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Acetylation of aromatic compounds over H-BEA zeolite: the influence of the substituents on the reactivity and on the catalyst stability

Matteo Guidotti [a,c,*,1], Christine Canaff [a], Jean-Marie Coustard [b], Patrick Magnoux [a], Michel Guisnet [a]

[a] *Faculté des Sciences Fondamentales et Appliquées, Université de Poitiers, UMR CNRS 6503, 40 av. du Recteur Pineau, 86022 Poitiers cedex, France*
[b] *Faculté des Sciences Fondamentales et Appliquées, Université de Poitiers, UMR CNRS 6514, 40 av. du Recteur Pineau, 86022 Poitiers cedex, France*
[c] *CNR – Istituto di Scienze e Tecnologie Molecolari, via Venezian 21, 20133 Milano, Italy*

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Abstract

The acylation with acetic anhydride of six aromatic substrates with different features (degree of activation of the aromatic ring towards electrophilic substitution, number of rings, i.e., 1 or 2) was carried out in a batch reactor at 373 K over a H-BEA zeolite (Si/Al = 15) with nitrobenzene as a solvent. The acetylation rate was found to be very dependent on the degree of ring activation, with diffusion limitations playing only a limited role. The decrease of the rate with reaction time, which was very pronounced with poorly activated and deactivated substrates, is mainly due to the inhibiting effect of acetic acid and of the products of acetic anhydride condensation.

Keywords: Acetylation; Acetic anhydride; Aromatic ketones; BEA zeolite; Reaction rate; Catalyst poisoning

1. Introduction

Aromatic ketones are useful intermediates for the synthesis of a wide range of compounds used in the fine and speciality chemical industry, such as pharmaceuticals, pesticides, flavours, perfumes, UV adsorbers, and dyes [1,2]. The acylation reactions are generally carried out in batch reactors over corrosive conventional Friedel–Crafts catalysts, such as $AlCl_3$, $FeCl_3$, or other Lewis acid metal chlorides. Because of the formation of very stable complexes between the metal chloride and the arylketone [3], more than stoichiometric amounts of catalysts and a final hydrolysis step of the 1:1 molar adduct are required. Therefore, such a process leads to the production of huge quantities of acidic by-products to be neutralised, treated, and properly discharged. Furthermore, the use of Brønsted acids, such as polyphosphoric or hydrofluoric acid, involves similar problems, the latter being much more volatile than the conventional metal chlorides.

Acid zeolites, with their shape-selective properties and the easy tailoring of their acidity and porosity, are particularly adapted to the selective synthesis of arylketones, their main limitation being in the size of the synthesised molecules. In the late 1960s, Venuto and Landis reported *m*-xylene acetylation over X zeolite [4]. Since that pioneering work, several recent studies have dealt with the acylation of aromatics catalysed by acidic zeolites [5], and two industrial processes using zeolites (H-BEA or H-FAU) were developed for the selective synthesis of acetoanisole and acetoveratrole, which are, respectively, precursors of a sun protector (Parsol) and of a component in an insecticide formulation (Verbutin). In both cases, noteworthy improvements were achieved by replacement of conventional technology (Lewis acid catalysts, acetylchloride as acylating agent, and batch reactor) with innovative technology (zeolite catalysts, acetic anhydride, and fixed-bed reactor) [6].

* Corresponding author. Fax: +39-02-50314405.
E-mail address: m.guidotti@istm.cnr.it (M. Guidotti).
[1] Temporarily in Poitiers (France) as a visiting researcher.

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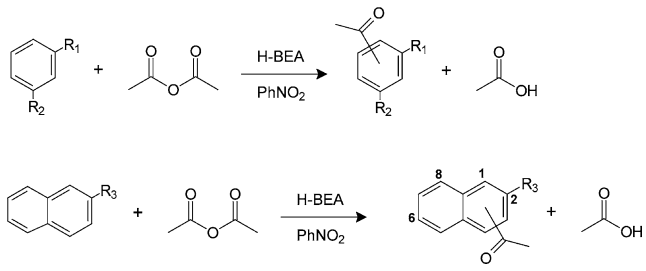


Scheme 1.

As in the last two decades many zeolitic catalysts have been tested under various conditions and with different acylating agents, it is now possible to evaluate critically their performance in the synthesis of aromatic ketones [5]. However, only a limited number of substrates have been used. Most of the works were carried out on alkylarenes or alkoxyarenes such as benzene, toluene, xylene, anisole, veratrole, and methoxynaphthalene [7–18]. Furthermore, since the authors focused their attention mainly on finding the best reaction conditions for each substrate, a systematic and comparative study of the performance of a catalyst in the acylation of different aromatics under the same conditions is still lacking.

Likewise, one of the main drawbacks to be solved in the use of zeolites as acylation catalysts is the decrease with time of the reaction rate, which is due either to the deposition of heavy by-products within the pore system and on their external surface or to inhibition of acylation by products of the main and secondary reactions. Nevertheless, since the conditions under which the reaction is carried out may affect largely the extent of the rate decrease, the reasons for the gradual loss of zeolite activity during the acylation reaction have not been unequivocally determined so far.

In this work, the reactivity in acetylation with acetic anhydride of six aromatic molecules with different features (monocyclic or bicyclic arenes, activated or nonactivated substrates towards electrophilic substitution) is systematically compared over an acidic BEA zeolite (Scheme 1). The effect of the substrate on the decrease with time of the acylation rate is also evaluated, and various experiments are carried out to specify the origin of this loss in activity.

2. Experimental

H-BEA zeolite (CP811B25; total Si/Al ratio = 15) was provided by PQ Zeolites. The total pore volume of the zeolite was 0.787 $cm^3\,g^{-1}$ (micropore volume = 0.282 $cm^3\,g^{-1}$; mesopore volume = 0.505 $cm^3\,g^{-1}$), and the average crystallite size (estimated from TEM) was smaller than 0.02 μm. The concentrations of Brønsted and Lewis acid sites were determined by pyridine adsorption at 423 K followed by IR spectroscopy and were found to be 345 and 372 $\mu mol\,g^{-1}$, respectively. Nitrogen adsorption measurements on the used catalyst (after reaction with fluorobenzene) were performed after a 1-h pretreatment period at 363 K in vacuo.

Six mono- and bicyclic aromatic compounds were used as substrates: anisole (Acros Organics; 99%), toluene (Aldrich; 99.5%), *m*-xylene (Fluka; 99%), fluorobenzene (Aldrich; 99%), 2-methoxynaphthalene (Lancaster; 98%), and 2-methylnaphthalene (Aldrich; 98%). The catalytic tests were carried out in liquid phase, at 373 K, under a dry nitrogen atmosphere, in a three-necked round-bottomed flask connected to a reflux condenser and equipped with magnetic stirring (750 rpm). Before each catalytic test, the zeolite was pretreated for 8 h under dry air flow (100 $mL\,min^{-1}$) at 773 K. The standard conditions were as follows: 500 mg of activated zeolite was added to a mixture containing 35 mmol of substrate, 7 mmol of acetic anhydride (AA) (Fluka; 99%), and 15 mL of nitrobenzene (Lancaster; 99%) as solvent. Solvent and reagents had previously been dried on 3A molecular sieves. Time zero of the reaction was taken at the time when the catalyst was introduced in the mixture heated at the reaction temperature. Small samples (0.1 mL) were periodically taken and analysed by GC-FID on a capillary Varian CP-Sil-8 CB column. Products were identified by reference samples or by mass spectrometry.

Since the acetic anhydride was present in a substoichiometric amount, the conversion of substrate (X_{SUB}) has been referred to the maximum possible conversion into monoacetylated products (here 20%):

$$X_{SUB} = \frac{X(\text{converted substrate})}{X(\text{maximum substrate conversion})},$$

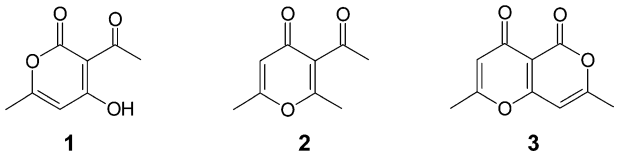
where

$$X(\text{converted substrate}) = 1 - \frac{\%(\text{SUB at time} = t)}{\%(\text{SUB at time} = 0)}.$$

The conversion of acetic anhydride (X_{AA}) has been computed from the amount of consumed acetic anhydride:

$$X_{AA} = 1 - \frac{\%(\text{AA at time} = t)}{\%(\text{AA at time} = 0)}.$$

The organic compounds retained on the external zeolite surface (including the intercrystallite mesopores) and in the micropores were recovered at the end of the experiment. For that, the used catalyst underwent a double-extraction methodology, as previously described [19]. First, the deactivated catalyst was treated in a Soxhlet extraction apparatus with dichloromethane, and the obtained solution was analysed by GC-FID. Then, the resulting solid was dissolved in hydrofluoric acid (40% aq.; Labosi), and the organic species was extracted with dichloromethane and analysed by GC-MS. With such a methodology, the largest part of the adsorbed compounds was recovered during Soxhlet extraction. In the following zeolite dissolution step, a much less significant part (< 3% of the retained compounds after reaction), which was neither extracted by Soxhlet treatment nor dissolved in aqueous HF, was recovered by the final dichloromethane extraction. Elemental analysis of the deactivated catalyst was carried out before and after Soxhlet treatment by dichloromethane.



Scheme 2.

In the inhibition tests, 7 mmol of acetic acid (Aldrich; 99.8%, dried on molecular sieves) or 3.5 mmol of dehydroacetic acid **1** (DHA) (Scheme 2; Acros Organics; 98%) or 7 mmol of *p*-methoxyacetophenone (Aldrich; 99%) or 2,4-dimethylacetophenone (Lancaster; 97%) were added at time 0 to the reaction mixture described above. In two experiments, the activated zeolite (500 mg), the acetic anhydride (7 mmol), and the solvent (15 mL) were mixed and left at 373 K for 1 h, and only after that time was the substrate (35 mmol of either anisole or *m*-xylene) added.

3. Results and discussion

3.1. Acylation rate and product distribution

Nitrobenzene, which has an intermediate polarity, was chosen as a solvent. Indeed, in previous studies [7,20] it was shown that in the presence of nonpolar solvents there was a strong inhibition of acetylation by the very polar products (acetic acid, acetylated products), whereas highly polar solvents competed with the reactant molecules to enter the micropores and adsorb on the acidic sites, with, therefore, a significant limitation in the acetylation rate.

Regardless of the substrate and the reaction time, the products of the substrate transformation resulted essentially from its monoacetylation. The other main product observed in the reaction mixture was acetic acid, which resulted from acetic anhydride consumption.

Figs. 1 and 2 show, respectively, the conversion profile of the substrates and of acetic anhydride (AA) vs time. At the beginning and after a reaction time of 60 min, the order of substrate reactivity was anisole > 2-methoxynaphthalene > *m*-xylene ≅ toluene > 2-methylnaphthalene > fluorobenzene.

The initial rates of acetylation of the six substrates were estimated from the slope of the tangent at time zero to the curves in Fig. 1: anisole was found to be 2.5, 12, 13, 75, and 340 times more reactive than 2-methoxynaphthalene, *m*-xylene, toluene, 2-methylnaphthalene, and fluorobenzene, respectively. We also calculated turnover frequency (TOF) values by admitting, in agreement with the literature [2,8,9], that the acetylation reaction with acetic anhydride occurs on the protonic sites without direct participation of the Lewis acid sites. Whereas the values of TOF found for anisole and 2-methoxynaphthalene are relatively high, indicating the possibility of using H-BEA as a catalyst for the acetylation of the substrates with methoxy groups, this is not the case with the other substrates, especially with

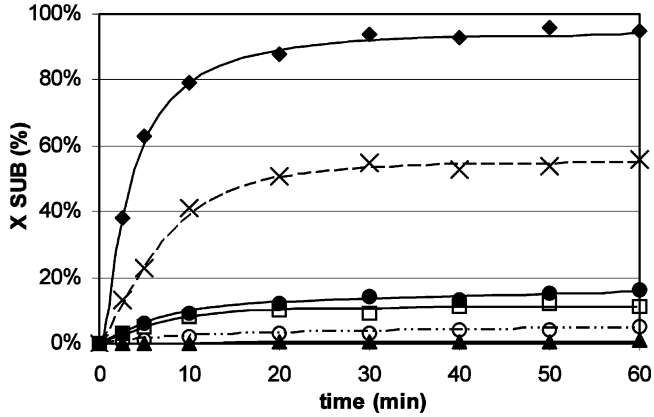


Fig. 1. Conversion (X_{SUB}) of anisole (◆), 2-methoxynaphthalene (×), *m*-xylene (●), toluene (□), 2-methylnaphthalene (○) and fluorobenzene (▲) vs time.

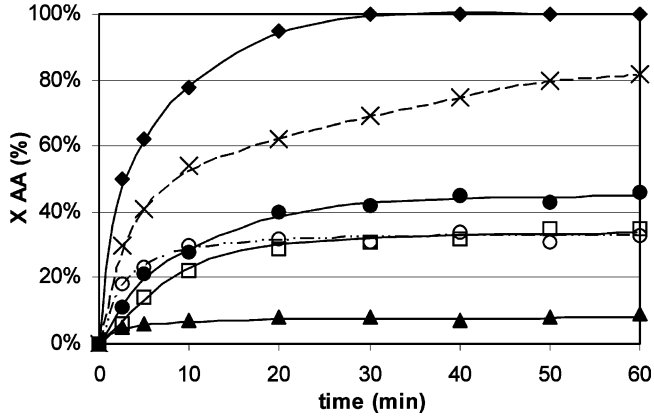


Fig. 2. Conversion of acetic anhydride (X_{AA}) during the acetylation of anisole (◆), 2-methoxynaphthalene (×), *m*-xylene (●), toluene (□), 2-methylnaphthalene (○) and fluorobenzene (▲) vs time.

2-methylnaphthalene and fluorobenzene. Moreover, there is no further conversion of these latter substrates after a reaction time of a few minutes.

The order of initial reactivities of the benzenic substrates is the one expected from the activating/deactivating effect of the substituents. The polarity properties, which affect the approach and the entrance of the aromatic molecule into the zeolite pores, play a more limited role. Actually, even though anisole and fluorobenzene have practically the same polarity parameter, as proposed by Reichardt (0.198 and 0.194, respectively) [21], their reactivities in heterogeneous acylation with AA are dramatically different.

It should be noted that, even though *m*-xylene acetylation should be much faster than toluene acetylation (7 times with $AlCl_3$ catalyst [2]), in this case it occurs practically at the same rate. This behaviour suggests the presence of limitations in the desorption of the relatively bulky 2,4-dimethylacetophenone molecules from the zeolite micropores. Furthermore, as could be expected from the most activating character of the methoxy group, acetylation of 2-methoxynaphthalene is much faster (30 times) than acetylation of 2-methylnaphthalene. However, the acetylation of

Table 1
Rate and selectivity of the acetylation of substituted arenes over H-BEA[a]

Substrates	X_{SUB}[b] (%)	r_0[c] (mmol h^{-1} g^{-1})	TOF[d] (h^{-1})	Product[e]	Isomer	Distribution[f] (%)
Anisole	95	130	370	Methoxyacetophenone	*para*	99.2
					ortho	0.8
2-Methoxynaphthalene	56	50	150	Methoxyacetonaphthone	1,2-	74.1
					2,6-	22.0
					2,8-	2.1
					others	1.8
m-Xylene	16	11	32	Dimethylacetophenone	2,4-	98.0
					3,5-	1.1
					2,6-	0.9
Toluene	11	10	29	Methylacetophenone	*para*	98.7
					ortho	1.3
2-Methylnaphthalene	5	1.7	5	Methylacetonaphthone	2,6-	70.5
					2,8-	15.7
					1,2-	3.1
					others	10.7
Fluorobenzene	1	0.35	1.1	Fluoroacetophenone	*para*	>99[g]

[a] Reaction conditions: 500 mg H-BEA-15 zeolite; substrate:AA ratio = 5; 15 mL $PhNO_2$; 373 K; 1 bar; 60 min.
[b] Conversion of substrate after 60 min.
[c] Initial rate of monoacetylation.
[d] Turn-over frequency ($[mol_{SUB}]\,[mol_{H^+}\ s^{-1}]^{-1}$) after 2.5 min. The amount of H^+ was computed according to the amount of Brønsted acid sites.
[e] In all cases selectivity to acetylated products was > 98% after 60 min.
[f] Obtained from GC-analysis of the reaction mixture after 60 min.
[g] Only *p*-fluoroacetophenone isomer was detected.

naphthalene derivatives is slower than that of benzenic derivatives with the same substituting group, whereas the reverse could be expected [22]. This is most likely due to limitations in the desorption from the BEA micropores of the acetylated naphthalenic products, which are bulkier than the acetylated benzenic products.

With regard to the chemoselectivity of the reaction, in all cases no other products but acetylated derivatives were detected in the GC analysis of the reaction mixture. Therefore the selectivity for acetylated species can be considered higher than 98%.

As far as regioselectivity is concerned, *para*-disubstituted acetophenones were almost exclusively obtained in the case of anisole, toluene, and fluorobenzene (Table 1). As the formation of *para*-disubstituted products is strongly favoured also with homogeneous and nonzeolitic solid acid catalysts (> 97% in almost all cases [2,8,23]), such very high *para*-selectivity is likely due to the intrinsic features of the substrate (electronic effects and intramolecular steric constraints) rather than to the shape selectivity of the BEA zeolite. In the case of *m*-xylene, the synergic *ortho,para*-orienting effect of the two methyl groups led mainly to 2,4-dimethylacetophenone. In any event, very small amounts of the other two less favoured isomers were detected, namely 3,5-dimethylacetophenone and 2,6-dimethylacetophenone.

With the bicyclic aromatic substrates, 2-methoxynaphthalene and 2-methylnaphthalene, a wider number of acetylated derivatives was possible, and, in this case, the presence of the oxygen atom affected markedly the isomer distribution of the products:

– The acylation of 2-methoxynaphthalene led predominantly to 2-methoxy-1-acetonaphthone (Table 1). The preferential acetylation of this molecule in position 1 has been shown previously [7,11] and is consistent with the lower charge density on carbon 1 with respect to that on the other carbon atoms obtained from semi-empirical MO calculations [24]. However, at long reaction times, 2-methoxy-1-acetonaphthone was found to undergo isomerisation through a transacylation process (from 2-methoxy-1-acetophenone to the residual 2-methoxynaphthalene) to the more thermodynamically favoured species, that is, to 6-methoxy-2-acetonaphthone [11]. In fact, a more detailed examination of the evolution of the isomer distribution versus the reaction time showed that the fraction of the 2,6-isomer increased gradually from 14% after 5 min to 22% after 60 min. It is worth highlighting that there was still an increase in the 2,6-isomer after the complete consumption of AA (after 30 min), in agreement with the proposed transacylation mechanism [11].
– The acylation of 2-methylnaphthalene led predominantly to 6-methyl-2-acetonaphthone, and only a small amount of the product resulting from acetylation in position 1 (2-methyl-1-acetonaphthone) could be observed (Table 1). Such behaviour was also observed

with $AlCl_3$ in the presence of nitromethane as a solvent [25], whereas 2-methyl-1-acetonaphthone was the main product in the presence of non-nitro-containing solvents, such as $CHCl_3$ or CS_2 [26]. The large difference found on this substrate with respect to the selectivity of 2-methoxynaphthalene acetylation in the same solvent (nitrobenzene) seems surprising. Indeed, on both reactants carbon 1 is the most activated position for electrophilic substitution [22]. Therefore, the most likely explanation is that the large difference in the distribution of acetylated products comes from differences in the relative rates of acetylation (in position 1) and of the following isomerisation into the 2,6-isomer. That is to say, the ratio between the rates of isomerisation and acetylation would be greater in 2-methyl than in 2-methoxynaphthalene transformations. However, since no papers in the open literature dealt with the heterogeneous acetylation of 2-methylnaphthalene, further studies are needed to confirm this assertion.

3.2. Origin of the decrease in the acetylation rate with time

Fig. 1 shows that, with all of the substrates, the formation of monoacetylated derivatives stopped after a reaction time of 20–30 min. However, whereas with anisole this can be related to the complete consumption of acetic anhydride, it is not the case with the other substrates (Fig. 2). Thermodynamic limitations can also be excluded, as was shown in the case of 2-methylnaphthalene acetylation. Indeed, no reaction of 6-methyl-2-acetonaphthone with acetic acid (the reverse reaction of the 2-methylnaphthalene acetylation) occurred over H-BEA at 373 K.

Another important difference between the transformation of anisole and that of the other substrates is shown in Fig. 3, in which the ratio of the substrate conversion to the AA conversion (X_{SUB}/X_{AA}) is plotted versus time. With anisole, this ratio is close to 1, which indicates a selective transformation of AA into methoxyacetophenones. With the other substrates, it is smaller than 1, that is, 0.7–0.8 with 2-methoxynaphthalene, 0.3 with *m*-xylene and toluene, 0.1–0.15 with 2-methylnaphthalene, and lower than 0.1 with fluorobenzene. This means that a part of AA (most of it with the poorly activated aromatics) was not used for the formation of monoacetylated products, but for the production of other compounds. Moreover, the catalyst deactivation seems to be related to the formation of these compounds, which, therefore, could poison the active sites or block the access to the reactant molecules. Deactivation of H-BEA zeolite during acetylation reactions was attributed to highly polar species strongly retained in the zeolite pores [12–16,18]. These species could be:

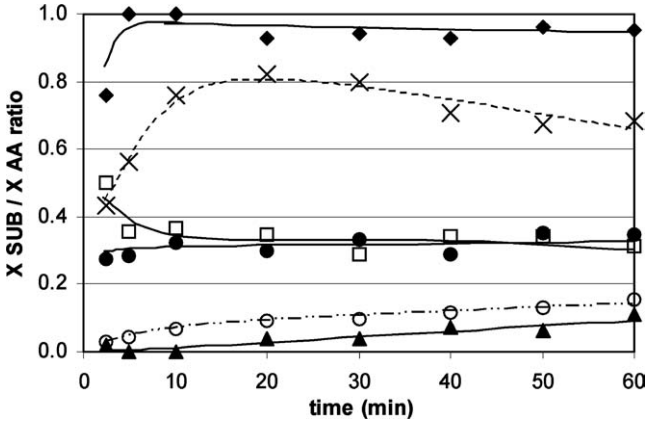


Fig. 3. Substrate conversion (X_{SUB}) to acetic anhydride conversion (X_{AA}) ratio vs time in the acetylation of anisole (◆), 2-methoxynaphthalene (×), *m*-xylene (●), toluene (□), 2-methylnaphthalene (○) and fluorobenzene (▲).

– acetylated products: polyacetylated products and even the desired monoacetylated products, which are bulkier and more polar than the reactant molecules and hence could be more strongly retained by the hydrophilic zeolite;

or

– products resulting from the transformation of AA molecules: acetic acid, condensation products.

These two possibilities are critically examined hereafter on the basis of the composition of the products retained on the zeolite and the effect of some of these products on the rate of acetylation.

3.2.1. Analysis of the products retained on the zeolite

The products retained on the H-BEA zeolite after acetylation of each substrate for 60 min were extracted and analysed. They can be classified into two groups: the organic materials that can be recovered by simple Soxhlet extraction with dichloromethane of the used catalyst and those that could be extracted only after destruction of the zeolite by means of concentrated hydrofluoric acid. The first group corresponds roughly to the products adsorbed to the external surface of the zeolite and in the intercrystallite mesopores, whereas the second group is formed by the organic species strongly retained in the microporous channels of the zeolite.

The composition of the mixture obtained by Soxhlet extraction (first group) was approximately the same as that of the reaction mixture. In fact, the largest part of the compounds recovered by this extraction procedure was due to a layer of reaction mixture physisorbed to the catalyst particles.

The composition of the second group (i.e., the compounds trapped within the zeolite micropores) is reported in Table 2. First of all, it is worth noting that the carbon content on the catalyst after Soxhlet extraction, which is a rough measure of the global amount of these organic deposits, was approximately of the same order of magnitude in all cases. Actually, the carbon content was slightly higher after the reaction on bicyclic aromatics. In general, these

Table 2
Composition of organic deposits strongly retained inside the zeolite pores after 1 h reaction

Substrates	Carbon content[a] (wt%)	Organic compound extracted after HF mineralisation of used catalyst[b]	(wt%)
Anisole	1.45	Monoacetylated anisole	93
		Diacetylated anisole	6
		Others[c]	1
2-Methoxynaphthalene	2.01	Monoacetylated methoxynaphthalene	43
		Diacetylated methoxynaphthalene	32
		Others	19
		Unreacted methoxynaphthalene	6
m-Xylene	1.90	Monoacetylated xylene	37
		Diacetylated xylene	35
		AA derivatives[d]	14
		Others	14
Toluene	1.80	Diacetylated toluene	81
		Triacetylated toluene	7
		AA derivatives	6
		Monoacetylated toluene	4
		Others	2
2-Methylnaphthalene	2.64	Monoacetylated methylnaphthalene	43
		AA derivatives	21
		Others	19
		Diacetylated methylnaphthalene	17
Fluorobenzene	1.74	AA derivatives	80
		Others	20

[a] From CHNS elemental analysis on the used catalyst after Soxhlet extraction and before HF mineralisation.
[b] See Section 2 for details.
[c] "Others" corresponds to a large number of minor heavy compounds (e.g., polycyclic aromatic compounds linked by carbonyl bridges).
[d] Compounds derived from AA condensation and/or oligomerisation only.

data mean that the large differences between the decreases in acetylation rates of the substrates are not due simply to large differences in the total quantity of organic deposits. As an example, even though the carbon contents on the BEA samples used in anisole and fluorobenzene acetylation was similar (Table 2; 1.45 and 1.74%, respectively), the loss in activity appeared to be negligible in the first case and complete in the second (Fig. 1). Furthermore, nitrogen adsorption measurements showed that the significant decrease in rate observed with poorly reactive substrates was not due to a blockage of the access to the active sites of the zeolite. Indeed, neither the total pore volume (V_{TOT}) nor the micropore volume (V_{μ}) of the H-BEA-15 zeolite changed noticeably before and after reaction with fluorobenzene (before reaction: $V_{TOT} = 0.787\ cm^3\,g^{-1}$, $V_{\mu} = 0.282\ cm^3\,g^{-1}$; after reaction and Soxhlet extraction: $V_{TOT} = 0.723\ cm^3\,g^{-1}$, $V_{\mu} = 0.222\ cm^3\,g^{-1}$; i.e., a decrease of only 8% of the total pore volume and 20% of the micropore volume). Therefore, the decrease in acetylation rate is likely due to inhibition of acetylation by strongly adsorbed species on the active sites rather than to a plugging of the zeolite channels by organic deposits.

The main compounds recognised after the zeolite mineralisation are listed in Table 2, together with their relative abundances. It is worth noting that a large part of organic compounds, which are either hydrolysable or soluble in acidic aqueous solutions, could not be recovered because of the use of a concentrated hydrofluoric acid aqueous solution. However, the list in Table 2 displays a representative although partial picture of the carbonaceous compounds retained in the zeolite channels.

These compounds can be classified into two main categories:

1. The species resulting from mono- or poly-(di- and sometimes tri-)acetylation of the substrate. As was previously shown in anisole [13] and veratrole acetylation [10], most of these di- and tri-acetylations do not occur on the deactivated aromatic ring but on the side chain. The relative amount of mono- and polyacetylated compounds depends very much on the substrate: practically only monoacetylated products from anisole; comparable amounts of monoacetylated and diacetylated products from 2-methoxynaphthalene, *m*-xylene, and 2-methylnaphthalene; essentially polyacetylated (mainly diacetylated) products from toluene; last, no acetylated products from fluorobenzene (Table 2). This large difference in the amount of acetylated products retained

within the zeolite micropore results most likely from different causes, such as the difference in polarity between the substrate and the acetylated products, the difference between the size of substrate molecules and pore openings, and the reactivity of the substrate.

2. The species resulting from AA condensation (so-called AA derivatives in Table 2). Three compounds were recognised as major components, namely, 3-acetyl-4-hydroxy-6-methyl-2-pyrone **1** (dehydroacetic acid; DHA), 3-acetyl-2,6-dimethyl-4-pyrone **2**, and 2,7-dimethylpyrano[4,3-*b*]pyran-4,6-dione **3** (Scheme 2), and they all can be obtained by multiple condensation of AA mediated by an acidic zeolite. In particular, DHA can be obtained from the condensation of four molecules of AA over a zeolitic acid site [27]. An important observation is that these AA derivatives do not appear in the acetylation of anisole and 2-methoxynaphthalene substrates, which occur quickly and with only a limited decrease in the rate with the reaction time. On the other hand, these derivatives are the major products retained on the zeolite during the acetylation of fluorobenzene, which occurs very slowly and with a significant decrease in reaction rate. This suggests that the AA derivatives play a more significant role than acetylated compounds in the inhibition of the acetylation reaction.

3.2.2. Effect of acetylated products and AA derivatives on the acetylation rate

First, the role of acetylated products as inhibiting species in the acylation reaction was tested, by the addition, from the beginning, of 7 mmol of acetylated products (4-methoxyacetophenone and 2,4-dimethylacetophenone for anisole and *m*-xylene acetylation, respectively) in the reaction mixture. A decrease in the initial reaction rate and TOF (ca. 1.4–1.8 times less) was observed in both cases. However, after 60 min of reaction, the conversions of anisole and *m*-xylene were close to those observed in the absence of acetylated products (96% for anisole and 14% for *m*-xylene, respectively). Therefore, the autoinhibition of acetylation cannot explain the complete poisoning of the catalyst that is observed during the acylation of poorly activated or deactivated substrates.

Since acetic acid and the "AA derivatives" are the typical products obtained from the reaction of the AA on the zeolite, further acylation tests were carried out in which the acylating agent (AA) and the presumed inhibiting species (acetic acid or dehydroacetic acid **1**, as the most representative of the AA derivatives recognised in the organic deposit analysis) were added. In these experiments, the presence of either acetic acid or DHA led to an almost complete inhibition of the acetylation of *m*-xylene (Fig. 4), whereas it had no detrimental effect on the acetylation of anisole (Fig. 5). On the other hand, previous tests in which AA was replaced by either acetic acid or DHA confirmed that none of them is an effective acetylating agent under these conditions.

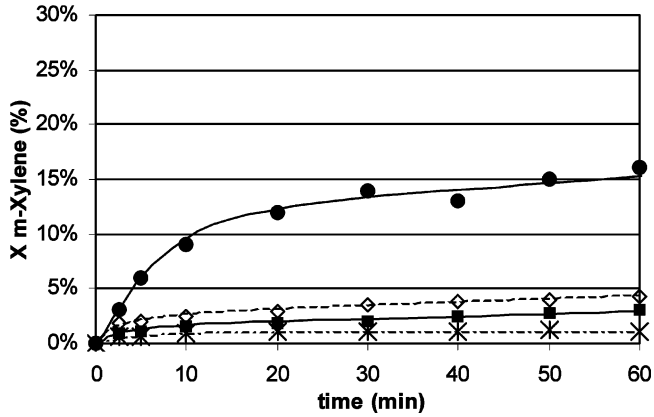


Fig. 4. Effect of inhibiting agents on the conversion of *m*-xylene. Simultaneous addition of zeolite, AA and *m*-xylene (●); addition of zeolite and AA and, after 1 h aging at 373 K, addition of *m*-xylene (◇); simultaneous addition of zeolite, AA, *m*-xylene and 3.5 mmol of DHA (■); simultaneous addition of zeolite, AA, *m*-xylene and 7 mmol of acetic acid (×).

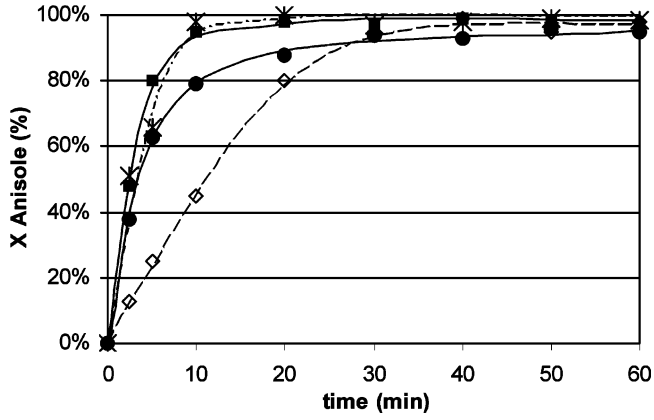


Fig. 5. Effect of inhibiting agents on the conversion of anisole. Simultaneous addition of zeolite, AA and anisole (●); addition of zeolite and AA and, after 1 h aging at 373 K, addition of anisole (◇); simultaneous addition of zeolite, AA, anisole and 3.5 mmol of DHA (■); simultaneous addition of zeolite, AA, anisole and 7 mmol of acetic acid (×).

To confirm these observations, AA, the solvent, and the activated zeolite were mixed without the substrate at the reaction temperature for a period of 60 min. The substrates were then added and the reaction was followed as a function of time. The 1 h "aging" of AA on the zeolite led to a significant decrease in the rate of *m*-xylene acetylation (Fig. 4). On the other hand, the same treatment had only a small inhibiting effect on the initial rate of anisole acetylation, and a full conversion of the substrate was obtained after 60 min (Fig. 5). It is worth highlighting that, after the 1 h "aging" of AA and before the substrate addition, a partial consumption of AA with acetic acid formation was recorded. This consumption could be due to the interaction of AA with the activated zeolite with formation of the active acylating species and of AA derivatives from these species. Several active acylating species have been postulated to be formed: acylium ions [16], electrophilic complexes between AA and zeolitic Brønsted acid sites [17], or ketene molecules [28].

All of them may play a role not only in the arene acetylation, but also in the formation of the AA derivatives.

Another series of experiments was carried out to determine the inhibiting effect of the products formed during the acetylation of poorly activated or nonactivated substrates on anisole transformation. Thus *m*-xylene was acetylated under typical conditions for 60 min, and, after that time, an aliquot (7 mmol) of fresh anisole was added to the reaction mixture without the addition of fresh AA. As soon as anisole was added, a high rate of methoxyacetophenone formation was detected, and, after the following 60 min, the anisole conversion was close to the maximum value (ca. 80%) expected from the residual amount of AA after *m*-xylene transformation. A similar behaviour was observed with the addition of anisole to the fluorobenzene reaction mixture: the H-BEA zeolite was completely nonactive towards fluorobenzene acetylation, but the addition of fresh anisole (without the addition of fresh AA) gave rise to rapid formation of methoxyacetophenone. Such observations show that the inhibiting species, which are formed on the catalyst surface, are able to stop the acetylation of weakly activated substrates but unable to stop that of anisole. Thanks to their high polarity and hydrophilicity and to the presence of an electron-rich coordinating oxygen atom, the molecules of anisole are probably able to compete with the AA derivatives and the acetic acid molecules for access to the hydrophilic zeolite micropores and to the acidic protonic sites, which is not the case for *m*-xylene and fluorobenzene molecules.

4. Conclusions

The initial rate and stability of acetylation of aromatic substrates with acetic anhydride over a H-BEA zeolite were shown to be very dependent on the substrate. Thus the initial rate of anisole acetylation is 340 times greater than that of fluorobenzene acetylation; the decrease in rate with reaction time is much faster in the latter case than in the former one. The reactivity of the aromatic compounds is primarily controlled by electronic factors: activating substituents on the aromatic ring have a strong positive influence on the reactivity of the substrates, deactivating substituents, a strong negative influence. Diffusion limitations play a more limited role, as shown by the small decrease in the acetylation rate from the monocyclic to the bicyclic aromatic substrates.

The decrease in acetylation rate is mainly due to an inhibiting effect of the products of acetic anhydride transformation: acetic acid and condensation products. Such an effect is small in the acetylation of substrates such as anisole, which are highly polar and hydrophilic and can therefore favourably compete with the inhibiting species to enter the H-BEA zeolite micropores and approach the active sites. On the other hand, it is very pronounced with hydrophobic substrate molecules such as methyl- and fluorosubstituted aromatics, which cannot easily enter the zeolite micropores in presence of the inhibiting species.

From a practical point of view, the acidic zeolites (especially the BEA zeolite) are a viable alternative to Friedel–Crafts catalysts, insofar as very activated and polar aromatic substrates are used. In contrast, whenever poorly activated or nonactivated substrates are concerned, the rapid decrease with time of the acetylation rate could represent a major drawback in the development of zeolite-catalysed acetylation processes.

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