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Molecular sieve catalysts as substitutes for metal chlorides in the chemical industry: Some selected examples*

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Abstract: The current main concern of global sustainable development pushes toward the substitution of corrosive and highly waste-producing chlorine-containing conventional catalysts (such as the strongly acidic $AlCl_3$–HCl mixture, still widely used in the production of chemicals) by environmentally friendly systems. The outstanding benefits in terms of environmental sustainability as well as of economic advantage related to the use of acid and micro- and/or mesoporous molecular sieves are here depicted, analyzing some selected examples in the field of oil refining, petrochemicals, and fine chemicals production: namely, n-C_5–C_6 alkane isomerization, isobutane/butene (I/B) alkylation, benzene ethylation, aromatic acylation, and Fries rearrangement. In the large-scale processes of refining and petrochemistry, the shift toward this kind of green and efficient solid catalysts is an established reality. In contrast, in fine chemicals synthesis, most of the novelties are still at a lab-scale level, and additional hurdles, related to the large differences between the national legislations about environmental protection, strongly limit this substitution.

Keywords: acid catalysis; acylation; alkylation; catalysts; isomerization; molecular sieves; rearrangements; zeolites.

INTRODUCTION

The predominant role played by catalysis in the development of the chemical industry throughout the decades, since the understanding of its fundamentals from the 19th century, has been the object of various recent review works [1–5]. Catalysis is today involved in the production of more than 90 % of all industrial chemicals [1,6]. This important role in chemistry shows that catalysis is a mature discipline, and it might suggest that it is now unable to cope with the new industry challenges. Luckily, this is not the case, probably because industrial catalysis has always been closely connected with changes in society [4] and is thus ready to meet the present crucial challenges: the decrease in fossil resources, push-

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ing toward the production of fuels and platform chemicals from biomass, and an ever-increasing attention to sustainability, implying, in particular, the set-up of cleaner and "greener" catalytic processes [6–9].

In this paper, we focus on the last topic and describe some selected examples where micro- or mesoporous molecular sieves can efficiently replace conventional inorganic metal chlorides in catalytic processes of interest for the chemical industry. Naturally, the examples deal with acid-catalyzed transformations: alkylation, alkane isomerization, acylation, and Fries rearrangement. Indeed, in this important industrial field, significant advances were accomplished by developing solid catalyst substitutes for the previously used highly toxic and corrosive strong mineral acids (HF, H_2SO_4) or inorganic Lewis acids ($AlCl_3$, etc.). However, even though this substitution has large positive effects, in terms of both environmental protection and economic profit, it remains generally incomplete. Moreover, in certain cases, other acid solid catalysts (e.g., sulfated zirconia [10]) or even ionic liquids (ILs) based on $AlCl_3$ [11] can favorably compete with micro- and mesoporous molecular sieves.

WHY ARE INORGANIC MOLECULAR SIEVES SO EFFICIENT AND SUCH ENVIRONMENTALLY FRIENDLY CATALYSTS?

Microporous molecular sieves (zeolites and zeotypes) are the most commercially used solid catalysts [6]. Already involved in most processes of production of petrochemicals and fuels, they are playing an increasing role in the selective synthesis of intermediate and fine chemicals as well as in pollution abatement [6,8,12–15]. Moreover, as shown in the section "Isomerization of n-C_5–C_6 alkanes", their molecular sieving properties can be exploited to develop environmentally friendly separation processes which, coupled to catalytic transformations, achieve a favorable total economic performance.

The main features of zeolites responsible for their success as catalysts are:

- A molecular-sized pore system (or systems), where the catalytic reactions occur. Zeolite crystals can be considered as perfectly ordered arrays of *nanoreactors* (channels, cages, or channel intersections). Therefore, rate, selectivity, and stability of all the zeolite-catalyzed reactions are affected not only by the characteristics of the active sites, but also by the properties of the nanoreactors (shape and size) and of their openings and interconnections. The concept of *shape selectivity* was proposed by Weisz and Frilette [16] to explain such an effect of the zeolite micropore system on the reactions. While this denomination has the great advantage to be simple and striking, it may appear too restrictive, since micropore *shape* (and not the size of the channels or pore apertures, which play a significant role too) and *selectivity* only seem to be concerned as critical factors. In detail, the positive effect that geometric characteristics of the micropore system have generally on the desired catalytic reactions results from: (i) the spatial constraints on the diffusion of reactant and product molecules within the micropore network (*reactant and product shape selectivity*); (ii) the spatial constraints on the formation of transition states (*transition-state shape selectivity*); and (iii) the confinement within the micropore network of reactant and product molecules (*confinement effect*), which can originate an increase in the reaction rate, especially of bimolecular mechanisms. The shape selectivity in zeolites prompted the design and development of many cheaper and more sustainable petrochemical catalytic processes [17–19] [especially after the discovery of medium pore-sized zeolites, such as mordenite framework inverted (MFI) zeolite]. Moreover, the recent commercial advances based on new types of shape selectivity, such as pore mouth and key-lock catalysis [20], in which the sites at (or close to) the outer surface of the zeolite crystals play a major role in influencing the reaction, show that *shape selectivity* is still a fruitful concept.
- A rich variety of active sites that can be present in zeolites, namely: (i) Brønsted acid sites, which catalyze many hydrocarbon reactions of commercial importance (isomerization, cracking, alkylation, etc.); (ii) Lewis acid sites, which can act alone or in cooperation with basic sites

(bifunctional acid–base catalysis); (iii) basic sites; (iv) and redox-active sites, either incorporated in the framework (e.g., Ti in TS-1) or within channels or cages (e.g., Pt clusters); and (v) redox and acid (or basic) sites, which can act in a concerted way to catalyze bifunctional redox-acid reactions (hydroisomerization, hydrocracking, etc.). Nevertheless, even if the potential of sites i, iv, and v is widely exploited at commercial scale, a major research effort is still needed to develop highly selective zeolite catalysts, which may be cheap enough to compete with the polluting, but inexpensive conventional systems that are currently used (e.g., NaOH or KOH, in base catalysis) [21].

- Active sites and pores that are easily adapted, case by case, to the catalytic applications. This can be made, either by varying the operating synthesis conditions, with the possibility to obtain ca. 180 different prestructures and a broad range of chemical compositions, or through a variety of well-mastered postsynthesis treatments, the most common being ion exchange, dealumination, and desilication.
- Environmentally friendly properties (e.g., no corrosive or hazardous nature, even for the most acidic zeolitic species). Thanks to these characteristics and their high thermal stability, zeolites can be easily handled and applied to continuous processes under a wide range of operating conditions as well as can be efficiently recovered and regenerated by coke oxidation at very high temperatures.

However, despite their outstanding properties, zeolites cannot be considered as *magic* catalysts. That is obvious particularly in the field of fine and intermediate chemicals production, in which the relatively small size of the micropore openings limits, or even blocks, the access to large and highly functionalized reactant intermediate and product molecules and hence their transformation [22]. Steric limitations affect the desorption of bulky product molecules and inhibit the formation of intermediates, too bulky to be accommodated within channels, channel intersections, or cages. In addition, the long contact time of bulky molecules with the active sites favors coke formation and deactivation. Various ways have been tested, in the last few decades, to increase both the accessibility of active sites to bulky molecules and the catalyst lifecycle: synthesis of extra-large pore zeolites or open-structure aluminophosphates (AlPOs) [23], synthesis of nano-sized zeolites [24,25], delamination of layered zeolite precursors [26], and creation of hierarchical pore structures combining zeolite micropores with inner mesopores [27,28] generated by incorporating carbon templates in the synthesis mixture or by steam, acid, or alkaline postsynthesis treatments.

In such scenario, starting from the 1990s, an ever-increasing variety of silicate and aluminosilicate-based mesoporous molecular sieves were synthesized. With these catalysts, larger substrate molecules can enter the pore network, be processed there, and leave it [29,30]. Ordered mesoporous materials, such as MCM-41 [31], MCM-48 [32], HMS, MSU [33], KIT-6 [34], SBA-15, or SBA-16 [35], compared to microporous crystalline zeolites, exhibit higher surface area (600–1300 $m^2 g^{-1}$) and larger pore size (2–30 nm) and, in principle, possess various potential applications in industrial catalytic reactions [36]. However, they often need expensive (mainly due to costly structure-directing agents) and time-consuming synthesis routes, and this is a main hurdle against a profitable industrial exploitation of these materials. Moreover, most of these materials present a poor hydrothermal stability, due to their ordered but noncrystalline nature, and they cannot be employed under severe conditions often found in continuous-production plants [37]. Indeed, so far, they have found mainly commercial niche applications as sorbents for high-performance adsorption or separation methods (e.g., as stationary phases in size-exclusion chromatography) or as catalyst supports for specific fine chemical transformations, where the high added-value of the product can justify the use of materials prepared by costly methods.

Anyway, the recent start-up of production plants at large-scale level (up to 20 t yr^{-1}) for the production of nanostructured mesoporous silicas could make these materials now suitable for a number of different applications in the synthesis of commodity and fine chemicals [38,39].

CASE STUDIES

Hydrocarbon transformation or production

Three refining and petrochemical processes were chosen as examples. Isomerization of light straight-run naphtha (a) and isobutane/butene (I/B) alkylation (b) play an essential role in the production of clean gasoline, while ethylbenzene (EB) production (c) is the most important aromatic alkylation process. In the last few decades, significant advances in terms of economy and environmental protection were accomplished in processes a and c, with, in particular, the substitution of environmentally friendly zeolite catalysts for corrosive and polluting ones (essentially $AlCl_3$). This is not yet the case in I/B alkylation even though the clean heterogeneous technology seems now able to compete economically with corrosive and polluting conventional technologies.

Isomerization of n-C_5–C_6 *alkanes*

Main characteristics

n-C_5–C_6 alkane isomerization generates a high octane number for the gasoline pool, avoiding the formation of undesired olefins or aromatics [40–42]. Indeed, isoalkanes have much higher octane numbers than linear ones (research octane number, RON: *iso*-C_5 = 92, n-C_5 = 62, 2,3-dimethylbutane = 102, and n-C_6 = 25). This reversible reaction is slightly exothermic, and it has to be preferably carried out at low temperatures. Some crucial points should also be underscored: (i) whatever the catalyst, the same rule applies, according to which the product composition can closely approach thermodynamic equilibrium and (ii) the possibility of separating branched isomers from the products and recycling lower-octane isomers makes the choice of low reaction temperatures less critical.

The isomerization was first performed with a purely acid catalyst: $AlCl_3$–HCl, a system considered as a superacid protonic catalyst: $AlCl_4^-$, H^+ [43], hence active at low temperatures. Then, it was run over bifunctional Pt/acid solid catalysts, which can work at higher temperatures. In both acid and bifunctional reactions, the skeletal isomerization of carbenium ions via protonated cyclopropane intermediates is a key step. The difference between the catalytic cycles lies in the way carbenium ions can be formed. In the acid mechanism, after the initiation step (either protolytic dehydrogenation of the linear alkanes (step 1) or simply protonation of alkene impurities), the carbenium ions result from hydride transfer from linear alkanes to branched carbenium ions, with isoalkane desorption (step 2).

$$n\text{-}C_6H_{14} + H^+ \rightleftharpoons n\text{-}C_6H_{15}^+ \rightleftharpoons n\text{-}C_6H_{13}^+ + H_2 \qquad (1)$$

$$n\text{-}C_6H_{14} + i\text{-}C_6^+ \rightleftharpoons n\text{-}C_6H_{13}^+ + i\text{-}C_6 \qquad (2)$$

In the bifunctional mechanism, carbenium ion formation (step 3) involves successively alkane dehydrogenation on the metallic sites then protonation of the resulting alkene.

$$n\text{-}C_6H_{14} \rightleftharpoons n\text{-}C_6H_{12} + H_2 \rightleftharpoons n\text{-}C_6H_{13}^+ + H_2 \qquad (3)$$

The secondary reactions depend on the catalyst and operating temperature. With the strongly acidic $AlCl_3$–HCl catalyst, low T isomerization can be accompanied by alkylation steps with formation of heavy products, whereas with the bifunctional catalysts, light products can be formed through hydrogenolysis over Pt sites and hydrocracking of the branched products.

Pt/chlorinated alumina catalysts were the first substitute for $AlCl_3$–HCl isomerization catalyst, the basic idea being to associate an acid function similar in strength with a hydrogenating agent in order to increase the catalytic stability. This catalyst, prepared by activation of a Pt/Al_2O_3 material by extensive chlorination with HCl (added as such or resulting from the in situ degradation of an organic chloride) can be used at relatively low temperatures (120–160 °C). The main drawback of the Pt/chlorinated alumina catalyst is the continuous evolution of HCl, which has to be compensated by a continuous adding of chloride activators to maintain the activity. The elimination from the feed of water and ammonia contaminants limits this HCl evolution. The poisoning of Pt by sulfur, although reversible, is another point of concern. This great sensitivity to poisons requires a very strict control of the pretreatment units. However, the Penex process from Universal Oil Products (UOP), which is the oldest process, is still in use, thanks to the relatively high octane number of the products (research octane number, RON, of 84–85 in once-through operation) and to successive catalyst improvements, leading to the reduction of the operating costs, e.g., decrease in Pt content without loss in activity.

A major advantage of Pt-zeolite isomerization catalysts over chlorinated catalysts is their outstanding robustness and their far higher tolerance to all kinds of feed contaminants [41]. This advantage compensates the necessity to operate at unfavorable higher temperatures (typically 240–280 °C) owing to the lower acid strength of the protonic zeolite component (H-MOR), even if chosen amongst the strongest acidic zeolites [44]. Mordenite (MOR) is a large pore-size zeolite with a micropore system constituted by 12-MR channels (0.65×7.0 Å) interconnected by 8-MR channels that are too narrow for the diffusion of organic molecules. Consequently, the one-directional diffusion of organic molecules within this pore system presents, as an inconvenience, an easy blockage of the channels, for instance, by coke precursors. For this, MOR zeolite is largely sensitive to deactivation by coking. However, thanks to the inner mesopores created by postsynthesis treatments, which make the molecular diffusion quasi three-directional, this problem can be circumvented [45,46]. The first commercial process (Hysomer), developed by Shell [47], operates through a once-through mode (fixed-bed reactor) at 30 bar of hydrogen pressure at ca. 250 °C. Aromatics of the feed are quantitatively hydrogenated to naphthenes, and concentrations of up to 2 wt % have no effect on the catalyst selectivity. Water can be tolerated up to very high concentrations, avoiding the need for expensive drying facilities. Sulfur was claimed to be tolerable up to 35 ppm, but, so far, no commercial Hysomer unit is known to operate at such high S content [41]. The catalyst can be regenerated in situ. In addition, a significant improvement in octane number was obtained by coupling the Isosiv process of separation of *n*- and *iso*-alkanes by adsorption over an A zeolite with the Hysomer process. Thanks to the recycling of the lower-octane products in the Hysomer unit, the resulting process, referred to as total isomerization package (TIP), commercialized in 1975, produces a gasoline with octane number similar to that obtained with the Pt/chlorinated alumina processes [42]. Improvements were made in the robustness of zeolite catalysts to contaminants, leading to the development of Süd-Chemie's Hysopar catalyst [41]. The sensitivity to S was significantly decreased, and this permits desulfuration lower than 100 ppm of S in the feed to be avoided. This is the most important feature, as the desulfuration of feeds containing more than 100 ppm of S can be carried out by caustic extraction, i.e., a regenerable process significantly more economical in capital and in operating costs than hydrotreatment. Moreover, this catalyst is very active in benzene hydrogenation, and it can withstand up to 15 wt % of benzene in the feed, obviating the need for separate processing of benzene by hydrogenation [41].

Pt/sulfated zirconia catalysts ($Pt/SO_4^{2-}/ZrO_2$) can compete with Pt/zeolite as alternative to Pt/chlorinated alumina catalysts. Indeed, they have the advantage of being more active and hence can be used at lower temperatures (180–210 °C against 240–280 °C), with as a consequence a gasoline with a higher octane number (Table 1). Furthermore, like Pt/zeolite, their sensitivity to water is low, they are regenerable, and their lifetime is very long. They present, however, some disadvantages, namely: (i) their sulfur tolerance is lower, but, however, better than that of Pt/chlorinated alumina; and (ii) great care has to be taken during the start-up procedure (in order to limit the undesired formation of gases) [41]. According to [48], this type of catalyst would be ideally suited for once-through operations.

Table 1 Comparison among isomerization processes for conventional C_5–C_6 feedstock.

	$AlCl_3$–HCl	Pt/Cl–Al_2O_3	Pt/ZrO_2–SO_4	Pt/H-MOR
Phase	Liquid	Vapor	Vapor	Vapor
Temperature (°C)	60–100	120–180	180–210	240–280
Feed limitations (ppm)				
Sulfur	Very low	0.1–0.5	1–5	50
Water	Very low	0.1	≤20	50
Catalyst lifetime (year)	Low	4	8–10	10
Yield (vol %)	≥96	≥99	≥97	97–98
RON				
One-through	90–94	83–86	81–83	78–80
With recycle		88–93	90–92	90

Alkylation of isobutane with butene

Generalities

I/B alkylation is an essential process for the production of *reformulated gasolines* [6,40,49–52]. For thermodynamic reasons, this exothermic alkylation has to be performed at low temperatures, which explains why strong acid sites are required for its catalysis. Furthermore, to favor alkylation against the facile secondary butene oligomerization, high values of the I/B ratio have to be chosen (from 10 up to 20). The complexity of the acid-catalyzed transformation of the I/B mixture appears clearly when considering the diversity of the products: mixture of trimethylpentanes (TMP) and not only the isomer resulting from the direct transformation of the reactants (e.g., 2,2,3-TMP from the isobutane/2-butene mixture); dimethylhexanes; C_5–C_7 and C_9–C_{14} isoalkanes; and tars [49–52].

Commercial processes

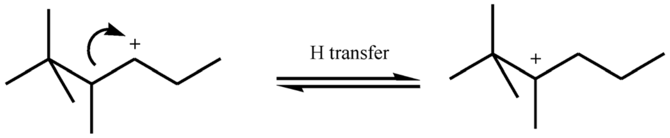
Strong protonic liquid acids, either hydrofluoric acid or sulfuric acid, are used as catalysts in commercial alkylation processes. The alkylation products (mainly TMP) have a high octane number (RON around 95) and very low contents in aromatics, alkenes, and S. So, they constitute a high-quality and environmentally benign gasoline cut. Unfortunately, both alkylation processes suffer from severe environmental drawbacks owing to significant safety risks: the use of hydrofluoric acid, that is, at the same time, highly toxic and volatile and a very high consumption of sulfuric acid (70–100 kg per t of alkylate), with, as a consequence, a costly regeneration for removing tarry hydrocarbons and water. This is the reason why, in the last two decades, much effort has been devoted to replacing hydrofluoric or sulfuric acids with more environmentally friendly acid catalysts, in particular, (but not only) solid catalysts. The suitable alternatives are large-pore zeolites and immobilized traditional liquid or gaseous strong acids ($AlCl_3$, HF–SbF_5, CF_3SO_3H, etc.) on suitable carriers.

Main characteristics of I/B alkylation

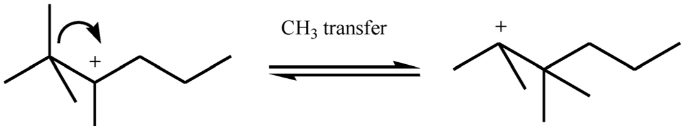
It is generally admitted that protons (e.g., those of bridging OH groups of zeolites) are the active species in alkylation. The following steps, involving carbenium ions as intermediates, are proposed to explain the formation of TMP products.

$$C_4H_8 + H^+ \rightleftharpoons C_4H_9^+ \quad (4)$$

$$i\text{-}C_4H_9^+ + n\text{-}C_4H_8 \rightleftharpoons i\text{-}C_8H_{17}^+ \quad (5)$$



(6)



(7)

$$i\text{-}C_4H_{10} + i\text{-}C_8H_{17}^+ \rightleftharpoons i\text{-}C_4H_9^+ + i\text{-}C_8H_{18} \quad (8)$$

This latter step of hydride transfer from isobutane to the TMP^+ carbenium ion plays an essential role in the catalytic alkylation cycle. Furthermore, it should be underscored that additional steps are required to explain the formation of other C_8 alkanes and of products with a number of C atoms different from eight.

Alkylation over zeolite catalysts

The transformation of isobutene/butene mixtures over acid large pore zeolites (FAU, BEA) leads initially to products with a composition similar to that of the alkylate obtained with HF or H_2SO_4. Unfortunately, a fast decline in activity can be observed, combined with a shift in selectivity from alkylation toward butene dimerization (reaction 9) and with the formation of dimethylhexenes instead of TMP. This is the main problem that has stopped so far an effective industrial use of solid acid catalysts.

$$C_4H_8 + C_4H_9^+ \rightleftharpoons C_8H_{17}^+ \rightleftharpoons H^+ + C_8H_{16} \quad (9)$$

The reasons for the fast zeolite deactivation by carbonaceous deposits (“coke”) and for the simultaneous disappearance of the hydride transfer capacity are well understood. Owing to the mild operating temperature, hydride transfer would require strong acid sites to occur catalytically, but these sites are the most active in coking and the most sensitive to poisoning by carbonaceous compounds [45]. Furthermore, over acid zeolite catalysts (even with weak acid character) alkenes are known to be the most probable precursors of “coke” deposits at low temperatures [53]. Therefore, despite a high value of isobutane/butene ratio, secondary transformations of butene (oligomerization or reactions with higher olefins even formed in traces) easily occur on the inner protonic sites and the relatively bulky olefinic products undergo secondary transformations leading to “coke” deposits. Moreover, hydride transfer (step 5), which is a bimolecular reaction involving C_{12} bulky intermediates and/or transition states, is sterically demanding, hence it is very sensitive to any diminution of the free space around the active sites [40]. Some guidelines for choosing the optimal zeolite-catalyzed alkylation system (including the catalyst regeneration by “coke” removal) can be drawn from these observations and are reported in Table 2.

Table 2 Optimal zeolite-catalyzed I/B alkylation system.

Operating conditions	Liquid phase; no diene and oxygenate impurities; high I/B ratio*
Reactor	Ensure high internal I/B ratios and avoid butene gradients (fluidized bed or expanded bed, rather than fixed bed)
Regeneration	Rejuvenation through hydrocracking or treatment with liquid or supercritical isobutane; oxidative regeneration
Characteristics of the zeolite catalyst	High concentration of strong protonic sites (low Si/Al ratio), low concentration of Lewis and weak protonic sites Large cages for accommodating the bulky hydride-transfer transition state; small crystallites or hierarchical pore systems to favor fast molecular diffusion and to limit product retention

*De-isobutanizer column for isobutane recycling.

The composition of the carbonaceous deposits responsible for the deactivation of FAU and BEA zeolite catalysts ("coke") is now well known [49,50,54,55]. On samples deactivated under classical alkylation conditions, the "coke" was shown to be constituted by a complex mixture of highly branched species with 35–40 carbon atoms maximum, containing unsaturations and cyclic structures. A change in "coke" composition can be observed with reaction time. An increase in molecular size and a progressive shift from butene oligomers to species with more double bonds and branchings, with aliphatic and aromatic cycles, was observed in the last stage. This change in "coke" composition and the simultaneous decrease in TMP formation suggest that periodic regeneration under mild conditions should be carried out on partially deactivated samples. Two possible rejuvenation methods were found to be suitable for reactivating partially deactivated catalysts, namely: (i) "coke" hydrocracking at ca. 300 °C in the presence of a small amount of Pt on the zeolite catalyst and (ii) treatment with liquid or supercritical isobutene.

Process developments

No zeolite-catalyzed alkylation processes at production scale are in operation yet [49]. However, two processes using zeolite catalysts, ABB Lummus Alkyclean and Exelus ExSact, were successfully tested in demonstration plants. Furthermore, a commercial plant based on the Alkylene process from UOP in which the catalyst is constituted of $AlCl_3$ supported on alumina, doped with K and Pt, would be in operation in Azerbaijan [49]. This shows that solid acid alkylation technologies are now able to economically compete with the conventional HF and H_2SO_4 processes. However, these significant advances deserve to be discussed in comparison to those made in the use of IL as alkylation catalysts [11]. Thus, Petrochina has recently developed an alkylation process (Ionikylation), which uses as catalyst a mixture of a conventional chloroaluminate-IL with CuCl [55,56]. This noncorrosive and highly stable catalyst has been substituted for the H_2SO_4 catalyst of a commercial unit with, as a result, an increase in TMP yield and in process unit capacity.

Ethylbenzene production

Generalities

Benzene alkylation with olefins is an electrophilic substitution catalyzed by protonic acids. This alkylation is performed on a large scale for producing petrochemical intermediates. The major products are EB, converted into styrene for polymer use, and cumene (C), a precursor of *phenol* and *acetone*, with a consumption of respectively ca. 50 and 20 % of benzene production [57,58]. The focus will be placed here on benzene ethylation, which is, at the same time, the most important process and the one in which the advances in terms of economy and environmental protection progress were the most evident and instructive.

Main characteristics of benzene ethylation [57–60]

Benzene ethylation is highly exothermic ($\Delta H = -113$ kJ mol^{-1}). This reaction, which implies the formation of an unstable primary carbenium-ion intermediate, is much slower than isopropylation (1500 times with $AlCl_3$–HCl catalyst), which involves a secondary one. Owing to the activation of the aromatic ring by alkyl substituents, consecutive alkylation is favored, giving rise to diethyl- (DEB) and polyethylbenzene (PEB) as main secondary products. There are various ways to minimize the yield into these undesired products and hence to maximize the formation of EB: choice of a benzene/ethylene (B/E) molar ratio much higher than 1; development of catalysts selective in monoethylation; and recycling of DEB and PEB in the reactor or association of a transalkylation unit to the alkylation unit. Other secondary transformations of EB can occur, but very slowly, such as the isomerization into xylenes and diphenylethane formation by alkylation of benzene with EB. Lastly, ethylene oligomerization-cracking is at the origin of other by-products: aliphatics, but also higher alkylbenzenes (*sec*-butyl benzene, C, etc.) resulting from the easy benzene alkylation with oligomerization-cracking products. Some of these by-products, mainly C_7–C_9 aliphatics and C boil close to EB, and may end up as EB impurities, which affects the quality of the final styrene product.

Traditional process

The original process of EB production, developed in the 1930, was performed in a bubble column reactor in the presence of superacid $AlCl_3$–HCl. Thanks to the high activity of the catalyst, it is possible to operate at low temperature (160 °C) with the drawback of recovering the heat of reaction only at low pressure. The possibility of operating with a low B/E ratio (typically 2.5) makes this process economically attractive [58,59]. High-boiling PEBs are simply recycled by transalkylation up to thermodynamic equilibrium in the alkylation reactor. It is also worth noting the very slow formation of xylenes at low reaction temperatures. Unfortunately, this process presents important environmental drawbacks: (a) $AlCl_3$ is corrosive and causes problems in handling and in industrial use; (b) the catalyst is consumed in large amounts (2–4 kg of $AlCl_3$ and 1 of HCl per ton of EB produced and 5 kg of caustic solution for neutralization); and (c) the large catalyst consumption implies significant waste production.

Zeolite-catalyzed processes

Various vapor- and liquid-phase zeolite-catalyzed processes were developed [57–60]. Mobil was the most active company in the field, with the first industrial application in 1980 (Mobil–Badger process). In this process, benzene ethylation is carried out in a vapor-phase fixed-bed reactor using the average pore size MFI (ZSM-5) zeolite. To limit the formation of DEB and PEB, a high B/E molar ratio, 5 to 20 (generally ca. 7), has to be chosen. The process operates at high temperatures, from 370 to 420 °C. Fresh and recycled benzene is combined with a DEB-rich recycle stream and fed with fresh ethylene to the reactor. Although the MFI zeolite is known for its strong resistance to coking, one of the initial problems was the relatively fast catalyst deactivation with the need of frequent regenerations (cycle length of only 40–60 days). This problem was solved in the next generation processes, leading to cycle lengths longer than one year. In addition, an increase of the EB yield from 98 % to more than 99.5 % was achieved thanks to the addition of a transalkylation unit (Table 3). The Mobil–Badger process presents great advantages over the traditional process: (a) there are no problems of corrosion, practically no catalyst consumption, and no waste production; (b) the process has high energy efficiency, with recovery at high temperature of essentially all the exothermic heat of alkylation; and (c) the use of dilute ethylene from catalytic cracking off-gas streams is possible, even if after some modifications. Unfortunately, the Mobil–Badger process presents an important disadvantage. Indeed, a high B/E ratio is required, and, as a consequence, a large distillation capacity for benzene recovery is needed.

Table 3 Comparison of the most representative EB processes.

	Monsanto–Lummus	Mobil–Badger III	Mobil–Raytheon EBMax
Reactor		Fixed bed	Fixed multibed
Catalyst	$AlCl_3$–HCl	H-MFI (H-ZSM5)	H-MWW (H-MCM-22)
Phase	Liquid	Vapor	Liquid
T (°C)	160	370–420	220
Molar B/E ratio	2.5	7.5	4
Life (years)	–	1	3
Transalkylation	No	Gas Phase/ H-MFI	Liquid or gas phase
EB yield (%)	99.7	>99.5	>99.5
Main advantages	Low B/E ratio	Clean process; high energy efficiency, possible use of low cost feedstocks	Clean process, long catalyst life, relatively low B/E ratio
Main drawbacks	Corrosion, catalyst consumption, and wastes	High B/E ratio	High sensitivity to feedstock contaminants

Additional advances in benzene ethylation were achieved thanks to the discovery of MWW (MCM-22) zeolite, presenting a high selectivity toward monoalkylated products and a high stability. Further advantages were drawn from significant process improvements: operation in liquid phase instead of in gas phase, use of multibed reactors with ethylene alimentation between the beds, etc. (EBMax process). The average pore size of MCM-22 zeolite presents unique structural features [61]. Indeed, the pore structure comprises two independent systems: (i) large supercages (1.82 nm in height and inner diameter of 0.71 nm), each one being connected with six others through 10-MR apertures (0.4 × 0.5 nm) and (ii) bidimensional sinusoidal channels (10-MR, 0.41 × 0.51 nm). Moreover, the outer surface of the crystals presents large cups corresponding to hemi-supercages (0.70 × 0.71 × 0.71 nm), which, like the inner micropores, contain protonic sites.

Some methods were developed for determining the distribution of these acid sites within the three types of micropores as well as their respective role in the reactions of various aromatics. By poisoning a MCM-22 zeolite with collidine (i.e., a basic molecule with a kinetic diameter of 0.7 nm, hence unable to enter the 10-MR inner micropores), it was clearly demonstrated that in the liquid phase at 220 °C, benzene ethylation takes place almost exclusively at the sites of the outer cups [62]. Indeed, poisoning caused a drop in ethylene conversion from 75 to ca. 1 %. This quasi inactivity of the inner pores, whose size is large enough to accommodate EB molecules, could seem surprising. The generally proposed explanation is that under the operating conditions (liquid phase and low temperature), the diffusion of organic molecules within these micropores is significantly limited. An additional explanation was recently advanced, based on the change in conversion and product distribution as a function of time-on stream (TOS) during toluene alkylation with propene at 200 °C [63]. Indeed, the inner micropores were shown to be active at short TOS values: heavy products were formed (and trapped) within the supercages while oligomerization-cracking of propene and the formation of a small amount of alkylaromatics occurred within the sinusoidal channels. However, owing to the blockage of their access (demonstrated by nitrogen adsorption), the activity of these inner micropores is rapidly suppressed. Therefore, on the stabilized catalyst, only the outer protonic sites remain active, catalyzing selectively the toluene alkylation. The high stability of the stabilized MWW zeolite, as well as its low selectivity to the undesired DEB, was ascribed to the very facile desorption of organic molecules from the outer cups and hence to the very low probability of secondary reactions of EB responsible for the formation of DEB, PEB, and coke precursor molecules.

The EBMax process presents the same environmental advantages over the traditional process than the Mobil–Badger process and, in addition, it operates with a low B/E ratio and thus it does not require a large distillation capacity for benzene recovery. Moreover, the cycle length of the catalyst is three times higher and the selectivity is much better, since almost no formation of undesired xylenes and propyl- and butyl-benzene products was observed. However, the use of low-cost feedstock such as dilute ethylene feed from fluid catalytic cracking (FCC) units or of lower-quality benzene is strongly limited by the lower catalyst tolerance to poisons under the operating conditions (liquid phase, low temperature) of the EBMax process [58].

Future of ethylation technologies

Table 3 shows that no zeolite-catalyzed process can still operate at the low B/E ratio that makes the traditional $AlCl_3$–HCl process so attractive. New catalysts and process innovations are needed to meet this challenge [58]. Note, however, that an improved technology based on a catalytic distillation process was already introduced by CDTech. A large-pore zeolite (FAU [64] or possibly BEA [59]) is chosen as catalyst. The reaction products are continuously removed from the reaction zone, which allows one to minimize the DEB/PEB production. Many other opportunities exist for improving EB production: (i) development of liquid-phase ethylation catalysts highly resistant to feedstock contaminants, hence able to process low-cost ethylene and benzene; (ii) development of more active transalkylation catalysts making it possible to operate at lower temperatures, at which by-products formation can be minimized; (iii) better integration of the alkylation and transalkylation units (in particular by using similar operating temperatures) [58].

Synthesis of aromatic ketones

Aromatic ketones are key intermediates for the production of a wide range of compounds used as pharmaceuticals, pesticides, flavors, perfumes, UV screens, and dyes [65–68]. They are mainly obtained via Friedel–Crafts acylation of arenes or via Fries rearrangement of aryl esters over Lewis acids. So, for instance, acetylation is the starting step in the synthesis of Ibuprofen, (2-(4-isobutylphenyl)propionic acid, which is one of the top-ten nonsteroidal antiinflammatory drugs marketed worldwide. Analogously, by Fries rearrangement of phenylacetate (PA), one can obtain *p*-hydroxyacetophenone (*p*-HAP), a key intermediate in the Hoechst Celanese process for the manufacturing of paracetamol (*p*-acetaminophenol) [69], a widely used analgesic and antipyretic accounting for a 160.000 t yr^{-1} world market, as well as *o*-hydroxyacetophenone (*o*-HAP), a key intermediate for producing 4-hydroxycoumarin and warfarin, both used as anticoagulant drugs [70], and for the synthesis of flavonones [71,72].

The alternative methods for performing these transformations under heterogeneous conditions over molecular sieve catalysts will be described in the following sections.

Acylation of aromatics

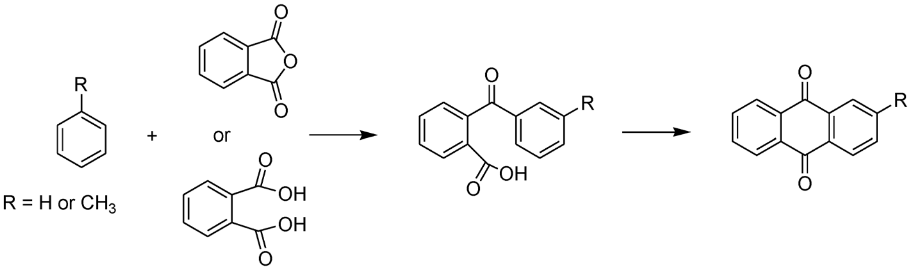
Generalities

In contrast to alkylation processes, currently carried out in flow units in the presence of solid catalysts, aromatic ketones are still often commercially prepared through the homogeneous Friedel–Crafts acylation of arenes in batch reactors with acyl chlorides as acylating agents and using Lewis acid metal chlorides ($AlCl_3$, $FeCl_3$, $SnCl_4$, etc.) as catalysts. Such a method implies the use of large amounts of solvents as reaction medium and the problems linked to costly separation and purification steps to recover the solvent. In addition, important environmental concerns arise from the use of acidic metal chlorides and especially from the consumption of more than stoichiometric amounts of catalysts owing to the intermediate formation of very stable 1:1 molar complexes between the metal chloride and the arylketone. Their hydrolysis leads to huge quantities of corrosive hydrochloric acid to be neutralized, treated, and properly disposed of. Furthermore, the use of acyl chlorides as acylating agents is an additional source of chlorine-containing wastes.

Acylation over acid molecular sieves

In the last few decades, several research teams have investigated the liquid-phase acylation of aromatics and heteroaromatics over acid zeolites using anhydrides as acylating agents and operating the reaction often in batch reactors. Most of the works deal in particular with aromatic acetylation over large-pore H-FAU and H-BEA zeolites and the medium-pore H-MFI (H-ZSM-5). A good understanding of the acylation scheme and the definition of the problems to be solved can be drawn from these works [67,73]. As expected from the classical mechanism of electrophilic aromatic substitution, the acylation rate strongly depends on the degree of activation of the aromatic ring by substituents and the formation of polyacylated aromatics is inhibited by the deactivating effect of the acyl group. Moreover, when the arene is a sterically demanding molecule, the selectivity to monacylated products can be significantly enhanced by the shape-selective properties of the zeolite. This is the case, for instance, of the acylation of ferrocene with acetic anhydride over H-MOR or H-BEA zeolites, in which very high selectivity to monoacetylferrocene was recorded at conversion higher than 80 % [74]. Furthermore, deliberate attempts to prepare 4,4'-diacylated biphenyls via double acylation of biphenyl with carboxylic acids or acid anhydrides over H-BEA or H-FAU gave only modest results (below 12 %) in the desired diacylated compound because of steric constraints [75].

Kinetic and adsorption studies, however, have shown a strong effect of the competition between reactants, solvent, and product molecules for adsorption within the zeolite micropores (for their occupancy) and on the protonic acid sites [76–78]. As a consequence, a gradual autoinhibition during arene acylation is generally observed, owing to the preferred adsorption on the acid sites of the acylated products (more polar and bulkier than the reactants they are formed from) and also of the very polar carboxylic acid co-product. Such autoinhibition is responsible for a rapid decrease in the reaction rate, causing even a stop in acylation after short times under batch conditions. This effect is much more marked with hydrophobic substrate molecules such as methyl- and fluoro-substituted aromatics, because of the large difference in polarity between the reactant substrate and the product molecules [79,80]. Therefore, it constitutes an additional limitation for the substitution of Friedel–Crafts catalysts by acid zeolites in the acylation of weakly activated and hence poorly reactive substrates. Lastly, owing to their long residence time within the zeolite micropores, the polar products often undergo secondary condensation reactions, leading to bulkier and, generally, more polar products which are consequently more strongly retained and, sometimes, block the pores. These bulky and polar trapped compounds (the so-called "coke") were shown to block the access of the reactants to the micropores, and this is generally the main cause of deactivation [76,79,81]. To counteract gradual coking, the synthesis of nano-sized materials, highly resistant to agglomeration, should open the way to the development of more active and stable catalysts [82–84]. For instance, 2-methylanthraquinone was obtained by liquid-phase two-step reaction from toluene and phthalic acid (Scheme 1) over nano-sized H-BEA with promising results (with yields up to 82 %) and, in particular, negligible deactivation over time, thanks to the shorter pore channels, in which the diffusion of the products is easier than in conventional micro-sized catalysts [85].

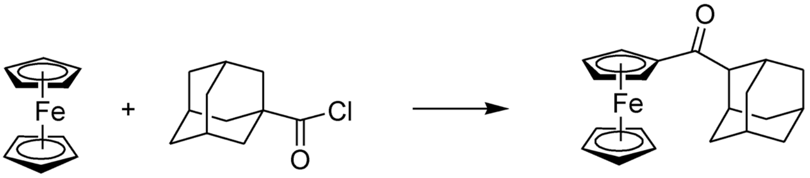


Scheme 1

The use of solvents as reaction medium is generally avoided, if possible. The acylation can be performed under solvent-free conditions in the presence of the acid anhydride, acting as acylating agent and solvent at the same time [86]. Nevertheless, in some peculiar cases, since the general acylation mechanism involves highly polar intermediate species, as the acylium ion and the σ-complex [87], in liquid-phase batch reactors, the reactions are performed in highly polar aprotic solvents, such as nitrobenzene or sulfolane. Otherwise, flow reactors (e.g., fixed-bed tubular reactors), in which the detrimental effect of competitive adsorption of substrate and products on the catalytic performance is lower than in batch reactors, can be an alternative to batch systems. Under these conditions, bulky and functionalized molecules can be synthesized too, as in the case of the vapor-phase bis-acylation of benzene with phthalic anhydride (Scheme 1), in which anthraquinone is obtained with very high selectivity (>95 %), even if at low conversion values [88].

Finally, in order to overcome the limitations when bulky molecules are used, several authors focused their attention onto mesoporous acid molecular sieves. Nevertheless, since mesoporous aluminosilicates possess, in general, far weaker acid sites than a common zeolite, in many cases strong acid centers were introduced by a postsynthesis modification, i.e., by depositing metal triflates (Zn, La-, Ce-, or Y-triflates) or post-transition metal oxides (In_2O_3, Ga_2O_3, or ZnO) onto a preformed mesoporous silica (MCM-41 or SBA-15) [89,90]. These materials proved to be active in the acylation of aromatics with benzoyl chloride or *p*-toluoyl chloride, respectively, and stable toward recycling, with minimal losses in activity (5 %).

However, the potentiality of mesoporous acid molecular sieves, which can accommodate very large reactants, has been exploited only in rare cases so far. One of these is the acylation of ferrocene with 1-adamantoyl chloride (Scheme 2) over mesoporous aluminum-containing silicate Al-KIT-5 over which the bulky monoacylated product, (1-adamantoyl)ferrocene, was obtained with yields up to 45–40 % and with 100 % selectivity, even in consecutive recycle runs [91].



Scheme 2

Anisole and veratrole acetylation over zeolites

From 1997 until 2005, Rhodia (formerly Rhône-Poulenc) has operated two industrial processes for the acetylation of anisole and veratrole over zeolitic catalysts. H-BEA and H-FAU are used as catalysts, respectively. In the new technology, an up-flow fixed-bed reactor is used and the reaction mixture (i.e., the substrate ether plus acetic anhydride) is recirculated over the catalytic bed as many times as it is needed to obtain the desired degree of acetylation. The reaction is typically operated at atmospheric pressure, at 90 °C and with a high ether/acetic anhydride molar ratio. To eliminate the carbonaceous compounds responsible for deactivation, the catalyst is periodically regenerated by oxidative treatment, which is made easier by adding a small amount of one metal of the groups 8, 9, or 10 (typically Pt) to the zeolite [92].

The new processes represent a major breakthrough in the 4-methoxyacetophenone and 3,4-dimethoxyacetophenone syntheses, and they are not only environmentally friendly, but also economically more sustainable than the conventional $AlCl_3$-based ones [66,93]. The most striking differences in anisole acetylation are summarized in Table 4.

Unfortunately, the classical route with $AlCl_3$ catalysts appears cheaper, when the cost of environmental problems (formation of huge quantities of corrosive hydrochloric acid and disposal of large amounts of salts) is not considered. This is the reason why the zeolite-based acetylation process was temporarily discontinued in 2005, the $AlCl_3$-based acetylation process being nowadays widely run in countries where less severe environmental restrictions are in force.

Table 4 Acetylation of anisole. A direct comparison between the conventional (old) and zeolite-based (new) technology. Adapted from [66,93].

Old process	New process
$AlCl_3$ > stoichiometric amount	Zeolite catalyst
1,2-Dichloroethane as solvent	No solvent
Batch reactor	Continuous reactor
Hydrolysis at the end of reaction	No water
Destruction of the catalyst	Periodic catalyst regeneration
Eight synthetic steps	Two synthetic steps
Separation of organic/aqueous phases Treatment and discharge of aqueous phase Distillation of organic phase Recycling of the solvent	Distillation of organic phase
Aqueous effluents: 4500 kg per ton of ketone 5 wt % Al^{3+} and 24 % Cl in the wastes	Aqueous effluents: 35 kg per ton of ketone, 0.8 % acetic acid, and <0.2 % of other organics in the wastes
Yield/anisole: 85–95 %	Yield/anisole: 95 % Higher purity of the final product

Guidelines for further development of acylation catalysts

According to these considerations, the liquid-phase acetylation of activated substrates, such as aromatic ethers (anisole, veratrole, methoxynaphthalene) or heterocyclic compounds (furans, thiophenes, pyrroles), can be efficiently and selectively carried out over zeolites under mild conditions. The key point is to favor the desorption of bulky and polar desired products. This can be done by: (1) choosing the adequate zeolite type and tuning its physicochemical properties (e.g., by using a three-dimensional large-pore zeolite under the form of nano-sized crystals and with hydrophobic properties); (2) using a flow reactor rather than a batch reactor; (3) choosing the proper operating conditions: high substrate/acylating agent molar ratio, eventual use of a suitable solvent, optimal temperature (high enough to favor the desorption of the products, but low enough to avoid extensive secondary reactions), high space velocity values to enhance the sweeping of the products and of the poisoning species out of the catalyst. The strict application of these rules can even permit the acetylation of poorly activated substrates such as toluene [94,95] and the acylation with bulkier acylating agents (benzoylation, etc.), also over mesoporous acid molecular sieves, provided their acid sites are strong enough.

Fries rearrangement

Generalities

The Fries rearrangement consists of the acid-catalyzed transformation of an arylester into hydroxyarylketones, as, for example, in the case of PA into *o*- and *p*-HAP.

The reaction protocol, as described in the original paper [96], is based on the heating at 140 °C of a mixture of 4-cresylchloroacetate and $AlCl_3$ (1:2 molar ratio), resulting in 90 % yield of 2-hydroxy-5-methyl-ω-chloroacetophenone. Similarly to acylation reactions, the formation of a stable adduct arylketone-catalyst requires the use of more than stoichiometric amounts of the Lewis acid, thus strongly worsening the drawbacks related to the use of a chlorine reagent. The recovery of the products requests a hydrolysis step involving the destruction of the catalyst and the unavoidable formation of large amounts of inorganic wastes. The alternative use of mineral acid catalysts, such as HF or H_2SO_4, is not certainly advantageous from the environmental point of view.

Solid-catalyzed processes

The importance of hydroxyarylketones as intermediates in several chemical processes makes the switch to solid acids as catalysts highly appealing in terms of economical and environmental impact. Both gas- and liquid-phase processes have been proposed for this transformation involving the use of zeolites or clays as catalysts. Here we report some selected examples aimed at highlighting the application to industrial products.

Fries rearrangement of phenylacetate

Since from the acid-catalyzed rearrangement of PA, *p*-HAP and *o*-HAP can be obtained, the reaction outcome is strongly related not only to selectivity toward Fries product, but also to the *p*/*o* value.

Earlier studies on the application of zeolites and alumina, namely, fluorinated alumina and H-FAU, in the rearrangement of PA into 4-HAP rely on the use of gas-phase conditions at atmospheric pressure at 420 °C [97,98]. Under the reaction conditions used, a low selectivity into *o*- and *p*-HAP was observed owing to the side dissociation of PA into ketene and phenol, in addition to a rapid catalyst deactivation by coke formation and zeolite dehydroxylation.

In order to overcome these drawbacks, different strategies have been reported, among which performing the reaction in liquid phase and modifying the catalyst features. The use of Ga, Ni, Pt, Pd, Sm, or W-modified MFI (ZSM-5) zeolite has been proposed [99]. On the other hand, the tuning of surface and acidic properties of BEA zeolites by means of SiO_2 and Ce_2O_3 modifications leads to more active and selective materials, allowing 70 % selectivity and conversions of ca. 60–80 % to be reached [100].

The proper choice of the solvent turned out to be crucial in influencing different parameters, such as initial reaction rate, catalyst stability, and product distribution. In particular, polar solvents such as sulfolane significantly promote the formation of the *para*-products and also limit the formation of heavy reaction products such as bisphenol derivatives and hence catalyst deactivation [101].

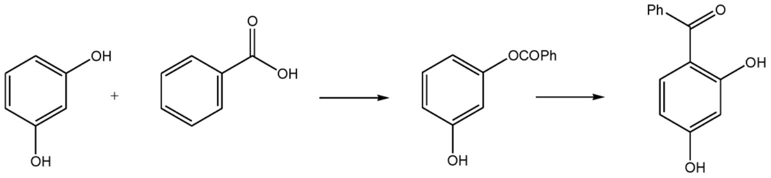
The effect of zeolite variables on catalyst performance has been also studied [102]. In particular, the *p*/*o*-HAP ratio decreases with increasing zeolite pore diameter, in agreement with the hypothesis of intra- and intermolecular mechanisms for *o*- and *p*-HAP formation, respectively. H-MFI (H-ZSM-5) showed indeed the highest conversion, the highest yield of *o*- and *p*-HAP and a high *para*-selectivity, conversely to that observed with narrow-pore-sized TON (Nu-10) zeolite.

The effect of porosity on *o*-selectivity is confirmed by the use of mesoporous materials. Thus, the application of Al-MCM-41 with three different Si/Al ratios to the direct reaction of phenol and acetic acid as the acylating agent, leads to 100 % selectivity in the *ortho* isomer, though with low yield in the Fries product [103]. Similarly, the use of SiO_2–Al_2O_3 and tungstophosphoric acid supported on MCM-41 under gas-phase conditions gives primarily the *ortho* product in the direct C-acylation of phenol with acetic acid [104].

A different approach was proposed relying on the use of Nafion in silica composites [105] obtained by entrapping nano-sized particles of Nafion (13–40 wt %) in a high porous silica matrix. Conversion and selectivity obtained are comparable to those observed by using H-BEA, thus showing that also mesoporous materials with proper acidic properties can be employed for this reaction. Authors underline the strong influence of the reaction solvent on selectivity, which reaches values up to 94 % in the presence of phenol.

Esterification + Fries reaction

The first report on this topic is based on the one-pot liquid-phase esterification of resorcinol followed by the Fries rearrangement into 2,4-dihydroxybenzophenone [106], precursor of the UV-absorbent 4-octyl-2-hydroxybenzophenone (Scheme 3).



Scheme 3

The preparation of 2,4-dihydroxybenzophenone can be accomplished in good yield by the metal chloride-catalyzed reaction of resorcinol with benzotrichloride, with the coproduction of 3 mol of hydrochloric acid and spent metal chloride. H-BEA was shown to be slightly less active than Amberlyst 15 resin, but it had the advantage to give fewer by-products (particularly the bulky and poisoning 3,6-dioxy-9-phenyl-xanthydrol) and to be regenerable by simple air burn-off. It would appear to have environmental benefits compared to the existing industrial process which generates substantial amounts of chloride wastes. A likely explanation of such good performance can be attributed to the small size of zeolite crystallites and to the shape selectivity induced by its microporosity.

Future of solid-catalyzed Fries rearrangement

The studies on Fries rearrangements promoted by solid acid catalysts rely almost exclusively on the transformation of PA and hydroxyphenylacetate, and zeolites reveal excellent performances with these substrates. In addition, an industrial exploitation of molecular sieves for Fries rearrangement is still at a primordial level. Nevertheless, this reaction finds wide application in traditional synthetic organic chemistry. Both the acid and the phenol, from which the phenol esters are derived, can be varied, thus offering the opportunity to directly obtain various synthons required for the preparation of polycyclic compounds such as benzofurans, steroids, coumarins and isocumarins, frequently used as intermediates for biologically active compounds [107]. The potentiality of mesoporous molecular sieves merits to be investigated as to be also exploited with bulky substrates and highly functionalized molecules and to widen the substrate scope of the reaction without the use of metal halides.

CONCLUSIONS

In the synthesis of molecules with industrial interest, solid catalysts and, in particular, molecular sieves, proved to be a viable alternative to chloride-containing Lewis acid catalysts. Outstanding advances have already been made in the field of oil refining and petrochemistry, wherein most acid-catalyzed process zeolites have taken the place of these corrosive and polluting catalysts. However, the three examples presented here show that this trend toward greener processes always occurs very gradually.

In contrast, a lot is still to be done in the field of fine and specialty chemical synthesis, where, according to some manufacturers' unilateral point of view, the high added-value of the products may justify the use of well-established, yet environmentally unfriendly, synthetic routes. However, such a shift toward more sustainable pathways could become possible, provided that, worldwide, all industrial producers are forced to comply with the same strict environmental laws. Otherwise, companies paying more attention to economical profit than to environmental sustainability will go on producing chemicals via old-fashioned chloride-based processes in countries with permissive regulations.

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