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Additional Information

**Chemicals from Biomass: Synthesis of biologically active  
furanochalcones by Claisen-Schmidt condensation of biomass-derived  
5-hydroxymethylfurfural (HMF) with acetophenones**

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**ABSTRACT**

Furanochalcones have been synthesized through the Claisen-Schmidt condensation of acetophenones and 5-hydroxymethylfurfural (HMF) using different solid base catalysts such as MgO, Al/Mg mixed oxide (HTc) with Lewis basic sites, and a hydrated Al/Mg mixed oxide (HTr) with Brønsted basic sites. The three catalysts provide high selectivity in absence of solvent or in the presence of polar solvents such as ethanol or acetonitrile, however catalysts become rapidly deactivated due to the strong adsorption of HMF and the furanochalcone obtained on the catalyst surface. A further increase in solvent polarity by using a mixture ethanol-water allows obtaining high conversion and high selectivity to furanochalcone using HTc and HTr as catalysts. However, MgO becomes rapidly deactivated which was mainly attributed to structural changes on MgO that is *in situ* rehydrated into Mg(OH)<sub>2</sub> with low activity for aldol condensations. When the reaction was performed using the homogeneous NaOH catalyst, it was found that their activity is higher than that of the solid catalyst, but the selectivity of the later is

clearly better. The results indicate that the active phase of the Al/Mg mixed oxide (HTc) in the ethanol-water medium corresponds to a partially restored hydrotalcite with basic hydroxyl groups. The HTc sample could be applied to the synthesis of a variety of furanochalcones with excellent success, while the catalyst could be reused several reaction cycles without loss of activity.

**KEYWORDS:** chemicals from biomass, 5-hydroxymethylfurfural, Claisen-Schmidt condensation, furanochalcones, MgO, Al/Mg mixed oxides.

## **INTRODUCTION**

In recent years extensive work has been done to maximize the sustainable utilization of biomass feedstocks while minimizing the CO<sub>2</sub> emissions and avoiding competition with human and animal food. It is therefore desirable to obtain chemical products and liquid biofuels from lignocellulose biomass which does not compete with food production. The most interesting approximation to convert lignocelluloses biomass into valuable chemicals is through the utilization of the platform molecules produced from biomass by enzymatic and chemical processes [1]. Platform molecules such as lactic acid, levulinic acid, furfural, 5-hydroxymethyl furfural,  $\gamma$ -valerolactone, succinic acid etc, are highly functionalized molecules which can be converted in some cases with minimal derivatization in new materials, polymers and pharmaceuticals [2]. Among them, furans derived from biomass such as furfural and 5-hydroxymethylfurfural (HMF) obtained by dehydration of pentoses and hexoses respectively, are versatile molecules that have increasingly attracted the attention as starting materials for the production of a variety of valuable compounds [3].

On the other hand, chalcones with structure of 1,3-diphenyl-2-propen-1-one, belong to the flavonoids family and are widespread in plants. Naturally occurring and synthetic chalcones are associated with several biological activities such as antioxidant, anti-inflammatory, antibacterial, ant hyperglycemic, antifungal, antimalarial, anticancer, etc. [4].

An interesting family of chalcones is the furan based chalcones or furanochalcones [5], which are produced by the Claisen-Schmidt condensation between furfural derivatives and acetophenones. These compounds exhibit a variety of biological activities such as antiproliferative activity on breast cancer cells [6], antimicrobial activity [7], antileishmanial activity [8], antifungal [9], nitrification inhibitors [10] and some of them are used in the treatment of neoplastic diseases as cytotoxic drugs [11] and in neurodegenerative disorders such as Alzheimer's and Parkinson's [12]. More specifically, furanochalcones derivatives produced from HMF and acetophenones show activities in the treatment of pancreatic cancer [13] and breast cancer [14].

The most general method to obtain chalcones is by Claisen-Schmidt condensation between substituted acetophenones and substituted aromatic aldehydes using homogeneous basic catalysts such as aqueous or alcoholic alkali metal hydroxide solutions [4]. These homogeneous processes present drawbacks associated to the catalyst recovery, and the manufacturing process requires an additional step to neutralize the metal hydroxide, generally with HCl, resulting in processes with a large E factor. These drawbacks can be avoided by using heterogeneous base catalyst, however the synthesis of furanochalcones are mainly based on the homogeneous method, being the use of heterogeneous catalysts really scarce. In this sense Yadav et al. [15] have recently reported the Claisen-Schmidt condensation of furfural and acetophenone

derivatives in the presence of  $\text{Al}_2\text{O}_3$  on  $\text{CaO}$ , achieving 98 % yield of the corresponding furanochalcone.

However, and despite the pharmaceutical interest of HMF derived furanochalcones, the condensation of HMF with acetophenone derivatives has not been performed up to now using heterogeneous solid catalysts. Therefore, in this work, we have studied the Claisen-Schmidt condensation of HMF with acetophenones in the presence of different heterogeneous basic catalysts, and a series of furanochalcones derived from HMF have been obtained in high yields and selectivities, improving the results obtained with homogeneous catalysts.

## **EXPERIMENTAL SECTION**

### *Catalyst*

Al/Mg hydrotalcite was prepared from gels produced by mixing two solutions: solution A containing 2.25 mol of  $\text{Mg}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$  and 0.75 mol of  $\text{Al}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$  in the (Al+Mg) concentration of 1.5 mol/L for a molar ratio of 0.25, the solution B containing of 6.75 mol of NaOH and 2 mol of  $\text{Na}_2\text{CO}_3$  dissolved in the same volume of the solution A. Both solutions are co-added at a rate of 1 mL/min under a vigorous mechanical stirring at room temperature. The suspension was left at 60 °C for 18 h. The hydrotalcite formed was filtered and washed until the pH of the filtrate was 7. The resultant solid was dried at 60 °C for 12 h. The hydrotalcite was transformed in an Al/Mg mixed oxide by calcination at 450 °C in a dry nitrogen flow. The temperature was raised at a rate of 2 °C/min to reach 450 °C and was maintained at this temperature for 6 h. The solid was then cooled until room temperature and used in reaction (labeled as HTc).

Rehydrated hydrotalcite (HTr) was obtained by rehydration of the calcined sample (HTc) by directly adding 36 wt% of CO<sub>2</sub> free water on the HTc just before reaction [16]. A MgO sample with crystallite size of 3 nm and 670 m<sup>2</sup>/g surface area was purchased from NanoScale Materials and was calcined at 450 °C for 8 h first in air and finally in a stream of nitrogen to remove absorbed impurities and carbonates.

X-ray diffraction measurements were recorded with a Philips X'PERT (PN 3719) diffractometer (Cu-K $\alpha$  radiation provided by a graphite monochromator) equipped with an automatic variable divergence slit and working in the constant irradiated area mode. Data were collected stepwise over the  $2^\circ \leq 2\theta \leq 40^\circ$  angular region with steps of  $0.02^\circ 2\theta$ , a 20 s/step accumulation time, and Cu KR ( $\lambda = 1.54178 \text{ \AA}$ ) radiation.

Chemical analyses of the samples were performed by atomic absorption after disintegration of the solids. N<sub>2</sub> and Ar adsorption/desorption isotherms were performed at -196 and -185.7 °C, respectively, in an ASAP 2010 apparatus from Micromeritics, after pre-treating the samples under vacuum at 400 °C overnight (for the calcined hydrotalcite) and at 120 °C (for the rehydrated hydrotalcite). The BET surfaces were obtained using the BET methodology. The physicochemical characteristics of the samples are summarized in Table 1.

Table 1. Physicochemical characteristics of the catalysts

Catalyst	Al/(Al+Mg)	Surface area BET (m <sup>2</sup> /g)	Crystallite size (nm)	Average pore diameter (Å)
MgO	-	600	3	nm
HTr	0.25	25	-	277
HTc	0.25	245	< 50	103

## General Procedure for the Synthesis of Furanochalcones

A mixture of 5-hydroxymethylfurfural (HMF) (1 mmol, 126 mg) and acetophenone (1 mmol, 120 mg), and solvent (2 mL) was added to the catalyst and purged with nitrogen. The reaction mixture was vigorously stirred at 90 °C. To check if the reaction was controlled by external diffusion, the condensation was by stirring the mixture of reactants at 500, 800 and 1000 rpm, and the results showed similar reaction rates when working at 800 and 1000 rpm, indicating that under these stirring speeds the reaction is not controlled by external diffusion. Therefore, the selected stirring speed for the catalytic experiments was 1000 rpm. At the end of the reaction, the catalyst was filtered off and washed successively with a mixture water/ethanol. After removing the solvent under reduced pressure, the furanochalcone was crystallized from ethanol.

In all reactions, samples were taken at regular intervals, diluted with ethanol, dried with anhydrous sodium sulfate and analyzed by gas chromatography (GC) equipped with a HP-5 column (30 m x 0.25 mm x 0.25  $\mu$ m) and a FID as the detector, using nonane as external standard. In all cases the molar balance was  $\geq 95\%$ .

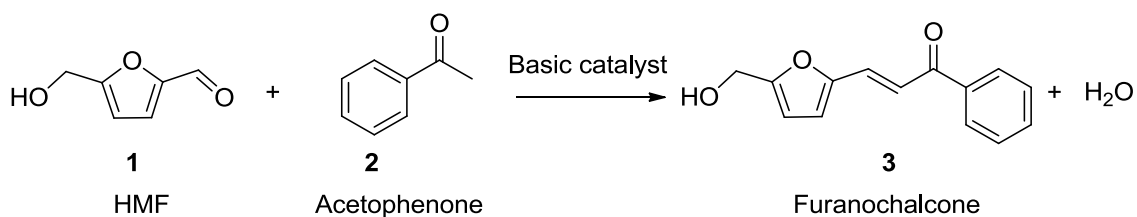
The identification of the products was carried out by MS-GS (Agilent MDS-5973 with HP5 capillary column) and NMR spectroscopy with a Bruker Avance 300 spectrometer working at 300 MHz for  $^1\text{H}$  and 75 MHz for  $^{13}\text{C}$ .

### *Recycling test of HTc*

For catalyst recycling studies, the solid was collected by filtration, washed with water/ethanol and calcined at 450 °C for 7 h in air.

## RESULTS AND DISCUSSION

In order to find the most adequate solid base catalyst to perform the synthesis of furyl substituted chalcones, the Claisen-Schmidt condensation between HMF and acetophenone was taken as reaction model (Scheme 1).



**Scheme 1.** Claisen-Schmidt condensation of HMF with acetophenone.

Under basic catalysis, and depending on the nature of the catalyst and reaction conditions different side reactions can also occur such as the self-condensation of acetophenone leading to the formation of dypnone, the Cannizzaro disproportionation of the aldehyde that in the case of HMF affords 5-hydroxymethylfurfanoic acid and 2,5-dihydroxymethylfuran as by-products [17], while oligomerization reactions of the  $\alpha$ - $\beta$ -unsaturated ketone can also take place. Therefore the optimization of the catalyst and reaction conditions is of paramount importance to achieve high selectivity to the furanochalcones.

To do that, we selected as catalysts different solids with basic sites able to abstract the proton in the methyl group of acetophenone, such as a high surface area MgO, an Al/Mg mixed oxide (HTc) produced from calcination of an Al/Mg hydrotalcite, and a rehydrated Al/Mg mixed oxide (HTr).

MgO and Al/Mg mixed oxides have strong Lewis basicity associated to  $O^{2-}M^{+2}$  ion pairs [18] that have shown excellent activity for aldol condensations including the



Claisen-Schmidt condensation [19,20,21,22,23,24,25]. Moreover, it is known that the hydration of the Al/Mg mixed oxide with CO<sub>2</sub> free water lead to the partial restoration of the layered structure of the hydrotalcite in which some of the CO<sub>3</sub><sup>2-</sup> compensation anions in the interlayer space are replaced by OH<sup>-</sup> anions which operate as strong Bronsted basic sites [26,27,28] able to perform a variety of aldol type condensations [16, 26, 29, 30].

The catalytic activity of these materials was tested in the Claisen-Schmidt condensation of acetophenone and HMF at 90 °C in the presence of 15 wt% of catalyst and in absence of solvent. In Table 2 are presented the results obtained for each catalyst. In the three cases the only product detected was the corresponding chalcone ((*E*)-3-(5-(hydroxymethyl)furan-2-yl)-1-phenylprop-2-en-1-one)(**3**), while in absence of catalyst no product was detected (Table 2). As can be observed in Table 2, the MgO was the most active catalyst, being the order of activity measured as per the initial reaction rate: MgO > HTr > HTc. The higher activity exhibited by the high surface area MgO compared with HTc and HTr can be attributed to the higher concentration of strong basic sites in this sample. Since the aldol condensation is a reaction sensitive to the structure [25], the very small crystallites (3 nm) of the MgO sample used presents a high ratio of atoms located at corners and steps of the crystallites, and these have been associated to the presence of stronger basic oxygen sites in MgO [31]. Nevertheless, if one calculates the intrinsic activity of each catalyst by dividing the initial reaction rate per surface area unit (Table 2), the highest specific activity corresponds to HTr sample bearing Bronsted basic sites associated to OH<sup>-</sup> which are formed during the rehydration. In other words, it is clear that Bronsted basicity works much better than Lewis basicity present on the catalysts studied for the condensation reaction between acetophenone and HMF.

On the other hand, it should be noted that the reaction stops before reaching full conversion on the three solid catalysts. This would be an indication that a deactivation of the catalyst occurs. The deactivation of the catalysts can be attributed to a strong adsorption of reactants and/or products on the catalyst surface. Then, the catalysts were recovered after use and extracted in a Soxhlet apparatus using dichloromethane as a solvent, it was observed that the amounts of organic material retained on the surface were 0.88, 2.73 and 1.34 wt% (respect to the amount of catalyst) for MgO, HTr and HTc respectively. The amount of organic extracted from each catalysts, as well as the products found in the extracts are summarized in Table 3. As can be observed there, the main component of the extracted products corresponds to HMF (95, 56 and 79 wt% for MgO, HTr and HTc respectively). At the same time the amount of furanochalcone **3** that remains adsorbed on the catalyst is particularly significant in the case of HTc ( 15.9 wt %) and HTr (28.8 wt%). Moreover, the TG analysis of the samples indicate that a considerable amount of organic material still remains strongly adsorbed on the catalysts after Soxhlet extraction, being 28.1%, 11.2% and 16.5% for MgO, HTc and HTr, respectively. Considering the composition of the organic extracts (Table 3) it appears that although the adsorption of furanochalcone contributes to catalyst decay (in the cases of HTc and HTr) the strong adsorption of HMF, is the main cause of deactivation of the catalysts in all cases. To avoid or at least decrease the deactivation of the catalysts due to the strong adsorption of HMF, we thought on using a solvent that can help to avoid complete surface coverage by HMF and the product.

Table 2. Claisen-Schmidt condensation of acetophenone and HMF in absence of solvent using different heterogeneous basic catalysts.<sup>a</sup>

Catalyst	$r^o 10^5$ (mol min <sup>-1</sup> g <sup>-1</sup> )	$r^o 10^5$ (mol min <sup>-1</sup> m <sup>-2</sup> )	Conv HMF (%)	Yield (%) of <b>3</b>	Selectivity (%) of <b>3</b>
Blank	-	-	-	-	-
HTr	59.7	238.0	44	43	99
HTc	2.2	0.9	17	16	99
MgO	123.7	20.6	67	66	99

<sup>a</sup>Reaction conditions: HMF (1 mmol), acetophenone (1 mmol), 15 wt% of catalyst at 90 °C, 5 h, without solvent.

Table 3. Amount of extracted organic material and distribution of compounds in the organic for each used catalyst.

Catalyst	Organic material (wt%) <sup>a</sup>	Distribution of compounds in the extracted organic material (wt %)		
		acetophenone	HMF	furanochalcone
HTc	1.3	5.0	79.1	15.9
HTr	2.7	14.9	56.3	28.8
MgO	0.8	1.8	95.8	2.4

<sup>a</sup> amount of organic material (with respect to the amount of catalyst) extracted by Soxhlet using dichloromethane.

### Influence of the solvent

The condensation between HMF and acetophenone was performed with two polar solvents with different dielectric constants that are able to solubilize both reactants (HMF and acetophenone). These solvent are acetonitrile, and ethanol, with dielectric constants ( $\epsilon$ ) of 37 and 24 respectively.

As can be observed in Table 4 in all catalysts, the highest initial activity is obtained with the most polar solvent and the order of reactivity is higher for the solvent with the higher dielectric constant: acetonitrile. A possible reason of these results can be based on differences on activation energy of the solvated transition states. If the reaction is performed with a polar solvent, the transition state complex could be better solvated decreasing the activation free enthalpy, enhancing the reaction rate as the solvent polarity is increased [32]. Moreover, it is observed that in the presence of polar solvents the order of activity (initial reaction rates) of the catalysts changes with respect to the results obtained when the reaction was performed in absence of solvent (see Table 2), being HTr>MgO>HTc. In other words, it appears that the most “ anionic” transition state, which should be formed on the strongest Bronsted basic sites present in HTr sample will be further stabilized, giving therefore the highest reaction rate.

On the other hand, the presence of solvent has not decreased the extent of catalyst deactivation and again the extraction of the used catalysts with dichloromethane in a Soxhlet apparatus showed that also when using solvent the extract is mainly composed of HMF and furanochalcone **3**, being the HMF the main component. This confirms that the main cause of catalyst deactivation is the strong adsorption of these compounds. The strong adsorption of the HMF and furanochalcone on the catalyst surface could be attributed to the presence in their structure of weakly acidic hydroxymethyl group that can strongly interact with the basic sites. In order to check that, the reaction was performed using furfural that unlike HMF, has not a hydroxymethyl group in the molecule. HTr was used as catalyst and ethanol as solvent. As can be observed in Figure 1, very good results were obtained in this case achieving 100% yield after 6h of reaction, and the amount of furfural adsorbed (< 1 %wt %) was sensibly lower than HMF.

Table 4. Influence of the solvent in the condensation of HMF and acetophenone using MgO, HTr and HTc as catalyst.<sup>a</sup>

Entry	Catalyst	Solvent	$r^o 10^5$ (mol min <sup>-1</sup> g <sup>-1</sup> )	Time (h)	Conv. (%)	Yield (%)	Selec (%)
					HMF	of <b>3</b>	of <b>3</b>
1	MgO	EtOH	11.6	4	35	30	86
				24	54	45	83
2	MgO	ACN	14.7	4	34	33	97
				24	49	47	96
3	HTr	EtOH	22.2	4	39	38	99
				24	50	49	98
				0.25	36	36	99
4	HTr	ACN	73.5	4	55	54	99
				24	61	60	98
5	HTc	EtOH	4.9	4	12	12	100
				24	18	18	100
6	HTc	ACN	10.2	4	13	13	100
				24	17	17	100

<sup>a</sup>Reaction conditions: HMF (1 mmol), acetophenone (1 mmol), solvent (2 mL), Catalyst 15 wt% with respect to the mass of reactants, at 90 °C.

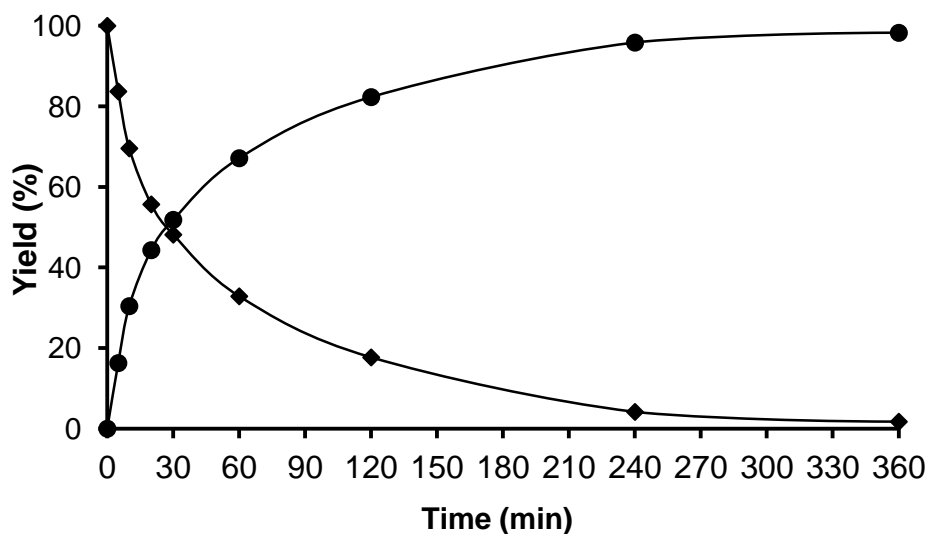


Figure 1. Claisen- Schmidt condensation of furfural and acetophenone. Reaction conditions: furfural (1 mmol), acetophenone (1 mmol), ethanol (2 mL); Catalyst: HTr (15 wt% respect to the total amount of reactants), at 90 °C. furfural (◆), chalcone (●).

On these bases, the polarity of the solvent has been further increased by working with mixtures of ethanol-water. Thus, when the reaction was performed with the three catalysts (Table 5) using mixtures of ethanol-water (1mL:1mL) as a solvent, a considerable increase of the initial reaction rate with respect to the values obtained before with ethanol is observed, showing again the benefit of increasing the solvent polarity. Gratifyingly, the catalyst decay was considerably depressed with HTr and HTc catalysts, achieving in both cases practically total conversion of HMF with 100 % selectivity to chalcone **3** after 4 h reaction time. These results would indicate that, the presence of water limits the strong adsorption of HMF and furanochalcone on the catalyst surface, decreasing the deactivation rate of the catalyst. Indeed, the amount of HMF and furanochalcone that remains adsorbed on those two catalysts is now clearly lower (0.9 and 1.6 wt % for HTc and HTr respectively, instead of 1.7 wt % 3.2 when using ethanol as solvent). Notice that in the case of HTc water works as both solvent and rehydrating agent. Thus, the increase in activity of HTc when a mixture of ethanol-

water is used, besides the positive effect of the polarity of the solvent, the *in situ* rehydration of the HTc that generates HTr (see the XRD of the used catalyst in Figure 2) can also play a positive role on the activity of the HTc sample.

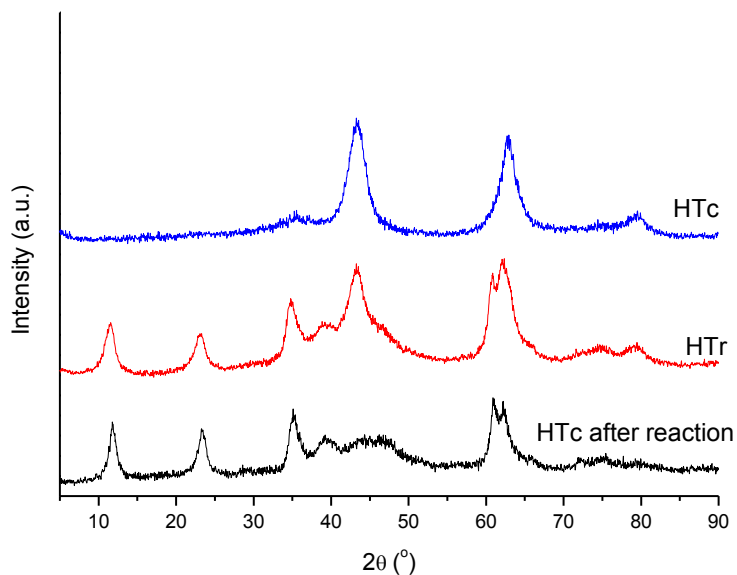


Figure 2. Powder X-ray diffraction (XRD) patterns of the fresh HTc, HTr and HTc after reaction in the Claisen-Schmidt condensation of HMF and acetophenone using ethanol-water as a solvent.

On the contrary, in the case of MgO a strong deactivation of the catalyst is observed with the ethanol-water mixture, since conversion of HMF does not surpass 39 % after 24 h of reaction time. In this case, the deactivation can be mainly attributed to structural changes on MgO that is *in situ* rehydrated into Mg(OH)<sub>2</sub> during the reaction, and which possesses negligible catalytic activity for aldol condensations compared with rehydrated Al/Mg mixed oxides [33]. In fact, the XRD of the used MgO catalyst (see Figure 3) showed the typical diffractogram of the Mg(OH)<sub>2</sub>, with characteristic peaks (XRD) of Mg(OH)<sub>2</sub> with 2θ values of : 18.4, 38.0, 50.9, 58.7, 62.2, 68.4, 72.1.

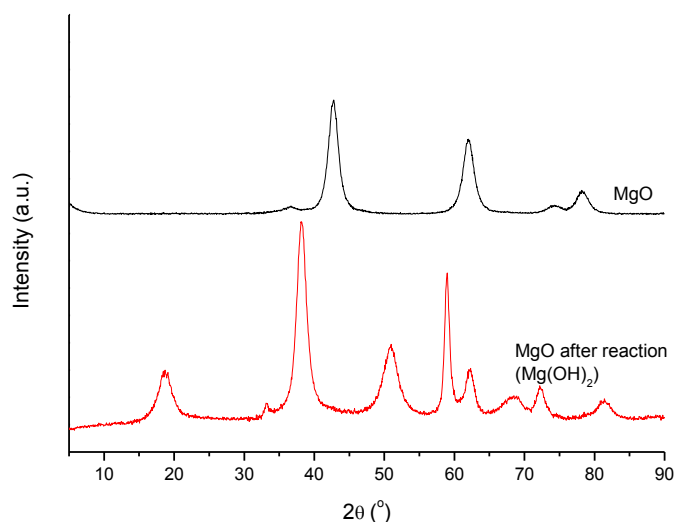


Figure 3. Powder X-ray diffraction (XRD) patterns of MgO before and after use in the Claisen-Schmidt condensation of HMF and acetophenone using ethanol-water.

Table 5. Claisen- Schmidt condensation of HMF and acetophenone using ethanol-water as a solvent in the presence of MgO, HTr and HTc catalysts.<sup>a</sup>

Entry	Catalyst	$r^o 10^5$	Time (h)	Conv.(%)		Yield (%)	Selec (%)
		( $\text{mol min}^{-1}\text{g}^{-1}$ )		HMF	of <b>3</b>		
1	MgO	21.0	4	36	34	94	
			24	39	37	95	
			0.17	39	39	100	
2	HTr	106.2	4	96	96	100	
			24	99	99	100	
			0.33	40	40	100	
3	HTc	46.3	4	99	99	100	
			1	95	75	75	

<sup>a</sup>Reaction conditions: HMF (1 mmol), acetophenone (1 mmol),; Catalyst 15 wt% with respect to the mass of reactants, at 90 °C. Solvent: 1mL ethanol plus 1mL water. <sup>b</sup>The reaction was performed using NaOH (4 wt% respect to the mass of reactants) in 1 mL ethanol plus 1 mL water at room temperature.



For comparison purposes, the reaction was performed using as homogeneous base an aqueous-ethanolic solution (1 mL ethanol-1 mL H<sub>2</sub>O) and NaOH (4 wt% with respect to the mass of reactants) (Table 5, entry 4). 95 % conversion of HMF was achieved but only 75 % yield of furanochalcone (**3**). The lack of selectivity in this case is consistent with the presence of products coming from the Cannizzaro disproportionation of HMF and polymerization. These results are similar to those previously reported in the patent literature for the condensation of HMF and acetophenone at room temperature using an ethanolic solution of NaOH [14]. It appears then that either the HTc or HTr catalysts studied here are clearly superior in terms of yield and selectivity to furanochalcone **3**, to the conventional homogeneous process.

The effect of the water on the initial reaction rate and catalyst decay was confirmed by doing the reaction using mixtures of water with different polar solvents (methanol, acetonitrile and isopropanol) using HTc as catalyst. As can be observed in Table 6, good results were achieved in all cases, being ethanol-water mixture the best solvent in terms of HMF conversion and furanochalcone yields.

Table 6. Claisen- Schmidt condensation of HMF and acetophenone using as a solvent different mixtures of organic solvent-water in the presence of HTc catalysts<sup>a</sup>.

Solvent	$r^o 10^5$ (mol min <sup>-1</sup> g <sup>-1</sup> )	Conv (%) HMF	Yield (%) of <b>3</b>	Selec (%) of <b>3</b>
Methanol/H <sub>2</sub> O	98.0	94	90	95
Ethanol/H <sub>2</sub> O	46.3	99	99	100
Isopropanol/H <sub>2</sub> O	76.9	93	88	94
ACN/H <sub>2</sub> O	62.5	84	82	98

<sup>a</sup>Reaction conditions: HMF (1 mmol), acetophenone (1 mmol), solvent (1mL organic solvent plus 1mL of water), 15 wt% HTc respect to the total amount of reactants, temperature 90 °C, 4 h.

### Catalyst reusability

For reducing the cost and environmental impact of the process, an important advantage of using heterogeneous catalysis is that the catalyst can be easily recovered by filtration and reused. In order to study the reusability of HTc, after a first cycle of reaction using ethanol-water as a solvent, the catalyst was filtered off, thoroughly extracted with dichloromethane in a Soxhlet apparatus and used in a second cycle under the same reaction conditions. However, only 16% conversion of HMF was observed after 24 h, indicating that the catalyst is strongly deactivated during the first cycle. The analysis of the organic extracted by Soxhlet (0.9 wt%) of the used catalyst showed that it was mainly composed by furanochalcone (70 wt%) indicating that this compound is the main poison on the catalyst, being the cause of deactivation. IR analysis of the used catalyst (Figure 4) showed a increased adsorption band around 1643 cm<sup>-1</sup> which can be attributed to the carbonyl group of the furanochalcone. Thus, in order to regenerate the catalytic activity of the solid, after their use, the adsorbed organic material was removed

by calcination of the catalyst at 450 °C, and applying this protocol, the catalyst could be recycled up to four consecutive cycles without any significant loss of activity (Figure 5).

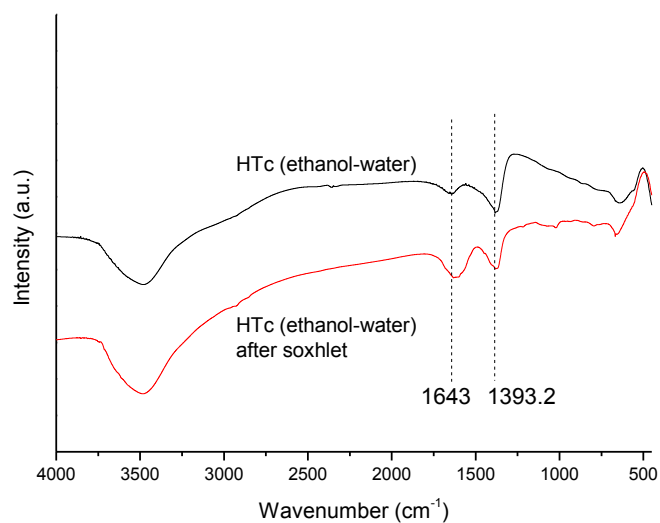


Figure 4. IR spectra of HTC (ethanol-water) before and after use in the Claisen- Schmidt condensation of HMF and acetophenone using ethanol-water.

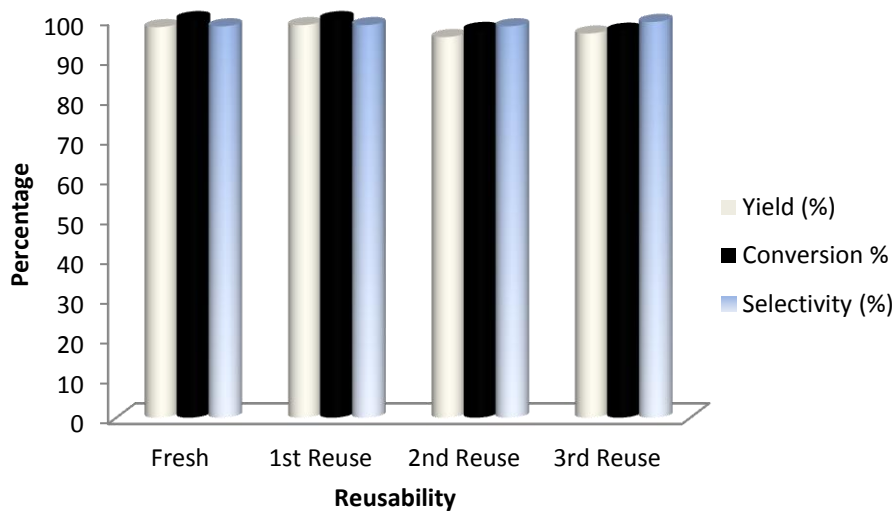
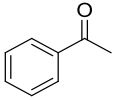
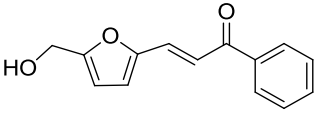
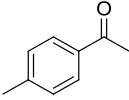
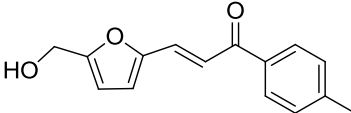
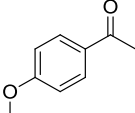
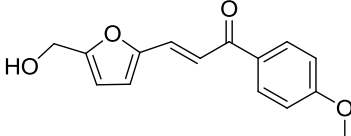
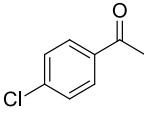
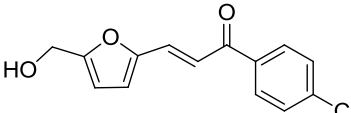


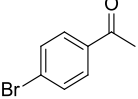
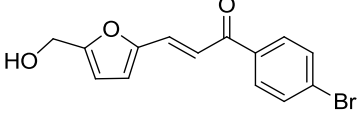
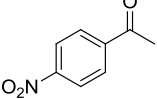
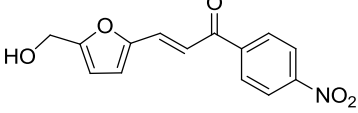
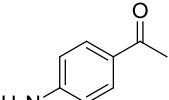
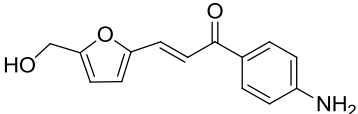
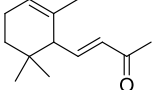
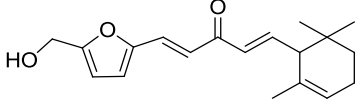
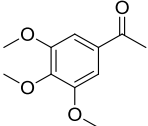
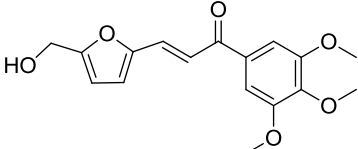
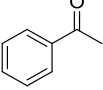
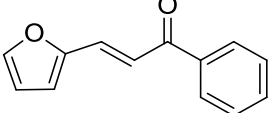
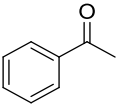
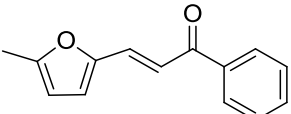
Figure 5. Reusability of catalyst. Reaction conditions: HMF (1 mmol, 126 mg), acetophenone (1 mmol, 120 mg), 15 wt% HTc with respect the total amount of reactants, solvent EtOH:H<sub>2</sub>O (1 mL:1 mL), temperature 90 °C, 4 h

### Scope of the reaction

HTc in ethanol-water as a solvent was used to perform the Claisen-Smidth condensation of various *p*-substituted acetophenones and furfuraldehydes derivatives (HMF, furfural and 5-methylfurfural). As can be observed in Table 7, good conversion and selectivities to the corresponding furanochalcones derivatives were obtained in all cases.

Table 7. Synthesis of furanochalcones using HTc as catalyst <sup>a</sup>.

Acetophenone	Aldehyde	Furanochalcone	Yield (%)	Selec (%)
	HMF	 <b>3</b>	98 (4 h)	99
	HMF	 <b>3a</b>	86 (8 h) 93 (24 h)	99
	HMF	 <b>3b</b>	95 (3 h) 99 (6,5 h)	99
	HMF	 <b>3c</b>	99 (2 h)	99

	HMF		98 (3 h)	98
		<b>3d</b>		
	HMF		83 (8 h)	95
		<b>3e</b>		
	HMF		59 (8 h)	99
		<b>3f</b>		
	HMF		70 (6 h)	98
			82 (20 h)	99
		<b>3g</b>	83 (10 h) <sup>b</sup>	99
			93 (22 h) <sup>b</sup>	99
	HMF		83 (8 h)	99
			94 (24 h)	99
		<b>3h</b>		
	Furfural		100 (6 h)	100
		<b>3i</b>		
	methylfurfural		93 (6 h)	99
			99 (20 h)	99
		<b>3j</b>		

<sup>a</sup>Reaction conditions: aldehyde (1 mmol), substituted acetophenone (1 mmol), 15 wt% HTc respect to amount of reactants, solvent EtOH:H<sub>2</sub>O (1 mL : 1 mL), at 90 °C. <sup>b</sup> at 110 °C.

## CONCLUSIONS

We have seen that HMF can react with different acetophenones using HTc, HTr and MgO as solid basic catalysts. The three catalysts can give high selectivity in absence of solvent, but unlike furfural, catalysts become rapidly deactivated. The deactivation is due to the strong adsorption of HMF and the furanochalcone obtained. Introducing polar solvents in the reaction do not allow increasing HMF conversion while important catalyst decay still occurs. A further increase in polarity by using a mixture ethanol-water allows finally obtaining high conversion and high selectivity to furanochalcone. While the activity of the homogeneous NaOH catalyst is higher than that of the solid catalyst the selectivity of the later is clearly better. It appears that the active phase of the calcined hydrotalcite in the ethanol-water medium corresponds to a partially restored hydrotalcite with basic hydroxyl groups. This is formed by the transformation of the mixed oxide fraction generated by calcinations at 450 °C, when it was contacted with water. The calcined hydrotalcite allows a wide reaction scope when working in ethanol-water as a solvent. After use, the HTc catalyst was regenerated by calcination at 450 °C, maintaining their catalytic activity through four consecutive runs.

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