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The effect of solvents on the heterogeneous synthesis of flavanone over MgO

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Abstract

The effect of several solvents on the heterogeneous synthesis of flavanone from benzaldehyde and 2-hydroxyacetophenone over a solid MgO catalyst was examined experimentally through kinetic and FTIR spectroscopic studies. High-boiling-point solvents considered were dimethyl sulfoxide, tetralin, mesitylene, benzonitrile, and nitrobenzene. Kinetic results indicate that the presence of different solvents in this reaction system affects the rate, kinetic dependencies, and selectivities toward flavanone and 2′-hydroxychalcone. Dimethyl sulfoxide (DMSO) in particular, significantly promotes the rates of both steps used in this synthesis (i.e., the Claisen–Schmidt condensation reaction of benzaldehyde with 2-hydroxyacetophenone and the subsequent isomerization of the 2′-hydroxychalcone intermediate to flavanone). The effect is more pronounced for the second reaction. Even the presence of small amounts of DMSO in other solvents, such as benzonitrile and nitrobenzene, results in strong promotion of the flavanone synthesis scheme. Results of FTIR spectroscopic studies indicate that the interaction of MgO with DMSO results in the formation of stable surface sulfate species. The presence of these species on the catalyst surface affects the adsorption behavior of benzaldehyde and 2-hydroxyacetophenone.

1. Introduction

Heterogeneous catalysis is considered an environmentally friendly alternative for the synthesis of fine chemicals and pharmaceuticals, since the use of heterogeneous catalytic processes allows for easier catalyst separation, recovery, and recycling [1,2]. Progress has been reported during the past decade in developing selective catalytic systems for the production of fine chemicals that are cost-effective in terms of raw materials, energy consumption, and waste generation [3,4]. Nevertheless, the number of available examples of successful transformations from stoichiometric or homogeneous catalytic syntheses to heterogeneous ones is rather limited. The complexity of the surface chemistry involved in the heterogeneous syntheses and the limited understanding of the kinetic and mass transfer effects incorporated in liquid–solid reaction systems are believed to represent major obstacles to such efforts [5].

Solvents play an important role in fine chemical and pharmaceutical syntheses. While the ultimate goal of many heterogeneous catalytic systems is to eliminate the use of solvents, which in turn minimizes the amount of waste generated, it is important to understand the role of solvents in these syntheses. In particular, solvents are used to facilitate liquid-phase reactions by improving the heat and mass transfer characteristics of the system and by limiting coke build-up on the catalyst surface, hence extending the catalyst life [6]. Variations in solvent polarity, solubility, reactivity, and chemisorption properties can influence the chemo-, regio-, and in some cases stereoselectivity of the products.

The synthesis of flavanone represents a textbook example of a relatively simple homogeneously catalyzed condensation reaction, for which the mechanism and kinetics are fairly well understood [7–10]. At the same time, flavanone represents a significant intermediate in many pharmaceutical syntheses, and members of the flavanoid family are attracting increased attention due to recent studies documenting their anticancer [11], antiinflammatory [12], antibacterial [13], and anti-AIDS [14] pharmacological activity. Consequently, flavanone synthesis represents, in our opinion, an opportunity to demonstrate the potential of replacing a homogeneous synthetic process by a heterogeneous one for the production of an important family of compounds.

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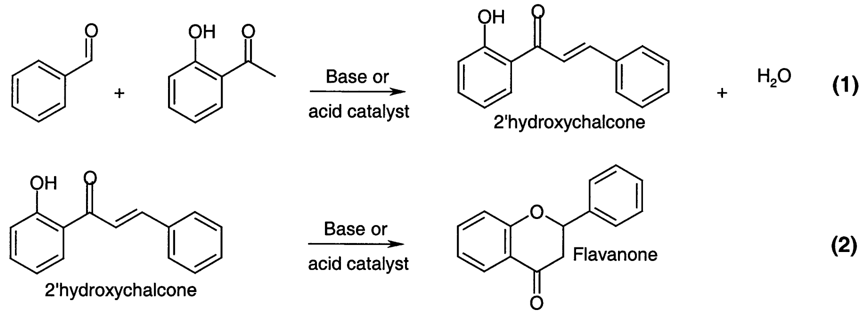

Fig. 1. Flavanone synthesis scheme: (1) Claisen–Schmidt condensation of benzaldehyde and 2-hydroxyacetophenone; (2) isomerization of 2′-hydroxychalcone to flavanone.

Flavanones are commonly synthesized via the Claisen–Schmidt condensation of benzaldehyde and 2-hydroxyacetophenone [15,16] and the subsequent isomerization of the 2′-hydroxychalcone intermediate formed in the first reaction to flavanone (Fig. 1). Both reactions are catalyzed by acid or base catalysts. The feasibility of utilizing the same reaction scheme to produce flavanone heterogeneously has been demonstrated by Corma et al. [16] and Blanco et al. [17]. However, no kinetic or mechanistic data are available to allow one to develop an understanding of the surface chemistry taking place during this heterogeneous synthesis or to draw analogies between homogeneous and heterogeneous cases.

Recently, we reported the first detailed kinetic results for the synthesis of flavanone over MgO, both in the presence and in the absence of dimethyl sulfoxide (DMSO) solvent [18,19]. Comparison of these results indicates significant differences in the two cases.

In this paper we explore solvent effects for the heterogeneous synthesis of flavanone over MgO. Activity measurements were obtained for both reactions involved in the synthetic scheme in a variety of different solvents frequently used in high-temperature syntheses. The results demonstrate a very significant promoting effect of DMSO. The kinetic studies were complemented by FTIR studies conducted at reaction temperature. The results of these studies suggest that DMSO modifies the MgO surface and the adsorption/desorption behavior of the two reactants on the catalyst. Thus, elements of the heterogeneous reaction mechanism are emerging from this study.

2. Experimental

2.1. Catalyst preparation

Pure magnesium oxide (Aldrich; 99.+% purity; SA = 65 m^2/g) was used in the form of small particles (175–250 µm). Prior to each experiment the catalyst was calcined at 475 °C for 5 h, to remove any adsorbed impurities. MgO was chosen as the catalyst because of its strong basicity and its high initial rate for flavanone synthesis as compared to other metal oxide catalysts [16,20].

2.2. Kinetic measurements

The batch reactor utilized in this study consisted of a four-port flat-bottom Pyrex reaction kettle. The four ports of the reactor were fitted with a stirring rod (attached to a motor), a reflux condenser, a thermocouple, and a sampling apparatus (with a nitrogen purge line). The reactor was engulfed in a heating mantle, the operation of which was controlled by a temperature controller connected to the reactor thermocouple.

Prior to each experiment, the empty reactor was purged with nitrogen to remove oxygen from the system. Removal of oxygen is necessary to avoid the oxidation of benzaldehyde to benzoic acid [13]. Following this purging procedure, benzaldehyde (Aldrich; 99.+% purity), 2-hydroxyacetophenone (Aldrich; 99.0% purity), and the solvent were placed in the reactor in the appropriate amounts (total volume of 150 ml). The solvents tested were obtained from Aldrich and included dimethyl sulfoxide (99.9% purity), nitrobenzene (99.+% purity), benzonitrile (99% purity), and tetralin (99% purity). Methyl sulfone (Aldrich, 98% purity) was also used as an additive in an effort to explore the role of the S=O group in the synthesis over MgO. After the reactor was charged, nitrogen was continuously bubbled through the system. The reactor was then heated and the catalyst was added when the desired reaction temperature was reached ($t = 0$). Following this point the reactor was operated under total reflux.

Samples of 1 ml were taken intermittently with a specially designed sampling apparatus. Each sample was centrifuged (VWR Scientific Model V Micro centrifuge) at 10,000 rpm for 10 min to separate any solid catalyst particles that might have been trapped in the sample. Analysis was carried out offline using a SRI 8610 gas chromatograph equipped with a 5% phenylmethylsiloxane capillary column (Supelco) and a flame ionization detector. For the GC analysis, 5- and 50-µl aliquots of the samples obtained during the Claisen–Schmidt condensation and 2′-hydroxychalcone isomerization reactions, respectively, were diluted in 1 ml of CH_2Cl_2. This dilution was necessary to obtain final sample concentrations in the range of optimum detector sensitivity. The general reproducibility of the analysis and concentration measurements was determined to be within 5%, based on several repeat measurements.

Initial reaction rates were calculated utilizing the concentration versus time data collected during the first 10 min of the reaction (i.e., first 4–6 data points). During this initial time period, the concentration of the reactants decreased almost linearly with time, and hence, the reaction rate (i.e., the derivative of the reactant concentration with respect to time) can be calculated from the slope of a simple linear fit to the data. For the Claisen–Schmidt condensation reaction, where two reactants are involved, similar values for the initial rates were obtained whether the benzaldehyde or 2-hydroxyacetophenone concentrations were used, consistent with the absence of any side reactions and the 1 : 1 reaction stoichiometry. The values reported in this manuscript are averages of the values obtained from the two reactants.

Yields for the 2′-hydroxychalcone and flavanone products were defined as the amounts of the specific product formed divided by the initial amount of the limiting reactant. No stoichiometric adjustment is needed in this definition, due to the 1 : 1 stoichiometries for both reactions involved. The selectivity toward a specific product was defined as the amount of this product formed divided by the total amount of 2′-hydroxychalcone and flavanone formed. Once again, as a result of the 1 : 1 stoichiometries involved, a stoichiometric adjustment is not required in this definition.

Baseline experiments were conducted in the absence of the MgO catalyst and did not indicate any significant homogeneous activity in the benzaldehyde/2-hydroxyacetophenone/solvent system for either the Claisen–Schmidt condensation or any other side reaction.

Furthermore, based on the results of a detailed investigation of potential mass transfer limitations [19,20] operating conditions of stirring rate of 500 rpm, catalyst particle size between 175 and 250 µm, and catalyst loading of 0.1 wt% MgO were chosen. Under these conditions, the experimental setup used operates in the kinetic regime.

2.3. FTIR spectroscopy studies

All FTIR spectra presented were collected with a Thermo Nicolet Nexus 470 spectrometer operated in the single-beam transmission mode with a resolution of 4 cm^{-1}. Reference spectra of the clean MgO surface in flowing nitrogen were collected separately and difference spectra between samples and the corresponding references collected at the same temperature are shown herein. A stainless steel IR cell with NaCl windows and a 10-cm path length was used. A heating element wrapped around the cell allowed collection of spectra at temperatures up to 250 °C. The temperature was monitored and controlled through a thermocouple located in the cell and in close proximity to the catalyst sample.

MgO catalyst samples were prepared as thin (∼ 20 mg/cm^2) self-supported wafers. Prior to each experiment, the samples were heated for 2 h at 150–200 °C under flowing nitrogen to remove any adsorbed water. Reactants and solvents were introduced into the cell in the gas phase. For this purpose, a nitrogen stream (approximately 100 ml/min) was saturated with the organic species of interest via passage through a saturator maintained at room temperature. The vapor pressures of the different organic compounds studied and the resulting concentrations in the saturated nitrogen streams used are shown in Table 1.

Table 1
Vapor pressures and concentrations of flavanone synthesis reactants and solvents used in the FTIR spectroscopic studies

Compound	Vapor pressure at 30 °C (Torr)[a]	Concentration (ppm)
DMSO	0.86	1100
Benzaldehyde	1.08	1400
2-Hydroxyacetophenone	0.20	260
Nitrobenzene	0.38	500
Benzonitrile	0.87	1100

[a] Obtained from the Antoine equation.

Spent MgO samples recovered from the slurry reactor used in the activity measurements were also studied via FTIR. Vacuum filtration of the reactor contents with acetone was used for the recovery of these samples. The samples were subsequently pressed into thin pellets and placed in a sample holder in the path of the IR beam. Spectra were then collected without any further treatment and were referenced against the room temperature spectrum of fresh MgO.

3. Results and discussion

3.1. Synthesis of flavanone in different solvents

Benzaldehyde conversions and flavanone yields obtained in different solvents are shown as a function of time in Figs. 2 and 3. The results are quantified in Table 2, where the initial rates for the Claisen–Schmidt condensation reaction are presented. Conversions of 2′-hydroxychalcone to flavanone obtained during a separate study of the isomerization reaction over MgO at 160 °C are shown in Fig. 4. Initial rates obtained for this reaction are also summarized in Table 2.

The results in Figs. 2–4 and Table 2 demonstrate the strong promoting effect of DMSO on the flavanone synthesis scheme. In the presence of DMSO, the observed yields and rates (especially for the isomerization of 2′-hydroxychalcone) are higher by at least one order of magnitude. DMSO is relatively polar and can effectively stabilize charge. Polar and nonpolar solvents are expected to show very different behavior for the synthesis of flavanone if an enolate anion type of intermediate needs to be stabilized, as suggested by some authors [13]. Indeed, in the presence of the nontpolar solvents (i.e., mesitylene and tetralin), no significant production of flavanone was observed even after 90 min of reaction (Fig. 3). Significant differences, however, were observed in the yields and rates obtained in the presence of the three polar solvents used (i.e., DMSO,

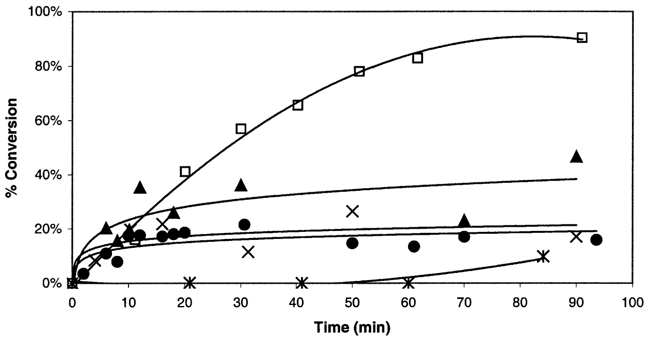

Fig. 2. Benzaldehyde conversion vs time obtained in the presence of different solvents at 160 °C: (□) DMSO; (⁎) nitrobenzene; (×) benzonitrile; (●) tetralin; (▲) mesitylene (initial concentrations: 1.5 mol/l benzaldehyde, 1.5 mol/l 2-hydroxyacetophenone; 0.1 wt% MgO).

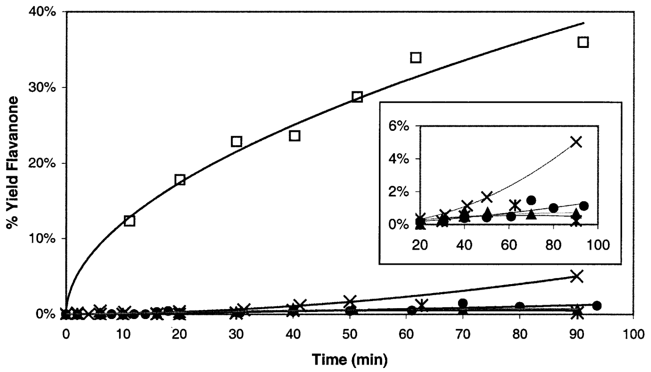

Fig. 3. Flavanone yields vs time obtained in the presence of different solvents at 160 °C: (□) DMSO; (⁎) nitrobenzene; (×) benzonitrile; (●) tetralin; (▲) mesitylene (initial concentrations: 1.5 mol/l benzaldehyde, 1.5 mol/l 2-hydroxyacetophenone; 0.1 wt% MgO). Inset represents a magnification of the plot for nitrobenzene, benzonitrile, tetralin, and mesitylene solvents.

nitrobenzene, and benzonitrile), although the polarity (as expressed by the dipole moment values in Table 1) is the same in all three cases. In the presence of nitrobenzene, the flavanone synthesis scheme did not proceed to any considerable extent and the results were similar to those obtained with the nonpolar solvents. However, as discussed later in the FTIR section, it is possible that the behavior of nitrobenzene can be attributed to a "blocking effect" of the catalyst's active sites that is not related to polarity. A delayed increase in the benzaldehyde conversion and the flavanone yield was evident in this case when the reaction time exceeded 30 min (i.e., the conversion of benzaldehyde over MgO in nitrobenzene increased from less than 1% after 30 min to approximately 24% after 180 min). A similar delay, but of lower magnitude (i.e., on the order of 5–10 min), was also observed with nitrobenzene during the isomerization of 2′-hydroxychalcone (Fig. 4). Currently, it is not clear why such an induction period is needed with this solvent.

No correlation between solvent polarity and reaction rate can be supported by the data obtained separately for the 2′-hydroxychalcone isomerization reaction (Fig. 4 and Table 2). In fact, the promoting effect of DMSO is more pronounced in this case, and the rate for this reaction over MgO in DMSO is two orders of magnitude higher than for any other observed. The reaction reaches the equilibrium conversion within 2 min of reaction time. Flavanone selectivity data obtained during the full synthesis (Table 3) are in agreement with these results, since they show that within the first 10 min of reaction, the DMSO system reaches 69% selectivity to flavanone and this value remains constant for the duration of the run. These results are consistent with a scheme in which the isomerization reaction in the presence of DMSO is very fast and the flavanone yield is limited solely by the rate of the Claisen–Schmidt condensation reaction. Much lower selectivities to flavanone are observed in Table 3 for all other cases, suggesting that the isomerization reaction is rate-limiting in all these cases.

The results obtained in the presence of DMSO, nitrobenzene, and benzonitrile indicate that solvent polarity and polarizability cannot simply be correlated to the effect of these solvents on the rate of the 2′-hydroxychalcone isomerization reaction, since very different kinetic behavior is observed in these three systems of similar polarity. Consequently, the origin of these differences should be explored further through the study of the interaction of the different solvents with the MgO catalyst. In particular, competitive adsorption between the solvent and the reactants and products on the catalyst surface can limit the number of available active sites and slow down the reaction. In contrast, functionalization of the catalyst surface caused by solvent adsorption may create new active sites.

Table 2
Initial reaction rates at 160 °C for the Claisen–Schmidt condensation reaction and isomerization of 2′-hydroxychalcone over MgO in different solvents

Solvent	Dipole moment (debye) measured in benzene at 20–25 °C	Dielectric constant (20 °C)	Claisen–Schmidt rate × 10^4 (mol/g-cat/s)	Isomerization rate × 10^4 (mol/g-cat/s)
DMSO	3.9	48.9	6.3[a]	1.8[b]
Nitrobenzene	4.0	35.6	0.7[a]	0.04[b]
Benzonitrile	3.9	26.5	1.6[a]	0.02[b]
Mesitylene	0	2.3	1.6[a]	–
Tetralin	0.6	2.8	0.9[a]	–

[a] Initial concentrations: 1.5 mol/l benzaldehyde, 1.5 mol/l 2-hydroxyacetophenone.

[b] Initial concentration: 0.02 mol/l 2′-hydroxychalcone.

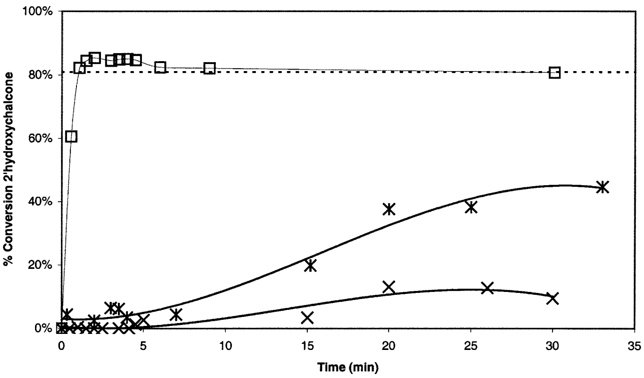

Fig. 4. Conversion of 2′-hydroxychalcone to flavanone over MgO at 160 °C as a function of time in different solvents: (□) DMSO; (⁎) nitrobenzene; (×) benzonitrile. (Initial concentration: 0.02 mol/l 2′-hydroxychalcone; 0.1 wt% MgO.)

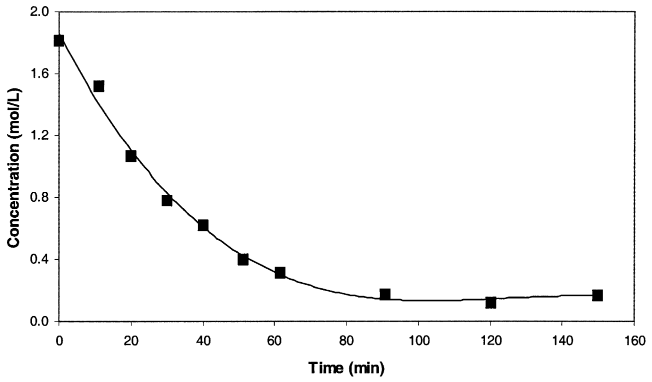

Fig. 5. Concentration of benzaldehyde as a function of time during the reaction with 2-hydroxyacetophenone at 160 °C over MgO in the presence of DMSO.

The kinetic results also indicate a deactivation of the MgO catalyst in the presence of DMSO after approximately 1 h of reaction. This becomes apparent in benzaldehyde concentration versus time data shown in Fig. 5. No complete conversion of benzaldehyde can be achieved in the presence of DMSO, and the reaction is terminated after approximately 100 min. Results obtained in the presence of nitrobenzene and benzonitrile, as well as in the absence of a solvent, indicate no deactivation in these cases. In fact, in all three examples the concentration of benzaldehyde continued to decrease with time until complete conversion was achieved. Consequently, the deactivation of the MgO catalyst is specific to the interaction of this catalyst with the DMSO solvent.

To further investigate the role of DMSO in the synthesis of flavanone, experiments were conducted with small amounts of this solvent added to benzonitrile and nitrobenzene. Figures 6 and 7 show the results of these studies and, in particular, the yields of flavanone obtained when different amounts of DMSO were added to nitrobenzene and benzonitrile, respectively, and these mixtures were used as solvents for the synthesis of flavanone. Even the presence of small amounts of DMSO (i.e., 3 vol%) promotes the production of flavanone for both the nitrobenzene- and benzonitrile-containing systems. The effect becomes more pronounced at higher DMSO concentrations and is not linear. In fact, when the solvent composition is 25 vol% DMSO 75 vol% nitrobenzene, higher flavanone yields are obtained after 50 min of reaction time than the yields obtained when pure DMSO is used as solvent. This phenomenon could be attributed to the deactivation of the MgO catalyst in pure DMSO, which is apparently slowed down in the DMSO–nitrobenzene system. It is possible that the same effect could be observed in the DMSO–benzonitrile system at higher concentrations of DMSO (i.e., an optimum mixture could be achieved that promotes the reaction more than pure DMSO).

Table 4 summarizes the initial rates for both reactions involved in the flavanone synthesis scheme for the different solvent combinations. Although a small increase is observed in the rate of the Claisen–Schmidt condensation reaction when DMSO is added to nitrobenzene and benzonitrile, the most significant effect is observed in the rate for the 2′-hydroxychalcone isomerization reaction. In particular, the rate increases by a factor of 40 with the addition of 25 vol% DMSO to nitrobenzene and by a factor of 60 with the addition of 25 vol% DMSO to benzonitrile. This behavior is consistent with the results reported previously, which show DMSO to affect primarily the 2′-hydroxychalcone isomerization reaction.

Table 3
Selectivity to flavanone over MgO in the presence of various solvents

Solvent	Selectivity flavanone (%)			
	10 min	30 min	90 min	180 min
No solvent	5	9	18	32
DMSO	69	67	64	66
Nitrobenzene	0	0	7	23
Benzonitrile	3	6	16	–
Mesitylene	0	12	3	–
Tetralin	0	5	7	–

Conditions: 150 °C, 0.1 wt% MgO catalyst, initial concentrations of 1.5 mol/l for both 2-hydroxyacetophenone and benzaldehyde.

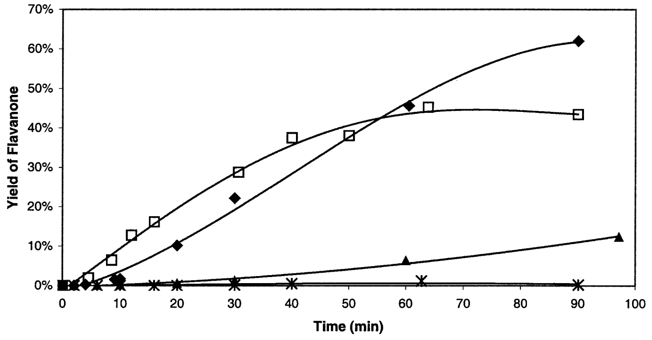

Fig. 6. Yield of flavanone as a function of time in systems containing the following solvent compositions: (□) 100% DMSO; (⁎) 100 vol% nitrobenzene; (▲) 3 vol% DMSO/97 vol% nitrobenzene; and (◆) 25 vol% DMSO/75 vol% nitrobenzene. (Initial concentration of reactants: 1.5 mol/l; 0.1 wt% MgO at 160 °C.)

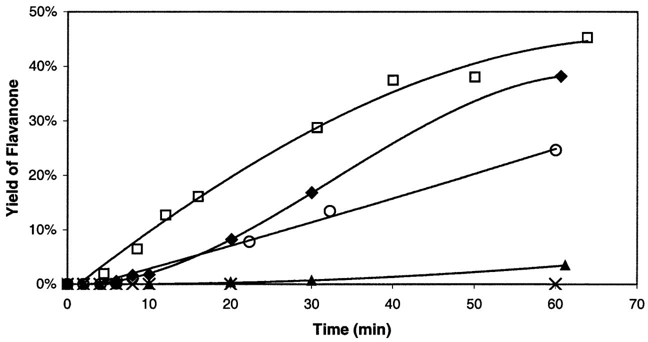

Fig. 7. Yield of flavanone as a function of time in systems containing the following solvent compositions: (□) 100% DMSO; (×) 100 vol% benzonitrile; (▲) 3 vol% DMSO/97 vol% benzonitrile; (○) 18 vol% DMSO/82 vol% benzonitrile; and (◆) 25 vol% DMSO/75 vol% benzonitrile. (Initial concentration of reactants: 1.5 mol/l; 0.1 wt% MgO at 160 °C.)

Finally, activity measurements were conducted with systems containing different amounts of methyl sulfone in benzonitrile. Methyl sulfone is similar with DMSO since it contains S=O groups. In the case of methyl sulfone, the molecule contains two S=O groups and adding this compound, therefore, allowed us to study the possible effects of the S=O group on this reaction. The initial rates observed in this case are also summarized in Table 4. The results indicate that the addition of small amounts of methyl sulfone also promotes the isomerization of 2′-hydroxychalcone, but this effect is not as dramatic as in the case of DMSO. Increasing the amount of methyl sulfone does not result in an additional benefit. Furthermore, the presence of methyl sulfone appears to inhibit the Claisen–Schmidt condensation reaction, and this inhibition increases with increased amounts of methyl sulfone in the reaction system.

Table 4
Initial rate constants at 160 °C for Claisen–Schmidt condensation reaction and 2′-hydroxychalcone isomerization over MgO for systems with DMSO and methyl sulfone additives

Solvent system	Claisen–Schmidt rate × 10^4 (mol/g-cat/s)	Isomerization rate × 10^4 (mol/g-cat/s)
100% DMSO	6.3[a]	1.8[b]
100% nitrobenzene	0.7[a]	0.04[b]
100% benzonitrile	1.6[a]	0.02[b]
3% DMSO in nitrobenzene	2.8[a]	0.09[b]
25% DMSO in nitrobenzene	2.1[a]	1.7[b]
3% DMSO in benzonitrile	2.3[a]	0.05[b]
18% DMSO benzonitrile	2.6[a]	0.9[b]
25% DMSO in benzonitrile	2.6[a]	1.3[b]
3% methylsulfone in benzonitrile	1.0[a]	0.04[b]
10% methylsulfone in benzonitrile	0.5[a]	0.03[b]
30% methylsulfone in benzonitrile	0.6[a]	0.07[b]

[a] Initial concentrations: 1.5 mol/l benzaldehyde, 1.5 mol/l 2-hydroxyacetophenone.

[b] Initial concentration: 0.02 mol/l 2′-hydroxychalcone.

3.2. FTIR studies

In situ FTIR gas phase adsorption studies were conducted at temperatures in the range 150–250 °C with benzaldehyde, 2-hydroxyacetophenone, dimethyl sulfoxide, nitrobenzene, and benzonitrile. These studies allowed the identification of different surface species formed on the MgO surface. These species can be used as models of the surface species formed in the liquid phase synthesis of flavanone. In fact, a comparison of spectra obtained during the gas phase adsorption studies with the spectrum of a recovered catalyst sample exposed to liquid phase synthesis conditions indicates that similar surface species are present in both cases. Current work in progress is designed to further validate this point by the use of attenuated total reflection infrared (ATR-IR) spectroscopy.

In situ FTIR spectra obtained during the adsorption and desorption of benzaldehyde and 2-hydroxyacetophenone on the MgO catalyst are shown in Figs. 8 and 9, respectively. Important features in these spectra appear in the carbonyl (1500–1750 cm^{-1}) and the C–H stretching (2700–3100 cm^{-1}) regions. The spectra of Fig. 8 suggest two different types of benzaldehyde adsorption on the MgO surface. The first mode of adsorption is represented by the IR peak at approximately 1700 cm^{-1}. This feature has been previously assigned to a surface aldehyde species adsorbed through the carbonyl oxygen [21,22]. Alternatively, the strong IR peak at 1622 cm^{-1} is characteristic of a surface aldehyde species adsorbed through the carbonyl carbon [21,22]. Koutstaal et al. [23] reported that benzene itself does not adsorb strongly to the surfaces of many oxide catalysts, and therefore, all strong adsorption of compounds containing phenyl groups is caused by the interaction of the specific substituents, such as the carbonyl group in benzaldehyde, with the surfaces. Finally, the gas phase carbonyl stretch is present at approximately 1720 cm^{-1}. The presence of surface aldehyde species is also evident in the spectra of Fig. 8, with the appearance of the peaks corresponding to C–H stretches for the carbonyl groups (at 2732 and 2821 cm^{-1} for the oxygen-bonded, and 2715 and 2841 cm^{-1} for the carbon-bonded benzaldehyde, respectively). Furthermore, during the adsorption of benzaldehyde the aromatic ring remains intact, as indicated by the C–H stretches of the aromatic hydrogens observed at 3026 and 3066 cm^{-1}, as well as the ring "breathing" mode at 1615 cm^{-1} [21–24]. All relevant peak assignments are summarized in Table 5.

The surface benzaldehyde species adsorbed through the carbonyl carbon is more stable than the corresponding species adsorbed through the carbonyl oxygen. This is clearly indicated in the spectra of Fig. 8, where the intensity of the corresponding peak at 1622 cm^{-1} remains unchanged even after flushing with N_2 at 195 °C. In contrast, the peak at 1700 cm^{-1} corresponding to benzaldehyde adsorbed through the carbonyl oxygen decreases significantly in intensity upon flushing with N_2 at 150 °C, almost at the same rate as the peak corresponding to the gas phase carbonyl

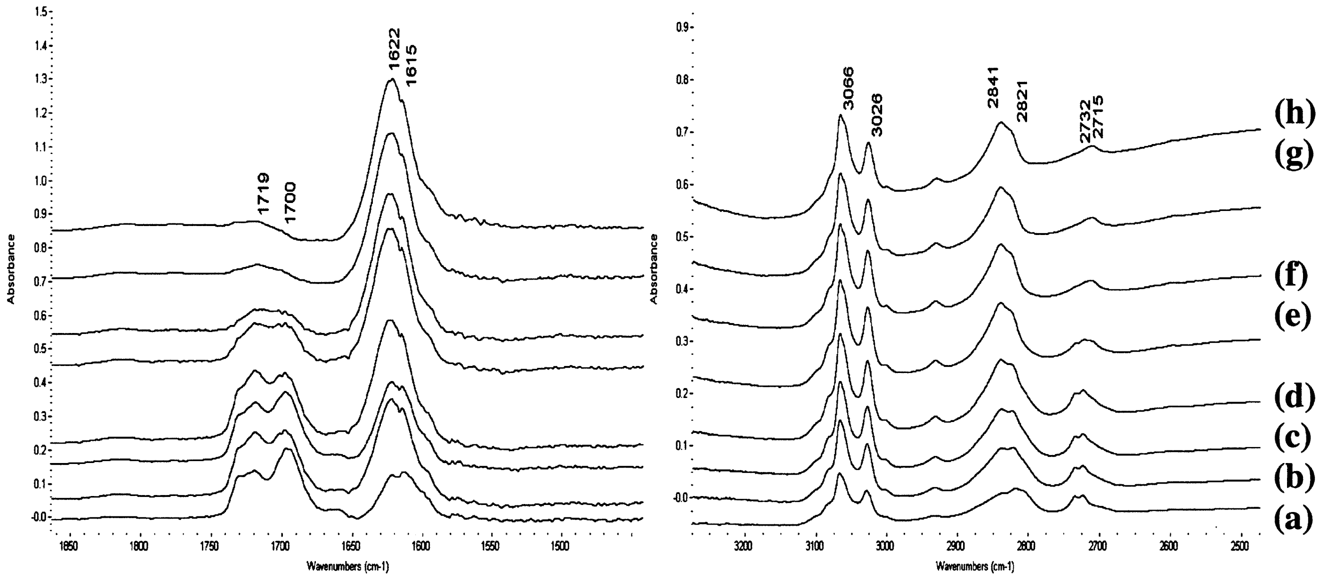

Fig. 8. In situ FTIR spectra of adsorbed benzaldehyde on MgO: (a)–(d): spectra obtained after exposure to MgO to a benzaldehyde-containing stream at 150 °C for 3, 9, 15, and 30 min; (e), (f): spectra obtained after flushing of (d) with N_2 at 150 °C for 15 and 30 min; (g) spectrum obtained after flushing of (f) with N_2 at 175 °C for 3 min; (h) spectrum obtained after flushing of (g) with N_2 at 195 °C for 3 min.

group (1719 cm^{-1}). The same behavior is observed in the C–H stretching region, with the peaks corresponding to the C–H stretches of the carbon-bonded benzaldehyde (2715 and 2841 cm^{-1}) remaining unchanged in intensity upon flushing with N_2 at 195 °C, while the peaks corresponding to the C–H stretches of the oxygen-bonded benzaldehyde (2732 and 2821 cm^{-1}) decrease significantly in intensity upon flushing with N_2 at 150 °C.

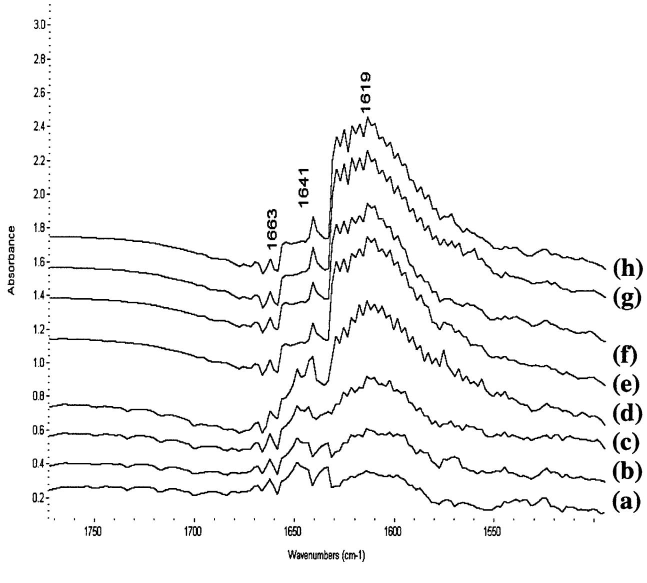

Fig. 9. In situ FTIR spectra of adsorbed 2-hydroxyacetophenone on MgO: (a)–(d): spectra obtained after exposure of MgO to a 2-hydroxyacetophenone-containing stream at 150 °C for 3, 9, 15, and 30 min; (e), (f): spectra obtained after flushing (d) with N_2 at 150 °C for 15 and 30 min; (g) spectrum obtained after flushing (f) with N_2 at 175 °C for 3 min; (h) spectrum obtained after flushing (g) with N_2 at 200 °C for 3 min.

Similar to the case of adsorbed benzaldehyde, a ring vibration is also observed in the spectra of adsorbed 2-hydroxyacetophenone at 1619 cm^{-1} (Fig. 9). No evidence is present in these spectra, however, of an O–H stretch. According to Hunsberger [28], the hydrogen bonding of the *ortho* hydroxyl group with the oxygen on the carbonyl causes shifts in the frequency or even the complete absence of the O–H absorption. Weak peaks present at 1641 and 1663 cm^{-1} can be assigned to the adsorbed C=O group of the ketone, which is weakened due to the loss of a methyl hydrogen. These vibrational modes along with the skeletal ring-breathing mode at 1619 cm^{-1} indicate that, similarly to the case of benzaldehyde adsorption, the carbonyl is again the vehicle of adsorption for the aryl molecule, while the aromatic ring remains intact. Furthermore, the C=O stretching vibrations are much less intense than was observed in the case of benzaldehyde (Fig. 8). This can be explained by hydrogen bonding between the carbonyl and the hydroxyl group, which is expected to decrease the freedom of movement of the C=O group.

Spectra collected during the adsorption of DMSO on MgO are shown in Fig. 10. The prominent feature of these spectra is a strong peak at approximately 1339 cm^{-1}. This vibrational mode is characteristic of a surface sulfate (SO_4^{2-}) species [25,29]. The spectra of Fig. 10 suggest that the formation of these surface sulfate groups occurs relatively quickly (i.e., after 3 min on stream). Furthermore, these species are strongly held to the catalyst surface and are not removed even under purge with an inert atmosphere for 30 min. Two additional peaks at 1032 and 1066 cm^{-1} can be assigned to weakly adsorbed sulfoxide groups, which quickly disappear upon removal of the gas phase DMSO and flushing of the cell with nitrogen (Fig. 10f).

Table 5
Summary of IR spectral assignments for different adsorbed species on MgO

Position (± 4 cm^{-1})	Assignment	Characteristic frequency
	Benzaldehyde and 2-hydroxyacetophenone	
3082, 3054, and 3018	Phenylic C–H stretch vibration	Aromatic ring (ketone) [27]
3067, 3028	Phenylic C–H stretch vibration	Aromatic ring (aldehyde) [21]
2932	Symmetric C–H stretching vibration of methylene (CH_2) group	Adsorbed benzyl species [21,23]
2841, 2715	Aldehydic C–H stretching vibration	Adsorbed aldehyde species [21,23]
1735	C=O stretching vibration	Physisorbed ketone [27]
1720	C=O stretching vibration	Physisorbed aldehyde [21,27]
1700	C=O stretching vibration	Adsorbed aldehyde species, attached through carbonyl oxygen [21–23]
1663 (ketone), 1641	Weakened C=O stretching vibration (attached through carbonyl C) due to loss of aldehydic hydrogen	Carboxylate structure formed during dissociative adsorption of aromatic ketone or aldehyde [22]
1622	C=O stretching vibration	Adsorbed aldehyde species, attached through carbonyl carbon [21–23]
1600–1619	C–C stretching vibration	Aromatic ring [21–23]
1540	C–O stretching vibration	Adsorbed benzoate species [23]
1067, 1025	C–H bending/semicircle in-plane stretching	Aromatic ring [27]
	DMSO	
1341	S=O stretching vibration	Surface sulfate species [25,26]
1059, 1020	S=O stretching vibration	Physisorbed sulfoxide [27]

Spectra of the MgO catalyst obtained in the presence of both DMSO and benzaldehyde (Fig. 11) suggest that the presence of DMSO significantly affects the adsorption of benzaldehyde on the MgO surface. In particular, while the ring vibration at 1606 cm^{-1} and the C–H aromatic stretches at 3020 and 3076 cm^{-1} are still present, no indication can be found in the spectra of the presence of the stable carbonyl-bound surface benzaldehyde species observed previously during the adsorption of benzaldehyde on MgO in the absence of DMSO (Fig. 8). Instead, the only carbonyl stretch present is that corresponding to a physisorbed C=O vibration at 1730 cm^{-1}. These results suggest that the carbonyl group of benzaldehyde is destroyed upon interaction with the sulfated MgO surface. Similar results were also obtained when the MgO surface was first exposed to DMSO for 1 h, purged with N_2 for 30 min, and then exposed to benzaldehyde. Following these treatments, surface sulfate groups are still present on the MgO surface. Spectra collected under these conditions (Fig. 12) indicate that once again benzaldehyde adsorption through the carbonyl group is inhibited, since the corresponding peaks at 1624 and 1699 cm^{-1} are weak. In contrast, the ring vibration at 1606 cm^{-1} remains strong and is accompanied by the presence of two new bands at 1556 and 1540 cm^{-1}, indicating the formation of surface benzyl and benzoate species [21–24]. The appearance of a new peak at 1639 cm^{-1} (Fig. 12e) can be attributed to a carboxylate-like structure that is being formed and can be explained by the loss of the aldehydic hydrogen to the surface and the subsequent weakening of the C=O bond [22]. Formation of benzoate species was not observed during the interaction of benzaldehyde with the untreated MgO surface. It is also important to note that even small amounts of DMSO in the benzaldehyde stream result in this change in adsorption behavior and the formation of the sulfate and benzoate surface species.

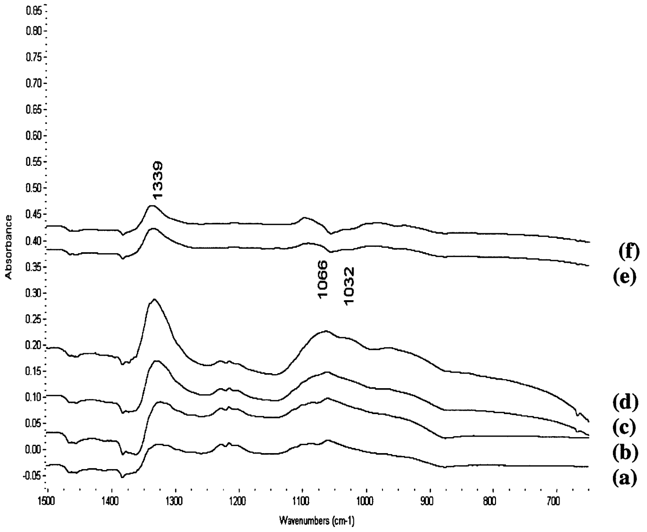

Fig. 10. In situ IR spectra of the adsorbed dimethyl sulfoxide on MgO at 150 °C for the region 1500–700 cm^{-1} (a)–(d): spectra obtained after exposure of MgO to a DMSO containing stream for 3, 9, 15, and 30 min; (e), (f) spectra obtained after the flushing of (d) with N_2 for 15 and 30 min.

Two types of surface benzoate species can be formed on oxide surfaces. They can attach to the surface through a surface oxygen and the carbonyl oxygen (or through two surface oxygens) and form a bidentate benzoate complex around a surface metal atom (Fig. 13a). Alternatively,

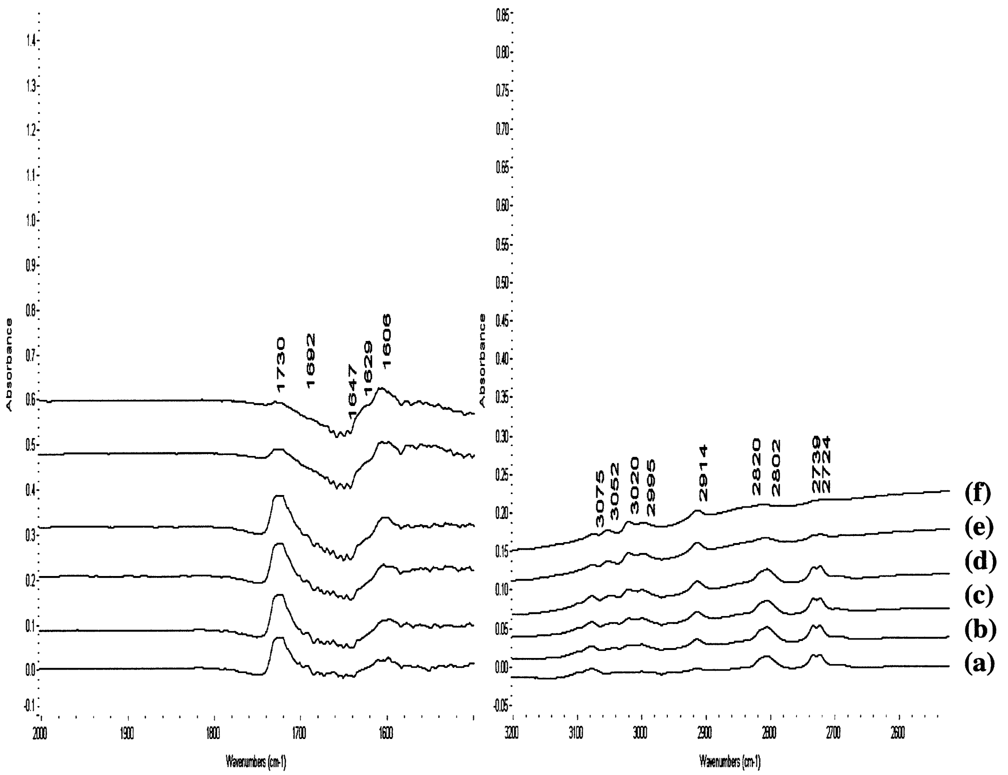

Fig. 11. In situ FTIR spectra of the MgO catalyst obtained during exposure to a mixture of benzaldehyde and DMSO at 150 °C: (a)–(d): spectra obtained after exposure of MgO to a benzaldehyde/DMSO-containing stream for 3, 9, 15, and 30 min; (e), (f) spectra obtained after flushing of (d) with N_2 for 15 and 30 min.

a bridging benzoate complex (Fig. 13b) can be formed, once again involving two surface oxygens or the carbonyl and a surface oxygen [22]. The bridging benzoate complex is a strongly bound species. The presence of such strongly bound surface species could account for the change in the kinetic order of benzaldehyde from 1 to 0.5 in the presence of DMSO [9,10]. Finally, Fig. 13c shows an intermediate species that is probably formed during the adsorption of benzaldehyde on the sulfated-MgO catalyst prior to the formation of the benzoate species. In this carboxylate structure, the aldehydic hydrogen has already been removed and the C=O bond has been weakened to facilitate the formation of the benzoate species. The results of our FTIR studies suggest that these species are formed on the surface of the MgO catalyst only when DMSO is present. It is important to note that the formation of benzoate species has been also observed during the adsorption of benzaldehyde on an untreated MgO surface [30]. The presence of surface hydroxyls facilitates their formation in this case. However, when MgO is thermally activated in an inert atmosphere, as is the case during flavanone synthesis, its surface is stripped of the hydroxyl groups. Therefore, it loses the vehicle through which benzoate species are formed. It appears that the presence of the surface sulfate species provides another medium through which the adsorbed benzaldehyde can be converted to surface benzoate species.

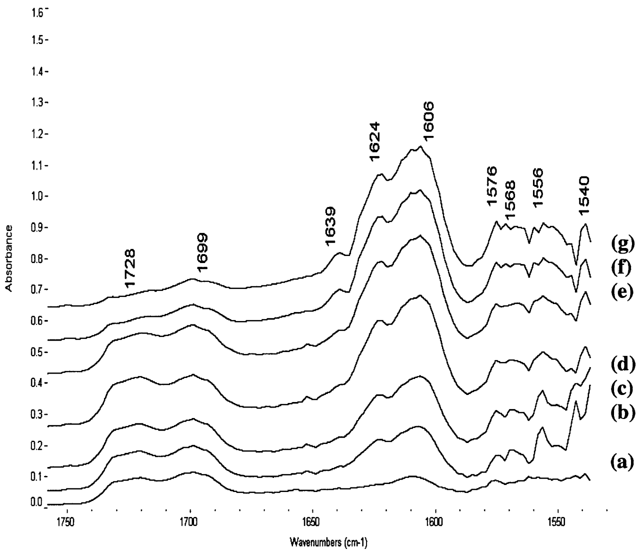

Fig. 12. In situ FTIR spectra of adsorbed benzaldehyde on MgO surface preexposed to DMSO at 150 °C: (a)–(d) spectra obtained after exposure of sulfated MgO to a benzaldehyde-containing stream for 3, 9, 15, and 30 min; (e)–(g) spectra obtained after flushing (d) with N_2 for 3, 15, and 30 min.

Similar experiments were also conducted with 2-hydroxyacetophenone/DMSO mixtures. Once again, differences were observed in the adsorption of 2-hydroxyacetophenone on the sulfated-MgO catalyst, although the kinetic results did not indicate any changes in the kinetic dependencies in this case. The presence of surface sulfate species weakens the carbonyl adsorption and facilitates the formation of surface

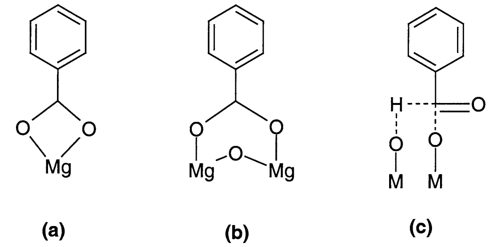

Fig. 13. Surface species formed during the adsorption of benzaldehyde on a sulfated MgO surface: (A) bidentate and (B) bridging benzoate complex and (C) carboxylate intermediate leading to benzoate formation.

benzoate species, although the effect is not as strong as in the case of benzaldehyde.

Finally, the interaction of different solvents and their mixture with the MgO surface was examined by in situ FTIR studies. Exposure of the MgO surface to benzonitrile indicates weak adsorption of the nitrile group to the surface, as the nitrile species corresponding to the peak at 2227 cm^{-1} disappears quickly in flowing nitrogen. Spectra of the MgO surface exposed to nitrobenzene indicate that this molecule adsorbs on the surface through the nitro group, while no ring vibrations were observed. As discussed by Itoh et al. [31], this type of behavior may indicate that the nitrobenzene ring is laying flat on the surface of the MgO catalyst upon adsorption. This conformation in turn could block the active sites of the catalyst and could account for the observed decrease in the rate when nitrobenzene was used as the solvent in the synthesis of flavanone.

4. Conclusions

Among the different high-boiling-point solvents examined for the synthesis of flavanone from benzaldehyde and 2-hydroxyacetophenone over a MgO catalyst, the use of dimethyl sulfoxide (DMSO) was found to significantly promote the yield of flavanone. The effect of DMSO on the rate of the second step of the synthesis (i.e., the isomerization of the 2′-hydroxychalcone) is more dramatic. In this case, a 40- to 100-fold increase in the activity of MgO was observed as compared to other solvents. The same promoting effect was also observed when relatively small amounts of DMSO were added to other solvents. No apparent correlation was obtained between the polarities of the solvents and the reactivity of MgO in the presence of these solvents. The results of FTIR studies indicate the formation of strongly held surface sulfate species following the interaction of DMSO with the MgO surface. The presence of these sulfate species affects the adsorption behavior of benzaldehyde and 2-hydroxyacetophenone on the surface of the MgO catalyst and leads to the formation of surface benzoate species. These differences may be responsible for the observed change in the catalytic behavior of MgO during the synthesis of flavanone in the presence on DMSO.

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