CATALYZED SYNTHESIS OF CHALCONES UNDER INTERFACIAL SOLID-LIQUID CONDITIONS WITH ULTRASOUND

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<u>SUMMARY</u>.-The sonochemical synthesis of chalcones, catalyzed by an activated barium hydroxide catalyst under interfacial solid-liquid conditions, is carried out with very good yields. The sonochemical process takes place at room temperature and with a lower catalyst weight and reaction time than the thermal process.

Ultrasound has been used in many organic reactions $^{1-3}$. It is very useful since it diminishes the reaction time and increases the yield. On the other hand, reaction products that are not accessible by conventional methods are obtained by this way.

Recently we have shown that the organic reactions catalyzed by the activated barium hydroxide C-200 in interfacial solid-liquid conditions can be favoured by ultrasound e.g.yields obtained in the Wittig-Horner reaction under ultrasound are similar to those under the sonochemical conditions but in shorter reaction time. On the other hand, C-200 catalyzes under ultrasound reactions that do not take place under thermal conditions such as Cannizzaro reaction^{4,5}.

In the present paper we describe the synthesis of chalcones by Claisen-Schmidt condensation under sonochemical conditions catalyzed by C-200. The chalcones are very common in Natural Products Chemistry⁶. Some chalcones are useful as sweeteners and drugs^{7,8}.



The synthesis of chalcones was carried out by mixing 0.0196mols of aldehyde,1, 0.0196mols of acetophenone,2, 10mL of solvent and 0.01g. of catalyst. Then the mixture was sonicated in an ultrasound bath P.Selecta model 513 for 10min. The mixture was left standing for 24h. at 0-4°C to produce the sedimentation of the solid.

The mixture was analyzed by HPLC using a Perkin-Elmer Serie 2 chromatograph using a UV-visible detector (λ =254nm) and anthracene as the internal standard. MeOH/H₂O=80/20(v/v) was used as the eluent. Flux=0.8mL/min. 5mC₁₈column.

All the products were from Merck p.a. The pure solvents:THF;EtOH;DMF and the 1.4-dioxane were from Ferosa S.A.

The results obtained are shown in Table 1. We can observe that the reaction takes place slowly without sonication at room temperature (entry 2). It is necessary to heat

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the mixture to obtain, at 60min. a similar yield that obtained at room temperature after 10min. of sonication time (entry 3vs 4). Therefore, the ultrasound diminishes the temperature and reaction time as in the case of the Wittig-Horner reaction 4 .

This fact is not exclusively related to the ultrasound waves because of the null conversions obtained in the absence of the catalysts (entry 1). The barium hydroxide catalyst C-200 is necessary to produce the reaction (entry 4). Therefore we must say that the active sites of the catalyst are activated by ultrasound favouring their catalytic activity.

These active sites are the strong basic sites without steric hindrance titrated by TBMPHE according to the data from the selective poisoning experiments (Table 2). This agrees with the weak acid character of α -hydrogen from acetophenone which needs a strong base to produce the carbanion. On the other hand the bulky molecule of chalcone, produced in the reaction, can only be formed in the active sites of the solid without steric hindrance All these assumptions are confirmed by the detection of the carbanion from acetophenone and C-200 by IR spectroscopy¹³. This carbanion remains adsorbed on the solid surface because it is not trapped by Merrifield's resin Ega Chemie (Imeq Cl/g, resin)¹³. Therefore we can say that the sonochemical synthesis of chalcones catalyzed by C-200 is produced on the solid surface in the strong basic sites titrated by TBMPHE. This general reaction way is equal to that described for the thermochemical process¹⁴.

The sonication time is important when very small amounts of solid are used (w 50mg).Nevertheless catalyst weights equal or greater than 0.1g. lead to similar yields (74-79%). This fact can be explained by the activation of solid catalytic sites by ultrasound that could be related to an increasing the vibrational state of the lattice which makes it laxer. So,the OH would go further away from Ba(II), in the presence rather than in the absence of ultrasound. Thus the negative charge of OH would be more important as would its basicity. This fact favours the catalytic activity of the basic site increasing the turnover number of the catalyst and therefore diminishing the reaction time. When very small amounts of basic sites are present to transform the same amount of reagents, then , the sonication time must be increased.

The reaction can be carried out with small amounts of catalyst (w=0.1g) comparable to the thermal process (w=1.0g) (entry 3).

The process takes place using solvents with moderate or high dielectric constants (entries 6,8,9 and 10) with similar yields. Solvents with very low dielectric constants such as 1,4-dioxane ($\boldsymbol{\varepsilon}$ =2.2) give small yields (65% entry 7). this can be explained by assuming an interfacial ionic mechanism for the process.

The presence of water in the medium seems not to be important because similar yields are obtained with pure EtOH,80%(entry 9) and with EtOH(96%),76% (entry 4). This behaviour is different from that observed in other thermal reactions such as Claisen-Schmidt or Wittig-Horner^{14,15} where the presence of water dramatically increases the yield. From this fact we can say that the activating character of the water in the thermal process is not present in this sonochemical process. Therefore the postulated activation of the basic site 0^{-} by ultrasound would be consistent with this observation.

under sonochemical conditions. Room temperature.							
Entry	R ¹	R ²	catalyst	solvent / g a	sonication	Yield in 3	
		_	weight(g)	ti	me (min) .	(%molar)	
1	Cl	Н	0.0	EtOH(96%)/26.5	10 (r.T.)	0	
2	Cl	н	1.0	U.	0.0(60min.r.T)	5	
3	C1	Н	1.0	11	0.0(60min.) ^b	70 ^b	
4	C1	Н	0.10	11	10-60	76-79	
5	C1	Н	0.05-0.2		10	74-77	
6	Cl	Н	0.10	DMF(99%)/37	10	76	
7	C1	Н	0.10	1,4-dioxane(99%)/2.2	10	65	
8	C1	Н	0.10	THF(99%)/7.9	10	73	
9	Cl	Н	0.10	EtOH(99.8%)/24.5	10	80	
10	Н	NO2	0.10	EtOH(96%)/26.5	10	50 [°]	
11	NO2	н	0.10	11	10	52 [°]	
12	CH	Н	0.10	11	10	36	
13	OCH3	Н	0.10	н	10	47	
14	н	Н	0.10	11	10	36	

Table 1 Synthesis of chalcones by Claisen-Schmidt condensation,catalyzed by C-200

^aDielectric constant at 25°C

^bREflux of EtOH.The obtained yield is at 4h. 94%

^CRecrystallized product from EtOH. a very dark solid is obtained in these cases.

Table 2

Active sites selective poisoning experiments in the synthesis of chalcones Sonication time=10min. 0.0196mol.of 1 and 2. 0.1g: of C-200.solvent EtOH(96%)

Catalyst	active sites	moles of poison adsorbed	yield in 3	
	(eq/g.cat)	per g. of catalyst	(%molar)	
	reducing sites	DNB		
C-200	(3.5 <u>+</u> 0.4) 10 ⁻⁵	-	76	
C-200	(3.5 <u>+</u> 0.4) 10 ⁻⁵	(1.3 ± 0.5) 10 ⁻⁴	77	
	Strong basic sites	TBMPHE		
C-200	(6.3 <u>+</u> 0.2) 10 ⁻⁶	_	76	
C-200	$(6.3+0.2)$ 10^{-6}	(4.4+1) 10 ⁻⁵	0	

Solvents such as benzene,toluene and cyclohexane do not lead to appreciable yields (<5%). this can be explained by their hydrophobic character which impedes the formation of a water rich interface between the solid and the solvent.

The electron-donating groups do not favour the process while the electron-withdrawing groups do.(entries 4,10-14 table 1). Unfortunately, secondary reactions are produced in the case of NO_2 group and the reported yields (entries 10-11) are obtained for the recrystallized product. They must be compared to the 71% obtained from the recrystallized product in the case of p-C1-benzaldehyde. Therefore we must suppose that a carbanionic species attacks the aldehyde 16.

On the other hand we can say that the Cannizzaro reaction was not observed.According to the experimental evidence we could postulate a catalytic mechanism where the active site of the catalyst is regenerated in order to explain that the reaction takes place with low amounts of catalyst and, so with a very small number of active sites.

0.1g. C-200 = 6.3 10^{-7} strong basic sites produce a 76% yield (entry 4). so,this amount of basic sites produces 1.49 10^{-2} moles of chalcone in 10min. Therefore 2.3 10^{3} moles of chalcone are produced by one strong basic site per minute.



adsorbed carbanion, detected by IR

REFERENCES AND NOTES

- 1.-J.Elguero; P.Goya; J.Lissavetzky and A.M.Valdeolmillos.-<u>C.R.Acad.Sci.Paris.</u> 1984,t-298, Serie II,977
- 2.-J.Einhorn and J.L.Luche.-Tetrahedron Lett.1986,27(16),1791; Ibid.1986,27(16),1793
- 3.-J.Brennan and F.H.S. Hussian.-Synthesis 1985,749
- 4.-A.Fuentes; J.M.Marinas and J.V.Sinisterra.-Tetrahedron Lett.-In press
- 5.-A.Fuentes and J.V.Sinisterra.-Tetrahedron Lett. 1986,27(26),2967
- 6.-G.Comdes, P.Vassort and F.Winternitz.-Tetrahedron Lett. 1986, 26, 5981
- 7.-S.S.Misra and R.S.Tenari.-J.Indian Chem Soc. 1973,50(1),68
- 8.-L.Lafon-Ger Offen 2,010,180(1970), Chem. Abstr. 1970, 73:120342s
- 9.-A.Garcia-Raso; J.A.Garcia-Raso; B.Campaner; R.Mestres and J.V.Sinisterra-Synthesis 1982,1037
- 10.-J.V.Sinisterra;F.Garcia-Blanco;M.Iglesias and J.M.Marinas.-<u>React.Kinet.Catal.Lett</u>. <u>1984</u>,25,277
- 11.-J.Barrios; J.M.Marinas and J.V.Sinisterra.-Bull.Soc.Chim.Belges 1986,95,107
- 12.-J.V.Sinisterra; M.Iglesias; F.Garcia-Blanco and J.M.Marinas.-React.Kinet.Catal.Lett. 1985,27,263
- 13.-A.Fuentes.-Thesis-University of Cordoba.December 1986
- 14.-A.Alcantara; A.Aguilera; J.V.Sinisterra and J.M.Marinas.-can.J.Chem.-in press.
- 15.-J.V.Sinisterra;Z.Mouloungui;M.Delmas and A.Gaset.-Synthesis 1985,1097
- 16.-Under sonochemical conditions the aldehyde is not adsorbed on the solid surface as has been proved by the IR spectroscopy of adsorbed species¹.