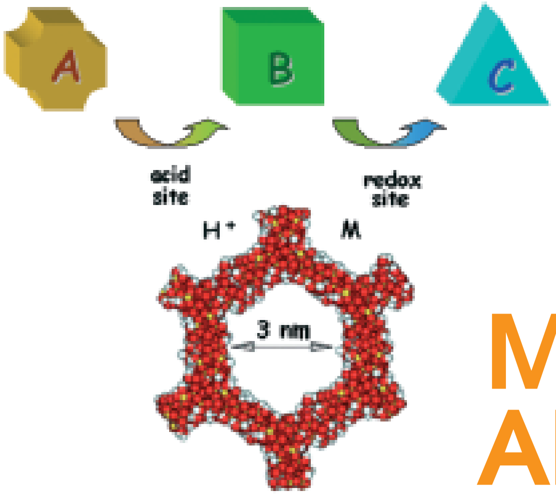

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MICROPOROUS AND MESOPOROUS MOLECULAR SIEVES AS MULTIFUNCTIONAL CATALYSTS

A general trend in academic and industrial research is the transformation of homogeneously catalysed reactions into heterogeneous processes, using solids as supports of the active sites, in order to develop greener and economically competitive processes for the synthesis of chemicals.

Multifunctional heterogeneous catalysts offer the additional important advantage of avoiding isolation as well as purification of intermediates in a complex multi-step synthesis of fine chemicals. Micro- and mesoporous molecular sieves, like zeolites, zeotypes and ordered inorganic oxides, create unique synthetic opportunities to achieve one-pot reactions.

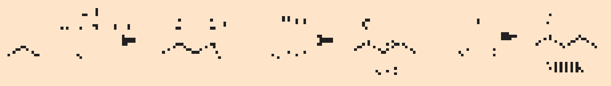
The reduction in the number of synthetic and separation steps has several positive consequences: environmentally more sustainable processes (higher atom economy and lower E-factors), lower operating costs, reduced production of wastes and in general an improvement in the safety conditions [1]. Indeed, the economical benefits of one-pot catalytic syntheses of fine chemicals, in which various successive chemical steps are accomplished in the same reaction vessel are obvious, but the environmental advantages can be still more remarkable if the catalytic transformation takes place on renewable raw materials, such as mixtures of natural terpenes or carbohydrates.

One-pot reactions usually occur over heterogeneous bifunctional (or multifunctional) catalysts, obtained by associating redox sites to acid-base sites. However, in some cases, a unique site is able to catalyse both redox and acid consecutive reaction steps. It is worth noting that the number of examples of bifunctional catalysis carried out on microporous or mesoporous molecular sieves is not so large in the open and patent literature. Indeed, whenever it is possible and mainly in industrial patents, amorphous porous inorganic oxides (*e.g.* Al_2O_3, SiO_2 gels or mixed oxides) are preferred to zeolite or zeotypes materials because of their better commercial availability and their lower cost (especially with respect to ordered mesoporous materials). Nevertheless, in some cases, as it will be shown hereafter, the use of ordered and well-structured molecular sieves leads to unique performances. In addition, mainly in fine chemicals synthesis, the wide use of bulky reactants addresses to the choice of mesoporous materials, more accessible than microporous sieves.

The simplest way to perform a multi-step synthesis is to carry out the successive steps, not only in the same pot, but also under the same conditions. However, when this is not possible, the one-pot reaction is carried out in two stages under different optimised conditions in order to avoid the formation of undesired by-products. In the following section, some relevant examples of bifunctional catalytic systems hosted in or supported on either microporous or mesoporous molecular sieves are reported.

Transformations involving consecutive hydrogenation and acid-base steps

A widely studied example of this kind is the synthesis of methyl isobutyl ketone (MIBK, used as a solvent for inks and lacquers) from acetone. The former was previously prepared from the latter through a catalytic three-step process: base-catalysed production of 4-hydroxy-4-methylpentan-2-one, acid dehydration into mesityloxide (MO), then hydrogenation of MO on a Pd catalyst. Since acetone aldolisation occurs through acid catalysis as shown over a H-MFI zeolite at 433 K (MO is the main reaction product, the aldolisation product being rapidly dehydrated [2]), it is possible, by associating to the acid catalyst a hydrogenation phase, to synthesise MIBK in one apparent step (Scheme 1). Most of the studies have been carried out in gas phase by using fixed-bed reactors.



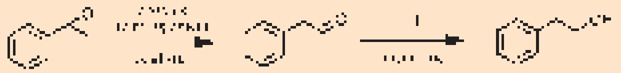
Scheme 1

Excellent selectivity to MIBK (98%) was obtained on a 0.5% Pd/HMFI in H_2-stream at 453 K at 29% conversion [3], but the highest yield value so far has been obtained on a 1% Pd/Cs-HMFI catalyst at 523 K under H_2, with a selectivity to MIBK of 82% at an acetone conversion of 42% [4]. The main by-products are propane and 2-methylpentane resulting from three-step transformations of acetone and MIBK, respectively (C=O hydrogenation, dehydration and C=C hydrogenation). For this reason Pd, which is more selective for the desired hydrogenation of the C=C rather than of the C=O double bonds, is generally chosen. In addition, diisobutyl ketone (DIBK) may also result from trimeric condensation of acetone and it was shown to be the main responsible for the catalyst deactivation [5]. However, its formation is minimised on MFI thanks to the narrowness of the zeolite channels, whereas over non-zeolitic catalysts (*e.g.* Pd/γ-Al_2O_3), large amounts of DIBK are obtained [4]. Also Pd supported on aluminophosphate molecular sieves, thanks to their tuneable acidity and basicity features, are suitable systems for such a transformation. A good selectivity to MIBK (72%), though at low conversion values (11%), is achieved on Pd/SAPO-11 material. Similar Pd-containing acidic zeolites were also applied to the vapour-phase synthesis of bulkier ketones, such as cyclohexylcyclohexanone (a precursor of *o*-phenylphenol, an important wide spectrum conservative) from cyclohexanone [6] or 1,3-diphenylbutan-1-one (an ingredient for plastifying agents) from acetophenone [7].

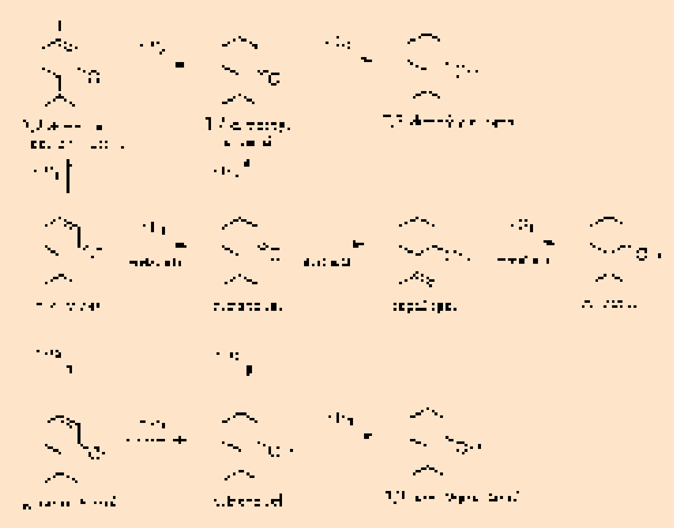
Otherwise, by impregnating a Pd precursor onto a basic K-exchanged FAU zeolite a highly selective bifunctional catalyst is obtained for the low-pressure one-step synthesis of 2-ethylhexanal (a component of perfumes and fragrances) from *n*-butyraldehyde and H_2 in a fixed-bed reactor [8]. Under optimum reaction conditions, over a 0.5% Pd/KX zeolite, 2-ethylhexanal is produced with 91% selectivity at 70% conversion. Once again, the zeolitic basic materials show better performances than non-zeolitic ones (under the same conditions 0.5% Pd/MgO displays a maximum *n*-butyraldehyde conversion of 8%).

Anyway, it is worth noting that almost with all of the above-mentioned catalysts a very important loss in activity with the time-on-stream (TOS) is observed, such a behaviour being more marked when the final product is a bulky ketone. This decrease in activity is ascribed to the strong retention of heavy reaction products inside the zeolite pores ("coke" precursors) as well as to a sintering of the metal particles, owing to the presence of water resulting from the dehydration reaction [6].

Furthermore, Pd or Cu/ alumino- and borosilicate pentasil zeolites are suitable for catalysing in one apparent step the successive dehydration of α-hydroxyketones to α,β-unsaturated ketones and their hydrogenation to unsymmetrical saturated ketones [9]. Thus, on a Pd-containing Ce/B-MFI zeolite 3-hydroxy-2-methylbutan-2-one is converted quantitatively to MIBK in a fixed-bed reactor at 648 K under H_2. Under similar conditions, non-zeolitic catalysts, *e.g.* Pd-containing alumina, show relatively poor performances. The same kind of catalyst displays also interesting results in the consecutive acid-catalysed rearrangement and hydrogenation reaction of terminal aromatic epoxides (Scheme 2) [10]. In particular, over a Cu/borosilicate pentasil zeolite, 2-phenylethanol (a fra-



Scheme 2



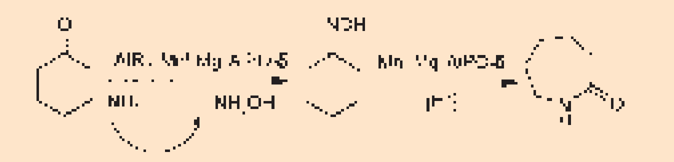
Scheme 3

grance with sweet and floral odour) is obtained in high yields (up to 85%) from styrene oxide.

The bifunctional properties of highly dispersed metal modified zeolites have also been applied to the transformation of raw materials obtained from renewable sources, such as the one-pot conversion of polysaccharides to polyhydric alcohols, which are important ingredients in pharmaceutical and alimentary use [11]. In this process the cleavage of the polysaccharide (*e.g.* corn starch, sucrose or lactose) by hydrolysis on the acidic sites of the zeolite and the following hydrogenation of the aldehydes and ketones on the metal, such as Ru, Co, Cu or Ni, occur in one apparent step. In particular, a 25 wt.% aqueous suspension of corn starch is converted in an autoclave at 453 K and 55 bar of H_2 in the presence of a 3% Ru-exchanged H-USY zeolite and after 35 min a product mixture containing 96% D-glycitol, 1% D-mannitol and 2% xylitol is obtained. In this case, the Brønsted acidity required for the hydrolysis of the polymer could be provided by the outer zeolite surface, whereas the hydrogenation step takes place both on the external surface and within the supercages of the FAU zeolite, which are accessible to glucose.

Recently, great attention has been paid to the selective synthesis of menthols (employed in flavouring and pharmaceutical applications) directly from either citronellal or citral in a one-pot process on a bifunctional catalyst (Scheme 3). A 3% Ir-impregnated H-BEA zeolite was shown to catalyse both the consecutive acid-catalysed cyclisation of citronellal into isopulegol and the Ir-catalysed hydrogenation of the unsaturated terpenic alcohol [12]. To improve the citronellal conversion, the reaction is conducted under N_2 for the first 4 hours, after which H_2 is added. In this way, 95% selectivity for the menthol isomers (of which 75% of the desired (-)-menthol) and complete citronellal conversion is achieved after 30 h. The authors underline the high productivity of this catalyst, since up to 17 g of menthol can be obtained per gram of catalyst in a single run. In addition, it is worth noting that the isomerisation activity (in absence of H_2) clearly increases upon the zeolite is loaded with Ir, calcined and reduced. This indicates that not only the protonic acidity of the zeolite, but also the Lewis acidity of non-reduced Ir might play a role in the isomerisation step. Furthermore, when other metals, such as Ru or Pd, are used instead of Ir under similar conditions, undesired side products are preferentially formed: the C=O hydrogenating aptitude of Ru leads to high yields in citronellol , whereas the strong C=C hydrogenating activity of Pd leads to the dominant production of the saturated aldehyde 3,7-dimethyloctanal. However, it is worth highlighting that, in this reaction, copper-based catalysts supported over non-zeolitic silica (Cu/SiO_2) exhibited excellent performances (very good yields) with a metal which is by far less expensive and more available than iridium [13].

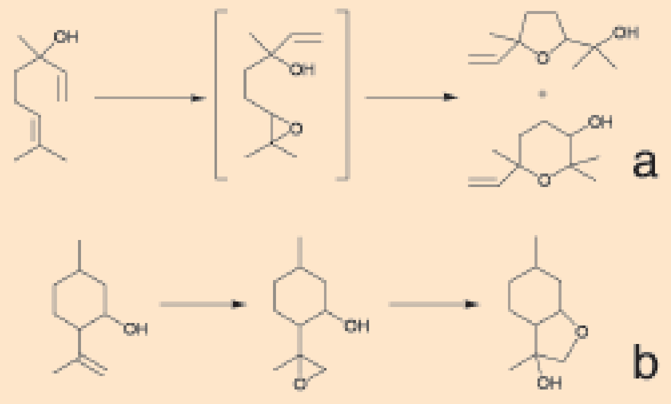
Alternatively, starting from citral, which has the advantage to be a renewable raw material obtained via distillation of essential oils, it is possible to exploit a three-step pathway: i) hydrogenation of citral to citronellal; ii) isomerisation/cyclisation of citronellal to isopulegol; iii) hydrogenation of isopulegol to menthol [14]. For this purpose, a single catalyst (3% Ni/Al-MCM-41) joins the good selectivity displayed by Ni in hydrogenating the α,β C=C bond in citral and the good activity shown by strong Lewis/weak Brønsted sites of Al-MCM-41, required for an efficient citronellal cyclisation. Such a system yields 90% menthols at 343 K and 5 bar and produces 70-75% racemic (±)-menthol in the final mixture after 300 min. Under the same conditions, a 3% Ni/BEA catalyst gives rise to higher formation of by-products, probably via decarbonylation and cracking reactions on the zeolite acid sites, which are stronger than those in Al-MCM-41. Ni is the metal of choice, as it is more selective than Co, Ir or Pt towards the C=C bond hydrogenation (*i.e.* Ni forms negligible amounts of geraniol/nerol isomers), but not as active as Pd in the



Scheme 4

hydrogenation of all C=C bonds (*i.e.* on Ni the formation of 3,7-dimethyloctanal is virtually absent). A further investigation has been recently carried out on the citral transformation into menthols, using a H-MCM-41 support, with a comparison of different metal catalysts: Ni, Pd, Ru and Ir [15]. It has been demonstrated that at conversion higher than 80% Ni/H-MCM-41 is the most promising catalyst, even if, under these conditions, suppressing the parallel hydrogenolysis reactions starting from citral still remains a challenge. A different pathway worth studying is the trifunctional one-pot conversion of geraniol into menthol. Very interesting results were reported over a non-ordered Cu/Al_2O_3 (mixtures rich in citronellal and menthol, the latter with a stereoselectivity in (±)-menthol of 80%) [16], whereas, at the moment, no examples are known over zeolite or zeotype materials.

Another example in which bifunctional catalysts are applied to the transformation of renewable sources is the manufacture of *p*-cymene (used in the fragrance industry and as intermediate in the *p*-cresol production) from terpenes. High yields (up to 80%) in *p*-cymene are obtained in vapour-phase from α-limonene by using a multifunctional zeolite system for catalysing the successive double-bond isomerisation and dehydrogenation steps [17]. In this case, the preparation of the catalyst (1% Pd / 2% Ce / Na-ZSM-5) and the process conditions have to be properly tuned to avoid secondary product formation and rapid deactivation due to coke deposition and presumably Pd agglomeration. In particular, Ce increases catalyst stability, apparently by an anchoring effect towards the Pd particles, whereas the *p*-cymene selectivity is enhanced by using a quasi neutral support (Na-ZSM-5) and careful ion-exchange and activation procedures. These catalysts can be applied directly to the conversion of mixtures of terpenes from natural source, such those obtained as by-product in pulp and paper industry. In this case, Pd-based systems proved to be efficient catalysts, but amorphous supports provide higher yields than zeolitic carriers (90% vs. 70%, respectively), because of diffusion limitations and significant deposition of carbonaceous compounds over zeolites.



Scheme 5

Scheme 6

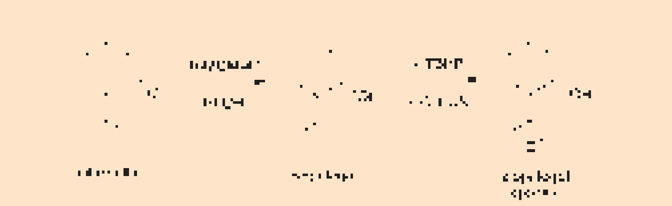
Transformations involving consecutive oxidation and acid-base steps

The presence of a metal in low oxidation state however is not essential to have a bifunctional system. Indeed, both the acid/base and the redox-active sites can be in high oxidation state, as, for example, in Mg(II)Mn(III) AlPO-36 and Mg(II)Mn(III) AlPO-5 molecular sieves, where M(II) ions with marked acidity and M(III) with oxidating activity coexist [18,19]. Such systems were shown to catalyse in one apparent step the synthesis of ε-caprolactam, a pre-

Setacci molecolari micro- e mesoporosi come catalizzatori multifunzionali

ABSTRACT

Lo sviluppo di catalizzatori eterogenei efficaci per i processi sintetici di composti d'interesse in chimica fine rappresenta una delle sfide più stimolanti per i ricercatori dell'accademia e dell'industria. L'utilizzo di supporti solidi può portare un reale contributo nella ricerca di metodi ecocompatibili ed economicamente competitivi. I catalizzatori eterogenei multifunzionali offrono inoltre la vantaggiosa opportunità di evitare l'isolamento e la purificazione degli intermedi nelle sintesi che prevedono più passaggi. I setacci molecolari micro- e mesoporosi, come le zeoliti e gli ossidi inorganici a struttura ordinata, possono talvolta rivelarsi degli strumenti unici per la realizzazione di reazioni multifunzionali in un unico stadio.



Scheme 7

cursor of nylon 6, from cyclohexanone, ammonia and oxygen, which involves three successive steps: i) hydroxylamine formation from NH_3 and O_2; ii) conversion of cyclohexanone to the related oxime and iii) its subsequent Beckmann rearrangement (Scheme 4). These catalysts have the great advantage of working under solvent-free conditions and using air as oxidant.

However, Ti-containing molecular sieves are the high-oxidation state bifunctional systems over which the largest number of organic syntheses have been carried out. Over such catalysts, where both epoxidating and acidic sites are present, it is often difficult to get high yields in the desired epoxide because of the production of large amounts of acid-catalysed by-products. Nevertheless, whenever these by-products are commercially valuable compounds, the bifunctional pathway (epoxidation + acid reaction) could be interesting for the synthetic chemist.

The most remarkable examples deal with the formation of substituted tetrahydrofurans, tetrahydropyrans or cineols, which are valuable compounds for the flavours and fragrances industry (two examples in Scheme 5) [20-24]. These classes of syntheses are run over Ti-containing large-pore zeolites (especially BEA) or mesoporous materials (mainly of the MCM-41 family) because of the bulkiness of the terpenic substrates. Indeed, Ti medium-pore zeolites (*e.g.* TS-1) display low conversion rates of bulky alkenes because of diffusion limitations within the micropores and of their too small external surface [23]. In certain cases, the catalyst contains no aluminium (hence has no protonic acid sites) and the acid-catalysed cyclisation is solely due to Ti(δ+) species [22]. Thus, from a formal point of view, titanium centres act effectively as "bifunctional" catalysts, as the two steps (oxidation + ring closure) are catalysed by the same metal site. The intermediate epoxides can be transformed through acid catalysis into either vicinal diols (by epoxide-ring opening) or aldehydes (by rearrangement), such as 1,2-pinanediol or campholenic aldehyde (Scheme 6) [20, 25, 26]. In general, the conversion of the starting terpenes is rather low (10-30%), but the high value of the desired product (they all are intermediates in the synthesis of fragrances) makes up for the poor yields obtained overall. In one case, the acid-catalysed step is not consecutive to epoxidation, but it occurs before it. Citronellal is converted into isopulegol, by acid-catalysed cyclisation, which in turn is epoxidised to isopulegol epoxide, a compound with fungicidal and insect-repellent activity (Scheme 7) [27]. To do so and to avoid the undesired epoxidation of the starting reagent, the oxidant (*tert*-butylhydroperoxide) is added only after the complete conversion of citronellal into isopulegol; moreover, the cyclisation step is performed in a poorly polar solvent (toluene) and the epoxidation step in an aprotic polar mixture (toluene + acetonitrile). With such precautions a 68% yield in isopulegol epoxide can be obtained.

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