in the presence of sodium butoxide at a mild temperature of 110–140 °C and atmospheric pressure. Although all the catalytic systems lost activity over time, the Rh and Ru systems were found to be the most stable ones. The improved catalytic activity shown by the rhodium precursors was correlated with the ease of hydrogen abstraction from the alcohol by Rh^{III}, Rh^{I} and Rh^{0} complexes, which form stable metal hydrides. In fact, Pd and Au-based complexes were found inactive because of the difficulty of metal hydride formation during the reaction. Burk *et al.* used Rh complexes together with alkoxides to study the role of the different catalysts in the condensation of primary[92] as well as secondary[147] alcohols. Their results indicate that Rh facilitates the initial dehydrogenation step, whereas the alkoxide promotes the aldol condensation and reduction of the reaction intermediates, coinciding with the reaction steps in Scheme 6. Water appeared to have a deactivating effect on the catalytic system and had to be removed. Hydrolysis of the alkoxide produced alkali hydroxides, which catalyze the formation of carboxylic acids and esters *via* Tishchenko or Cannizzaro reactions.

Iridium complexes were also found to be very efficient in catalyzing the Guerbet reaction of various primary alcohols (from *n*-butanol to *n*-dodecanol) in the presence of KOH or *tert*-BuOK and using an alkene as the hydrogen acceptor.[148,149] Contrary to the Rh-based catalysts studied by Burk *et al.*,[92,147] Ir complexes remained active even without removal of water and with KOH instead of potassium alkoxides. However, 1,7-octadiene was used as a hydrogen acceptor, promoting dehydrogenation in order to obtain high yields of Guerbet alcohols, and the reaction took place at 120 °C with the reagents diluted in *p*-xylene. Under these conditions, high yields of dimer alcohols were obtained. By using Ir–phenanthroline types of complexes, Xu *et al.*[150] did not require a hydrogen acceptor to achieve a high Guerbet selectivity of ethanol and *n*-butanol condensation reactions with KOH, even in the presence of water. Fujita *et al.*[151] also reported the utilization of the [Cp*IrCl$_2$]$_2$ complex as an efficient catalyst for the β-alkylation of secondary alcohols with primary alcohols at 110 °C in the presence of NaOH or NaO*t*Bu. Moreover, the studied system does not require the addition of an extra hydrogen acceptor or donor. The electronic and steric effects of the Cp* ligand were demonstrated to be essential in the performance of the Ir complex as a hydrogen transfer catalyst.[152] High selectivity for *n*-butanol, *viz.* 94% at 20% conversion, was also achieved by Dowson *et al.*[77] using a Ru phosphine complex and EtONa in the self-condensation of ethanol without a solvent. The catalyst shows remarkable control over the aldol condensation reaction, preferring the production of dimeric products over subsequent reactions.

So far, most of the homogeneous catalytic systems described in the literature for the synthesis of higher alcohols have been based on Ru or Ir complexes. In general, these catalysts were found to be very efficient for the cross-condensation of a lot of different types of primary and secondary alcohols. In 2011, Saito *et al.*[153] reported that a relatively simple Cu^{I}/H_2/NaOH system was able to catalyze the cross-coupling of various alcohols, showing a wide substrate scope with the best practicality for the selective synthesis of higher alcohols. Optimal reaction conditions were established as follows: 100 mol% alcohol 1, 100 mol% alcohol 2, CuBr (0.2 mol%), H_2 (1 atm), NaOH (4 mol%), and *p*-xylene as the solvent, at 135 °C. It should be noted that these reactions involve a secondary or conjugated alcohol, hence facilitating the dehydrogenation step at 135 °C. The authors describe a Meerwein–Ponndorf–Verley and Oppenauer types of transfer hydrogenation, in which the reagent alcohol is simultaneously dehydrogenated, while the unsaturated aldol product is reduced. The catalyst is not reduced during the reaction.

Homogeneous Ni, Ru, Rh and Pd complexes were also studied at higher temperatures (200 °C) by Carlini and co-workers.[5,81] Using MeONa, Pd(0) and Pd(II) complexes showed remarkable activity for the production of isobutanol from methanol and *n*-propanol. The oxidation state of the palladium precursor appeared to be unimportant with respect to its activity. However, during the reaction, solid deposition was observed and the results suggest that both homogeneous and heterogeneous species, in equilibrium with each other, contribute to the catalytic activity.[81] The same observations were made for Pd phosphine complexes in the self-condensation of *n*-butanol with BuONa. The complexes showed good activity, but a black solid, probably consisting of Pd(0), was formed during the reaction.[5] The authors consider the possibility that the deactivation of the Pd catalysts, reported by Gregorio *et al.*,[146] could be due to the lower temperature (120 °C) applied in the reaction. Similar to the Pd precursors, Burk *et al.*[92] noticed the formation of a heterogeneous phase when employing Rh complexes. Only in the presence of this heterogeneous phase did the system display good activity for Guerbet condensation.

The synthesis of higher molecular weight alcohols (C$_{16+}$) by the Guerbet reaction has been mostly described in the patent literature, since the β-branched primary alcohols formed in this way have a great practical value for the production of detergents, alcohols, lubricants, and personal care products.[2] Table 1 summarizes the main aspects of the aforementioned homogeneous catalytic systems reported in the patent literature.

4.1.2 Homogeneous base and heterogeneous transition metal. The industrial production of Guerbet alcohols employs homogeneous catalysts with disadvantages such as in product purification, recovery and cost of the catalyst and waste treatment. As an alternative way to deal with these drawbacks, the implementation of mixed homogeneous and heterogeneous systems have been reported for the synthesis of higher alcohols. Therefore, many research studies focus on the heterogenization of the catalytic systems. These mixed catalytic systems are normally composed of one heterogeneous dehydrogenation–hydrogenation catalyst complemented by the

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Table 1 Chronological overview of the patent literature describing homogeneous catalyst systems for the production of Guerbet alcohols

Catalytic system	T (°C)	P (bar)	Yield (%)	Starting alcohols	Reference (publ. date) (applicant)
Boric anhydride or alkyl borate + KOH	270–300	Autog.	23–39	C3–C8 (ex. C4, C5)	132 (1951)
Alkaline catalyst	200–370	100–190		C3 + C4	154 (1952) (Phillips Petroleum)
Alkali metal phosphate, pH >9	150–290	Atm., autog.		C2–C10 (ex. C4, C6)	135 (1956) (Monsanto)
NaOH + Fe(III) salts (Fe(NO)$_3$)	200–260	1(−7)	44	C10–C16 (ex. C10)	138 (1958) (Exxon Res. Eng.)
KOH (1–3 mol%)	200–300 (240–270)	Atm. or higher	47–64	C3–C20 (ex. C12)	134 (1967) (Continental Oil)
1–10 ppm Pd(II) alkyl carboxylate or Pd(II) halides + KOH	80–300 (200–300)	1	47	C2–C30 (ex. C10)	139 (1976) (Continental Oil)
Alkali catalyst + organic zinc compound	80–300	1	45–51	C1–C10 (ex. C10)	141 (1975) (Continental Oil)
Alkali catalyst + organic silver compound	80–300 (200–300)	1	54	C6–C20 (ex. C10)	140 (1975) (Continental Oil)
Alkali + metals of platinum series, ligands of organic compounds of arsenic, antimony and phosphorus	80–220 (110–180)	1	15–54	C4, C5	142 (1969) (Montecatini Edison)
Metal alkoxide (*in situ* formed) + saturated or unsaturated aldehyde or allyl alcohol	100–220	1	43–53	C6–C17 (ex. C8)	136 (1991) (Exxon Chemical)
Cr(III), Mn(II), Fe(II), Pb(II), Co(II) salts + alkali, alkaline earth hydroxides	200–245	0.65–6		C6–C22 (ex. C8)	143 (1998) (Henkel)
Group VIII to X phosphine compounds (*e.g.* Ru, Rh, Ir, Ni, Pd, and Pt) + base	180	Partial H$_2$ pressure 1–200	10–20	C2–C4	145 (2010) (Mitsubishi Chemical Corp.)
Group VIII TMI (Fe, Ru, and Os) + phosphine ligand + base	150	Partial H$_2$ pressure < 1	10–24	C2–C4 (ex. C2)	144 (2013) (BP Biofuels)

presence of a homogeneous base (*e.g.* alkali/alkaline earth hydroxides). Examples of heterogeneous catalysts described in the patent literature are ZnO,[155,156] PbO, NiO, Pd, PbSiO$_3$, PbTiO$_3$ or PbZrO$_3$,[157,158] Ni powder,[159,160] Cu powder[161] or a combination thereof[162] and supported metal catalysts such as Pt/C[163] or Pd/C.[164] Dual metal-supported systems, such as Cu–Ni/Al$_2$O$_3$, are also described.[165,166] Nanoscale metal oxides give very high yield (92%) and selectivity (96%) after purification.[167] In the open literature, heterogeneous catalysts based on Cu, Ni, Rh, Ru, Pd and Ir are described.[5,81,83,85,100,150,168]
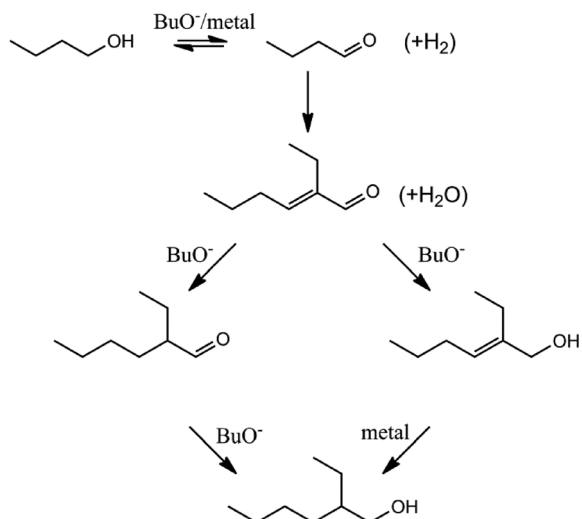
The selective synthesis of isobutanol from methanol/*n*-propanol and methanol/ethanol mixtures was thoroughly investigated by Carlini *et al.*[81,83] The authors achieved significant yield (up to 77%, after 6 hours at 200 °C) and near complete selectivity to isobutanol using copper chromite or nickel on kieselguhr together with MeONa. The high selectivity results from the fact that isobutanol does not proceed to further condensation reactions, because it lacks a second hydrogen atom at the α-carbon, which is required for aldol condensation. Higher temperatures up to 220 °C or a higher MeONa/Cu ratio increased the productivity. Replacement of H$_2$ atmosphere with N$_2$ also caused significantly higher productivity, confirming alcohol dehydrogenation to be the rate determining step under the applied conditions. A large excess of MeONa is required because water is formed in the condensation reaction and deactivates the basic catalyst through hydrolysis. Nevertheless, copper leaching from copper chromite was not observed, confirming exclusively heterogeneous activity.

The same group of authors also reported the selective synthesis of 2-ethyl-1-hexanol (2EH) by self-condensation of *n*-butanol in the presence of catalysts based on homogeneous and heterogeneous palladium systems as well as copper chromite and BuONa.[5] By using Pd/C together with BuONa,

n-butanol conversions up to 43.3% were achieved after reaction for 12 h, maintaining complete selectivity to 2EH. Nevertheless, the high leaching of palladium during the reaction (about 50% of the original Pd catalyst) reduces the interest for industrial application perspectives. When the Cu chromite/BuONa system was tested, the total selectivity to 2EH was conserved. The conversion was limited by hydrolysis of the basic component due to the water formed in the process. Although the presence of CaO as a water scavenger showed certain improvement of the catalytic performance, the best *n*-butanol conversion was obtained by increasing the reaction temperature up to 280 °C (61% after reaction for 6 h).

Burk *et al.*[92,147] evidenced the synergistic interaction between the metal and the basic component when the self-condensation of *n*-butanol to 2-ethyl-1-hexanol at low temperatures in the presence of Rh/C and sodium butoxide was performed. It was concluded that the initial dehydrogenation step requires the catalysis of both the transition metal and the base, whereas the α,β-unsaturated aldehyde derived from aldol condensation might be reduced to the Guerbet alcohol through two pathways; one is promoted only by the base and the other characterized by the successive assistance of both catalytic components. The mechanism is shown in Scheme 7, based on visualization by Carlini *et al.*[5]

In a recent report, Xu *et al.*[150] showed the heterogenization of homogeneous Ir–phenanthroline complexes as a suitable way to obtain a highly active catalyst for the synthesis of 2-ethyl-1-hexanol. In fact, the self-condensation of *n*-butanol was performed in aqueous phase by using KOH as the base. The heterogeneous catalyst was prepared *via* immobilization and pyrolysis of the *in situ*-generated Ir–phenanthroline complexes supported on carbon (5 wt% Ir). The catalyst was highly stable and no loss of activity nor Ir leaching was observed after five consecutive catalytic runs.

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Scheme 7 Schematic representation of the reaction mechanism described by Carlini *et al.*[5] for the self-condensation of *n*-butanol in the presence of BuONa.

About 42% conversion and 37% yield were obtained after 16 hours. Another heterogeneous Ir catalyst was reported by Cano *et al.*[168] who prepared a magnetite-supported IrO_2 catalyst. This reusable heterogeneous catalyst was used for the cross-alkylation of primary alcohols using KOH as the base and toluene as the solvent. A wide scope of aromatic primary alcohols were explored, reporting yields between 71 to 98% after reaction for 5 days. After recovering the catalyst from the reaction media (using a magnet) and washing it with toluene, the catalyst was re-used up to ten times without practically losing its activity. Although 3.3% of the initial amount of iridium leached out, no significant modifications were found on the surface properties of the catalyst. In addition, a blank test without a solid catalyst showed that the reaction does not proceed by leaching of iridium into the organic medium. It should be noted that these reactions always involve the most reactive alcohols, hence facilitating the dehydrogenation step at 110 °C.

In an attempt to reduce carboxylic acid formation and increase catalyst activity with regard to alkali alkoxides and hydroxides, early publications describe the use of weaker bases such as carbonates or phosphates in liquid phase Guerbet reactions. Dvornikoff and Farrar[112,169] employed potassium carbonate together with anhydrous magnesium oxide and copper chromite in the condensation of ethanol at 230 °C. After 8 hours, the conversion remained at 20%. Molar selectivity to carboxylic acids was less than 5%. Contrary to the addition of a fresh catalyst, it was the removal of water by distillation that permitted further reaction of the reagent alcohol, hence the conversion was doubled. Another detrimental effect of water was published by Miller and Bennett.[111,135,170,171] Employing tripotassium phosphate together with calcium oxide and activated copper powder in the condensation of *n*-butanol at 300 °C, the authors achieved 42% conversion at a selectivity of 76% after 4.5 hours.

Although tripotassium phosphate appeared to be an active catalyst and acid formation was reduced, water removal by azeotropic distillation further reduced the formation of acids significantly. Molar selectivity to the unwanted acid was reduced from about 20% to about 10%. The use of potassium triphosphate with Cu and Ni–Cu dehydrogenation catalysts was also published by the same authors in several patents.[115,150,151] Regarding the (de)hydrogenation catalyst, gaseous products such as H_2, CO_2, CO and CH_4 were produced, especially by RANEY® Ni.[111] Using $CuCrO_4$, this decomposition was minimized.

Kao Corporation discovered that the combination of copper and nickel on a supported catalyst is better than either copper chromate or RANEY® nickel.[166] Reaction rates per unit metal weight were several times higher in Cu–Ni/Al_2O_3 catalysts (Cu : Ni = 1 : 9 to 9 : 1; 10–60 wt.% metals), which allows the reaction to be carried out at lower temperatures. As a consequence, the formation of carboxylic acid salt (soap formation) by-products was reduced and high yields above 85% were obtained. A physical mixture of Ni and Cu metal powders was also discovered to be beneficial for the condensation of mixed alcohols by Chevron.[162]

Even with the use of a dehydrogenation catalyst, the Guerbet reaction is sometimes further accelerated by the addition of carbonyl promoters.[172] Several examples give high yields (>80%) for the conversion of *n*-decanol (Table 2). Aldehydes or ketones were added at a temperature above 180 °C, not only to initiate and promote the condensation reaction but also to resume conversion after substantial completion of the reaction, resulting in increased conversion to the Guerbet alcohol. After completion of the reaction, alcohols, alkoxides and hydrides can also be used to reduce the levels of unsaturated compounds and carbonyls.[172]

The use of homogeneous bases poses some implications for industrial applicability, such as stability of the dehydrogenation catalyst, reactor vessel corrosion and intensive product purification. Leaching (*i.e.* the formation of reaction-soluble components that are difficult to recover for recycling) is a problem encountered with the basic activation of dehydrogenation catalysts. Copper, zinc and lead oxides generally leach and in the case of lead oxides, sintering and formation of hard balls can also be troublesome.[173] High yields and conversions are obtained by the use of insoluble lead salts (of an oxyacid from a group IV element) that are stable under the reaction conditions.[158] In a different patent report, the stabilization of the hydrogenation catalysts, *i.e.* Pd supported on activated carbon,[164] was achieved by confinement of Pd in a hydrophobic environment. This situation protects the hydrogenation catalyst from leaching in alkaline medium (Tables 3–5).

Several Henkel patents pay attention to the purification process. The poorly soluble soap is removed by filtration, centrifugation or extraction, and then distillation.[157] However, a filter cake is obtained during filtration, which results in increased waste. The described extraction with water gives rise to strongly heavy metal-polluted wastewater. In another

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Table 2 Chronological overview of the patent literature describing homogeneous/heterogeneous catalytic systems for the synthesis of Guerbet alcohols

Catalytic system	T (°C)	P (bar)	Operation mode: batch (B) or continuous (C)	Yield (%)	Starting alcohols	Reference (publ. date) (applicant)
MgO, BeO, ZnO, CaO, CuO, NiO and mixtures	240–400	60–300	B	30–34	C2	175 (1933)
Copper chromite or copper on alumina gel (reduced in H_2) + K_2CO_3 (+ Al_2O_3)	200–230 (>150)	10–70	B	65	C2	176 (1935) (Du Pont)
NaOH (formation alcoholate) + Zn dust + ZnO	120–300	1	B	37–54	Prim. + sec.	177 (1949) (Carbide)
Soda lime copper oxide–chromium oxide (condensation zone) + RANEY® nickel (hydrog. zone)	375–580	1–70	C	4–27	C2–C10 (to 2n − 1)	178 (1953) (Phillips Petroleum)
Alkali metal phosphate, pH >9 + copper dehydrogenation catalyst	150–290	1–autog.	B		C2–C10 (ex. C4, C6)	135 (1956) (Monsanto)
Tripotassium phosphate + 1 : 1 nickel–copper catalyst + inert liquid (bp. 60–150 °C)	150–250	1–autog.	B	17–54	Unsaturated C10–C24	171 (1958) (Monsanto)
Tripotassium phosphate + 1 : 1 nickel–copper catalyst + inert liquid (bp. 60–150 °C)	206–210	1–autog.	B	49–85	ex. C13	170 (1958) (Monsanto)
K_2CO_3, MgO, copper chromite + alkali	225–250	autog.	B	47–70	C2–C8 (ex. C2, C4)	169 (1961) (Monsanto)
NaOH + Ni on kieselguhr + lead acetate trihydrate	165	1	B	53–72	C2–C18 (ex. C8)	179 (1964) (Gulf R&D Comp.)
Metal of platinum group deposited on support (e.g. Pd/C) + alkaline	80–300 (110–160)	1	B	35	C1–C20 (ex. C4–C6)	180 (1970) (Montecatini Edison)
Base + insoluble Pb catalyst (oxyacid from group IV elem., e.g. silicate, titanate, zirconate, germanate, and hafnate)	80–400 (150–240)	1–autog.	B	72–84	C2–C20 (ex. C8)	158 (1977) (Henkel)
Cu–Ni/Al_2O_3 (Cu : Ni = 1 : 9 to 9 : 1) + KOH	200–230	1	B	85–90	C3–C27 (ex. C8, C10)	166 (1985) (Kao Corp.)
KOH + ZnO (aldehyde (or ketone) promoted Guerbet reaction)	180–250	1	B	77	C10	172 (1991) (Henkel)
Pt/C + NaOH or KOH	175–210	1	B		C1–C20 (ex. C10)	163 (1989) (Exxon Chemical Patents)
Catalyst mixture of (i) $Fe_2(SO_4)_3$, (ii) $CuCO_3 \cdot Cu(OH)_2$, and (iii) Ni powder + KOH	180–250	1	B and C	60–75	C6–C22 (ex. C8)	174 (1991) (Henkel)
ZnO, PbO, NiO, Pd, $PbSiO_3$, $PbTiO_3$ or $PbZrO_3$ + alkali, alkaline earth oxides, hydroxides	200–280	1–4	B	78–83	C2–C30 (ex. C8, C10)	157 (1996) (Henkel)
ZnO + alkali, alkaline earth hydroxides	200–245	0.65–6	B	67	C6–C22 (ex. C8)	143 (1998) (Henkel)
KOH, ZnO	180–350 (250–320)	1(−30)	B		C2–C30 (ex. C6, C10)	156 (1999) (RWE-Dea)
Alkali metal hydroxide + amorphous nickel	160–260	1	B	90	C6–C30 (ex. C8, C10, and C12)	160 (2002) (China Petrochemical Corp.)
KOH, Ni powder	100–270	2–20	B	91	C4–C20 (ex. C12)	159 (2010) (Shijiazhuang)
Nanoscale metal oxide + strong alkaline substance (e.g. CuO/BaO)	140–200	1	B	92	C6–C14	167 (2009) (Lanzhou Chem. Phys. Inst.)
Pd/C + KOH + carbonyl compound (e.g. aldehyde)	120–250 (140–230)	0.1–6	B	30–75	C8 + C10; C5	164 (2012) (Cognis IP Manag.)
Cu/Ni (80 : 20) metal powder + KOH	228–250	1	B	58–90	C12 + C14; C10 + C12 + C14	162 (2014) (Chevron)

patent,[156] alcohols are condensed in the presence of alkaline and/or heavy metal catalysts at a high temperature, while water is removed from the reaction, whereby the product is then directly separated from the reaction by distillation, with no additional purification process and providing metal-free and soap-free Guerbet alcohols. A process using distillation with at least two stages was also developed to produce high purity Guerbet alcohols.[174]

4.2 Heterogeneous systems

The use of homogeneous bases in the Guerbet reaction imposes thorough purification of the product stream as well as recovery of the basic compound together with waste treatment. Also, these bases cause metal leaching and corrosion of reactor vessels and are often deactivated by the co-produced water resulting in incomplete conversions and by-product formation. In order to develop cost-efficient production processes for Guerbet alcohols, the use of solid acid–base catalysts is required. Completely heterogeneous catalytic systems are easily separated from the reaction mixture, do not cause corrosion and metal leaching and can ideally be reused multiple times without extensive regeneration. They can be fixed in a catalyst bed, thus facilitating continuous operation e.g. in a simple plug flow reactor set-up. This

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Table 3 Chronological overview of the patent literature describing purely heterogeneous systems for the synthesis of Guerbet alcohols

Catalytic system	T (°C)	P (bar)	Operation mode: batch (B) or continuous (C)	Yield (%)	Starting alcohols	Reference (publ. date) (applicant)
Magnesium oxide + copper oxide (+ Al_2O_3)	200–400	(+ H_2)	C	20	C2	181 (1935)
Composed of MgO, CuO, and Al_2O_3	150–450	up to 50 (H_2)	B and C		C4+	182 (1937)
Alkali or alkaline earth metal supported on high surface support (*e.g.* γ-Al_2O_3) (a Pt group metal)	200–400	70–345	C		C1 + C2	201 (1976) (Celanese Corporation)
MgO/NaY + Ni powder	100–270	1	B	(95% after distillation)	C6–C30 fatty alcohols	199 (2007) (China Petrochemical Corp.)
Partially or fully decomposed hydrotalcite	200–500	1–200	B and C	1–20	C2	190 (2009) (Du Pont)
Group II metal salts supported on lanthanum promoted oxide containing alumina	200–500	1–200	C	8–10	C2	200 (2010) (Du Pont)
(1) Decomposed hydrotalcite (HT) or (2) combination of HT and metal carbonates or (3) HT surface impregnated with a TMI nitrate. ((2) and (3) have also been thermally decomposed.)	200–500	1–200	C	18–50	C2	191 (2012) (Du Pont)
$(M_wM'_xM''_yM'''_z)_5(PO_4)_3(OH)$ (M = Mg, M' = Ca, M'' = Sr, M''' = Ba (and base treated catalyst compositions))	150–500	1–200	C	1–21	C2	196 (2012) (Du Pont)
Ca or Sr hydroxyapatite, hydrotalcite, $Mg(OH)_2$ or Rb–Li ion-exch. zeolite X	200–450	<1 (gas phase)	C	10–58	C1–C3 (ex. C2)	197 (2012) (Sangi, Yoshioka Tetsuya)
Sr phosphate apatite Sr/P: 1.5–2	200–350		C	6–13 (sel.: 80–86)	C2	195 (2012) (Sangi, Kochi University)
Metal coated hydrotalcite (metal = Mg, Al, Ga, Ge, Sn, Pd or Cu, or combination *e.g.* Cu–Mg/Al-HT)	250–400	1–51	C	13–39	C2	192 (2014) (Celanese Int. Corp.)
CuO + ZnO + traces of aluminium	275–350	1–3	C	1–15 (-63^a)	C2	203 (2014) (ECN)

[a] Yield of crotonaldehyde + butyraldehyde + 1-butanol (to be hydrogenated to the Guerbet alcohol).

Table 4 Overview of the most important heterogeneous catalysts for the vapor phase synthesis of Guerbet alcohols at atmospheric pressure (open literature)

Catalyst	Reactant (ratio)	T (°C)	$GHSV^a$ (std cm^3 g_{cat}^{-1} h^{-1})	$Conversion^b$ (%)	$Yield^b$ (%)	$STY^{b,c}$ (g_{prod} kg_{cat}^{-1} h^{-1})	Ref.
MgO	C1 + C2 (20 : 1)	390	~950	60	45	55	80
MgO	C1 + C2–C5 (20 : 1)	380	~950	50–60	40	55–80	105
MgO	C2	450	—	55	11	—	67
MgO	C3	450	—	27	13	—	99
Mg_3AlO_x	C2	350	~960	35	14	~400	72
$Mg_3Fe_nAl_{1-n}O_x$	C2	400	~1000	50	10	~220	187, 188
$Cu_{10}MgAlO_x$	C1 + C3 (6.25 : 1)	280	~1200	100	80	~400	84
$Cu_{25}MgAlO_x$	C1 + C2 (4 : 1)	250	3000	70	—	65	109
$Ca_{1.64}$-P HAP	C2	350	$~880^d$	25	18	~470	65
$Sr_{1.7}$-P HAP	C2	300	$~570^d$	11	9	~160	73
Na_2CO_3/NaX	C1 + C2 (20 : 1)	300	~950	40	—	45	198

[a] GHSV = alcohol gas-hourly space velocity at stp (298 K, 101 kPa), inert gas excluded. [b] Based on the heaviest reagent alcohol. [c] Space time yield of Guerbet-type condensation alcohols. [d] Considering the specific volume of HAP = 3 ml g^{-1}.

allows for easier integration with subsequent post-treatment steps such as an extra hydrogenation step or purification by distillation. Performing the reaction in vapor phase allows higher temperatures to be attained without pressure build-up, which generally imposes practical limitations to liquid phase systems. At high temperatures, typically 350–450 °C, the basic catalyst also catalyzes dehydrogenation and hydrogenation reactions. Therefore, many publications describing high temperature (>300 °C) vapor phase reactions do not report the use of transition metal catalysts. On the other hand, in every single publication reporting about heterogeneous

liquid phase Guerbet reactions, a transition metal catalyst is applied.

MgO. Various basic oxides have been investigated as heterogeneous catalysts for the Guerbet reaction. The reaction rates of light alcohols on heterogeneous catalysts have already been reviewed extensively by Kozlowski and Davis.[7] MgO is by far the most used due to its superior activity and selectivity and often serves as a reference catalyst. A number of publications describe the use of MgO in vapor phase reactions without a transition metal catalyst. According to the studies of Ueda,[80,105] who studied the cross-condensation of

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Table 5 Overview of the most important heterogeneous catalysts for the liquid phase synthesis of Guerbet alcohols (open literature)

Catalyst (atomic ratio M/Mg/Al)	Reactant (ratio)	T (°C)	P (bar)	Time (hours)	Conversion[a] (%)	Yield[a,b] (%)	STY[c] (g_{prod} kg_{cat}^{-1} u^{-1})	Ref.
Cu chromite (19 wt%[d]) + MgAlOx (66:34)	C1 + C3 (12.5:1)	200	30	12	30	30	87.8	82
CuMgAlOx (2:69:29)	C1 + C3 (12.5:1)	210	30	12	40	40	93.6	84
CuMgAlOx (5:71:24)	C2	200	Autog.	5	4	1.6	203.4	110
PdMgAlOx (5:71:24)	C2	200	Autog.	5	4	2.9	368.6	76
20% Ni/Al2O3	C2	250	70	72	27	22	78.8	68

[a] Based on the heaviest reagent alcohol. [b] Space time yield of Guerbet-type condensation alcohols. [c] Calculated at the specified reaction time. [d] Weight percentage of the physical mixture of catalysts.

methanol with various primary alcohols, Guerbet condensation occurs as the basic surface promotes both condensation and hydride shift, facilitating the formation of saturated higher alcohols. It is interesting to note that such a multi-step reaction readily takes place on an oxide surface and that MgO in particular has a high ability to yield fully-hydrogenated higher alcohols. At a temperature of 380 °C, a selectivity of up to 80% was obtained for a conversion of 50%.

MgO was also applied in the vapor phase self-condensation of propanol by Ndou and Coville.[99] The reaction gave 2-methylpentanol and propionaldehyde as the major products. The introduction of hydrogen before and during the reaction enhanced the catalyst selectivity to 2-methylpentanol. Again, the important role of hydrogen transfer in the reaction was mentioned. The highest selectivity (69%) was achieved in the presence of hydrogen at 450 °C with a propanol conversion of 24%.

Note that, in order to catalyze hydrogen transfer, high temperatures are applied. 300 °C appears to be the minimum temperature at which detectable activity for the Guerbet reaction is reported for catalytic systems consisting solely of MgO.[7,99,115] Modification of the MgO surface with alkali, alkaline earth or transition metals did not result in an increased coupling rate.[67,80] Addition of Ni to MgO supported on activated carbon increased the selectivity to the saturated Guerbet alcohol.[79] Increasing the basicity of the material, e.g. by addition of alkali metals, resulted in an increased selectivity to dehydrogenation products but did not increase C–C bond formation.

A mixture of CuO and MgO with small amounts of Al2O3 was already patented in 1935 for vapor phase ethanol condensation.[181] Contrary to the general consensus that hydrogen atmosphere slows down the reaction, a beneficial effect was mentioned for the use of hydrogen as a carrier gas, most probably due to reasons of selectivity. By bringing ethanol vapor (40 mol%) into contact with the CuO/MgO/Al2O3 catalyst bed at a temperature of 260 °C, an n-butanol yield of 15% was obtained at 56% conversion. Similar catalytic systems are described in a second patent for the cross-condensation of n-pentanol with ethanol.[182]

Mg/Al mixed oxides. Often it is argued that the coupling reaction requires paired acid–base sites, for instance, by incorporation of more acidic metals into MgO. An extensively studied material is Mg/Al mixed oxides, in which Lewis acidic Al is incorporated into the MgO structure. These materials are generally synthesized by calcination of hydrotalcites. A hydrotalcite is an anionic layered material or layered double hydroxide (LDH) that is considered to be a predominantly basic support. Al atoms are partially substituted in the layered brucite structure of $Mg(OH)_2$, causing an excess of positive charges. In between the hydroxide layers, the positive charges are neutralized by intercalated anions.[183] Upon calcination, the layered structure collapses upon removal of the anions and a mixed Mg/Al oxide is obtained. It is well known that these Mg/Al mixed oxides possess several sorts of active sites. Weak Brønsted basic sites are associated with surface hydroxyl groups remaining after activation; medium-strength Lewis sites are related to Mg^{2-}–O^{2-} and Al^{3+}–O^{2-} acid–base pairs; strong Lewis basic sites are due to the presence of low-coordinated O^{2-} species. Mg/Al mixed oxides are well-known catalysts for C–C bond formation reactions such as the aldol self-condensation of acetone or cross-condensation with e.g. citral.[184–186]

A very important property of hydrotalcites and their activated mixed oxides is their versatility. Mg or Al atoms can be substituted by transition, noble or lanthanide atoms introducing new metal–O^{2-} acid–base pairs, thereby changing the overall acid–base properties of the material. Also, the Mg/Al ratio can be adjusted, changing the number and strength of the acid and basic sites. Di Cosimo et al.[95,115] studied the influence of the Mg/Al ratio on the acid and base properties of mixed oxides and published a detailed mechanistic study of all reactions that can occur when reacting alcohols in vapor phase over calcined hydrotalcites with varying Mg/Al ratios. The incorporation of a small amount of Al into the brucite layer significantly increases the density of acid–strong base pair sites. Higher contents (5 > Mg/Al > 1) lead to an increased density of basic sites due to the formation of coordinatively unsaturated oxygen sites. As evidenced by CO2 and NH3 sorption experiments, higher amounts of Al also lead to an increased density of acidic sites. Materials with a high amount of Al incorporated (Mg/Al < 1) therefore favor dehydration of the alcohols instead of dehydrogenation and condensation reactions. By varying the Mg/Al ratios, hence changing the acid–base properties, the selectivity can be optimized towards dehydrogenation, aldolization and hydride shift. Strong acid sites are to be avoided due to their dehydration properties, yet a moderate amount of acidity facilitates coupling of the intermediates.[95,115,187]

Similar findings were also reported by León et al.[187,188] for vapor phase ethanol condensation. The authors show that a 'medium base pair' can selectively transform ethanol into acetaldehyde. Mg^{2+}–O^{2-} pairs are believed to be the active sites for hydrogen abstraction. Moreover, by replacing the Al sites with Fe sites, the acidity of the catalyst is significantly reduced, thereby limiting the dehydration of ethanol in favor of the condensation towards desired C_4 fragments.[187]

Carlini et al.[82] substituted Mg/Al mixed oxides for the homogeneous alkali alkoxides previously used in the liquid phase Guerbet condensation of methanol and n-propanol. In combination with pre-activated copper chromite, Mg/Al mixed oxides obtained by calcination of the corresponding hydrotalcite precursors appeared to be active catalysts. In all cases, an almost complete selectivity to isobutanol was found in the conversion of n-propanol. Contrary to the alkali alkoxides, the activity of these systems was not affected by the co-produced water, with no evidence of inhibition during the course of the reaction being observed. Again, the activity was found to be affected by the Mg/Al atomic ratio in the hydrotalcite precursor, in correspondence to the variation of the relative amount of medium/strong and strong basic sites. The heterogeneous catalyst with the lowest Mg/Al ratio and the highest basic strength showed the maximum selectivity to isobutanol. 30% n-propanol conversion was achieved after 12 hours of reaction at 200 °C.

As the next step, the same group developed a single bifunctional heterogeneous catalyst to replace the copper chromite–Mg/Al mixed oxide system. Aiming to simplify the catalytic system and exploit potential synergistic effects in Guerbet condensation, the Mg/Al mixed oxide was doped with Cu^{2+} ions into the hydrotalcite.[84] Particularly when Cu/Mg/Al mixed oxides prepared by co-precipitation were adopted, an activity similar to that of the physical mixture with copper chromite was measured. Upon increasing the temperature to 210 °C, an increase in conversion of 10% was achieved, keeping 100% selectivity to isobutanol. These promising results were also confirmed in preliminary experiments carried out in a continuous flow reactor adopting a vapor phase. In this vapor phase plug flow reactor, the yield further improved to 80% at a reasonable temperature of 280 °C. The authors have tried several other (de)hydrogenating metals (Ni, Pd, Ag, and Pt) but concluded that only Cu enhanced the activity of the hydrotalcite catalyst to an appreciable level while all the other doped elements showed no synergistic effect. Similarly, Bravo-Suárez et al.[109] noticed that catalyst deactivation in vapor phase reactions was minimized upon incorporation of Cu into the Mg/Al mixed oxide. The authors report the requirement of moderate Cu loadings and intermediate temperatures to favor the selective formation of C–C coupled products. Upon Cu addition to the hydrotalcite-derived Mg/Al mixed oxides, a significant increase in ethanol dehydrogenation at 250 °C was also reported by Hosoglu et al.[189]

It should be noted that the cross-condensation of methanol with ethanol cannot simply be compared to self-condensation reactions of primary alcohols nor to condensation reactions between methanol and n-propanol. The rates of dehydrogenation differ according to the reagent alcohol and contrary to higher aldehydes, methanol cannot form an enolate.[7] Nevertheless, the observed catalytic characteristics can be extended to general trends in Guerbet condensation.

Marcu et al.[76,110] made an analysis of different transition metals supported on Mg/Al mixed oxides for the liquid phase Guerbet reaction of ethanol to butanol. In their studies, they did not focus so much on the optimal conditions for the highest yield, but rather on obtaining a fundamental understanding of the role of catalytic sites, as well as the role of acetal intermediates at the temperature applied (200 °C). The authors identified an optimum loading of Cu between 5 and 10 at.%. Contrary to the coupling of methanol to n-propanol previously mentioned,[82,85] a detrimental effect of water on the catalytic activity was observed.[110] Investigating several other transition metals (Pd, Ag, Mn, Fe, Cu, Sm, and Yb), the highest n-butanol yields were obtained with the Pd-containing mixed oxide which exhibited remarkable stability during the reaction.[76] A good correlation was found between the amount of basic sites of medium and high strength and the selectivity towards n-butanol.

Several patents describing the use of (modified) calcined hydrotalcites in the vapor phase condensation of ethanol have also been published. Using partially or fully decomposed Mg/Al hydrotalcites, n-butanol was obtained in 20% yield at 45% conversion and a temperature of 300 °C.[190] Introduction of Ni, either during the hydrotalcite synthesis or via impregnation, allows the reaction to proceed at lower temperatures. At 215 °C, a feed of ethanol containing 8% water was converted to higher alcohols with a selectivity of 75% at conversions between 45 and 67%.[191] Good results were also obtained with Cu- and Pd-coated hydrotalcites. The Pd–Mg/Al oxide mentioned in the examples achieved an n-butanol yield of 34% at 54% conversion under the conditions of 3.4 MPa and 290 °C.[192]

Hydroxyapatites. The mineral hydroxyapatite (HAP) or $Ca_{10}(PO_4)_6(OH)_2$ is known to function as a catalyst with both acid and base sites, depending on the manner in which it is synthesized. Tsuchida et al. studied the Guerbet reaction of ethanol over HAP at 300 °C using catalysts of different Ca/P molar ratios.[65,121] These were prepared by controlling the pH of the solution during precipitation synthesis. They found that the distribution of acidic and basic sites on the catalyst surface varied with the Ca/P ratio of the HAP. Analogous to the aforementioned Mg/Al mixed oxides, the rates of dehydration and dehydrogenation are influenced by the Ca/P ratio, hence the amount of acidic and basic sites. Ca-deficient materials, e.g. with a Ca/P ratio of 1.59, have a higher density of acid sites. Upon increasing the Ca/P ratio up to a stoichiometric value of 1.67, the material surface contains less acidic and more basic sites, as evidenced by CO_2 and NH_3 sorption experiments.[121] The authors concluded that HAP catalysts – without the addition of noble metals, transition metals, or halogens – can be used for the highly selective synthesis of

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valuable compounds like *n*-butanol and 1,3-butadiene from ethanol merely by controlling the catalyst's Ca/P molar ratio.

In a study by Ogo *et al.*, the selectivity to *n*-butanol was further increased by replacing Ca with Sr, creating strontium hydroxyapatites, whereas substitution of phosphate with vanadate ions strongly decreased the selectivity due to extensive dehydration of ethanol.[73,96] The overall conclusion remained the same: the more basic the catalyst is or the more basic sites the catalyst possesses, the higher the selectivity will be towards the Guerbet alcohol and the less the other side reactions will occur.

The importance of acid–base bifunctionality has once more been confirmed in two recent papers.[193,194] Hanspal *et al.*[193] compared HAP and MgO for ethanol condensation using isotopic transient kinetic analysis together with acid–base characterization. HAP was found to expose a higher density of both basic and weak acidic sites which explained why it was about three times more active. As compared to MgO, a greater fraction of the acetaldehyde formed undergoes aldol condensation on HAP. Silvester *et al.*[194] synthesized modified hydroxyapatites and found an optimal *n*-butanol yield on materials with an acidity/basicity ratio of 5. Fine-tuning of both the nature and the amount of acid–base sites is a key to optimize both conversion and selectivity of the Guerbet reaction.

The use of Ca- and Sr-hydroxyapatites for ethanol condensation is disclosed in several patents, reporting similar catalytic performance. The best results are obtained on Sr-HAP either used directly after synthesis[195] or treated with Sr(OH)$_2$ solution[196] at temperatures of 300–400 °C. Operating under reduced pressures greatly increases the conversion.[197]

Other catalysts. Basic zeolites have also been reported as condensation catalysts for the production of short chain alcohols in vapor phase.[75,197–199] Yang and Meng[75] prepared various alkali-zeolites *via* combination of ion-exchange and impregnation. By reacting ethanol at a temperature of 400 °C, the best selectivity was obtained with a Rb–LiX zeolite. Remarkably, without excess Rb, only dehydrogenation activity was observed. An excess of Rb species was required for the condensation step in the reaction. Similarly, Gotoh *et al.*[198] prepared impregnated NaX with Na$_2$CO$_3$ and obtained decent selectivity to higher alcohols for the condensation of methanol and ethanol at 300 °C. Impregnating the zeolites with alkali salts results in an increased reactivity for base-catalyzed reactions, a trend that was also reported for CsNaX zeolites in the dehydrogenation of *n*-propanol.[102]

Zirconia, generally regarded as an amphoteric oxide, has also been reported to be active for Guerbet condensation reactions. Kozlowski *et al.* studied the acid–base properties of pure and modified ZrO$_2$ and their effect on the selectivity in vapor phase ethanol condensation. In one report, the authors prepared Mg/Zr mixed oxides by various methods for the Guerbet condensation of ethanol.[103] Addition of Zr to the MgO catalyst however increased the acid site density and hence dehydration reactions of ethanol to ethane. The addition of Zr therefore appeared detrimental to the catalytic

performance of MgO. In another publication, the same authors loaded ZrO$_2$ with different amounts of Na (0–1 wt%).[69] Addition of 1 wt% Na to the catalyst was efficient to neutralize the acid sites, as evidenced by NH$_3$ sorption, and therefore greatly increased *n*-butanol selectivity at 400 °C. The coupling rate, however, did not increase due to Na modification.

Another mixed oxide reported for condensation reactions is the potassium-doped Mg/Ce oxide reported by Gines and Iglesia.[94] The authors studied ethanol reactivity on K–Mg$_5$CeO$_x$ with and without copper addition in the vapor phase. Reactions were carried out in a recirculating batch reactor at 300 °C and atmospheric pressure. Again, addition of copper was proven to have a beneficial effect. Dehydrogenation as well as condensation reactions were greatly increased for the sample containing 7 wt.% Cu. Copper facilitates dehydrogenation of the reagent alcohol as well as hydrogenation of the coupled intermediates.

Another catalyst reported for vapor phase Guerbet condensation of ethanol is La-promoted Al$_2$O$_3$ impregnated with alkaline earth compounds.[200] Impregnating La-promoted alumina with Ca, Sr or Ba salts resulted in catalysts that produced *n*-butanol at 400 °C. Selectivities between 23–35% were obtained at conversions of 30–38%. The use of Pt group metals on Rb-impregnated alumina has also been patented.[201]

The vast majority of Guerbet catalysts described so far contain either an alkali or an alkaline earth metal. Yet, there are a few materials, free of alkali and alkaline earth metals, that were shown to be active Guerbet condensation catalysts. Riittonen *et al.* studied different transition metals (Ru, Rh, Pd, Pt, Au, Ni and Ag) supported on alumina for liquid phase ethanol condensation without addition of a specific base at a temperature of 250 °C.[68] Interestingly, a commercial Ni/Al$_2$O$_3$ catalyst showed high selectivity for *n*-butanol. After optimization of the reaction conditions, a high selectivity (80%) was obtained at a conversion of about 25% after 72 hours. The authors report the detrimental effect of water on ethanol conversion, which was increased from 20 to 30% after addition of water-absorbing molecular sieves. The authors have recently published a second paper in which they compare different materials of Co, Ni and Cu on Al$_2$O$_3$.[202] The most active materials found were those with a low copper loading or a high amount of Ni. On the other hand, Co and higher loadings of copper produced more ethyl acetate. The authors investigated the catalyst's structure and concluded that the reaction is highly sensitive to the crystal structure; octahedrally-coordinated metal cations catalyze Guerbet condensation, whereas tetrahedrally-coordinated cations stimulate esterification reactions due to differences in the strength of metal–support interactions. It is proposed that the inverse spinel metal aluminate structure is the catalytically active site for Guerbet condensation.[202]

Recently, Van Hal *et al.* have reported the use of a catalyst for vapor phase ethanol condensation that preferably exhibits acid character.[203] The catalyst comprises at least 20 mol% copper and between 20–80 mol% Mg, Al, Si and Zn,

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preferably in the forms of Mg_2SiO_4, $Zn_6Al_2O_9$ and boehmite. While the yields remain modest at atmospheric pressure, increasing the pressure to 3 bar oddly resulted in an increase of selectivity to the desired C4 products. At 350 °C, a conversion of 96% and a yield of 50% were obtained at a contact time of 8 s.

The self-coupling of secondary alcohols at low temperatures (80–144 °C) was studied by Shimura and co-workers.[204] Various secondary alcohols (2-octanol, 2-hexanol, 2-butanol, 3-methyl-2-butanol, cyclopentanol and 2-propanol) were converted using 3 or 5 wt% Ni/CeO$_2$ catalysts and o-xylene as the solvent. It should be noted that the main product formed was not the secondary alcohol dimer but its corresponding ketone. After pre-reduction of the catalyst in the presence of hydrogen at medium temperatures (250–300 °C), the self-coupling reaction to mainly higher ketones is highly favored, even at low temperatures (80–144 °C). The catalyst was reused at least two times without any indication of deactivation or Ni leaching, proving its robustness under the tested reaction conditions. A reaction mechanism was proposed in which Ni^0 acts as a hydrogen-transfer component, while ceria facilitates the aldol condensation step (Scheme 8).

5. Technological considerations and challenges

Since Marcel Guerbet first discovered the chemistry of alcohol condensation, numerous patents and publications have been published describing many different catalytic systems applied in the coupling of various alcohols for both mixed and pure feeds. Different alcohols as well as divergent types of catalysts pose specific technological needs for the reaction system. Appropriate reactor design is therefore necessary in order to achieve optimal reaction conditions and facilitate separation and purification operations, for instance, the continuous separation of co-generated water or an extra hydrogenation step when needed.

One of the problems frequently reported is the detrimental effect of water. Water can deactivate the catalyst and limit aldol condensation rates, thereby decreasing the selectivity to C–C coupled products and facilitating Cannizzaro- or Tishchenko-type disproportionation generating unwanted carboxylic acids (vide supra)[5,35,68,92,110–112,175] These acids have a poisoning effect on the typically basic catalysts. The development of water-stable catalysts that are less strongly influenced by carboxylic acids is a key challenge in current developments. Nevertheless, the Guerbet reaction requires water to be removed in order to drive aldol condensation to equilibrium and to prevent side reactions. This can be achieved by filtration, extraction and centrifugation,[157] as well as addition of water scavengers[5,131,132] but most often azeotropic distillation is applied.

A second consideration is the dehydrogenation reaction, which is considered to be the rate-limiting step at lower temperatures, typically in liquid phase systems. A transition metal compound is very frequently incorporated into the

catalytic system in order to facilitate dehydrogenation. Few catalytic systems without transition metals show appreciable activity for Guerbet condensation.[65,69,75,80] This is only the case for reactions at high temperatures (300–450 °C). Under these conditions, enough energy is supplied to activate these basic catalysts for dehydrogenation. Yet, as high temperatures are indispensable for these basic materials, the catalytic system is less sustainable when it comes to energy consumption.[123] Transition metals are far more efficient in catalyzing (de)hydrogenation, so addition of a metal function to the catalytic system can greatly decrease the reaction temperature.[29,205] Furthermore, thermodynamic considerations should be taken into account; high temperatures and low partial pressures favor dehydrogenation of the reagent alcohols (vide supra).

An interesting method to increase the rate of water removal and speed up the reaction is the operation under reduced pressure, as patented by Mueller et al.[143] With water being distilled off, the pressure is continuously reduced to the vapor pressure of the reaction mixture (e.g. final pressure of 0.65 bar). This way, reaction times are reduced significantly and better selectivities towards the dimer alcohol are obtained. The desired reactor pressure can be calculated by $P = x_M P_M^S + (P_D^S - P_M^S)C$, where P_M^S and P_D^S are the pure vapor pressures of the monomer and the dimer, respectively, x_M is the mole fraction of the monomer and C is the conversion. The initial pressure in the reaction corresponds to the vapor pressure of the alcohol components used. During the reaction, the pressure is continually reduced to the vapor pressure of the reaction mixture at a particular temperature. Similarly, the beneficial effect of reduced pressure in vapor phase ethanol condensation over various basic catalysts has been described.[197] Under the same conditions, decreasing the pressure resulted in a significant increase of n-butanol yield.

The kind of reagent alcohol used for the condensation reaction dictates certain requirements for the reactor system. Water miscibility, azeotrope formation and pressure generation in a closed system are important factors that influence the reaction rate and selectivity, and should be taken into account when designing a reactor. Application of alcohols in vapor phase condensation reactions is limited by the boiling
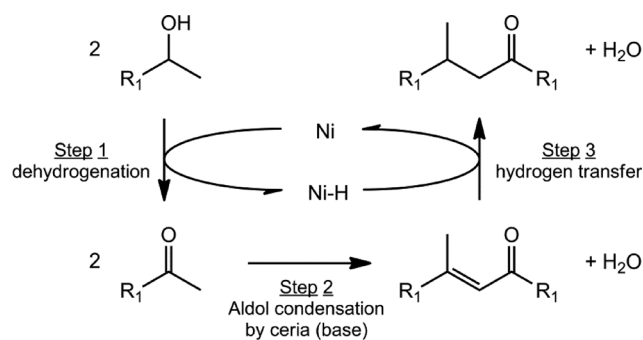
Scheme 8 Reaction mechanism described by Shimura and co-workers[204] for the self-condensation of different secondary alcohols.

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point of the corresponding products. Heavier alcohols are of course coupled in liquid phase reactions. Due to their higher boiling points, higher temperatures can be reached at moderate pressures favoring the dehydrogenation equilibrium. Also, higher alcohols don't mix well with water, allowing for simple and continuous separation techniques, such as application of the Dean-Stark apparatus frequently used in lab-scale experiments. Likewise, heavier alcohols form azeotropes containing a high amount of water, thus permitting more efficient separation and removal of water. As discussed earlier for liquid phase reactions, continuously reducing the pressure to the vapor pressure of the reaction mixture was found to increase the reaction rate and selectivity to the dimer product.[143]

The principles are reversed when short-chain alcohols are considered. Heating these low boiling reagents in a closed system to temperatures higher than 200 °C implicates increased pressures, posing extra safety requirements and a more expensive reactor system, as well as limiting the thermodynamic equilibrium.[29,206] These lighter alcohols mix well with water and their azeotropes prevent efficient separation, making it hard to eliminate water from the reaction mixture efficiently. Application of lighter alcohols in the vapor phase should seriously be considered when designing the reactor system. In vapor phase reactions, high temperatures can be achieved without increased pressure favoring the thermodynamic equilibrium, while co-produced water, also in the vapor phase, is continuously removed from the catalytic system.

A recent feasibility study by Dias et al.[206,207] investigated the economic potential of Guerbet condensation for the production of n-butanol from bio-ethanol. The authors evaluated the catalytic condensation reaction in both vapor and liquid phase, basing their calculations on the catalytic properties published by Riittonen et al.[68] and Tsuchida et al.[121] For the Ni/Al$_2$O$_3$ catalyst employed in the liquid phase ethanol condensation at 250 °C and 70 bar, Riitonen et al.[68] reported 80% selectivity to n-butanol at a conversion of 25% after 72 hours of reaction. Tsuchida et al.,[121] on the other hand, achieved 20% conversion and 70% selectivity at a contact time of 1.78 s using hydroxyapatite at about 300 °C and atmospheric pressure. The techno-economic analysis by Dias et al.[206] predicts a higher internal rate of return (financial efficiency of the project) for the vapor phase reaction, mainly because of the higher specific n-butanol production and lower reactor investment costs. Due to the long reaction time (72 h), the liquid phase reactor is considered much larger in order to be industrially relevant. Next to its size, it also has to operate under high pressure (70 bar). Both its size and requirements for safe operation increase the cost of the liquid phase reactor. It should be noted that the authors assumed a series–parallel arrangement of vapor phase plug flow reactors in which unconverted ethanol is assumed to react in the subsequent reactors. With contact times less than 2 s, this could be a useful reactor set-up to increase the conversion efficiently.

Another feasibility study was published by Patel et al.[29] and focuses on the vapor phase production of higher alcohols from ethanol. The authors combined their economic and environmental assessments with lab-scale catalytic experiments in a vapor phase plug flow reactor. The best results were obtained when a physical mixture of MgO and Cu, both supported on carbon nanofibers, was tested at 200 °C. Again, the addition of Cu to the catalytic system greatly increased the selectivity to n-butanol and allowed the reaction to proceed at only 200 °C, affording a more sustainable system in terms of energy consumption.[29,123] Upon developing a more detailed analysis method, the authors pointed out that compared to the aldol condensation and hydrogenation steps, the dehydrogenation step thermodynamically requires different reaction conditions. It was found that the Guerbet reaction should preferably be carried out in two separate reactors: a dehydrogenation reactor operating at high temperature (350 °C) and low pressure (1 bar) and a hydro-condensation reactor converting the produced hydrogen and acetaldehyde to n-butanol at lower temperature (200 °C) and increased pressure (20 bar). For the double Guerbet condensation of ethanol via n-butanol to 2-ethyl-1-hexanol, four reactors with multiple intermediate separation steps were used for calculation. Although these separation steps assure good selectivity, they consume a lot of energy and possibly decrease the system's sustainability. The feasibility studies by Dias et al.[206,207] and Patel et al.[29] clearly show the advantages of vapor phase reaction systems when coupling short-chain alcohols. Both publications are limited to the catalytic properties that are currently reported and require more extensive catalytic studies in order to expand and adjust their analyses.

Currently, the industrial production of branched-chain higher alcohols is carried out from aldehydes, which are produced by hydroformylation.[4] The aldehydes undergo aldol condensation catalyzed by aqueous NaOH and subsequently are hydrogenated on a transition metal catalyst.[90] 30% of the selling price of these Guerbet alcohols is estimated to be caused by purification, recovery and waste treatment due to the homogenous base.[29,208] Using solid base catalysts together with a hydrogenation catalyst, researchers are developing more sustainable systems for condensation–hydrogenation reactions.[209–212] In these systems, implementation of the Guerbet reaction only implies a preliminary dehydrogenation step, which can easily be integrated for instance in continuous vapor phase reactors. An elegant example is the multistep condensation of ethanol to higher alcohols recently patented by Eastman Chemical Company.[213] Instead of using two different reactors to accommodate optimal conditions for all reaction steps, the patent describes a single-reactor multi-bed approach. A dehydrogenation catalyst bed, an aldol condensation catalyst bed and a hydrogenation catalyst bed are all fixed in the same plug flow reactor. Yet, the temperature at the dehydrogenation bed is higher to favor the thermodynamic equilibrium. By heating the catalyst beds separately, the temperature can be optimized for every reaction step. Putting two of these reactors in series, ethanol is first

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coupled into *n*-butanol and subsequently condensed to 2-ethyl-1-hexanol, minimizing separation units between the different reaction steps. Conceptually, the patent describes the recirculation of H$_2$ from the dehydrogenating to the hydrogenating catalyst bed, promoting the thermodynamic equilibrium in both steps.

6. Conclusions and perspectives

Driven by the increasing availability of bio-based alcohols, Guerbet chemistry is currently experiencing a revival. Short bio-alcohols and their commercially available mixtures are coming to the market at a reasonable price. The Guerbet reaction foresees access to bio-derived alcohols of industrial interest. Depending on the target Guerbet alcohols, one can choose for the self- or cross-coupling reactions using both well-known and less explored substrate alcohols. Self-condensation can provide interesting Guerbet reactions starting *e.g.* from bio-propanol, bio-butanol or other bio-based alcohols. By cross-condensation, a mixture composition is obtained while the product properties are easily changed by varying the initial ratio of the different alcohols. The mixed Guerbet reaction produces a broader pallet of branched alcohols; new product mixtures of branched alcohols are formed directly that today are not available through blending and mixing.

Recent patents and publications describe the use of mixed feedstock such as C$_{10-14}$ alcohols,[162] fusel oils or acetone–butanol–ethanol mixtures.[34–36] These kinds of mixtures could be used without the need for excessive cleaning or separation, reducing the environmental footprint and process costs. The bio-based sources could be mixtures obtained from fermentation or through extraction of plant oils.[214]

The Guerbet reaction proceeds *via* a sequence of reactions, receiving general acceptance, *viz.* dehydrogenation, aldol condensation, dehydration and hydrogenation. In this study, the equilibrium compositions of the Guerbet reaction and intermediate steps at different temperatures for the *n*-butanol model substrate at atmospheric pressure were calculated. Other than this four-step reaction mechanism, a few direct mechanistic routes have also been suggested in the literature, but so far only for the Guerbet condensation of ethanol to *n*-butanol on purely basic heterogeneous catalysts at relatively high temperatures.

The Guerbet reaction can be accompanied by a complex series of side reactions (Scheme 5) producing by-products such as olefins, esters, ethers, acids, aldehydes and ketones, as well as heavier byproducts. The most important by-products were also determined for the model reaction with *n*-butanol at atmospheric pressure. It is a crucial factor in the development of a selective and robust Guerbet condensation catalyst to find an optimal balance in the acid–base properties and to suppress the formation of side products that poison the catalyst system.

The coupling of various alcohols has been investigated under a wide range of conditions with various types of catalysts, both in liquid and in vapor phase. In this review paper, the various homogeneous, heterogeneous and combined homogeneous and heterogeneous systems are described in detail. In homogeneous systems, strong alkali hydroxides can be used, most often in combination with homogeneous transition metal salts or complexes. Ir complexes seem to be very promising as efficient catalysts for producing Guerbet alcohols. It is remarkable that the open literature is relatively scarce on investigations using C$_{8+}$ starting alcohols, whereas many patents describe their findings using longer starting alcohols. This can be explained by the interesting industrial applications in the field of detergents, alcohols, lubricants, and personal care products.[215]

In mixed homogeneous/heterogeneous systems, an insoluble dehydrogenation catalyst is used in combination with an alkali or alkaline earth hydroxide. One can add a carbonyl compound to initiate and promote the condensation reaction. Attention must be paid to water removal as soon it is formed, *e.g.* using a Dean-Stark water separator, a purification process and catalyst leaching. For purely heterogeneous systems, four main families are frequently reported and patented for Guerbet chemistry: MgO, hydrotalcites (and their related mixed oxides), hydroxyapatites and alkaline zeolites; however, there is room for improvement and optimization of specific catalyst compositions for the variety of reactions.

The search for optimal reaction conditions in either gas or liquid phase plays a key role in the optimization of the Guerbet process. Short alcohols are suggested to react in the gas phase; high temperatures are highly favorable for the conversion rate (Arrhenius), but also for the equilibrium conversion (Le Chatelier) of the endothermic dehydrogenation reaction. On the other hand, the liquid phase is favorable for Guerbet reactions with larger alcohols. Pressure should be kept low for equilibrium reasons. If the pressure of H$_2$ is to be kept low, the mechanism could also be stimulated by hydride shift mechanisms, requiring Lewis acids like Al, Zr, Ga or Sn. The hydrogenation step usually requires analogue metals as in the dehydrogenation step, like Cu or more expensive noble metals, and ultimately leads to the branched alcohol. This reaction pulls the equilibrium of the Guerbet reaction and may thus be regarded as the main driver of the conversion rate. As the rate determining steps and the substrate reactivity are completely different in gas phase, when compared to liquid phase, distinct catalyst compositions and reaction conditions are needed.

Acknowledgements

References

1 M. Guerbet, *C. R. Hebd. Séances Acad. Sci.*, 1899, **128**, 511–513.
2 A. J. O'Lenick, *J. Surfactants Deterg.*, 2001, **4**, 311–315.

3   L. D. Rhein, M. Schlossman, A. J. O'Lenick and P. Somasundaran, *Surfactants in Personal Care Products and Decorative Cosmetics*, Taylor & Francis Group, 3rd edn, 2007.

4   C. Kohlpaintner, M. Schulte, J. Falbe, P. Lappe and J. Weber, in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, 2000.

5   C. Carlini, A. Macinai, A. M. Raspolli Galletti and G. Sbrana, *J. Mol. Catal. A: Chem.*, 2004, **212**, 65–70.

6   G. Knothe, in *The Lipid Handbook*, ed. F. G. Gunstone, J. L. Harwood and A. J. Dijkstra, CRC Press, 3rd edn., 2007, ch. 8, pp. 587–590.

7   J. T. Kozlowski and R. J. Davis, *ACS Catal.*, 2013, **3**, 1588–1600.

8   G. R. C. Market, *MarketsandMarkets Research*, Wilmington, USA, 2013.

9   S. Kim and B. E. Dale, *J. Ind. Ecol.*, 2003, **7**, 147–162.

10   G. Genti and R. A. van Santen, Wiley-VCH Verlag GnbH & Co. KGaA, 2007, pp. 287–411.

11   C. A. Cardona and Ó. J. Sánchez, *Bioresour. Technol.*, 2007, **98**, 2415–2457.

12   L. Panella, *Sugar Tech*, 2010, **12**, 288–293.

13   C. S. Goh and K. T. Lee, *Renewable Sustainable Energy Rev.*, 2010, **14**, 842–848.

14   R. P. John, G. S. Anisha, K. M. Nampoothiri and A. Pandey, *Bioresour. Technol.*, 2011, **102**, 186–193.

15   M. Y. Menetrez, *Environ. Sci. Technol.*, 2012, **46**, 7073–7085.

16   V. Menon and M. Rao, *Prog. Energy Combust. Sci.*, 2012, **38**, 522–550.

17   R. C. Saxena, D. K. Adhikari and H. B. Goyal, *Renewable Sustainable Energy Rev.*, 2009, **13**, 167–178.

18   A. Singh, P. S. Nigam and J. D. Murphy, *Bioresour. Technol.*, 2011, **102**, 10–16.

19   J. O. B. Carioca, *Biotechnol. J.*, 2010, **5**, 260–273.

20   J. J. Spivey and A. Egbebi, *Chem. Soc. Rev.*, 2007, **36**, 1514–1528.

21   F. R. Bengelsdorf, M. Straub and P. Dürre, *Environ. Technol.*, 2013, **34**, 1639–1651.

22   J. R. Phillips, K. T. Klasson, E. C. Clausen and J. L. Gaddy, *Appl. Biochem. Biotechnol.*, 1993, **39–40**, 559–571.

23   A. M. Henstra, J. Sipma, A. Rinzema and A. J. M. Stams, *Curr. Opin. Biotechnol.*, 2007, **18**, 200–206.

24   D. W. Griffin and M. A. Schultz, *Environ. Prog. Sustainable Energy*, 2012, **31**, 219–224.

25   M. Köpke, C. Mihalcea, J. C. Bromley and S. D. Simpson, *Curr. Opin. Biotechnol.*, 2011, **22**, 320–325.

26   L. Zhang, C. Xu and P. Champagne, *Energy Convers. Manage.*, 2010, **51**, 969–982.

27   INEOSBio, Advanced bioethanol production and renewable energy generation from ligno-cellulosic materials, biomass waste and residues, http://www.ineos.com/businesses/ineos-bio/technology/, Accessed September 2014.

28   A. D. Webb and J. L. Ingraham, in *Advances in Applied Microbiology*, ed. W. W. Umbreit, Academic Press Inc., London, 1963, vol. 5, pp. 317–354.

29   A. D. Patel, S. Telalović, J. H. Bitter, E. Worrell and M. K. Patel, *Catal. Today*, 2015, **239**, 56–79.

30   T. Lütke-Eversloh and H. Bahl, *Curr. Opin. Biotechnol.*, 2011, **22**, 634–647.

31   S. Atsumi, T. Hanai and J. C. Liao, *Nature*, 2008, **451**, 86–89.

32   T. C. Ezeji, N. Qureshi and H. P. Blaschek, *Curr. Opin. Biotechnol.*, 2007, **18**, 220–227.

33   A. Güvenç, N. Kapucu, H. Kapucu, Ö. Aydoğan and Ü. Mehmetoğlu, *Enzyme Microb. Technol.*, 2007, **40**, 778–785.

34   K. Breitkreuz, A. Menne and A. Kraft, *Biofuels, Bioprod. Biorefin.*, 2014, **8**, 504–515.

35   P. Anbarasan, Z. C. Baer, S. Sreekumar, E. Gross, J. B. Binder, H. W. Blanch, D. S. Clark and F. D. Toste, *Nature*, 2012, **491**, 235–239.

36   S. Sreekumar, Z. C. Baer, E. Gross, S. Padmanaban, K. Goulas, G. Gunbas, S. Alayoglu, H. W. Blanch, D. S. Clark and F. D. Toste, *ChemSusChem*, 2014, **7**, 2445–2448.

37   K. C. Waugh, *Catal. Today*, 1992, **15**, 51–75.

38   G. W. Huber, S. Iborra and A. Corma, *Chem. Rev.*, 2006, **106**, 4044–4098.

39   J. R. Rostrup-Nielsen, *Catal. Rev.: Sci. Eng.*, 2004, **46**, 247–270.

40   P. Forzatti, E. Tronconi and I. Pasquon, *Catal. Rev.: Sci. Eng.*, 1991, **33**, 109–168.

41   V. R. Surisetty, A. K. Dalai and J. Kozinski, *Appl. Catal., A*, 2011, **404**, 1–11.

42   G. Prieto, S. Beijer, M. L. Smith, M. He, Y. Au, Z. Wang, D. A. Bruce, K. P. de Jong, J. J. Spivey and P. E. de Jongh, *Angew. Chem., Int. Ed.*, 2014, **53**, 6397–6401.

43   M. Scates, R. D. Shaver, J. Zink, R. Zinobile and O. Oyerinde, WO2013/070216, 2013.

44   G. Prieto, P. Concepción, A. Martínez and E. Mendoza, *J. Catal.*, 2011, **280**, 274–288.

45   X. Pan, Z. Fan, W. Chen, Y. Ding, H. Luo and X. Bao, *Nat. Mater.*, 2007, **6**, 507–511.

46   Y. Choi and P. Liu, *J. Am. Chem. Soc.*, 2009, **131**, 13054–13061.

47   P. Courty, D. Durand, E. Freund and A. Sugier, *J. Mol. Catal.*, 1982, **17**, 241–254.

48   W. X. Pan, R. Cao and G. L. Griffin, *J. Catal.*, 1988, **114**, 447–456.

49   K. Xiao, X. Qi, Z. Bao, X. Wang, L. Zhong, K. Fang, M. Lin and Y. Sun, *Catal. Sci. Technol.*, 2013, **3**, 1591–1602.

50   T. Ishida, T. Yanagihara, X. Liu, H. Ohashi, A. Hamasaki, T. Honma, H. Oji, T. Yokoyama and M. Tokunaga, *Appl. Catal., A*, 2013, **458**, 145–154.

51   Z. Bao, K. Xiao, X. Qi, X. Wang, L. Zhong, K. Fang, M. Lin and Y. Sun, *J. Energy Chem.*, 2013, **22**, 107–113.

52   Y. Xiang, V. Chitry, P. Liddicoat, P. Felfer, J. Cairney, S. Ringer and N. Kruse, *J. Am. Chem. Soc.*, 2013, **135**, 7114–7117.

53   S. Van de Vyver, J. Thomas, J. Geboers, S. Keyzer, M. Smet, W. Dehaen, P. A. Jacobs and B. F. Sels, *Energy Environ. Sci.*, 2011, **4**, 3601–3610.

54   D. W. Rackemann and W. O. S. Doherty, *Biofuels, Bioprod. Biorefin.*, 2011, **5**, 198–214.

55   P. P. Upare, J.-M. Lee, Y. K. Hwang, D. W. Hwang, J.-H. Lee, S. B. Halligudi, J.-S. Hwang and J.-S. Chang, *ChemSusChem*, 2011, **4**, 1749–1752.

This journal is © The Royal Society of Chemistry 2015

Catal. Sci. Technol., 2015, **5**, 3876–3902 | **3899**

56 M. G. Al-Shaal, A. Dzierbinski and R. Palkovits, *Green Chem.*, 2014, **16**, 1358–1364.

57 S. Liu, Y. Okuyama, M. Tamura, Y. Nakagawa, A. Imai and K. Tomishige, *ChemSusChem*, 2015, **8**, 628–635.

58 B. Op de Beeck, M. Dusselier, J. Geboers, J. Holsbeek, E. Morre, S. Oswald, L. Giebeler and B. F. Sels, *Energy Environ. Sci.*, 2015, **8**, 230–240.

59 A. Corma, S. Iborra and A. Velty, *Chem. Rev.*, 2007, **107**, 2411–2502.

60 G. Knothe, J. Van Gerpen and J. Krahl, *The Biodiesel Handbook*, AOCS Press, Champaign, Illinois, 2005.

61 P. Handke, S. A. Lynch and R. T. Gill, *Metab. Eng.*, 2011, **13**, 28–37.

62 E. J. Steen, Y. Kang, G. Bokinsky, Z. Hu, A. Schirmer, A. McClure, S. B. del Cardayre and J. D. Keasling, *Nature*, 2010, **463**, 559–562.

63 J. Clomburg and R. Gonzalez, *Appl. Microbiol. Biotechnol.*, 2010, **86**, 419–434.

64 M. Holtzapple, R. Davison, M. K. Ross, S. Aldrett-Lee, M. Nagwani, C.-M. Lee, C. Lee, S. Adelson, W. Kaar, D. Gaskin, H. Shirage, N.-S. Chang, V. Chang and M. Loescher, *Appl. Biochem. Biotechnol.*, 1999, **79**, 609–631.

65 T. Tsuchida, S. Sakuma, T. Takeguchi and W. Ueda, *Ind. Eng. Chem. Res.*, 2006, **45**, 8634–8642.

66 T. Tsuchida, T. Yoshioka, S. Sakuma, T. Takeguchi and W. Ueda, *Ind. Eng. Chem. Res.*, 2008, **47**, 1443–1452.

67 A. S. Ndou, N. Plint and N. J. Coville, *Appl. Catal., A*, 2003, **251**, 337–345.

68 T. Riittonen, E. Toukoniitty, D. K. Madnani, A.-R. Leino, K. Kordas, M. Szabo, A. Sapi, K. Arve, J. Wärnå and J.-P. Mikkola, *Catalysts*, 2012, **2**, 68–84.

69 J. T. Kozlowski and R. J. Davis, *J. Energy Chem.*, 2013, **22**, 58–64.

70 V. Nagarajan and N. R. Kuloor, *Indian J. Technol.*, 1966, **4**, 46–54.

71 J. Scalbert, F. Thibault-Starzyk, R. Jacquot, D. Morvan and F. Meunier, *J. Catal.*, 2014, **311**, 28–32.

72 D. L. Carvalho, R. R. de Avillez, M. T. Rodrigues, L. E. P. Borges and L. G. Appel, *Appl. Catal., A*, 2012, **415–416**, 96–100.

73 S. Ogo, A. Onda, Y. Iwasa, K. Hara, A. Fukuoka and K. Yanagisawa, *J. Catal.*, 2012, **296**, 24–30.

74 K. W. Yang, X. Z. Jiang and W. C. Zhang, *Chin. Chem. Lett.*, 2004, **15**, 1497–1500.

75 C. Yang and Z. Y. Meng, *J. Catal.*, 1993, **142**, 37–44.

76 I.-C. Marcu, N. Tanchoux, F. Fajula and D. Tichit, *Catal. Lett.*, 2013, **143**, 23–30.

77 G. R. M. Dowson, M. F. Haddow, J. Lee, R. L. Wingad and D. F. Wass, *Angew. Chem., Int. Ed.*, 2013, **52**, 9005–9008.

78 J. Sun, K. Zhu, F. Gao, C. Wang, J. Liu, C. H. F. Peden and Y. Wang, *J. Am. Chem. Soc.*, 2011, **133**, 11096–11099.

79 E. Olson, R. Sharma and T. Aulich, in *Proceedings of the Twenty-Fifth Symposium on Biotechnology for Fuels and Chemicals Held May 4–7, 2003*, ed. M. Finkelstein, J. McMillan, B. Davison and B. Evans, Humana Press, Breckenridge, CO, 2004, ch. 74, pp. 913–932.

80 W. Ueda, T. Kuwabara, T. Ohshida and Y. Morikawa, *J. Chem. Soc., Chem. Commun.*, 1990, 1558–1559.

81 C. Carlini, M. Di Girolamo, A. Macinai, M. Marchionna, M. Noviello, A. M. Raspolli Galletti and G. Sbrana, *J. Mol. Catal. A: Chem.*, 2003, **200**, 137–146.

82 C. Carlini, C. Flego, M. Marchionna, M. Noviello, A. M. Raspolli Galletti, G. Sbrana, F. Basile and A. Vaccari, *J. Mol. Catal. A: Chem.*, 2004, **220**, 215–220.

83 C. Carlini, M. D. Girolamo, M. Marchionna, M. Noviello, A. M. R. Galletti and G. Sbrana, *J. Mol. Catal. A: Chem.*, 2002, **184**, 273–280.

84 C. Carlini, M. Marchionna, M. Noviello, A. M. Raspolli Galletti, G. Sbrana, F. Basile and A. Vaccari, *J. Mol. Catal. A: Chem.*, 2005, **232**, 13–20.

85 C. Carlini, A. Macinai, M. Marchionna, M. Noviello, A. M. R. Galletti and G. Sbrana, *J. Mol. Catal. A: Chem.*, 2003, **206**, 409–418.

86 D. Seddon, *Catal. Today*, 1992, **15**, 1–21.

87 E. V. Makshina, M. Dusselier, W. Janssens, J. Degreve, P. A. Jacobs and B. F. Sels, *Chem. Soc. Rev.*, 2014, **43**(22), 7917–7953.

88 M. Henry, M. Bulut, W. Vermandel, B. Sels, P. Jacobs, D. Minoux, N. Nesterenko, S. Van Donk and J. P. Dath, *Appl. Catal., A*, 2012, **413–414**, 62–77.

89 S. M. Sen, E. I. Gurbuz, S. G. Wettstein, D. M. Alonso, J. A. Dumesic and C. T. Maravelias, *Green Chem.*, 2012, **14**, 3289–3294.

90 D. F. Cadogan and C. J. Howick, in *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH Verlag GmbH & Co. KGaA, 2000.

91 J. D. Wagner, G. R. Lappin and J. R. Zietz, in *Kirk-Othmer Encyclopedia of Chemical Technology*, John Wiley & Sons, Inc., 2000.

92 P. L. Burk, R. L. Pruett and K. S. Campo, *J. Mol. Catal.*, 1985, **33**, 1–14.

93 K. Rettinger, C. Burschka, P. Scheeben, H. Fuchs and A. Mosandl, *Tetrahedron: Asymmetry*, 1991, **2**, 965–968.

94 M. J. L. Gines and E. Iglesia, *J. Catal.*, 1998, **176**, 155–172.

95 J. I. Di Cosimo, C. R. Apesteguía, M. J. L. Ginés and E. Iglesia, *J. Catal.*, 2000, **190**, 261–275.

96 S. Ogo, A. Onda and K. Yanagisawa, *Appl. Catal., A*, 2011, **402**, 188–195.

97 V. Nagarajan, *Indian J. Technol.*, 1971, **9**, 380–386.

98 C. H. Weizmann, E. Bergmann and M. A. X. Sulzbacher, *J. Org. Chem.*, 1950, **15**, 54–57.

99 A. S. Ndou and N. J. Coville, *Appl. Catal., A*, 2004, **275**, 103–110.

100 S. Veibel and J. I. Nielsen, *Tetrahedron*, 1967, **23**, 1723–1733.

101 R. Olcese and M. M. Bettahar, *MATEC Web Conf.*, 2013, 3.

102 P. E. Hathaway and M. E. Davis, *J. Catal.*, 1989, **119**, 497–507.

103 T. W. Birky, J. T. Kozlowski and R. J. Davis, *J. Catal.*, 2013, **298**, 130–137.

104 C. F. de Graauw, J. A. Peters, H. van Bekkum and J. Huskens, *Synthesis*, 1994, **1994**, 1007–1017.

105 W. Ueda, T. Ohshida, T. Kuwabara and Y. Morikawa, *Catal. Lett.*, 1992, **12**, 97–104.

3900 | *Catal. Sci. Technol.*, 2015, **5**, 3876–3902

This journal is © The Royal Society of Chemistry 2015

106 A. Gangadharan, M. Shen, T. Sooknoi, D. E. Resasco and R. G. Mallinson, *Appl. Catal., A*, 2010, **385**, 80–91.

107 W. Shen, G. A. Tompsett, R. Xing, W. Curtis Conner Jr and G. W. Huber, *J. Catal.*, 2012, **286**, 248–259.

108 M. E. Sad, M. Neurock and E. Iglesia, *J. Am. Chem. Soc.*, 2011, **133**, 20384–20398.

109 J. J. Bravo-Suárez, B. Subramaniam and R. V. Chaudhari, *Appl. Catal., A*, 2013, **455**, 234–246.

110 I.-C. Marcu, D. Tichit, F. Fajula and N. Tanchoux, *Catal. Today*, 2009, **147**, 231–238.

111 R. Miller and G. Bennett, *Ind. Eng. Chem.*, 1961, **53**, 33–36.

112 M. N. Dvornikoff and M. W. Farrar, *J. Org. Chem.*, 1957, **22**, 540–542.

113 F. C. Meunier, J. Scalbert and F. Thibault-Starzyk, *C. R. Chim.*, 2015, **18**, 345–350.

114 A. Chieregato, J. Velasquez Ochoa, C. Bandinelli, G. Fornasari, F. Cavani and M. Mella, *ChemSusChem*, 2015, **8**, 377–388.

115 J. I. Di Cosimo, V. K. Díez, M. Xu, E. Iglesia and C. R. Apesteguía, *J. Catal.*, 1998, **178**, 499–510.

116 M. Xu, M. J. L. Gines, A.-M. Hilmen, B. L. Stephens and E. Iglesia, *J. Catal.*, 1997, **171**, 130–147.

117 H. Tsuji, F. Yagi, H. Hattori and H. Kita, *J. Catal.*, 1994, **148**, 759–770.

118 S. V. Lebedev, *Zh. Obshch. Khim.*, 1933, **3**, 698–717.

119 M. Y. Kagan, G. D. Lyubarskii and O. M. Podurovskaya, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1947, 173–181.

120 W. M. Quattlebaum, W. J. Toussaint and J. T. Dunn, *J. Am. Chem. Soc.*, 1947, **69**, 593–599.

121 T. Tsuchida, J. Kubo, T. Yoshioka, S. Sakuma, T. Takeguchi and W. Ueda, *J. Catal.*, 2008, **259**, 183–189.

122 V. T. Tishchenko, *J. Russ. Phys.-Chem. Soc.*, 1906, **38**, 355.

123 H. Hattori, *Chem. Rev.*, 1995, **95**, 537–558.

124 S. Cannizzaro, *Justus Liebigs Ann. Chem.*, 1853, **88**, 129–130.

125 K. Takeshita, S. Nakamura and K. Kawamoto, *Bull. Chem. Soc. Jpn.*, 1978, **51**, 2622–2627.

126 D. J. Elliott and F. Pennella, *J. Catal.*, 1989, **119**, 359–367.

127 S. E. Davis, M. S. Ide and R. J. Davis, *Green Chem.*, 2013, **15**, 17–45.

128 S. E. Davis, B. N. Zope and R. J. Davis, *Green Chem.*, 2012, **14**, 143–147.

129 J. Bussi, S. Parodi, B. Irigaray and R. Kieffer, *Appl. Catal., A*, 1998, **172**, 117–129.

130 M. Renz, *Eur. J. Org. Chem.*, 2005, **2005**, 979–988.

131 M. Sulzbacher, *J. Appl. Chem.*, 1955, **5**, 637–641.

132 M. Sulzbacher, GB655864, 1951.

133 L. E. Gast, E. D. Bitner, J. C. Cowan and H. M. Teeter, *J. Am. Oil Chem. Soc.*, 1958, **35**, 703–707.

134 R. L. Poe, US3328470, 1967.

135 G. E. Bennett and R. E. Miller, US2762847, 1956.

136 D. A. Young, J. A. Jung and M. L. McLaughlin, US5068469, 1991.

137 C. Waykole, D. Bhowmick and A. Pratap, *J. Am. Oil Chem. Soc.*, 2014, **91**, 1407–1416.

138 N. L. Cull and J. K. Mertzweiller, US2829177, 1958.

139 J. E. Yates, US3979466, 1976.

140 J. E. Yates, US3864407, 1975.

141 J. E. Yates, US3916015, 1975.

142 C. Francesco, G. Guglielmo and P. Gianfranco, US3479412, 1969.

143 G. Mueller, B. Gutsche, L. Jeromin, U. Steinberner, R. Sedelies, R. Bohlander, R. Ridinger, D. Springer, F. Buettgen and F. Bartschik, US5777183, 1998.

144 D. F. Wass and G. R. M. Dowson, US20130116481, 2013.

145 Y. Tanaka and M. Utsunomiya, US20100298613, 2010.

146 G. Gregorio, G. F. Pregaglia and R. Ugo, *J. Organomet. Chem.*, 1972, **37**, 385–387.

147 P. L. Burk, R. L. Pruett and K. S. Campo, *J. Mol. Catal.*, 1985, **33**, 15–21.

148 K. Koda, T. Matsu-Ura, Y. Obora and Y. Ishii, *Chem. Lett.*, 2009, **38**, 838–839.

149 T. Matsu-ura, S. Sakaguchi, Y. Obora and Y. Ishii, *J. Org. Chem.*, 2006, **71**, 8306–8308.

150 G. Xu, T. Lammens, Q. Liu, X. Wang, L. Dong, A. Caiazzo, N. Ashraf, J. Guan and X. Mu, *Green Chem.*, 2014, **16**, 3971–3977.

151 K. Fujita, C. Asai, T. Yamaguchi, F. Hanasaka and R. Yamaguchi, *Org. Lett.*, 2005, 7, 4017–4019.

152 K. Fujita, C. Kitatsuji, S. Furukawa and R. Yamaguchi, *Tetrahedron Lett.*, 2004, **45**, 3215–3217.

153 T. Miura, O. Kose, F. Li, S. Kai and S. Saito, *Chem. – Eur. J.*, 2011, **17**, 11146–11151.

154 C. Alfred and F. E. Condon, US2593009, 1952.

155 G. D. Mueller, B. D. Gutsche, L. D. Jeromin, U. D. Steinberner, R. D. Sedelies, R. D. Bohlander, R. Ridinger, D. D. Springer, F. Buettgen and F. Bartschik, DE19524245C1, 1996.

156 E. D. Scherf, H. J. Letsch, C. D. Schroeder and A. T. D. Herrmann, DE19734673A1, 1999.

157 R. D. Bohlander, R. Reisberg, H. Kienast, T. Kwiatkowski, R. Ridinger and E. D. Reuter, DE19531714A1, 1996.

158 P. G. Abend and P. Leenders, US4011273, 1977.

159 L. Qiao, F. Liu, X. Li, C. Wang and X. Hao, CN101659597A, 2010.

160 X. Chen, M. Wang and Y. Liang, CN1436762A, 2003.

161 DE20303420U1, 2003.

162 V. Dwarakanath and R. Shong, WO/2014/149419, 2014.

163 R. L. Pruett, D. A. Young, C. B. Duncan and E. J. Mozeleski, EP0299720A2, 1989.

164 A. Wick and E. U. Mahnke, US20120220806, 2012.

165 M. Matsuda and M. Horio, EP0089569B2, 1992.

166 M. Matsuda and M. Horio, US4518810, 1985.

167 W. Liu, C. Sun, Y. Liang and P. Gao, CN102020533A, 2011.

168 R. Cano, M. Yus and D. J. Ramon, *Chem. Commun.*, 2012, **48**, 7628–7630.

169 M. W. Farrar, US2971033, 1961.

170 G. E. Bennett and R. E. Miller, US2862013, 1958.

171 R. E. Miller, US2836628, 1958.

172 J. A. Miller and M. Virnig, WO1991004242, 1991.

173 F. Engelhardt and W. Schritt, US3558716, 1971.

174 K. Reinhold, DE4014736A1, 1991.

175 P. W. Johan, US1910582, 1933.

176 N. D. Scott, US2004350, 1935.

177 C. A. Carter, US2457866, 1949.

This journal is © The Royal Society of Chemistry 2015

Catal. Sci. Technol., 2015, **5**, 3876–3902 | **3901**

178 E. E. Burgoyne, US2645667, 1953.

179 D. S. J. Gustav and J. Kollar, US3119880, 1964.

180 G. Guglielmo and P. Gianfranco, US3514493, 1970.

181 F. Otto and Q. Wilhelm, US1992480, 1935.

182 O. Fuchs and W. Querfurth, US2092450, 1937.

183 B. F. Sels, D. E. De Vos and P. A. Jacobs, *Catal. Rev.: Sci. Eng.*, 2001, **43**, 443–488.

184 S. Abello, F. Medina, D. Tichit, J. Perez-Ramirez, J. C. Groen, J. E. Sueiras, P. Salagre and Y. Cesteros, *Chem. – Eur. J.*, 2005, **11**, 728–739.

185 P. Kustrowski, D. Sulkowska, L. Chmielarz, A. Rafalska-Lasocha, B. Dudek and R. Dziembaj, *Microporous Mesoporous Mater.*, 2005, **78**, 11–22.

186 S. Ordonez, E. Diaz, M. Leon and L. Faba, *Catal. Today*, 2011, **167**, 71–76.

187 M. León, E. Díaz, A. Vega, S. Ordóñez and A. Auroux, *Appl. Catal., B*, 2011, **102**, 590–599.

188 M. León, E. Díaz and S. Ordóñez, *Catal. Today*, 2011, **164**, 436–442.

189 F. Hosoglu, J. Faye, K. Mareseanu, G. Tesquet, P. Miquel, M. Capron, O. Gardoll, J.-F. Lamonier, C. Lamonier and F. Dumeignil, *Appl. Catal., A*, 2014, DOI: 10.1016/j.apcata.2014.10.005.

190 K. Kourtakis, M. B. D'Amore and L. E. Manzer, US20090054705, 2009.

191 K. Kourtakis, R. Ozer and M. B. D'Amore, US8318989, 2012.

192 C. Zhang, M. Borlik and H. Weiner, WO/2014/100131, 2014.

193 S. Hanspal, Z. D. Young, H. Shou and R. J. Davis, *ACS Catal.*, 2015, **5**, 1737–1746.

194 L. Silvester, J.-F. Lamonier, J. Faye, M. Capron, R.-N. Vannier, C. Lamonier, J.-L. Dubois, J.-L. Couturier, C. Calais and F. Dumeignil, *Catal. Sci. Technol.*, 2015, DOI: 10.1039/C5CY90023A.

195 A. Onda, S. Ogo and K. Yanagisawa, US8232433, 2012.

196 P. J. Fagan, T. G. Calvarese, R. J. Davis and R. Ozer, US20120165577, 2012.

197 J. Kubo, S. Sakuma, T. Tsuchida and T. Yoshioka, WO2012035772A1, 2012.

198 K. Gotoh, S. Nakamura, T. Mori and Y. Morikawa, in *Studies in Surface Science and Catalysis*, ed. F. V. M. S. M. Avelino Corma and G. F. José Luis, Elsevier, 2000, vol. 130, pp. 2669–2674.

199 X. Chen and Y. Liang, CN1939886A, 2007.

200 K. Kourtakis and R. Ozer, US20100160692, 2010.

201 R. T. Clark, US3972952, 1976.

202 T. Riittonen, K. Eränen, P. Mäki-Arvela, A. Shchukarev, A.-R. Rautio, K. Kordas, N. Kumar, T. Salmi and J.-P. Mikkola, *Renewable Energy*, 2015, **74**, 369–378.

203 J. W. Van Hal and J. H. Grisel, WO/2014/137212, 2014.

204 K. Shimura, K. Kon, S. M. A. Hakim Siddiki and K.-I. Shimizu, *Appl. Catal., A*, 2013, **462–463**, 137–142.

205 M. A. Landau and V. V. Shchekin, *Russ. Chem. Bull.*, 1960, **9**, 885–887.

206 M. O. S. Dias, L. G. Pereira, T. L. Junqueira, L. G. Pavanello, M. F. Chagas, O. Cavalett, R. Maciel Filho and A. Bonomi, *Chem. Eng. Res. Des.*, 2014, **92**, 1441–1451.

207 L. G. Pereira, M. O. S. Dias, T. L. Junqueira, L. G. Pavanello, M. F. Chagas, O. Cavalett, R. Maciel Filho and A. Bonomi, *Chem. Eng. Res. Des.*, 2014, **92**, 1452–1462.

208 G. J. Kelly, F. King and M. Kett, *Green Chem.*, 2002, **4**, 392–399.

209 F. King and G. J. Kelly, *Catal. Today*, 2002, **73**, 75–81.

210 C. A. Hamilton, S. D. Jackson and G. J. Kelly, *Appl. Catal., A*, 2004, **263**, 63–70.

211 C. J. Barrett, J. N. Chheda, G. W. Huber and J. A. Dumesic, *Appl. Catal., B*, 2006, **66**, 111–118.

212 C. U. Pittman and Y. F. Liang, *J. Org. Chem.*, 1980, **45**, 5048–5052.

213 D. W. Norman, D. R. Billodeaux and M. D. Page, US 2014/0088326, 2014.

214 S. Thach, R. Shong, V. Dwarakanath and G. Winslow, US20130068457, 2013.

215 P. Kempers, R. Kawa, S. Brüning, J. Milardovic, E. U. Mahnke, H.-J. Krüppel, M. Dierker and B. Beckedahl, WO2013120757A1, 2013.