

Update 1 of: Use of Solid Catalysts in Friedel–Crafts Acylation Reactions

Giovanni Sartori^{*,†,‡} and Raimondo Maggi^{†,‡}

[†]Clean Synthetic Methodologies Group and [‡]National Interuniversity Consortium “Chemistry for Environment” (INCA), Unit PR2, Dipartimento di Chimica Organica e Industriale, Università degli Studi di Parma, Parco Area delle Scienze 17A, I-43100 Parma, Italy

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1. INTRODUCTION

“The first mention of acylation related to the later Al_2Cl_6 method of Friedel and Crafts appeared in 1873 in a preliminary

communication by Grucarevic and Merz....”¹ With these words G. A. Olah in an historical review about Friedel–Crafts chemistry² reported the earliest reference on the metal-catalyzed acylation of aromatic compounds. The Friedel–Crafts acylation reaction essentially consists of the production of an aromatic ketone by reacting an aromatic substrate with an acyl component in the presence of a catalyst.³

Since the above communication, an impressive number of papers and books have been published and numerous patents have been registered on this topic.³ The reaction quickly became a fundamental pillar of synthetic organic chemistry at both the academic and industrial levels. The great interest in electrophilic acylation studies and in the optimization of preparative processes was spurred by the considerable practical value of the aromatic ketone products. In fact, these compounds constitute fundamental intermediates in the pharmaceutical, fragrance, flavor, dye, and agrochemical industries.^{4–6}

Conventionally, the electrophilic acylations are catalyzed by Lewis acids (such as ZnCl_2 , AlCl_3 , FeCl_3 , SnCl_4 , and TiCl_4) or strong protic acids (such as HF and H_2SO_4). In particular, the use of metal halides causes problems associated with the strong complex formed between the ketone product and the metal halide itself which provokes the use of more than stoichiometric amounts of catalyst. The workup commonly requires hydrolysis of the complex, leading to the loss of the catalyst and giving large amounts of corrosive waste streams. For these reasons, during the past decade, the setting up of more ecocompatible Friedel–Crafts acylations has become a fundamental goal of the general “green revolution” that has spread in all fields of synthetic chemistry⁷ through a revision of the preparation methods mainly based on the exploitation of new and increasingly efficient catalysts.⁸

Great efforts have been made by different research groups to achieve the goal of making the Lewis acid role catalytic in Friedel–Crafts acylation. Interesting results have been achieved, such as the use of catalytic amounts of lanthanide trifluoromethanesulfonates alone⁹ or microencapsulated on polyacrylonitrile¹⁰ as reusable catalysts, as well as the more ecocompatible methods based on the use of graphite as a solid catalyst¹¹ or even the possibility to perform the reaction without any catalyst.¹²

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Even though these results could suggest some practical developments, they have not led to any very important industrial application. However, maximum effort has been directed toward the use of solid acid catalysts. In fact, heterogeneous catalysts can be easily separated from the reaction mixture and reused; they are generally not corrosive and do not produce problematic side products. Different classes of materials have been studied and utilized as heterogeneous catalysts for Friedel–Crafts acylations: these include zeolites, (acid treated) metal oxides, and heteropoly acids already utilized in the hydrocarbon reactions.¹³ Moreover, the application of clays, perfluorinated resinsulfonic acids, and supported (fluoro) sulfonic acids, mainly exploited in the production of fine chemicals, is the subject of intensive studies in this area.

Owing to the great interest in the argument, minireviews can be found on the use of solid catalysts in Friedel–Crafts acylation. Kouwenhoven and van Bekkum in a chapter of the *Handbook of Heterogeneous Catalysis* faced the basic problem of the use of zeolites in the reaction.¹⁴ A further essential overview of the same argument was reported by Métivier in *Fine Chemicals through Heterogeneous Catalysis*.¹⁵ Furthermore, Bezouhanova described the synthetic aspects of the zeolite-catalyzed aromatic ketones preparation.^{16a} **Very recently, Čejka et al. reported the development in the acylation reactions of arenes, aromatic ethers, and phenols catalyzed by zeolites and mesoporous materials.**^{16b}

The present review deals with the developments, mainly during the past decade, in the use of heterogeneous catalysts for Friedel–Crafts acylation of aromatic compounds. The whole argument is organized in five sections, namely, acylation of arenes, aromatic ethers, aromatic thioethers, phenolic substrates (split up into Fries rearrangement and direct acylation), and heterocycles. It is structured according to a mechanistic point of view, taking into special account the role played by the surface active sites in the activation of reagents as well as in the different modes of regioselectivity encountered in the acylation of arenes, aromatic ethers, and phenols.

Even if the great majority of the papers reviewed concern reactions carried out in batch conditions, where the blocking of pores and active sites can have a negative effect on catalyst efficiency, we particularly stressed results obtained in the gas phase or under continuous fixed-bed reaction conditions, where the continuous removal of products and poisons from the catalyst surface enhances performance.

When we decided to face the problem of writing a review on the Friedel–Crafts acylation reaction, immediately our minds went back to the fruitful discussions on this topic with our mentor Prof. Giuseppe Casnati and to the passionate studies performed under his guidance about the physicochemical factors that control the C-regioselectivity in the acylation of ambidental phenol substrates.^{17,18} For these reasons, with high regard and much affection, we dedicate this review to his memory on the occasion of the 18th anniversary of his death.

2. ACYLATION OF ARENES

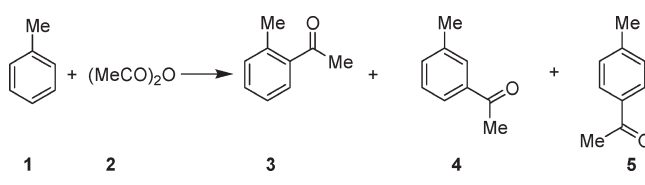
In this section, the Friedel–Crafts acylations of simple arenes (benzene, toluene, xylenes, etc.), condensed arenes, and biphenyls are analyzed. These aromatic substrates are examined together since their reactions with acylating reagents follow the same direct mechanism and usually they do not involve secondary transformations such as transposition and deacylation-reacylation processes. The ketones derived from these kinds of arenes

Table 1. Pore Types and Dimensions of the Zeolites Utilized

entry	zeolite	pore type	dimensions
1 ^a	Beta (BEA)	interconnected channels	7.6 Å × 6.4 Å channel 5.5 Å × 5.5 Å channel
2 ^a	Y (FAU)	interconnected spheres	7.4 Å diameter pore 11.8 Å diameter cavity
3 ^a	ZSM-5 (MFI)	interconnected channels	5.5 Å × 5.6 Å channel 5.1 Å × 5.5 Å channel
4 ^a	Mordenite (MOR)	interconnected channels	6.5 Å × 7.0 Å channel 2.6 Å × 5.7 Å channel
5 ^b	Nu-10 (TON)	one-dimensional channels	5.5 Å × 4.5 Å channel
6 ^a	X (FAU)	interconnected spheres	7.4 Å diameter pore 11.8 Å diameter cavity

^a Meier, W. M.; Olson, D. H. *Zeolites* **1992**, 12, special issue *Atlas of Zeolites Structure Type*. ^b Kokotalio, G. T.; Schlenker, J. L.; Dwyer, F. G.; Walyocsk, E. W. *Zeolites* **1985**, 5, 349.

Scheme 1



represent important chemicals utilized in different areas of applied organic chemistry.^{19,20}

2.1. Acylation with Zeolites

Zeolites are well-known microcrystalline porous materials largely studied and applied in the petrochemical industry for a long time;¹³ more recently they have been utilized in the fine chemicals industry.²¹ As these materials have been fully described and characterized, we report here (Table 1) only the essential data concerning the pore types and dimensions of the zeolites most employed for Friedel–Crafts acylation reactions.

Zeolites should be best considered as solid solvents when they are used as catalysts for liquid-phase organic reactions.^{22,23} In fact, adsorption equilibrium constants can be effectively considered as partition coefficients determining the distribution of the reactants and products between the bulk liquid phase and the zeolite “solid solvent” phase. The partitioning of the reactants and products is determined by their nature and relative amount, the type of zeolite, the temperature, and other conventional factors. This statement can account for the different behaviors observed when zeolites are utilized in the liquid-phase Friedel–Crafts acylation.

BEA zeolites are the most useful zeolite catalysts applied at academic and industrial levels for Friedel–Crafts acylation of arenes.²⁴ A detailed comparison of the activity of different HBEA zeolites in the acylation of toluene 1 with acetic anhydride 2 (1/2 ratio = 20) was reported by Corma et al.²⁵ (Scheme 1). The reaction afforded *p*-methylacetophenone (5; *p*-MAP) with a selectivity close to 100%, accompanied by *ortho*- and *meta*-isomers 3 and 4, whose amount was less than 2% of the total yield in acetylated products. The yield of MAPs increased by increasing the time on stream (TOS), and after 120 min the constant value of ~42% was achieved, suggesting that an

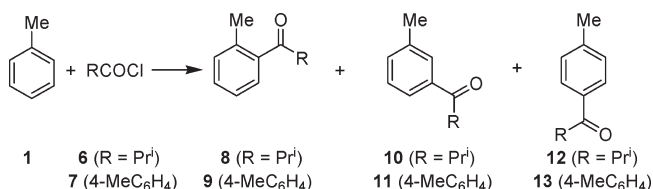
important deactivation of the catalyst occurred during the reaction. This is probably due to the inhibiting effect of MAPs, which can be strongly adsorbed on the catalyst (product inhibition).²⁶ Moreover, the adsorbed MAPs can further react, giving larger byproducts (coke) which remain adsorbed and further limit the diffusion of reactants within the channels of the catalyst. The catalyst activity is influenced by the Brönsted acidity and the SiO₂/Al₂O₃ ratio (SAR) of the zeolite; in fact, a low SAR framework led to better yields of MAPs, and a lowering in the catalytic activity was observed when increasing the SAR value. The conclusion is that neither the higher hydrophobicity nor the higher acidity alone produce an important increase of the catalytic activity in the present reaction. On the contrary, the zeolite crystallite size is an important factor and affects both conversion and catalyst decay. Thus, use of a sample with very small crystallites (crystal size $\sim 0.05 \mu\text{m}$) and a high density of Brönsted acid sites resulted in an important increase in the activity and a decrease of catalyst deactivation, allowing faster diffusion of the products out of the catalyst and minimizing the coke deposition. Similar activity enhancement of microcrystalline HBEA zeolites was very recently described in a study of the acylation of aromatic and heteroaromatic compounds with different acid anhydrides.²⁷

The effect of the pore dimensions and the hydrophobicity of the zeolite catalyst was confirmed in the acylation of toluene **1** with isobutyryl chloride **6**²⁸ (**1/6** ratio = 4) (Scheme 2). The catalytic activity increased from medium- to large-pore zeolites and from one- to three-dimensional channel systems. The highest conversion of the acylating reagent was observed with large-pore zeolites such as HBEA (71%) and USY (62%). The reaction rate increased by increasing the hydrophobicity of the zeolite; therefore, the highest initial TOF values were obtained for HBEA zeolite with the lowest concentration of acid sites. With an increase of the zeolite hydrophobicity, toluene can easily diffuse to the channels system and adsorb more efficiently, and also the desorption of the polar ketone product is much easier.

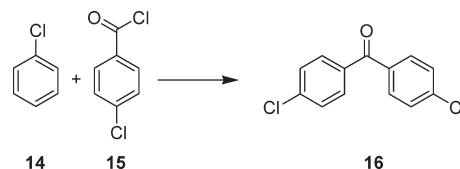
The same catalyst was utilized by Singh et al.²⁹ in the reaction of chlorobenzene **14** with *p*-chlorobenzoyl chloride (**15**) to produce 4,4'-dichlorobenzophenone (**16**) (**14/15** ratio = 2) (Scheme 3). As expected, the process showed a modest conversion that was reagent **14** deactivated toward the electrophilic substitution reaction. Product **16** was obtained with >88% selectivity at 19.8 wt % **15** conversion. Small amounts of 2,4'-dichlorobenzophenone and dibenzoylated products were also obtained. It must be stressed that by using HBEA zeolite it was possible to activate not only 4-chlorobenzoyl chloride but also the greener and cheaper 4-chlorobenzoic acid, that, reacting with the more activated toluene (toluene/4-chlorobenzoic acid ratio = 300), afforded 4-chloro-4'-methylbenzophenone in 84% yield.³⁰

Davis et al.³¹ studied the possibility of preparing 4,4'-diacylated biphenyls **26** and **27** by regioselective 4,4'-bisacylation of biphenyl **17** with carboxylic acids **18** and **19** or anhydrides **2** and **20** (**17**/acylating agent ratio = 1) (Scheme 4) over HBEA and HY zeolites, with HBEA being the most efficient one. Unfortunately, in the model reaction with acetic anhydride (**2**), the monoacylated product **23** was near exclusively formed with a selectivity higher than 98 wt %, whereas the target diacetylated product **26** was isolated only in modest yield (8–10%). Moreover, acylation of **17** with hexanoic acid **19** at 150 °C afforded 4-hexanoylbiphenyl (**24**) with 8–14% yield (98% selectivity); an increase in temperature to 200 °C enhanced the yield of **24** to

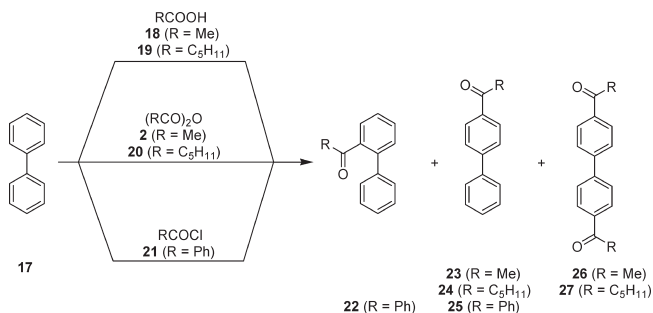
Scheme 2



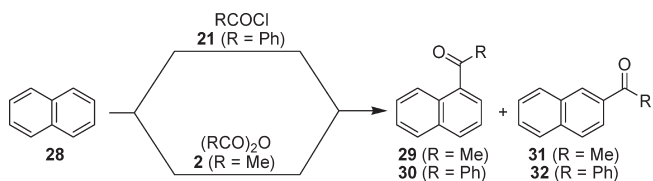
Scheme 3



Scheme 4



Scheme 5



53%, but as frequently observed in similar experiments, a slight lowering in selectivity to 92% was observed.

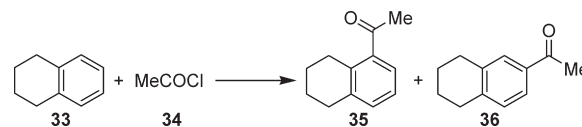
HBEA zeolite was again considerably more active than HZSM-5 and HY in the acylation of **17** with benzoyl chloride **21** (**17/21** ratio = 1) (Scheme 4) to give 4-phenylbenzophenone (**25**) in 41% yield and 97.5% selectivity.³² In the same reaction, AlCl₃ showed higher conversion of reagent **17** but lower selectivity to product **25**, as a considerable amount of 2-phenylbenzophenone **22** ($\sim 20\%$) was produced. A lowering of product **25** yield (from 41 to 33%) on catalyst recycling was observed. The hydrogen chloride liberated during the reaction probably promotes the extraction of aluminum to some extent from the framework of HBEA. The loss of aluminum and the decrease in crystallinity of the catalyst may be the cause for the lowering of catalytic activity after each cycle, in good agreement with similar experiments carried out with different zeolites.^{33,34}

The acylation of naphthalene (**28**) with benzoyl chloride (**21**) and acetic anhydride (**2**) was studied in the presence of different zeolites, including HBEA (**28/21** ratio = 2), in comparison with AlCl_3 (Scheme 5).^{35,36} With the number of active sites being equal, HBEA was more efficient and selective with respect to the production of 2-benzoylnaphthalene (**32**), in comparison with nonshape-selective AlCl_3 , which preferentially affords compound **30** because the 1-position of naphthalene is more active than the 2-position.^{37a} HBEA showed higher activity with respect to HZSM-type zeolites, which is ascribable to the narrow pore diameter of the latter catalysts which hampers the access of large molecules such as naphthalene to the active sites. In the reaction with acetic anhydride (**28/2** ratio = 2), HBEA still exhibited the highest activity in comparison with some other large-pore zeolites such as HY and HMOR. Significant differences in naphthalene conversion over HBEA were found with Decalin or sulfolane as solvents; the different hydrophilicities of these two solvents dramatically influence the resulting naphthalene conversion. The hydrophilic sulfolane interacts more strongly with the zeolite surface, blocking the acid sites that are unavailable for the acylation reaction; on the contrary, the hydrophobic Decalin enables the adsorption of acetic anhydride and increases the rate of acylation reaction. Due to the proper structure of the HBEA, the selective formation of isomer **31** was achieved probably via a restricted transition state selectivity (81% selectivity at 35% conversion of **28**). By comparing HBEA zeolites with different SARs, it was evident that for the best naphthalene conversion an optimum value (37.5) was required; at higher or lower aluminum contents, the catalyst showed lower activity. Moreover, since the catalyst deactivation was attributed to the formation of bulky byproducts that cannot desorb from the zeolite channels, the use of an excess of naphthalene resulted in a decrease of the deactivation rate.

2-Methylnaphthalene was acylated by HBEA zeolite in the absence of any solvent.^{37b} Short-chain acyl chlorides and carboxylic acids were found not to be the effective acylating agents; only acid anhydrides possessed considerable reactivity, which increased with the lengthening of the carbon chain. Butyric anhydride was chosen as a model acylating agent: the catalytic reaction did not proceed at 140 °C with as low as 0.2 g of catalyst loading (for 50 mmol of aromatic substrate), and the conversion of butyric anhydride increased steadily from 0 to 61% as the zeolite amount was raised from 0.2 to 4.0 g. Diacylated byproducts emerged when the catalyst amount was higher than 1.5 g. The best HBEA amount was found to be 3.5 g. The conversion of the acylating reagent increased steadily up to 83% as the temperature was raised from 140 to 200 °C; a bit of heavy products, which would block the zeolite channels, were detected when the acylation was conducted above 200 °C. The best reaction time was 1 h, and as with the increase of the reaction time, the competing adsorption between reactants and products as well as the emergence of heavy products brought on the deactivation of HBEA. In addition, the equimolar byproduct butyric acid, which was inevitably formed during the acylation reaction, may undergo competitive adsorption with butyric anhydride on the catalyst and consequently lead to its deactivation.

The problem of catalyst deactivation with particular attention to HY and HBEA zeolites was further investigated by Moreau et al.³⁸ during studies on the reaction of tetralin (**33**) with acyl chlorides. In particular, with acetyl chloride (**34**) (**33/34** ratio = 0.5) (Scheme 6) the reaction led to isomers **35** (~2%) and **36** (~15%) after 2 h. The **36/35** ratio remained constant with time,

Scheme 6



suggesting that both isomers were obtained by parallel reactions. Moreover, studies on the influence of the chain length of the acylating agent showed very good conversion of **33** (higher than 70% after 4 h of reaction) with octanoyl and butanoyl chloride, in agreement with the results reported by Geneste et al.³⁹ To avoid hydrolysis of acetyl chloride, the reaction was performed under a nitrogen atmosphere; however, even if a very fast conversion was obtained leading to a maximum amount of acetyltetralin after only 20 min (17% yield), different secondary products (naphthalene, ethyltetralin, and acetylnaphthalene) were produced on the surface of the catalyst due to the consecutive reactions of the acetyltetralin.

The rare-earth-exchanged HBEA zeolites (REBEA) were studied in the model reaction involving toluene (**1**) and acetic anhydride (**2**) (**1/2** ratio = 0.5) (Scheme 1) in nitrobenzene.⁴⁰ The catalysts were prepared by ion exchange with an aqueous solution of the rare earth acetate followed by calcination at 550 °C. With HBEA and LaBEA, a maximum conversion was observed after 6 h (50 and 66%, respectively) with high selectivity (86–100%) toward *para*-isomer **5**. Therefore, the observed difference in the catalytic activity could not be attributed to the rare earth content of the zeolite alone. In general, rare-earth-exchanged zeolites display both Lewis and Brønsted acidity; this is ascribable to the cation high charge density, which generates acid hydroxy groups inside the zeolitic cavities. Thus, the difference in the catalytic activity of these materials might be due to the following reasons: (i) acidity of the sample, (ii) SAR and crystallinity of the sample as the total number of Brønsted acid sites decreases with the increase of SAR,²⁵ and (iii) cation position in the lattice as cations present at different positions in the lattice result in different acidities depending on their immediate environment. Concerning the solvent effect, the highly polar solvent nitrobenzene showed the best activity, in agreement with the general mechanism of the acylation reaction involving highly polar active species such as the acylium ion and the σ -complex.³

The catalytic activity improvement of HBEA and HY zeolites by metal exchange was further studied by Singh et al.^{29,32,34,35,41} in the acylation of arenes with benzoyl chloride (arene/benzoyl chloride ratio = 5). The isomorphous substitution of Al by Ga and Fe in the HBEA sample resulted in the following order of efficiency (benzoyl chloride conversion after 18 h in the reaction with toluene): AlBEA (54.0) > GaBEA (32.8) > FeBEA (19.0). Indeed the acid strength of the exchanged metal decreases in the order Al > Ga > Fe.⁴² Similarly, when HY was transformed into REY by exchanging with rare earth metals, its catalytic activity was considerably enhanced [for example, compare the TOF values of benzoyl chloride conversion: 4.2 for HY vs 14.2 for REY].

Choudary et al.^{43,44} compared the activities of HBEA and HBEA-supported In_2O_3 (In_2O_3 -BEA) (20 wt % loading) in the acylation of benzene with benzoyl chloride (benzene/benzoyl chloride ratio = 17). In_2O_3 -BEA showed higher activity (80%

benzoyl chloride conversion in 1.5 h vs 50% benzoyl chloride conversion with HBEA in 3 h). This catalytic activity enhancement was explained by considering the activation of benzoyl chloride by both protonic acid and redox sites present in In_2O_3 –BEA. In fact, rare earth metal oxide species are known for their redox properties, which are expected to play a significant role in activating the benzoyl chloride according to the pathway depicted in Scheme 7. Thus, the benzoyl cation produced according to the redox process promotes the acylation reaction.

Singh et al.⁴⁵ thoroughly studied the vapor-phase acylation of aromatic hydrocarbons with acyl chlorides over different zeolites. Comparison experiments of the acetylation of toluene with acetyl chloride (toluene/acetyl chloride ratio = 2) over HZSM-5, HMOR, and REY zeolites showed that HZSM-5 was the best catalyst, affording *p*-MAP with 60.2% conversion of acetyl chloride (88.3% selectivity). The conversion increased with increasing reaction temperature and toluene to acetyl chloride molar ratio, while it decreased with the increase of the reaction time, space velocity, Na content, and SAR.

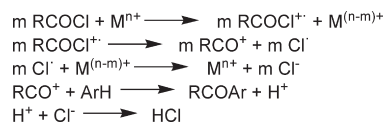
The vapor-phase benzene acylation with acetic anhydride (benzene/acetic anhydride ratio = 2) in the presence of CeZSM-5 was studied by Subrahmanyam et al.⁴⁶ This research is a part of a more extensive study on the use of CeY zeolites as catalysts for aromatic acylation with carboxylic acids.^{39,47,48} Comparison experiments showed that CeZSM-5 was a better catalyst in the reaction (86.4 wt % conversion of acetic anhydride, 95.0% selectivity to acetophenone) than unmodified HZSM-5 (70.6 wt % conversion of acetic anhydride, 86.4% selectivity to acetophenone). The reaction was favored by Brønsted acid sites even if no special mechanistic information is given.

The use of the greener acetic acid in the acetylation of benzene (benzene/acetic acid ratio = 2) over HZSM-5 was evaluated; the process was carried out in a flow reactor under atmospheric pressure at 275 °C, showing quite promising results (76% acetic acid conversion, 91.2 TOF value, and 88.1% selectivity with respect to acetophenone).^{49,50}

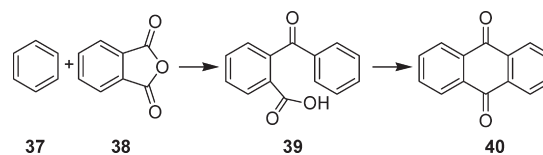
Results of studies on the application of HBEA in the anthraquinone (40) synthesis by gas-phase bis-acylation of benzene (37) with phthalic anhydride (38) were reported⁵¹ (Scheme 8). Compound 38 reacted even at relatively low temperature (<250 °C), and the anthraquinone selectivity was very high (>95%). An increase of phthalic anhydride conversion was observed by increasing the temperature or the TOS, unfortunately accompanied by a lowering in selectivity toward anthraquinone, particularly for temperatures higher than 350 °C. The main byproducts are benzoylbenzoic acid 39 and biphenyl. FT-IR studies showed that at 50 °C benzene interacts with all bridged silanols and with 70% of the unbridged silanols, whereas at 250 °C these groups are completely free. Thus, at temperatures lower than 250 °C, a solution of phthalic anhydride in benzene can exist inside zeolite channels, whereas at higher temperatures benzene does not exist in the form of liquid film in the zeolite channels and phthalic anhydride forms H-complexes with acid OH groups. At 200 °C the formation of benzoylbenzoic acid as a H-complex was observed, and above 250 °C compound 39 was decarboxylated. This information allows the conclusion that anthraquinone should be better formed at 200 °C.

The cyclization step 39 → 40 was also investigated in the presence of a HZSM-type zeolite;^{52a} at 200 °C the reaction was complete in 100 min. Authors assumed that the cyclization takes place within the zeolite cavities.

Scheme 7



Scheme 8



2-Methylantraquinone (2MA) can be obtained by liquid-phase cascade reactions through bis-acylation of toluene with phthalic acid.^{52b} The process has been carried out with various zeolitic materials, namely, HBEA, HY and HMOR; HBEA appears to be the best active catalyst in terms of both conversion of phthalic acid and selectivity to 2MA. Because of the interconnected channel architecture, HBEA and HY zeolites allow for an easier diffusion of the products than HMOR. However, the lower SAR value of HY (5.5) compared with that of HBEA (22) will lead to a higher hydrophilicity, which may result in the absorption of some produced water; as a result, the HY zeolite can be easily passivated. Both conversion of phthalic acid and selectivity to 2MA increase rapidly with the increase of reaction temperature up to 250 °C, but then they drop-out beyond this. As recently nanomaterials and nanotechnology have received much attention for catalysis application, nanosized HBEA zeolite was prepared and tested in the above process. This nanocatalyst exhibited better catalytic performance in the one-pot synthesis of 2MA than the micro-sized catalyst, which may be attributed to the former's additional surface acid sites, larger surface area and pore volume, and shorter pore channels. Because of the shortened pore channel allowing materials and product to diffuse smoothly from the body of catalyst to the reaction system (which compresses the coke formation), there is no obvious decrease in conversion but a slight increase in selectivity after the catalyst is recycled four times.

Acetylferrocene has been prepared by liquid phase acylation reaction over zeolites of ferrocene with acetic anhydride in decahydronaphthalene under an atmospheric pressure at 140 °C.^{52c} The exclusive formation of monoacetylferrocene was detected. The conversion of ferrocene in acylation reaction was significantly influenced by the zeolite structure, SAR value, and ferrocene/acetic anhydride molar ratio. The lowest ferrocene conversion was achieved with 10-membered ring zeolite, indicating that some steric hindrances limit the formation of acetylferrocene inside the catalyst. Some increase in the conversion of ferrocene was observed with 12-membered HMOR. The highest conversions of ferrocene were achieved with 12-membered HBEA (100% conversion after 180 min) and HY (80% conversion after 300 min). Very high selectivity to acetylferrocene could be explained by the shape-selective properties of these zeolites: because of the steric hindrances imposed by zeolite structures, the formation of more acylated ferrocenes can probably proceed only in the large cavities of zeolite Y. However,

these bulky products if formed might be strongly retained inside the cages of this zeolite. In addition, the higher concentration of acid sites (despite the structural type of zeolite used), the higher the conversion of ferrocene. To this end, three different types of HBEA zeolite, with different SAR values (25, 75, and 300) were tested: HBEA(25) achieved 100% ferrocene conversion after 180 min, while HBEA(75) reached the same conversion in 300 min; the lowest activity in ferrocene acylation was found for HBEA-(300) (30% after 300 min). It must be underlined that while total ferrocene conversion was obtained after 120 min when 0.8 g of HBEA(25) zeolite was employed, 300 min of the reaction were not sufficient to reach the same conversion when only half of this amount of catalyst was used.

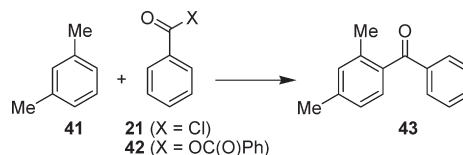
Strongly dealuminated HY zeolites, prepared from commercially available NaY by a triple treatment with NH_4NO_3 followed by calcination (3YH) and further treatment with HNO_3 (3YHA), were utilized as catalysts in the acylation of *m*-xylene (41) with benzoyl chloride (21) and benzoic anhydride (42) (41/acylating agent ratio = 2)^{53,54} (Scheme 9). 3YH and 3YHA have a substantial pore volume in mesopores and contain an appreciable amount of nonframework aluminum. Contrary to the results reported by other authors,³⁶ the 3YH catalyst showed a much higher activity in sulfolane (94% xylene conversion) with respect to decane (46% xylene conversion). To account for these results, it was assumed that a polar solvent like sulfolane enhances the reaction rate by stabilizing ionic species.³ However, a more realistic leaching of acid active species in the highly polar medium can help to account for the apparently positive sulfolane effect.

Acylation of arenes with benzoyl chloride over FeNaY zeolite (arene/benzoyl chloride ratio = 5) in comparison with homogeneous FeCl_3 was studied by Hutchings et al.⁵⁵ The activity of the heterogeneous catalyst was very similar to that of the homogeneous one (74–99% arene conversion with FeCl_3 vs 64–96% conversion with FeNaY) even if longer reaction times were needed. Kinetic studies of the reaction show typical product inhibition phenomena.^{26,35,41}

In a series of valuable studies, Geneste et al.^{39,48,56} investigated the activity of various cation-exchanged HY zeolites in the acylation of toluene and xylenes with aliphatic carboxylic acids (arene/carboxylic acid ratio = 300). In a model reaction between toluene and octanoic acid (Scheme 10) the activity of rare earth, transition metal, and alkaline earth cation exchanged HY zeolites was considered.³⁹

REY exhibited the highest activity (47 yield = 75%), in agreement with the results published in an earlier study;⁵⁷ on the contrary, HY showed a lower activity (47 yield < 40%) and transition metal and alkaline earth exchanged HY were nearly inactive. Figure 1 shows the dependence of the reaction rate on the cerium content in the Y zeolite. The catalyst activity increased with the degree of exchange of Na^+ ions by Ce^{3+} . There is a threshold of exchange ($\sim 20\%$) below which no activity was observed, but above that threshold a rapid increase in activity occurred. A possible explanation for this phenomenon was recognized by the authors in the particular structure of the HY zeolite that contains five distinct cation sites which are located respectively at the center of the hexagonal prism (type I), in the sodalite unit (types I' and II'), and in the supercage (types II and III)⁴⁸ (Figure 2). When the zeolite is in the hydrate form, all cations are in the supercage because of the solvation by water. However, upon dehydration, the cation position shifts and for low degree of exchange the trivalent cations tend to migrate toward inaccessible sites I and I', showing very reduced activity.

Scheme 9



Scheme 10

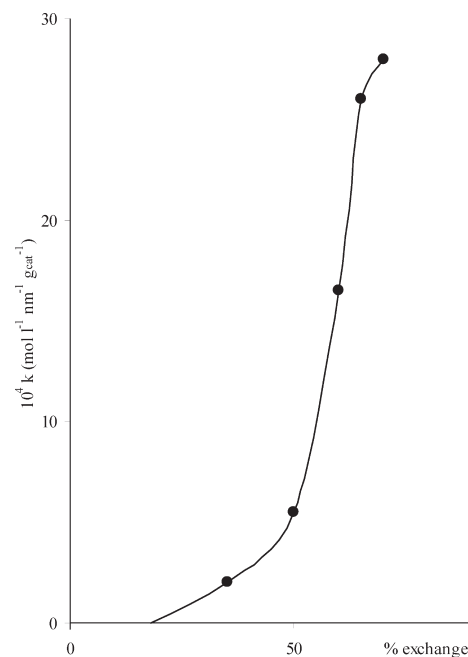
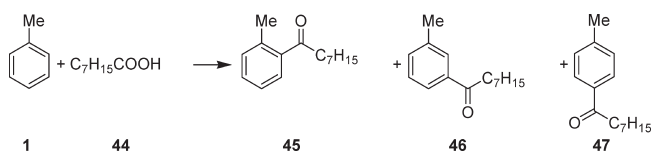


Figure 1. Dependence of the degree of exchange of Na^+ by Ce^{3+} on the activity of Y-zeolite in the acylation of toluene by octanoic acid at 200 °C.

For exchange entities greater than 40%, part of the cations remains in the supercage and considerable catalytic activity can be observed. The nature of the acid sites and consequently the catalyst activity depend on the thermal pretreatment. For HY zeolite the activity remains practically constant for calcination temperatures between 300 and 600 °C; for CeNaY the maximum acylation activity was obtained at a calcination temperature of 300 °C: this relatively low activation temperature may be a consequence of the easier removal of adsorbed water, and the decrease in activity for temperatures above 350 °C is probably due to dehydroxylation of the lattice and conversion of Brönsted acid sites into Lewis ones. These results confirm that the Brönsted rather than Lewis acids are the active sites in the present reaction. A quite interesting behavior was observed by evaluating the activity of CeY in the acylation of toluene with linear carboxylic acids of increasing chain length (from acetic

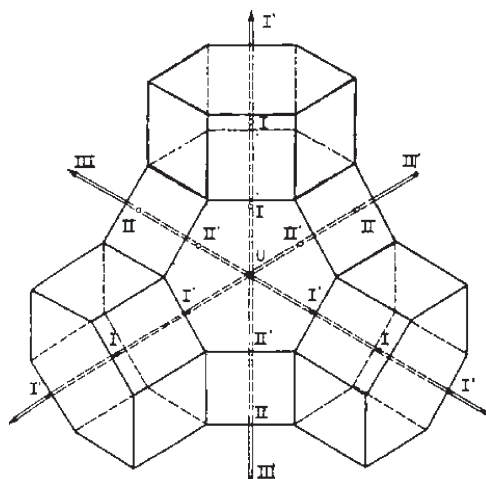


Figure 2. Schematic drawing of cation positions in faujasite. Reprinted with permission from ref 48. Copyright 1989 Elsevier.

[C₂] to behenic acid [C₂₂]) (Figure 3).³⁹ The acylation with fatty acids took place with yields higher than 50%. Acylation of toluene showed an extraordinary high *para* shape-selectivity effect, and in all cases the yield of *para*-isomer was at least 94%, whereas in classical Friedel–Crafts acylation with AlCl₃, the *para*-selectivity was ~80% due to the competitive attack at the *ortho*-position. For short alkyl chain carboxylic acids, the yield increased linearly with the number of carbon atoms, although all molecules could diffuse through the porous network. This phenomenon is not encountered in the homogeneous Friedel–Crafts acylation, and it is probably due to the same reason as previously mentioned, i.e., the intracrystalline reaction combined with the hydrophobic interaction of reactants with the catalyst surface.

The effect of the catalyst modification on the activity in the acylation of toluene with acetyl and propionyl chlorides (toluene/acyl chloride ratio = 150 and 230) was further investigated;⁴⁷ two HY zeolites containing different amounts of lanthanum, namely, La(26)Y and La(70)Y, were utilized, affording the *para*-isomers as the major products (44 and 65%, respectively) accompanied by trace amounts of *meta*- and *ortho*-isomers (2–3%).

From a synthetic point of view, REY zeolites were utilized in the preparation of cycloalkanones via intramolecular electrophilic acylation of variously substituted arylalkanoic acids (Scheme 11).⁵⁸ CeY catalyzed the reaction, affording bicyclic and tricyclic ketones in satisfactory to good yield (20–72%). As well documented in previous studies, the efficiency of the process parallels the lipophilic character of the reagent.

The use of HY and HBEA zeolites in the Friedel–Crafts acylation of aromatics showed some limitations when large-sized molecules were utilized. In fact, due to the dimensions of their pores, the access to the internal active sites of these zeolites is restricted to molecules with kinetic diameter up to 8 Å. The mesoporous molecular sieve MCM-41, a silicate-type material, possesses an hexagonal arrangement of uniformly sized unidimensional mesopores with a diameter which can be systematically varied from 20 to 80 Å,⁵⁹ and it should, therefore, be an interesting catalyst for reactions involving larger molecules.

Choudary et al.^{60,61a} thoroughly investigated the preparation and the use of InCl₃, GaCl₃, and ZnCl₂ supported on MCM-41 as Lewis acids in Friedel–Crafts acylation of aromatics with acyl

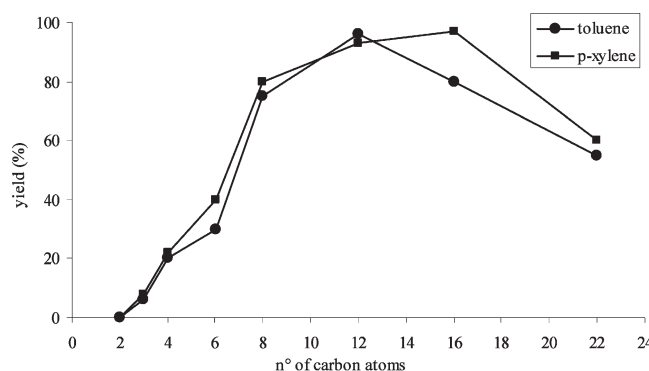
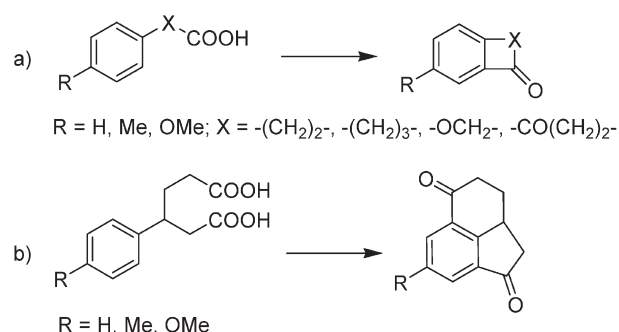


Figure 3. Dependence of the chain length of the linear carboxylic acid on the toluene (●) and *p*-xylene (■) acylation yield.

Scheme 11



chlorides (arene/acyl chloride ratio = 17). The support itself showed no catalytic activity, whereas the highest activity was shown by the supported InCl₃. The order for acylation activity of the supported metal chloride (InCl₃ > GaCl₃ >> ZnCl₂) was quite similar to that of the redox potential of the metals [$E^\circ_{In^{3+}/In} (-0.34\text{ V}) > E^\circ_{Ga^{3+}/Ga} (-0.53\text{ V}) > E^\circ_{Zn^{2+}/Zn} (-0.74\text{ V})$] and confirms a possible relationship between the redox potential and the catalytic activity of the supported metal chloride, in agreement with further studies by the same authors.^{43,44} The reaction could be efficiently applied to a variety of aromatic compounds (70–90% yield), confirming the moisture insensitivity of the InCl₃/MCM-41 catalyst.^{61a}

A good improvement was realized by grafting GaCl₃ or a mixture of GaCl₃/AlCl₃ on MCM-41.^{61b} The acylation reactions were carried out by magnetically stirring the catalyst, the benzoyl chloride, and the aromatic substrate at 80 °C for 2 h. No leaching of gallium or aluminum from the catalysts was observed during the acylation reactions. For both catalysts, reaction induction periods, strongly depending on the nature of the aromatic substrate utilized (anisole, cumene, mesitylene, *p*-xylene, toluene, benzene, and naphthalene), were found, but with the bimetal catalyst these induction periods are quite small. This was mostly attributed to a synergetic effect produced, due to the presence of strong Lewis acid sites, (–O–)₂AlCl and (–O–)₃Al, along with the weaker Lewis acid sites, (–O–)₂GaCl and (–O–)₃Ga. Both the catalysts also showed excellent reusability and stability.

More interesting are the results on the support of In₂O₃, Ga₂O₃, and ZnO on MCM-41.^{62–64} In particular, In₂O₃/MCM-41

proved to be a highly active catalyst for the acylation of aromatic compounds with benzoyl chloride (arene/benzoyl chloride ratio = 17) even in the presence of moisture. The activity order of the three supported metal oxides was found to be the same as that for the supported metal halides.⁶³ The times requested for the half of the benzene benzoylation in different solvents in the presence of $\text{In}_2\text{O}_3/\text{MCM-41}$ were in the following order: dichloromethane (2.8 h) < acetonitrile (3.2 h) < heptane (6.2 h). These results indicate that the catalyst is more active for the reaction in the presence of polar solvents even if a parallel correlation with Reichardt E_T^N polarity parameters^{65a} [dichloromethane (0.309), acetonitrile (0.460), heptane (0.012)] was not observed.

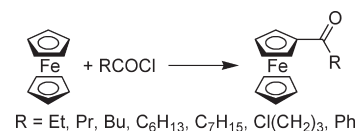
Several metal triflates, $\text{La}(\text{OTf})_3$, $\text{Ce}(\text{OTf})_4$, $\text{Y}(\text{OTf})_3$ and $\text{Zn}(\text{OTf})_2$, were incorporated into the pores of mesoporous SBA-15.^{65b} The so-obtained catalysts were employed in the acylation of naphthalene using *p*-toluoyl chloride as acylating agent. The SBA-15 with no triflate loading showed no measurable catalytic activity in the naphthalene acylation; with the triflate-functionalized mesoporous material, the conversion of naphthalene was found to progressively increase with the increase in the triflate loading (from 35 to 55% for the increase in the $\text{Zn}(\text{OTf})_2$ loading from 5 to 30 mol %). The 2-acyl naphthalene was the major reaction product (~92% selectivity), the minor product being 1-acyl naphthalene. This product distribution was almost independent of the supported-metal triflate utilized, but the zinc-based catalyst showed much higher catalytic activity. This catalyst can be utilized for five-six consecutive test runs, showing only a 5% activity loss in the process. The results of IR studies revealed that, while large triflate groups may assist in the geometric confinement within the pores of the mesoporous SBA-15, the zinc cations are basically responsible for the direct binding of the reactant molecules and hence for the catalytic properties.

An interesting catalyst, namely, ALKIT-5, obtained with varying ratios of Si/Al by sol gel procedure through the addition of aqueous HCl to a mixture of tetraethoxysilane, aluminum isopropoxide, and Pluronic F127 as template polymer, was utilized in the acylation of ferrocene with acyl chlorides.^{65c} The reaction carried out with 1-adamantoyl chloride shows a substantial increase in ferrocene conversion during the first 30 min at 100 °C reaching ~50%; also with other acyl chlorides the reaction affords selectively the monoacylated products. The catalyst can be recycled after filtration and regeneration by heating to 500 °C in a stream of air for 2 h: for four consecutive kinetic runs of ferrocene acylation with 1-adamantoyl chloride ALKIT-5 catalyst can afford the corresponding product with more than 40% yield.

2.2. Acylation with Clays

From a general point of view,⁶⁶ clays consist of crystalline sheets of aluminosilicate that are negatively charged. These sheets can have a 1:1 (i.e., kaolin) or 2:1 (i.e., montmorillonite) structure; in the latter case, a central layer of alumina in octahedral coordination with oxygen is sandwiched between two layers of silicon tetrahedrally coordinated with oxygen. Although the ideal aluminosilicate is electrically neutral, random substitutions for the aluminum and silicon resulted in a net negative charge within the sheets; typical substitutions include Al^{3+} for Si^{4+} and Mg^{2+} for Al^{3+} . To balance this negative charge, cations such as Na^+ , K^+ , or Ca^{2+} are located in an amorphous interlayer between the sheets. The interlayer also includes water

Scheme 12



molecules, some of which are complexed to the interlayer cations. Clay particles are composed of alternating sheets and interlayers. Different clay materials (natural, acid-treated, cation-exchanged,⁶⁷ and pillared clays⁶⁸) are effective catalysts for a wide variety of organic reactions,⁶⁶ including Friedel–Crafts acylation; both Brønsted and Lewis acidity play a role in the catalytic activity.

Among the different applications of modified clays in catalysis, Laszlo et al.^{69–72} described their use in Friedel–Crafts acylation. Two groups of materials were studied in catalytic reactions, namely, clays modified through exchange of the interlamellar cations or through impregnation of metal chlorides. The acid Fe-K10, obtained by exchanging K10 montmorillonite clay with $\text{Fe}(\text{III})$ ions, gave outstanding results in the acylation of mesitylene and *p*-xylene with benzoyl chloride or benzoic anhydride (arene/acylating agent ratio = 7) (98–100% yield). The catalyst is described as a material of low cost and low toxicity since the metal ions remain trapped in the double layer. In a comparative study on the acylation of mesitylene and anisole with benzoyl chloride promoted by Fe-K10,⁷⁰ it was observed that mesitylene reacted faster (by a factor of 3) when the reactions were carried out separately. However, when the two substrates were reacted jointly, competition favored anisole (by the same factor of 3). A tentative explanation for this reversal activity could be based on the assumption that benzoylation of mesitylene and anisole follows two different mechanisms characterized by different levels of interaction of the catalyst surface with the aromatic substrate and the benzoyl cation, the actual electrophilic reagent. In particular, it must be taken into consideration that anisole interacts more strongly than mesitylene with the acid centers of the catalyst and, consequently, both its intrinsic higher reactivity toward the acyl cation can be dramatically lowered and the acid sites are less available for mesitylene acylation reaction.

Cation-exchanged montmorillonites were utilized by Geneste et al.^{73,74} in the acylation of aromatics with carboxylic acids. As the clay acidity depends on the nature of the exchanged cation, a series of exchanged montmorillonites was studied in the model acylation of toluene with dodecanoic acid (toluene/dodecanoic acid ratio = 190). Best results were achieved with Al^{3+} -exchanged montmorillonite (60% yield of the *ortho*-, *meta*-, and *para*-isomers). The influence of the chain length of different carboxylic acids on the yield of acylation appeared to be similar on clays and on zeolites.³⁹ Indeed, acylation of toluene with $\text{CH}_3(\text{CH}_2)_n\text{COOH}$ over Al^{3+} -montmorillonite gave 12% yield for $n = 1$, 45% for $n = 6$, and 80% for $n = 14$.

K10 montmorillonite impregnated with zinc chloride (ZnK10) was also utilized for similar reactions. Unfortunately, carboxylic acids (i.e., benzoic acid) were inactive, and benzoic anhydride underwent activation of only one of the two acyl groups. Nevertheless, the reaction was applied at an industrial level.⁷⁵ However, some doubt still remains on the effective heterogeneity and reusability of these kinds of catalysts.

Some interest shows the results of the study on the use of bentonite-supported polytrifluoromethanesulfosiloxane (B-PTMSS) as catalyst in the acylation of ferrocene with different acyl chlorides⁷⁶ (ferrocene/acyl chloride ratio = 0.5) (Scheme 12). The catalyst was prepared by mixing the selected bentonite with tetraethyl orthosilicate (TEOS) in water and by adding a solution of trifluoromethanesulfonic acid in ethanol; the material was then dried at 200 °C.⁷⁷ The conversions of acyl chlorides increased in the following order: aromatic acyl chlorides (~20%) < chlorobutyl chloride (~30%) << long chain acyl chlorides (70–80%). The catalyst could be utilized for at least three cycles in the acylation of ferrocene with butyryl chloride, showing similar activity (81.3, 73.3, and 86.4% ferrocene conversion, respectively).

The influence of hydrogen chloride pretreatment of a Ga–Mg-hydrotalcite anionic clay⁷⁸ on its catalytic activity in the acylation of aromatics by benzoyl chloride (arene/benzoyl chloride ratio = 14) was studied by Choudary et al.^{79,80} The hydrotalcite was dried at 80 °C, and the sample was designated as Ga–Mg–HT-80. Hydrogen chloride pretreatment of Ga–Mg–HT-80 was performed by bubbling gaseous hydrogen chloride through a mixture of the catalyst and the aromatic substrate, and then flushing with nitrogen to remove the physically adsorbed or absorbed hydrogen chloride from the reaction mixture. After this pretreatment, the surface area of the catalyst decreased from 9.0 to 2.9 m²/g. The fresh Ga–Mg–HT-80 catalyst showed no activity; however, after the hydrogen chloride pretreatment, the catalyst was activated, showing almost no reaction induction period. The activity values measured in terms of the time required for half the reaction for different aromatic substrates followed this order: mesitylene > *p*-xylene > toluene. The catalyst could be reused repeatedly in the reaction even in the presence of moisture (~90% benzoyl chloride conversion in the model reaction with toluene).

2.3. Acylation with Metal Oxides

Metal oxides were utilized in their pure form or in different mixtures as solid catalysts in fine chemicals preparation since they are commercially available or easily synthesized, they are stable toward moisture, and their properties can be tailored by doping with convenient metal ions.⁸¹

Dimethylbenzophenones can be obtained in high yield (88–97%) by reaction between benzoyl chloride and the three isomeric xylenes (xylene/benzoyl chloride ratio = 1.5) in the presence of iron(III) oxide, zinc oxide, tin(II) oxide, or molybdenum(VI) oxide, with iron(III) oxide showing the greatest activity.⁸² The inertia of some metal oxides, such as those of aluminum and titanium, in the same reaction is puzzling, since all the respective halides are powerful Friedel–Crafts catalysts.³ On the basis of comments made by different authors on the leaching of active FeCl₃, produced by reaction of iron oxide with HCl, into solution, the possible contribution of the homogeneous iron-based Lewis acid form is strongly suspected.

The acylation of toluene with benzoyl chloride (toluene/benzoyl chloride ratio = 40) over ferrous and ferric sulfates previously heat treated at 500, 700, and 900 °C was studied by Arata et al.;⁸³ the catalysts prepared by calcination of the two sulfates at 700 °C showed good activity [FeSO₄, initial rate = 7.7 × 10³ (mol/L·min·g); Fe₂(SO₄)₃, initial rate = 10.1 × 10³ (mol/L·min·g)]. The product distribution was 18–22% *o*-, 2–4% *m*- and 74–78% *p*-methylbenzophenone. Both ferrous and ferric sulfates are mainly remaining as sulfate forms when

calcined at 500 °C and decompose to form iron oxides containing 0.15% of sulfur at 700 °C.

Thallium oxide supported on different materials was studied by Choudary et al.⁸⁴ as catalyst in the benzene acylation with benzoyl chloride (benzene/benzoyl chloride ratio = 17). In general, TiO_x deposited on low-surface-area supports showed high catalytic activity (80% benzoyl chloride conversion after ~1.5 h), whereas that deposited on high-surface-area supports had almost no activity. This behavior is indicative of a different interaction between TiO_x and the supports. Strong metal–support interactions are well-known and are observed for many supported metals,^{81,85} however, the information on the chemical nature of the strong metal oxide–support interaction is scarce.^{86a} In the present case, since TiO_x is basic, it can chemically interact with the weak or strong acid hydroxy groups of high-surface-area supports. The low-surface-area supports are highly sintered macroporous materials and hence have no surface hydroxy groups; thus, the supported TiO_x keeps unchanged its catalytic properties.

P₂O₅/SiO₂ catalyst has been employed in the ecoefficient reaction of carboxylic acids with aromatic substrates to produce the corresponding aryl ketones.^{86b} The acylation reactions were carried out at reflux under solventless conditions or by using 1,2-dichloroethane as solvent. The reactions are so clean that no chromatographic separation was necessary to obtain spectroscopically pure compounds (except in a few cases). The acylation occurs at the *para* position with good selectivity; of course, in cases where this position is blocked, the acyl group is introduced at the *ortho* position. These reactions are rapid even with higher carboxylic acids; as expected, deactivated aromatic rings such as bromobenzene, chlorobenzene, and nitrobenzene gave low or no yields. The present acylation method occurs by *in situ* generation of a carboxylic anhydride derived from a mixed carboxylic-phosphoric anhydride. Interestingly, in the absence of the siliceous support the yields were lower (average, 20%); the effect of SiO₂ may be due to a good dispersion of P₂O₅ on the surface of silica gel leading to significant improvements in its reactivity. In addition, SiO₂ as a support may also minimize cross contamination between the product and the H₃PO₄ generated during the reaction.

The same reaction was also carried out by using Cu_xMn_(1-x)-Fe₂O₄ spinel catalyst (benzene/benzoyl chloride ratio = 10).⁸⁷ A relationship between the concentration of strong acid sites on the catalyst surface and the reaction rate was shown. Moreover, the incorporation of copper drastically decreased the number of Brønsted acid sites; the relatively high catalytic activity of copper-substituted systems for benzene benzoylation is due to the generation of Lewis acid sites at higher copper loadings.

2.4. Acylation with Acid-Treated Metal Oxides

Sulfated metal oxide catalysts represent a class of extremely attractive strong solid acids showing widespread application in different areas of chemical transformations.⁸⁸ Arata et al.^{89,90} reported that sulfated zirconia (SZ), prepared by treatment of zirconia with sulfuric acid or ammonium sulfate, exhibits extremely strong acidity and that it is able to catalyze the isomerization of butane to isobutane at room temperature. This behavior represents a unique catalytic performance, compared to those of typical solid acids, such as zeolites, which show no activity for the reaction at such low temperatures. Using Hammet indicators, Hino and Arata⁹⁰ claimed that SZ is an acid 10⁴ times stronger than 100% sulfuric acid; therefore, SZ, with $-H_0 = 16$, was

considered as the strongest halide-free solid superacid.^{91–94} However, the superacidity of SZ has been recently questioned by several authors,^{95–98} who claimed that SZ is only a strong solid acid with an acid strength comparable to that of sulfuric acid or some acid zeolites.

In an early study, Arata et al.⁹⁹ showed that SZ was catalytically active in the acylation of toluene with acetic and benzoic acids (toluene/carboxylic acid ratio = 145). In the latter case, the yield of methylbenzophenones was 60% and the product's distribution was 30–35% *o*-, 5% *m*-, and 60–65% *p*-methylbenzophenone. The same reaction carried out with benzoic anhydride took place readily even at 30 °C, and it seems to be also accomplished by the benzoic acid produced. The real heterogeneity of the catalyst was confirmed by the inertia observed when the catalyst was removed from the reaction medium. The acylation of toluene with acetic acid was also performed in a flow system by passing the vaporized reaction mixture through the SZ catalyst bed at 280 °C with a nitrogen carrier. The system seems to be quite promising even if no further development of the research was performed (51% acetic acid conversion; 89% selectivity with respect to all ketones; *ortho*-, *meta*-, and *para*-isomer selectivity 16, 13, and 71%).

Further studies were performed to evaluate the efficiency of SZ and sulfuric acid-treated alumina (SA) in the acylation of arenes with different benzoylating reagents (arene/benzoyl chloride ratio = 10).^{100–103} SZ catalyzed the reaction of *p*-chlorobenzoyl chloride with benzene, affording *p*-chlorobenzophenone in 80% conversion and 100% selectivity. The catalyst showed partial reusability without any further treatment. The loss of about 20% of particles during filtration can account for the partial loss of activity. Comparison experiments showed that the activity of SZ was slightly higher than that of SA for the reaction with benzoyl chloride (28% vs 22% benzophenone yield after 1 h) but much lower for the reaction with benzoic anhydride (45% vs 80% benzophenone yield after 1 h). The authors concluded that strong Brønsted acid sites are responsible for the production of the benzoyl cation although the Friedel–Crafts acylation with acyl chlorides is generally known to be catalyzed by Lewis acids.

The promoting effect of alumina on various types of sulfated metal oxides, namely, sulfated zirconia-alumina (SZA), sulfated titania-alumina (STA), and sulfated iron oxide-alumina (SFA), was reported.^{104,105} The catalyst efficiency in the acylation of toluene with benzoyl chloride (toluene/benzoyl chloride ratio = 22) was dependent on the content of alumina. For example, in the case of SZA, the catalyst activity increased with alumina content up to a maximum (~3 mol % Al₂O₃) and then decreased as the alumina content was further increased. The yields in isomeric methylbenzophenones of the reactions carried out with the catalysts were in the order SZA (91%) > SFA (78%) > STA (45%). The high or good activity of SZA and STA is consistent with the formation of strong acid sites on the catalyst surface due to the production of Al–O–Zr and Al–O–Ti bonds in the mixed oxides; these strong bonds lead to an increase of the concentration and thermal stability of the sulfate surface species and generate additional acid sites. On the contrary, the high activity of SFA was explained assuming that the reactions were homogeneously catalyzed by iron chloride formed by reaction of benzoyl chloride or hydrogen chloride evolved with the iron component of the catalyst.¹⁰⁶

The catalytic properties of mesoporous zirconias (Zr-TMSs) functionalized with triflic acid were studied by Singh et al.^{107,108} The catalysts were prepared via a postsynthesis method by reaction of Zr-TMS with triflic acid; for comparison, the

amorphous zirconia [Zr(OH)₄] was functionalized in the same manner. Physicochemical analyses revealed that triflic acid was bonded in the same fashion on both Zr(OH)₄ and Zr-TMS at all loading values: triflate groups bound via three equivalent oxygen atoms to zirconium atoms forming a tripod structure. Acylation of biphenyl (17) with benzoyl chloride (21) (17/21 ratio = 1) (Scheme 4) showed a comparable low conversion with both unfunctionalized amorphous and mesoporous zirconia (3.1 and 3.2%, respectively). The conversion of substrate 17 increased for both catalysts after the functionalization with triflic acid [41.0% for Zr-TMS and 20.5% for Zr(OH)₄], and the selectivity with respect to product 25 ranged from 93 to 100%; these results demonstrate that the benzoylation of 17 essentially needs a porous catalyst with uniform porous size and high acidity. The activity of the same triflic acid-functionalized Zr-TMS was studied in the acylation of toluene (1) with *p*-toluoyl chloride (7) (1/7 ratio = 1) to give 4,4'-dimethylbenzophenone (13) (1 conversion = 82 wt %, 9 selectivity = 21.4 wt %, 13 selectivity = 44.1 wt %) (Scheme 2). Results of catalyst-recycling studies showed a modest decrease in *p*-toluoyl chloride conversion after one cycle (from 50.7 to 49.2 wt %) which was related to a minor loading of CF₃SO₃H (from 15.0 to 14.1 wt %); this result seems to be rationalized with some leaching of CF₃SO₃H into the solution during the reaction.

2.5. Acylation with Heteropoly Acids

Heteropoly acids (HPAs) are Brønsted acids composed of heteropolyanions and protons as counteranions; the most commonly utilized HPA is the phosphotungstic acid (H₃PW₁₂O₄₀). HPAs are stronger than many conventional solid acids such as mixed oxides and zeolites. One important advantage of HPAs is that they can be utilized both homogeneously and heterogeneously. The homogeneous reactions occur in polar media at ~100 °C; on the other hand, when using nonpolar solvents, the reactions proceed heterogeneously. In the latter case, supported HPAs are the catalysts of choice, as bulk HPAs possess a low surface area (1–5 m²/g).¹⁰⁹ The HPA catalysts are easily separated from the heterogeneous reaction mixture by filtration and from the homogeneous systems by extraction with water.

The use of HPAs and multicomponent polyoxometalates as catalysts in liquid-phase reactions was reviewed by Kozhevnikov¹⁰⁹ in 1998. Moreover, an interesting minireview was published in 2003 by the same author¹¹⁰ concerning the Friedel–Crafts acylation of arenes and the Fries rearrangement catalyzed by HPA-based solid acids.^{111–113} The author concluded that HPA-based solid acids, including bulk and supported heteropoly acids as well as heteropoly acid salts, are efficient and environmentally friendly catalysts for all reactions analyzed.

The insoluble Cs_{2.5}H_{0.5}[PW₁₂O₄₀] was applied in the acylation of benzene with benzoic anhydride (benzene/benzoic anhydride ratio = 180) in 100% yield.¹¹⁴ The initial rate was almost proportional to the amount of catalyst. Repeated use of the catalyst was possible by washing the used one with benzene. However, the activity gradually decreased after the third run caused by the adsorption of both benzophenone and benzoic acid.

The alkali metal and ammonium salts of HPAs were studied by Izumi et al.^{115–117} In the acylation of *p*-xylene with benzoyl chloride (*p*-xylene/benzoyl chloride ratio = 20), the catalytic activity of sodium and potassium salts decreased with increasing metal content expressed as *x* in the formula M_{*x*}H_{3–*x*}[PW₁₂O₄₀].

For rubidium and cesium salts, however, the activity first decreased with increasing x and then jumped to attain a maximum at $x = 2.5$. Although the acid alkali metal salts, as well as the parent free acid $\text{H}_3\text{PW}_{12}\text{O}_{40}$, are protonic acids in nature, they worked as efficient catalysts to activate benzoyl chloride. In contrast, typical strong protonic acids such as sulfuric and perchloric acids were quite inactive for the present benzoylation reaction. The reason is that the heteropolyanion $\text{PW}_{12}\text{O}_{40}^{3-}$ has the ability to stabilize cationic intermediates^{118a} such as benzoyl cations, whereas simple oxoanions such as sulfate and perchlorate anions are unable of stabilizing such cations. However, it is important to take into account that a similar behavior was observed with acid-treated metal oxides.^{100–103} No dissolution of catalytically active species from the salts was observed (the reaction ceased completely if the heterogeneous salt was removed from the reactor). $\text{Rb}_{2.5}\text{H}_{0.5}[\text{PW}_{12}\text{O}_{40}]$ and $\text{Cs}_{2.5}\text{H}_{0.5}[\text{PW}_{12}\text{O}_{40}]$ are highly porous materials with mesopores showing 2–7 nm average diameter; this mesoporous structure seems to favor the benzoylation since the reaction takes place not only on the surface but also in the bulk near the surface, owing to the highly polar nature of benzoyl chloride and the deriving cationic intermediate. It must be underlined that not only can $\text{Cs}_{2.5}\text{H}_{0.5}[\text{PW}_{12}\text{O}_{40}]$ act as an efficient catalyst for electrophilic acylation with acid chlorides or anhydrides but also, more and more advantageously, it can directly activate the carboxylic acids.

The polyvalent transition metal salts of dodecatungstophosphate can act as highly effective and recyclable heterogeneous catalysts for Friedel–Crafts acylation of both activated and less activated aromatic substrates with carboxylic acids.^{118b} In the model reaction of toluene with dodecanoic acid, $\text{H}_3\text{PW}_{12}\text{O}_{40}$ and $\text{Cs}_{2.5}\text{H}_{0.5}\text{PW}_{12}\text{O}_{40}$ show low yields (<35%), suggesting that a catalyst with strong Brønsted acidity is not able to catalyze this kind of reaction. On the contrary, salts of polyvalent transition metal ions (Fe^{3+} , Ti^{4+} , Sn^{4+} , Zr^{4+} , Bi^{3+} , Ru^{3+}) and $\text{PW}_{12}\text{O}_{40}^{3-}$ show good to excellent yield (65–94%) with only 3 mol % of the catalyst; the *para* isomer was the major product (86–90% selectivity). The highest yield (94%) was achieved in the presence of $\text{FePW}_{12}\text{O}_{40}$. This catalyst was found to be truly heterogeneous, and after its separation from the reaction mixture by a simple centrifugation, it can be recycled at least three times keeping excellent yield without any reactivation treatment. The catalyst was also employed to acylate other aromatic compounds with dodecanoic acid: electronrich arenes such as *p*-xylene and anisole gave the corresponding acylation products in 89 and 97% yield, respectively, but even nonactivated arenes such as benzene and chlorobenzene gave satisfactory yield (53 and 39%, respectively). Finally, the acylation of toluene with a variety of straight chain C6–C19 carboxylic acids and benzoic acid gave the corresponding acylated products in 87–94% yield. The yield increases with carbon number of linear carboxylic acids from C2 to C6, which suggests that the hydrophobic reactant is more favorable for this reaction. Interestingly, the acylation rate strongly depends on the type of metal cation: the rate increases with electronegativity of cation. This suggests that the catalytic activity increases with Lewis acid strength, originated from the exchanged metal cation. The effect of Keggin anions on the activity of Ru salts was also tested; the initial rate and the final yield show the following order: $\text{PW}_{12}\text{O}_{40}^{3-} > \text{SiW}_{12}\text{O}_{40}^{4-} > \text{PMo}_{12}\text{O}_{40}^{3-}$, which is consistent with the order of the acid strength of the proton form of HPAs. From these results, the cooperation of strong Brønsted acid sites and Lewis acid sites

Scheme 13

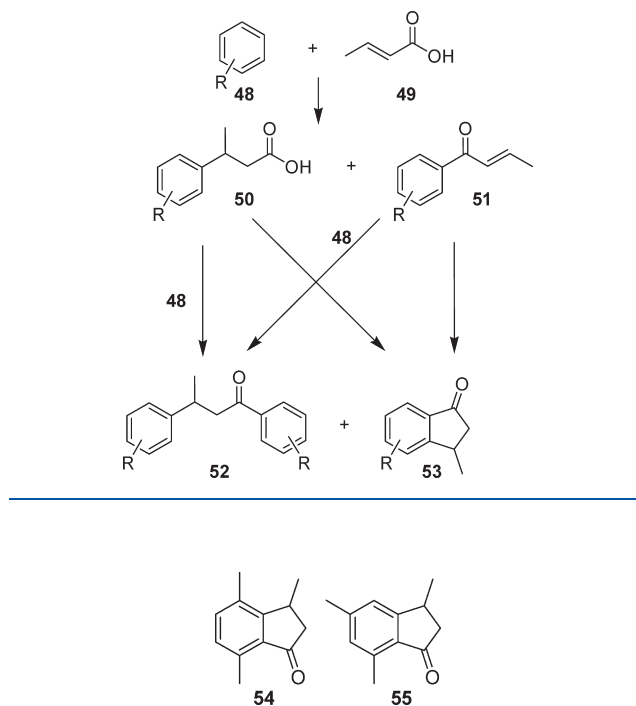


Figure 4. Indanones obtained by Friedel–Crafts reactions of *p*- and *m*-xylene with crotonic acid.

may be responsible for the high activity of the polyvalent transition metal salts of $\text{PW}_{12}\text{O}_{40}^{3-}$.

It is well-known that one of the major problems associated with HPAs in the bulk form is their low efficiency due to low surface area, rapid deactivation, and relatively poor stability. Attempts to improve the efficiency and stability of HPAs were made by using various supports including mesoporous silica,¹¹⁹ mesoporous aluminosilicates,¹²⁰ zirconia, and alumina.¹²¹ Because of their basic nature, alumina and zirconia tend to decompose HPAs, resulting in deformation of the parent Keggin structure, thereby reducing the overall acidity. The use of pure phosphotungstic acid and its cesium salt supported on silica as solid catalysts for the acylation of aromatics 48 with crotonic acid 49 (48/49 ratio = 85) was studied by Corma et al.¹²² The protonation of crotonic acid in the presence of a Brønsted acid produces an electrophilic reactive intermediate that can be either an alkyl or an acyl carbocation which can react with the aromatic ring to produce either the alkylated product 50 or the acylated product 51, respectively (Scheme 13). Products 50 and 51 can further react either via intramolecular acylation/alkylation reaction to produce the corresponding indanone 53 or via an intermolecular acylation/alkylation process to form the corresponding ketone 52. Products 52 and 53 could be obtained in different proportions depending on the relative rates of the different reactions. Analysis of products obtained with *p*- and *m*-xylene showed that all the catalysts were more active for the acylation than for the alkylation reaction. Indeed, indanones 54 and 55 (Figure 4) were obtained in 65 and 79% yield. The silica-supported HPA was more active than the unsupported one, due to the increase of the surface area. However, in the case of cesium-exchanged HPA, the surface area concept could not be directly extrapolated since the surface area increased when

cesium ions were introduced, but the total Brønsted acidity decreased when H^+ was replaced by Cs^+ . A good correlation could be, however, observed between the specific surface acidity and the catalyst activity.^{123a}

Similarly, the catalytic performance of $\text{H}_4\text{SiW}_{12}\text{O}_{40}$ supported on silica was tested in the reaction of *p*-xylene with γ -butyrolactone to produce the 5,8-dimethyl- α -tetralone.^{123b} The process, carried out in a stainless autoclave at 210 °C, showed a high activity and selectivity when 20 wt % $\text{H}_4\text{SiW}_{12}\text{O}_{40}/\text{SiO}_2$ was employed; the unsupported heteropolyacid $\text{H}_4\text{SiW}_{12}\text{O}_{40}$ was found to convert γ -butyrolactone but mainly yielded byproducts adhering tenaciously to the catalyst. The reaction of *p*-xylene with vinylacetic acid to give 3,4,7-trimethyl- α -indanone was also performed with the same supported catalyst (40 wt %): the process was carried out for 4 h at 190 °C and afforded the product in 44% yield.

As already underlined by Kozhevnikov,^{109,110} it is quite evident that HPAs and related compounds represent materials to be efficiently utilized as catalysts in organic reactions, including Friedel–Crafts acylation. However, a serious problem with the use of these compounds as heterogeneous catalysts is their deactivation because of coking. In fact, conventional regeneration by calcining at 500–550 °C, which is routinely used in the case of oxides and zeolites, cannot be applied to HPAs because their thermal stability is not high enough. However, some tricks useful in alkane isomerization processes, that include doping with transition metal ions (i.e., Pd) and controlled addition of water to the catalyst, can be successfully utilized to prolong the lifetime of HPA catalysts.

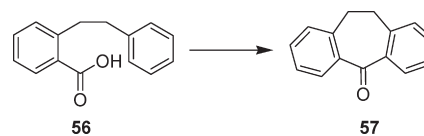
2.6. Acylation with Nafion

The use of Nafion, a solid perfluorinated resinsulfonic acid, was reported early by Olah et al.¹²⁴ for the acylation of toluene with benzoyl chlorides (toluene/benzoyl chloride ratio = 2). The reaction could be simply carried out by heating under reflux the mixture of the reagents with the solid catalyst, affording substituted benzophenones in 81–87% yield. The optimum catalyst amount was 30 wt %, as higher quantities significantly decreased the yields due to adsorption of appreciable amounts of products and starting materials. Concerning the isomeric composition of methylbenzophenones, when benzoyl chloride was employed as acylating agent, the reaction gave predominantly *para*- and *ortho*-substitution (in accordance with the typical electrophilic aromatic reaction), but the *o/p* ratio (2.34–4.81) was, in general, higher than that obtained under homogeneous (AlCl_3) catalysis (0.02–0.62). The reaction could be applied to *p*-nitrobenzoyl chloride and various substituted benzenes, giving the corresponding benzophenones in 60–90% yield.

More problems resulted with the acetylation of aromatic compounds; in fact, with acetyl chloride the preferential formation of ketene degradation products was observed, whereas neither acetic anhydride nor acetic acid alone proved to be effective. On the contrary, when an equimolecular mixture of acetic acid and acetic anhydride was refluxed with toluene, *m*-xylene, or mesitylene in the presence of Nafion, the corresponding acetophenones were isolated in 3, 21, and 72% yield, respectively.

Nafion was also successfully utilized as catalyst for the intramolecular Friedel–Crafts acylation.^{125,126} The cyclization of diphenylethane-2-carboxylic acid (**56**) (Scheme 14) was carried out in refluxing *p*-xylene, affording the 10,11-dihydro-5*H*-dibenzo[*a,d*]cyclohepten-5-one (**57**) in nearly quantitative

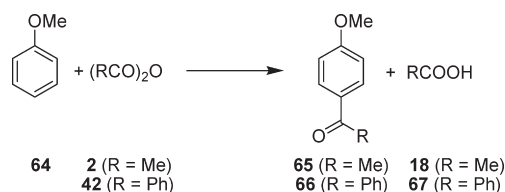
Scheme 14



Scheme 15



Scheme 16



yield. The procedure was then applied to other aromatic carboxylic acids by using 1,2- and 1,3-dichlorobenzene as solvent, and the cyclization products were isolated in 82–95% yield. The reactivity of the aliphatic carboxylic acids **58–60** was also investigated (Scheme 15). Even though the yield of 1-indanone (**61**) from 3-phenylpropionic acid (**58**) was very low (~5%), 4-phenylbutyric acid (**59**) and 5-phenylvaleric acid (**60**) afforded the corresponding α -tetralone (**62**) and 1-benzosuberone (**63**) in 90 and 83% yield, respectively.

3. ACYLATION OF AROMATIC ETHERS

Aromatic ethers are described to be very reactive substrates toward electrophilic substitution and are therefore successfully acylated by using catalysts that normally show modest activity with arenes. However, this statement must be carefully considered each time, since the alkoxy group represents a good donor for the acid sites of the catalyst and it can interact so strongly with the catalyst itself that the original activity of both aromatic ether and catalyst can be greatly lowered. The Friedel–Crafts acylation of aromatic ethers has attracted considerable interest in organic synthesis and in industrial chemistry because of the widespread application of the corresponding ketones as valuable intermediates in fine chemistry.^{26,127–130} An example is the selective acetylation of 2-methoxynaphthalene (2MN) at the carbon in position 6 owing to the great interest in 2-methoxy-6-acetylnaphthalene (2Ac6MN), an intermediate in the preparation of the anti-inflammatory drug (*S*)-Naproxen.^{58,131}

3.1. Acylation with Zeolites

Derouane et al. reported the acylation of anisole (**64**) with acetic anhydride (**2**) (**64/2** ratio = 2) over HBEA zeolite.²² The reaction afforded *p*-methoxyacetophenone (**65**) as the sole

aromatic product (Scheme 16). Compound **65** and acetic acid **18** were produced in equal amounts at short reaction times, confirming that reagent **2** was not noticeably hydrolyzed under the reaction conditions. However, a deficit of acetic acid was observed at long reaction times, probably due to its reaction with the silanols of the zeolite, ultimately resulting in the dealumination of the zeolite framework. This partial and uncontrollable dealumination led to the irreversible loss of acid sites, giving rise to an irreversible catalyst deactivation. The inhibition of the catalyst in the batch reaction was also shown by detailed kinetic analyses using a Langmuir–Hinshelwood model that allowed the authors to quantify its nature and extent. The adsorption equilibrium constant for product **65** exceeded by a factor of at least 6 the adsorption equilibrium constant for any reactant, and the occupancy of the intracrystalline volume of the zeolite by compound **65** increased rapidly with conversion, thereby reducing the access of reactants to the catalytic sites and resulting in a catalyst deactivation as the conversion increased.¹³²

The origin of the HBEA deactivation in the same reaction was further investigated by the research groups of Derouane^{23,133} and Guisnet.²⁶ The authors showed that, by performing the model reaction (**64/2** ratio = 1) under batch conditions, a rapid catalyst deactivation occurred, which could be attributed, to a large extent, to the inhibiting effect of the product. However, when the reaction was performed in a fixed bed reactor, the catalyst deactivation was much slower, particularly when an anisole-rich mixture (**64/2** molar ratio = 5) was used, with product **65** being obtained in high selectivity (>98%). The conclusion is that the use of an excess of anisole enhances the catalyst stability and limits both retention of product **65** and formation of polyacetylated byproducts which deactivate the catalyst even if, as previously underlined, the reaction product **65** continued to be the major poison of the catalyst. A possible acylation mechanism was proposed in which the acylating agent **2** reacts first with the zeolite to form an acyl cation–zeolite complex **68** (Scheme 17) which then acts as acylating reagent.

Controlled dealumination was reported^{134a} as an instrument to enhance the activity of zeolites by tailoring their acidity. Dealuminated HBEA showed, in the same reaction (**64/2** ratio = 1), higher activity in the initial period compared to the case of untreated HBEA (48.1% vs 26.4% anisole conversion after 15 min), whereas at longer reaction times the same conversion was achieved (~70% after 240 min). Dealumination provokes changes in acidity and in pore distribution; the initial higher activity of the dealuminated HBEA zeolite could be due to the improved diffusion; this effect continues until coking reactions dominate. However, the spent catalyst restored its activity upon exposure to fresh reaction mixture, which was likely able to extract the deposited higher molecular weight compounds, or by calcination in air at 500 °C for 4 h, which removed coke by oxidation. After the above treatments, the catalyst could be reused in the model reaction of Scheme 16 for at least four cycles, showing quite unchanged activity (product **65** yield = 75%).¹³⁰ Therefore, two types of coke exist in the channels system and in the external surface: (i) extractable (“reversible”) and (ii) nonextractable (“irreversible”) coke. On the basis of these conclusions, the authors tried a further increase of the catalyst activity by using the reactor in Figure 5.^{134a} In this Soxhlet-like extractor-reactor, the zeolite was placed in the reflux chamber containing the condensing reaction mixture. However, the conversion was lower compared to that obtained in batch experiments (30% vs 70% after 240 min), probably due to the different vapor pressures of both reactants.

Scheme 17

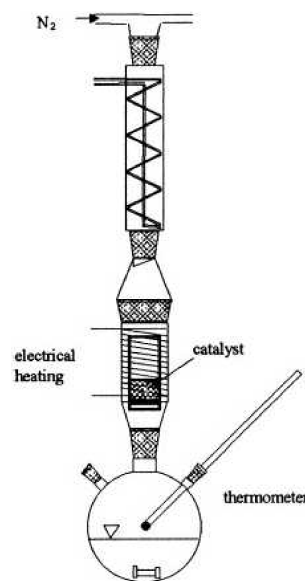
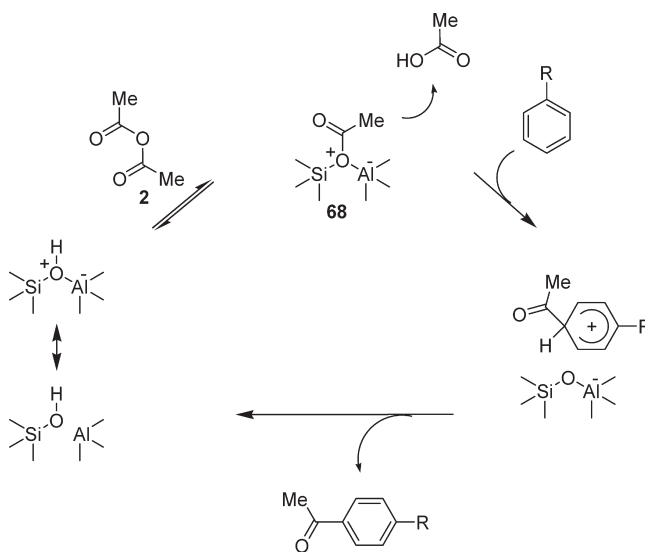


Figure 5. Trickle bed reactor. Reprinted with permission from ref 134a. Copyright 1999 Elsevier.

In the same model acylation reaction, the catalytic activity of cation-exchanged NaY zeolites was found to be strongly influenced by the nature of the exchanged cation.^{134b} Rare earth cation (Ce^{3+} , La^{3+} , and Nd^{3+}) exchanged zeolites exhibit the highest activity showing 66, 24, and 21% anisole conversion, respectively. Among the various zeolites studied, HBEA showed the highest catalytic activity (81% anisole conversion). The correlation of the catalytic activity with acidity (evaluated by FT-IR and DSC studies) revealed that the Brønsted acid sites in the zeolite are responsible for the anisole acylation.

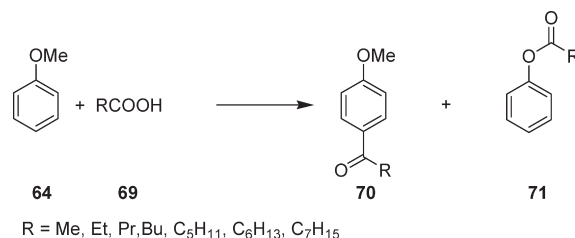
Acylation of anisole (**64**) with carboxylic acids **69** (**64/69** ratio = 45), in particular with octanoic acid (Scheme 18), was studied by Beers et al.^{135,136} over variously activated HBEA zeolites. Treatment of HBEA with steam or acid did not result in any significant

change in the surface area and pore volume. However, treating the zeolite with oxalic acid after steaming resulted in a significant decrease of the surface area (from 670 to 500 m²/g) and an increase of the bulk SAR (from 13 to 51). This led to an increase in activity and selectivity: in fact, HBEA itself exhibited an activity, defined as the initial apparent first-order constant k , of 0.03 L/g_{cat}·h and a selectivity toward compound **70** (R = C₇H₁₅) of 80% at 50% conversion, whereas a great activity increase ($k = 0.12$ L/g_{cat}·h) and a selectivity improvement (up to 95%) were observed with the acid-treated catalyst. It was reported⁵⁴ that the activity enhancement observed in steamed zeolites could be due to the migration of the extraframework aluminum (EFAL) into the reaction mixture, hereby acting as an homogeneous catalyst. However, the model reaction did not continue after hot filtration,^{137a} indicating that no active species were leached from the zeolite during the reaction. More likely, the activity and selectivity enhancement could be due to the increased accessibility or participation of active sites, rather than the formation of additional active species. Indeed, removal of EFAL and, in general, of “site-blocking” species resulted in an increase of the number of active sites that are accessible.

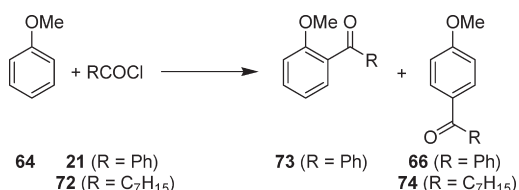
The acylation of anisole with long chain carboxylic acids (hexanoic, octanoic, and decanoic acid) has been also investigated by Mayadevi et al. over large pore zeolites HBEA, HFAU, and HMOR with different SAR (in brackets).^{137b} According to Scheme 18, the products of the acylation with hexanoic acid (**69**, R = C₅H₁₁) are the ketone **70** (major), the ester **71** (minor), and a trace amount of the *ortho*-isomer. The activity of HBEA increases with dealumination (according to previous studies). This is again attributed to the generation of mesopores during dealumination and the corresponding ease diffusion of the reactants and products. The conversion of hexanoic acid after 6 h at 140 °C follows the order HFAU(6) > HBEA(15) > HMOR(11), whereas for decanoic acid the order was HBEA(15) > HFAU(6) > HMOR(11). In the acylation of anisole with hexanoic acid, the reaction rate constant of zeolites showing a SAR value of 49 reveals that HBEA is about seven times more active than HMOR but only slightly more active (by about 17%) than HFAU.

The handling of unsupported zeolites in batch reactions frequently shows some drawbacks since these materials have a colloidal form and the small size of the particles renders difficult their recovery and purification. The transformation of powders into extrudates or tablets requires the introduction of binders such as α -Al₂O₃ that can increase the diffusion barrier between the reactants and the active sites. For these reasons, different groups devoted their efforts to the preparation of zeolites supported over special materials to obtain a macroscopic shaping easily recoverable from the reaction mixture and more utilizable in a fixed bed reactor.^{138,139} To this end, HBEA zeolite supported on macroscopic preshaped SiC material (HBEA/SiC) was investigated as a high-performance catalyst for benzylation of anisole (**64**) with benzoyl chloride (**21**) (**64**/**21** ratio = 1.5) (Scheme 19).¹⁴⁰ The SiC support exhibited high thermal conductivity, high resistance toward oxidation, high mechanical strength, and chemical inertness, properties required for a good support. HBEA zeolite was synthesized and in situ deposited on SiC extrudates previously prepared by a reported technology.^{141a} A high-magnification SEM image showed the presence of small zeolite particles homogeneously dispersed on the entire surface of the support. The deposition of HBEA on the SiC surface significantly increased the overall surface area of the material

Scheme 18



Scheme 19



from 25 (for pure SiC) to more than 100 m²/g (for HBEA/SiC) along with a large microporous contribution (~60 m²/g). This composite catalyst showed relatively high activity with a total 71% conversion of benzoyl chloride after 24 h on stream (95% selectivity with respect to ketone **66** and less than 5% selectivity for ketone **73**). The catalyst could be reused after washing with methylene chloride, showing quite similar results for three tests. Similar experiments carried out with unsupported more highly acidic HBEA showed that in the first cycle similar activity and ketone selectivity were achieved, but significant catalyst deactivation was observed during the second cycle. The higher activity of the HBEA/SiC was tentatively attributed, by authors, to the dispersion of the zeolite on the support surface, leading to a larger contact surface with reactants.

The zeolite deactivation during electrophilic acylation was attributed to the site blockage due to the accumulation of heavier products. Moreover, the aromatic ketones (i.e., *p*-methoxybenzophenone) are the main inhibitors for the Friedel–Crafts reaction due to their strong adsorption on the active sites. Temperature programmed oxidation (TPO) analysis carried out on the commercial HBEA catalyst clearly highlights the important coke formation when compared to that which was observed on the SiC supported HBEA catalyst, that is, 7 instead of 1.25 wt %.^{141b} In addition, coke formed on the bulk zeolite catalyst also exhibits a higher resistance toward combustion (i.e., maximum combustion peak at 600 instead of 400 °C for the supported zeolite). The dispersion of the zeolite crystals on the SiC support also allows a high diffusion rate of ketones out of the pores of the HBEA-SiC catalyst, thus lowering the deactivation rate as a function of TOS when compared to that observed on the bulk HBEA.

With the aim of achieving a supported HBEA with higher performance, the same authors¹⁴² prepared HBEA zeolite nano-wire material by using mesoporous multiwalled carbon nanotubes (MWNTs) as directing templates. The catalyst was obtained by growing the BEA zeolite in the presence of carbon nanotubes favoring the formation of carbon templates. It was assumed that the confinement effect inside the tubes could

induce an increase in pressure, thus promoting the synthesis of nanoparticles of BEA zeolite by replacing the hydrothermal pressure increase by the internal pressure increase. The final carbon template was removed by submitting the sample to calcination in air at 750 °C. The as-prepared BEA zeolite was then converted into the H-form, and it was employed in the acylation of anisole (**64**) with benzoyl chloride (**21**) (**64/21** ratio = 8), showing a satisfactory activity (anisole conversion ~65%) and selectivity toward *p*-methoxybenzophenone (~95%). However, it must be emphasized that similar and even better results could be obtained in the same reaction promoted by simpler and less expensive catalysts.

The preparation and use of active catalysts coated on a structure packing represents a further attractive replacement for conventional catalysts in randomly packed beds or slurry reactions.¹⁴³ A method was developed in which catalytically active and selective HBEA coatings could be prepared on ceramic monoliths constituted either of pure silica or of cordierite ($2\text{Al}_2\text{O}_3 \cdot 5\text{SiO}_2 \cdot 2\text{Mg}$) (Figure 6a) and on metallic wire gauze packings¹⁴⁴ (Figure 6b). The average loading values of the HBEA coatings were the following: silica monolith, 6.6 wt %; cordierite monolith, 5.4 wt %; silica precoated wire gauze packing, 5.6 wt %. The activity of the coated structures was measured batchwise in the acylation of anisole (**64**) utilized as solvent-reagent with octanoic acid (**64**/octanoic acid ratio = 45) (Scheme 18). The liquid reaction mixture was carried through the monoliths using a nitrogen flow. The silica monolith showed the highest activity ($k = 0.05 \text{ L/g}_{\text{cat}} \cdot \text{h}$), which was only 10% lower than that of HBEA particles in slurry. The activities of the coated cordierite monolith and the metal wire gauze packing were much lower than that of the HBEA particles in slurry. All monoliths gave a similar selectivity of about 77–85% toward the main *para*-isomer **70** ($\text{R} = \text{C}_7\text{H}_{15}$) compared to the 84% selectivity of the original HBEA tested in slurry. Since, in the solid acid-catalyzed acylation with carboxylic acids, inhibition of the active sites occurred due to water adsorption, a monolithic structured reactor could make it possible to remove water in situ by a stripping operation using a gas flow through the reactor. The HBEA-coated monoliths could be reused after regeneration by washing with acetone, drying at 120 °C (16 h), and calcining at 450 °C for 4 h.

The HZSM-5 zeolite was utilized as catalyst in the acylation of anisole (**64**) with various linear carboxylic acids **69** (**64/69** ratio = 4) (Scheme 18), showing some interesting results.¹⁴⁵ As expected, a drop in activity from propanoic (92%) to stearic acid (0%) was observed; this order of activity, reversed to that previously described by Geneste³⁹ in the presence of REY zeolites, is evidently due to the small micropore size of HZSM-5, in which the formation of large product molecules was difficult (in the case of pentanoic to octanoic acids) or impossible (in the case of longer chain carboxylic acids). Only two kinds of products were obtained in all experiments, namely, the 4-acylanisoles **70** and the carboxylic acid phenyl esters **71**. The selectivity for the C-acylated products **70** increased from 0.5% with acetic acid to 80% with butanoic acid and then remained constant for C_5 – C_7 acids. A great effect of temperature on both the conversion and selectivity of the reaction with acetic, propanoic, and butanoic acids was evidenced: phenyl esters **71** were mainly produced at lower temperature (<130 °C), while at higher temperature (>130 °C) 4-acylanisoles **70** were the predominant products.

Detailed studies on the characterization of acylating intermediates formed on HZSM-5 with acetic acid, acetic anhydride, and acetyl chloride were performed.¹⁴⁶ In the case of acetic acid,

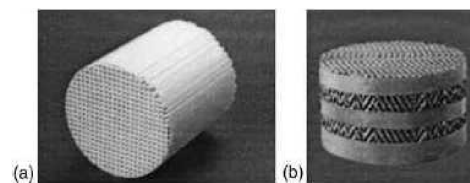


Figure 6. Examples of a structured reactor packing: (a) monolithic packing; (b) wire gauze packing. Reprinted with permission from ref 144. Copyright 2003 Elsevier.

Scheme 19bis



the molecules are primarily hydrogen bonded to the Brönsted sites, whereas, in the case of acetic anhydride and acetyl chloride, a reaction easily occurs at the Brönsted sites, forming an acetyl-zeolite intermediate. The comparison of interaction between the Brönsted sites in HZSM-5 and the three above-mentioned acylating reagents and other polar organic compounds, such as ketones, shows that molecules having a gas-phase proton affinity equal to or greater than that of ammonia are protonated by HZSM-5; on the contrary, molecules that have a proton affinity less than that of ammonia tend to form hydrogen bonds with Brönsted sites and the strength of the hydrogen bonding appears to vary in a regular manner with the proton affinity of the adsorbate. These results lead the authors to the conclusion that the acylium-ion-like acetyl-zeolite intermediate is completely analogous to the carbenium-ion-like alkoxide intermediate formed at Brönsted acid sites by an alkylating reagent. In conclusion, HZSM-5 is readily capable of forming the acylium-ion-like intermediates required for the Friedel–Crafts acylation reaction; the main problem of the reaction carried out with this catalyst is still the interaction of ketone products and byproducts with the catalyst active sites. These continuous interactions are well-known to produce coke in the zeolite, leading to deactivation of active sites. A possible way to overcome these problems should be the investigation of materials that are less acidic but more resistant to coke formation, such as HZSM-5 zeolites containing Fe^{3+} in place of Al^{3+} in the framework, that are reported to effectively produce less coke in butene isomerization.^{147a}

Acylation of aromatic ethers with carboxylic acids smoothly proceeds at 190–230 °C in the presence of zeolite catalyst under microwave irradiation (maximum power 300 W) to efficiently afford aromatic ketones.^{147b} HY(30–80) and HBEA(40) zeolites were active for this acylation giving the aromatic ketones in good yields (Scheme 19bis). Hexanoic and butyric acid smoothly underwent the acylation, while propanoic acid showed lower reactivity; anisole gave the *para*-acylation products nearly selectively. 2,3-Dihydrobenzofuran also reacted at the *para*-position with respect to the oxygen atom, predominantly. The microwave assisted reactions were, in general, faster than the

conventional oil bath heated reactions and gave higher yields in the acylation products.

Corma et al.¹⁴⁸ showed that the activities of HY zeolites with different levels of Na⁺ exchange in the acylation of anisole with phenylacetyl chloride (anisole/phenylacetyl chloride ratio = 1) were independent of their acid strength distributions; on the contrary, a linear dependence between the Na⁺-exchange level of the zeolite and the initial rate for the ketone formation (r_0) was observed (Figure 7). The linearity suggests that all the acid sites with weak, medium, and strong acidity are active in the present reaction. This was also confirmed by the small increase in the TON values (from 73 to 90 based on anisole) when the SAR framework changed from 9 to 24, with the zeolites with higher silica content being slightly more active. This behavior can be explained by taking into account that hydrolysis and acylation are competitive processes, both being catalyzed by the zeolite. Since in the heterogeneous catalysis the real reaction medium is the solid surface, and the concentration of water is lower in the more dealuminated samples, it is expected that acylation becomes comparatively favored over hydrolysis when more hydrophobic catalysts are used. The results confirm that a good catalyst does not need very strong acid sites, but a high-SAR framework is better in order to achieve an appreciable hydrophobicity and consequently a good catalytic performance.

LaY zeolites showed enhanced activity with respect to the starting HY sample in the acylation of anisole with acetyl chloride and acetic anhydride (anisole/acetylating agent ratio = 140).¹⁴⁹ The enhancement of the Brönsted acid strength of the LaY was attributed to the presence of La²⁺(OH) ions which may be formed during the calcination $[\text{La}^{3+}(\text{H}_2\text{O})_n(\text{O-zeol}^-)_3 \rightarrow \text{La}^{2+}(\text{H}_2\text{O})_{n-1}(\text{OH})(\text{O-zeol}^-)_2 + \text{HO-zeol}]$.¹⁵⁰

Some attractive results deserving of further attention and development were reported by Wang et al.¹⁵¹ concerning the acylation of anisole with alkanolic acids, alkanolic anhydrides, and aromatic carboxylic acids (anisole/acetylating agent ratio = 4) over different HY and HZSM-5 zeolites. Results achieved with one HZSM-5 zeolite (SAR = 60) and four HY zeolites (SAR = 5.8–18.4) in the acylation of anisole with propanoic acid showed an order of activity consistent with the order of the Lewis sites' strengths and opposite to the order of the Brönsted sites' strengths. The byproducts formed were phenyl propionate and 2-hydroxypropionophenone, originated respectively from the attack of the propionic acid at the oxygen atom of anisole and from the Fries rearrangement of phenyl propionate. C-acylation was preferentially catalyzed by Lewis acid sites, and instead, the esterification reaction was promoted by strong Brönsted sites, which were at first absent in all HY zeolites but were produced from the Lewis acid sites by reaction with water coming from the carboxylic acid. The reaction showed a quite interesting synthetic application in the benzoylation of anisole with a series of substituted benzoic acids. In general, the substituted benzophenones were produced with satisfactory yield (20–80%); however, a great effect of the substituent groups at the aromatic ring of the benzoic acid was observed: in particular, the conversion decreased when the electron-donating nature of the substituent decreased (for example: 87% conversion of *p*-methoxybenzoic acid vs 60% conversion of *p*-bromobenzoic acid).

The limitation imposed by small pore dimensions could be overcome, as already observed in the acylation of arenes, by using MCM-41 mesoporous materials. The preparation of mesoporous aluminosilicate MCM-41-type material was performed from HBEA zeolite seeds.¹⁵² This catalyst was utilized in the acylation

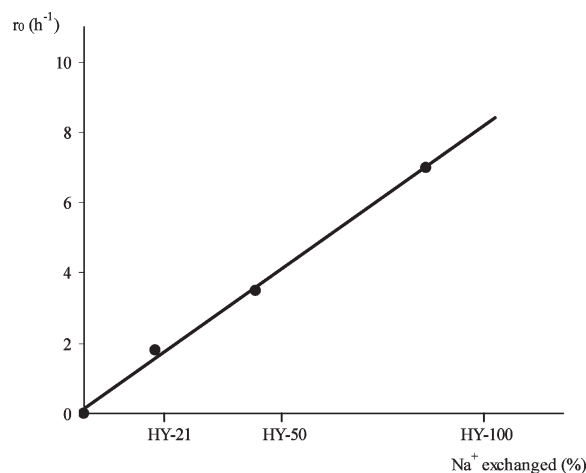
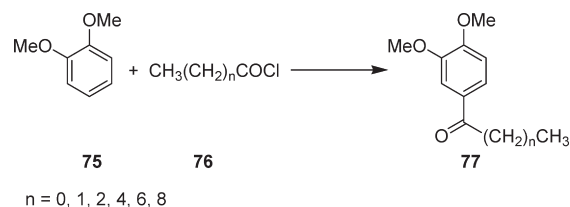


Figure 7. Influence of the percentage of the Na⁺ exchange on the initial rate of formation of 1-(4-methoxyphenyl)-2-phenylethanone (r_0).

Scheme 20



of anisole (64) with octanoyl chloride (72) (64/72 ratio = 45) (Scheme 19) with the aim of improving the transport of the reactants, especially for the relatively hindered molecules such as 72. The catalyst showed a good activity, with product 74 being obtained in 90% yield after 1 h. As commonly observed, the use of the carboxylic acid as acylating agent resulted in a slower process (~20% yield after 26 h) due to its lower electrophilicity and to the production of water that inhibits the active sites of the zeolite, as previously observed by Beers et al.¹⁴⁴

The regioselective propanoylation of veratrole (75) to 3,4-dimethoxypropiophenone (77) with propanoyl chloride (76) (75/76 ratio = 1) was explored by Singh et al.¹²⁷ over HBEA, HMOR, HY, and REY zeolites in comparison with AlCl₃ (Scheme 20, $n = 1$). In all experiments, 3,4-dimethoxypropiophenone was the main product accompanied by small amounts of other (consecutive) products. Compared with AlCl₃, all zeolites showed higher selectivity (90–100% vs 70%), and HBEA catalyzed the reaction more efficiently than other zeolite catalysts (40% vs 10% veratrole conversion for HY). The catalyst could be recycled after washing with acetone and calcining at 500 °C for 16 h in air; its activity, however, progressively decreased to a small extent on recycling, but the selectivity remained nearly unaffected (93.4% fresh catalyst, 95.8% in the second cycle).

The activities of some HY zeolites showing different Lewis and Brönsted acid site densities were studied by Sartori et al.¹⁵³ in the acylation of dimethoxyarenes (with particular attention to veratrole, Scheme 20) with different acyl chlorides (dimethoxyarene/acetyl chloride ratio = 5) as a function of zeolite acidity and chain length and lipophilic nature of the acyl chlorides. Due to the particularly soft reaction conditions, 3,4-dimethoxyphenyl

ketones **77** were the sole isomers recognized in the reaction mixture. Results of the catalytic tests (yield of compounds **77**) confirm that the best catalyst was the HY zeolite with a SAR value of 14, characterized by an optimum ratio between Lewis and Brönsted acidity (medium-strength acid site densities for Lewis and Brönsted acids = 17.0 and 11.0 mmol/g py respectively), whereas more strongly or weakly acidic materials gave lower yields. This evidence suggests that the reaction requires both a delicate balance between the Lewis and Brönsted acid sites and a low density of hydrophilic hydroxy groups that can strongly and preferentially interact with methoxy and carbonyl groups, resulting in the pore-blocking by product molecules. The chain length effect of the acyl chloride on the ketone yields showed the typical trend already reported by Geneste et al.³⁹

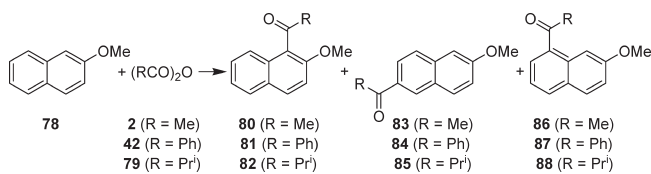
The remarkable effect of pore dimensions and structural properties on zeolite efficiency was further confirmed by Moreau et al.^{154,155} in the acylation of veratrole with acetic and benzoic anhydrides (veratrole/anhydride ratio = 1). The following r_0 value order was observed with some commonly utilized zeolites: HY (0.125) > HBEA (0.050) > HMOR (0.015). These results can be directly related to the microporous structures of the different catalysts, for which the pores of the tridimensional HY framework allow a readier diffusion of both substrate and product than those of the interconnected channel architecture of HBEA and those of the bidimensional HMOR framework.

Extensive studies were carried out to investigate the electrophilic acylation of 2MN (**78**) with acetic anhydride (**2**) in the presence of different zeolites (Scheme 21) mainly for two reasons: (i) 2Ac6MN (**83**) represents, as underlined in the introduction of this section, a valuable intermediate in pharmaceutical chemistry and (ii) reagent **78** represents a suitable model substrate since it can afford different isomeric ketones via direct acylation or isomerization and consequently it makes it possible to evaluate the effect of the catalyst properties and experimental conditions on the regioselectivity of the reaction.

Acetylation of **78** generally occurs at the kinetically controlled 1-position, leading to 1-acetyl-2-methoxynaphthalene (1Ac2MN (**80**)). However, over acid zeolites a different product distribution was frequently obtained, mainly depending on the type of the framework, solvent, and temperature.¹⁵⁶

In a series of independent studies the research groups of Hölderich,¹⁵⁷ Guisnet,^{158–160} and Lenarda¹⁶¹ thoroughly investigated the acetylation of 2MN with acetic anhydride in the presence of HBEA zeolites with particular attention to the acid-treated materials. Concerning the special activity of HBEA, in addition to its generally large outer surface,^{157,162–164} it possesses particular acid properties related to local defects, i.e., aluminum atoms which are not fully coordinated to the framework.^{164–166} The reactions performed over this catalyst showed a common behavior: initially, isomer **80** was largely predominant between the reaction products; however, it disappeared afterward at the benefit of isomers **83** and, in a minor amount, **86**; the higher the reaction temperature, the faster this disappearance. This transformation is due both to direct isomerization of **80** into **83** and **86** and to deacetylation-transacetylation reactions in an intermolecular mechanism. From molecular modeling and analysis of the compounds entrapped in the zeolite pores during isomerization, Guisnet et al.¹⁶⁰ concluded that acetylation and isomerization mainly occurred inside the zeolite pores. 2Ac6MN was obtained in 80% yield at relatively high temperature (≥ 170 °C) and in the presence of a polar solvent such as nitrobenzene. The positive effect of solvent polarity was

Scheme 21



also exploited in the industrial acylation of 2MN with a series of carboxylic acid anhydrides (C₂–C₅).¹⁶⁷

Hölderich et al.¹⁵⁷ deeply analyzed the influence of the acid pretreatment of HBEA on its activity in the model reaction between 2MN and acetic anhydride. The contribution of the inner and outer surfaces of the catalyst was examined by considering the selectivity with respect to the bulky product 1Ac2MN and the linear product 2Ac6MN, which were assumed to be formed on the outer surface and on both the inner and the outer surfaces, respectively, as also evidenced by the research groups of Fajula,¹⁶⁸ Davis,¹⁶⁹ and Lee.¹⁷⁰ Authors showed that the production of EFAL species located in the micropores of HBEA subjected to high heating rate calcination provoked the increase in the selectivity of the less hindered 2Ac6MN since the formation of the bulky 1Ac2MN was sterically hampered. On the contrary, acid treatment increased the catalytic activity of the outer surface due to the extraction of the catalytically active EFAL species out of the micropores, leading to the preferential formation of the bulky 1Ac2MN.

Competitive adsorption studies of a mixture of reagent **78**, product **80**, and sulfolane or 1,2-dichlorobenzene over HBEA zeolite showed that compound **80** can be formed inside the pores by acetylation of **78**. Isomerization of **80** into **83** was also shown to occur inside the zeolite micropores, with the desorption of **83** being slower than its production. Moreover, these experiments confirmed that highly polar solvents such as sulfolane ($E_T = 0.410$; $r_0 = 184$ mmol/h·g) limited the entrance into the zeolite micropores of reactant **78** (which is less polar) and hence the rate of the acetylation; on the contrary, solvents of intermediate polarity such as 1,2-dichlorobenzene ($E_T = 0.225$; $r_0 = 224.5$ mmol/h·g) favored the reaction, in good agreement with results reported by Guisnet et al.¹⁶⁰

Acetyl chloride was tested in the comparative acylation of **78** (**78**/acetyl chloride ratio = 1) over HBEA, HY, and HMOR zeolites.¹⁷¹ All three catalysts showed about 30–40% conversion of **78** in sulfolane in the temperature range 100–150 °C. At 100 °C HY showed higher activity than the other two catalysts. However, as the reaction temperature was raised to 150 °C, the initial high conversion dropped rapidly, indicating faster deacetylation of the primary product **80**. HBEA and HMOR zeolites also showed some deacetylation at higher temperatures, but the drop in conversion was not as sharp as that observed with HY. At 150 °C yields of isomer **83** were found to be similar with all three catalysts (70–80%) due to the faster isomerization of compound **80**.

The SAR value, which directly affects some properties of the zeolite, such as the surface polarity, lipophilicity, and acidity, is expected to play a major role in the distribution of isomers **80**, **83**, and **86** in the reaction between 2MN (**78**) and acetic anhydride **2** (**78**/**2** ratio = 0.5). In a comparative study with three HY zeolites, namely, HY-15, HY-40, and HY-100, an increase of the initial activity was observed with the increase of the SAR value.¹⁷²

These results confirm that the activity does not come from an increase of the acid strength of the catalyst¹⁷³ and suggest, in agreement with some conclusions by Corma,¹⁴⁸ that the catalytic activity could be better related to a more hydrophobic character of dealuminated HY zeolites. In all cases, the reaction led to the formation of compound **80** as major product (95% yield), **83** (obtained only up to 4% yield), and traces of **86**. These products were formed by a parallel reaction since the **80/83** ratio remained constant to a value of 24 even after 24 h.

Acylation of **78** with different anhydrides (**78**/anhydride ratio = 2) at low temperature (100 °C) in the presence of the moderately protic acid MCM-41 mesoporous zeolite was studied by van Bekkum et al.^{174a} The selectivity for isomer **80** was practically 100% with the less bulky acetic anhydride whereas with the more bulky isobutyric anhydride a small amount of isomer **85** was produced. At higher temperature (~130 °C) the reversibility of the acylation at the 1-position played a fundamental role in the distribution of products and a decrease in the selectivity for the 1-position was observed. The catalyst could be recycled three times; after each cycle, the catalyst was filtered, washed, dried, and reactivated by calcination for 2 days at 450 °C, showing quite similar conversion (~40%) and selectivity (~97%) with respect to isomer **80**.

Hölderich et al. studied the acylation of 2MN with acetic anhydride over Nafion/silica composite (SAC5-80) ion-exchanged with Lewis acids.^{174b} The higher the Nafion content, the higher conversion and selectivity (up to 69%) to the desired 2Ac6MN. Unpolar solvents such as toluene or methylene chloride favor the formation of 1Ac2MN, while polar solvents such as nitrobenzene or sulfolane promote the 2Ac6MN formation. The difference between SAC-13 in the H⁺ form and the metal-exchanged SAC-13 was in the ratio between the selectivity of 2Ac6MN and 1-acetyl-7-methoxynaphthalene (1Ac7MN). The best results in terms of selectivity toward 2Ac6MN were achieved with SAC-80(Cu) (49%) and SAC-80(Ag) (69%).

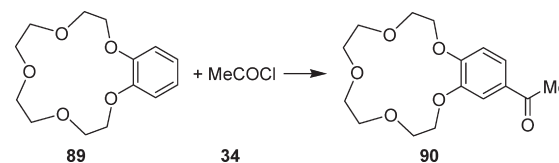
The tridimensional large pore zeolite named ITQ-7 was formerly prepared in the silica form not useful in catalysis.¹⁷⁵ More recently, Corma et al.¹⁷⁶ developed a methodology to perform the synthesis of ITQ-7 with different T^{III} and T^{IV} elements isomorphically incorporated into the framework, such as Al-ITQ-7; this zeolite has two channels of 6.2 Å × 6.1 Å and a third one of 6.3 Å × 6.1 Å, which are smaller than the two major channels of the HBEA zeolite (7.2 Å × 6.2 Å). Al-ITQ-7 was studied as a catalyst in the reaction of Scheme 21 (R = Me) (**78/2** ratio = 2) in comparison with HBEA.^{177,178} Both catalysts showed quite similar activity (~70% 2MN conversion), but Al-ITQ-7 decays much faster due to its smaller pore dimension.

3.2. Acylation with Clays

Thermally activated rare-earth chlorides or oxychlorides deposited on clays and silica showed high activity in the acylation of aromatic ethers with acyl chlorides (aromatic ether/acyl chloride ratio = 0.6).¹⁷⁹ Among the supports used, K10 montmorillonite gave the more effective catalysts, as the clay itself has its own activity. All the rare-earth-supported catalysts were active in the benzoylation of anisole; ScK10 showed the best activity (~98% anisole conversion in 20 h), whereas the untreated K10 montmorillonite showed a good anisole conversion (~95%) but with a lower reaction rate (~60 h).

Envirocat EPIC (commercially available FeCl₃-exchanged montmorillonite) was utilized as a catalyst for the benzoylation of anisole with aromatic carboxylic acids (anisole/aromatic

Scheme 22



carboxylic acid ratio = 35).¹⁸⁰ The reaction showed limited applicability, with the yield ranging from 20 to 70%. No information is reported on the possible recycling of the catalyst and on the leaching phenomena.

Yadav et al.^{181,182} compared the activity of ZnK10 with those of some cesium-substituted HPAs on K10 clay (CsHPAK10) in the acylation of anisole (**64**) with benzoyl chloride (**21**) (**64/21** ratio = 7) (Scheme 19). *p*-Methoxybenzophenone was the sole isomer produced, and ZnK10 showed the higher activity; nevertheless, the reusability of this catalyst was found to be unfavorable, whereas the CsHPAK10 catalyst showed an excellent reusability for at least three times (36, 35, and 33% anisole conversion for each cycle).

Choudary et al.^{79,80,183} described the preparation of cation-exchanged clays and their use in Friedel–Crafts acylation of aromatic ethers with anhydrides (aromatic ether/anhydride ratio = 0.5). The best results were obtained with Fe³⁺- and Zn²⁺-exchanged clays. In the case of the reaction of 2MN (**78**) with acetic anhydride (**2**) (Scheme 21), 1Ac2MN (**80**) was selectively formed and only small amounts of the thermodynamically favored 6Ac2MN (**83**) were produced (82% yield, 90% 1Ac2MN selectivity, 8% 6Ac2MN selectivity). The higher activity of Fe³⁺- and Zn²⁺-exchanged montmorillonites can be ascribed to the synergistic effect of Brönsted and Lewis acidities.

A further application of metal-exchanged K10 clay is represented by the preparation of ketones of benzo crown ethers by reaction of crown ether **89** with acetyl chloride (**34**)¹⁸⁴ (**89/34** ratio = 0.2) (Scheme 22). The best catalyst in the reaction was SnK10, which afforded product **90** in 90% yield after 30 min. The redox mechanism depicted in Scheme 7 could represent an alternative pathway for the formation of acyl cation, that can account for the higher activity of the SnK10.

3.3. Acylation with Metal Oxides

The regioselective acylation of aromatic ethers with carboxylic acids (aromatic ether/carboxylic acid ratio = 1) was performed in the presence of an equimolecular mixture of trifluoroacetic anhydride adsorbed on the surface of alumina without any solvent.¹⁸⁵ The process could be applied, with nearly quantitative yields, to anisole and the three isomeric dimethoxybenzenes by using cyclic and C₂–C₁₆ linear carboxylic acids. Authors outlined that in the case of anisole the acylation occurred selectively at the position *para* to the methoxy group. The reaction required a large amount of alumina and trifluoroacetic anhydride, and consequently, it could only be applied at the laboratory scale.

A merely synthetic application was reported concerning the acylation of aromatic ethers with acyl chlorides (aromatic ether/acyl chloride ratio = 1) in the presence of hydrated zirconia.¹⁸⁶ Thus, anisole, 2-methoxynaphthalene, and 3,5-dimethoxytoluene were reacted with acetyl or benzoyl chloride in the presence of zirconium oxide. The corresponding ketones were produced in 60–80% yield. Unfortunately, no comments are made concerning the isomeric distribution.

Mixed oxides WO_3/ZrO_2 showed catalytic activity in the acylation of anisole with acetic anhydride (anisole/acetic anhydride ratio = 9).^{187a} These catalysts have both Brønsted and Lewis acid sites; the maximum Brønsted acidity and catalytic activity was achieved with a WO_3 loading of 19 wt %. The highest conversion (89% with 92% selectivity) was obtained when the reaction was carried out at 100 °C; higher reaction temperature and increasing the WO_3 loading on ZrO_2 resulted in a lower activity.

$\text{P}_2\text{O}_5/\text{SiO}_2$ catalyst, simply prepared by mixing equal amounts of the two reagents at room temperature, can be efficiently used for the acylation of methoxyarenes.^{86b} The reactions were performed by refluxing for 1–5 h an excess of the liquid aromatic reagent, the carboxylic acid, and the solid catalyst; in a few cases methylene chloride was utilized as solvent. Aromatic ketones were obtained in satisfactory to good yields according to the reactivity rules of the electrophilic substitution. Lower yields were obtained by performing the reaction with P_2O_5 alone. The positive effect of the support is probably due to the dispersion of P_2O_5 on the surface of the silica.

Quite similar results were achieved by using a mixture of P_2O_5 and alumina.^{187b} Similar solid acid catalysts WO_3/ZrO_2 , prepared by wet impregnation method using zirconium dichloride and ammonium metatungstate, were utilized in the acylation of veratrole with acetic anhydride.^{187b} The most active catalyst, which contains 15 wt % of WO_3 calcined at 800 °C, gave 67% conversion of acetic anhydride at 70 °C with a veratrole/acylating agent = 2 and a reaction time of 4 h. The catalyst was reused without appreciable loss of activity by calcination.

3.4. Acylation with Acid-Treated Metal Oxides

SZ was reported by Deutsch et al.¹⁸⁸ to show high performance in the acylation of anisole with benzoic anhydride or benzoyl chloride (anisole/acylating agent ratio = 10). The authors compared the activity of several solid acid catalysts in the reaction with benzoic anhydride (42) (Scheme 16). They showed that SZ exhibited a dramatically higher activity with respect to those of HBEA and HMOR; in addition, they found that the performance of SZ in the reaction of the sterically demanding benzoic anhydride was less dependent on the acidity level and more dependent on the pore size. Comparative experiments surprisingly confirmed that benzoyl chloride (21) (Scheme 19) (yield of 73 + 66 = 52%) was less active than benzoic anhydride (yield of 73 + 66 ≈ 100%); this result would require further investigations. However, the method showed synthetic utility since the anisole acylation with carboxylic acid anhydrides and chlorides (anisole/acylating agent ratio = 10) over SZ^{189–192a} afforded the corresponding ketones in 88–96% yield and 94–99% selectivity.

Signoretto et al. showed that in the benzoylation of anisole with benzoic anhydride catalyzed by SZ, the calcination temperature as well as the precipitation pH applied in the preparation of the catalyst played an important role in the catalyst activity.^{192b} Thus, calcination at temperatures higher than 550 °C resulted in a nearly quantitative conversion of anhydride, with a 70–80% selectivity and a *o/p* ratio = 97:3; lower temperatures led to incomplete conversion. The precipitation pH had a minor influence, pH 10 being slightly better than pH 8 in terms of yield (70 and 64% yield, respectively). Activation temperature was demonstrated to have a strong effect on the selectivity: lower activation temperatures (150–300 °C) led to catalysts able to promote high benzoic anhydride hydrolysis rate at the expense of

the acylation (~30% yield). On the contrary, 73% yield was achieved with a catalyst activated at 450 °C. The different catalytic activity is related to the combination of different phenomena such as physisorbed water elimination, dehydroxylation, sulphating agent decomposition, phase transition and sulfate species removal.

According to the positive results achieved with different solid catalysts, the metal ion doping of SZ was tried with the aim of improving the catalytic performance of the parent material. Thus, the so-called metal-promoted SZs were prepared by impregnation of SZ with a solution of the selected metal salt. Iron-promoted SZ samples were synthesized by freeze-drying as well as by conventional and aerogel synthesis followed by impregnation with $\text{Fe}(\text{NO}_3)_3$ and $\text{Mn}(\text{NO}_3)_2$, and their catalytic efficiency was evaluated in the anisole (64) acylation with benzoyl chloride (21) (64/21 ratio = 40) (Scheme 19).¹⁹³ Besides the ketones, benzoic acid and phenyl benzoate were formed as side products; *p*- and *o*-methoxybenzophenones were obtained in 95 and 5% selectivity. Again, pure zirconia was catalytically inactive, and all modified samples showed good acylation activity (68–85% yield). This catalytic behavior might be mainly due to the large pore volume. An increase of the catalytic activity of SZ was also observed after promotion with iron (63 vs 42% anisole conversion), whereas no such effect was observed for manganese-promoted samples (41% anisole conversion). The product inhibition and coke deposition still represent the major drawback of these catalysts;^{194a} nevertheless, the catalytic activity of the spent SZ could be completely restored by burning off the deposited carbonaceous materials.

SZs supported on MCM-41 silica promoted with metal oxides (Ga_2O_3 and Fe_2O_3) were employed in the catalytic acylation of veratrole with acetic anhydride.^{194b} In the preparation of the catalyst, SZ was supported on MCM-41 silica by incipient wetness impregnation. The metal promoted catalysts were prepared by impregnation of MCM-41 silica with a methanol solution of $\text{Zr}(\text{SO}_4)_2$ and $\text{M}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$ (*M* = Ga or Fe). All catalysts were active in the mentioned reaction (70–78% yield, 88–93% selectivity). A marked enhancement in catalytic activity was observed as the veratrole/anhydride molar ratio was increased. For example, with the gallium-promoted catalyst, at a molar ratio 5:1, the anhydride conversion was 72% after 3 h reaction; as the molar ratio was increased to 20:1, the conversion was complete after 30 min. The gallium-promoted catalyst was the best catalyst because of the presence of Lewis acid sites, absent in the sample promoted by iron oxide. On the other hand, the presence of Fe_2O_3 was important because it enhances the redox properties of the catalytic system, allowing the complete restoration of the catalytic activity by calcination at 450 °C even after three catalytic runs.

Kemnitz et al.¹⁹⁵ reported the preparation and use of borate zirconia catalyst ($\text{B}_2\text{O}_3/\text{ZrO}_2$), prepared from zirconyl nitrate and boric acid, in the same reaction (64/21 ratio = 0.8). Phenyl benzoate, formed by *O*-benzoylation, was still found to be the major side product. The activity of the catalyst was almost constant during three cycles (data not reported). It was found that the stronger surface acid sites were mainly responsible for the catalytic reaction and the weaker sites were active at higher reaction temperatures. The advantage of $\text{B}_2\text{O}_3/\text{ZrO}_2$ over SZ may be that it is a suitable catalyst because of the presence of weaker surface sites that lead to a longer catalyst life. There is also evidence to confirm the assumption that the acylation occurred exclusively at Brønsted acid sites which can activate the acylating

agent through a hydrogen bond (Figure 8). In fact, by comparing acylation with 1-butene isomerization as a probe of Brønsted acid-catalyzed reactions, high catalytic activity in the acylation was observed for samples that showed high conversion degrees in the 1-butene isomerization. Therefore, it can be concluded that both reactions take place on the same kind of acid sites of the SZ sample used.

The acylation 1-methoxynaphthalene (1MN) with acetic anhydride (1MN/acetic anhydride ratio = 0.5) was performed by Deutsch et al.¹⁹⁶ in the presence of SZ. The catalyst exhibited a higher performance than other mesoporous solid acids such as $\text{Cs}_{2.5}\text{H}_{0.5}[\text{PW}_{12}\text{O}_{40}]$, Nafion on SiO_2 , Amberlyst-15, and K10. Indeed, 1-acetyl-4-methoxynaphthalene was isolated in nearly quantitative yield after 3 h. The formation of very reactive acylating species and thermodynamically favored leaving groups on the catalyst surface may explain the high catalytic performances of SZ.

Sulfonic acids supported on mesostructured SBA-15 silica were studied as catalysts in the acylation of anisole and 2MN with acetic anhydride (aromatic ether/acetic anhydride ratio = 0.95).^{197a} The catalysts were prepared by hydrolyzing a mixture of TEOS and 3-mercaptopropyl trimethoxysilane in the presence of hydrogen peroxide. These catalysts showed a greater activity as compared to those of other homogeneous and heterogeneous sulfonated materials. The selectivity toward *p*-methoxyacetophenone was higher than 95% for all catalysts regardless of the pore size, showing that it would not be the consequence of a shape selectivity effect but rather that of the specific anisole reactivity. The supported catalysts displayed the highest activity (TON = 85–93) with respect to both heterogeneous Amberlyst-15 (TON = 40) and homogeneous *p*-toluenesulfonic acid (TON = 5) catalysts. The significant decrease of conversion rate per acid center observed with Amberlyst-15 could be related to the low accessibility of the acid sites arising from its low specific surface area ($45 \text{ m}^2/\text{g}$).

High activity in the acylation of anisole with acetic anhydride has been observed by using propylsulphonic acid supported on MCM-41 mesoporous silica as catalyst.^{197b} The catalyst was produced through a sol–gel method by using a mixture of TEOS and bis(3-trimethoxysilylpropyl)tetrasulfide followed by oxidation with bromine/hydrogen chloride. The material showed a mesoporous highly ordered structure. The anisole conversion was 98%, accompanied by the same yield of *p*-methoxyacetophenone. Lower activity was observed in the same reaction performed with a catalyst produced by using a mixture of TEOS and mercaptopropyl trimethoxysilane followed by oxidation (68% conversion, 65% yield).

In a comparative study, different sol–gel silica immobilized triflate compounds such as $\text{La}(\text{OTf})_3$, *tert*-butyldimethylsilyl trifluoromethanesulfonate (BDMST) and triflic acid (TfOH) were tested in the acylation of 2MN with acetic anhydride (Scheme 21) leading to 1Ac2MN as the major product.^{197c} The reaction proceeded with good yield only on silica supported BDMST and TfOH . In particular, the reaction performed at 50°C for 4 h in the presence of silica supported BDMST (30 mg for 5 mmol of 2MN) without solvent afforded 1Ac2MN with 89% conversion and 98% selectivity. Quite interestingly, the TOF was superior to that reported in the literature for other heterogeneous catalysts and even for homogeneous triflates.

An efficient MCM-41-based catalyst ($\text{SO}_4^{2-}/\text{Al-MCM-41}$) was set up by impregnating sulfuric acid on Al-MCM-41;^{198a} this composite material showed a good catalytic efficiency in the

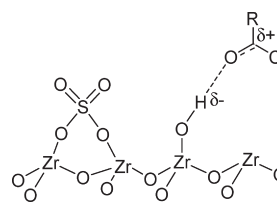


Figure 8. Hydrogen bond activation of acyl chloride by Brønsted sites of SZ.

preparation of 2Ac6MN (**83**) by acetylation of **78** with acetic anhydride (**2**) (**78/2** ratio = 1–0.25) (Scheme 21), giving a 43.3% yield of **83** and a 60% conversion of reagent **78**.

3.5. Acylation with Heteropoly Acids

The sustainable heterogeneous acid catalysis by HPAs in different carbon–carbon bond forming reactions, including electrophilic acylation of aromatics and oxidations, has been recently reviewed by Kozhevnikov.^{198b}

The acylation of anisole with C_2 – C_{12} carboxylic acids (anisole/carboxylic acid ratio = 1) was carried out with HPAs and multicomponent polyoxometalates affording the corresponding products in 62–65% yield. These solid acids were superior in activity to the conventional acid catalysts such as sulfuric acid and zeolites. The HPA catalysts could be reused after a simple workup, albeit with reduced activity.^{110,199}

Silica-supported HPA catalysts were also studied in the acylation of anisole with acetic anhydride (anisole/acetic anhydride ratio = 0.33),^{200a} showing very high anisole conversion (~90%) combined with high selectivity in *p*-methoxyacetophenone (90%). Nevertheless, the catalyst seemed to deactivate after 0.5 h. Cleaning the spent catalyst by washing with dichloromethane restored its activity, indicating that the active HPA was not fairly leached from the silica support; however, a slower but progressive coking completely deactivated the catalyst.

The silica-supported HPA with a loading of 30 wt % (HPW30), prepared using an incipient wetness method by slurring the phosphono-12-tungstic acid with silica, has been compared with the lanthanum-exchanged HYzeolite (LaY) and SZ in the model acylation of anisole with dodecanoic acid under conventional heating and microwave stimulation.^{200b} The microwave irradiated experiments exhibited increased reaction rates, the extent of which was dependent upon the nature of the catalyst and in general the activity order was $\text{HPW30} > \text{SZ} > \text{LaY}$ under microwave irradiation and $\text{HPW30} > \text{LaY} > \text{SZ}$ under conventional heating. The origin of the microwave enhancement has been attributed to the selective desorption of water from the surface of the catalyst.

The activities of two HPA catalysts, one supported on a commercial silica (HPA/SiO_2) and the other supported on a silica-zirconia mixed oxide (HPA/SiZr), were compared in the same reaction (anisole/acetic anhydride ratio = 10).²⁰¹ Both supported catalysts and the SiZr support were active, even if the maximum yield (65%) was observed with HPA/SiO_2 , whereas low yields (~20%) were obtained with SiZr and HPA/SiZr . Differences in the nature and number of the acid sites were recognized, and dispersion of HPA over the silica surface resulted in the generation of a catalyst possessing Brønsted acid properties. However, addition of HPA to a support with inherent Lewis and Brønsted acid properties modifies the number and distribution of the acid sites usually by increasing their number and

strength; these effects depend on the extent of interaction of the HPA with the support. The interaction of HPA with the silica surface, which is much weaker than that for zirconia,^{202a} is attributed to the formation of $(\equiv\text{SiOH}_2^+)(\text{H}_2\text{PW}_{12}\text{O}_{40}^-)$ species¹⁰⁹ and would account for the different activities of the two HPA-supported catalysts.

The benzylation of veratrole with benzoic anhydride to yield 3,4-dimethoxybenzophenone was studied using silicotungstic acid (STA) supported on zirconia as catalyst.^{202b} A series of catalysts with different STA loadings (5–25 wt %) and calcination temperatures (600–850 °C) were prepared by suspending zirconium oxyhydroxide, prepared by controlled hydrolysis of zirconyl chloride, in the presence of STA followed by drying and calcination. Raman spectroscopy of the catalyst with the optimum STA loading (15 wt %) showed the presence of zirconia-anchored monooxotungstate as the major tungsten species up to 750 °C. This material, named 15SZ-750, showed also the highest Brönsted acidity. The catalytic activity was found to strongly depend on STA coverage; comparison of the catalytic activity of zirconia- and silica-supported STA revealed that the silica-supported catalyst was leached, whereas the zirconia-supported one acted as efficient and stable catalyst. At 120 °C and with a veratrole/benzoic anhydride molar ratio = 5, the most active catalyst 15SZ-750 showed 99% benzoic anhydride conversion; the used and deactivated catalyst was regenerated by calcination without any appreciable loss of activity.

The catalytic activity of HPA-impregnated zirconia (HPA/ ZrO_2) was also analyzed in the acylation of 2MN with acetic anhydride (2MN/acetic anhydride ratio = 0.33).²⁰³ The maximum activity (~50 wt % 2MN conversion) was achieved with a HPA loading of 15 wt %, corresponding to a maximum surface acidity. The reaction was highly selective since the 1Ac2MN was the sole product isolated.

The same catalyst showed good activity in the acylation of diphenyl ether with benzoyl chloride (diphenyl ether/benzoyl chloride ratio = 7).^{204a} The maximum conversion of benzoyl chloride was ~60%, and 4-benzoyldiphenyl ether was obtained with a selectivity higher than 97%. The catalyst could be efficiently recycled three times, affording the same benzoyl chloride conversion. However, a drawback in the use of these interesting catalysts is represented by their solubility in polar organic compounds such as aromatic ethers even in the case of silica-supported HPAs. These results suggest that more studies are needed to point out an efficient HPA-based solid catalyst for Friedel–Crafts acylation.

Zirconia-supported HPAs with 3–20 wt % loading were also prepared by impregnating zirconia with aqueous solution of 12-heteropolyacid of tungsten and molybdenum followed by evaporation of water, drying at 110 °C, and calcination at 500 °C.^{204b} The 15 wt % sample was found to be the most active in the acylation of anisole with acetic anhydride, giving 89% conversion of acetic anhydride with 97% *para*-selectivity. The catalyst was recycled for two runs after washing and calcination at 500 °C giving only a 3% yield lowering.

The more complex solid catalysts constituted of TPA supported on zirconia and uniformly dispersed in mesoporous silica channels of MCM-41 and MCM-48 were prepared and characterized.^{204c} These catalysts with different TPA loadings (5–50 wt %) on 22.4 wt % ZrO_2 /MCM-41 and 15 wt % TPA on different ZrO_2 /MCM-41 loadings (10–70 wt %) were tested in the acylation of veratrole with acetic anhydride. The mesoporous silica support plays an important role in stabilizing catalytically

active TPA along with the tetragonal phase of zirconia. Results confirmed that MCM-41 was better than MCM-48 support. Among the catalysts, 15 wt % TPA/22.4 wt % ZrO_2 /MCM-41 calcined at 850 °C was found to have the highest acidity and to be at least four times more reactive than neat 15 wt % TPA/ ZrO_2 , giving 44% conversion of acetic anhydride. The reaction was demonstrated to be truly heterogeneous, and no contribution of homogeneous (leached) TPA was found.

3.6. Acylation with Nafion

Nafion/silica composite materials were reported by Hoelderich et al.²⁰⁵ to work as promising catalysts for the acylation of aromatic compounds. These very strong solid acids, made by entrapping highly dispersed nanosized Nafion particles within a silica matrix, combine the advantages of both components, namely, the acid strength of the Nafion resin and the accessibility of the high surface area of silica. The composite materials were more active than the original acid resin in the acylation of anisole with phenyl acetic and phenyl propionic acid chlorides (anisole/acyl chloride ratio = 11). By using phenyl acetyl chloride in the presence of Nafion at 100 °C, the acyl chloride conversion was 77% whereas 100% conversion was achieved with the composite material. Surprisingly, the selectivity for the *para*-acylated product steadily increased with increasing temperature and conversion. More likely, by enhancing the reaction temperature, the solubility of the hydrogen chloride in the reaction mixture was distinctly reduced and consequently the selectivity for the desired ketones was enhanced.

Beers et al.²⁰⁶ faced the problem of the use of carboxylic acids in the anisole acylation (anisole/carboxylic acid ratio = 40) over Nafion catalyst. Unfortunately, carboxylic acids, when present in large amounts, adsorbed so strongly on the catalyst surface that the aromatic substrates had no chance to react.^{207a} A continuous process was preferred since it operated at low acid concentrations. This could be achievable by using a fixed-bed catalyst with a recirculation of the reaction mixture. A structured catalyst was therefore needed to allow for higher recirculation rates and to avoid a high pressure drop over the catalyst; the choice fell on Nafion/silica composite materials, that resulted to be more active in the acylation of anisole with octanoic acid than HBEA and USY zeolites and Amberlyst-15 resin. The highest activity was exhibited by the Nafion/silica composite containing more accessible Nafion nanoparticles, even if a modest *para*-selectivity was obtained ranging from 44 to 72% and being the major byproduct the O-acylated compound. Removal of water produced during the reaction had a beneficial effect, and a 4-fold growth of catalyst activity was observed. The use of coated monoliths as supports was further studied; the catalyst was present as a thin layer on the channel walls. The advantages of such a system were that no filtering of catalyst was necessary, no attrition of catalyst occurred and the reactor had a low pressure drop, and the reaction was performed in the liquid phase and the water was removed through the gas phase. Two different types of silica monoliths were employed: a monolith with 400 cells per square inch (cps) and a loading of 1.05 wt % Nafion and one with 600 cps and 1.27 wt % Nafion loading; also a 400 cps silica-coated monolith with 0.96 wt % Nafion loading was tested. The 400 and 600 cps monoliths exhibited the same selectivity (46–47%) as the pure Nafion tested in batch reaction (47%), whereas the silica-coated 400 cps monolith showed a higher selectivity (70%); these results indicate that the silica matrix led to higher selectivities, probably due to the interaction of Nafion with the silica surface.

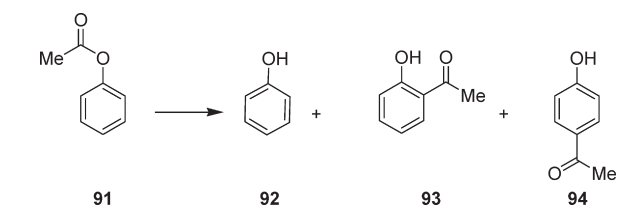
Silica-supported Nafion catalyst (SAC-13) was studied in comparison with HPA on the same support in the model acylation of anisole with acetic anhydride.^{207b} Reactions were performed in a continuous slurry reactor at 70 °C using an anisole-rich feed (molar ratio 5:1). Acetic anhydride conversions of 40–50% with excellent selectivity (>95%) toward the primary product, *p*-methoxyacetophenone, were observed at TOS of few hours. The Keggin ions from the supported HPA-based catalyst leached completely during the liquid-phase operation in less than 24 h. The SAC-13 type catalyst displayed the best combination of stability and leach resistance during liquid-phase operations. The deactivation of the catalyst could be caused by the inclusion of *p*-methoxyacetophenone and/or multiply acetylated products in the mesopores of Nafion catalyst aggregates. Treating the spent catalyst with boiling nitric acid solution restored completely the activity of the SAC-13 type catalyst.

Nafion resin was supported on mesostructured SBA-15 material by means of impregnation with different resin content.^{207c} An optimum Nafion loading has been achieved by Nafion(15)/SBA-15 material with ~13 wt % of Nafion. This sample has been the most effective in the acylation of anisole with acetic anhydride even if the anisole conversion (~14%) remains quite modest. Similar results have been achieved by increasing the Nafion loading above 15 wt %. The catalyst activity of this material was superior to those of other perfluorosulfonic acid based catalysts such as the commercial Nafion SAC-13 or the material prepared by reactive-grafting perfluoroalkylsulphonic acid precursor over SBA-15 mesoporous silica. The impregnated catalyst showed high stability, although a remarkable deactivation was observed by a strongly chemisorbed polyacetylated byproduct. Treatment with nitric acid allows regaining of 93% of the initial catalyst activity.

Perfluorinated alkylsulfonic groups grafted onto the high-surface-area MCM-41 silica were utilized as strong solid acid catalysts stable up to 350 °C.^{208a} With these catalysts the acylation of anisole with acetic anhydride (anisole/acetic anhydride ratio = 1) was carried out, showing a good anisole conversion (35–45%) and a very high selectivity (97%) for the desired *para* isomer at 60 °C. The best results in terms of conversion were achieved with the catalyst showing the highest loading; an increase in reaction temperature up to 120 °C allowed isolation of the product in ~60% yield. A limit of the exploitation of such a catalyst was represented by its deactivation; further studies are needed to establish the stability of the covalent bonds between the alkyl sulfonic groups and silica to the hydrolysis under strong acid conditions and the influence of the residual silanols on the acid strength of the perfluoroalkylsulfonic groups.

The acylation of 1,4-dimethoxybenzene to 2,5-dimethoxyacetophenone with acetic anhydride was studied as a model reaction to compare the efficiency of different solid acid catalysts.^{208b} Results confirmed that the cation exchange resins Amberlyst-15 and Indion-125 gave quite similar results and were superior to other inorganic solid acids such as SZ, HPA, and mesoporous solid superacids prepared by the authors. A systematic study was performed to achieve instruments to rationalize the reaction mechanism, that could be controlled by one of the following steps: (a) adsorption, (b) surface reaction, and (c) desorption. The catalyst was deactivated over repeated use at lower temperature. Analysis of the adsorption of the reactants and products gave the possibility to overcome the drawback. Thus, the deactivation could be avoided by using a temperature of

Scheme 23



120 °C at a 1,4-dimethoxybenzene/acetic anhydride molar ratio of 1:5 in chlorobenzene as solvent, and by using a Indion-125 loading of 0.05 g/cm³ (with respect to the total volume of the reaction mixture): under these conditions the acetic anhydride conversion reached 60%.

4. ACYLATION OF AROMATIC THIOETHERS

HBEA showed good activity and shape selectivity in the acylation of thioanisole with acetic anhydride (thioanisole/acetic anhydride ratio = 1) to 4-(methylthio)acetophenone (32% conversion of thioanisole, 99.9% selectivity). The catalyst showed rapid deactivation by product inhibition; however, its activity could be restored by calcination at 500 °C, showing quite similar activity for at least three cycles.^{209,210}

Better results for the same reaction (thioanisole/acetic anhydride ratio = 0.33) were achieved by using the commercially available Amberlyst-15 resin;²¹¹ in this case after 2 h at 120 °C 4-(methylthio)acetophenone was isolated in 69% yield (98.6% selectivity); nevertheless, the production of this important pharmaceutical intermediate requires further studies since a marked decay of the catalyst activity was observed during recycling tests.

5. ACYLATION OF PHENOLIC SUBSTRATES

Aromatic hydroxyketones are valuable intermediate compounds in the synthesis of important pharmaceuticals and fragrances. In particular, *o*-(*o*-HAP) and *p*-hydroxyacetophenone (*p*-HAP) are widely used for the synthesis of aspirin and paracetamol (4-acetaminophenol), respectively.²¹² *o*-HAP is also a key intermediate for the production of 4-hydroxycoumarin and warfarin, which are both used as anticoagulant drugs in the therapy of thrombotic disease,²¹³ and it is also employed for the synthesis of flavonones.^{214,215} In addition, the acylation of resorcinol is a very important process as the corresponding products are utilized for the production of valuable fine chemicals such as ipriflavone (antiosteopenic drug) and 4-*O*-octyl-2-hydroxybenzophenone (UV-light absorbent for polymers).

5.1. Fries Rearrangement

The Fries reaction consists of the acid-catalyzed rearrangement of phenolic esters with production of phenolic ketones.²¹⁶ In general, both *o*- and *p*-hydroxyaryl ketones are formed at the same time (Scheme 23). It was assumed early on that the *ortho*-rearrangement is an intramolecular reaction while the production of the *p*-hydroxyketone occurs via an intermolecular process. However, the analysis of a great number of papers dealing with the Fries reaction promoted under both homogeneous and heterogeneous catalysis prompted us and others to conclude that the mechanistic problems are more and more entwined. To help the reader to draw general conclusions from the wealth of

sometimes conflicting information from the chemical literature, we have summarized some general trends, allowing a possible parallelism between the reaction promoted by classic Lewis acids (i.e., AlCl_3) and that promoted by solid catalysts: (a) the yield of *o*-hydroxyketone (**93**) is greater at high temperatures than that for the reaction at low temperatures, with other conditions being equal; (b) the *p/o* ratio increases with time of the reaction carried out with a lower amount of Lewis or solid acid, and it remains constant with a higher amount of acid catalyst; (c) solvents of great polarity favor the formation of the *para*-isomer, as in homogeneous conditions the *p/o* ratio is determined by the electron densities at the *ortho*- and *para*-positions in the phenoxy radical; this is not the controlling factor within zeolites. Mechanistic details merit clarification in order to discriminate between the intra- and intermolecular pathways.^{217–219} From an experimental point of view, the presence of phenol in the reaction medium is indicative of intermolecular acylation (Scheme 24a) or deacylation (Scheme 24b).

While the first process represents a positive event since acetoxyacetophenone (**95**) (normally the *para*-isomer) is convertible into *p*-HAP, the second one produces ketene, which, being highly reactive, represents the most important source of coke responsible for catalyst deactivation. Moreover, compound **95** can give further intermolecular phenol acylation, affording both *o*-HAP and *p*-HAP.

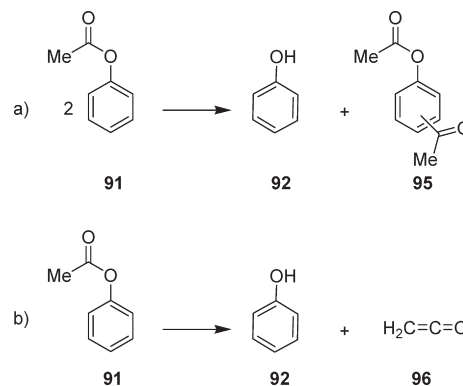
5.1.1. Fries Rearrangement with Zeolites. In the Fries rearrangement of phenyl acetate (PA) carried out in the presence of HZSM-5 zeolite (Scheme 23),²²⁰ a good shape selectivity (*p/o* = 6.0) was reached after 24 h by keeping modest the conversion of the starting ester (~20%). When the reaction was repeated over Nu-10 zeolite, a 1/1 mixture of *ortho*- and *para*-products was isolated; this different behavior can be ascribed to the smaller pore dimension of Nu-10 zeolite that hampers the entrance of the reagents producing both isomers.

The same reaction was comparatively performed at 170 °C under both batch liquid-phase and continuous liquid-phase conditions.²²¹ In the first experiment, HZSM-5 showed a 69% phenyl acetate conversion with a relatively low formation of phenol and byproducts, but a not exciting selectivity toward *para*-product (*p/o* = 1.5). Treatment of the catalyst with triphenylchlorosilane, which deactivates its outer surface, showed an appreciable effect on the performance as well as on *p/o* ratio, that were somewhat higher than those of the starting material (81% conversion, *p/o* = 2.0). This suggests that the reaction mainly occurs in the pores of HZSM-5 material. A catalyst deactivation was observed after 20 h (45–47% conversion); in continuous liquid-phase reaction at the same temperature the catalyst showed a lower deactivation rate, clearly attributable to the shorter contact time between the catalyst and the products due to the washing effect which can remove deactivating species from the catalyst surface; however, a modest selectivity was observed (*p/o* = 1.1).

Ga-exchanged HZSM-5 was employed to promote the reaction in the gas-phase at 250 °C,²²² showing 71% conversion, 46 wt % of *o*-HAP and 5 wt % of *p*-HAP. The high *ortho*-selectivity of the process was attributed to the easy migration of acetyl cation to the *ortho*- compared to the *para*-position, particularly in the gas-phase, in agreement with the temperature effect on the *o/p* ratio already underlined.²¹⁶

The same model reaction was studied in the presence of HZSM-5 zeolite in the pure form or as agglomerates joined with Al_2O_3 and SiO_2 .²²³ Low temperatures favor adsorption of PA on

Scheme 24



the catalyst, while at higher ones the formation of undesired byproducts was increased. The best results were achieved by carrying out the reaction on pure HZSM-5 at 265 °C, showing 86% conversion accompanied by a very high *ortho*-selectivity (*o/p* = 35.5) and only 27% of phenol production. On the contrary, the performance of the same catalyst containing ~40% of a binder worsened slightly with Al_2O_3 (75% conversion, 18.2 *o/p* ratio, 23% phenol) and more dramatically with SiO_2 (44% conversion, 5.4 *o/p* ratio, 63% phenol), evidencing the role of a delicate balance between Lewis and Brønsted acid sites. The FT-IR analyses²²⁴ of the catalysts showed significant differences with other HZSM-5-type zeolites, with probably a partial silylation of the external surface, resulting in the production of a large amount of very weak acid external silanols and an increase in the hydrophobic character. ACD/3D program calculations allowed the conclusion that *ortho*-isomer was slightly compatible with the porosity of the HZSM-5, in which the formation of the *para*-isomer should be favored.²²⁵ Thus, the high level of *ortho*-selectivity observed allowed the authors to hypothesize that with the present catalyst the reaction occurred on the external surface. The partial silylation of the external surface increased its hydrophobic character, with a pronounced decrease of the amount of Lewis acid sites, and promoted the adsorption of both ester feed and ketones formed, while decreasing that of the polar phenol, thus reducing the formation of *para*-product.²²⁶

A series of studies was performed on the Fries reaction carried out under photocatalytic conditions.²²⁷ Various Li^+ , Na^+ , and K^+ -exchanged HX, HY, and HZSM-5 zeolites were tested; the irradiation in hexane as a slurry was conducted to about 30% conversion. The photoreaction within LiX, NaX, LiY, and NaY zeolites gave a small percentage (<10%) of the *para*-isomer, while within KX and KY zeolites the *ortho*-isomer was the exclusive product. This selectivity is not the result of a shape exclusion since both the *ortho*- and the *para*-isomers fit very well within the supercage. On the contrary, it probably results from the restriction imposed on the mobility of the phenoxy and the acyl fragments by the supercage framework and from the interaction between the cations and the two reactive fragments.²²⁸ Although the shape and size of pentasils are such that only the *para*-isomer could fit within the channels of these materials, no selectivity was achieved when the photolysis of PA included within HZSM-5 was conducted as a hexane slurry (0.9 *o/p* ratio). Hexane displaces the reactant from the interior of HZSM-5, and most of the reactants are present in the hexane

solvent and not inside the zeolite, thus giving a significant yield of the *ortho*-isomer. On the other hand, *para* selectivity was achieved by using solvents which did not displace the included PA from the interior of HZSM-5. Since the internal structure of HZSM-5 is highly hydrophobic, water is not expected to fill its channels. Similarly, 2,2,4-trimethylpentane solvent molecules, being too large, are not expected to enter the channels. These solvents would keep both the reactants and the reactive fragments within the channels of HZSM-5; thus, the reaction would be forced to occur inside the channels showing high *para* selectivity (water: *ortho* = 6%, *para* = 62%; 2,2,4-trimethylpentane: *ortho* = 5%, *para* = 63%).

The influence of the solvent on the rate and on the selectivity of PA transformation over HBEA was thoroughly investigated by Guisnet et al.²²⁹ Large differences were observed in both catalyst activity and product distribution by carrying out the reaction in sulfolane or dodecane. Sulfolane ($E_T^N = 0.410$) significantly favored the formation of the *para*-product with respect to dodecane ($E_T^N = 0.012$), and production of *o*-HAP was seven times slower in sulfolane than in dodecane. The reaction orders were quite likely due to differences in adsorption of the solvents on the acid sites: sulfolane would compete with PA and the reaction products for adsorption on the acid sites whereas the adsorption of dodecane could be considered as negligible. Of consequence, sulfolane also limited the catalyst deactivation.

Concerning the catalyst deactivation, it was also found that the phenolic products (phenol, *o*-HAP, and *p*-HAP) were strong inhibitors of PA conversion.^{230,231} While all the phenolic compounds contributed to reaction inhibition during the initial reaction period, phenol was replaced by competitive adsorption of *o*-HAP and *p*-HAP after a longer reaction time, when they were formed to a greater extent. When adding fresh PA, they were extracted from the catalyst so that the catalyst activity was mostly regained. The deactivation by coke^{221,226} only played a role after prolonged reaction times.

The zeolite deactivation could be lowered by performing the Fries reaction in the trickle bed reactor (Figure 5) already utilized in the anisole acylation.^{134a} In the initial period the conversion in the batch reactor was higher than that in the trickle bed reactor (15% vs 8% conversion after 30 min); this fact was probably caused by the higher heat capacity of the latter. Moreover, after 180 min, with the trickle bed reactor the conversion exceeded that in the batch reactor (27 vs 14%). In addition, the higher the catalyst-to-reactant ratio, the higher the conversion. It is expected that the continuous extraction effect should be improved by using convenient solvents.

The modification of HBEA zeolite by surface deposition of SiO₂ and impregnation with cerium oxide was studied as a tool to improve the selectivity of the reaction.²³² The number of acid sites, particularly the strong ones, on HBEA zeolite decreased with increasing amount of SiO₂ deposited on its surface. Moreover, there was no severe pore blocking after deposition. On the contrary, the cerium oxide impregnation afforded a catalyst with a decreased adsorption capacity, since part of the cerium oxide is deposited in the channels of the zeolite crystals and blocks the porous system. In addition, Ce₂O₃ modification created new weak acid sites on the zeolite surface. The SiO₂ modification decreased the catalytic activity but slightly increased the selectivity with respect to *o*-HAP, *p*-HAP, and *p*-acetoxyacetophenone (*p*-AXAP), in comparison to the case of the unmodified HBEA zeolite, and the stability of the catalyst was also improved after modification. The best reaction results were obtained over

16 wt % cerium oxide-modified catalyst, with the selectivity increased to about 70% while the conversion remained 60–80%.

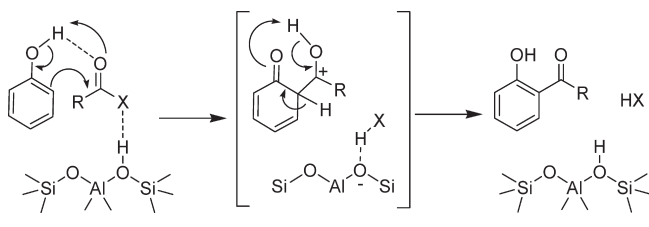
5.1.2. Fries Rearrangement with Heteropoly Acids. HPA- and HPA-salts-catalyzed Fries rearrangement was deeply investigated by Kozhevnikov et al.^{110,198b,233–236} Three kinds of catalysts, namely bulk HPA, silica-supported HPA (SiO₂/HPA)¹¹⁹ (including its Cs⁺ and Ce³⁺ salts), and sol–gel silica-supported HPA (SiO₂–HPA),^{237,238} were compared. The insoluble salt Cs_{2.5}H_{0.5}PW (CsHPA) catalyzed the reaction in polar media such as nitrobenzene with 8.7% PA conversion and with a TOF of 15 min^{−1}; although less active per unit weight than the homogeneous HPA or SiO₂/HPA, it was more selective to HAPs, making less phenol. The explanation of this behavior may be that the less hydrophilic CsHPA^{239a} possesses stronger proton sites than HPA or SiO₂/HPA. Some leaching of HPA from SiO₂/HPA (ca. 10% per run) was observed during recycling studies, probably due to the ready solubility of HPA in PA at elevated temperatures.^{233,234} These observations repropose the question about the real heterogeneity of the catalyst. Much better reusability showed the more stable CsHPA that is insoluble, and the reaction is truly heterogeneous. In addition, the low-porosity CsHPA made much less coke (ca. 2%) than the high-porosity SiO₂–HPA; the amount of coke remains constant in successive runs. However, CsHPA reuse showed a decline of activity and selectivity to C-acylated products, which indicated loss of catalyst acidity. Pd doping (2.1%) of CsHPA (Pd/CsHPA) further improved the catalyst performance upon reuse. The Pd-doped catalyst performed no better than the undoped one, but it could be regenerated with full recovery of both activity and selectivity over five successive runs. Only a small decrease in activity in the first run for Pd/CsHPA compared with undoped CsHPA could be noted, probably because the palladium partly exists as Pd(II) in the first run, whereas in the subsequent runs it mostly exists as Pd(0) due to reduction of Pd(II) by the reaction medium.

Platinum (0.3–1%) can also be utilized for doping HPAs.^{239b} The doped CsHPA catalysts were prepared by treating CsHPA with H₂PtCl₆; the reduction of Pt(IV) to Pt(0) was then carried out by a hydrogen flow at 250 °C for 2 h. The phenyl acetate rearrangement was carried out in nitrobenzene at 130 °C and it was found that Pt doping (0.3–1%) of CsHPA greatly improved the catalyst reuse (22% conversion in four successive cycles) after oxidative treatment of the used catalysts by air at 350 °C followed by steaming at 200 °C. The regeneration is necessary to completely remove coke from the Pt/CsHPA catalyst. The reaction is truly heterogeneous (CsHPA is insoluble in nitrobenzene), and tungsten did not leach from the catalyst (throughout all successive runs its content in the catalyst was constant). Comparing the performance of CsHPA and Pt/CsHPA catalysts, one can conclude that the Pt doping has little effect on the catalyst activity and selectivity but a great improvement in catalyst reuse, even better than that observed with Pd/CsHPA.

5.1.3. Fries Rearrangement (Miscellaneous). Nafion was utilized by Olah et al.²⁴⁰ for the Fries rearrangement. The catalyst showed general applicability (~70% ketones yield) for phenol esters of aromatic carboxylic acids bearing electron-donating as well as electron-withdrawing groups on both the aromatic rings. In all cases, the *para*-isomer was usually predominant. The catalyst could be reused after simple regeneration involving washing with acetone and deionized water and drying.

Silica composite materials constituted by Nafion entrapped in a high porosity silica matrix (13 and 40 wt % Nafion) were

Scheme 25



utilized as catalysts for the Fries rearrangement.²²⁶ The conversions of the reactions performed in cumene were 10 and 16%, respectively, and the selectivity with respect to *p*-HAP (**94**) and *o*-HAP (**93**) was in a range from 20% up to 56%, with phenol being the main side product accompanied by deposition of carbonaceous materials; these results were comparable to those obtained with USY. By using phenol as solvent instead of cumene, a tremendous change of the chemical pathway was found: in particular, by using a 13 wt % Nafion in the silica composite catalyst, a selectivity of more than 90% (with respect to the two HAPs) was obtained at a conversion of about 21%. In the case of HBEA, a higher conversion was observed (41%), but accompanied by a lower selectivity (76%). Unfortunately, it was impossible to reuse the catalysts without reactivation as only traces of product could be obtained.

A silica-supported $\text{AlCl}_3/\text{ZnCl}_2$ mixture was employed under solventless conditions and under microwave irradiation to promote the reaction;²⁴¹ the *o*-HAP was isolated in 95% yield with 100% selectivity. It is worth noting that the reaction did not proceed on ZnCl_2 or AlCl_3 supported alone on silica gel. An elegant application of this procedure is represented by the Fries rearrangement of the cinnamyl esters of phenols and naphthols. In fact, when using these substrates, the *ortho*-rearranged product chalcones spontaneously cyclized by intramolecular conjugate addition of the phenolic hydroxy group to give flavones, biologically active compounds, in 70–90% isolated yields. To demonstrate the efficiency of the methodology, α -naphthyl acetate mixed with the support was heated at 300 °C for 7 min and the corresponding product was isolated in only 10% yield compared to the 95% yield gained under microwave irradiation.

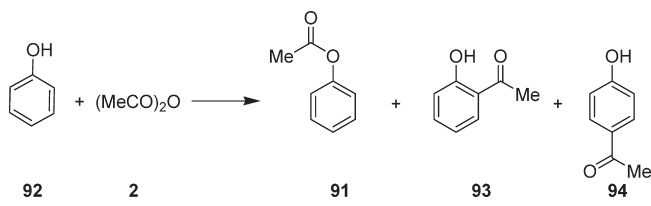
5.2. Direct Acylation

The direct acylation of phenols represents an extremely complex reaction. Phenol is a typical ambidental system and reacts with acylating reagents such as acetyl chloride in the presence of convenient homogeneous or heterogeneous acid catalysts to give phenyl acetate (PA) by O-acetylation as well as *o*-HAP and *p*-HAP by C-acetylation of the aromatic ring. Furthermore, PA can undergo Fries rearrangement, complicating the entire process.

The O-acylation process is much more rapid than the C-acylation one and, in general, the *o*-HAP is prevalent with respect to *p*-HAP.²⁴² In our opinion, this is due to the *ortho*-directing effect of the hydroxy group, which can stabilize by hydrogen bonding the transition state leading to the *ortho* attack (Scheme 25) in a way resembling the so-called “complex-induced proximity effect” (CIPE).²⁴³

In addition, it must be underlined that the mode of *p*-HAP formation is probably different from that of *o*-HAP. Indeed the *ortho*-isomer is a primary product while the *para*-one seems to be a secondary product. Of course, other ways for the formation of

Scheme 26



o-HAP can result from the acylation of phenol with PA, which is a better acylating agent than acetic acid.

5.2.1. Direct Acylation with Zeolites. The acylation of phenol (**92**) with acetic anhydride (**2**) (**92/2** ratio = 1) (Scheme 26) performed over HZSM-5 zeolite showed a very high *ortho*-selectivity (72.4% phenol conversion, 20.1% PA yield, 47.8% *o*-HAP yield, 0.6% *p*-HAP yield).²⁴⁴ The modified MZSM-5 catalysts (M = Zr, V, Pd, Cr, La, and Rh) did not improve the yield of *o*-HAP (68.4–74.6% phenol conversion, 24.5–32.0 PA yield, 35.4–42.7% *o*-HAP yield, 0.5–3.3% *p*-HAP yield); however, the *p*-HAP formation increased with TOS, probably because of the channel/pore tailoring due to coking.

The SAR value showed a remarkable influence on the selectivity of the phenol acylation. When the reaction was catalyzed by HZSM-5-type zeolites with 30, 150, and 280 SAR values, the *o*-HAP yields were 41.8, 39.7, and 15.1, respectively, whereas the O-acylation was noticeably increased. These results mean that C-acylation requires higher Brønsted acidity and that lower acidity leads to PA formation. In addition, an amorphous aluminosilicate acid catalyst gave mostly PA and there was no isomer selectivity, confirming that the C-acylation of phenol occurs in the channels of zeolites and not on the external surface.

The activation of acetic acid in the gas-phase phenol acylation was studied by Guisnet et al.²⁴² in the presence of HZSM-5 zeolite. The products were PA, HAPs, and acetone; the last one was produced from acetic acid according to the equation ($2\text{CH}_3\text{COOH} \rightarrow \text{CH}_3\text{COCH}_3 + \text{CO}_2 + \text{H}_2\text{O}$). Only a small amount of *p*-AXAP was detected. *o*-HAP still represents the major isomer (initial yield = 16%) with respect to *p*-HAP (initial yield = 0.8%). By increasing the TOS, an increase in PA yield together with a decrease in *o*-HAP yield was observed.

Dealumination of HZSM-5 zeolite²⁴⁵ showed a great effect on the *o/p* selectivity in the acylation of phenol by acetic acid.²⁴⁶ Thus, for a phenol conversion of 20%, the *o/p* selectivity was 7.0 when HZSM-5 with 41.8 SAR was utilized, and it became 13.0 in the presence of a HZSM-5 with 42.4 SAR.

In the same reaction, HY showed the highest initial selectivity values to *o*-HAP and *p*-HAP (69.1 and 8.9%, respectively),²⁴⁷ but after 4 h, the *o*-HAP selectivity decreased to only 10.4%. The most stable catalyst still was confirmed to be HZSM-5 zeolite; in fact, with this catalyst no significant activity decay for the *o*-HAP formation rate during the catalytic runs was observed (from 67.1% to 65.3%). HZSM-5 did not deactivate by increasing the conversion of phenol up to 25%, contrary to what was observed for the HY sample. The superior stability of HZSM-5 was explained by considering that its narrow pore size structure hampers the formation of coke precursor compounds.

Singh et al.²⁴⁸ studied the acylation of phenol (**92**) with propanoyl chloride (**97**) (**92/97** ratio = 3) over HBEA, HY, HMOR, and HZSM-5 zeolites (Scheme 27). The main product was phenylpropionate (**98**); moreover, HBEA was the most

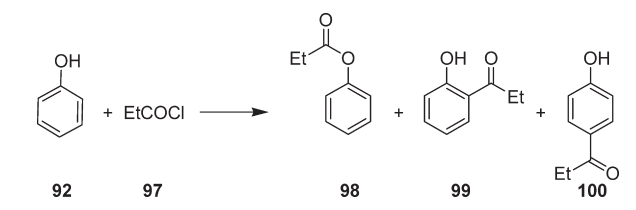
active in the C-acylation and selective for *p*-hydroxypropiophenone production ($p/o = 1.9$) compared to other zeolite catalysts. The conventional catalyst AlCl_3 was less active and selective ($p/o = 0.9$), and a higher yield of other byproducts (3.6 wt %) was obtained due to its nonshape-selective character. The modest activity of HZSM-5 in the formation of C-acylated products may be due to the fact that its pore openings are smaller than the size of the various reactants (intermediates). Among the catalysts studied, HBEA was recycled two times, but unfortunately, the recycled material was less active in the formation of C-acylated products than the fresh sample.

HBEA again showed the highest activity in the acylation of phenol with benzoic anhydride (phenol/benzoic anhydride ratio = 21).²⁴⁹ Phenyl benzoate was the main product (61.2% yield) accompanied by C-acylated products (34.7%), with an interesting *para*-selectivity ($p/o = 2.1$). When the reaction time was increased from 4 to 20 h, an increase in *p*-hydroxybenzophenone yield (from 11.1 to 23.0 wt %) together with a decrease in phenyl benzoate yield (from 79.0 to 63.6 wt %) was observed; however, a small increase in the *o*-hydroxybenzophenone yield (from 8.5 to 10.2 wt %) could not be avoided. The activity of the catalyst together with its selectivity did not distinctly decrease when the catalyst was used from fresh to first cycle; nevertheless, no quantitative results on the reuse of the zeolitic material were reported.

The vapor-phase phenol acylation with acetic acid and acetic anhydride (phenol/acylating agent ratio = 0.5–0.25) was studied in the presence of CeBEA in comparison with undoped catalyst.²⁵⁰ In general, over HBEA the product formation depended on the nature of the acylating agent employed. Acetic acid, being a weak acylating agent compared to acetic anhydride, produced only PA and *o*-HAP, whereas acetic anhydride gave PA, *o*-HAP, *p*-HAP, and other condensed products. Undoped HBEA showed the higher phenol conversion with acetic anhydride (67%; 75% PA selectivity, 20% *o*-HAP selectivity, 3% *p*-HAP selectivity), whereas higher activity and selectivity with acetic acid was observed with CeBEA (48% phenol conversion, 80% PA selectivity, 19% *o*-HAP selectivity). These results are indicative of a strong effect of the Brönsted/Lewis acid ratio on the catalyst performance, which is tightly related to the nature and amount of the doping cation.

The same reactions were studied in batch conditions (phenol/acylating agent = 0.2) over mesoporous Al-MCM-41.²⁵¹ Phenyl acetate still was the major product, and in all experiments, *o*-HAP was the predominant C-acylated product, without any detectable amount of *p*-HAP; instead, a double acylated product was isolated in trace amounts. Different behaviors were found with increasing temperature with the two acylating agents. When acetic anhydride was utilized, the overall conversion of the phenol decreased with the temperature increase; this was ascribed to the decomposition of the PA back to phenol, which resulted in an apparent conversion decline (from 98.9 to 51.6%). At the same time, the selectivity for *o*-HAP increased from 0.8 to 20.8%, indicating that at lower temperatures the O-acylation was the predominant process, but as the temperature increased, O-acylation was gradually replaced by C-acylation. When acetic acid was utilized, the overall conversion was much lower, but it increased from 33.4 to 46.6% together with the *o*-HAP selectivity (from 0.5 to 24.2%). Finally, an increase in the SAR value resulted in a lowering of the phenol conversion, while the selectivities of *o*-HAP and double acetylated products were enhanced.

Scheme 27



The CeNaY zeolite was utilized for the preparation of 4-methylcoumarin by reaction of phenol with acetic anhydride (phenol/acetic anhydride ratio = 1).²⁵² The formation of PA represented the first step; the subsequent acylation at the *ortho*-position followed by an intramolecular aldol-like condensation afforded the final 4-methylcoumarin in 75% yield. In the whole process, the cerium catalyst showed a bifunctional character: the active centers in the supercage of CeNaY zeolite, the Ce^{3+} ions, acted as Lewis catalysts whereas the acid centers H^+ , formed in the dissociation of water according to the equation $\text{Ce}^{3+} + \text{H}_2\text{O} \rightarrow [\text{Ce}(\text{OH})]^{2+} + \text{H}^+$, acted as Brönsted catalysts.

Phenol acylation with PA (phenol/PA ratio = 1) was also studied by Guisnet et al.²³⁰ in the presence of HBEA zeolite; the authors mainly investigated the catalyst deactivation: to this end, they recovered the organic material entrapped into the zeolite following two methodologies: (i) Soxhlet extraction of the zeolite [Ext] and (ii) extraction of coke by dissolution of the zeolite itself in a 40% solution of hydrofluoric acid [Coke]. The acylation reaction was carried out in the two classical solvents, dodecane and sulfolane. In both cases, a significant lowering of the rate of HAPs' formation with time was observed: this deactivation was faster in dodecane (~ 1 h) than in sulfolane (~ 2 h). Whatever the solvent, the two reactants were the main components of the material retained in the catalyst; nevertheless, in the case of sulfolane, their contents in Ext and Coke were similar to that of the reaction mixture, whereas when the less polar solvent dodecane was utilized, their contents in Ext and Coke were greater than that in the reaction mixture. In addition, sulfolane constituted a very significant part of Ext and Coke, whereas practically no dodecane was found. As already stressed in this review, these differences can be related to the difference in solvent polarity: the polar sulfolane enters the pores of the zeolite while dodecane cannot enter them. For the same reason, the amount of PA found in Coke is very small compared to those of the more polar phenol and sulfolane. The authors also confirmed the catalyst deactivation by product inhibition; the reaction rate was very low when PA was added to the zeolite impregnated with phenol, with the higher rate being obtained when phenol was added to the zeolite impregnated with the less polar PA. The conclusion is that the decrease in catalyst activity is not necessarily due to formation of the heavy secondary products but most likely to a limitation of the access of PA to the zeolite pores occupied by the very polar phenol.

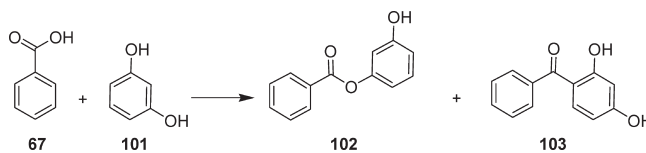
Hoefnagel and van Bekkum²¹⁹ studied the acylation of resorcinol with different substituted benzoic acids (resorcinol/carboxylic acid = 1) in the presence of some solid catalysts with special focus on the use of benzoic acid (67) with HBEA zeolite (Scheme 28). The progress of the reaction in *p*-chlorotoluene was examined, and after 18 h, 2,4-dihydroxybenzophenone (2,4-DHB, 103) was isolated in 70% yield together with 20% of resorcinol monobenzoate (RMB, 102), 3% of resorcinol

dibenzoate, 5% of benzoic acid, and 2% of resorcinol. The fact that the concentration of resorcinol in the final mixture was somewhat lower than that of benzoic acid was thought to be due to the preferred adsorption of the former one. The process was then studied by using different substituted benzoic acids: the different conversions of 2-methyl-, 4-methyl-, and 2,6-dimethylbenzoic acids (70, 80, and 28%, respectively) were ascribed to the transition-state shape selectivity; this was confirmed by the higher yield (98%) observed when the resorcinol was reacted with 2,6-dimethylbenzoic acid in the presence of Amberlyst-15.

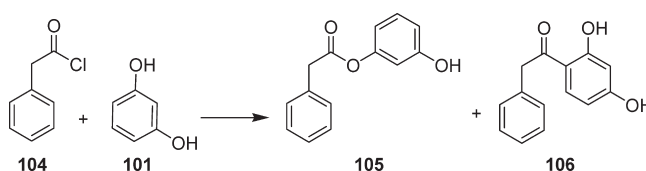
5.2.2. Direct Acylation with Clays. Clays were utilized as catalysts for the direct acylation of resorcinol **101**; Figueras et al.^{253,254} studied the use of phenyl acetyl chloride (**104**) (**101/104** ratio = 1) (Scheme 29) in the presence of different montmorillonites. In all cases, a high resorcinol conversion was reached (65–80%), and phenyl acetyl chloride had completely reacted. However, the yield of the desired ketone **106** was poor and the best yield (25%) was achieved with KS montmorillonite, with the ester **105** being the main product. The ketone/ester ratio was practically constant during the reactions with every catalyst and in all cases was much lower than 1. Moreover, the concentration of the ester **105** showed no maximum, which means that the ketone was not formed by a rearrangement of the ester but directly by ring acylation. The FeK10 and FeKS clays were slightly more active than the undoped ones (i.e., 39% **105** yield and 25% **106** yield for KS and 37% **105** yield and 42% **106** yield for FeKS). In the presence of FeK10 without solvent in a melted phase, although the resorcinol conversion was slightly lower (~70%) than that in dichloroethane (80%), a good ketone selectivity made possible a 60% preparative yield of the ketone **106**. The solvent-free reaction gave some other advantages: in fact, while the catalysts used in dichloroethane were generally deactivated after one cycle, the solvent-free reaction showed a satisfactory catalyst reusability after washing and drying (80% resorcinol conversion in the second cycle).

In a more environmentally benign way, Cavani et al.²⁵⁵ employed benzoic acid (**67**) as a resorcinol (**101**) acylating agent (**101/67** ratio = 1) (Scheme 28) in the presence of montmorillonite clay. RMB and 2,4-DHB were the sole products; the former is claimed by the authors to be a primary product whereas the latter is a secondary one, being exclusively formed by Fries rearrangement. These results seem to be not in complete agreement with mechanistic conclusions by Figueras et al., probably because they were obtained with different acylating agents.²⁵³ On the basis of these data, authors concluded that RMB first diffuses out of the catalyst pores and then, successively, is activated and transformed into 2,4-DHB. One possible explanation is that the high hydrophilic character of the clay surface, especially in samples having higher alumina content, makes the pores filled with more polar substances, such as benzoic acid and resorcinol, while less polar compounds rapidly diffuse out of the clay porosity and undergo consecutive transformation at the active sites located at the external particle surface. The reaction between resorcinol and benzoic acid to yield RMB was fully reversible, and the hydrolysis of RMB to yield resorcinol and benzoic acid occurred with water retained in clays; the removal of water from the bulk liquid by azeotropic distillation made it possible to considerably increase the conversion, which reached 80.6% since the esterification reaction was favored; in this case the 2,4-DHB was obtained with 61.8% selectivity.

Scheme 28



Scheme 29



Fe³⁺-exchanged clays underwent microwave activation that allowed them to achieve catalytic reactions in short reaction periods.^{256a} For example, the acetylation of methyl salicylate by acetic anhydride (methyl salicylate/acetic anhydride ratio = 1) under microwave irradiation for 0.13 h afforded the C-acetylated product in higher yield (13.3 vs 6.3%), TON (4.09 vs 8.56), and TOF (0.04 vs 64.19) with respect to the case of traditional heating carried out for 92 h. However, as in most microwave activation studies of heterogeneous catalysts, there are still many doubtful points about the role played by the catalysts and their reusability.

5.2.3. Direct Acylation (Miscellaneous). H₃PO₄ impregnated on TiO₂–ZrO₂ material has been successfully employed for the direct acylation of phenol with ethyl acetate under solventless conditions.^{256b} TiO₂–ZrO₂ was prepared through the sol–gel method by reacting zirconium(IV) isopropoxide, titanium(IV) butoxide, and cetyl pyridinium bromide (surfactant); this material was successively impregnated with varying H₃PO₄ contents and calcined in air at 500 °C for 6 h.^{256c} The best catalytic activity was found for 15 wt % content of H₃PO₄: at 350 °C and with a total phenol conversion, *o*-HAP was obtained in 97% yield, the only byproduct being PA (<3%) and alkylated products (<1%). It is well-known that strong acid sites are responsible for the formation of alkyl cation, whereas weak ones are responsible for formation of acetyl cation and therefore acylated products. By loading H₃PO₄ on the TiO₂–ZrO₂ support, the number of Lewis acid sites increases by a huge amount; this might happen probably by removing the adsorbed water on the Lewis sites or by esterifying the remaining M–OH groups on the support. The final catalyst has some weak Brønsted acid sites (P–OH) and a lot of Lewis acid sites, which are eligible for acylation reaction; the strong Brønsted acid sites that are the main active sites for producing ethyl cation are missing. Therefore, the most beneficial property of this new catalyst is that it prevents the ethylation of phenol. The effect of the temperature was also examined: by carrying out the process at 400 instead of 350 °C, the amount of byproduct (AAP, *p*-HAP, and alkylated products) was increased.

Graphite in methanesulfonic acid showed very good activity in the direct acetylation of phenol with benzoic acid.^{256d} After 3 h at 120 °C, the *ortho* isomer can be isolated in 81% yield; on the contrary, in the absence of graphite the yield drops to 20% and

with graphite alone a complete inactivity was found. By using different substituted benzoic acids, the process was applied to a variety of phenol and naphthol derivatives, obtaining high yields and high levels of *ortho*-regioselectivity; as expected, the reactions were faster when the aromatic moiety of the acylating agent carries an electron-releasing group (50–90% yield). In addition, acetic acid, cyclohexyl carboxylic acid, phenylacetic acid, hexanoic acid, and 11-bromoundecanoic acid can be utilized in obtaining the final ketones in very good yields (60–90%). Concerning the recyclability of the catalyst, the yield of the *ortho* product for three successive cycles did not decrease; of course, after each cycle, as methanesulfonic acid was not adsorbed onto graphite, it was necessary to add it again for the successive run.

6. ACYLATION OF HETEROCYCLES

Great attention has been devoted to the selective Friedel–Crafts acylation of heterocycles since the corresponding ketones represent valuable intermediates for the production of fine chemicals and, in particular, of biologically active compounds.²⁵⁷

The acylation of thiophene (**107**) by butyryl chloride (**108**) (**107**/**108** ratio = 1) was studied in the presence of various solid catalysts, including HZSM-5, HMOR, and HY zeolites²⁵⁸ (Scheme 30). It was observed that HZSM-5, which does not contain Lewis acid sites in a measurable amount, had a very low activity (initial rate = 0.9; Lewis acid content = 0.00 mmol/g); HMOR was much more active (initial rate = 28.3; Lewis acid content = 0.21 mmol/g). The highest activity was observed in the presence of USY with the maximum Lewis sites content (initial rate = 63.5; Lewis acid content = 0.88 mmol/g). These results indicate an increase in the acylation rate with an increase of the number of Lewis acid sites irrespective of the pore size, whereas the variation with respect to the number of Brönsted sites is incoherent, showing no correlation with the catalytic activity.

In agreement with these observations, Finiels et al.^{259a} showed that over HY zeolite the process followed a Langmuir–Hinshelwood kinetic law (which involves the adsorption of the two reactants on identical sites of the catalyst surface). Moreover, the Hammett ρ – σ relationship showed that there was no significant effect of the benzoyl chloride substituent on the initial reaction rate.

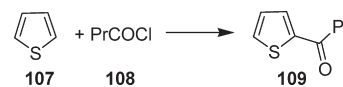
Thiophene was also acylated with benzoyl and anisoyl chlorides in the presence of Si–Fe catalyst, prepared from sodium trisilicate and ferric nitrate in the presence of ammonia and ammonium carbonate.^{259b} The corresponding α -acylated products were isolated in 77–79% yield.

More interesting are the results regarding the use of carboxylic acids as acylating agents. Zarei et al.^{86b} reported the use of phosphorus pentoxide on silica (P_2O_5/SiO_2), a catalyst easy to prepare and to handle,^{259c} for the acylation of thiophene and 2-methylthiophene with *p*-nitrocarboxylic acid and *p*-nitrophenylacetic acid (52–58% yield) at reflux in 1,2-dichloroethane for 3 h. The method occurs by in situ generation of a carboxylic anhydride derived from a mixed carboxylic-phosphoric anhydride.^{259d}

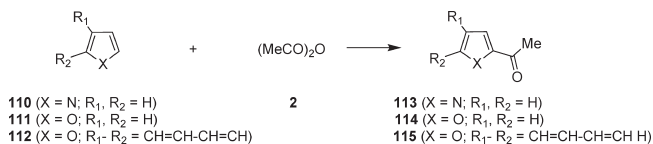
Thiophene was also acylated with hexanoic acid through HBEA catalysis.^{147b} The reaction was carried out at 190 °C for 30 min under microwave irradiation, and 1-(2-thienyl)-1-hexanone was isolated in 57% yield. The yields were increased up to 78% by prolonging the reaction time to 120 min.

HBEA showed interesting results in the acetylation of thiophene, 2-methylthiophene, and 3-methylthiophene with acetic anhydride.^{259e} The only products observed were the α -monoacylated (positions 2 or 5) derivatives. As expected, thiophene

Scheme 30



Scheme 31



and 2-methylthiophene reacted faster than 3-methylthiophene (that has the methyl group in a position that is not effectively activating); in addition, with the latter reagent there are two available positions for acylation, and, in fact, a mixture of 2,3- and 3,5-dimethylthiophene was obtained, with predominance of the less hindered product.

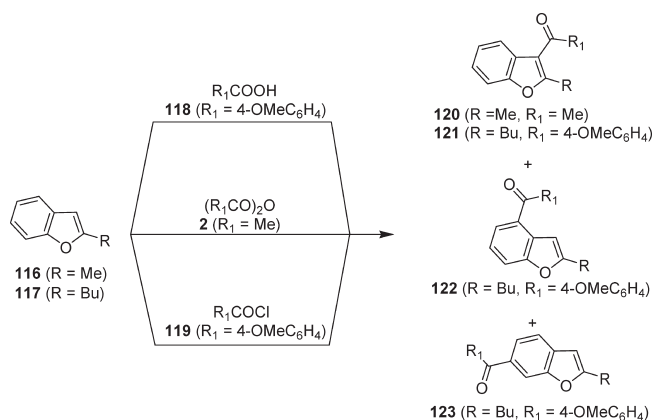
The same catalyst was utilized for the acetylation of furan and indole under similar reaction conditions. On the contrary, with pyrrole the reaction was slower and less selective, mainly due to the fact that pyrrole is more adsorbed by the catalyst than the other heteroaromatic compounds (which may also mean that pyrrole partially poisons the catalyst). For this reason, a modification of the zeolite catalyst was made by impregnation with indium chloride (20% metal loading):^{259e} in 2 h 2-acetylpyrrole was obtained in 74% yield by reacting pyrrole with acetic anhydride. Probably, indium promotes the reaction by increasing the number of Lewis acid sites.

The vapor-phase acetylation of pyrrole (**110**) and furan (**111**) with acetic anhydride (**2**) (heterocycle/**2** ratio = 2–0.5) over HZSM-5 zeolites was studied by Subrahmanyam et al.²⁶⁰ (Scheme 31). The reaction proceeded largely at the 2-position of the heteroaromatic substrate to yield a somewhat sterically bulkier product. The comparison of the activities of different acid zeolites led the authors to the conclusion that the Brönsted acid centers were suitable for the Friedel–Crafts acylation of furan and pyrrole and that the catalysts having moderate acid strength (SAR = 30) showed higher activity (70% pyrrole conversion, 97% 2-acetylpyrrole selectivity). The selectivity for both furan and pyrrole acylation as well as the catalytic activity were less favorable at high temperature. The decrease in the yield of acylated product at higher temperatures was attributed to the conversion of Brönsted acid centers into Lewis acid centers.⁴⁸ The role of Brönsted or Lewis sites on the catalyst activity in the present acetylation seems to be somewhat conflicting with studies on thiophene.²⁵⁸

Furan was efficiently and selectively acylated at the 2-position with a large variety of carboxylic acids (furan/carboxylic acid ratio = 1) in the presence of phosphonic ion-exchanged resins (62–96% yield).²⁶¹ However, the process seems to be not particularly exciting since it required large amounts of trifluoroacetic anhydride to activate the carboxylic acid.

The acylation of benzofuran (**112**) with acetic anhydride (**2**) (**112**/**2** ratio = 1–0.07) (Scheme 31) in the presence of HY zeolites was particularly studied by Pérot et al.^{262–265} The conversion of benzofuran (**112**) into 2-acetylbenzofuran (**115**) was

Scheme 32



strongly dependent on the order of introduction of reactants: in particular, it was lower when reagent **112** was introduced first (2-acetylbenzofuran conversion 0.4% vs ~22.0%). This could be due to the oligomerization of the substrate through a Diels–Alder-type reaction and the subsequent acylation of its dimer or trimer, which would give products entrapped in the zeolite, causing a rapid deactivation.²⁶³ There was a competition toward adsorption between the two reactants which was in favor of benzofuran. Moreover, the activity of the catalyst decreased significantly with time.

Acetylation of 2-methylbenzofuran (**116**) with acetic anhydride (**2**) (**116/2** ratio = 0.08) in the presence of HY zeolite gave 3-acetyl-2-methylbenzofuran (**120**) in high yield (95% **116** conversion with 95% selectivity with respect to compound **120**)²⁶⁴ (Scheme 32). The reaction could be performed with the same pelletized catalyst in a dynamic flow reactor at 60 °C under atmospheric pressure. Comparative experiments with benzofuran and 2-methylbenzofuran showed a behavior similar to that observed under batch conditions. Deactivation was significant for benzofuran but much less for 2-methylbenzofuran, with which high yield and selectivity could be obtained. 2-Methylbenzofuran was about twice as reactive as benzofuran, with position 3 in 2-methylbenzofuran being at least 2 orders of magnitude more reactive than position 3 in benzofuran. The system represents a promising tool to conveniently carry out the above acylation in a flow reactor.

The acylation of 2-butylbenzofuran (**117**) with *p*-anisoyl chloride (**119**) and *p*-anisic acid (**118**) (**117/acylating agent** = 0.33) in the presence of faujasite-type zeolites was reported by Geneste et al.²⁶⁶ (Scheme 32). The reaction with both acylating reagents led to the formation of the three isomers **121**, **122**, and **123** with a good initial selectivity in the 3-acylated derivative **121** (87 and 82% selectivity after 1 h, respectively). The selectivity decreased with time, due to a consecutive deacylation of this compound, followed by a reacylation which favored the formation of the other two isomers (mainly the 6-acylated one **123**), similar to the behavior of 2MN.

A Fe³⁺-exchanged K10 clay showed high activity in the electrophilic acetylation of five-membered heterocycles with acetic anhydride (**2**) (heterocycle/**2** ratio = 4)²⁶⁷ (Scheme 31). The reaction proceeded selectively at the 2-position to yield the bulkier products **113**–**115** (97–98% conversion). The high selectivity (95–100%) was attributed to electronic and kinetic effects which determine the course of the reaction. The reusability of the catalyst for several cycles in the pyrrole acetylation was emphasized.

7. CONCLUDING REMARKS

The analysis of several articles and patents has shown that numerous examples of the use of solid catalysts in Friedel–Crafts acylation have not been directly followed by an extensive industrial application, although some positive instances have been reported.¹²⁸

The reaction carried out under heterogeneous catalysis follows a mechanism similar to that occurring under homogeneous conditions, and the surface active acid sites interact with reagents and products in the same manner. In particular, the great drawback is the fact that the ketonic products strongly adsorb on the catalytic sites, ultimately poisoning the catalyst (product inhibition). Moreover, in the case of the heterogeneous catalysis, the adsorbed products can undergo further reactions, giving larger byproducts (coke), which remain adsorbed and further limit the access of reactants to the active sites. This provokes low conversions and the need for laborious and expensive recovering, washing, and reactivating of the catalyst. Nevertheless, many positive suggestions can be inferred. First, it is clearly ascertained that a catalyst showing a too strong acidity will be more rapidly poisoned. Better performances seem to be achievable through a convenient combination of parameters such as balanced acidity, hydrophobicity, and crystallite size. In regard to the catalyst acidity, we can conclude, in agreement with Corma,¹³ that the great number of studies by researchers from different areas make it today possible to prepare specific catalysts with adequate acidic strength for almost any particular acid-catalyzed reaction. Positive results deserving further investigations come from experiments carried out under continuous fixed-bed reaction conditions even with monolithic reactors. In fact, with these systems, the continuous flow of reagents and solvents can remove the ketone products from the active sites of the catalyst, thereby enhancing performance. To minimize the problem of catalyst decay by coke formation and to prolong its lifetime, some stratagems can be utilized: these include doping with transition metal ions and addition of controlled amounts of an adequate solvent. **More recently, the problem of the catalyst deactivation has been deeply considered: different metals and metal couples can be incorporated into the framework of zeolites, mesoporous supports, and other materials, obtaining more recyclable and stable catalysts.**

Improvements have been achieved from both the economic and ecological perspectives. For example, by using solid catalysts, it has been possible to avoid complex workup procedures and production of great quantities of spent catalysts, and to minimize the corrosion of plants. In addition, the greenest acylating agents, namely, the carboxylic acids, have been successfully utilized in some reactions with promising results. Of course, their use is correlated with the development of systems, such as the mentioned monolithic structured reactors, that can allow the removal of water by a stripping operation using a gas flow, with the aim of avoiding catalyst deactivation by water.

Unlike alkylation, acylation does not necessitate a rigid control of both zeolite SAR and operating conditions (temperature and reagent pressure); in addition, by using solid catalysts having tailored channels and pores, better selectivity can be achieved with respect to that obtained with the homogeneous ones.

We would like to conclude this review with an optimistic view for the future expansion of heterogeneous catalysis in Friedel–Crafts acylation: this positive view comes from the certainty that the cooperation between researchers of different scientific and technological areas will result in an extraordinary synergic strength aimed at hitting the most difficult targets.

AUTHOR INFORMATION

Corresponding Author

*Phone: +39 0521 905551. Fax: +39 0521 905472. E-mail: giovanni.sartori@unipr.it.

BIOGRAPHIES



Giovanni Sartori was born in Casalmaggiore (Italy) in 1944. He studied chemistry at the University of Parma, where he obtained his laurea degree under the guidance of Prof. Giuseppe Casnati in 1971. In 1972 he began his career at the University of Parma working in the group of Prof. Casnati on the regio- and stereoselective functionalization of ambidental reagents. He was promoted to Associate Professor of Organic Chemistry in 1985 and to Full Professor in 1994. He is the Head of the "Clean Synthetic Methodologies Groups" of the University of Parma. His research interests include all aspects of heterogeneous catalysis applied to fine chemicals and pharmaceuticals production with particular attention to the preparation and use of supported organic (chiral) catalysts. A special area of extensive interest is also represented by the development of new ecocompatible synthetic methods mainly based on the exploitation of solvent-free and multicomponent reactions. **The more recent research topics concern the continuous-flow processes with heterogeneous catalysts including application of sequentially linked column reactors.** He has published about **150** original studies and **11** chapters of books and filed approximately 20 patents.



Raimondo Maggi was born in Parma (Italy) in 1963. He graduated from the University of Parma in 1989 (under the guidance of Prof. Giuseppe Casnati), and he received his Ph.D. in Organic Chemistry (under the direction of Prof. Giovanni Sartori)

from the same university in 1992. In 1994 he carried out his postdoctoral research with Prof. Manfred Schlosser at Lausanne University. He began his career at the University of Parma in 1997 as Researcher, and in 2002 he was promoted to Associate Professor of Organic Chemistry. His research interests include the preparation and use of heterogeneous (chiral) catalysts for the environmentally friendly synthesis of fine chemicals and pharmaceuticals **and the set up of microstructured catalytic flow reactors.** He has published about **100** original studies and **11** chapters of books.

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DEDICATION

Dedicated to the memory of Professor Giuseppe Casnati on the **18th** anniversary of his death.

REFERENCES

- (1) Grucarevic, S.; Merz, V. *Chem. Ber.* **1873**, *6*, 60.
- (2) Olah, G. A. *Friedel-Crafts Chemistry*; Wiley: New York, 1973.
- (3) Gore, P. H. in *Friedel-Crafts and Related Reactions*; Olah, G. A., Ed.; John Wiley & Sons Inc.: London, 1964; Vol. III, Part 1, p 1.
- (4) Franck, H. G. *Industrial Aromatic Chemistry*; Springer: Berlin, 1988.
- (5) Horsely, J. A. *CHEMTECH* **1997**, 45.
- (6) Bauer, K.; Garbe, D.; Surberg, H. *Common Fragrance and Flavor Materials*; WHC Verlagsgesellschaft: Weinheim, 1990; p 83.
- (7) Sheldon, R. A.; Downing, R. S. *Appl. Catal. A: Gen.* **1999**, *189*, 163.
- (8) Anastas, P. T.; Bartlett, L. B.; Kirchhoff, M. M.; Williamson, T. C. *Catal. Today* **2000**, *55*, 11.
- (9) Kawada, A.; Mitamura, S.; Kobayashi, S. *J. Chem. Soc., Chem. Commun.* **1993**, 1157.
- (10) Kobayashi, S.; Nagayama, S. *J. Am. Chem. Soc.* **1998**, *120*, 2985.
- (11) Kodomari, M.; Suzuki, Y.; Yoshida, K. *J. Chem. Soc., Chem. Commun.* **1997**, 1567.
- (12) Milto, V. I.; Mironov, G. S.; Kopelkin, V. V. *Zh. Org. Khim.* **1989**, *25*, 2372.
- (13) Corma, A. *Chem. Rev.* **1995**, *95*, 559.
- (14) Kouwenhoven, H. W.; van Bekkum, H. In *Handbook of Heterogeneous Catalysis*; Ertl, G., Knözinger, H., Weitkamp, J., Eds.; VCH: Weinheim, 1997; Vol. 5, p 2358.
- (15) Métivier, P. In *Friedel-Crafts Acylation in Fine Chemicals through Heterogeneous Catalysis*; Sheldon, R. A., van Bekkum, H., Eds.; VCH: Weinheim, 2001; p 161.
- (16) (a) Bezouhanova, C. P. *Appl. Catal. A: Gen.* **2002**, *229*, 127. (b) Bejblova, M.; Procházková, D.; Cejka, J. *ChemSusChem* **2009**, *2*, 486.
- (17) Sartori, G.; Casnati, G.; Bigi, F.; Predieri, G. *J. Org. Chem.* **1990**, *55*, 4371.
- (18) Sartori, G.; Bigi, F.; Canali, G.; Maggi, R.; Casnati, G.; Tao, X. *J. Org. Chem.* **1993**, *58*, 840.
- (19) Beck, U. In *Ullmann's Encyclopedia of Industrial Chemistry*; Gerhart, W., Campbell, F. T., Pfefferkorn, R., Rounsaville, J. F., Eds.; VCH: Weinheim, 1986; Vol. 15, p 91.
- (20) Szmant, H. *Organic Building Blocks of the Chemical Industry*; Wiley: New York, 1989.
- (21) Sen, S. E.; Smith, S. M.; Sullivan, K. A. *Tetrahedron* **1999**, *55*, 12657.
- (22) Derouane, E. G.; Dillon, C. J.; Bethell, D.; Derouane-Abd Hamid, S. B. *J. Catal.* **1999**, *187*, 209.
- (23) Derouane, E. G.; Crehan, G.; Dillon, C. J.; Bethell, D.; He, H.; Derouane-Abd Hamid, S. B. *J. Catal.* **2000**, *194*, 410.

- (24) Myata, A.; Matsunaga, K.; Ishikawa, M. JP 07089894, 1995; *Chem. Abstr.* **1995**, 123, 82946.
- (25) Botella, P.; Corma, A.; López-Nieto, J. M.; Valencia, S.; Jacquot, R. *J. Catal.* **2000**, 195, 161.
- (26) Rohan, D.; Canaff, C.; Fromentin, E.; Guisnet, M. *J. Catal.* **1998**, 177, 296.
- (27) Kantam, M. L.; Ranganath, K. V. S.; Sateesh, M.; Kumar, K. B. S.; Choudary, B. M. *J. Mol. Catal. A: Chem.* **2005**, 225, 15.
- (28) Klisáková, J.; Červený, L.; Čejka, J. *Appl. Catal. A: Gen.* **2004**, 272, 79.
- (29) Venkatesan, C.; Jaimol, T.; Moreau, P.; Finiels, A.; Ramaswamy, A. V.; Singh, A. P. *Catal. Lett.* **2001**, 75, 119.
- (30) Bourgogne, J. P.; Aspisi, C.; Ou, K.; Geneste, P.; Durand, R.; Mseddi, S. FR 2667063, 1992; *Chem. Abstr.* **1992**, 117, 233598.
- (31) Escola, J. M.; Davis, M. E. *Appl. Catal. A: Gen.* **2001**, 214, 111.
- (32) Chidambaram, M.; Venkatesan, C.; Moreau, P.; Finiels, A.; Ramaswamy, A. V.; Singh, A. P. *Appl. Catal. A: Gen.* **2002**, 224, 129.
- (33) Singh, A. P.; Bhattacharya, D.; Sharma, S. *J. Mol. Catal. A: Chem.* **1995**, 102, 139.
- (34) Jacob, B.; Sugunan, S.; Singh, A. P. *J. Mol. Catal. A: Chem.* **1999**, 139, 43.
- (35) Bhattacharya, D.; Sharma, S.; Singh, A. P. *Appl. Catal. A: Gen.* **1997**, 150, 53.
- (36) Cervený, L.; Mikulcová, K.; Čejka, J. *Appl. Catal. A: Gen.* **2002**, 223, 65.
- (37) (a) Friedman, H. M.; Nelson, A. L. *J. Org. Chem.* **1969**, 34, 3211. (b) Yuan, B.; Li, Z.; Liu, Y.; Zhang, S. *J. Mol. Catal. A: Chem.* **2008**, 280, 210.
- (38) Moreau, P.; Finiels, A.; Pelorgeas, S.; Vigneau, O.; Lasperas, M. *Catal. Lett.* **1997**, 47, 161.
- (39) Chiche, B.; Finiels, A.; Gauthier, C.; Geneste, P. *J. Org. Chem.* **1986**, 51, 2128.
- (40) Sheemol, V. N.; Tyagi, B.; Jasra, R. V. *J. Mol. Catal. A: Chem.* **2004**, 215, 201.
- (41) Singh, A. P.; Bhattacharya, D. *Catal. Lett.* **1995**, 32, 327.
- (42) Chu, C. T. W.; Chang, C. D. *J. Phys. Chem.* **1985**, 89, 1569.
- (43) Choudary, V. R.; Jana, S. K.; Patil, N. S.; Bhargava, S. K. *Microporous Mesoporous Mater.* **2003**, 57, 21.
- (44) Choudary, B. M.; Sateesh, M.; Kantam, M. L.; Ranganath, K. V. S.; Raghavan, K. V. JP 2001278833, 2001; *Chem. Abstr.* **2001**, 135, 288581.
- (45) Jaimol, T.; Pandey, A. K.; Singh, A. P. *J. Mol. Catal. A: Chem.* **2001**, 170, 117.
- (46) Ram Reddy, P.; Subrahmanyam, M.; Kumari, V. D. *Catal. Lett.* **1999**, 61, 207.
- (47) Akporiaye, D. E.; Daasvatan, K.; Solberg, J.; Stöcker, M. *Stud. Surf. Sci. Catal.* **1993**, 78, 521.
- (48) Gauthier, C.; Chiche, B.; Finiels, A.; Geneste, P. *J. Mol. Catal.* **1989**, 50, 219.
- (49) Pandey, A. K.; Singh, A. P. *Catal. Lett.* **1997**, 44, 129.
- (50) Singh, A. P.; Pandey, A. K. *J. Mol. Catal. A: Chem.* **1997**, 123, 141.
- (51) Kikhtyanin, O. V.; Ione, K. G.; Snytnikova, G. P.; Malysheva, L. V.; Toktarev, A. V.; Paukshtis, E. A.; Spichtner, R.; Schüth, F.; Unger, K. K. *Stud. Surf. Sci. Catal.* **1994**, 84, 1905.
- (52) (a) Cundy, C. S.; Higgins, R.; Kibby, S. A. M.; Lowe, B. M.; Paton, R. M. *Chem. Ind. (London)* **1991**, 629. (b) Hou, Q.; Zheng, B.; Bi, C.; Luan, J.; Zhao, Z.; Guo, H.; Wang, G.; Li, Z. *J. Catal.* **2009**, 268, 376. (c) Bejblova, M.; Zones, S. I.; Čejka, J. *Appl. Catal. A: Gen.* **2007**, 327, 255.
- (53) Fang, R.; Harvey, G.; Kouwenhoven, H. W.; Prins, R. *Appl. Catal. A: Gen.* **1995**, 130, 67.
- (54) Fang, R.; Kouwenhoven, H. W.; Prins, R. *Stud. Surf. Sci. Catal.* **1994**, 84, 1441.
- (55) Laidlaw, P.; Bethell, D.; Brown, S. M.; Hutchings, G. J. *J. Mol. Catal. A: Chem.* **2001**, 174, 187.
- (56) Chiche, B.; Finiels, A.; Gauthier, C.; Geneste, P. *Appl. Catal.* **1987**, 30, 365.
- (57) Kladnig, W. J. *Phys. Chem.* **1976**, 80, 262.
- (58) Badri, R.; Tavakoli, L. J. *Inclusion Phenom. Macrocyclic Chem.* **2003**, 45, 41.
- (59) Beck, J. S.; Vartuli, J. C.; Roth, W. J.; Leonowicz, M. E.; Kresge, C. T.; Schmitt, K. D.; Chu, W.; Olson, D. H.; Sheppard, E. W.; McCullen, S. B.; Higgins, J. B.; Schlenker, J. L. *J. Am. Chem. Soc.* **1992**, 114, 10834.
- (60) Choudary, V. R.; Jana, S. K.; Patil, N. S. *Catal. Lett.* **2001**, 76, 235.
- (61) (a) Choudary, V. R.; Jana, S. K.; Patil, N. S. *Tetrahedron Lett.* **2002**, 43, 1105. (b) Choudary, V. R.; Jha, R. *Appl. Catal. A: Gen.* **2007**, 333, 42.
- (62) Choudary, V. R.; Jana, S. K. *J. Mol. Catal. A: Chem.* **2002**, 184, 247.
- (63) Choudary, V. R.; Jana, S. K.; Kiran, B. P. *J. Catal.* **2000**, 192, 257.
- (64) Choudary, V. R.; Jana, S. K. *Synth. Commun.* **2002**, 32, 2843.
- (65) (a) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; VCH: Weinheim, 1988. (b) Selvakumar, S.; Gupta, N. M.; Singh, A. P. *Appl. Catal. A: Gen.* **2010**, 372, 130. (c) Procházková, D.; Bejblova, M.; Vlk, J.; Vinu, A.; Štěpnička, P.; Čejka, J. *Chem.—Eur. J.* **2010**, 16, 7773.
- (66) Balogh, M.; Laszlo, P. *Organic Chemistry Using Clays*; Springer-Verlag: New York, 1993.
- (67) Alberti, G.; Costantino, U. In *Comprehensive Supramolecular Chemistry*; Atwood, J. L., Davies, J. E. P., MacNicol, D. D., Vögtle, F., Eds.; Pergamon Press: Oxford, 1996; Vol. 7, pp 1–23.
- (68) Gil, A.; Gandía, L. M.; Vicente, M. A. *Catal. Rev. Sci. Eng.* **2000**, 42, 145.
- (69) Cornélis, A.; Gerstmans, A.; Laszlo, P.; Mathy, A.; Zieba, I. *Catal. Lett.* **1990**, 6, 103.
- (70) Laszlo, P.; Montaufer, M.-T. *Tetrahedron Lett.* **1991**, 32, 1561.
- (71) Cornélis, A.; Laszlo, P.; Wang, S. *Tetrahedron Lett.* **1993**, 34, 3849.
- (72) Cornélis, A.; Laszlo, P.; Wang, S.-F. *Catal. Lett.* **1993**, 17, 63.
- (73) Chiche, B.; Finiels, A.; Gauthier, C.; Geneste, P.; Graille, J.; Pioch, D. *J. Mol. Catal.* **1987**, 42, 229.
- (74) Chiche, B. H.; Geneste, P.; Gauthier, C.; Figueras, F.; Fajula, F.; Finiels, A.; Graille, J.; Pioch, D. FR 2599275, 1987; *Chem. Abstr.* **1988**, 109, 172531.
- (75) Fujita, T.; Takahata, K. JP 61152636, 1986; *Chem. Abstr.* **1987**, 106, 18104.
- (76) Hu, R.-J.; Li, B.-G. *Catal. Lett.* **2004**, 98, 43.
- (77) Zhou, D.-Q.; Zhang, Y.-H.; Huang, M.-Y.; Jiang, Y.-Y. *Polym. Adv. Technol.* **2002**, 14, 360.
- (78) López-Salinas, E.; Garcia-Sanchez, M.; Ramon-Garcia, M. L.; Schifter, I. *J. Porous Mater.* **1996**, 3, 169.
- (79) Choudary, V. R.; Jana, S. K.; Narkhede, V. S. *Appl. Catal. A: Gen.* **2002**, 235, 207.
- (80) Choudary, V. R.; Jana, S. K.; Mandale, A. B. *Catal. Lett.* **2001**, 74, 95.
- (81) Tauster, S. J. *Acc. Chem. Res.* **1987**, 20, 389.
- (82) Morley, J. O. *J. Chem. Soc., Perkin Trans. 2* **1977**, 601.
- (83) Arata, K.; Yabe, K.; Toyoshima, I. *J. Catal.* **1976**, 44, 385.
- (84) Choudary, V. R.; Jana, S. K. *J. Catal.* **2001**, 201, 225.
- (85) Haller, G. L.; Resasco, D. E. *Adv. Catal.* **1989**, 36, 173.
- (86) (a) Choudary, V. R.; Mulla, S. A. R.; Uphade, B. S. *Ind. Eng. Chem. Res.* **1997**, 36, 2096. (b) Zarei, A.; Hajipour, A. R.; Khazdooz, L. *Tetrahedron Lett.* **2008**, 49, 6715.
- (87) Nishamol, K.; Rehna, K. S.; Sugunan, S. *React. Kinet. Catal. Lett.* **2004**, 81, 229.
- (88) Song, X.; Sayari, A. *Catal. Rev. Sci. Eng.* **1996**, 38, 329.
- (89) Hino, M.; Kobayashi, S.; Arata, K. *J. Am. Chem. Soc.* **1979**, 101, 6439.
- (90) Hino, M.; Arata, K. *J. Chem. Soc., Chem. Commun.* **1980**, 851.
- (91) Arata, K. *Adv. Catal.* **1990**, 37, 165.
- (92) Arata, K.; Hino, M. *Mater. Chem. Phys.* **1990**, 26, 213.
- (93) Arata, K. *Trends Phys. Chem.* **1991**, 2, 1.
- (94) Misono, M.; Okuhara, T. *CHEMTECH* **1993**, 23, 23.
- (95) Umansky, B.; Engelhardt, J.; Keith, W. J. *Catal.* **1991**, 127, 128.

- (96) Kustov, L. M.; Kazansky, V. B.; Figueras, F.; Tichit, D. *J. Catal.* **1994**, *150*, 143.
- (97) Adeeva, V.; Dehaan, J. W.; Janchen, J.; Lei, G. D.; Schunemann, V.; Vandeven, L. J. M.; Sachtler, W. M. H.; Vansanten, R. A. *J. Catal.* **1995**, *151*, 364.
- (98) Babou, F.; Bigot, B.; Coudurier, G.; Sautet, P.; Védrine, J. C. *Stud. Surf. Sci. Catal.* **1994**, *90*, 519.
- (99) Hino, M.; Arata, K. *J. Chem. Soc., Chem. Commun.* **1985**, 112.
- (100) Yadav, G. D.; Pujari, A. A. *Green Chem.* **1999**, *1*, 69.
- (101) Arata, K.; Hino, M. *Appl. Catal.* **1990**, *59*, 197.
- (102) Arata, K.; Nakamura, H.; Shouji, M. *Appl. Catal. A: Gen.* **2000**, *197*, 213.
- (103) Goto, S.; Goto, M.; Kimura, Y. *React. Kinet. Catal. Lett.* **1990**, *41*, 27.
- (104) Xia, Y.; Hua, W.; Gao, Z. *Catal. Lett.* **1998**, *55*, 101.
- (105) Hua, W.; Xia, Y.; Yue, Y.; Gao, Z. *J. Catal.* **2000**, *196*, 104.
- (106) Suja, H.; Deepa, C. S.; Sreeja Rani, K.; Sugunan, S. *Appl. Catal. A: Gen.* **2002**, *230*, 233.
- (107) Chidambaram, M.; Curulla-Ferre, D.; Singh, A. P.; Anderson, B. G. *J. Catal.* **2003**, *220*, 442.
- (108) Landge, S. M.; Chidambaram, M.; Singh, A. P. *J. Mol. Catal. A: Chem.* **2004**, *213*, 257.
- (109) Kozhevnikov, I. V. *Chem. Rev.* **1998**, *98*, 171.
- (110) Kozhevnikov, I. V. *Appl. Catal. A: Gen.* **2003**, *256*, 3.
- (111) Castro, C.; Corma, A.; Primo, J. *J. Mol. Catal. A: Chem.* **2002**, *177*, 273.
- (112) Kaur, J.; Kozhevnikov, I. V. *Chem. Commun.* **2002**, 2508.
- (113) Kaur, J.; Griffin, K.; Harrison, B.; Kozhevnikov, I. V. *J. Catal.* **2002**, *208*, 448.
- (114) Tagawa, T.; Amemiya, J.; Goto, S. *Appl. Catal. A: Gen.* **2004**, *257*, 19.
- (115) Izumi, Y.; Natsume, N.; Takamine, H.; Tamaoki, I.; Urabe, K. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2159.
- (116) Izumi, Y.; Ogawa, M.; Nohara, W.; Urabe, K. *Chem. Lett.* **1992**, 1987.
- (117) Izumi, Y.; Ogawa, M.; Urabe, K. *Appl. Catal. A: Gen.* **1995**, *132*, 127.
- (118) (a) Izumi, Y.; Matsuo, K.; Urabe, K. *J. Mol. Catal.* **1983**, *18*, 299. (b) Shimizu, K.-i.; Niimi, K.; Satsuma, A. *Catal. Commun.* **2008**, *9*, 980.
- (119) Kozhevnikov, I. V.; Kloetstra, K. R.; Sinnema, A.; Zandbergen, H. W.; van Bekkum, H. *J. Mol. Catal. A: Chem.* **1996**, *114*, 287.
- (120) Blasco, T.; Corma, A.; Martínez, A.; Martínez-Escolano, P. *J. Catal.* **1998**, *177*, 306.
- (121) Kapustin, G. I.; Brueva, T. R.; Klyachko, A. L.; Timofeeva, M. N.; Kulikov, S. M.; Kozhevnikov, I. V. *Kinet. Catal.* **1990**, *31*, 1017.
- (122) De Castro, C.; Primo, J.; Corma, A. *J. Mol. Catal. A: Chem.* **1998**, *134*, 215.
- (123) (a) Okuhara, T.; Nishimura, T.; Misono, M. *Stud. Surf. Sci. Catal.* **1996**, *101*, 581. (b) Kamiya, Y.; Ooka, Y.; Obara, C.; Ohnishi, R.; Fujita, T.; Kurata, Y.; Tsuji, K.; Nakajyo, T.; Okuhara, T. *J. Mol. Catal. A: Chem.* **2007**, *262*, 77.
- (124) Olah, G. A.; Malhotra, R.; Narang, S. C.; Olah, J. A. *Synthesis* **1978**, 672.
- (125) Yamato, T.; Hideshima, C.; Prakash, G. K. S.; Olah, G. A. *J. Org. Chem.* **1991**, *56*, 3955.
- (126) Olah, G. A.; Mathew, T.; Farnia, M.; Prakash, G. K. S. *Synlett* **1999**, 1067.
- (127) Jaimol, T.; Moreau, P.; Finiels, A.; Ramaswamy, A. V.; Singh, A. P. *Appl. Catal. A: Gen.* **2001**, *214*, 1.
- (128) Spagnol, M.; Gilbert, L.; Guillot, H.; Tirel, P.-J. *WO 9748665*, 1997; *Chem. Abstr.* **1998**, *128*, 90668.
- (129) Spagnol, M.; Gilbert, L.; Benazzi, E.; Marcilly, C. *WO 9635656*, 1996; *Chem. Abstr.* **1997**, *126*, 46970.
- (130) Smith, K.; Zhenhua, Z.; Hodgson, P. K. G. *J. Mol. Catal. A: Chem.* **1998**, *134*, 121.
- (131) Zoeller, J. R.; Sumner, C. E. *J. Org. Chem.* **1990**, *55*, 319.
- (132) Derouane, E. G. *J. Mol. Catal. A: Chem.* **1998**, *134*, 29.
- (133) Derouane, E. G.; Schmidt, I.; Lachas, H.; Christensen, C. J. H. *Catal. Lett.* **2004**, *95*, 13.
- (134) (a) Freese, U.; Heinrich, F.; Roessner, F. *Catal. Today* **1999**, *49*, 237. (b) Hsu, H.-L.; Selvin, R.; Her, T.-M. *J. Therm. Anal. Calorim.* **2007**, *89*, 379.
- (135) Beers, A. E. W.; van Bokhoven, J. A.; de Lathouder, K. M.; Kapteijn, F.; Moulijn, J. A. *J. Catal.* **2003**, *218*, 239.
- (136) Beers, A. E. W.; Nijhuis, T. A.; Kapteijn, F.; Moulijn, J. A. *Microporous Mesoporous Mater.* **2001**, *48*, 279.
- (137) (a) Lempers, H. E. B.; Sheldon, R. A. *J. Catal.* **1998**, *175*, 62. (b) Wagholikar, S. G.; Niphadkar, P. S.; Mayadevi, S.; Sivasanker, S. *Appl. Catal. A: Gen.* **2007**, *317*, 250.
- (138) Xu, M.; Cheng, M.; Bao, X. *Chem. Commun.* **2000**, 1873.
- (139) García-Martínez, J.; Cazorla-Amorós, D.; Linares-Solano, A.; Lin, Y. S. *Microporous Mesoporous Mater.* **2001**, *42*, 255.
- (140) Winé, G.; Tessonnier, J. P.; Pham-Huu, C.; Ledoux, M. J. *Chem. Commun.* **2002**, 2418.
- (141) (a) Ledoux, M. J.; Pham-Huu, C. *CATTECH* **2001**, *5*, 226. (b) Winé, G.; Tessonnier, J.-P.; Rigolet, S.; Marichal, C.; Ledoux, M.-J.; Pham-Huu, C. *J. Mol. Catal. A: Chem.* **2006**, *248*, 113.
- (142) Nhut, J.-M.; Pesant, L.; Tessonnier, J.-P.; Winé, G.; Guille, J.; Pham-Huu, C.; Ledoux, M.-J. *Appl. Catal. A: Gen.* **2003**, *254*, 345.
- (143) Nijhuis, T. A.; Beers, A. E. W.; Vergunst, T.; Hoek, I.; Kapteijn, F.; Moulijn, J. A. *Catal. Rev.* **2001**, *43*, 345.
- (144) Beers, A. E. W.; Nijhuis, T. A.; Aalders, N.; Kapteijn, F.; Moulijn, J. A. *Appl. Catal. A: Gen.* **2003**, *243*, 237.
- (145) Wang, Q. L.; Ma, Y.; Ji, X.; Yan, H.; Qiu, Q. *J. Chem. Soc., Chem. Commun.* **1995**, 2307.
- (146) Kresnawahjuesa, O.; Gorte, R. J.; White, D. J. *J. Mol. Catal. A: Chem.* **2004**, *208*, 175.
- (147) (a) Kresnawahjuesa, O.; Kühl, G. H.; Gorte, R. J.; Quierini, C. A. *J. Catal.* **2002**, *210*, 106. (b) Yamashita, H.; Mitsukura, Y.; Kobashi, H. *J. Mol. Catal. A: Chem.* **2010**, *327*, 80.
- (148) Corma, A.; Climent, M. J.; García, H.; Primo, J. *Appl. Catal.* **1989**, *49*, 109.
- (149) Gaare, K.; Akporiaye, D. *J. Mol. Catal. A: Chem.* **1996**, *109*, 177.
- (150) Lee, E. F. T.; Rees, L. V. C. *Zeolites* **1987**, *7*, 545.
- (151) Ma, Y.; Wang, Q. L.; Jiang, W.; Zuo, B. *Appl. Catal. A: Gen.* **1997**, *165*, 199.
- (152) Shih, P.-C.; Wang, J.-H.; Mou, C.-Y. *Catal. Today* **2004**, *93–95*, 365.
- (153) Bigi, F.; Carloni, S.; Flego, C.; Maggi, R.; Mazzacani, A.; Rastelli, M.; Sartori, G. *J. Mol. Catal. A: Chem.* **2002**, *178*, 139.
- (154) Raja, T.; Singh, A. P.; Ramaswamy, A. V.; Finiels, A.; Moreau, P. *Appl. Catal. A: Gen.* **2001**, *211*, 31.
- (155) Moreau, P.; Finiels, A.; Meric, P. *J. Mol. Catal. A: Chem.* **2000**, *154*, 185.
- (156) Harvey, G.; Mader, G. *Collect. Czech. Chem. Commun.* **1992**, *57*, 862.
- (157) Heinichen, H. K.; Hölderich, W. F. *J. Catal.* **1999**, *185*, 408.
- (158) Fromentin, E.; Coustard, J.-M.; Guisnet, M. *J. Catal.* **2000**, *190*, 433.
- (159) Berreghis, A.; Ayrault, P.; Fromentin, E.; Guisnet, M. *Catal. Lett.* **2000**, *68*, 121.
- (160) Fromentin, E.; Coustard, J.-M.; Guisnet, M. *J. Mol. Catal. A: Chem.* **2000**, *159*, 377.
- (161) Casagrande, M.; Storaro, L.; Lenarda, M.; Ganzerla, R. *Appl. Catal. A: Gen.* **2000**, *201*, 263.
- (162) Harvey, G.; Binder, G.; Prins, R. *Stud. Surf. Sci. Catal.* **1995**, *94*, 397.
- (163) Cambor, M. A.; Pérez-Pariente, J. *Zeolites* **1991**, *11*, 202.
- (164) Jansen, J. C.; Creyghton, E. J.; Njo, S. L.; van Koningsveld, H.; van Bekkum, H. *Catal. Today* **1997**, *38*, 205.
- (165) Jia, C.; Massiani, P.; Barthomeuf, D. *J. Chem. Soc., Faraday Trans.* **1993**, *89*, 3659.
- (166) Kiricsi, I.; Flego, C.; Pazzuconi, G.; Parker, W. O., Jr; Millini, R.; Perego, C.; Bellussi, G. *J. Phys. Chem.* **1994**, *98*, 4627.

- (167) Kantam, M. L.; Satees, M.; Choudary, B. M.; Ranganath, K. V. S.; Raghavan, K. V. JP 2001278832, 2001; *Chem. Abstr.* **2001**, 135, 288592.
- (168) Moreau, P.; Finiels, A.; Meric, P.; Fajula, F. *Catal. Lett.* **2003**, 85, 199.
- (169) Andy, P.; Garcia-Martinez, J.; Lee, G.; Gonzalez, H.; Jones, C. W.; Davis, M. E. *J. Catal.* **2000**, 192, 215.
- (170) Kim, S. D.; Lee, K. H.; Lee, J. S.; Kim, Y. G.; Yoon, K. E. *J. Mol. Catal. A: Chem.* **2000**, 152, 33.
- (171) Das, D.; Cheng, S. *Appl. Catal. A: Gen.* **2000**, 201, 159.
- (172) Meric, P.; Finiels, A.; Moreau, P. *J. Mol. Catal. A: Chem.* **2002**, 189, 251.
- (173) Barthomeuf, D. *Mater. Chem. Phys.* **1987**, 17, 49.
- (174) (a) Gunnewegh, E. A.; Gopie, S. S.; van Bekkum, H. *J. Mol. Catal. A: Chem.* **1996**, 106, 151. (b) Schuster, H.; Hölderich, W. F. *Appl. Catal. A: Gen.* **2008**, 350, 1.
- (175) Villaescusa, L. A.; Barrett, P. A.; Cambor, M. A. *Angew. Chem., Int. Ed.* **1999**, 38, 1997.
- (176) Corma, A.; Díaz-Cabañas, M. J.; Fornés, V. *Angew. Chem., Int. Ed.* **2000**, 39, 2346.
- (177) Botella, P.; Corma, A.; Sastre, G. *J. Catal.* **2001**, 197, 81.
- (178) Botella, P.; Corma, A.; Navarro, M. T.; Rey, F.; Sastre, G. *J. Catal.* **2003**, 217, 406.
- (179) Baudry-Barbier, D.; Dormond, A.; Duriau-Montagne, F. *J. Mol. Catal. A: Chem.* **1999**, 149, 215.
- (180) Bandgar, B. P.; Sadavarte, V. S. *Synth. Commun.* **1999**, 29, 2587.
- (181) Yadav, G. D.; Asthana, N. S.; Kamble, V. S. *J. Catal.* **2003**, 217, 88.
- (182) Yadav, G. D.; Asthana, N. S.; Kamble, V. S. *Appl. Catal. A: Gen.* **2003**, 240, 53.
- (183) Choudary, B. M.; Sateesh, M.; Kantam, M. L.; Ram Prasad, K. V. *Appl. Catal. A: Gen.* **1998**, 171, 155.
- (184) Biró, K.; Békássy, S.; Ágai, B.; Figueras, F. *J. Mol. Catal. A: Chem.* **2000**, 151, 179.
- (185) Ranu, B. C.; Ghosh, K.; Jana, U. *J. Org. Chem.* **1996**, 61, 9546.
- (186) Patil, M. L.; Jnaneshwara, G. K.; Sabde, D. P.; Dongare, M. K.; Sudalai, A.; Deshpande, V. H. *Tetrahedron Lett.* **1997**, 38, 2137.
- (187) (a) Sakthivel, R.; Prescott, H.; Kemnitz, E. *J. Mol. Catal. A: Chem.* **2004**, 223, 137. (b) Hajipour, A. R.; Zarei, A.; Khazdooz, L.; Ruoho, A. E. *Synth. Commun.* **2009**, 39, 2702. (c) Bordoloi, A.; Mathew, N. T.; Devassy, B. M.; Mirajkar, S. P.; Halligudi, S. B. *J. Mol. Catal. A: Chem.* **2006**, 247, 58.
- (188) Deutsch, J.; Trunschke, A.; Müller, D.; Quaschnig, V.; Kemnitz, E.; Lieske, H. *J. Mol. Catal. A: Chem.* **2004**, 207, 51.
- (189) Deutsch, J.; Trunschke, A.; Müller, D.; Quaschnig, V.; Kemnitz, E.; Lieske, H. *Catal. Lett.* **2003**, 88, 9.
- (190) Deutsch, J.; Quaschnig, V.; Kemnitz, E.; Auroux, A.; Ehwald, H.; Lieske, H. *Topics Catal.* **2000**, 13, 281.
- (191) Quaschnig, V.; Auroux, A.; Deutsch, J.; Lieske, H.; Kemnitz, E. *J. Catal.* **2001**, 203, 426.
- (192) (a) Quaschnig, V.; Deutsch, J.; Druska, P.; Niclas, H.-J.; Kemnitz, E. *J. Catal.* **1998**, 177, 164. (b) Zane, F.; Melada, S.; Signoretto, M.; Pinna, F. *Appl. Catal. A: Gen.* **2006**, 299, 137.
- (193) Parida, K.; Quaschnig, V.; Lieske, E.; Kemnitz, E. *J. Mater. Chem.* **2001**, 11, 1903.
- (194) (a) Trunschke, A.; Deutsch, J.; Müller, D.; Lieske, H.; Quaschnig, V.; Kemnitz, E. *Catal. Lett.* **2002**, 83, 271. (b) Breda, A.; Signoretto, M.; Ghedini, E.; Pinna, F.; Cruciani, G. *Appl. Catal. A: Gen.* **2006**, 308, 216.
- (195) Patil, P. T.; Malshe, K. M.; Kumar, P.; Dongare, M. K.; Kemnitz, E. *Catal. Commun.* **2002**, 3, 411.
- (196) Deutsch, J.; Prescott, H. A.; Müller, D.; Kemnitz, E.; Lieske, H. *J. Catal.* **2005**, 231, 269.
- (197) (a) Melero, J. A.; van Grieken, R.; Morales, G.; Nuño, V. *Catal. Commun.* **2004**, 5, 131. (b) Kwon, O.; Park, S.; Seo, G. *Chem. Commun.* **2007**, 4113. (c) Pârvulescu, A. N.; Gagea, B. C.; Pârvulescu, V. I.; De Vos, D.; Jacobs, P. A. *Appl. Catal. A: Gen.* **2006**, 306, 159.
- (198) (a) Selvaraj, M.; Lee, K.; Yoo, K. S.; Lee, T. G. *Microporous Mesoporous Mater.* **2005**, 81, 343. (b) Kozhevnikov, I. V. *J. Mol. Catal. A: Chem.* **2007**, 262, 86.
- (199) Firouzabadi, H.; Iranpoor, N.; Nowrouzi, F. *Tetrahedron Lett.* **2003**, 44, 5343.
- (200) (a) Cardoso, L. A. M.; Alves, W., Jr.; Gonzaga, A. R. E.; Aguiar, L. M. G.; Andrade, H. M. C. *J. Mol. Catal. A: Chem.* **2004**, 209, 189. (b) Thakuria, H.; Borah, B. M.; Das, G. *J. Mol. Catal. A: Chem.* **2007**, 274, 1.
- (201) Bachiller-Baeza, B.; Anderson, J. A. *J. Catal.* **2004**, 228, 225.
- (202) (a) López-Salinas, E.; Hernández-Cortéz, J. G.; Schifter, I.; Torres-García, E.; Navarrete, J.; Gutiérrez-Carrillo, A.; López, T.; Lottici, P. P.; Bersani, D. *Appl. Catal. A: Gen.* **2000**, 193, 215. (b) Devassy, B. M.; Halligudi, S. B. *J. Catal.* **2005**, 236, 313.
- (203) Devassy, B. M.; Halligudi, S. B.; Hegde, S. G.; Halgeri, A. B.; Lefebvre, F. *Chem. Commun.* **2002**, 1074.
- (204) (a) Sawant, D. P.; Devassy, B. M.; Halligudi, S. B. *J. Mol. Catal. A: Chem.* **2004**, 217, 211. (b) Parida, K. M.; Mallick, S.; Pradhan, G. C. *J. Mol. Catal. A: Chem.* **2009**, 297, 93. (c) Sawant, D. P.; Vinu, A.; Lefebvre, F.; Halligudi, S. B. *J. Mol. Catal. A: Chem.* **2007**, 262, 98.
- (205) Heidekum, A.; Harmer, M. A.; Hoelderich, W. F. *J. Catal.* **1999**, 188, 230.
- (206) Beers, A. E. W.; Hoek, I.; Nijhuis, T. A.; Downing, R. S.; Kapteijn, F.; Moulijn, J. A. *Top. Catal.* **2000**, 13, 275.
- (207) (a) Gunnewegh, E. A.; Hoefnagel, A. J.; van Bekkum, H. *Stud. Surf. Sci. Catal.* **1996**, 97, 447. (b) Sarsani, V. R.; Lyon, C. J.; Hutchenson, K. W.; Harmer, M. A.; Subramaniam, B. *J. Catal.* **2007**, 245, 184. (c) Martínez, F.; Morales, G.; Martín, A.; van Grieken, R. *Appl. Catal. A: Gen.* **2008**, 347, 169.
- (208) (a) Alvaro, M.; Corma, A.; Das, D.; Fornés, V.; García, H. *J. Catal.* **2005**, 231, 48. (b) Yadav, G. D.; Pimparkar, K. P. *J. Mol. Catal. A: Chem.* **2007**, 264, 179.
- (209) Sawant, D. P.; Halligudi, S. B. *Catal. Commun.* **2004**, 5, 659.
- (210) Gilbert, L.; Spagnol, M. WO 9717324, 1997; *Chem. Abstr.* **1997**, 127, 4923.
- (211) Yadav, G. D.; Bhagat, R. D. *J. Mol. Catal. A: Chem.* **2005**, 235, 98.
- (212) Fritch, J. R.; Fruchey, O. S.; Horlenko, T. US 4 954 652, 1990; *Chem. Abstr.* **1991**, 114, 81258.
- (213) Uwaydah, I. M.; Aslam, M.; Brown, C. H.; Fitzhenry, S. R.; McDonough, J. A. US 5 696 274, 1997; *Chem. Abstr.* **1997**, 127, 135720.
- (214) Climent, M. J.; Corma, A.; Iborra, S.; Primo, J. *J. Catal.* **1995**, 151, 60.
- (215) Drexler, M. T.; Amiridis, M. D. *J. Catal.* **2003**, 214, 136.
- (216) Gerecs, A. In *Friedel-Crafts and Related Reactions*; Olah, G. A., Ed.; John Wiley & Sons Inc.: London, 1964; Vol. III, Part 1, p 449.
- (217) Pouilloux, Y.; Gnep, N. S.; Magnoux, P.; Pérot, G. *J. Mol. Catal.* **1987**, 40, 231.
- (218) Pouilloux, Y.; Bodibo, J.-P.; Neves, I.; Gubelmann, M.; Pérot, G.; Guisnet, M. *Stud. Surf. Sci. Catal.* **1991**, 59, 513.
- (219) Hoefnagel, A. J.; van Bekkum, H. *Appl. Catal. A: Gen.* **1993**, 97, 87.
- (220) Cundy, C. S.; Higgins, R.; Kibby, S. A. M.; Lowe, B. M.; Paton, R. M. *Tetrahedron Lett.* **1989**, 30, 2281.
- (221) Vogt, A.; Kouwenhoven, H. W.; Prins, R. *Appl. Catal. A: Gen.* **1995**, 123, 37.
- (222) Subba Rao, Y. V.; Kulkarni, S. J.; Subrahmanyam, M.; Rama Rao, A. V. *Tetrahedron Lett.* **1993**, 34, 7799.
- (223) Borzatta, V.; Poluzzi, E.; Vaccari, A. In *Science and Technology in Catalysis 2002*; Anpo, M., Onaka, M., Yamashita, H., Eds.; Elsevier: Amsterdam, 2003; p 439.
- (224) Borzatta, V.; Busca, G.; Poluzzi, E.; Rossetti, V.; Trombetta, M.; Vaccari, A. *Appl. Catal. A: Gen.* **2004**, 257, 85.
- (225) Armaroli, T.; Bevilacqua, M.; Trombetta, M.; Gutiérrez Alejandre, A.; Ramirez, J.; Busca, G. *Appl. Catal. A: Gen.* **2001**, 220, 181.
- (226) Heidekum, A.; Harmer, M. A.; Hoelderich, W. F. *J. Catal.* **1998**, 176, 260.
- (227) Pitchumani, K.; Warrier, M.; Ramamurthy, V. *J. Am. Chem. Soc.* **1996**, 118, 9428.

- (228) Hepp, M. A.; Ramamurthy, V.; Corbin, D. R.; Dybowski, C. *J. Phys. Chem.* **1992**, *96*, 2629.
- (229) Jayat, F.; Sabater Picot, M. J.; Guisnet, M. *Catal. Lett.* **1996**, *41*, 181.
- (230) Rohan, D.; Canaff, C.; Magnoux, P.; Guisnet, M. *J. Mol. Catal. A: Chem.* **1998**, *129*, 69.
- (231) Heitling, E.; Roessner, F.; van Steen, E. *J. Mol. Catal. A: Chem.* **2004**, *216*, 61.
- (232) Wang, H.; Zou, Y. *Catal. Lett.* **2003**, *86*, 163.
- (233) Kozhevnikova, E. F.; Derouane, E. G.; Kozhevnikov, I. V. *Chem. Commun.* **2002**, 1178.
- (234) Kozhevnikova, E. F.; Quartararo, J.; Kozhevnikov, I. V. *Appl. Catal. A: Gen.* **2003**, *245*, 69.
- (235) Kozhevnikova, E. F.; Rafiee, E.; Kozhevnikov, I. V. *Appl. Catal. A: Gen.* **2004**, *260*, 25.
- (236) Kaur, J.; Kozhevnikova, E. F.; Griffin, K.; Harrison, B.; Kozhevnikov, I. V. *Kinet. Catal.* **2003**, *44*, 175.
- (237) Izumi, Y.; Ono, M.; Kitagawa, M.; Yoshida, M.; Urabe, K. *Microporous Mater.* **1995**, *5*, 255.
- (238) Molnár, Á.; Keresztesi, C.; Török, B. *Appl. Catal. A: Gen.* **1999**, *189*, 217.
- (239) (a) Misono, M. *Chem. Commun.* **2001**, 1141. (b) Musawir, M.; Kozhevnikova, E. F.; Kozhevnikov, I. V. *J. Mol. Catal. A: Chem.* **2007**, *262*, 93.
- (240) Olah, G. A.; Arvanaghi, M.; Krishnamurthy, V. V. *J. Org. Chem.* **1983**, *48*, 3359.
- (241) Matloubi Moghaddam, F.; Ghaffarzadeh, M.; Abdi-Oskoui, S. H. *J. Chem. Res. (S)* **1999**, 574.
- (242) Neves, I.; Jayat, F.; Magnoux, P.; Pérot, G.; Ribeiro, F. R.; Gubelmann, M.; Guisnet, M. *J. Mol. Catal.* **1994**, *93*, 169.
- (243) Jackman, L. M.; Petrei, M. M.; Smith, B. D. *J. Am. Chem. Soc.* **1991**, *113*, 3451.
- (244) Subba Rao, Y. V.; Kulkarni, S. J.; Subrahmanyam, M.; Rama Rao, A. V. *Appl. Catal. A: Gen.* **1995**, *133*, L1.
- (245) Wang, Q. L.; Torrealba, M.; Giannetto, G.; Guisnet, M.; Pérot, G.; Cahoreau, M.; Casso, J. *Zeolites* **1990**, *10*, 703.
- (246) Neves, I.; Jayat, F.; Magnoux, P.; Pérot, G.; Ribeiro, F. R.; Gubelmann, M.; Guisnet, M. *J. Chem. Soc., Chem. Commun.* **1994**, 717.
- (247) Padró, C. L.; Apesteguía, C. R. *J. Catal.* **2004**, *226*, 308.
- (248) Chaube, V. D.; Moreau, P.; Finiels, A.; Ramaswamy, A. V.; Singh, A. P. *J. Mol. Catal. A: Chem.* **2001**, *174*, 255.
- (249) Chaube, V. D.; Moreau, P.; Finiels, A.; Ramaswamy, A. V.; Singh, A. P. *Catal. Lett.* **2002**, *79*, 89.
- (250) Kumari, V. D.; Saroja, G.; Ratnamala, A.; Noorjahan, M.; Subrahmanyam, M. *React. Kinet. Catal. Lett.* **2003**, *79*, 43.
- (251) Bhattacharyya, K. G.; Talukdar, A. K.; Das, P.; Sivasanker, S. *Catal. Commun.* **2001**, *2*, 105.
- (252) Subba Rao, Y. V.; Kulkarni, S. J.; Subrahmanyam, M.; Rama Rao, A. V. *J. Chem. Soc., Chem. Commun.* **1993**, 1456.
- (253) Farkas, J.; Békássy, S.; Ágai, B.; Hegedüs, M.; Figueras, F. *Synth. Commun.* **2000**, *30*, 2479.
- (254) Békássy, S.; Farkas, J.; Ágai, B.; Figueras, F. *Topics Catal.* **2000**, *13*, 287.
- (255) Bolognini, M.; Cavani, F.; Cimini, M.; Dal Pozzo, L.; Maselli, L.; Venerito, D.; Pizzoli, F.; Veronesi, G. C. R. *Chim.* **2004**, *7*, 143.
- (256) (a) Gronnow, M. J.; Macquarrie, D. J.; Clark, J. H.; Ravenscroft, P. *J. Mol. Catal. A: Chem.* **2005**, *231*, 47. (b) Ghiaci, M.; Kalbasi, R. J.; Mollahasani, M.; Aghaei, H. *Appl. Catal. A: Gen.* **2007**, *320*, 35. (c) Ghiaci, M.; Abbaspur, A.; Kalbasi, R. J. *Appl. Catal. A: Gen.* **2005**, *287*, 83. (d) Sharghi, H.; Hosseini-Sarvari, M.; Eskandari, R. *Synthesis* **2006**, 2047.
- (257) Tomiyama, T.; Tomiyama, I.; Shirai, T.; Wakabayashi, S.; Futamura, M.; Ichikawa, S. JP 03261778, 1991; *Chem. Abstr.* **1992**, *116*, 151553x.
- (258) Isaev, Y.; Fripiat, J. J. *J. Catal.* **1999**, *182*, 257.
- (259) (a) Finiels, A.; Calmettes, A.; Geneste, P.; Moreau, P. *Stud. Surf. Sci. Catal.* **1993**, *78*, 595. (b) Borate, H. B.; Gaikwad, A. G.; Maujan, S. R.; Sawargave, S. P.; Kalal, K. M. *Tetrahedron Lett.* **2007**, *48*, 4869. (c) Hajipour, A. R.; Zarei, A.; Khazdooz, L.; Zahmatkesh, S.; Ruoho, A. E. *Phosphorus, Sulfur, Silicon* **2006**, *181*, 387. (d) So, Y. H.; Heeschen, J. P. *J. Org. Chem.* **1997**, *62*, 3552. (e) Álvaro, V. F. D.; Brigas, A. F.; Derouane, E. G.; Lourenço, J. P.; Santos, B. S. *J. Mol. Catal. A: Chem.* **2009**, *305*, 100.
- (260) Ram Reddy, P.; Subrahmanyam, M.; Kulkarni, S. J. *Catal. Lett.* **1998**, *54*, 95.
- (261) Fayed, S.; Delmas, M.; Gaset, A. *J. Mol. Catal.* **1985**, *29*, 19.
- (262) Richard, F.; Drouillard, J.; Carreyre, H.; Lemberton, J. L.; Pérot, G. *Stud. Surf. Sci. Catal.* **1993**, *78*, 601.
- (263) Richard, F.; Carreyre, H.; Pérot, G. *J. Mol. Catal. A: Chem.* **1995**, *103*, 51.
- (264) Richard, F.; Carreyre, H.; Pérot, G. *J. Mol. Catal. A: Chem.* **1995**, *101*, L167.
- (265) Richard, F.; Carreyre, H.; Pérot, G. *J. Catal.* **1996**, *159*, 427.
- (266) Amouzegh, P.; Finiels, A.; Geneste, P.; Ginestar, E.; Moreau, P. *Catal. Lett.* **1995**, *34*, 389.
- (267) Choudary, B. M.; Sateesh, M.; Kantam, M. L.; Ranganath, K. V. S.; Raghavan, K. V. *Catal. Lett.* **2001**, *76*, 231.