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Journal of Molecular Catalysis A: Chemical 159 (2000) 377–388

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

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Acetylation of 2-methoxynaphthalene with acetic anhydride over a HBEA zeolite

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Received 15 February 2000; accepted 27 March 2000

Abstract

Acetylation of 2-methoxynaphthalene (2MN) with acetic anhydride (AA) was carried out over a HBEA 15 zeolite (framework Si/Al ratio of 15) under the following conditions: batch reactor, 500 mg of zeolite, 35 mmol of 2MN and 7 mmol of AA, 4 cm^3 of solvent, temperature of 90°C, 120°C or 170°C (generally 120°C). In addition to acetic acid, the main reaction products are 1-acetyl-2-methoxynaphthalene (I) and 2-acetyl-6-methoxynaphtalene (II); 1-acetyl-7-methoxynaphthalene (III) is formed in low amounts and 2-acetyl-3-methoxynaphthalene (IV) in trace amounts. I, which initially is preferentially formed, undergoes isomerization into II and III and also deacylation afterwards. However, high yields into isomer II, which is a precursor of the anti-inflammatory Naproxen, can be obtained by operating at relatively high temperatures ($\geq$ 170°C) in the presence of a solvent of intermediate polarity such as nitrobenzene. The solvent polarity has a significant effect on the reaction rates and on the selectivity to acetylation, isomerization and deacylation. Very polar solvents such as sulfolane, which compete with the reactant molecules for diffusion inside the zeolite micropores and for adsorption on the acid sites, reduce significantly the reaction rates. Low acetylation and isomerization rates and high deacetylation rates are found with non-polar solvents, such as 1-methylnaphthalene which cannot solvate the acylium ion intermediates. Adsorption experiments suggests that all the acetylmethoxynaphthalene products are mainly formed inside the zeolite micropores.

Keywords: 2-Methoxynaphthalene; Acetylation; HBEA; Solvent effects; 1-Acetyl-2-methoxynaphthalene isomerization

1. Introduction

Aromatic ketones are important intermediates in the synthesis of fragances and pharmaceuticals. Indeed, many synthetic fragances of the musk type contain an acetyl group while the synthesis of various pharmaceuticals such as Paracetamol, Ibuprofen, Naproxen etc… involves acylation of aromatics [1–4]. Acylation processes are generally carried out in batch reactors by using acid metal chlorides such as $AlCl_3$ as catalysts and acid chlorides as acylating agents. As the aryl ketone forms a 1:1 molar adduct with the catalyst, more than stoichiomet-

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1381-1169/00/$ - see front matter
PII: S1381-1169(00)00225-9

ric amounts are required. The recovery of the products requires a hydrolysis step with the destruction of the catalyst and production of a large amount of valueless salts (more than 4 mol of Cl^- per mol of ketone produced). Therefore, the substitution of these polluting and corrosive solutions by solid acid catalysts such as zeolites which do not present these inconveniences is most attractive. Besides the environmental improvement, heterogeneous catalysis has many technical advantages: easy separation of products, possibility of developing continuous processes, of regenerating the catalyst, etc... The potential of zeolite catalysts for acylating various aromatics by acetic anhydride (AA) has been well demonstrated [5–22]. In particular, BEA zeolites were found to be efficient catalysts for the selective synthesis of *p*-methoxyacetophenone by acetylation of anisole [14] and FAU zeolites for the selective synthesis of 3,4-dimethoxyacetophenone by veratrol acetylation [15].

This paper deals with the acetylation of 2-methoxynaphthalene (2MN) with AA over a HBEA zeolite. Acylation at the 6-position (Fig. 1) is of particular interest, 2-acetyl-6-methoxynaphthalene (II, Fig. 1) being a precursor of the anti-inflammatory Naproxen [16]. Acetylation of 2MN has been carried out over various acidic zeolites: FAU [17,18], MFI, MOR [18], MTW [17], BEA [17,19,20], mesoporous MCM41 molecular sieves [21] and clays [18,22]. Generally, acetylation occurs preferentially at the kinetically controlled 1-position with formation of 1-acetyl-2-methoxynaphthalene (I, Fig. 1). Differences in selectivity observed between zeolites such as FAU, BEA and MTW [17] were interpreted by shape selectivity effects. Thus, the more favourable formation of the more linear isomer II molecules with HBEA compared with HFAU was proposed to be due to pronounced steric constraints in the narrow pores of HBEA [17]. Afterwards, it has been proposed that only the linear isomer II could be formed in the micropores of HBEA, the bulky isomer I being formed on the outer surface of the crystallites which is known to be up to one third of the total surface area [19]. On the other hand, secondary reactions of isomer I were demonstrated on HBEA [17]. These secondary reactions: migration of the acetyl group from the 1- to the 6-position (i.e. isomerization of I into II) and protodeacylation of isomer I, allow the selective formation of the thermodynamically stable 6-

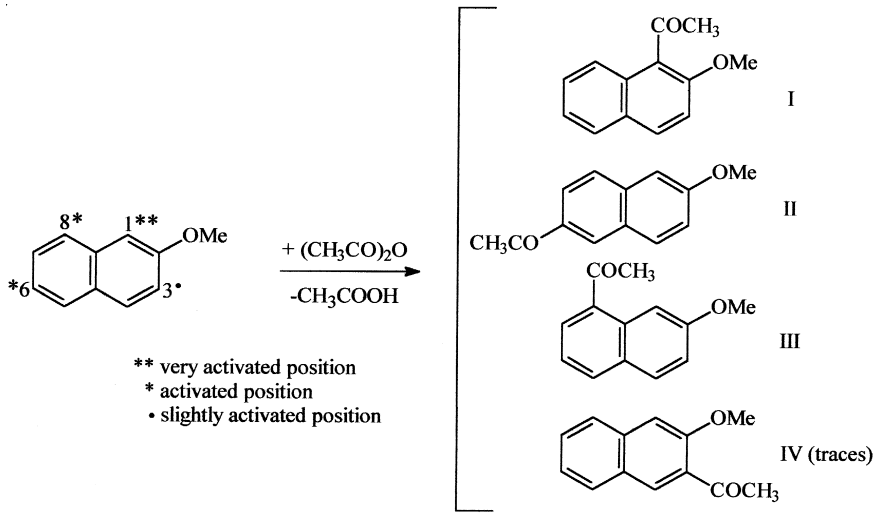


Fig. 1. Acetylation of 2-methoxynaphthalene (2MN). Reaction products.

acylated product (II). Recently, the isomerization of I into II was shown to occur through an intermolecular transacylation mechanism, the acetyl group being transferred from molecules of I to molecules of 2MN [23].

As the melting point of 2MN and acylated products is very high, acetylation of 2MN was carried out in a batch reactor and in presence of a solvent. The effect of the solvent polarity on the activity and the selectivity of the HBEA zeolite was firstly examined. Afterwards, the influence of the operating conditions in the chosen solvent (nitrobenzene) was determined, which allowed us to confirm the possibility of a selective formation of II (Fig. 1). The location of acetylation and isomerization steps, either inside the zeolite micropores or on the outer surface of the crystallites was also discussed.

2. Experimental

The HBEA zeolite (total and framework Si/Al ratios of 11 and 15.5, respectively), was provided by PQ Zeolites (CP 811-DL-25). Its physicochemical characteristics (porosity and acidity) were already reported [24,25].

2.1. Acetylation of 2MN

The reactions were carried out in a flask equipped with a cooler and a magnetic stirrer (500 rpm). The standard conditions were the following: temperature of 120°C, 500 mg of catalyst previously activated at 500°C overnight under dry air flow, solution containing 35 mmol of 2MN ($C_{2MN} = 3.43$ mol l^{-1}) and 7 mmol of AA ($C_{AA} = 0.68$ mol l^{-1}) and 4 cm^3 of solvent (generally nitrobenzene but also sulfolane or 1,2-dichlorobenzene or 1-methylnaphthalene). The E_T parameter defined by Dimroth and Reichardt [26,27] was used for characterising the solvent polarity. E_T derives from spectroscopic measurements based on a solvent-sensitive standard compound adsorbing light in spectral ranges corresponding to UV/Vis-, IR-, ESR-, and NMR-spectra. The effect of operating was determined in nitrobenzene solvent.

Time zero of the reaction was taken as the time of introduction of the zeolite in the reactant mixture heated at the reaction temperature. Small samples of the reaction mixture (0.1 cm^3) were taken periodically and analysed by GC on a capillary CP Sil 8 CB column. Identification of the products was carried out by using reference samples or by mass spectrometry.

The conversion of 2MN into acetylated products (isomers I, II, III (1-acetyl-7-methoxynaphthalene), Fig. 1) is taken as

$$X_R = \frac{\%(I,II)}{(\%2MN + \%I + \%II + \%III)} * 100$$

the yields into I, II or III as the conversion of 2MN into I, II and III. It should be emphasized that at the beginning of the reaction, a small part of AA is hydrolysed into acetic acid. Therefore, the conversion of AA into acetylated products was taken as

$$X = \frac{X_{2MN}}{X_{2MN}\text{max}} * 100 \quad \text{with}$$

$$X_{2MN}\text{max} = \frac{\%AA + \%(I + II + III)}{\%2MN + \%(I + II + III)} * 100$$

Up to total conversion of AA, X_{2MN}max can be considered as constant and is generally greater than 90% of the value calculated from the reactant mixture that was prepared. However, after total conversion of AA, there is a decrease in X_{2MN}max due to deacylation of I, II and III.

2.2. Adsorption experiments of I and 2MN

500 mg of a HBEA15 was added at 120°C in a stirred mixture of 2MN (20 mmol), isomer I (4 mmol) in nitrobenzene or in sulfolane (1 ml). After a 4-min reaction, the reaction mixture is

filtered to remove the solid catalyst. In order to recover the organic material on the external surface of the zeolite (or in the mesopores), the catalyst was treated in a soxhlet for 1 h with dichloromethane. Then, 300 mg of the HBEA zeolite was dissolved in a 40% solution of hydrofluoric acid. Threefold extraction with dichloromethane was carried out. All the carbonaceous compounds were found to be soluble in dichloromethane. After evaporation of the solvent, the carbonaceous components were weighted and analysed by GC-MS.

Isomer I, used in adsorption experiments, was synthesized according to Ref. [28] by reacting 1-acetyl-2-hydroxynaphthalene (1 eq.) with Me_2SO_4 (1 eq.) in the presence of K_2CO_3 (1 eq.) using acetone as a solvent (54 eq.) under stirring at room temperature for 24 h. The product was recovered and recristallised in petroleum ether (yield of 83%).

3. Results

Most of the experiments were carried out under the following conditions: batch reactor, 35 mmol of 2MN and 7 mmol of AA, 4 cm^3 of solvent (i.e. concentrations of 2MN and AA of 3.43 and 0.68 mol l^{-1}, respectively), 500 mg of zeolite, temperatures of 90°C, 120°C or 170°C (generally 120°C). Acetylation of 2MN leads to three isomers indicated as I, II , III in low amounts and to acetic acid. The other isomers and particularly the one that corresponds to the slightly activated 3-position of 2MN (Fig. 1) are observed in trace amounts.

3.1. Influence of the solvent

Acetylation of 2MN was carried out at 120°C with different solvents: sulfolane, nitrobenzene, 1,2-dichlorobenzene and 1-methylnaphtalene. Whatever the solvent, I, II and III appear as primary products, isomer I being largely predominant (Fig. 2). Initially, isomer I is formed at the same rate in sulfolane and in 1,2-dichlorobenzene and more slowly in nitrobenzene (1.2 times) and particularly in 1-methylnaphthalene

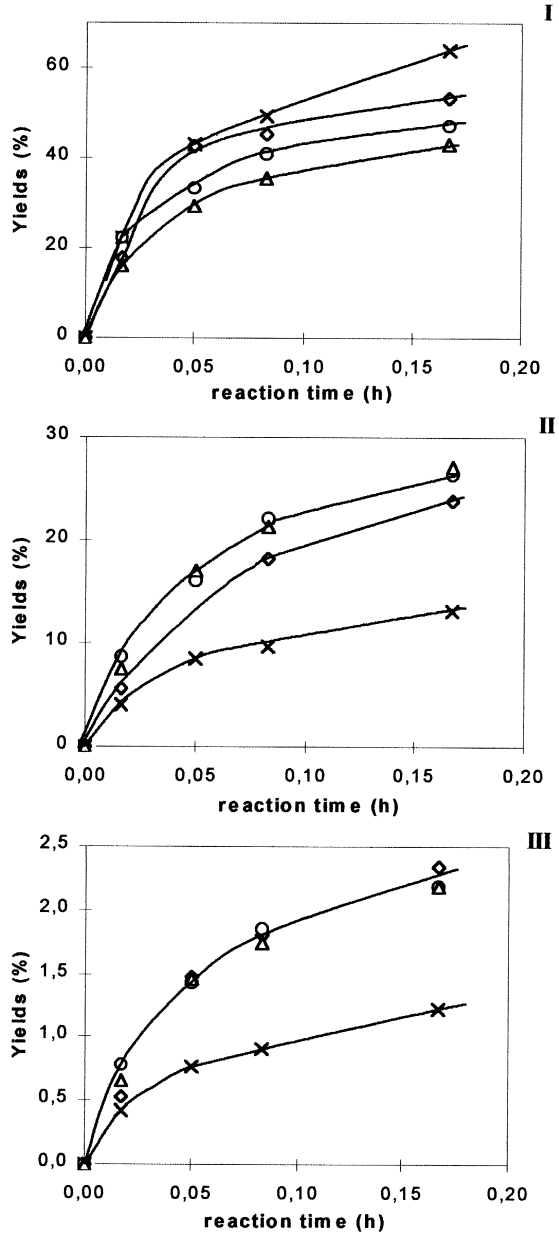


Fig. 2. Acetylation of 2-methoxynaphthalene with acetic anhydride in various solvents: sulfolane (×), nitrobenzene (◇), 1,2-dichlorobenzene (○) and 1-methylnaphthalene (△). Yields in 1-acetyl-2-methoxynaphthalene (I), 2-acetyl-6-methoxynaphthalene (II), 1-acetyl-7-methoxynaphthalene (III) vs. reaction time.

Table 1
Acetylation of 2MN with acetic anhydride in various solvents, E_T is the solvent polarity parameter proposed by Dimroth and Reichardt [26,27]. Initial rates (r_o) of formation of acetyl–methoxynaphthalene isomers I, II, III and rate ratios

Solvent	E_T	r_o^a (I + II + III)	r_o^a I	r_o^a II	r_o^a III	r_o I/r_o II	r_o I/r_o III
Sulfolane	0.410	184	153	28	3	5.5	51
Nitrobenzene	0.324	175	130	41	3.8	3.2	34
1,2-Dichlorobenzene	0.225	224.5	157	62	5.5	2.5	28.5
1-Methylnaphthalene	0.142	163.5	108	51	4.5	2.1	24
Without solvent	×	122.2	133.5	48	10.7	2.8	12.5

[a] r_o (mmol h^{-1} g^{-1}).

(1.4 times). On the other hand, the rates of formations of II and III are approximately 1.2 times lower in 1-methylnaphthalene than in 1,2-dichlorobenzene, 1.5 times lower in nitrobenzene and two times in sulfolane (Fig. 2 and Table 1). The ratio between the initial rates of formation of I and II passes from 5.5 in sulfolane to 3.2 in nitrobenzene, 2.5 in 1,2-dichlorobenzene and 2.1 in 1-methylnaphthalene, hence decreases with E_T (Table 1), the solvent polarity parameter proposed by Dimroth and Reichardt [26,27]. It is also the case for the ratio between the rates of formation of I and III isomers (Table 1).

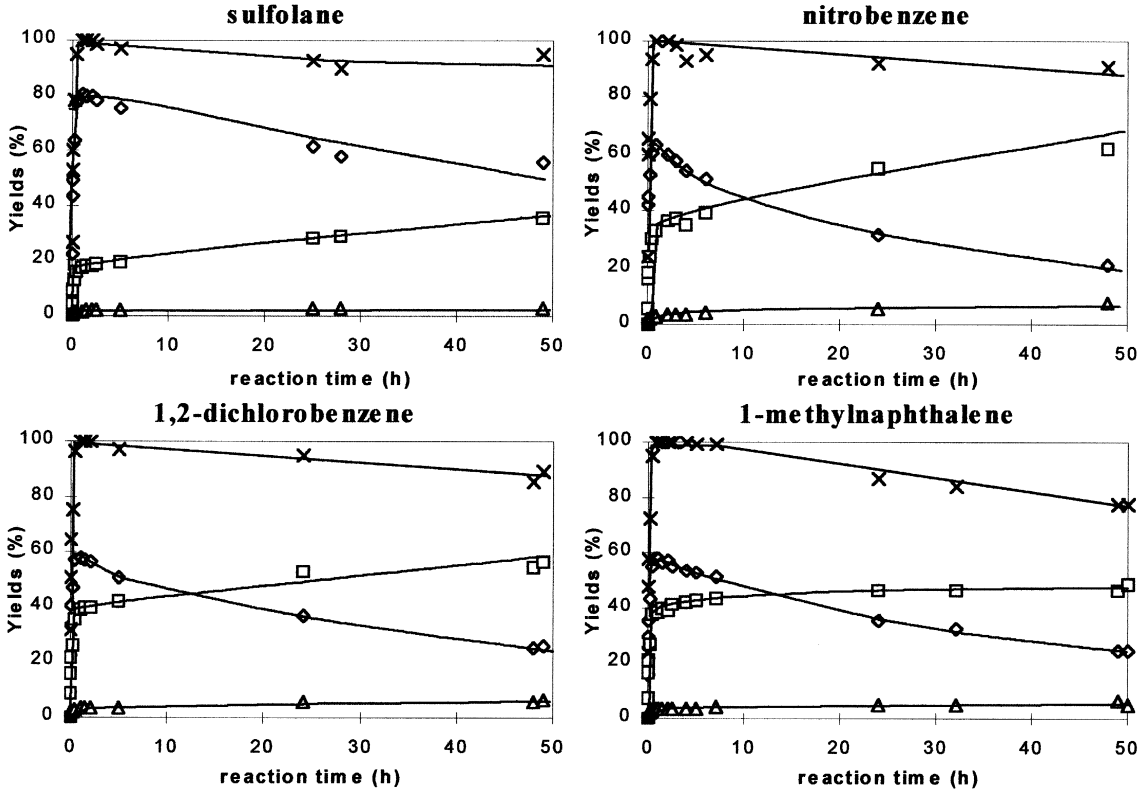


Fig. 3. Acetylation of 2-methoxynaphthalene with acetic anhydride in various solvents. Total yield in acetyl–methoxynaphthalene (I + II + III) (×) and yields in isomers I (◇),II (□),III (△).

A complementary experiment was carried out in the absence of solvent, hence with higher concentrations of 2MN and AA, 5.65 and 1.15 mol l^{-1}, respectively. The initial rates of formation of I and II were found to be similar to those measured in nitrobenzene, whereas the rate of formation of isomer III was 2.8 times higher (Table 1).

Whatever the solvent, a complete conversion of AA and a 100% yield in isomers I, II and III are obtained after a 45–60-min reaction. At longer times, a decrease in this yield is observed, which indicates a deacylation of the acetyl–methoxynaphthalene isomers (Fig. 3). However, Fig. 3 shows that this deacylation is accompanied by a faster isomerization of I into isomers II and III. This isomerization is clearly shown in Table 2 in which is reported the change in the distribution of acetyl–methoxynaphthalene isomers as a function of reaction time: whatever the solvent, the percentage of I in the I, II, III mixture decreases significantly. It should be remarked that part of the decrease in the percentage of I could be due to a preferential deacylation of this product. The rate of deacylation of I in nitrobenzene was furthermore found to be about twice greater than the rate of deacylation of II.

However, even if it is considered that only isomer I undergoes deacylation, this reaction can only be responsible for part of the decrease in the percentage of I. Indeed, the decrease in the yield in isomer I is always more pronounced than the decrease in the total yield (I + II + III). The difference is very large with the more polar solvent. Thus, in sulfolane, the yield in I decreases from 80.6% at total conversion of AA (at 1 h) to 56.1% at 50 h, i.e decrease of 24.5%, whereas the total yield decreases only by 4.9%. Likewise, in nitrobenzene the yield in I decreases by 42.3%, the total yield only by 9.1%. On the other hand, with the less polar solvents,

Table 2
Acetylation of 2MN with AA. Distribution of acetyl–methoxynaphthalene isomers (I, II and III), total yield, yields in I and II + III as a function of reaction time

Solvent	Reaction time (h)	Distribution (%)			Yield (%)		
		I	II	III	Total	I	(II + III)
Sulfolane	0	83.5	14.8	1.7	0	0	0
	1	80.6	17.7	1.7	100	80.6	19.4
	25	66.2	30.6	3.2	92.6	61.3	31.3
	50	59	37.6	3.4	95.1	56.1	39.0
Nitrobenzene	0	75.5	22.5	2.0	0	0	0
	0.75	63.6	33.2	3.2	100	63.6	36.4
	25	34.3	59.4	6.3	91.9	31.5	60.4
	50	23.4	68.4	8.2	90.9	21.3	69.6
1,2-Dichlorobenzene	0	71.7	26	2.3	0	0	0
	0.75	57.8	38.9	3.3	100	57.8	42.2
	25	38.9	55.3	5.8	95	36.9	58.1
	50	29.8	63.1	7.1	85.7	25.5	61.3
1-Methylnaphthalene	0	67.5	29.9	2.6	0	0	0
	0.75	57.8	38.9	3.3	100	57.8	42.2
	25	40.5	53.3	6.2	87	35.2	51.8
	50	31.3	62	6.7	77.9	24.4	53.5
Without solvent	0	70.5	23	6.5	0	0	0
	0.5	57.3	40.5	4.3	100	57.3	42.7
	24	22.1	65.7	12.2	65.3	14.4	50.9

the difference is more limited: i.e with 1,2-dichlorobenzene the yield in I decreases by 32.3%, the total yield by 14.7%, with 1-methylnaphthalene by 33.4% and 22.1%, respectively. The difference is even weaker in the absence of solvent: the yield in I decreases by 42.9% from 0.5 h (total conversion of AA), the total yield by 34.7%. Therefore, it can be concluded that in the absence of solvent as well as in the presence of 1-methylnaphthalene, deacylation is the main reaction, whereas in the presence of the more polar solvents it is the isomerization of I into II and III.

The percentage of deacylation of acetyl–methoxynaphthalenes (I, II, III) was taken as the decrease in the total yield in (I + II + III) after total conversion of AA (100% yield in I + II + III). On the other hand, in order to estimate the conversion of I into isomers II and III, it was supposed that only I undergoes deacylation and that the isomerization of I before total conversion of AA could be neglected, which is not the case with the less polar solvents: large change of the I, II, III distribution at short reaction times (Table 2). The conversion in isomerization was therefore taken as the decrease in the yield of II plus III after total conversion of AA.

Fig. 4a shows that whatever the solvent, deacylation increases with reaction time. At long reaction times, deacylation is very significant in the absence of solvent or with 1-methylnaphthalene and of lower and similar significance with the other solvents. On the other hand, the conversion of I into isomers II and III (X_I) is greater in nitrobenzene than in the other solvents (Fig. 4b and c). At the 50-h reaction, X_I nitrobenzene > X_I dichlorobenzene > X_I sulfolane > X_I 1-methylnaphthalene. The isomerization rates can be estimated from the initial slopes of the curves in Fig. 4b. They are equal to 0.07 mmol h^{-1} g^{-1} in sulfolane, 0.175 in nitrobenzene, 0.12 in dichlorobenzene, 0.13 in 1-methylnaphthalene. However, there is a rapid decrease in the rate of isomerization in dichlorobenzene, and more especially in 1-methylnaphthalene (Fig. 4b).

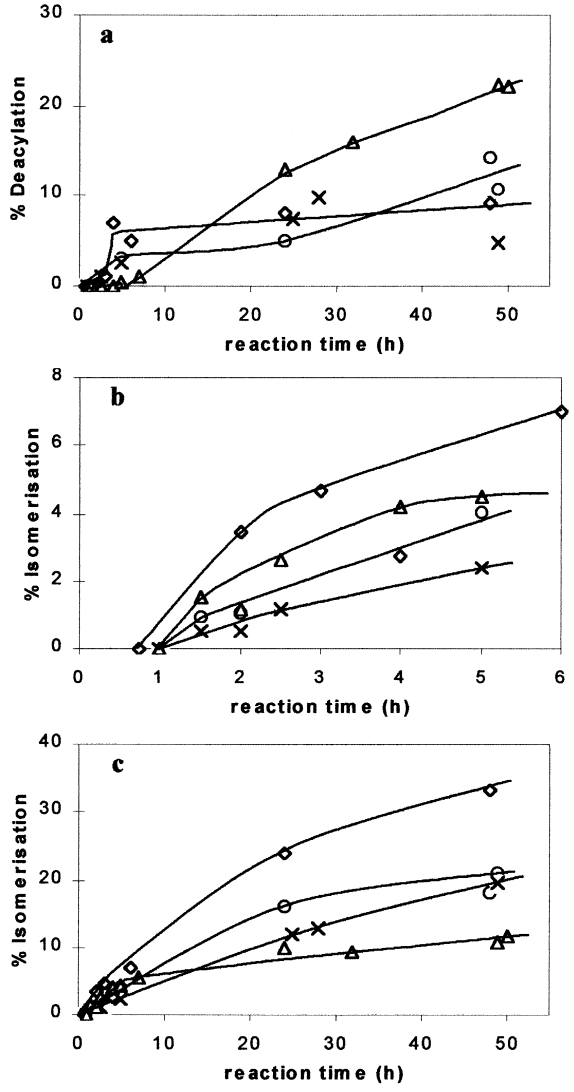


Fig. 4. Acetylation of 2-methoxynaphthalene with acetic anhydride in various solvents: sulfolane (×), nitrobenzene (◇), 1,2-dichlorobenzene (○) and 1-methylnaphthalene (△). Percentages in deacylation of acetyl–methoxynaphthalene isomers I + II + III (a) and in isomerization of 1-acetyl-2-methoxynaphthalene (I) (b and c) vs. reaction time.

3.2. Influence of operating conditions

The initial rates of formation of I, II, III were compared at 120°C with nitrobenzene as a solvent for standard conditions of concentrations $C_{2MN} = 3.43$ mol l^{-1}, $C_{AA} = 0.68$ mol l^{-1}, $C_{nitrobenzene} = 3.84$ mol l^{-1} and for the following concentrations, $C_{2MN} = 4.27$ mol l^{-1}, C_{AA} =

0.85 mol l^{-1}, $C_{nitrobenzene}$ = 2.37 mmol l^{-1}. Table 3 shows that the reaction rates were greater in the latter conditions, indicating a positive order with respect to 2MN and with respect to AA (and eventually a negative order with respect to nitrobenzene). However, this change in operating conditions has practically no effect on the initial product distribution and on the percentages of deacylation and isomerization after total conversion of AA.

The reaction temperature has a large effect on the initial distribution of the acetyl–methoxynaphthalene isomers as well as on the extent of deacylation and isomerization after complete conversion of AA (Table 4). The lower the reaction temperatures, the higher the initial selectivity to isomer I and the lower the selectivity to II and III, which means that the activation energy is greater for the production of II and III than for that of I (ΔE = 20–30 kJ mol^{-1} between I and II + III). Deacylation, which is limited at 90–120°C (10–15% in 24 h), becomes very fast at 170°C (23.7% in 4 h). Furthermore, isomerization, which is very slow at 90°C (3% in 24 h), increases rapidly with temperature. At 170°C, I can be completely converted after 4 h with a final yield in isomers II and III greater than 75% (Table 4); the maximum value of the yield in II + III (83%) was obtained after a 30-min reaction.

Table 3
Acetylation of 2MN with AA at 120°C under conditions: (1) C_{2MN} = 3.43 mol l^{-1}, C_{AA} = 0.68 mol l^{-1}, $C_{nitrobenzene}$ = 3.84 mol l^{-1} and under conditions; (2) C_{2MN} = 4.27 mol l^{-1}, C_{AA} = 0.85 mol l^{-1}, $C_{nitrobenzene}$ = 2.37 mol l^{-1}. Distribution of acetyl–methoxynaphthalene isomers (I, II and III), total yield, yields in I and II + III as a function of reaction time

Reaction time (h)	Distribution (%)			Yield (%)		
	I	II	III	Total	I	(II + III)
120°C, Condition 1						
0	75.5	22.5	2.0	0	0	0
0.75	63.6	33.2	3.2	100	63.6	36.4
25	34.3	59.4	6.3	91.9	31.5	60.4
50	23.4	68.4	8.2	90.9	21.3	69.6
120°C, Condition 2						
0	71.5	25.5	3.0	0	0	0
0.33	63.7	33.1	3.2	100	63.7	36.3
24	32.1	61.1	6.8	84.8	27.2	57.6
50	18.6	72.2	9.2	76.6	14.3	62.3

Table 4
Acetylation of 2MN with AA at various temperatures. Distribution of acetyl–methoxynaphthalene isomers (I, II and III), total yield, yields in I and II + III as a function of reaction time

Temperature	Reaction time (h)	Distribution (%)			Yield (%)		
		I	II	III	Total	I	(II + III)
90°C							
	0	88.8	8	3.2	0	0	0
	1	81.0	16.6	2.4	100	81	18.6
	24	74.5	21.7	3.8	84.3	62.8	21.5
120°C							
	0	75.5	22.5	2.0	0	0	0
	0.75	63.6	33.2	3.2	100	63.6	36.4
	25	34.3	59.4	6.3	91.9	31.5	60.4
170°C							
	0	50	46.5	3.5	0	0	0
	0.17	29.2	65.3	5.5	100	29.2	70.8
	4	0.2	86.9	12.9	76.3	0.15	76.15

4. Discussion

The operating conditions that were used here, liquid phase with or without solvent, temperature between 90°C and 170°C, direct acetylation of 2MN with AA over HBEA15, lead predominantly to 1-acetyl-2-methoxynaphthalene (I), despite that this compound is thermodynamically unfavoured with respect to the other acetylated products and, in particular, to the desired one: II. This preferential acylation of 2MN in position 1 was observed with various catalysts: acidic chlorides such as $AlCl_3$ and $InCl_3$ [28,29], less acidic chlorides such as $MnCl_2$ [28] at higher temperatures, zeolites [17–20,23], clays [18,22] and mesoporous aluminosilicates [21].

The greater reactivity in position 1 can be related to the lower charge density of carbon 1 (−0.21) compared to carbon 6 (−0.14) and carbon 8 (−0.13) [29]. Acetylation is followed by a very slow isomerization of I into II and III:

1000 times slower than acetylation in nitrobenzene at 120°C.

4.1. Optimal conditions for the synthesis of II

The total rate of acetylation is slightly greater in dichlorobenzene than in the other solvents (1.2 to 1.4 times): the initial selectivity to isomer II is better in 1-methylnaphthalene, but much better results are observed in isomerization of I in nitrobenzene (Fig. 3). Increasing concentrations of 2MN and AA in nitrobenzene leads to an increase in the rate of acetylation without changing its selectivity, but also to a decrease in the isomerization/deacylation rate ratio (Table 3). On the other hand, as expected from the higher thermodynamic stabilities of II and III with respect to I, the selectivity of acetylation to II and III significantly increases with reaction temperature. Moreover, this temperature increase causes a significant increase in isomerization rate but also in deacylation rate. However, at complete isomerization of I, a yield into II and III greater than 75% (83% at the maximum) can be obtained at 170°C. Therefore, isomer II, which is a precursor of (*S*)-Naproxen can be obtained selectively by liquid phase acetylation of 2MN with AA over a HBEA zeolite at high temperatures ($\geq$ 170°C).

4.2. Solvent effects

In the liquid phase synthesis of functional compounds, solvents are often used for practical reasons: solubilization of reactants and products, heat transfer with exothermic reactions etc... However, solvents can also play a direct role in the reaction, increasing the rate, the stability and the selectivity of the process [30–34].

A large effect of solvent is shown here in the acetylation of 2MN by AA. Thus, the initial rate and especially the initial selectivity depend on the solvent: acetylation is faster in 1,2-dichlorobezene than in the other solvents, hence is faster for a solvent of average polarity (see E_T in Table 1). Furthermore, the selectivity to the desired product (isomer II) increases when the solvent polarity (given by E_T) decreases. The secondary reactions undergone by acylation products (deacylation and isomerization) also depend on the solvent. At long reaction times, the highest yield in isomer II is obtained with nitrobenzene, a solvent of intermediate polarity. With more polar as well as with less polar solvents, II is obtained in lower amounts but for different reasons:

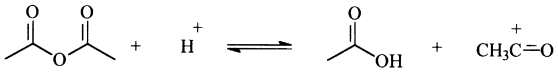
- In a very polar solvent such as sulfolane ($E_T = 0.41$), isomerization of I and deacylation are very slow.
- In a less polar solvent (e.g. 1-methylnaphthalene) or in the absence of solvent, the low yields in II are due both to a faster deacylation of acetyl–methoxynaphthalene isomers and to a slower isomerization process.

The effect of solvent polarity on the rates of acetylation and isomerization is similar to the one found by Espeel et al. [32] in phenol alkylation with cyclohexene over zeolites: the highest rates are obtained at intermediate solvent polarity. A very polar solvent, such as sulfolane, competes with the reactant molecules for diffusion inside the pores and for adsorption on the acid sites, reducing therefore the rates of the main reaction. It inhibits the secondary transformation of the primary products, for these products are rapidly expelled from the zeolite. Such competitive effects have also been found to play a significant role in Fries rearrangements [33] as well as in acetylation of phenol with phenyl acetate [34]. On the other hand, in the less polar solvents, the residence time of the primary products in the zeolite pores is very long with, as a consequence, a significant deacylation process; hence, an apparently slower isomerization.

However, the following two other parameters have to be considered.

(1) As shown in phenol acetylation with phenylacetate [34], solvents can also favour the dissociation of the acylating agent by solvating

the acylium ions. This solvation would displace to the right the thermodynamic equilibrium of reaction (1):



(1)

The more polar the solvents, the more significant the solvation and the higher the concentration of acylium ions; hence, the faster the acetylation. This solvation increase could explain the increase in the rates of acetylation of 2MN and isomerization of I from 1-methylnaphthalene to 1,2-dichlorobenzene.

(2) The HBEA zeolite having a large external surface area [19,20], part of the reactions could occur on the outer surface. Furthermore, based on adsorption experiments of I and II isomers, Harvey et al. [19] proposed that the bulky isomer I can only be formed on the outer surface whereas the linear isomer II would be formed on the outer and on the inner acid sites. This proposal would allow us to explain the increase in the I/II ratio with the solvent polarity (Table 1). Indeed, as emphasized above, a polar solvent limits the entrance of the reactant molecules inside the zeolite pores, hence should limit preferentially the formation of isomer II. However, molecular modelling [35] shows that isomer I can easily lodge in the pores of HBEA zeolite (minimum interaction energy of -27.4 kcal/mol), hence can be formed on the inner acid sites. Along the straight channel, the interaction energy is always negative (barrier of diffusion of approximately 10 kcal mol^{-1}), which suggests that the molecules of I can diffuse inside the pores and desorb from these pores.

Moreover, the following adsorption experiments allowed us to confirm that isomer I can enter the micropores of the HBEA15 zeolite. HBEA15 was added at 120°C in a stirred mixture of 2MN, isomer I in nitrobenzene or in sulfolane. The composition of the reaction mixture at a 4-min reaction can be compared to those of the products recovered by soxhlet treatment with dichloromethane and of the products blocked inside the pores (''coke''), which can be recovered in dichloromethane only after dissolution of the zeolite in a hydrofluoric solution (Table 5).

Whatever the solvent, isomer I is found in ''coke'', hence, can enter the micropores. Therefore, the proposal of formation of isomer I only on the outer acid sites of HBEA can be rejected. Moreover, the percentages of II and III in the acetyl–methoxynaphthalene (AMN) mixture are greater in ''coke'' than in Ext and MR, which suggests that I isomerization occurs mainly inside the micropores. Furthermore, whereas the compositions of Ext and MR are similar, the composition of ''coke'' is completely different and depends very much on the solvent. With nitrobenzene solvent, the percent-

Table 5
Reaction of 2MN with I at 120°C. Composition (wt.%) of the reaction mixtures (RM) at a 4-min reaction, of the mixtures obtained by soxhlet treatment, of the recovered catalysts (Ext) and of ''coke''

Solvent	Nitrobenzene			Sulfolane		
	RM	Ext	''Coke''	RM	Ext	''Coke''
Solvent	18.4	17.5	2.8	15.4	15.8	75.2
2MN	70.3	72.3	70	72.6	71.5	17.7
Acetyl–methoxynaphthalene I + II + III	11.3	10.2	14.1	12	12.9	7.1
I	10.6	9.6	12.0	12	12.6	6.5
II	0.6	0.3	1.8	0.06	0.2	0.5
III	0.1	0.3	0.3	0	0.1	0.1
Others	0	0	13	0	0	0

age of 2MN in ''coke'' is slightly greater than in Ext and MR; the one of AMN is 1.5 times greater, whereas the one of nitrobenzene is six times smaller (Table 5). This indicates that 2MN and especially AMN are more strongly adsorbed on the zeolite than nitrobenzene, which, therefore, should have no inhibiting effect on 2MN acetylation. On the other hand, with sulfolane, the percentages of AMN and especially of 2MN in ''coke'' are smaller than in Ext and MR, whereas the one of sulfolane is greater (Table 5). This suggests that this polar solvent limits the entrance in the micropores of less polar molecules such as I and especially 2MN.

4.3. Influence of the operating conditions

Since nitrobenzene has no inhibiting effect on acetylation, the positive effect of the increase in the concentrations of 2MN and AA (Table 3) is only due to this increase. A total reaction order of 1.8 was obtained. This reaction order is in agreement with a mechanism involving as a limiting step the attack of 2MN molecules in liquid phase by acylium ions in low amounts on the catalyst.

The positive effect of temperature on the selectivity to isomer II could be expected, the attack of acylium ions in position 6 being more difficult, hence, requiring a greater activation energy than the attack in the very activated position 1 [28].

5. Conclusion

Liquid phase acetylation of 2MN by AA leads preferentially to I, this compound being afterwards transformed into III and especially into II, which is a precursor of Naproxen [16]. Unfortunately, the isomerization is generally accompanied by deacylation of isomer I but also of isomers II and III into 2MN. High yields in isomer II can, however, be obtained over a commercial HBEA zeolite by operating at relatively high temperature ($\geq 170^{\circ}C$) and in presence of a solvent of intermediate polarity such as nitrobenzene.

As recently underlined by Derouane et al. [13], competitive adsorption effects play a major role in the liquid phase synthesis of polar compounds such as acetoxymethoxynaphthalenes, and more generally fine chemicals on zeolite catalysts and zeolites should be considered not only as catalysts but also as solid solvents. This competition explains the significant effect that the solvent polarity has on the rate and selectivity of direct acetylation as well as on the rates of subsequent reactions of isomerization and deacylation. Very polar solvents such as sulfolane compete with the reactant molecules for diffusion inside the zeolite pores and for adsorption on the acid sites, reducing therefore the rates of acetylation and isomerization. On the other hand, the solvent polarity plays also a positive role by solvating the acylium ion intermediates, hence, by allowing a better dissociation of AA into these acetylation intermediates. With non-polar solvents such as 1-methylnaphthalene or in the absence of solvents, deacylation is very significant, probably because of a too long residence time of acetyl–methoxynaphthalene isomers inside the micropores of the zeolite.

Adsorption over the HBEA zeolite of a mixture of I, 2MN and sulfolane or nitrobenzene demonstrates that despite its bulkiness, I enters the pores of this zeolite. This suggests that this compound can be formed inside the pores by acetylation of 2MN. Isomerization of I into II is also shown to occur inside the zeolite micropores, the desorption of II being slower than its isomerization. Moreover, these adsorption experiments confirm that polar solvents such as sulfolane limit the entrance into the zeolite micropores of the reactant molecules, which are less polar (e.g. 2MN); hence, the rate of their transformation.

References

[1] G. Franck, J.W. Stadelhofer, Industrial Aromatic Chemistry, Springer-Verlag, Berlin, 1988.
[2] H. Szmant, Organic Building Blocks of the Chemical Industry, Wiley, NY, 1989.
[3] P.B. Venuto, Microporous Mater. 2 (1994) 297.
[4] H.W. Kouwenhoven, H. van Bekkum, in: G. Ertl, H. Knözinger, J. Weitkamp (Eds.), Handbook of Heterogeneous Catalysis vol. 5 Wiley, 1997, p. 2358.
[5] G. Harvey, A. Vogt, H.W. Kouwenhoven, R. Prins, in: R. von Ballmoos, J.B. Higgins, M.M.J. Treacy (Eds.), Proceedings of the ninth International Zeolite Conference, Montreal 1992 vol. 2 Butterworth-Heinemann, Boston, 1993, p. 363.
[6] W.F. H–lderich, H. Lermer and M. Schwarzmann, Patent DE 3.618.964, to BASF A.G.
[7] F. Richard, H. Carreyre, G. Pèrot, J. Mol. Catal. 103 (1995) 51.
[8] F. Richard, H. Carreyre, G. Pèrot, J. Catal. 159 (1996) 427.
[9] K. Gaare, D. Akporiaye, J. Mol. Catal. A 109 (1996) 177.
[10] Y.V. Subba Rao, S.J. Kulkarni, M. Subrahmanyam, A.AV. Rama Rao, Appl. Catal. 133 (1995) L1–L6.
[11] M. Spagnol, L. Gilbert, D. Alby, Routes of organic development, Ind. Chem. Libr. 8 (1996) 29.
[12] D. Rohan, C. Canaff, E. Fromentin, M. Guisnet, J. Catal. 177 (1998) 296.
[13] E.G. Derouane, C.J. Dillon, D. Bethel, S.B. Derouane-Abd Hamid, J. Catal. 187 (1999) 209.
[14] M. Spagnol, L. Gilbert, E. Benazzi and C. Marcilly, Patent PCT, Int. Appl WO 96 35, 655, 1996.
[15] M. Spagnol, L. Gilbert, E. Benazzi and C. Marcilly, Patent PCT, Int. Appl WO 96 35, 656, 1996.
[16] J.R. Zoeller, C.E. Summer, J. Org. Chem. 55 (1990) 319.
[17] G. Harvey, G. Mäder, Collect. Czech. Chem. Commun. 57 (1992) 862.
[18] G.D. Yadav, M.M.S. Krishnan, Chem. Eng. Sci. 54 (1999) 4189.
[19] G. Harvey, G. Binder, R. Prins, Stud. Surf. Sci. Catal. 94 (1995) 397.
[20] H.K. Heinichen, W.F. Hölderich, J. Catal. 185 (1999) 408.
[21] E.A. Gunnewegh, S.S. Gopie, H. van Bekkum, J. Mol. Catal. 106 (1996) 151.
[22] B.M. Choudary, M. Sateesh, M.L. Kantam, K.V.R. Prasad, Appl. Catal. 171 (1998) 155.
[23] E. Fromentin, J.-M. Coustard, M. Guisnet, J. Catal. 190 (2000) 433.
[24] S. Morin, P. Ayrault, N.S. Gnep, M. Guisnet, Appl. Catal. 166 (1998) 281.
[25] M. Guisnet, P. Ayrault, C. Coutanceau, M.F. Alvarez, J. Datka, J. Chem. Soc., Faraday Trans. 93 (1997) 1661.
[26] K. Dimroth, C. Reichardt, T. Siepmann, F. Bohlmann, Liebigs Ann. Chem. 661 (1963) 1.
[27] C. Reichardt, Liebigs Ann. Chem. 752 (64) (1971).
[28] S. Pivsa-Art, K. Okuro, M. Miura, S. Mutara, M. Nomura, J. Chem. Trans. I (1994) 1703.
[29] M. Miura, H. Hashimato, K. Itok, M. Nomura, J. Chem. Soc., Perkin Trans. 1 (1990) 2207.
[30] C. Reichardt, Solvents and Solvents Effects in Organic Chemistry, VCH Weinheim, 1988.
[31] L. Gilbert, C. Mercier, Stud. Surf. Sci. Catal. 78 (1993) 51.
[32] P.H.J. Espeel, K.A. Vercruysse, M. Debaerdemaker, P.A. Jacobs, Stud. Surf. Sci. Catal. 84 (1994) 1457.
[33] F. Jayat, M.J. Sabater Picot, M. Guisnet, Catal. Lett. 41 (1996) 181.
[34] F. Jayat, M.J. Sabater Picot, D. Rohan, M. Guisnet, Stud. Surf. Sci. Catal. 108 (1997) 91.
[35] D. Martin, unpublished results.