Enhancement of furfural-cyclopentanone aldol condensation using binary water-ethanol mixtures as solvent

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BACKGROUND: Cyclopentanone (CPO) – furfural (FFL) aldol condensation is a very interesting reaction for upgrading the furfural obtained in the depolymerization – dehydration reaction of cellulosic materials. Reaction is faster with cyclopentanone than with other ketones, and resulting condensation adducts are attractive for manufacturing drop-in fuels. However, the most important problem is that this adducts present low water solubility.

RESULTS: Binary systems combining water (needed to promote the aldol condensation) and ethanol (for enhancing the condensation adducts solubility) at different ratios have been tested. Operation parameters, such as water/ethanol ratio, temperature and reaction time, were optimized for this reaction. Best results (global yield to condensation adducts higher than 36 %) were achieved using 1:2 water/ethanol ratio, and working at 303 K. Higher water ratios lead to the precipitation of condensation products, whereas higher ethanol concentrations hinder the catalyst performance. A reaction mechanism, considering a first order kinetic model on cyclopentanone concentration, was proposed. Kinetic constants have been empirically correlated with ethanol concentration in the reaction medium.

CONCLUSIONS: The use of binary ethanol-water binary mixtures with controlled solvent ratios can avoid the precipitation of condensation adducts. This precipitation leads to important operation problems in the reactor as well as to catalyst deactivation. The negative effect of the presence of ethanol on the reaction kinetics can be overcome by increasing reaction temperature.

KEYWORDS. Biorefinery; cyclopentanone; furfural; solvent effects; drop-in diesel fuels; MgZr oxides
1. INTRODUCTION

The increasing concern about global climate change has promoted the development of different routes that use biomass waste as raw material for obtaining biofuels and commodity chemicals\(^1\). One of the most promising routes to fulfil these purposes is the aqueous phase transformation of lignocellulosic biomass\(^2\). Aldol condensation can be a key step for these purposes, since it is an effective way for the selective conversion of small molecules (C5-C6) into larger ones with 8 to 15 carbon atoms\(^3,4\). These condensation adducts are precursors for a large variety of renewable chemicals and, upon total hydrogenation, drop-in diesel fuels. Aldol condensation involves the interaction between two molecules with carbonyl groups (aldehydes – furfural FFL or 5-hydroximethylfurfural 5-HMF – or ketones), being acetone the most studied linking molecule\(^5-8\).

There are several studies about the aldol condensation of acetone and furfural or 5-HMF using different homogeneous and heterogeneous catalysts, highlighting different hydroxides (NaOH and Ca(OH)\(_2\))\(^9,10\) and mixed oxides such as Mg-Zr or Mg-Al\(^5,8\). However, there are other bio-derived molecules with two \(\alpha\)-hydrogen positions that can be alternatively used for this purpose. Among these compounds, cyclopentanone (CPO) presents important advantages in comparison to acetone. Firstly, resulting condensation adducts are entirely renewable since both reactants (cyclopentanone and furfural or 5-HMF) can be quantitatively produced from ligno-cellulosic biomass\(^11\), whereas acetone is nowadays only renewably obtained as a side product in the ABE fermentation. On the other hand, considering the usefulness of the resulting products, condensation adducts obtained have longer and branched carbon chains, leading to
fuels of better quality\textsuperscript{12}. Despite these theoretical considerations, cyclopentanone-furfural condensation is still scarcely studied. Hronec \textit{et al.} studied this reaction using homogeneous catalyst (NaOH), with more than 95\% of the second adduct yield (C15) in less than two hours\textsuperscript{13}. Deng \textit{et al.} reported selectivities higher than 85\% (in solid phase) after 2 hours but working in solvent-free condensation and using NaOH as catalyst\textsuperscript{14}.

In spite of the well-known disadvantages of using homogeneous catalysts\textsuperscript{15}, and the wide use of solid base catalysts for these reactions\textsuperscript{7, 16, 17} there are few works dealing with the heterogeneously catalyzed cyclopentanone-furfural condensation\textsuperscript{18}. In our previous work, preliminary results using Mg-Zr mixed oxide as catalyst were reported, combining mild conditions (303 – 323 K) and aqueous media\textsuperscript{12}. A complete conversion of furfural, with more than 68\% of CPO conversion, was observed after 4 hours of reaction in a batch reactor. These results correspond to a 320 times faster reaction than the similar tests using acetone as linking molecule\textsuperscript{7}. At this time, the carbon balance closure in liquid phase decreases to 20\% and main products were obtained as solids, reaching a global yield of 77\%. The low solubility of these adducts in water, hinders further downstream processing, such as partial or total hydrogenations. Furthermore, the precipitation of these phases leads to catalyst fouling and deactivation. Performing the reaction in presence of organic solvents would be an alternative for overcoming these solubility problems. The high solubility of these adducts in these solvents was previously observed by Hronec \textit{et al.}, proposing the use of methanol or tetrahydrofuran\textsuperscript{13}. Nevertheless, both solvents are considering as toxic and incompatible with Green Chemistry principles\textsuperscript{19, 20}. 
Taking into account that alcohols and organic esters dissolve the condensation adducts, ethanol and ethyl acetate are proposed as valuable alternatives. Ethyl acetate is considered as a green solvent (low toxicity, stable, biodegradable, etc.) and it was used in our previous work for fully solving the condensation adducts and would allow studying the reaction in a biphasic system. On the other hand, ethanol is a green solvent, which can be obtained from lignocellulose feedstock, reducing greenhouse gas emissions in its production and it is less toxic than methanol (TLV is 1000 ppm; whereas for methanol is 200 ppm). Since ethanol is soluble in water, the reaction will be carried out in a binary but monophasic configuration.

In this paper, we try to select appropriate solvent (ethyl acetate, ethanol, and biphasic or monophasic mixtures of these solvents with water), as well as to study the influence of different parameters (initial volume ratios, time and temperature) in furfural – cyclopentanone condensation at mild conditions, using MgZr mixed oxide as catalyst and analysing the reaction mechanism as function of the obtained data.

2. Materials and methods

2.1. Catalysts preparation

MgZr mixed oxide with a Mg/Zr ratio of 4 was synthesized using the sol-gel technique optimized in our previous works. The gel was obtained dissolving nitrate salts in 1 L of deionized water and adding NaOH until pH 10 to produce the precipitation. The resulting solid was aged for 24 h at 353 K, filtered and washed with deionized water until pH 7. It was dried at 393 K for 24 h and, finally, it was calcined in He flow at 5
K·min\(^{-1}\) until 873 K and the temperature was held for 3 h. All the characterization results have been studied in detail in a previous work\(^7\).

### 2.2. Reaction system and procedure

Reactions were carried out in a 0.5 L stirred batch autoclave reactor equipped with a PID temperature controller and a backpressure regulator (Autoclave Engineers EZE Seal). The reactor was loaded with 0.25 L of a mixture of both reactants, cyclopentanone (Sigma Aldrich, 99%) and furfural (Sigma Aldrich, 99%), with a 5 wt.% of cyclic molecules in solution. The CPO:FFL initial ratio was 1:1 and 0.1 g of MgZr oxide (average diameter of 50 – 80 µm) was used as heterogeneous catalyst. Different solvents have been tested (ethyl acetate, ethanol, water, or water-organic solvent mixtures), varying the water/organic solvent volume ratios from 1:1 to 1:4 depending on the experiment. The mixture was heated up to reaction temperature, air was purged with N\(_2\) and the reaction took place under 10 bar of N\(_2\) with a stirring of 1000 rpm for different times. In order to evaluate the reaction evolution, samples were taken from the sampling port, filtered and analysed by gas chromatography in a Shimadzu GC-2010 equipped with a FID detector (using a 30 m long CP–Sil 8 CB capillary column). The identification of the main products was verified with GC–MS in a Shimadzu GC/MS QP2010 Plus instrument, using a 30 m long TRB–5MS capillary column. Calibration of cyclopentanone and furfural were done using commercial standards, whereas for the condensation adducts the relative carbon concept proposed by Scanlon\(^{25}\) was used. Conversion, atomic yields and carbon balance (equations 1 – 3) were calculated according to the following expressions.

\[
\psi_{C10}^\% = \frac{10 \cdot mol \ C10}{5 \cdot mol \ FFL_{2\rightarrow0} + 5 \cdot mol \ CPO_{2\rightarrow0}} \cdot 100 \quad [1]
\]
The final solid (either spent catalyst or a combination of the catalyst with the precipitated condensation adducts) was recovered, filtered, dissolved in organic solvent, and analyzed using the GC–FID (organics) or ICP-MS (metal leaching).

Conversions obtained in previous experiments performed in absence of Mg-Zr were negligible (less than 1% of conversion after 4 hours of reaction), discarding the presence of non-catalytic mechanisms. Furthermore, the self-condensation of these compounds (CPO or FFL) was discarded because no products were detected after 4 hours if only one reactant (and the catalyst) is present in the reactor. Only a weak signal evidencing the reaction between furfural and ethanol was observed. However, the relevance of this reaction of formation of acetal is almost negligible in all the cases, with maximum concentrations lower than 0.0005 mol·L⁻¹.

3. Results and discussion

3.1. Solvent selection

Preliminary solubility analyses of solids obtained after reaction in aqueous phase were carried out to identify the most appropriate organic solvents to perform this study. With this aim, non-polar compounds (hexane, diethyl ether), organic alcohols (methanol, ethanol) and aprotic polar organic compounds (THF, ethyl acetate) were tested, concluding that C15 adducts are entirely soluble in ethyl acetate, THF, methanol and ethanol. These results are congruent with the previously observed
behaviour for similar reactions, obtaining a good correspondence between the solubility and the dielectric constant of these solvents. This effect is even more evident in the case of alcohols, because of their both hydrophilic and hydrophobic groups that produce a strong interaction between the solvent and the steric arrangement of these molecules, increasing their solubility. Methanol and THF were discarded because of environmental considerations.

Initial tests were carried out using ethanol and ethyl acetate in a monophasic system. In both cases, the reaction does not take place, obtaining less than 1 % of cyclopentanone conversion after 4 h reaction time. The only reaction observed was the formation of furfural-ethanol acetal, when the alcohol was used as solvent. These results suggest that water is required to perform the reaction. However, as it was proved in our previous results, the adduct insolubility limits the results and leads to severe catalyst deactivation. According to these facts, a mixture of both solvents (water/ethyl acetate or water/ethanol) was selected in order to improve catalytic performance, avoiding the problems coming from adducts precipitation. Fig. 1 shows the results (considering only liquid phase analyses) after 4 h of reaction at 303 K, using a 1:1 mixture of water/ethyl acetate (biphasic system) and 1:1 water/ethanol (monophasic system). Results previously obtained in aqueous phase were also included for comparison purposes. ICP analyses of the liquid phase after each reaction were carried out in order to discard metal lixiviation and the subsequent homogeneous reaction pathway. For all the cases, negligible metal concentrations (Mg and Zr) were detected. The carbon balances with both water-organic solvent systems exceed 90 % versus 24 % working in aqueous phase (considering only liquid phase species). In contrast, conversions of furfural and cyclopentanone decrease to 30 and
29 %, respectively in the case of water/ethanol, and to 7 and 10 %, respectively in the case of water/ethyl acetate, whereas in aqueous phase values of 98 and 66 % of FFL and CPO were achieved. The atomic yields of both adducts (C10 and C15) are higher when using the water/ethanol mixture as solvent, obtaining a global yield of 29.6 %.

This value decreases to 6.4 % in water and 1.15 % in water/ethyl acetate. Separate experiments were performed with both water/ethanol and water/ethyl acetate systems at lower stirring velocity (600 rpm). In the first case, results obtained at 600 rpm were very similar to the previously reported experiments (reactant conversions around 30%), whereas in the case of the biphasic system, conversions of both reactants are below 5 %. These results suggest that mass transfer (enhanced as stirring rate increases) plays a key role in the biphasic system. Taking into account these results, the use of the water/ethyl acetate biphasic system was discarded. Aldol condensation does not take place in organic phase and the interphase transport of the adducts to the organic phase plays a relevant role, hindering the overall process. Reaction by-products derived from the organic solvent were not observed in these experiments.

Concerning to the water/ethanol system, reaction conditions must be optimised in order to determine further limitations of this configuration. For this purpose, the evolution of reactants and products with reaction time at 303 K using 0.1 g of MgZr and a 1:1 volume ratio water/ethanol as solvent is plotted in Fig. 2. This analysis was not possible with the water/ethyl acetate system, since the biphasic character of this configuration prevents sampling with time (the constant organic/aqueous volume ratio, modifies the temporal ratio evolution between both solvents and, hence, disturbing the whole reaction), thus only the final point was considered. As it is
observed in Fig. 2, the trend in the reactants with the water/ethanol system is analogous – although with lower values – than with water, a continuous decrease until similar final conversions for furfural and cyclopentanone (30 %, approximately). These lower values suggest an inhibition role of the organic phase in the whole condensation, as it was previously observed in other condensations\textsuperscript{27}. Water has a key role on catalyst performance, in agreement with the negligible reaction extent in the experiment performed in presence of pure ethanol. Concerning to the reaction products, the main one is the C10 adduct (in good agreement with the parallel evolution of both reactants), and the production of the C15 adduct is only significant after 3 hours reaction time. The final concentration of both reaction products (C10 and C15) is 0.07 and 0.01 mol·L\textsuperscript{-1}, respectively. The carbon balance in this experiment (considering only liquid phase analyses) was 96 %, discarding the presence of side reaction products and the precipitation of the condensation adducts. Accordingly, no solid phase was detected during the reaction when it is performed in the water/ethanol system, whereas in the case of the reaction carried out in aqueous phase, the presence of a solid product was detected from the beginning of the experiment. The absence of flat reactant or product profiles during the experiment suggests that this configuration is promising if these results are improved by modifying some parameters (reaction time, temperature or solvents ratio). The double character of this organic solvent (hydrophobic and hydrophilic) and the good interaction between ethanol and water justifies these results.

In order to identify the optimum reaction conditions, the influence of different parameters (water/ethanol ratio, reaction time and temperature) was studied. In order to discard any influence of the adducts solubility, the maximum theoretical
amount of C10 and C15 that could be obtained at the studied temperatures (from 303 to 323 K) was dissolved in the liquid phase. GC analyses corroborate that same concentration was detected in all the cases, demonstrating that C10 and C15 are entirely soluble in all the liquid mixtures tested.

3.2. Influence of the initial water / ethanol ratio

Experiments at different water/ethanol ratios (1:0.9 to 1:2) were carried out in order to balance the enhancement of the aldol condensation reaction and the minimization of the reaction products precipitation. Higher ethanol percentages inhibit the condensation, whereas lower amount of the alcohol leads to reaction products precipitation. The temporal evolution of all the compounds involved in the reaction is detailed in Fig. 3. In these studies, the temperature, catalyst loading, and reactant concentration were chosen considering the values previously optimized for the reaction in aqueous phase (303 K, 0.1 g of MgZr and 5 % of organics with 1:1 FFL:CPO ratio)\textsuperscript{12}. In general terms, same trends were observed in all the cases, concluding that the presence of ethanol in different ratios does not influence the whole mechanism of the reaction. According to this, furfural and cyclopentanone show the typical decreasing profiles of primary reactants (slightly more linear in the case of furfural). The parallel evolutions of both compounds suggest that reaction is mainly limited to the first step, the C10 formation, main reaction product detected. Only in the last points of the most favourable conditions, the signal of C15 can be clearly appreciated, with a typical behaviour of a secondary product. In order to make easier the analysis of these data, Fig. 4 compares the results after 4 h at 303 K. A strong influence of
The water/ethanol ratio is observed for all the considered parameters. Reactants conversions decrease as the ethanol concentration increases, until 36 % for CPO and 46 % for FFL at 1:0.9 water/ethanol ratio. These values strongly decrease to 8 % for CPO and 6 % for FFL at the opposite conditions (1:2 water/ethanol). A huge difference in FFL conversion is observed when water/ethanol changes from 1:0.9 to 1:1, since the furfural conversion is almost 33 % higher with 1:0.9. From the final carbon balance 96 %, the presence of solids is discarded for 1:1 test and larger alcohol concentrations. However, for a water/ethanol ratio of 1:0.9, a carbon balance of 89 % is obtained, suggesting a breaking point in the evolution (and a subsequent fast decrease) if higher amounts of water were used. In fact, reaction at these conditions produces the precipitation of condensation adducts (mainly C15), enhancing the formation of this compound and consuming more furfural. In fact, 8.75 moles of C15 were obtained after dissolving the solid recovered after this reaction in ethanol, whereas only 0.88 moles of C15 were detected in the liquid phase. The amount of solids obtained is supposed to be much higher at higher water/ethanol ratio, being these configurations discarded for this study.

The C10 and C15 formation patterns are very different. The C10 atomic yield decreases as the percentage of water increases, reaching final values of 27 and 6 % with 1:0.9 and 1:2 water/ethanol ratios, respectively. Considering the positive role of water in the aldol condensation, these data could suggest that higher amounts of water enhance the formation of the second adduct, C15. However, the C15 yield reaches a maximum (5.6 %) working with the 1:1 mixture. This behaviour is not the expected for a limiting reactant. Therefore, the study of different furfural/cyclopentanone ratios was discarded (the stoichiometric furfural/cyclopentanone ratio is 2:1), taking into account...
that reaction is not limited by the total consumption of the reactants, and the water/ethanol ratio is controlling the reaction extent. Therefore, and taking into account the possible side products derived for the furfural adsorption, it was concluded that working with furfural excess has a negative effect on the overall yield. Same conclusion was reported for the furfural-acetone aldol condensation, in which no significant improvement was observed when working with 2:1, being considered the 1:1 ratio as the optimum one.

In order to extrapolate the results to higher reactant conversions, reactions at the most representative water/ethanol ratios (1:1.35, 1:1.5, 1:2) were repeated, but increasing the reaction time to 24 h. Experiments with higher water concentrations were discarded because of the low carbon balances after only 4 h reaction time. These studies were carried out in order to identify if ethanol has any inhibitory effect in the reaction kinetics (in such a way similar results as in aqueous phase could be obtained at longer times) or if the reaction is limited at given ethanol concentrations. Obtained results are in a good agreement with previously reported trends in all the cases. The temporal evolution of reactants and products are shown in the supplementary information (Fig. S1), whereas the final results are summarized in Table 1 in comparison to the corresponding ones after 4 h, in order to facilitate the direct comparison. Experiments performed at the 1:2 ratio provide clearly different results to the parallel evolution of 1:1.35 and 1:1.5 reactions. In the two last mentioned experiments, carbon balances markedly decrease to values lower than 60 %, with the subsequent precipitation of a solid phase. This fact mainly affects to the C15, which never reaches yields higher than 2.6 %, despite conversions close to 80 % of furfural and around 50 % of cyclopentanone were observed. Best results were obtained
working at 1:2 water/ethanol ratio. At these conditions, 35 and 50 % of
cyclopentanone and furfural conversion were reached, remaining the carbon balance
close to 100 %, and observing significant increases in the C10 and C15 atomic yields.
Specically, the C10 atomic yield increases to 26 % and the C15 one to 10.5 %. These
values are the highest obtained in the liquid phase, even working with aqueous
phase\textsuperscript{12} or with water/ethanol mixtures, and correspond to an increase of more than
75 % of the highest yield reported in the literature.

3.3. Effect of the reaction temperature

The role of the temperature on the catalyst performance was studied in the range of
303–323 K, considering the 1:1, 1:1.5 and 1:2 water-ethanol ratios and keeping
constant the other parameters (0.1 g of catalyst, 5 % of organics at equimolar ratio).
These solvent ratios were chosen as function of the previous results at 303 K and the
expected positive effect of the temperature on the reaction rate. Results after 4 h of
reaction are summarized in Fig. 5. At 1:1 conditions, conversions higher than 50 % of
both reactants were obtained at 323 K. These values are the highest observed and are
in good agreement with the key role of water in this reaction. In relative terms, an
increment in the reaction temperature of 20 K corresponds to relative increments of
72.1 and 65.1 % for cyclopentanone and furfural conversions, respectively, at these
conditions. Despite conversion decreases when the amount of ethanol in the medium
increases, the role of temperature is more relevant, obtaining relative increases of
48.2 and 116.4 % for cyclopentanone and furfural conversions, working at 1:1.5; and
147 and 227 %, respectively, with the 1:2 solvent ratio. Less marked trends were
observed for the evolution of C10 and C15 adducts, except for the 1:1 ratio, where liquid phase yields seem to be limited by lateral reactions involving the C15 (yields constant at 3.5 %). In good agreement, the carbon balance only decreases in this case, suggesting that ethanol concentration is not high enough to dissolve the reaction products. This effect was not observed in the other cases because the maximum amount of C15 was 2.6 %. Considering that the aim of this study is to improve the aldol condensation but preventing the precipitation of products, results obtained allow us to conclude that the best configuration is working at 1:2 water/ethanol ratio. At these conditions, a temperature of 323 K is needed to partially compensate the decrease in the activity when the aldol condensation is carried out in organic solvent. After 4 h, a global yield of 19.5 % was reached, keeping the carbon balance close to 100 %.

Reaction at 1:2 solvent ratio and 323 K was repeated increasing the reaction time to promote the aldol condensation. Final results are summarized in Fig. 6, comparing the improvement between 4, 24 and 48 hours at 303 and 323 K. Concerning to the conversions, the highest improvement was obtained at 323 K, reaching a CPO conversion after 24 h more than ten times higher than the original one after 4 h (51.9 and 4.7 %, respectively). However, these conditions are discarded because of the lower carbon balance obtained (66 %), suggesting a high relevance of side reactions and/or product precipitation. In good agreement, reaction at 48 h was not considered for the study. On the other hand, the highest yields were obtained at 303 K after 24 h, with a global yield of 36.6 % and a C10/C15 ratio of 2.4. Longer times have not a positive effect in these data, reaching similar yields of the main product when the reaction time increases to 48 h. However, the increase in the conversion, mainly the furfural one, as well as the decrease in the carbon balance (from 93 to 78 %, after 24 and 48 h),
suggests that reaction times longer than 24 h promote side reactions. In order to
discard solubility limitations, an extra reaction at 1:4 (water/ethanol ratio) was carried
out, obtaining same results as in the previous at 1:2 (34.6 % global yield with less than
11 % of C15). Analysing all these results, the aldol condensation at 1:2 (water/ethanol
ratio) at 303 K for 24 hours was chosen as the optimum ones for this reaction. At these
conditions, global yields are similar as those reported for aldol condensations using
furfural as biomass-derived molecule\textsuperscript{10}.

3.4. Reaction mechanism and kinetic modelling

In order to get new insights about the reactivity, as well as to compare with the
reactivities reported for similar catalytic systems, initial conversion rate on a mass
basis were estimated according to the following equation:

\[ r_{\text{condensation}}^0 = \frac{1}{S_G} \cdot \left[ \frac{dX}{d(\frac{t \cdot W}{n^0})} \right]_{t = 0} \]  \[ [4] \]

Where “\(S_G\)” is the surface area of the catalyst (74 m\(^2\cdot\)g\(^{-1}\) for this Mg-Zr, as it was
previously reported\textsuperscript{7,8}); “\(X\)” the aldehyde conversion; “\(t\)” the reaction time in minutes;
“\(W\)” the mass of MgZr in grams; and “\(n^0\)” the initial moles of furfural. According to
experimental results, the initial conversion rate obtained with 1:2 water/ethanol ratio,
at 303 K using 0.1 g of Mg-Zr and 5 % of organics is 2.45 \(\mu\)mol\(\cdot\)min\(^{-1}\)\cdot\)m\(^{-2}\), whereas the
corresponding value working in aqueous phase has a value of 38.4 \(\mu\)mol\(\cdot\)min\(^{-1}\)\cdot\)m\(^{-2}\).
Despite the effect of ethanol, this reaction is still much faster than other
condensations using furfural and acetone (0.27 \(\mu\)mol\(\cdot\)min\(^{-1}\)\cdot\)m\(^{-2}\))\textsuperscript{7} or 5-HMF and acetone
(1.9 \(\mu\)mol\(\cdot\)min\(^{-1}\)\cdot\)m\(^{-2}\))\textsuperscript{8}. 
According to the temporal profiles obtained in all the experiments, and the similarity between these data and the previous ones reported in aqueous phase \(^{12}\), the first mechanistic conclusion is that the presence of ethanol does not modify the general reaction network, only limiting the reaction rate of the different steps. Considering this mechanism, acid-basic pairs are needed to catalyse these reactions. In fact, the aldol condensation requires the initial abstraction of one \(\alpha\)-proton from cyclopentanone, obtaining an enolate that attacks the carbonyl group of the furfural molecule. According to the literature, both molecules must be adsorbed on an acid site but Bronsted basicity is also needed to stabilize the proton\(^{7,15}\). These Bronsted basic sites are mainly generated by the partial rehydration of the MgZr mixed oxide. This mechanism, as well as the stabilisation of the resulting enolate, justifies the key role of water in the first stages of the reaction, and it is congruent with the negligible conversion observed when working with organic solvents. Once this enolate is stabilized, alcohol intermediate is formed by the nucleophilic attack of the enolate to the furfural carbonyl group. This intermediate is not observed because it undergoes fast dehydration in presence of medium acid sites, yielding the first condensation adduct (C10). The second condensation step is also possible since this molecule (C10) has another \(\alpha\)-proton, yielding the C15 alcohol and the subsequent C15 condensation adduct after the above-mentioned dehydration step.

In agreement with the proposed mechanism, both C10 and C15 adducts are obtained following a first-order dependence on the concentration of the compound undergoing enolization (cyclopentanone and C10, respectively) and zero-th order dependence on furfural. This zero-th order for the furfural is congruent with other kinetics models for the aldol condensation of other bio-platform molecules, such as furfural, 5-HMF\(^8\) and
citral with acetone and it is justified by the strong adsorption of furfural on these materials. According to these facts, the kinetic model is described in the following equations (5-8):

\[
\frac{dC_{cPO}}{dt} = -k_1 \cdot C_{cPO} \quad [5]
\]

\[
\frac{dC_{FRAL}}{dt} = -k_1 \cdot C_{cPO} - k_2 \cdot C_{c10} \quad [6]
\]

\[
\frac{dC_{c10}}{dt} = k_1 \cdot C_{cPO} - k_2 \cdot C_{c10} \quad [7]
\]

\[
\frac{dC_{15}}{dt} = k_2 \cdot C_{c10} \quad [8]
\]

Temporal profiles of reactants and products concentrations were fitted to this kinetic model using the Scientist® software. Ideal batch reactor behaviour has been considered in all the cases. The presence of mass-transfer effects has been discarded by both, ensuring that particle size and stirring reaction do not affect the results, and by theoretical considerations. The theoretical approach consisted on a kinetic model derivation considering the liquid-solid mass transfer and the Thiele modulus-based efficiency factor for internal diffusion. Taking into account the experimental conditions, the resistance due to the intrinsic kinetic is seven orders of magnitude higher than the mass-transfer resistance, the influence of both, external and internal diffusion, was discarded and reaction is considered to be under kinetic control\textsuperscript{29, 30}. Table 2 summarises the values $k_1$ and $k_2$ for all the experiments performed with water-ethanol mixtures. Values of these kinetic constants are normalised considering the catalytic loading and the feed volume in order to compare the results obtained in experiments at different conditions. The correlation coefficient obtained in each case, as well as confidence intervals, were also included in Table 2 for illustrating the
goodness of the fit ($r^2 > 0.99$ in all the cases). Other reaction orders were tested, such as first order dependence on FAL concentration or fractional reaction orders, with largely worst results. The correspondence between experimental results and model predictions is shown in the Figures 2 and 3, as well as in the Supplementary Information (Fig. S2). As it could be expected, values of $k_1$ were higher than $k_2$, concluding that the formation of the first condensation adduct is much faster than the second one. Considering the high amount of solids obtained when the reaction was performed in pure water, the direct comparison between these values and the corresponding ones in aqueous phase is not possible. However, there is a clear influence of the percentage of ethanol and the values of kinetic constants, decreasing as ethanol concentration in the reaction medium increases. If results at 1:0.9 and 1:2 are compared, there is a decrease of almost 85 and 63 % in the values of $k_1$ and $k_2$, respectively. This result is in a good agreement with the previous hypothesis about the key role of the water to promote the aldolization, and the negative effect of ethanol on the general rate. In order to illustrate this idea, Fig. 7 shows the relationship between the ethanol concentration in the different mixtures ethanol/water used in this work and the values of the kinetic constants, observing clearly the decreasing trend of both parameters, being more relevant in the case of the first constant. The observed behaviour suggests a value of this kinetic constants of 0.0114 and 0.0060 L·min$^{-1}$·g$^{-1}$ for $k_1$ and $k_2$, respectively, when reaction is carried out in aqueous phase. Observing the good fit between the kinetic constant and the ethanol percentage, a clear influence of the solvent polarity is suggested (ethanol/water polarity ratios is 0.654). At this point, the presence of polar molecules is considered as necessary for stabilizing the ketone-derived enolate species, needed for accomplishing the
By contrast, an effect of the presence of ethanol on surface chemistry or in the adsorption of reaction and/or products is ruled out since the affinity of the surface for ethanol is largely lower than the affinity for water, which is present in all the experiments.

Considering the influence of the temperature observed in this study, kinetic constants obtained with experiments at 1:1, 1:1.5 and 1:2 water/ethanol ratio were fit to an Arrhenius dependence. The fit of these constants to this model is plotted in Fig. 8a. The mathematical analysis of these results indicates a continuous increase in the apparent activation energy as the percentage of ethanol in the system increases, obtaining values of 22.8 kJ·mol⁻¹ for 1:1.5, and 49.4 kJ·mol⁻¹ for 1:2. In any case, these data are within the range of values reported in the literature for similar type of reactions. At this point, different physical and chemical constraints could influence this parameter when working in liquid phase, thus activation energies are not comparable to those obtained in gas phase. Considering that the apparent activation energy is obtained by the slope of the regression, the corresponding one for the aqueous phase system was estimated taking into account the variation in the initial conversion rates at different temperatures. Result obtained, 7.2 kJ·mol⁻¹, allows predicting the evolution of the reaction with the water/ethanol ratio, as it is observed in the Fig. 8b. In this figure, the clear inhibitory effect of the organic solvent is observed. The resulting exponential trend justifies ethanol ratios higher than 1:2 must be discarded because of the expected low activity. However, the best results obtained for 1:2 water:ethanol ratio (36.5 % of global yield with this configuration, whereas less than 6 % was obtained as liquids in aqueous solution at the optimized conditions) justify the use of ethanol in the reaction media. In addition, the presence of ethanol
minimises the deactivation caused by the permanent adsorption of main and side reaction products. Globally, this effect compensates the decrease in the kinetic rate, obtaining a net enhancement in the selectivity of C10 and C15.

4. Conclusions

The condensation yields obtained by the reaction between cyclopentanone and furfural are strongly improved by adding ethanol to the initial aqueous phase. According to experimental results, an equilibrium between condensation activity (being water needed) and products solubility (strongly enhanced by the presence of ethanol) is needed. Once reaction time, temperature and water/ethanol ratio were optimized, best results were obtained working at 303 K and a water/ethanol ratio of 1:2. At these conditions, after 24 hours, the global yield in the liquid phase (36.5 %) is more than six times the maximum ones reported in aqueous phase. The good carbon balance obtained at these conditions (higher than 90 % whereas it was only 24 % in aqueous phase) also corroborates the absence of side reactions and oligomerizations that could have a negative effect in the catalytic deactivation. Experimental data were successfully fit to a first-order reaction mechanism, obtaining a clear dependency between the activation energy and the percentage of ethanol in the mixture.

ACKNOWLEDGMENTS

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ABBREVIATIONS

FFL, furfural; CPO, cyclopentanone; HPLC, high performance liquid chromatography; 5-HMF, 5-hydroximethylfurfural; GC, Gas Chromatography.

REFERENCES


Fig. 1. Results obtained, considering only liquid phase composition, after 4 h of furfural and cyclopentanone aldol condensation at 303 K catalyzed by 0.1 g of MgZr using different systems: aqueous system (bars with horizontal lines) and two different water/organic systems: 1:1 water/ethanol (bars with twisted lines), and 1:1 water/ethyl acetate (bars with vertical lines). Results in terms of reactant conversions, product atomic yields and carbon balance.
Fig. 2. Reactants and products concentration temporal evolution of the cyclopentanone – furfural condensation (5 % organics, 1:1 water/ethanol ratio, 303 K and 0.1 g of Mg Zr). Symbols: (▲) furfural; (●) cyclopentanone; (♦) C10 and (●) C15. Maximum error: 4 %. Lines correspond to the predictions of the proposed kinetic model.
Fig. 3. Evolution of reactants and products concentration involved in the aldol condensation of cyclopentanone and furfural (303 K, 0.1 g Mg-Zr, 1:1 Furfural:Cyclopentanone) as function of reaction time for different ethanol-water mixtures: (a) 1:0.9; (b) 1:1.35; (c) 1:1.5; (d) 1:1.75; (e) 1:2. Symbols: (▲) furfural; (●) cyclopentanone; (♦) C10 and (■) C15. Maximum error of 3.75 %. Lines correspond to the predictions of the proposed kinetic model.
**Fig. 4.** Results obtained after 4 h of furfural and cyclopentanone aldol condensation at 303 K catalyzed by 0.1 g of MgZr using different initial water/ethanol ratio: 1:0.9 (white), 1:1 (bars with horizontal lines), 1:1.35 (bars with twisted lines), 1:1.5 (dotted bars), 1:1.75 (bars with vertical lines) and 1:2 (solid black). Results in terms of reactants conversions, product atomic yields and carbon balance (secondary axe).
**Fig. 5.** Results obtained after 4 h of furfural and cyclopentanone aldol condensation catalyzed by 0.1 g of MgZr using different water/ethanol ratios: (a) 1:1; (b) 1:1.5, (c) 1:2. Reaction temperature: 303 K (white); 313 K (grey); 323 K (black).
Fig. 6. Comparison of the results obtained in the CPO-FFL aldol condensation using 1:2 water/ethanol ratio and 0.1 g of MgZr as function of the temperature and the reaction time. Legend: 303 K and 4 h (white); 303 K and 24 h (bars with horizontal lines); 303 K and 48 h (dotted bars); 323 K and 4 h (bars with vertical lines); 323 K and 24 h (black).
Fig. 7. Kinetic constants for the fitting of the experimental results to the proposed kinetic model when different percentages of ethanol were used in the feed at 303 K. Symbols: (●) $k_1$; (♦) $k_2$. 
Fig. 8. Analysis of kinetic data with temperature. (a) Arrhenius adjustment for different water/ethanol ratios. Symbols: (▲) 1:2; (♦) 1:1.5 and (■) 1:1. (b) Activation energy evolution with the percentage of ethanol used in the feed.
**Table 1.** Results of condensation between furfural and cyclopentanone (5 % of cyclic molecules, 303 K) catalyzed by 0.1 g of MgZr at different times and solvent relations.

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Water/Ethanol</th>
<th>Conv. CPO (%)</th>
<th>Conv. FFL (%)</th>
<th>Ψ C10</th>
<th>Ψ C15</th>
<th>C. B.</th>
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<td>4</td>
<td>1:1.35</td>
<td>23.7</td>
<td>20.2</td>
<td>16.7</td>
<td>3.0</td>
<td>97.8</td>
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<td>24</td>
<td>1:1.35</td>
<td>50.0</td>
<td>79.4</td>
<td>22.1</td>
<td>2.6</td>
<td>59.9</td>
</tr>
<tr>
<td>4</td>
<td>1:1.5</td>
<td>19.7</td>
<td>14.0</td>
<td>13.6</td>
<td>1.3</td>
<td>98.0</td>
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<tr>
<td>24</td>
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<td>54.7</td>
<td>78.5</td>
<td>21.6</td>
<td>2.4</td>
<td>57.4</td>
</tr>
<tr>
<td>4</td>
<td>1:2</td>
<td>7.9</td>
<td>6.0</td>
<td>6.5</td>
<td>0.6</td>
<td>100.0</td>
</tr>
<tr>
<td>24</td>
<td>1:2</td>
<td>35.9</td>
<td>51.2</td>
<td>25.9</td>
<td>10.8</td>
<td>93.1</td>
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Table 2. Kinetic constants for the fitting of the experimental results to the proposed kinetic model when MgZr was used as catalyst (see equations 4-7 to identify the constants). Values reported with 95% confidence interval (CI).

<table>
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<tr>
<th>Temperature (K)</th>
<th>Water/Ethanol</th>
<th>$k_1$ (L·min$^{-1}$·g$^{-1}$)</th>
<th>$k_2$ (L·min$^{-1}$·g$^{-1}$)</th>
<th>$r^2$</th>
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<td>303</td>
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<td>0.0049 ± 0.0003</td>
<td>0.0025 ± 0.0005</td>
<td>0.996</td>
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<tr>
<td></td>
<td>1:1</td>
<td>0.0045 ± 0.0003</td>
<td>0.0023 ± 0.0007</td>
<td>0.996</td>
</tr>
<tr>
<td></td>
<td>1:1.35</td>
<td>0.0023 ± 0.008</td>
<td>0.0018 ± 0.0008</td>
<td>0.998</td>
</tr>
<tr>
<td></td>
<td>1:1.5</td>
<td>0.0021 ± 0.0005</td>
<td>0.0015 ± 0.0002</td>
<td>0.997</td>
</tr>
<tr>
<td></td>
<td>1:1.75</td>
<td>0.0020 ± 0.0006</td>
<td>0.0012 ± 0.0003</td>
<td>0.999</td>
</tr>
<tr>
<td></td>
<td>1:2</td>
<td>0.0007 ± 0.0002</td>
<td>0.0009 ± 0.0001</td>
<td>0.999</td>
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<tr>
<td>313</td>
<td>1:1</td>
<td>0.0057 ± 0.0005</td>
<td>0.0044 ± 0.0001</td>
<td>0.995</td>
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<tr>
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<td>1:1.5</td>
<td>0.0024 ± 0.0002</td>
<td>0.0018 ± 0.0003</td>
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</tr>
<tr>
<td></td>
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<td>0.0017 ± 0.0009</td>
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<tr>
<td>323</td>
<td>1:1.5</td>
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<td>0.0024 ± 0.0007</td>
<td>0.0008 ± 0.0001</td>
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ASSOCIATED CONTENT

Supporting Information

Comparison of experimental results and fitted data is available, for all the experiments of the study, in the supporting information.

AUTHOR INFORMATION

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