

1 **Enhancement of furfural-cyclopentanone aldol condensation** 2 **using binary water-ethanol mixtures as solvent**

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

11 **RESULTS:** Binary systems combining water (needed to promote the aldol condensation) and
12 ethanol (for enhancing the condensation adducts solubility) at different ratios have been
13 tested. Operation parameters, such as water/ethanol ratio, temperature and reaction time,
14 were optimized for this reaction. Best results (global yield to condensation adducts higher than
15 36 %) were achieved using 1:2 water/ethanol ratio, and working at 303 K. Higher water ratios
16 lead to the precipitation of condensation products, whereas higher ethanol concentrations
17 hinder the catalyst performance. A reaction mechanism, considering a first order kinetic model
18 on cyclopentanone concentration, was proposed. Kinetic constants have been empirically
19 correlated with ethanol concentration in the reaction medium.

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

25 **KEYWORDS.** Biorefinery; cyclopentanone; furfural; solvent effects; drop-in diesel fuels;
26 MgZr oxides

27

28 1. INTRODUCTION

29 The increasing concern about global climate change has promoted the development of
30 different routes that use biomass waste as raw material for obtaining biofuels and
31 commodity chemicals¹. One of the most promising routes to fulfil these purposes is the
32 aqueous phase transformation of lignocellulosic biomass². Aldol condensation can be a
33 key step for these purposes, since it is an effective way for the selective conversion of
34 small molecules (C5-C6) into larger ones with 8 to 15 carbon atoms^{3,4}. These
35 condensation adducts are precursors for a large variety of renewable chemicals and,
36 upon total hydrogenation, drop-in diesel fuels. Aldol condensation involves the
37 interaction between two molecules with carbonyl groups (aldehydes – furfural FFL or
38 5 – hydroxymethylfurfural 5 – HMF – or ketones), being acetone the most studied
39 linking molecule⁵⁻⁸.

40 There are several studies about the aldol condensation of acetone and furfural or 5-
41 HMF using different homogeneous and heterogeneous catalysts, highlighting different
42 hydroxides (NaOH and Ca(OH)₂)^{9,10} and mixed oxides such as Mg-Zr or Mg-Al^{5,8}.
43 However, there are other bio-derived molecules with two α -hydrogen positions that
44 can be alternatively used for this purpose. Among these compounds, cyclopentanone
45 (CPO) presents important advantages in comparison to acetone. Firstly, resulting
46 condensation adducts are entirely renewable since both reactants (cyclopentanone
47 and furfural or 5-HMF) can be quantitatively produced from ligno-cellulosic biomass¹¹,
48 whereas acetone is nowadays only renewably obtained as a side product in the ABE
49 fermentation. On the other hand, considering the usefulness of the resulting products,
50 condensation adducts obtained have longer and branched carbon chains, leading to

51 fuels of better quality¹². Despite these theoretical considerations, cyclopentanone-
52 furfural condensation is still scarcely studied. Hronec *et al.* studied this reaction using
53 homogeneous catalyst (NaOH), with more than 95 % of the second adduct yield (C15)
54 in less than two hours¹³. Deng *et al.* reported selectivities higher than 85 % (in solid
55 phase) after 2 hours but working in solvent-free condensation and using NaOH as
56 catalyst¹⁴.

57 In spite of the well-known disadvantages of using homogeneous catalysts¹⁵, and the
58 wide use of solid base catalysts for these reactions^{7, 16, 17} there are few works dealing
59 with the heterogeneously catalyzed cyclopentanone-furfural condensation¹⁸. In our
60 previous work, preliminary results using Mg-Zr mixed oxide as catalyst were reported,
61 combining mild conditions (303 – 323 K) and aqueous media¹². A complete conversion
62 of furfural, with more than 68 % of CPO conversion, was observed after 4 hours of
63 reaction in a batch reactor. These results correspond to a 320 times faster reaction
64 than the similar tests using acetone as linking molecule⁷. At this time, the carbon
65 balance closure in liquid phase decreases to 20 % and main products were obtained as
66 solids, reaching a global yield of 77 %. The low solubility of these adducts in water,
67 hinders further downstream processing, such as partial or total hydrogenations.
68 Furthermore, the precipitation of these phases leads to catalyst fouling and
69 deactivation. Performing the reaction in presence of organic solvents would be an
70 alternative for overcoming these solubility problems. The high solubility of these
71 adducts in these solvents was previously observed by Hronec *et al.*, proposing the use
72 of methanol or tetrahydrofuran¹³. Nevertheless, both solvents are considering as toxic
73 and incompatible with Green Chemistry principles^{19, 20}.

74 Taking into account that alcohols and organic esters dissolve the condensation
75 adducts²¹, ethanol and ethyl acetate are proposed as valuable alternatives. Ethyl
76 acetate is considered as a green solvent (low toxicity, stable, biodegradable, etc.)²² and
77 it was used in our previous work for fully solving the condensation adducts¹² and
78 would allow studying the reaction in a biphasic system. On the other hand, ethanol is a
79 green solvent, which can be obtained from lignocellulose feedstock, reducing
80 greenhouse gas emissions in its production²³ and it is less toxic than methanol (TLV is
81 1000 ppm; whereas for methanol is 200 ppm)²⁴. Since ethanol is soluble in water, the
82 reaction will be carried out in a binary but monophasic configuration.

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

88

89 **2. Materials and methods**

90 *2.1. Catalysts preparation*

91 MgZr mixed oxide with a Mg/Zr ratio of 4 was synthesized using the sol-gel technique
92 optimized in our previous works^{7, 8}. The gel was obtained dissolving nitrate salts in 1 L
93 of deionized water and adding NaOH until pH 10 to produce the precipitation. The
94 resulting solid was aged for 24 h at 353 K, filtered and washed with deionized water
95 until pH 7. It was dried at 393 K for 24 h and, finally, it was calcined in He flow at 5

96 K·min⁻¹ until 873 K and the temperature was held for 3 h. All the characterization
97 results have been studied in detail in a previous work⁷.

98 2.2. Reaction system and procedure

99 Reactions were carried out in a 0.5 L stirred batch autoclave reactor equipped with a
100 PID temperature controller and a backpressure regulator (Autoclave Engineers EZE
101 Seal). The reactor was loaded with 0.25 L of a mixture of both reactants,
102 cyclopentanone (Sigma Aldrich, 99%) and furfural (Sigma Aldrich, 99%), with a 5 wt.%
103 of cyclic molecules in solution. The CPO:FFL initial ratio was 1:1 and 0.1 g of MgZr oxide
104 (average diameter of 50 – 80 μm) was used as heterogeneous catalyst. Different
105 solvents have been tested (ethyl acetate, ethanol, water, or water-organic solvent
106 mixtures), varying the water/organic solvent volume ratios from 1:1 to 1:4 depending
107 on the experiment. The mixture was heated up to reaction temperature, air was
108 purged with N₂ and the reaction took place under 10 bar of N₂ with a stirring of 1000
109 rpm for different times. In order to evaluate the reaction evolution, samples were
110 taken from the sampling port, filtered and analysed by gas chromatography in a
111 Shimadzu GC-2010 equipped with a FID detector (using a 30 m long CP–Sil 8 CB
112 capillary column). The identification of the main products was verified with GC–MS in a
113 Shimadzu GC/MS QP2010 Plus instrument, using a 30 m long TRB–5MS capillary
114 column. Calibration of cyclopentanone and furfural were done using commercial
115 standards, whereas for the condensation adducts the relative carbon concept
116 proposed by Scanlon²⁵ was used. Conversion, atomic yields and carbon balance
117 (equations 1 – 3) were calculated according to the following expressions.

$$118 \quad \Psi_{C_{10}}\% = \frac{10 \cdot \text{mol } C_{10}}{5 \cdot \text{mol } FFL_{t=0} + 5 \cdot \text{mol } CPO_{t=0}} \cdot 100 \quad [1]$$

119
$$\Psi_{C15}\% = \frac{15 \cdot \text{mol } C15}{5 \cdot \text{mol } FFL_{t=0} + 5 \cdot \text{mol } CPO_{t=0}} \cdot 100 \quad [2]$$

120
$$C.B. (\%) = \frac{5 \cdot \text{mol } FFL + 5 \cdot \text{mol } CPO + 10 \cdot \text{mol } C10 + 15 \cdot \text{mol } C15}{5 \cdot \text{mol } FFL_{t=0} + 5 \cdot \text{mol } CPO_{t=0}} \cdot 100 \quad [3]$$

121 The final solid (either spent catalyst or a combination of the catalyst with the
122 precipitated condensation adducts) was recovered, filtered, dissolved in organic
123 solvent, and analyzed using the GC–FID (organics) or ICP-MS (metal leaching).

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

132

133 **3. Results and discussion**

134 *3.1. Solvent selection*

135 Preliminary solubility analyses of solids obtained after reaction in aqueous phase were
136 carried out to identify the most appropriate organic solvents to perform this study.
137 With this aim, non-polar compounds (hexane, diethyl ether), organic alcohols
138 (methanol, ethanol) and aprotic polar organic compounds (THF, ethyl acetate) were
139 tested, concluding that C15 adducts are entirely soluble in ethyl acetate, THF,
140 methanol and ethanol. These results are congruent with the previously observed

141 behaviour for similar reactions, obtaining a good correspondence between the
142 solubility and the dielectric constant of these solvents. This effect is even more evident
143 in the case of alcohols, because of their both hydrophilic and hydrophobic groups that
144 produce a strong interaction between the solvent and the steric arrangement of these
145 molecules, increasing their solubility²⁶. Methanol and THF were discarded because of
146 environmental considerations.

147 Initial tests were carried out using ethanol and ethyl acetate in a monophasic system.
148 In both cases, the reaction does not take place, obtaining less than 1 % of
149 cyclopentanone conversion after 4 h reaction time. **The only reaction observed was**
150 **the formation of furfural-ethanol acetal, when the alcohol was used as solvent.** These
151 results suggest that water is required to perform the reaction. However, as it was
152 proved in our previous results, the adduct insolubility limits the results and leads to
153 severe catalyst deactivation¹². According to these facts, a mixture of both solvents
154 (water/ethyl acetate or water/ethanol) was selected in order to improve catalytic
155 performance, avoiding the problems coming from adducts precipitation. **Fig. 1** shows
156 the results (considering only liquid phase analyses) after 4 h of reaction at 303 K, using
157 a 1:1 mixture of water/ethyl acetate (biphasic system) and 1:1 water/ethanol
158 (monophasic system). Results previously obtained in aqueous phase were also
159 included for comparison purposes¹². ICP analyses of the liquid phase after each
160 reaction were carried out in order to discard metal lixiviation and the subsequent
161 homogeneous reaction pathway. For all the cases, negligible metal concentrations (Mg
162 and Zr) were detected. The carbon balances with both water-organic solvent systems
163 exceeds 90 % versus 24 % working in aqueous phase (considering only liquid phase
164 species). In contrast, conversions of furfural and cyclopentanone decrease to 30 and

165 29 %, respectively in the case of water/ethanol, and to 7 and 10 %, respectively in the
166 case of water/ethyl acetate, whereas in aqueous phase values of 98 and 66 % of FFL
167 and CPO were achieved. The atomic yields of both adducts (C10 and C15) are higher
168 when using the water/ethanol mixture as solvent, obtaining a global yield of 29.6 %.
169 This value decreases to 6.4 % in water and 1.15 % in water/ethyl acetate. **Separate**
170 **experiments were performed with both water/ethanol and water/ethyl acetate**
171 **systems at lower stirring velocity (600 rpm). In the first case, results obtained at 600**
172 **rpm were very similar to the previously reported experiments (reactant conversions**
173 **around 30%), whereas in the case of the biphasic system, conversions of both**
174 **reactants are below 5 %. These results suggest that mass transfer (enhanced as stirring**
175 **rate increases) plays a key role in the biphasic system.** Taking into account these
176 results, the use of the water/ethyl acetate biphasic system was discarded. Aldol
177 condensation does not take place in organic phase and the interphase transport of the
178 adducts to the organic phase plays a relevant role, hindering the overall process.
179 **Reaction by-products derived from the organic solvent were not observed in these**
180 **experiments.**

181 Concerning to the water/ethanol system, reaction conditions must be optimised in
182 order to determine further limitations of this configuration. For this purpose, the
183 evolution of reactants and products with reaction time at 303 K using 0.1 g of MgZr
184 and a 1:1 volume ratio water/ethanol as solvent is plotted in **Fig. 2**. This analysis was
185 not possible with the water/ethyl acetate system, since the biphasic character of this
186 configuration prevents sampling with time (the constant organic/aqueous volume
187 ratio, modifies the temporal ratio evolution between both solvents and, hence,
188 disturbing the whole reaction), thus only the final point was considered. As it is

189 observed in Fig. 2, the trend in the reactants with the water/ethanol system is
190 analogous – although with lower values – than with water, a continuous decrease until
191 similar final conversions for furfural and cyclopentanone (30 %, approximately). These
192 lower values suggest an inhibition role of the organic phase in the whole condensation,
193 as it was previously observed in other condensations²⁷. Water has a key role on
194 catalyst performance, in agreement with the negligible reaction extent in the
195 experiment performed in presence of pure ethanol. Concerning to the reaction
196 products, the main one is the C10 adduct (in good agreement with the parallel
197 evolution of both reactants), and the production of the C15 adduct is only significant
198 after 3 hours reaction time. The final concentration of both reaction products (C10 and
199 C15) is 0.07 and 0.01 mol·L⁻¹, respectively. The carbon balance in this experiment
200 (considering only liquid phase analyses) was 96 %, discarding the presence of side
201 reaction products and the precipitation of the condensation adducts. Accordingly, no
202 solid phase was detected during the reaction when it is performed in the
203 water/ethanol system, whereas in the case of the reaction carried out in aqueous
204 phase, the presence of a solid product was detected from the beginning of the
205 experiment. The absence of flat reactant or product profiles during the experiment
206 suggests that this configuration is promising if these results are improved by modifying
207 some parameters (reaction time, temperature or solvents ratio). The double character
208 of this organic solvent (hydrophobic and hydrophilic) and the good interaction
209 between ethanol and water justifies these results.

210 In order to identify the optimum reaction conditions, the influence of different
211 parameters (water/ethanol ratio, reaction time and temperature) was studied. In
212 order to discard any influence of the adducts solubility, the maximum theoretical

213 amount of C10 and C15 that could be obtained at the studied temperatures (from 303
214 to 323 K) was dissolved in the liquid phase. GC analyses corroborate that same
215 concentration was detected in all the cases, demonstrating that C10 and C15 are
216 entirely soluble in all the liquid mixtures tested.

217

218 3.2. *Influence of the initial water / ethanol ratio*

219 Experiments at different water/ethanol ratios (1:0.9 to 1:2) were carried out in order
220 to balance the enhancement of the aldol condensation reaction and the minimization
221 of the reaction products precipitation. Higher ethanol percentages inhibit the
222 condensation, whereas lower amount of the alcohol leads to reaction products
223 precipitation. The temporal evolution of all the compounds involved in the reaction is
224 detailed in **Fig. 3**. In these studies, the temperature, catalyst loading, and reactant
225 concentration were chosen considering the values previously optimized for the
226 reaction in aqueous phase (303 K, 0.1 g of MgZr and 5 % of organics with 1:1 FFL:CPO
227 ratio)¹². In general terms, same trends were observed in all the cases, concluding that
228 the presence of ethanol in different ratios does not influence the whole mechanism of
229 the reaction. According to this, furfural and cyclopentanone show the typical
230 decreasing profiles of primary reactants (slightly more linear in the case of furfural).
231 The parallel evolutions of both compounds suggest that reaction is mainly limited to
232 the first step, the C10 formation, main reaction product detected. Only in the last
233 points of the most favourable conditions, the signal of C15 can be clearly appreciated,
234 with a typical behaviour of a secondary product. In order to make easier the analysis of
235 these data, **Fig. 4** compares the results after 4 h at 303 K. A strong influence of

236 water/ethanol ratio is observed for all the considered parameters. Reactants
237 conversions decrease as the ethanol concentration increases, until 36 % for CPO and
238 46 % for FFL at 1:0.9 water/ethanol ratio. These values strongly decrease to 8 % for
239 CPO and 6 % for FFL at the opposite conditions (1:2 water/ethanol). A huge difference
240 in FFL conversion is observed when water/ethanol changes from 1:0.9 to 1:1, since the
241 furfural conversion is almost 33 % higher with 1:0.9. From the final carbon balance 96
242 %, the presence of solids is discarded for 1:1 test and larger alcohol concentrations.
243 However, for a water/ethanol ratio of 1:0.9, a carbon balance of 89 % is obtained,
244 suggesting a breaking point in the evolution (and a subsequent fast decrease) if higher
245 amounts of water were used. In fact, reaction at these conditions produces the
246 precipitation of condensation adducts (mainly C15), enhancing the formation of this
247 compound and consuming more furfural. In fact, 8.75 moles of C15 were obtained
248 after dissolving the solid recovered after this reaction in ethanol, whereas only 0.88
249 moles of C15 were detected in the liquid phase. The amount of solids obtained is
250 supposed to be much higher at higher water/ethanol ratio, being these configurations
251 discarded for this study.

252 The C10 and C15 formation patterns are very different. The C10 atomic yield decreases
253 as the percentage of water increases, reaching final values of 27 and 6 % with 1:0.9
254 and 1:2 water/ethanol ratios, respectively. Considering the positive role of water in the
255 aldol condensation, these data could suggest that higher amounts of water enhance
256 the formation of the second adduct, C15. However, the C15 yield reaches a maximum
257 (5.6 %) working with the 1:1 mixture. This behaviour is not the expected for a limiting
258 reactant. Therefore, the study of different furfural/cyclopentanone ratios was
259 discarded (the stoichiometric furfural/cyclopentanone ratio is 2:1), taking into account

260 that reaction is not limited by the total consumption of the reactants, and the
261 water/ethanol ratio is controlling the reaction extent. Therefore, and taking into
262 account the possible side products derived for the furfural adsorption, it was
263 concluded that working with furfural excess has a negative effect on the overall yield.
264 Same conclusion was reported for the furfural-acetone aldol condensation, in which no
265 significant improvement was observed when working with 2:1, being considered the
266 1:1 ratio as the optimum one⁷.

267 In order to extrapolate the results to higher reactant conversions, reactions at the
268 most representative water/ethanol ratios (1:1.35, 1:1.5, 1:2) were repeated, but
269 increasing the reaction time to 24 h. Experiments with higher water concentrations
270 were discarded because of the low carbon balances after only 4 h reaction time. These
271 studies were carried out in order to identify if ethanol has any inhibitory effect in the
272 reaction kinetics (in such a way similar results as in aqueous phase could be obtained
273 at longer times) or if the reaction is limited at given ethanol concentrations. Obtained
274 results are in a good agreement with previously reported trends in all the cases. The
275 temporal evolution of reactants and products are shown in the supplementary
276 information (**Fig. S1**), whereas the final results are summarized in **Table 1** in
277 comparison to the corresponding ones after 4 h, in order to facilitate the direct
278 comparison. Experiments performed at the 1:2 ratio provide clearly different results to
279 the parallel evolution of 1:1.35 and 1:1.5 reactions. In the two last mentioned
280 experiments, carbon balances markedly decrease to values lower than 60 %, with the
281 subsequent precipitation of a solid phase. This fact mainly affects to the C15, which
282 never reaches yields higher than 2.6 %, despite conversions close to 80 % of furfural
283 and around 50 % of cyclopentanone were observed. Best results were obtained

284 working at 1:2 water/ethanol ratio. At these conditions, 35 and 50 % of
285 cyclopentanone and furfural conversion were reached, remaining the carbon balance
286 close to 100 %, and observing significant increases in the C10 and C15 atomic yields.
287 Specically, the C10 atomic yield increases to 26 % and the C15 one to 10.5 %. These
288 values are the highest obtained in the liquid phase, even working with aqueous
289 phase¹² or with water/ethanol mixtures, and correspond to an increase of more than
290 75 % of the highest yield reported in the literature.

291

292 3.3. *Effect of the reaction temperature*

293 The role of the temperature on the catalyst performance was studied in the range of
294 303 –323 K, considering the 1:1, 1:1.5 and 1:2 water-ethanol ratios and keeping
295 constant the other parameters (0.1 g of catalyst, 5 % of organics at equimolar ratio).
296 These solvent ratios were chosen as function of the previous results at 303 K and the
297 expected positive effect of the temperature on the reaction rate. Results after 4 h of
298 reaction are summarized in **Fig. 5**. At 1:1 conditions, conversions higher than 50 % of
299 both reactants were obtained at 323 K. These values are the highest observed and are
300 in good agreement with the key role of water in this reaction. In relative terms, an
301 increment in the reaction temperature of 20 K corresponds to relative increments of
302 72.1 and 65.1 % for cyclopentanone and furfural conversions, respectively, at these
303 conditions. Despite conversion decreases when the amount of ethanol in the medium
304 increases, the role of temperature is more relevant, obtaining relative increases of
305 48.2 and 116.4 % for cyclopentanone and furfural conversions, working at 1:1.5; and
306 147 and 227 %, respectively, with the 1:2 solvent ratio. Less marked trends were

307 observed for the evolution of C10 and C15 adducts, except for the 1:1 ratio, where
308 liquid phase yields seem to be limited by lateral reactions involving the C15 (yields
309 constant at 3.5 %). In good agreement, the carbon balance only decreases in this case,
310 suggesting that ethanol concentration is not high enough to dissolve the reaction
311 products. This effect was not observed in the other cases because the maximum
312 amount of C15 was 2.6 %. Considering that the aim of this study is to improve the aldol
313 condensation but preventing the precipitation of products, results obtained allow us to
314 conclude that the best configuration is working at 1:2 water/ethanol ratio. At these
315 conditions, a temperature of 323 K is needed to partially compensate the decrease in
316 the activity when the aldol condensation is carried out in organic solvent. After 4 h, a
317 global yield of 19.5 % was reached, keeping the carbon balance close to 100 %.

318 Reaction at 1:2 solvent ratio and 323 K was repeated increasing the reaction time to
319 promote the aldol condensation. Final results are summarized in **Fig. 6**, comparing the
320 improvement between 4, 24 and 48 hours at 303 and 323 K. Concerning to the
321 conversions, the highest improvement was obtained at 323 K, reaching a CPO
322 conversion after 24 h more than ten times higher than the original one after 4 h (51.9
323 and 4.7 %, respectively). However, these conditions are discarded because of the lower
324 carbon balance obtained (66 %), suggesting a high relevance of side reactions and/or
325 product precipitation. In good agreement, reaction at 48 h was not considered for the
326 study. On the other hand, the highest yields were obtained at 303 K after 24 h, with a
327 global yield of 36.6 % and a C10/C15 ratio of 2.4. Longer times have not a positive
328 effect in these data, reaching similar yields of the main product when the reaction time
329 increases to 48 h. However, the increase in the conversion, mainly the furfural one, as
330 well as the decrease in the carbon balance (from 93 to 78 %, after 24 and 48 h),

331 suggests that reaction times longer than 24 h promote side reactions. In order to
332 discard solubility limitations, an extra reaction at 1:4 (water/ethanol ratio) was carried
333 out, obtaining same results as in the previous at 1:2 (34.6 % global yield with less than
334 11 % of C15). Analysing all these results, the aldol condensation at 1:2 (water/ethanol
335 ratio) at 303 K for 24 hours was chosen as the optimum ones for this reaction. At these
336 conditions, global yields are similar as those reported for aldol condensations using
337 furfural as biomass-derived molecule¹⁰.

338

339 3.4. Reaction mechanism and kinetic modelling

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

$$343 \quad r_{condensation}^0 = \frac{1}{S_G} \cdot \left[\frac{dX}{d\left(\frac{t \cdot W}{n^0}\right)} \right]_{\left(\frac{t \cdot W}{n^0}\right)=0} \quad [4]$$

344 Where “ S_G ” is the surface area of the catalyst (74 m²·g⁻¹ for this Mg-Zr, as it was
345 previously reported^{7, 8}); “ X ” the aldehyde conversion; “ t ” the reaction time in minutes;
346 “ W ” the mass of MgZr in grams; and “ n^0 ” the initial moles of furfural. According to
347 experimental results, the initial conversion rate obtained with 1:2 water/ethanol ratio,
348 at 303 K using 0.1 g of Mg-Zr and 5 % of organics is 2.45 μmol·min⁻¹·m⁻², whereas the
349 corresponding value working in aqueous phase has a value of 38.4 μmol·min⁻¹·m⁻².
350 Despite the effect of ethanol, this reaction is still much faster than other
351 condensations using furfural and acetone (0.27 μmol·min⁻¹·m⁻²)⁷ or 5-HMF and acetone
352 (1.9 μmol·min⁻¹·m⁻²)⁸.

353 According to the temporal profiles obtained in all the experiments, and the similarity
354 between these data and the previous ones reported in aqueous phase ¹², the first
355 mechanistic conclusion is that the presence of ethanol does not modify the general
356 reaction network, only limiting the reaction rate of the different steps. Considering this
357 mechanism, acid-basic pairs are needed to catalyse these reactions. In fact, the aldol
358 condensation requires the initial abstraction of one α -proton from cyclopentanone,
359 obtaining an enolate that attacks the carbonyl group of the furfural molecule.
360 According to the literature, both molecules must be adsorbed on an acid site but
361 Bronsted basicity is also needed to stabilize the proton^{7, 15}. These Bronsted basic sites
362 are mainly generated by the partial rehydration of the MgZr mixed oxide. This
363 mechanism, as well as the stabilisation of the resulting enolate, justifies the key role of
364 water in the first stages of the reaction, and it is congruent with the negligible
365 conversion observed when working with organic solvents. Once this enolate is
366 stabilized, alcohol intermediate is formed by the nucleophilic attack of the enolate to
367 the furfural carbonyl group. This intermediate is not observed because it undergoes
368 fast dehydration in presence of medium acid sites, yielding the first condensation
369 adduct (C10). The second condensation step is also possible since this molecule (C10)
370 has another α -proton, yielding the C15 alcohol and the subsequent C15 condensation
371 adduct after the above-mentioned dehydration step.

372 In agreement with the proposed mechanism, both C10 and C15 adducts are obtained
373 following a first-order dependence on the concentration of the compound undergoing
374 enolization (cyclopentanone and C10, respectively) and zero-th order dependence on
375 furfural. This zero-th order for the furfural is congruent with other kinetics models for
376 the aldol condensation of other bio-platform molecules, such as furfural, 5-HMF⁸ and

377 citral²⁸ with acetone and it is justified by the strong adsorption of furfural on these
378 materials. According to these facts, the kinetic model is described in the following
379 equations (5-8):

$$380 \quad \frac{dC_{CPO}}{dt} = -k_1 \cdot C_{CPO} \quad [5]$$

$$381 \quad \frac{dC_{FRAL}}{dt} = -k_1 \cdot C_{CPO} - k_2 \cdot C_{C10} \quad [6]$$

$$382 \quad \frac{dC_{C10}}{dt} = k_1 \cdot C_{CPO} - k_2 \cdot C_{C10} \quad [7]$$

$$383 \quad \frac{dC_{15}}{dt} = k_2 \cdot C_{C10} \quad [8]$$

384 Temporal profiles of reactants and products concentrations were fitted to this kinetic
385 model using the Scientist[®] software. Ideal batch reactor behaviour has been
386 considered in all the cases. The presence of mass-transfer effects has been discarded
387 by both, ensuring that particle size and stirring reaction do not affect the results, and
388 by theoretical considerations. The theoretical approach consisted on a kinetic model
389 derivation considering the liquid-solid mass transfer and the Thiele modulus-based
390 efficiency factor for internal diffusion. Taking into account the experimental
391 conditions, the resistance due to the intrinsic kinetic is seven orders of magnitude
392 higher than the mass-transfer resistance, the influence of both, external and internal
393 diffusion, was discarded and reaction is considered to be under kinetic control^{29, 30}.
394 **Table 2** summarises the values k_1 and k_2 for all the experiments performed with water-
395 ethanol mixtures. Values of these kinetic constants are normalised considering the
396 catalytic loading and the feed volume in order to compare the results obtained in
397 experiments at different conditions. The correlation coefficient obtained in each case,
398 as well as confidence intervals, were also included in Table 2 for illustrating the

399 goodness of the fit ($r^2 > 0.99$ in all the cases). Other reaction orders were tested, such as
400 first order dependence on FAL concentration or fractional reaction orders, with largely
401 worst results. The correspondence between experimental results and model
402 predictions is shown in the Figures 2 and 3, as well as in the Supplementary
403 Information (Fig. S2). As it could be expected, values of k_1 were higher than k_2 ,
404 concluding that the formation of the first condensation adduct is much faster than the
405 second one. Considering the high amount of solids obtained when the reaction was
406 performed in pure water, the direct comparison between these values and the
407 corresponding ones in aqueous phase is not possible. However, there is a clear
408 influence of the percentage of ethanol and the values of kinetic constants, decreasing
409 as ethanol concentration in the reaction medium increases. If results at 1:0.9 and 1:2
410 are compared, there is a decrease of almost 85 and 63 % in the values of k_1 and k_2 ,
411 respectively. This result is in a good agreement with the previous hypothesis about the
412 key role of the water to promote the aldolization, and the negative effect of ethanol
413 on the general rate. In order to illustrate this idea, Fig. 7 shows the relationship
414 between the ethanol concentration in the different mixtures ethanol/water used in
415 this work and the values of the kinetic constants, observing clearly the decreasing
416 trend of both parameters, being more relevant in the case of the first constant. The
417 observed behaviour suggests a value of this kinetic constants of 0.0114 and 0.0060
418 $\text{L}\cdot\text{min}^{-1}\cdot\text{g}^{-1}$ for k_1 and k_2 , respectively, when reaction is carried out in aqueous phase.
419 Observing the good fit between the kinetic constant and the ethanol percentage, a
420 clear influence of the solvent polarity is suggested (ethanol/water polarity ratios is
421 0.654). At this point, the presence of polar molecules is considered as necessary for
422 stabilizing the ketone-derived enolate species, needed for accomplishing the

423 reaction^{27,31}. By contrast, an effect of the presence of ethanol on surface chemistry or
424 in the adsorption of reaction and/or products is ruled out since the affinity of the
425 surface for ethanol is largely lower than the affinity for water, which is present in all
426 the experiments.

427 Considering the influence of the temperature observed in this study, kinetic constants
428 obtained with experiments at 1:1, 1:1.5 and 1:2 water/ethanol ratio were fit to an
429 Arrhenius dependence. The fit of these constants to this model is plotted in **Fig. 8a**.
430 The mathematical analysis of these results indicates a continuous increase in the
431 apparent activation energy as the percentage of ethanol in the system increases,
432 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
433 data are within the range of values reported in the literature for similar type of
434 reactions^{8, 32, 33}. At this point, different physical and chemical constraints could
435 influence this parameter when working in liquid phase, thus activation energies are
436 not comparable to those obtained in gas phase. Considering that the apparent
437 activation energy is obtained by the slope of the regression, the corresponding one for
438 the aqueous phase system was estimated taking into account the variation in the initial
439 conversion rates at different temperatures. Result obtained, 7.2 kJ·mol⁻¹, allows
440 predicting the evolution of the reaction with the water/ethanol ratio, as it is observed
441 in the **Fig. 8b**. In this figure, the clear inhibitory effect of the organic solvent is
442 observed. The resulting exponential trend justifies ethanol ratios higher than 1:2 must
443 be discarded because of the expected low activity. However, the best results obtained
444 for 1:2 water:ethanol ratio (36.5 % of global yield with this configuration, whereas less
445 than 6 % was obtained as liquids in aqueous solution at the optimized conditions)
446 justify the use of ethanol in the reaction media. In addition, the presence of ethanol

447 minimises the deactivation caused by the permanent adsorption of main and side
448 reaction products. Globally, this effect compensates the decrease in the kinetic rate,
449 obtaining a net enhancement in the selectivity of C10 and C15.

450

451 **4. Conclusions**

452 The condensation yields obtained by the reaction between cyclopentanone and
453 furfural are strongly improved by adding ethanol to the initial aqueous phase.
454 According to experimental results, an equilibrium between condensation activity
455 (being water needed) and products solubility (strongly enhanced by the presence of
456 ethanol) is needed. Once reaction time, temperature and water/ethanol ratio were
457 optimized, best results were obtained working at 303 K and a water/ethanol ratio of
458 1:2. At these conditions, after 24 hours, the global yield in the liquid phase (36.5 %) is
459 more than six times the maximum ones reported in aqueous phase. The good carbon
460 balance obtained at these conditions (higher than 90 % whereas it was only 24 % in
461 aqueous phase) also corroborates the absence of side reactions and oligomerizations
462 that could have a negative effect in the catalytic deactivation. Experimental data were
463 successfully fit to a first-order reaction mechanism, obtaining a clear dependency
464 between the activation energy and the percentage of ethanol in the mixture.

465

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470

471 **ABBREVIATIONS**

472 FFL, furfural; CPO, cyclopentanone; HPLC, high performance liquid chromatography; 5-

473 HMF, 5-hydroxymethylfurfural; GC, Gas Chromatography.

474

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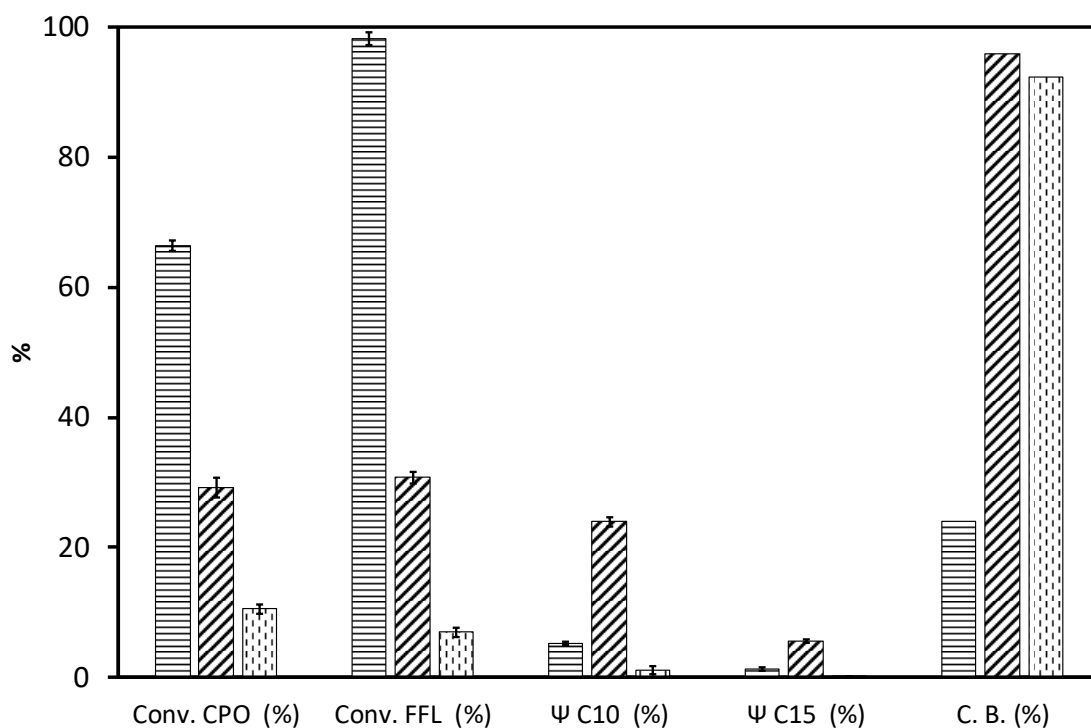
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573

574 **Fig. 1.** Results obtained, considering only liquid phase composition, after 4 h of furfural
 575 and cyclopentanone aldol condensation at 303 K catalyzed by 0.1 g of MgZr using
 576 different systems: aqueous system (bars with horizontal lines) and two different
 577 water/organic systems: 1:1 water/ethanol (bars with twisted lines), and 1:1
 578 water/ethyl acetate (bars with vertical lines). Results in terms of reactant conversions,
 579 product atomic yields and carbon balance.

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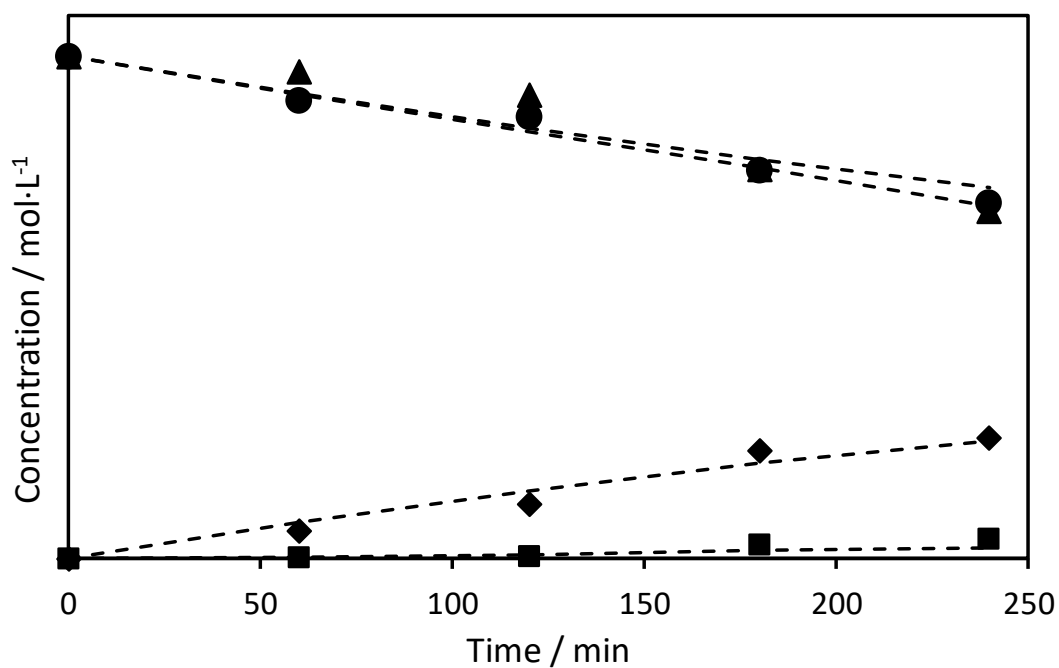
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590 **Fig. 2.** Reactants and products concentration temporal evolution of the cyclopentanone -
 591 furfural condensation (5 % organics, 1:1 water/ethanol ratio, 303 K and 0.1 g of Mg Zr).

592 Symbols: (▲) furfural; (●) cyclopentanone; (◆) C10 and (■) C15. **Maximum error: 4 %.**

593 **Lines correspond to the predictions of the proposed kinetic model.**

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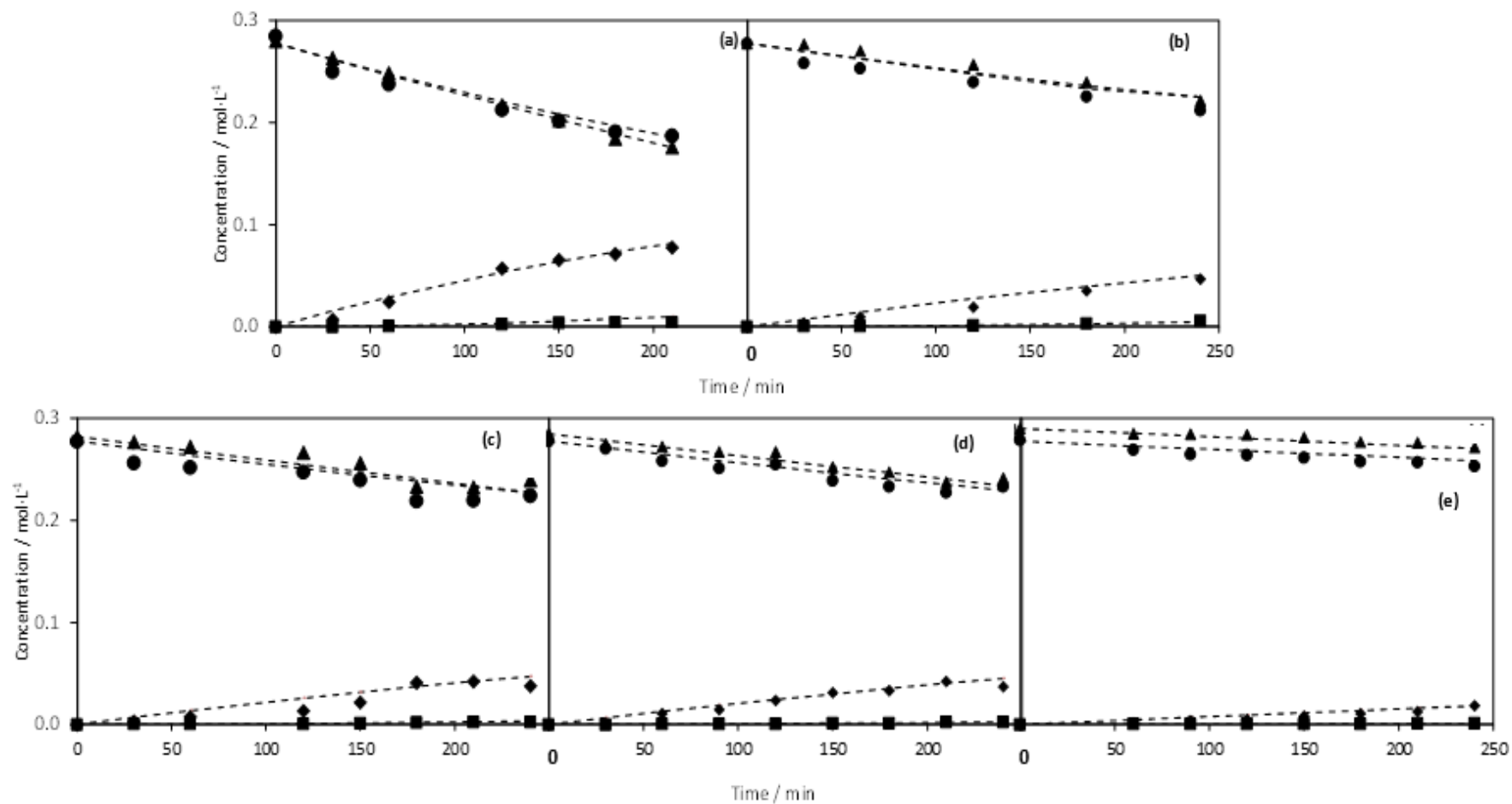


Fig. 3. Evolution of reactants and products concentration involved in the aldol condensation of cyclopentanone and furfural (303 K, 0.1 g Mg-Zr, 1:1 Furfural:Cyclopentanone) as function of reaction time for different ethanol-water mixtures: (a) 1:0.9; (b) 1:1.35; (c) 1:1.5; (d) 1:1.75; (e) 1:2. Symbols: (▲) furfural; (●) cyclopentanone; (◆) C10 and (■) C15. Maximum error of 3.75 %. **Lines correspond to the predictions of the proposed kinetic model.**

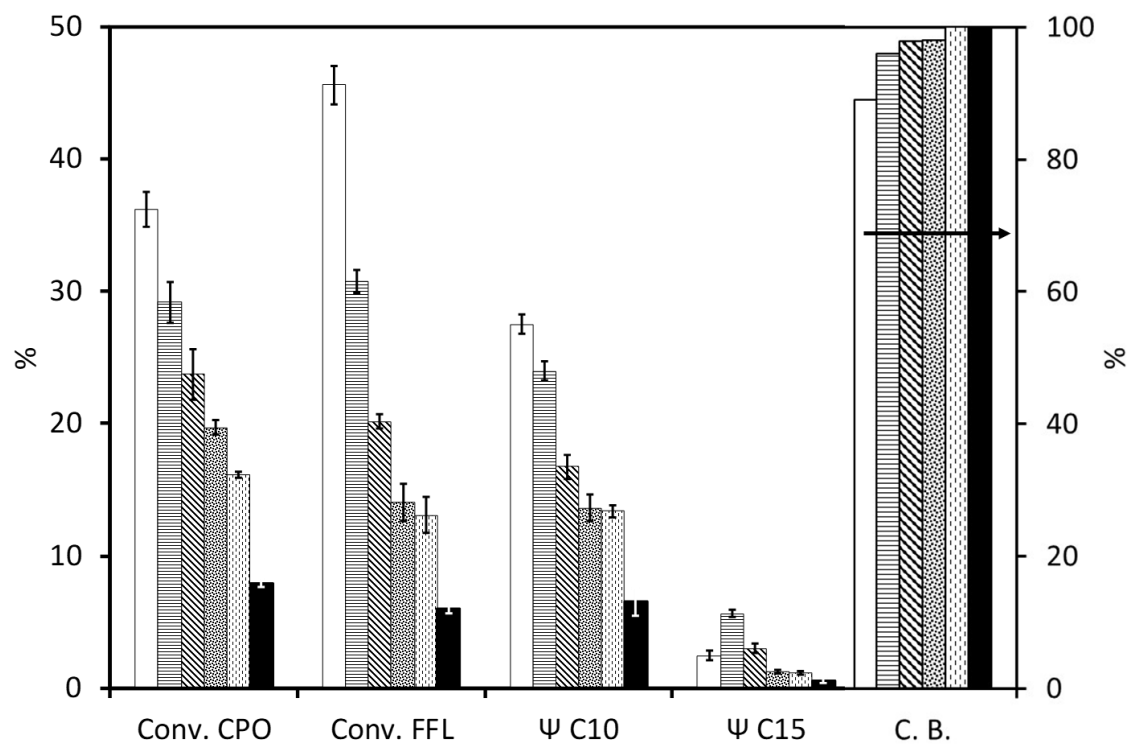


Fig. 4. Results obtained after 4 h of furfural and cyclopentanone aldol condensation at 303 K catalyzed by 0.1 g of MgZr using different initial water/ethanol ratio: 1:0.9 (white), 1:1 (bars with horizontal lines), 1:1.35 (bars with twisted lines), 1:1.5 (dotted bars), 1:1.75 (bars with vertical lines) and 1:2 (solid black). Results in terms of reactants conversions, product atomic yields and carbon balance (secondary axe).

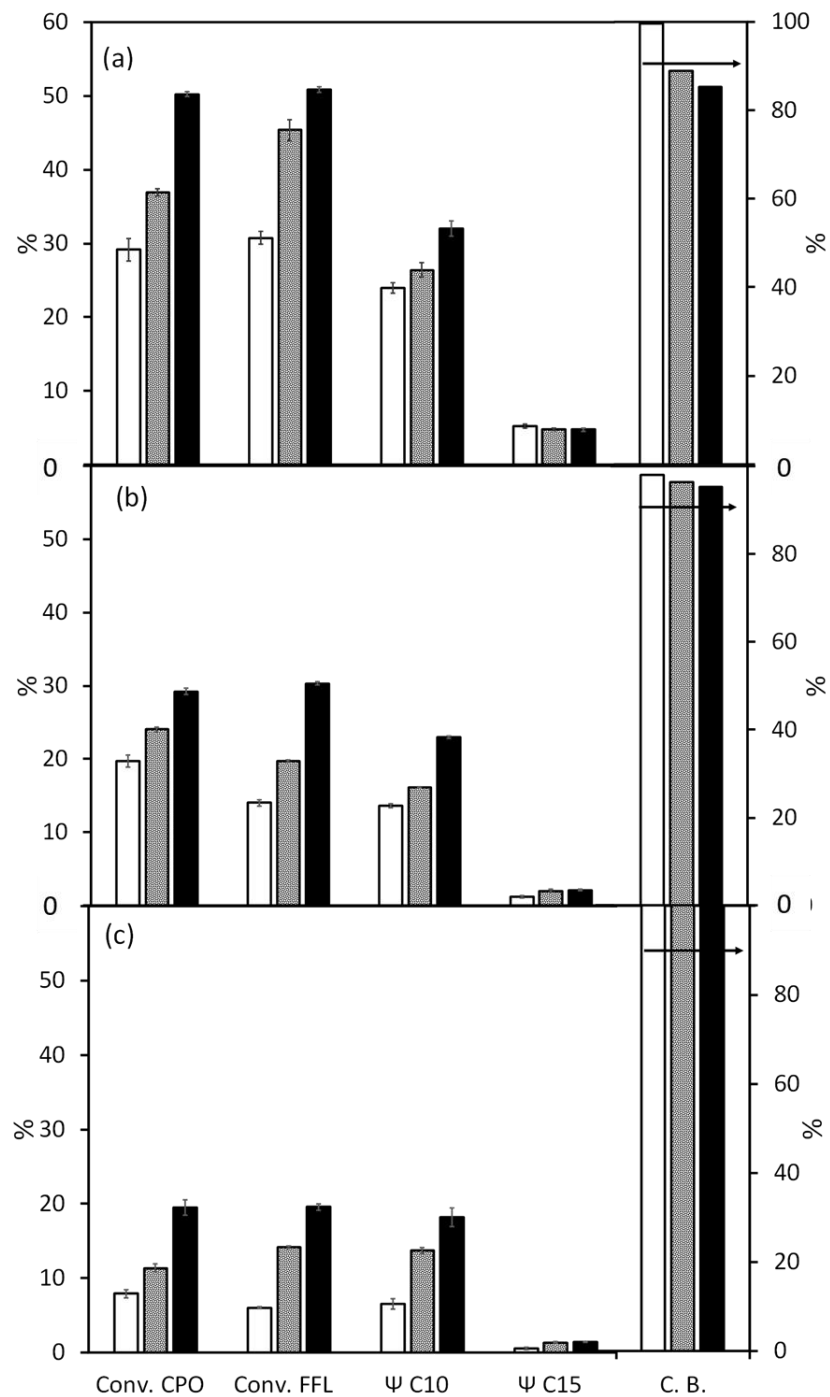


Fig. 5. Results obtained after 4 h of furfural and cyclopentanone aldol condensation catalyzed by 0.1 g of MgZr using different water/ethanol ratios: (a) 1:1; (b) 1:1.5, (c) 1:2. Reaction temperature: 303 K (white); 313 K (grey); 323 K (black).

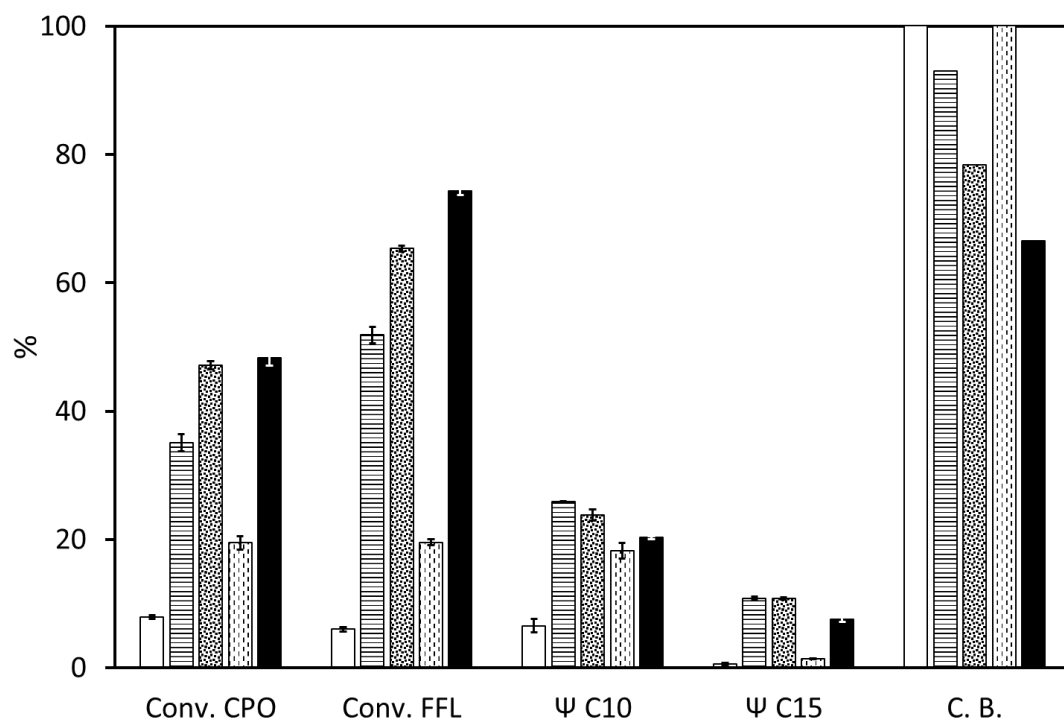


Fig. 6. Comparison of the results obtained in the CPO-FFL aldol condensation using 1:2 water/ethanol ratio and 0.1 g of MgZr as function of the temperature and the reaction time. Legend: 303 K and 4 h (white); 303 K and 24 h (bars with horizontal lines); 303 K and 48 h (dotted bars); 323 K and 4 h (bars with vertical lines); 323 K and 24 h (black).

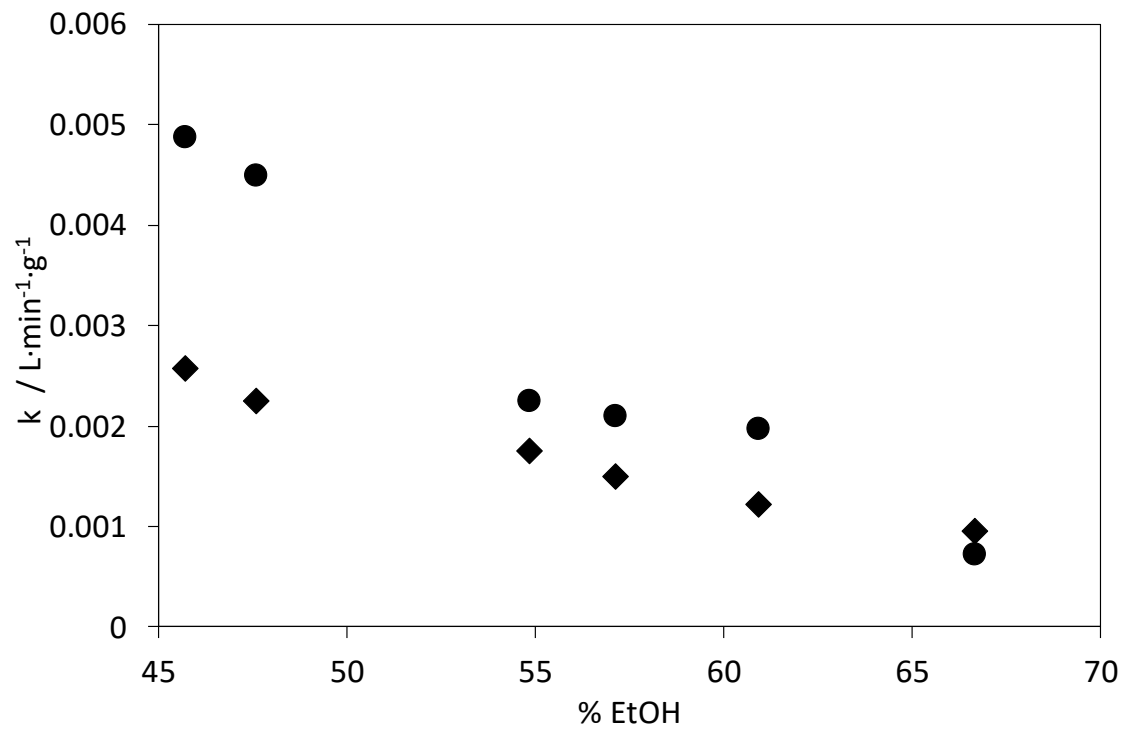


Fig. 7. Kinetic constants for the fitting of the experimental results to the proposed kinetic model when different percentages of ethanol were used in the feed at 303 K. Symbols: (●) k_1 ; (◆) k_2 .

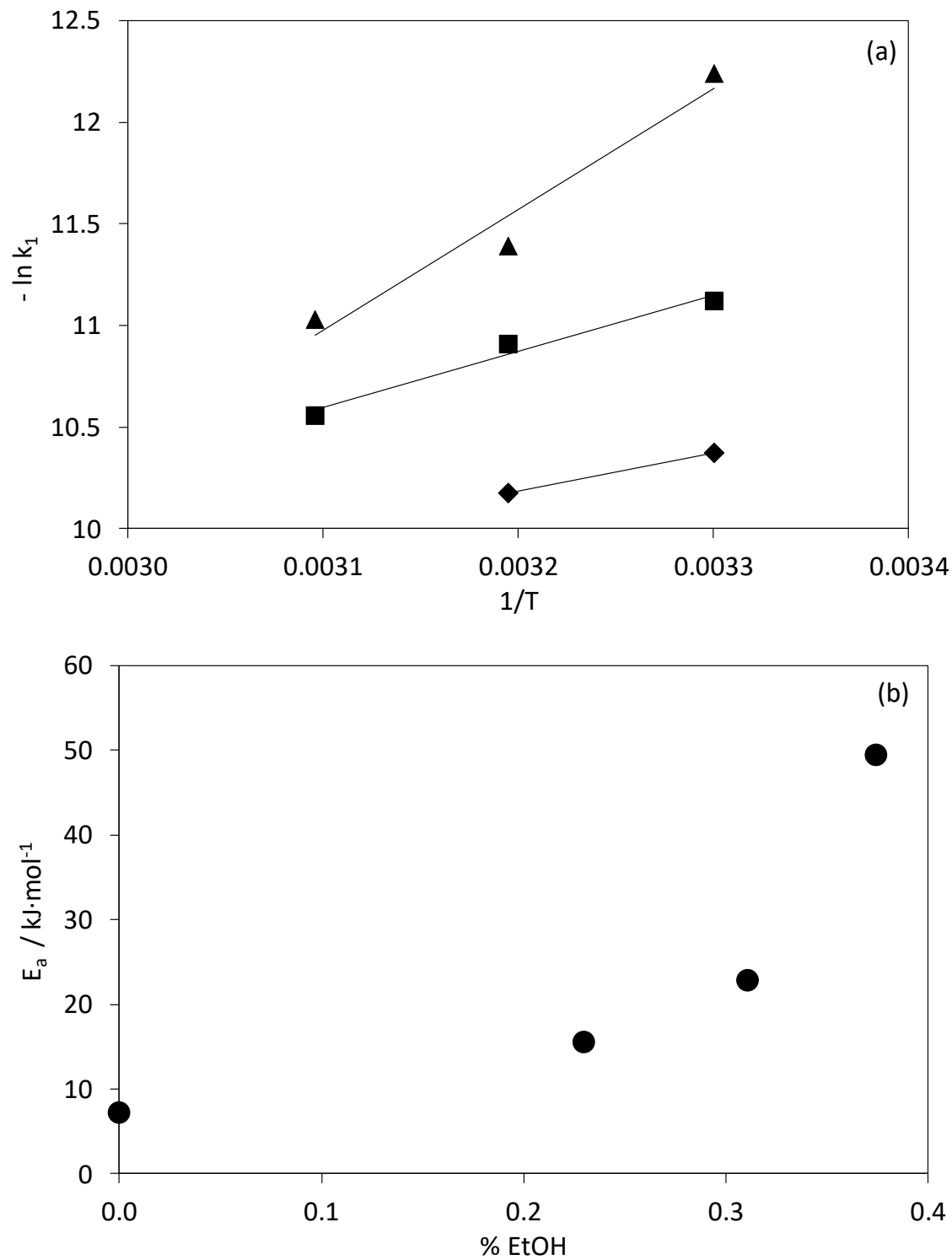


Fig. 8. Analysis of kinetic data with temperature. (a) Arrhenius adjustment for different water/ethanol ratios. Symbols: (▲) 1:2; (◆) 1:1.5 and (■) 1:1. (b) Activation energy evolution with the percentage of ethanol used in the feed.

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.

Time (h)	Water/Ethanol	Conv. CPO (%)	Conv. FFL (%)	Ψ C10	Ψ C15	C. B.
4	1:1.35	23.7	20.2	16.7	3.0	97.8
24	1:1.35	50.0	79.4	22.1	2.6	59.9
4	1:1.5	19.7	14.0	13.6	1.3	98.0
24	1:1.5	54.7	78.5	21.6	2.4	57.4
4	1:2	7.9	6.0	6.5	0.6	100.0
24	1:2	35.9	51.2	25.9	10.8	93.1

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).

Temperature (K)	Water/Ethanol	k_1 (L·min ⁻¹ ·g ⁻¹)	k_2 (L·min ⁻¹ ·g ⁻¹)	r^2
303	1:0.9	0.0049 ± 0.0003	0.0025±0.0005	0.996
	1:1	0.0045± 0.0003	0.0023± 0.0007	0.996
	1:1.35	0.0023 ± 0.008	0.0018 ± 0.0008	0.998
	1:1.5	0.0021 ± 0.0005	0.0015 ± 0.0002	0.997
	1:1.75	0.0020 ± 0.0006	0.0012 ± 0.0003	0.999
	1:2	0.0007 ± 0.0002	0.0009 ± 0.0001	0.999
313	1:1	0.0057 ± 0.0005	0.0044 ± 0.0001	0.995
	1:1.5	0.0024 ± 0.0002	0.0018 ± 0.0003	0.995
	1:2	0.0017 ± 0.0009	0.0003 ± 0.0001	0.999
323	1:1.5	0.0039 ± 0.0005	0.0021± 0.0002	0.999
	1:2	0.0024 ± 0.0007	0.0008 ± 0.0001	0.997

ASSOCIATED CONTENT

Supporting Information

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

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