Activities of Heterogeneous Acid-Base Catalysts for Fragrances Synthesis: A Review

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Abstract

This paper reviews various types of heterogeneous acid-base catalysts for fragrances preparation. Catalytic activities of the various types of heterogeneous acid and base catalysts in fragrances preparation, i.e. non-zeolitic, zeolitic, and mesoporous molecular sieves, have been reported. Generally, heterogeneous acid catalysts are more commonly used in fragrance synthesis as compared to heterogeneous base catalysts. Heteropoly acids and hydrotalcites type catalysts are widely used as heterogeneous acid and base catalysts, respectively. © 2013 BCREC UNDIP. All rights reserved.

1. Introduction

Until the mid-19th century, most perfumes were used personally by rich people due to the quite expensive isolation cost of perfume. In the nineteenth century, the development of organic chemistry has begun to make synthetic chemicals available and their use in perfumery thrived. For example, the nitromusks were discovered by Bauer while he was working on explosives related to TNT. However, techniques for the isolation, characterization, and chemical synthesis of organic chemicals still improved, therefore the techniques in the searching of new fragrance materials becoming more structured [1].

Nowadays, perfumers can afford to use certain natural products in fine fragrances only. Synthetic chemicals for fragrances are the most available in the market with wide range of prices. For example, the use of cheap perfumery is highly diversed from soaps, detergents to household materials [2]. The high demand of the perfumes led to industry sector to manufacture the synthetic perfume in a large

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scale. In fact, the statistical data showed that the perfume sales reached about $22 million in 2010 [3].

Synthesis of fragrances can be performed using homogeneous or heterogeneous catalysts. Currently, the use of homogeneous catalysts has been widely avoided due to several reasons such as the difficulty and recovery of the catalyst from the reaction medium, corrosion and toxic problem, and not environmentally friendly process [4, 5].

Concern to the environmental problem, many research groups have explored the development of new type of heterogeneous catalysts with the goal of high efficiency, clean, safe and environmentally friendly technology for chemical process industry [6]. In addition, the heterogeneous catalysts may improve the sustainability of the chemical processes in a manner of process intensification [7].

Some excellent publications covered a part of our theme up to *ca.* 2011. This review is intended to have a more practical character, giving preference to the process and synthesis of fragrances related to the heterogeneous acid-base catalysts and catalysis.

Currently, the industrial practices involve excessive stoichiometric amounts of metal halides (e.g. $AlCl_3$, $FeCl_3$) as catalysts, which resulted in a substantial amount of by-products and corrosion problems as well. The high amount of catalyst is related to the stronger coordination of the formed ketone to the catalyst compared with the acid chloride. The alternative use of zeolites which are reusable and very easily tailored to the desired reaction is very promising [8].

The need for more environmentally-friendly production technology in the chemical industry is universally acknowledged and much progress has already been made. In the past, the need to reduce costs has provided the driver for improvements in process efficiency, since wasteful processes are also uneconomical. However, recent publication concerns about the environment have accelerated this tendency by leading to regulatory activity by governments. Legislations enacted to control the discharge of waste products into the environment, and restrict the manufacture, transport, storage and use of certain hazardous chemicals, have acted as a spur to the introduction of cleaner technology [9]. Acid-base heterogeneous catalysis have the potential to replace liquid acid-base catalysis, thus, the corrosion problems and consequent environmental issues posed by the liquid acids and base can be avoided [10]. On the basis of the reported literature, the solid catalysts used for fragrances synthesis can be generally classified into acid-type and base-type catalysts, which are listed in the flow chart (Figure 1).
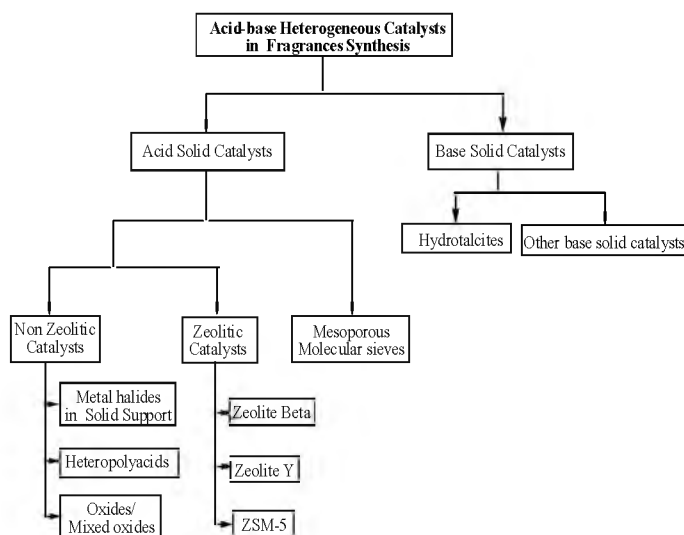

**Figure 1.** Classification of acid-base heterogeneous catalysts in fragrance synthesis

2. Solid Acid Catalysts

2.1. Non Zeolitic Catalysts

2.1.1. Metal halides on solids support

The use of metal chlorides M/PS-IL (M = Ga, Fe, Zn, Cu, In and Al) as catalyst were studied by Bao *et al.* [11]. They prepared imidazolium-styrene copolymer-supported metal chloride catalysts and used it in acetalization reactions of benzaldehyde (1) to (1-methoxyethyl) benzene (2) (Scheme 1). Acetals are widely used as ingredients or additives in fragrances. Compared with ionic liquid-modified silica gel, the imidazolium-styrene copolymers (denoted as PS–IL), were demonstrated to be a more efficient solid support for immobilization of metal chlorides M/PS-IL (M = Ga, Fe, Zn, Cu, In and Al). $GaCl_3$ immobilized on imidazolium-styrene copolymers can be used as an efficient and reusable heterogeneous catalyst for acetalization of carbonyl compounds with methanol, offering a catalytic performance that is on par with its homogeneous counterpart.

As shown in Table 1, when M/PS-IL[Cl] (M = Ga, Zn, Cu, In and Al) were used in the acetalization of benzaldehyde with methanol, Ga/PSIL[Cl]
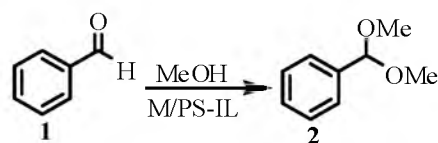
Scheme 1. Acetalization of benzaldehyde (1) with methanol

afforded the best result, giving a 94% yield of product within 30 min in the presence of a very small fraction of Ga (0.05% equiv.), which was a much higher yield than that of achieved using Al (33%), Cu (30), In (29%) and Zn (16%) (Runs 1–5). As Ga/PS-IL[Cl] was used as a heterogeneous catalyst, a pure product of dimethylacetal which can be easily obtained in a high yield (85%) after removing Ga/PS-IL[Cl] by centrifugation and vacuum-drying the remaining liquid phase.

The results also showed that Ga/PS-IL[Cl] could be used 5 times to catalyze the reaction without significant loss of activity and Ga/PS-IL [Cl] can be the best catalyst for acelization of benzaldehyde with methanol. To prove it, the same study also compared the results obtained with the use of Ga/PS-IL[Cl] with halide salts, like GaCl₃, other tetrachlorogallate ions liquid [VBIm] GaCl₄ and silica gel-supported Ga/SiO₂-IL[Cl]. The catalyst was also efficient to other acetalization reactions, shown with a high value, i.e. TOF 0.05% equiv, while other systems typically use a 5% equiv.

Table 1. The yield of acetalization of benzaldehyde with methanol in the presence of M/PS-IL

Entry	Catalyst	Loading amount of M $(10^{-3}$ mmol/g)	Yield (%)
1	Ga/PS-IL[Cl]	8.86	94
2	Al/PS-IL[Cl]	8.85	33
3	Cu/PS-IL[Cl]	0.92	30
4	In/PS-IL[Cl]	9.02	29
5	Zn/PS-IL[Cl]	1.12	16
6	Ga/PS-IL[Br]	2.12	90
7	Ga/PS-IL[BF₄]	6.82	89
8	Ga/PS-IL[PF₆]	5.95	87

2.1.2. Heteropolyacids

Heterogeneous acid catalysis using heteropoly acids (HPAs) is an environmentally-friendly process with high economic value. Unlike metal oxide or zeolite based catalysts, HPAs have discrete and mobile ionic structures. HPAs have very strong Bronsted acidity and redox properties. Both redox and acid properties can be obtained by varying the chemical composition of HPAs. Thus, the redox catalytic acid and selectivity is the main areas of catalytic application of HPAs. HPAs possess stronger (Bronsted) acidity than conventional solid acid catalysts such as acidic oxides and zeolites.

The majority of catalytic applications use the most stable and easily available Keggin HPAs, especially for acid catalysis. Most typical Keggin HPAs such as H₃PW₁₂O₄₀, H₄SiW₁₂O₄₀ and H₃PMo₁₂O₄₀ are commercially available. Its activities can be improved by doping with palladium or platinum, such as in the catalysis for Friedel–Crafts acylation in liquid-phase batch processes. This illustrated by studies of Fries rearrangement of phenyl acetate (**3**), yielding acylated phenols (**4-6**) (Scheme 2) [12].
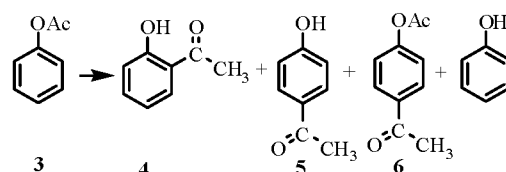

Scheme 2. Fries rearrangement of phenyl acetate

Silica-supported heteropoly acid H₃PW₁₂O₄₀ has been reported as an efficient solid acid catalyst for the cyclisation of (+)-citronellal (**7**) to (−)-isopulegol (**8**) (Scheme 3). More recently, silica-supported H₃PW₁₂O₄₀ doped with 5 wt% palladium has been reported as an active catalyst for one-pot transformation of (+)-citronellal to menthol via acid-catalyzed cyclisation followed by Pd-catalyzed hydrogenation, with a 92% yield of menthol at 100% citronellal conversion and 85% stereoselectivity for the desired (−)-menthol. The reaction occurs in cylohexane at 70°C and 35 bar H₂ pressure. This result is similar or better than those reported so far. It is important that no products of citronellal hydrogenation have been found. This indicates that in this system, citronellal cyclisation occurs much faster than the hydrogenation of isopulegol. The reaction appears to be truly heterogeneous [12].

Leng *et al.* [13] prepared a family of solid organic heteropolyacid (HPAs) salts by combining Keggin heteropolyanions with ionic liquid (IL)-forming cations functionalized by propane sultone (PS). They also evaluated the activity of catalyst in esterification processes including of the study on the organic cations effects, role of heteropolyanions, optimization of reaction and catalyst stability and reusability testing. The example of esterifica-
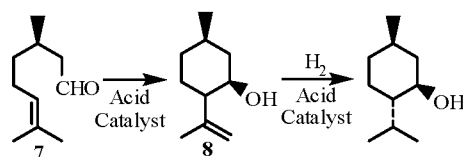
Scheme 3. Synthesis of menthol from citronellal

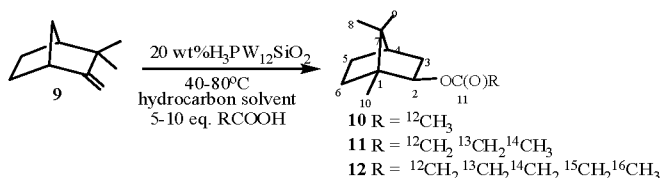$$RCOOH + R'OH \xrightarrow[110°C]{[MIMPS]_3PW_{12}O_{40}} RCOOR' + H_2O$$
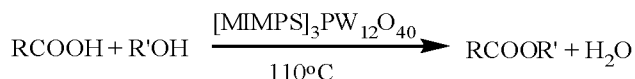
Scheme 4. Esterification of monocarboxylic acid with monohydric alcohol

tion reaction of acetic acid with n-butanol is as follow (Scheme 4).

Catalytic activities of PS-functionalized imidazole (MIMPS) salts of $PW_{12}O_{40}{}^{3-}$, $PMo_{12}O_{40}{}^{3-}$, $SiW_{12}O_{40}{}^{4-}$, and the conventional IL-forming anion $HSO_4{}^-$ in the esterification of acetic acid with n-butanol are compared in Table 2. It can be seen that PS-functionalized imidazole (MIMPS) salts of $PMo_{12}O_{40}{}^{3-}$ and $SiW_{12}O_{40}{}^{4-}$ anions (entries 5 and 6) showed similar phenomenon and comparable activities to that of $PW_{12}O_{40}{}^{3-}$, and their activities were clearly higher than those of pure $H_4SiW_{12}O_{40}$ and $H_3PMo_{12}O_{40}$ (entries 2 and 3). The conventional acidic IL catalyst [MIMPS]HSO$_4$ exhibited a low yield of 65.6% (entry 7), even in a homogeneous system with the amount of [MIMPS]HSO$_4$ being 0.33 mmol, which was much higher than 0.06 mmol for the other catalysts in Table 2.

Silica-supported $H_3PW_{12}O_{40}$ (PW) was also used as a solid acid catalyst for the liquid-phase esterification of camphene [14]. The results on camphene (9) esterification with acetic acid (5–10 fold excess) in the presence of PW/SiO$_2$ in cyclohexane solution at 40–80 °C have been reported. The reaction occurred with 100% selectivity to isobornyl acetate (10), with no other products being observed. The reaction of camphene with n-butyric acid occurred much slower than with acetic acid, reaching a non-

Table 2. Esterification of acetic acid with n-butanol over various with different inorganic anions[a]

Entry	Catalyst	Reaction phenomenon	Yield (%)[b]
1	H$_3$PW$_{12}$O$_{40}$	Homogeneous	88.2
2	H$_4$SiW$_{12}$O$_{40}$	Homogeneous	79.4
3	H$_3$P Mo$_{12}$O$_{40}$	Homogeneous	87.0
4	[MIMPS]$_3$ PW$_{12}$O$_{40}$	Heterogeneous (liquid-liquid)	94.5
5	[MIMPS]$_{-3}$ PMo$_{12}$O$_{40}$	Heterogeneous (liquid-liquid)	96.1
6	[MIMPS] $_4$SiW$_{12}$O$_{40}$	Heterogeneous (liquid-liquid)	90.2
7[c]	[MIMPS]HSO$_4$	Homogeneous	65.6

[a] Reaction conditions: catalyst (0.06 mmol), acetic acid (30 mmol), n-alcohol: n-acid (1.2 : 1), 110°C, 1,5 h, with water segregator.
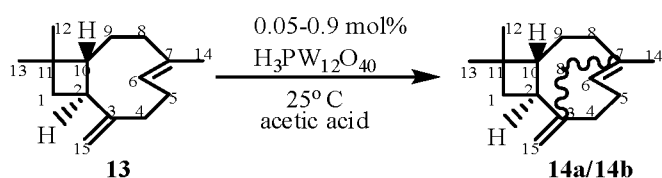[b] Yield of butil acetate based acetic acid
[c] Catalyst amount 0.33 mmol

equilibrium camphene conversion of 52% in 7 h with a TON of 1670. Reaction can be accelerated by increasing the amount of catalyst and attained a nearly equilibrium conversion of 80% in 1–2 h reaction time. After that the reaction became stagnant. This reaction gave isobornyl butyrate (11) in almost 100% selectivity. The esterification of camphene with n-hexanoic acid is also feasible with the PW/SiO$_2$ catalyst, although the performance is not as good as with n-butyric acid. With n-butyric acid, the reaction almost reached equilibrium in 4 h, whereas with n-hexanoic acid only 46% camphene conversion was obtained within the similar time interval. Thus, the longer the hydrocarbon chains of carboxylic acid, the slower the camphene esterification, which can be plausibly explained by steric constraints. Under optimized conditions, isobornyl caprylate (12) was obtained with 80% yield in 3 h. This yield was also limited by equilibrium as the selectivity to 12 was virtually 100% and continuing the reaction beyond the 3 h interval did not increase the conversion any more (Scheme 5). After the reaction, the catalyst was reused.

Scheme 5. Esterification of camphene (9)

Study of the HPAs-catalyzed transformations of β-caryophyllene (13), a bicyclic sesquiterpene compound containing two olefinic bonds has been conducted by Rocha et al. [15]. β-caryophyllene is one of the most abundant sesquiterpenes found in many essential oils. For example, it is the main hydrocarbon component of clove (*Eugenia caryophyllata*) and copaiba (Copaifera) oils. Various synthetic derivatives of β-caryophyllene finds its use as woody ingredient in perfumes. The application of $H_3PW_{12}O_{40}$ (PW), the strongest HPA in the Keggin series was used as the catalyst for the liquid-phase acetoxylation of β-caryophyllene in homogeneous and heterogeneous systems for producing of β-caryolanyl acetate (14) and β-caryolanol (15) (Scheme 7). As a result, they developed an efficient method for the synthesis of acetate with a virtually quantitative yield. The high solubility of PW in acetic acid prevents direct use of silica-supported PW catalysts for the acetoxylation of β-caryophyllene in this solvent due to PW leaching. To avoid leaching problems, the reaction was performed in cyclohexane as a solvent with the addi-
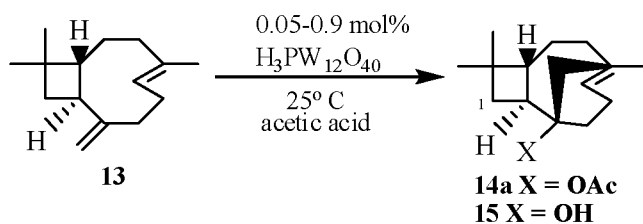
tion of small amounts of acetic acid, up to 10/1 mol/mol of the substrate. In blank tests, with no catalyst or pure silica were added. This result is different from that observed for the homogeneous system, where the 14a/14b molar ratio was about 80/20 (Scheme 6).

Rocha *et al.* [16] also used HPAs as catalyst for another application. They reported the application of silica-supported $H_3PW_{12}O_{40}$ (PW), the strongest HPAs in the Keggin series, as an efficient and recyclable solid catalyst for the liquid-phase isomerization of α-pinene and longifolene into their more valuable isomers-camphene and isolongifolene respectively, which are intermediates in the synthesis of expensive fragrances. The results of the isomerization of longifolene (**16**) indicated that PW/SiO_2 is an excellent catalyst for this reaction. At 80°C, more than half of the substrate was transformed into isolongifolene (**17**) in 5 h with a selectivity of 95% (Scheme 8).
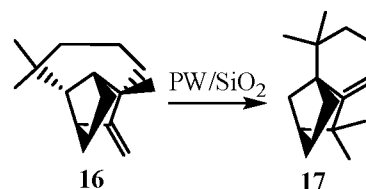
In the isomerization of α-pinene, a complex mixture of products is formed in the presence of an acid catalyst, because α-pinene (**18**) is a very reactive substrate. Therefore, with camphene, selectivity is strongly dependent on the reaction conditions and the amount of catalyst. Silica-supported PW showed excellent performance in α-pinene isomerization, that shown by 90% at 100°C in 1 h, with 50% camphene selectivity. The product distribution slightly varied over time. Under optimized conditions, the selectivity to camphene was 50%, with 28% limonene formed as a main by-product. The PW/SiO_2 catalyst was highly efficient in an amount as low as 0.6 wt %, with a turnover number of 5450 and turnover frequency of 91 min⁻¹. No
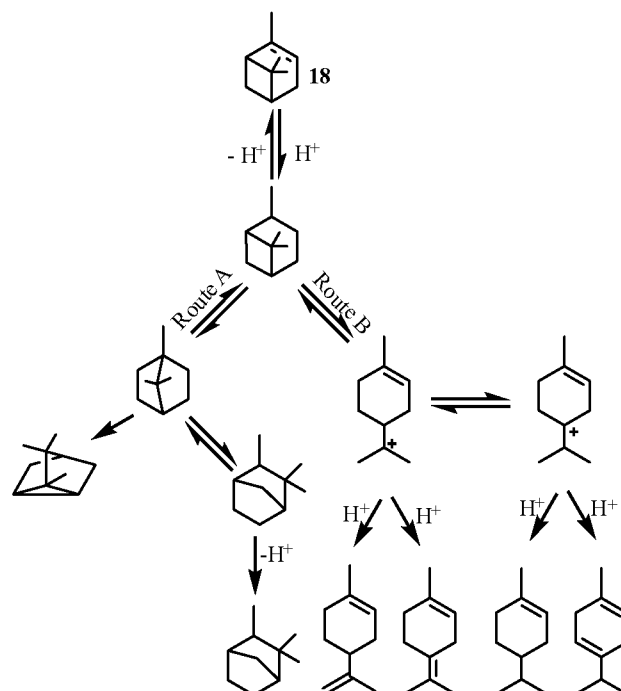
Scheme 8. Acid-catalyzed isomerization of longifolene

leaching of PW from silica was observed, as the reaction practically ceased to occur after removal of the catalyst from the reaction mixture. The catalyst was reused 3 times virtually without loss in activity and selectivity. The acid-catalyzed transformation of α-pinene is likely to occur via a carbenium-ion mechanism, which may be represented by Scheme 9.

The study of a non-zeolitic solid acid catalyst systems based on zirconia-supported isopoly and heteropoly acids was done for acetal and acylal (1,1-diacetates) formation reactions in liquid-phase [17].

Acetalization of aldehydes or ketones can be done using an acid catalyst through a simple reaction. Scheme 10 demonstrates the acetalization reaction of methyl 2-naphthyl (**19**) with propylene glycol (**20**) to give 2-methyl-2-naphthyl-4-methyl-1,3-dioxolane (**21**). This reaction occurs in the liquid phase. The reaction is performed by zirconia-supported isopoly and heteropoly tungstate catalysts in a distillation mode to remove water that

Scheme 6. Acetoxylation of β-caryophyllene

Scheme 7. Acetoxylation/hydration of β-caryophyllene

Scheme 9. Acid-catalyzed isomerization of α-pinene

formed during the reaction. The results are presented in Table 3 and Table 4. Table 3 indicates that higher concentration of a catalyst up to 7% showed the conversion of 1-methyl naphthyl ketone increased up to 97%. Meanwhile, Table 4 shows that the catalyst is better than both ZSM-5 and MCM-41. Similar results were also obtained in synthesis of fructone (24) (Scheme 11) through the reaction of ethyl acetoacetate (22) with ethylene glycol (23) (Table 5).

Atalay and Gunduz [18] studied 12-tungstophosphoric acid (HPW) supported on natural zeolite rich in clinoptiolite as a catalyst of isom-

erization of α-pinene in the liquid phase. Reaction formation of mono-, bi-, and tricyclic in isomerization of α-pinene (18) occurs through such parallel stages (Scheme 12). In these reactions, the formation of tricyclene (26), camphene (9), and limonene (28) and other secondary products were not the case in interconnected. Limonene (28) is more reactive than camphene (9), so that it could transform to other products such as terpinenes (29 and 30) and terpinolenes (31 and 32). The later compounds can then be subsequently disproportionated back into *p*-menthenes and *p*-cymene (37).

In addition, non-monoterpes can also be formed

Table 3. Effect of catalyst weight on the acetalization of 2-naphthyl methyl ketone with propylene glycol using 15 WZ-750

Entry	Catalyst weight (wt.%)	2-naphthyl methyl ketone conversion (mol%)	Selectivity (mol%)
1	1	70	100
2	3	84	100
3	5	90	100
4	7	97	100

Reaction conditions: 2-Naphthyl methyl ketone = 1.497 g (8.8 mmol), propylene glycol = 1.598 g (21 mmol), propylene glycol molar ratio/2-naphthyl methyl ketone = 2.4, toluene = 41 ml, temperature = 146 °C, time = 1 h

Table 4. Comparison of the catalytic activity of 15 WZ-750 on the acetalization of 2-naphthyl methyl ketone with propylene glycol with other catalysts

Entry	Catalyst weight (wt.%)	2-naphthyl methyl ketone conversion (mol%)	Selectivity (mol%)
1	15 WZ-750	90	100
2	15 SZ-750	84	100
3	15 PZ-750	63	100
4	H-ZSM-5	78	100
5	AlMCM-41	76	100

Reaction conditions: 2-Naphthyl methyl ketone = 1.497 g (8.8 mmol), propylene glycol = 1.598 g (21 mmol), propylene glycol molar ratio/2-naphthyl methyl ketone = 2.4, toluene = 41 ml, catalyst weight = 0.154 g (5 wt.% of total weight of reactants), temperature = 146 °C, time = 1 h.
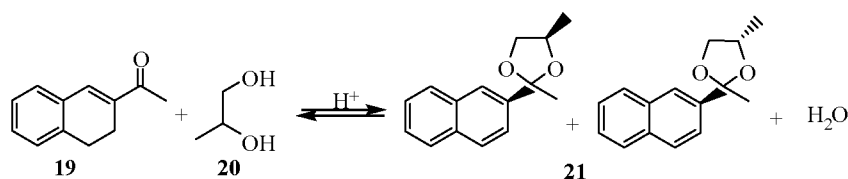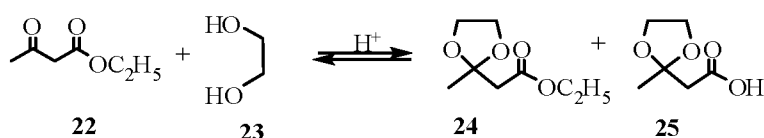

Scheme 10. Reaction scheme of the formation of 2-methyl-2-naphthyl-4-methyl-1,3-dioxalane

Table 5. Comparison of the catalytic activity of 15WZ-750 on the acetalization of ethyl acetoacetate with ethylene glycol with other catalysts

Entry	Catalyst	Ethyl acetoacetate conversion (mol%)	Selectivity (mol%)
1	15 WZ-750	95	100
2	15 SZ-750	87	100
3	15 PZ-750	80	100
4	H-ZSM-5	37	100
5	AlMCM-41	24	100

Reaction conditions: Ethyl acetoacetate = 1.561 g, ethylene glycol = 1.489 g, ethyl acetoacetate: ethylene glycol molar ratio = 1:2, toluene = 41 ml, catalyst weight = 0.09 g (3 wt.% of total weight of the reactants), temperature = 146 °C, time = 1 h.

Scheme 11. Reaction scheme of the formation of fructone (ethyl 3,3-ethylenedioxybutyrate)
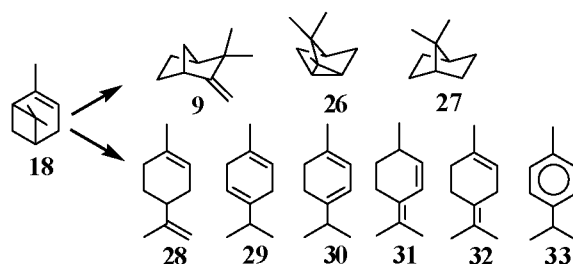
Scheme 12. Products observed by isomerization of α-pinene over HPW catalyst supported on natural zeolite

with higher retention times than terpinolene (HRTP), depending on the structure and formation of ketals. The main product from isomerization reactions α-pinene (**18**) and camphene (**9**) is limonene (**28**), with selectivity of around 40% and 3%, respectively, over the HPW catalyst supported on natural zeolite without heat treatment. One and a half order dependency on α-pinene consumption was observed and activation energy was estimated to be 65.4 kJ/mol. This study indicated that clinoptilolite-based natural zeolite can be used as a support for HPW catalysts in α-pinene isomerization with high catalytic activity.

Heteropolyacid (an exchanged Cs form) is also used as a solid acid catalyst in esterification of fatty acids with sorbitol (**34**). Synthesis of sorbitol fatty acid esters (**35**) can be conducted by reacting protected sorbitol (sorbitol ketalized with acetone). The catalyst is able to hydrolyze some of the ketal functions in a controlled way, thus deprotecting OH groups which can then react with the fatty acids (Scheme 13).

In this process, the amount of free hydroxyl groups that occur during the reaction is expected to be controlled, so as to inhibit the formation of higher esters (di-, tri-, tetraesters) as well as to avoid the anhydrization of the sorbitol with formation of dianhydride ethers. However, this has not yet demonstrated high selectivity of the catalyst on the mono-ester expected, as well as the use of zeolite beta catalyst [7].

2.1.3. Oxides/Mixed oxides

Mineral acids such as H_2SO_4 and HCl are excellence catalysts for alkylation, hydration, hydrolysis and esterification reactions. However, the utilization of oxide and/or mixed oxide in heterogeneous catalysis is explored widely in order to overcome the disadvantages of the homogenous catalysis such as corrosion, troublesome work-up procedures and excessive waste streams.

Dijs *et al.* [19] evaluated the catalytic properties of the surface-functionalised silicas in the solvent-free liquid-phase hydro-acyloxy addition of acetic acid to camphene (**9**), yielding the pine-fragrance
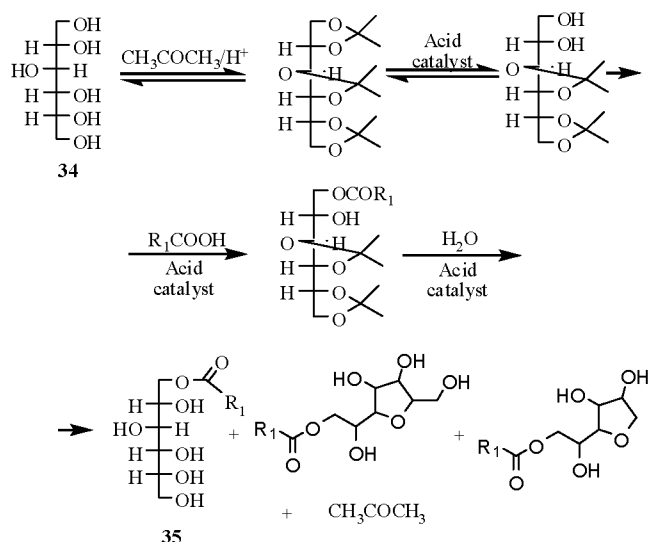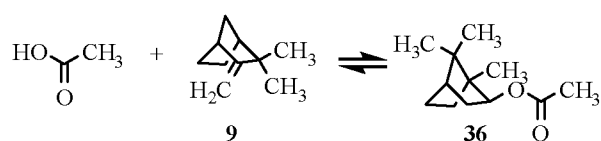
Scheme 13. One-pot synthesis of sorbitol fatty acid esters

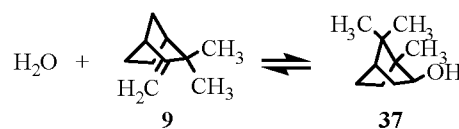**Scheme 15.** Reaction of camphene with water

isobornyl acetate (**36**) (Scheme 14).

Reaction rates (normalised on the concentration of sulphonic acid groups) were identical to those on the homogeneous CH₃SO₃H reference catalyst. The equal rates suggested that the reaction occurs through similar mechanism. The reaction rate for solid surface-functionalised silica catalysts increased by two orders of magnitude upon addition of a small amount of water. In the presence of water, the alcohol analogue of **36**, i.e. isoborneol (**37**) (Scheme 15), is an important intermediate. Generation of homogeneous alkyl sulphonic acids via hydrolysis, followed by leaching from the silica surface does not occur; the formation of **36** stopped after removal of the solid catalyst from the reaction mixture by filtration. Thus, the alkyl sulphonic acid functionalised silica's act as proper heterogeneous Bronsted acid catalysts.

Mesoporous MoO₃/SiO₂ was used as a solid acid catalyst in acetalization of glycerol with various aldehydes [20]. MoO₃/SiO₂ catalysts are studied with varying molybdenum oxide molar concentrations. Acetalization reaction of glycerol with aldehydes yields 1,3-dioxane (**38**) and 1,3-dioxalane (**39**) (Scheme 16). The results showed that benzaldehyde conversion reached 38 and 45 % for 1 and

10% MoO₃ loading catalyst, respectively, which increased to 72% in the presence of 20% MoO₃/SiO₂. This result is better than that of pure silica (benzaldehyde conversion = 23%), but lower than that of PTSA (81%). The catalyst was also used for acetalization of glycerol with various aldehydes. The results are shown in Table 6. The conversion of aldehydes decreased as the selectivity for six-membered acetals increased.

2.2. Zeolitic Catalysts

Zeolite is a porous crystal typically consisting of Si, Al, and O atoms, typically constructed from 12-, 10- and 8-rings, and sizes of the pores are roughly 0.7 nm, 0.55 nm, and 0.4 nm, respectively. There are around 190 kinds of framework type codes known by the end of 2010. The number and type of zeolite species is increases every year, but only a few type of zeolites has been used in industrial processes [21].

Zeolite in the form of H is a solid acid with varying acid strength. Variations in the acid strength can be achieved through modification of the zeolite by ion exchange, dealumination, and atomic partial isomorphous substitution of framework Al and Si atoms [1]. Various properties of zeolites with different textures and acidity have been widely synthesized. Zeolites can also be modified to possess a hydrophobic character without disturbing the function of acid sites by incorporating of certain organic species into the zeolite pore structure [10]. For example, heating of H-zeolite at high temperatures, water molecules will be desorbed leaving of to form coordinately unsaturated Al³⁺ ions. In Scheme 17 Lewis acids are shown [1].

Since zeolites possess Lewis and Bronsted acid, a lot of researches studied the use of zeolites as ac-

Scheme 14. Hydro-acyloxy addition of acetic acid to camphene
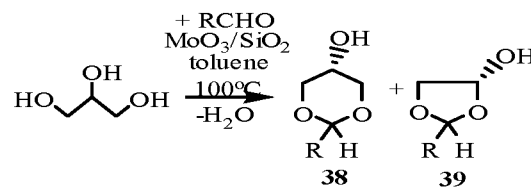
Scheme 16. Acetalization of glycerol with aldehydes

Table 6. Acetalization of glycerol with various aldehydes

No	Aldehyde compounds	Time (h)	Conversion	Six-membered (%)
1	*p*-Tert-butyl benzaldehyde	8	54	62
2	2-Hydroxy-5-nitro benzaldehyde	8	23	60
3	Anisaldehyde	8	45	99.5
4	*o*-Chloro Benzaldehyde	8	61	72
		16	70	70
5	*n*-Heptadehyde	8	78	62
6	*n*-Butyraldehyde	8	69	66
7	*Trans*-cinnamaldehyde	8	10	100
8	Phenylacetaldehyde	8	56	91

Charge: glycerol = 0.11 mol, aldehyde compounds = 0.1 mol, catalyst (20% MoO_3/SiO_2) = 10 wt% of glycerol, reaction temp. = 100 °C, solvent = toluene = 15 g

id catalyst. In the following description, several studies using zeolites as catalysts in the synthesis of fragrances are shown.

2.2.1. Beta Zeolites

Climent *et al.* [22] used beta zeolites and other zeolites, also mesoporous molecular sieves, as catalysts in the synthesis of phenylacetaldehyde glyceryl acetal (40 and 41), propylene glycol acetal of vanillin (42), and acetonaphthone (43) (Scheme 18 to 21).

Beta zeolites with different Si/Al ratio were investigated in the synthesis of hyacinth fragrance. The results showed that the catalytic activity of beta zeolite decreased when the Si/Al ratio exceeded 100. In the acetalization of phenylacetaldehyde with glycerol performed in the presence of zeolite beta, a fairly high conversion (92%) was shown, and the majoring product is (40) (61%), along with the product (41) with 31%. Scheme 19 shows isomerization reaction of 1,3-dioxolane into 1,3-dioxane catalyzed by acids. The results of the reaction showed that the ratio of the two isomers (1/2) is similar to the results by PTSA catalyst.

The synthesis of the vanillin propylene glycol acetal (42) is carried out by reacting of 4-hydroxy-3-methoxybenzaldehyde with propylene glycol (Scheme 20). In the reaction vanillin synthesis, zeolite beta showed a good performance, as indicated by the results 42 by 88%, which is almost the same in comparison with the use of homogeneous PTSA catalysts. However, in the synthesis of 2-methyl-2-naphthyl-4-methyl-1,3-dioxolane (43) which has a blossom orange fragrance (Scheme 21), the performance of zeolite beta was not as good as the catalyst ITQ-2 zeolite (Table 7).

Climent *et al.* [23] also used beta zeolite in the synthesis of fructone (ethyl 3,3- thylendioxybutyrate), a flavoring material, by acetalization of ethyl
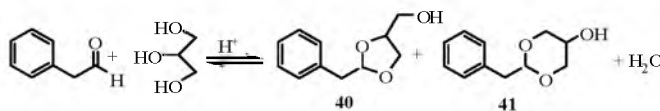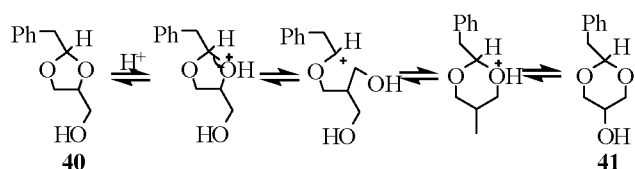
Scheme 18. Reaction scheme of the formation of 2-benzyl-4-hydroxymethyl-1,3-dioxolane (40) and 2-benzyl-5-hydroxy-1,3-dioxane (41)
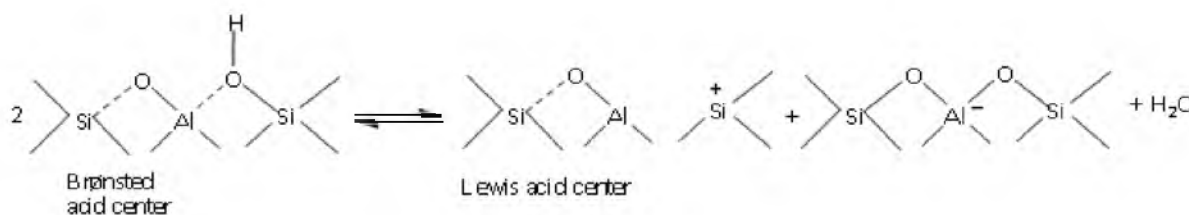
Scheme 17. Formation of Lewis acid center

acetoacetate with ethylene glycol. As can be inferred in Scheme 22, the reaction involves relatively bulky intermediates and therefore one may expect that the geometrical constraints imposed by different zeolite geometries could have an impact on both activity and selectivity.

As shown in Scheme 23, the process involves relatively large reaction intermediates, therefore it is to be expected that the geometric constraints on the different zeolites may have an impact on activity and selectivity. The results showed that beta zeolites is an active and selective catalyst, with conversion to fructone (**24**) was 91%, while to the conversion to 3,3-ethylenedioxy-butanoic acid (**25**) was only 4%. This result is lower than that of zeolite Y.


Scheme 19. General reaction mechanism of isomerization of 1,3-dioxolane into 1,3-dioxane catalyzed by acids
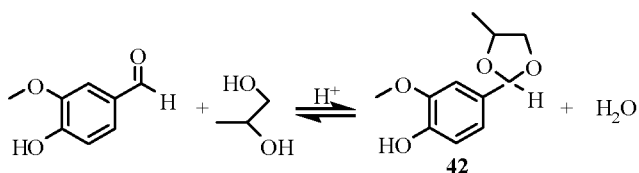
Scheme 20. Reaction scheme of the formation of vanillin propylene glycol acetal (**42**)

The use of beta zeolite as a catalyst in the acylation of methoxybenzene with acetic anhydride was also done by Freese *et al.* [8]. In addition, they also studied the Fries rearrangement of phenyl acetate on H-Beta zeolite in the liquid phase. The results showed H-Beta (Si/Al=12) and dealuminated H-Beta (Si/Al=90) has a high selectivity towards *p*-methoxyacetophenone (MAP) (**44**) (99% for H-beta and 98.5% for the dealuminated H-Beta) and only small amounts of ortho-isomer formed. The mechanism acylation on zeolite is as shown in Scheme 23.
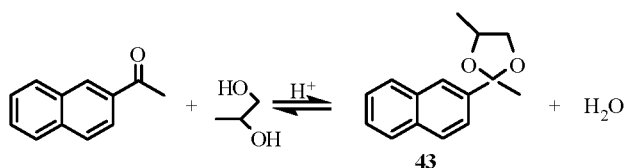
Scheme 21. Reaction scheme of the formation of 2-methyl-2-naphthyl-4-methyl-1,3-dioxolane (**43**)

Table 7. Result of acetalization of 2-acetonaphthone with propylene glycol using different solid acid catalysts

| Catalysts	Si/Al	r_0/Ba (min^{-1})	Yield 43 (%)
Beta-1	13	2.3	5
MCM-22	15	1.8	20
ITQ-2 (I)	15	12.3	63

Ba: Bronsted acidity, mmol pyridine per gram of catalyst, measured ad 523 K. Yield at 3 h reaction time

For Fries' rearrangement, the reactions were carried out in a trickle bed reactor which represents a combination of catalytic reaction with continuous extraction (Soxhlet-like). The catalyst was placed in the reflux of the condensing reaction mixture. All reactions were carried out in dry nitrogen atmosphere.

The results showed that the high conversion in trickle bed reactor maintain for a short time only at a significantly higher reactant-to-catalyst ratio. When the nitrogen flow passed through the trickle bed reactor, trace amounts of ketene were conformed (Scheme 24), while the acidic hydroxyl group catalyzes the scission of the ester bond (Scheme 25).

Candu *et al.* [24] used beta zeolite in the benzylation of benzene with benzyl alcohol (BnOH) as alkylating agent over the investigated H-beta zeolites and other catalysts. An important chemical compound obtained through the benzylation of benzene is diphenylmethane, which is mainly used in the fragrance industry and agrochemicals (Scheme 26). They used the commercial H-beta zeolites with Si/Al of 10.8 and 35.8.

The results showed that under optimal conditions following the drop-wise reactant addition methodology, selectivity of 77% in DPM (Scheme 27) was achieved for 58% BnOH conversion in 4 h
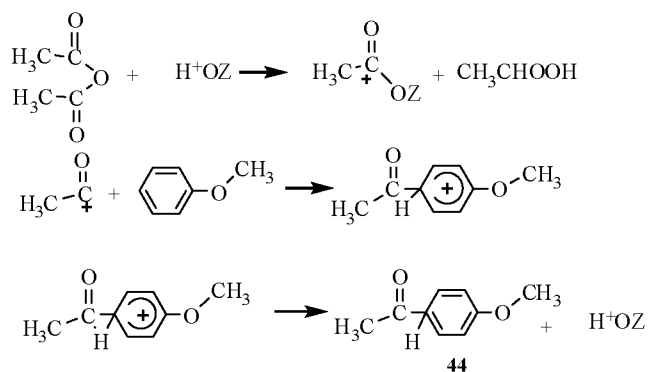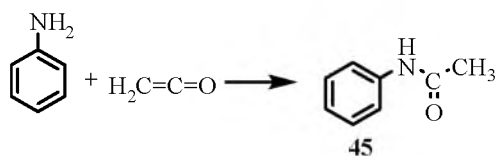

Scheme 23. Reaction mechanism of MAP formation on zeolite (Oz⁻ zeolite lattice)
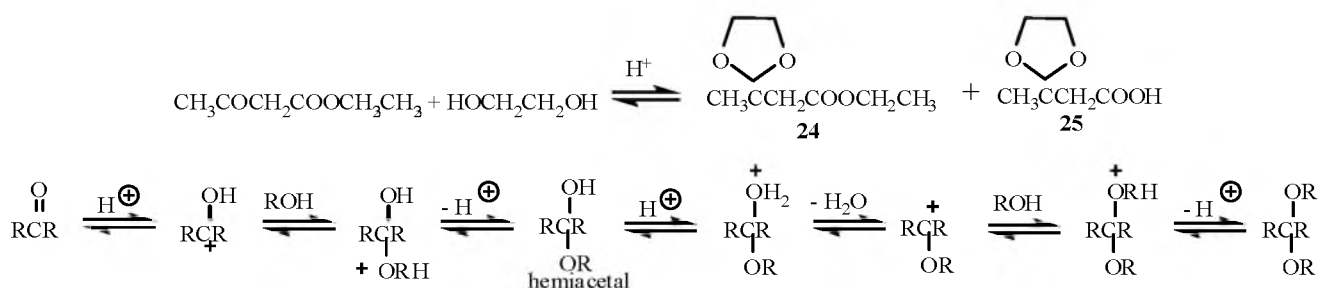
Scheme 22. Acetalization of ethyl acetoacetate with ethylene glicol

of reaction at 353 K.

Sn- and Zr- Beta zeolites as acid Lewis catalysts were used in one-pot synthesis of 4-methoxybenzyl -1-methylpropyl ether [7]. The 4-methoxybenzyl-1-methylpropyl ether (46) is a fragrance with a fruity pear odor. This reaction (Scheme 27) involves two steps. The first step consists of the reduction of 4-methoxybenzaldehyde into alcohol. Before entering into phase two (esterification), alcohol is separated and purified. This alternative preparation procedure involves the reduction of the 4-methoxybenzaldehyde to the corresponding alcohol through a Meerwein-Ponndorf-Verley reaction

with 2-butanol, followed by etherification of the benzyl alcohol intermediate with 2-butanol which is in excess. The results showed that both catalysts are actively giving the desired fragrance in high yield, Zr-Beta being more active for the global process (Table 8).

Other beta zeolite, namely Nb and Ta zeolite, were also used as catalyst in the one-pot process

Scheme 24. Formation of acetanilide (45)
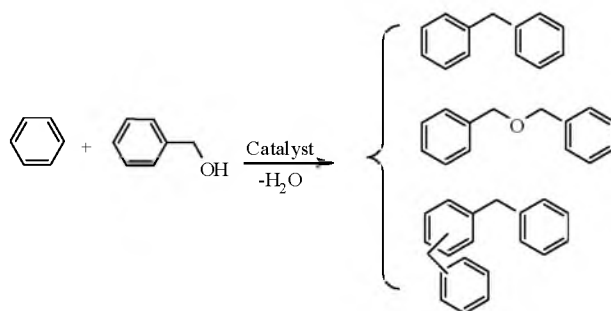
Scheme 26. Friedel-Crafts benzylation of benzene with benzyl alcohol
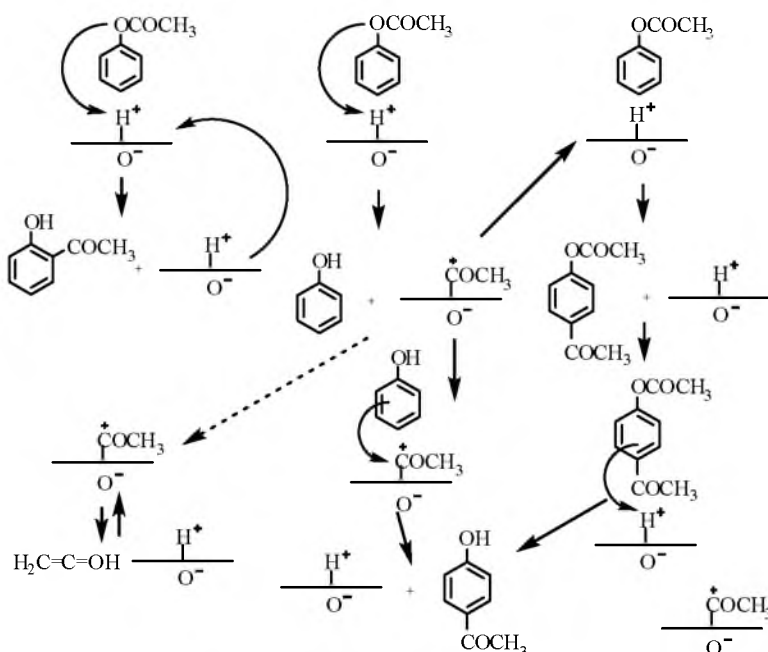

Scheme 25. Proposed reaction mechanism for the conversion of phenyl acetate on H-Beta

described above for the synthesis of 4-methoxybenzyl 1-methylpropyl ether. Ta-Beta exhibited similar activity and selectivity with Sn-Beta, while Nb-Beta resulted in a considerably lower selective to the target molecule [7]. Kantam *et al.* [25] used beta zeolite as a catalyst for the nitration of *o*-xylene (**47**) with high regio-selectivity in liquid phase with stoichiometric quantity of nitric acid (Scheme 28). From this research, it was known that among all the solid acid catalysts, beta zeolite with SiO_2/Al_2O_3 ratio: 22 displayed the best isomeric [4-nitro/3-nitro-*o*-xylenes (**48** and **49**)] ratio of 2.2.

Zr-beta zeolite was used as a catalyst in the cyclization of citronellal (**7**) to isopulegol isomers (**8**) (Scheme 29) by Yongzhong *et al.* [26]. They also studied the effect of zirconium on the formation of Zr-zeolite beta in a fluoride medium. The crystalization kinetics was determined for an initial Si/Zr ratio from 200 to 50. Good crystallinity can be obtained up to a Si/Zr ratio of 75; higher Zr content resulted in an amorphous phase. Without the use of seeds, it was still possible to form Zr-zeolite beta up to a Si/Zr ratio of 100, although a longer crystalization time was required. The yield was good, but the crystallinity was lower than that obtained with the seeded synthesis.

2.2.2. Y Zeolites

Hensen *et al.* [5] studied the use of H-USY zeolites and also other zeolite and heteropoly acids as heterogeneous catalysts for synthesis of 1-methyl-4-[α-alkoxy-isopropyl]-cyclohexenes or α-terpinylmethylether (**50**) (Scheme 30) through
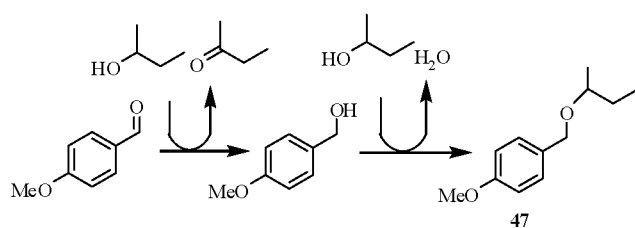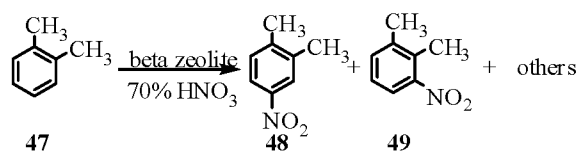
alkoxylation of limonene and *a*-pinene with C_1-C_5 alcohols to 1-methyl-4-[α-alkoxy-isopropyl]-1-cyclohexene in the liquid phase. The results of the synthesis, namely 1-methyl-4- [α-alkoxy-isopropyl]-cyclohexenes can be used as a flavor and fragrance for perfumes and cosmetic products, as additives to pharmaceuticals and agricultural chemicals, and also in the food industry.

The reaction procedure of alkoxylation with H-USY zeolite as catalyst was conducted in batches. Methanol reacts with limonene over acidic catalysts to 1-methyl-4-[alpha-methoxy-isopropyl]-1-cyclohexene (α-terpinyl methyl ether) as the main reaction product (Scheme 32: R- = CH_3-). Table 9 presents the conversion, selectivity and product yields for limonene methoxylation in the presence of various acidic catalysts. Table 9 shows that H-USY show only low activity, with selectivity of the desired product reaches values of about 70-80%, and only in the presence of a H-USY zeolite with the SiO_2/Al_2O_3 ratio of 40, the limonene conversion increases to 57%.

In contrast to the previous research presented, Climent *et al.* [27] used zeolite USY-2 (Si/Al = 35) as catalyst in the synthesis of hyacinth and vanilla fragrances (Scheme 18). In the acetalization of phenylacetaldehyde with glycerol for synthesis of hyacinth fragrance, reaction carried out at 420 K using toluene as the solvent. Observation after two hours of reaction showed that the conversion occurred was phenylacetaldehyde by 95%. The results of cyclic reaction is 1.2 (2-benzyl-4-hydroxymethyl-1,3-dioxolane (**40**) and the additional product 1.3 (2-benzyl-5-hydroxy-1,3-dioxane (**41**) and two geometrical isomers of 1), namely (cis and trans configurations) were obtained with 64 and 31%, respectively. The results also show that the 1,3-dioxolane (**40**) is an unstable primary product, while 1,3-dioxane (**41**) emerged as the major secondary product. This suggests that the 1,3-dioxolane (**1**) is preferred ki-

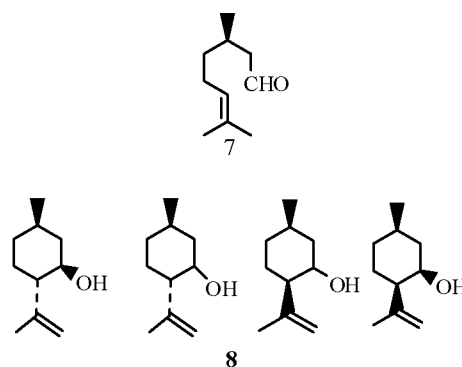**Scheme 27.** Cascade process for the synthesis of 4-methoxybenzyl 1-methylpropyl ether

Scheme 28. The nitration of *o*-xylene (**47**) with highest isomeric selectivity for 4-nitro-*o*-xylene (**48**) using beta zeolite catalyst

Scheme 29. Cyclisation of (+)-citronellal to isopulegol isomers

Table 8. Results for the synthesis of 4-methoxybenzyl 1-methylpropyl ether by a tandem hydrogenation / etherification sequence using solid Lewis Acid catalysts

Catalyst (mg)	Time (h)	Total Conversion (%)	Overall Selectivity to Other (%)
Sn-Beta (50)	8	71	100
Sn-Beta (100)	24	99	99
Zr-Beta (50)	8	100	100

Reaction conditions: p-methoxybenzaldehyde (1.1 mol), 2-butanol (3 g) at 100 °C

netically, and isomerizes to a more stable form (Scheme 19). The results of the reaction using H-USY-2 catalyst showed best results for conversion of phenylacetaldehyde compared with results of other reactions using heterogeneous catalysts (beta zeolite, mordenite, ZSM-5, and MCM-41), i.e. 93%. This research also studied the influence of the Si/Al ratio of zeolite decreased activity, the results show that increasing the ratio Si/Al 19-35 did not reduce the activity of the catalyst.

Synthesis of the vanillin propylene glycol acetal was conducted by reacting 4-hydroxy-3- methoxybenzaldehyde and propylene glycol with some of heterogeneous catalysts, included H-USY (Scheme 20). Results of acetalization of vanillin with propylene glycol using USY zeolite as catalyst showed that acetalization is lower than in the case where the water was removed by azeotropic distillation with toluene as solvent. Carrying out the azeotropic distillation, 99% conversion was achieved after 1 h reaction time.

Thomas *et al.* [28] used solid acid catalysts such as Mg-Y zeolites in the synthesis of dimethyl acetal of ketone to one-pot acetalization reaction. They used the H-ion exchange on zeolite HY with magnesium ion to form Mg-Y zeolite.
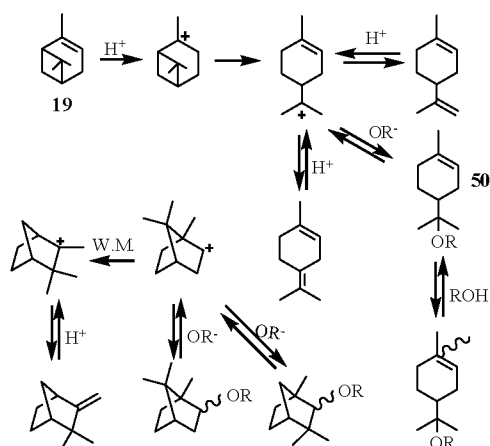
Scheme 30. The global reaction pathway, as suggested, based on the product distribution

One-pot acetalization reaction was carried out in a 50 ml flask equipped with magnetic stirrer, thermometer, water condenser, and temperature controller and nitrogen gas flowing slowly. Acetalization reaction is a reversible reaction. This reaction consists of two stages, namely the reaction of hemiacetal formation and the formation of ketals (Scheme 31). In the reaction of hemiacetal formation, cyclohexanone (51) is protonated by the-Bronsted acid sites (H^+ ions from zeolite) to produce an intermediate which then combine with methanol to form a hemiacetal (52). This reaction was followed by the removal of water molecules. At this stage of reaction, ketals are formed. Protonation occurs to form the resulting intermediate compounds formed after dehydration. After the intermediate compounds reacted with methanol, and then underwent a protons-elimination process, producing the acetal compounds (53).

Besides using the Mg-Y zeolite, they also used the same CeMg-Y zeolite as catalyst. The results showed that Ce Mg-Y zeolite catalyst is more reactive than the Mg-Y zeolite (69.8% *vs.* 42%). In addition, this researcher also compared with the use of other catalysts such as mesoporous K10-montmorillonite, and the results are better than using CeMg-Y zeolite, which is 71.8% (reaction for 2 hours). This suggests a difference between the acidity and the effect of clay zeolite on acetalization reaction. The difference is due to the acidic bridging hydroxy groups, which should be associated with the presence of tetrahedrally-coordinated aluminum in the structure, in an amount greater in zeolites than clays.

Padró *et al.* [29] have studied the use of Zn-NaY zeolites in the synthesis of ortho – hydroxy-acetophenone (*o*-HAP) (54), an intermediate compound for the synthesis of fragrance, by acylation of phenol with acetic acid in the gas-phase. For the formation of o-HAP, they proposed two possible mechanisms, as shown in Scheme 32. Direct formation was done via C-acylation of phenol in the ortho position, and indirectly through O-acylation of phenol forming the PA intermediate results,

Table 9. Methoxylation of limonene in the presence of H-USY catalysts in a batch reactor

Catalyst	Temperature (°C)	Conversion (%) (limonene)	Selectivity (%) (α-terpinyl methyl ether)	Yield (%) (α-terpinyl methyl ether)
H-USY (6)[a]	100	8.7	74.1	6.4
H-USY (40)[a]	60	57.1	78.8	45.0
H-USY (70)[a]	100	6.2	70.5	4.4

[a] The various SiO_2/Al_2O_3 ratios of the zeolites are put in parentheses
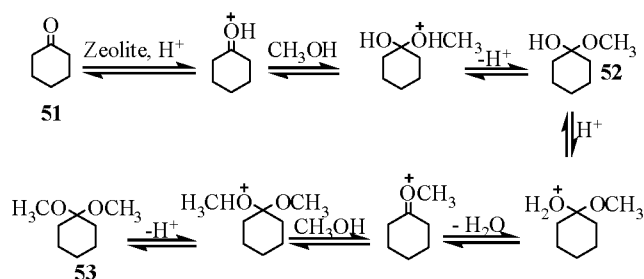
Scheme 31. General reaction mechanism for acetalization of ketones catalyzed by zeolite

Scheme 32. Reaction network for the acylation of phenol with acetic acid

then through the acylation of phenol with PA or Fries rearrangement to form o-HAP.

Acylation reaction of phenol in the gas phase with acetic acid carried out in a fixed bed, continuous-flow reactor at 513 K and 101.3 kPa. The catalyst was calcined in air at 773 K for 2 hours. Phenol (P) and acetic acid (AA) were introduced (P/AA = 1) via a syringe pump and vaporized into flowing N_2 to give a $N_2/(P + AA)$ ratio of 45. The results as analyzed by gas chromatography showed that the zeolite Zn (9:30) also formed only PA and o-HAP, but selectivity to PA increased with time on stream at the expense of o-HAP even though XP was relatively constant.

2.2.3. ZSM-5

As noted in Section 2.2.2, in addition to using NaY, Padro *et al.* [29] also used ZSM-5 as a catalyst in the synthesis of *ortho*-hydroxyacetophenone (o-HAP), an intermediate compound for the synthesis of fragrance, by acylation of phenol with acetic acid in the gas-phase (Scheme 33). They prepared zeolites Zn(0.82)ZSM-5 and Zn(1.19)ZSM-5 containing 0.82% and 1.19% Zn, respectively. Zeolite Zn(0.82)ZSM-5 was prepared from commercial ZSM-5 by performing one exchange with a 0.05 M $Zn(NO_3)_2.6H_2O$ solution while zeolite Zn(1.19)ZSM-5 was obtained by exchanging ZSM-5 three times, with a 0.5 M $Zn(NO_3)_2$ solution of commercial ZSM-5. Both the exchanged samples calcined in air at 723 K for 3 h, then washed with

hot distilled water before being dried at 373 K.

The use of ZSM-5 in the acetylation of benzene to acetophenon (55) was reported by Singh and Pandey [30]. ZSM-5 was prepared in accordance with the procedure in U.S. Patent 3,702,886. Conversion of acetic acid for the acetylation product in benzene was measured through a series of exchange of Na⁺ H-ZSM-5 zeolite at constant temperature (523 K) with benzene/ acetic acid molar ratio of the two. The results showed that the conversion rate of acetic acid decreased in the following order: H-ZSM-5> H-Na (28.9)-ZSM-5> H-Na (34.1)-ZSM-5> H-Na (37.3)-ZSM -5.

The Friedel-Crafts acylation is an electrophilic aromatic substitution in which an electron-deficient-species (electrophile) is generated by the activation of acetic acid at protonic sites of the zeolite which attacks the benzene ring resulting in the formation of asetofenon, in accordance with the equation in Scheme 33.

2.3. Mesoporous Molecular sieves

The solids of mesoporous molecular sieves, with uniform pores from 2 to 10 nm, have attracted attention as catalytic materials. These materials have very high surface area, around 1000 m^2/g [31].

The research used MCM-41 mesoporous aluminosilicate with Si/Al ratio of 14 to synthesis of jas-

minaldehyde. The jasminaldehyde (56) was formed by acetal formation followed by acetal hydrolysis and subsequent Aldol Condensation. The reaction consists of two steps (Scheme 34). In the first one, heptanal dimethyl acetal is formed by refluxing heptanal with an excess of methanol in the presence of the solid catalyst. In the second step and when the dimethyl acetal yield is around 80%, the methanol is removed by distillation, and then benzaldehyde is added. Under these reaction conditions, heptanal dimethyl acetal undergoes deacetalization at a controlled rate giving heptanal which condenses with benzaldehyde under acid catalysis. In this research, the concentration of aldehydes was controlled, as well as acidic conditions [7].

The use of mesoporous molecular sieves as heterogeneous catalyst was also done by Wang *et al.* [32]. They investigated the MSU-S (BEA) and MSU-S (Y) mesoporous molecular sieves with different Si/Al ratios for isomerization catalyst in α-pinene (9) (Scheme 35) and compared with conventional method.

3. Solid Base catalysts

Acid heterogeneous catalysts were commonly used compared with base heterogeneous catalysts. However, some kinds of solid base catalysts were used, such as oxide, hydroxides, and amides of alkali and alkaline earth metals (also on supports), anion exchangers, alkali and alkaline earth metal salts of weak acids (carbonates, carbides, nitrides, silicates, etc.) or superbases: MgO doped with Na are usually used as solid base catalysts [1]. This review includes the use of hydrotalcites for the synthesis of fragrances. Hydrotalcites are the most widely used as a base catalyst for synthesis of fragrances. In addition to hydrotalcites, applications of some other solid base catalysts such as basic zeolites, base alumina, talc and *etc.* in fragrances synthesis were also reported.
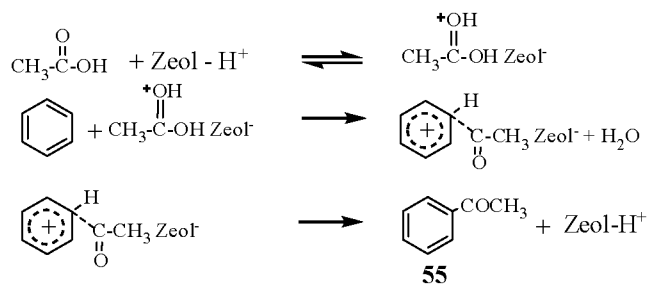
Scheme 33. The activation of acetic acid on the protonic sites of the zeolite in the Friedel-Crafts acylation
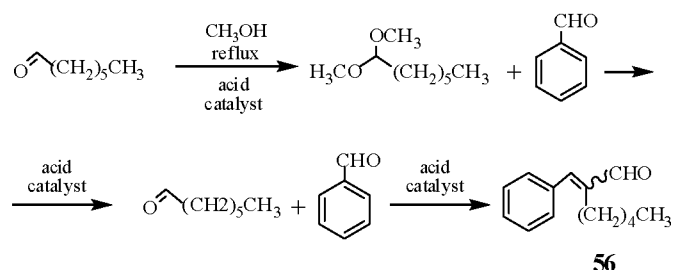
Scheme 34. Synthesis of jasminaldehyde
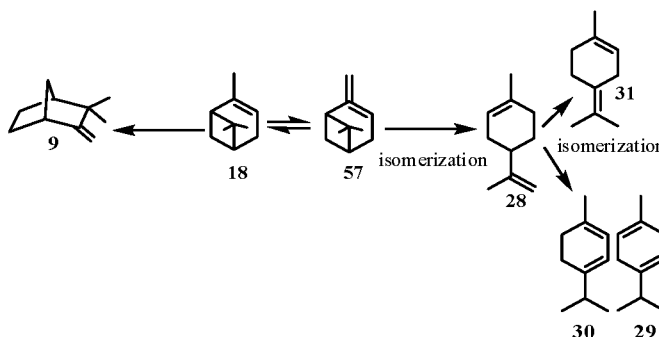
Scheme 35. Routes for α-pinene isomerization

3.1. Hydrotalcites

Layered double hydroxides (LDH) includes hydrotalcites and Hydrotalcites-like compounds, which can be expressed with a general formula: $[M(II)_{1-x} M(III)_x(OH)_2]^{x+}(A^{n-})_{x/n}.mH_2O]^x$ [34]. In this structure of molecules, they are formed by positively charged brucite-like layers $(Mg(OH)_2)$ in which some of Mg^{2+} are replaced by Al^{3+} in the octahedral sites of hydroxide layers and also there are CO_3^{2-} anions to compensate the positive charge, while in between two layers there are molecules of water [10, 33, 20].

Misra and Perrota [34] studied composition and properties of high aluminum synthetic hydrotalcite. They also pillared the hydrotalcite by molybdate, chromate, and silicate anion replacement. Products of the synthesis indicated the high aluminium content with the ratio of alumunium/alumunium + magnesium at more than 0.32. In addition, the synthetic hydrotalcite can be intercalated with some complex ions through a calcinaton-reformation method.

Condensation reaction between citral and acetone can be catalyzed by either acid or bases. Some commercial methods make use of conventional homogeneous bases as catalysts (i.e., aqueous alkali metal hydroxide solutions, alcoholates in alcohol, or benzene solvents), which lead to waste streams.

Climent *et al.* [20] used calcined hydrotalcites

as catalyst for the Knoevenagel condensation between citral (58) and acetone (Scheme 36). They also studied the use of hydrotalcites regenerated by rehydration for catalysts in the same condensation reaction. The results showed that the freshly calcined hydrotalcite was less active than the rehydrated samples and a maximum of activity was found when the condensation was carried out using freshly calcined hydrotalcite with the addition of 36% (wt/wt) water. Using these rehydrated hydrotalcites, it is possible to obtain yields of pseudoionones (59) of 96% with 99% of selectivity, in 15 min of reaction time working at a very low acetone/citral molar ratio.

Some authors also used combinations of hydrotalcite with some metal ions as catalysts of several organic compounds, for an example in the synthesis of benzylidene malononitrile (62) from benzaldehyde dimethyl acetal (60) and malononitrile (61). This reaction was performed in a one-pot procedure using a combination of Ti^{4+}-exchanged montmorillonite bearing Bronsted acid sites and a noncalcined Al/Mg hydrotalcite (HT) as basic catalyst (Scheme 37) [7]. The result showed that in the absence of HT, benzaldehyde was the only product detected while no reaction took place in the absence of Ti^{4+}-exchanged montmorillonite.

The Ti^{4+}-mont/HT can also catalyze the tandem reaction of Michael addition followed by acetalization. For this reaction, there were a synergistic effect between both Ti^{4+}-mont and HT support. Basic sites of HT promote the Michael addition, while acid sites of Ti^{4+}-mont play a role in the acetalization. For the first step, methyl vinyl kethone (63) was reacted with nitromethane. This chemical process was catalyzed by Ti^{4+}-mont/HT. In the second step, ethane 1,2-diol was reacted with the product of the first steps, and the acetalization process achieved 89% yield of 2-methyl-2-(3-nitropropyl)-1,3-dioxolane (64) (Scheme 38) [7].

The same catalyst was also used for epoxinitrile, an intermediate for the synthesis of several heterocyclic compounds. It was synthesized in high overall yield (91%) by coupling four sequential acid and base reactions (Scheme 39) using the Ti^{4+}-mont/HT catalytic system. The reaction consists of several steps. In the first step, the acid site of Ti^{4+}-mont catalyzed esterification of cyanoacetic acid

(65) with methanol, giving methyl cyanoacetate, which subsequently reacts with benzaldehyde (after dimethyl acetal hydrolysis). At the end step, the basic sites of the HT catalyst play the role with hydrogen peroxide to yield the R,a,b-unsaturated nitrile (66) [7].

Hydrotalcite is also used indirectly in the synthesis of 2-methyl-3-phenyl-propanal, a compound widely used as a fragrance. In this synthesis, reaction of benzaldehyde and propanal was catalyzed by acid and base sites of Pd-supported AlMgO. Preparation by supporting 0.2 wt % Pd on the AlMgO was used to perform the reaction between benzaldehyde and propanal under 1 MPa of hydrogen at 130°C. Conversion of benzaldehyde by a multifunctional catalyst achieved 43% after 24 h with 45% selectivity to 2-methyl-3-phenyl-propanal (67), while benzyl alcohol being the main by-product from the hydrogenation of benzaldehyde, as shown in Scheme 40 [7].
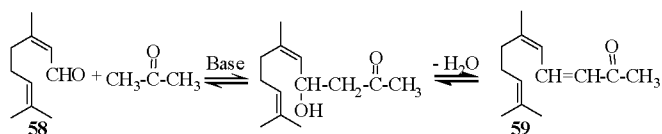
Padmasri *et al.* [35] studied the use of calcined hydrotalcites (CHTs) as catalyst for *tert*-butylation of phenol using *iso*-butanol. There are three kinds of CHTs prepared namely calcined Mg–Al (CMA), calcined Mg–Cr (CMC) and calcined Zn–Al (CZA) by different procedures of catalysts preparation. The main products of these synthesis are *o-tert*-butyl phenol (*tert*-butyl phenyl ether, OTBP) and 2-*tert*-butyl phenol (*o-tert*-butyl phenol, 2TBP) with o-butenyl phenol (butenyl phenyl ether, OBP) (68) and 2-butenyl phenol (*o*-butenyl phenol, 2BP) (69) (Scheme 41) as useful by-products. The results showed that the activities of catalysts increase in the following order: CMA >CZA > CMC, presented by conversion of phenol of 31, 30, and 29%, respectively.
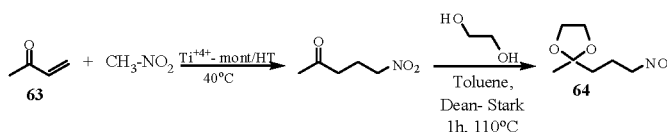
3.2. Other Base Solid Catalysts

In addition to hydrotalcite, some other solid-base catalysts, such as: basic alumina and zeolites,
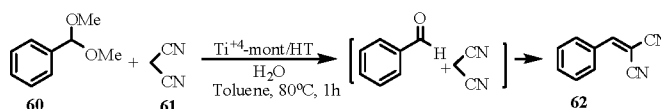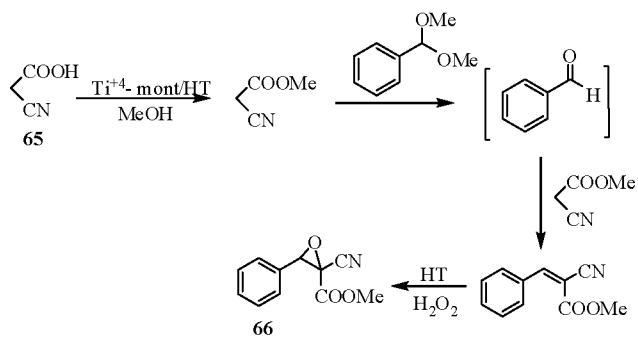

Scheme 37. One-pot hydrolysis of acetal followed by Knoevenagel condensation

Scheme 38. One-pot Michael addition followed by acetalization

Scheme 36. Condensation reaction between citral and acetone

Scheme 39. One-pot esterification followed by deacetalization, Knoevenagel condensation and subsequent epoxidation

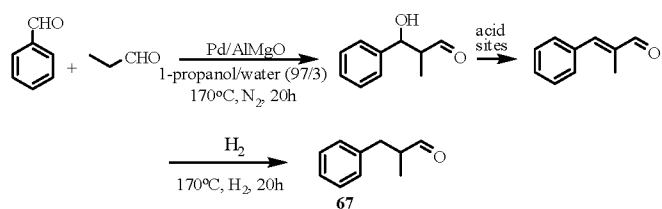**Scheme 40.** One-pot synthesis of 2-methyl-3-phenyl-propanal

were also used to catalyze the isomerization of 1-methoxy-4-(2-propen-1-yl) benzene (methyl chavicol) (**70**) to 1-methoxy-4-(1-propen-1-yl) benzene (trans-anethole) (**71**) (Scheme 42) [36].

They used zeolites powder (Si/Al=1.25) to prepare the zeolites Cs–X, Rb–X, K–X through cation exchange of Cs, Rb and K in Na–X zeolite with 1 M aqueous solution of corresponding chlorides at 353 K. The results showed that conversion data for isomerization of **71** using alkali ion exchanged zeolites which are known to be weak bases varying from 61% to 96% with 56–76% selectivity for **70**. The conversions obtained follow the order of Cs–X>Rb–X >K–X> Na–X, which is in consonance with the order of basicity. It was found that the conversions of **70** depended on the amount of impregnated KOH on alumina, and that the lower the KOH impregnation, the higher the conversion of **70** and selectivity for **71**.

As seen in Table 10 conversion and selectivity for transanethole obtained with 10% KOH/alumina (non-calcined) are comparable to those obtained when pure KOH was used as a catalyst. Non-calcined 10%KOH/alumina sample showed 97% and 95% conversion with 79% selectivity for 1 compared to 99% conversion and 76% selectivity with KOH, which shows that this catalyst can be used without heat treatment to obtain higher conversion and selectivity.

Sharma *et al.* [37] also used alkali ion-exchanged zeolites, alumina, and alkali-treated alumina besides hydrotalcite to produce 2-methylpentenal (**72**) from propanal (Scheme 43).

The result showed that the conversion of propanal varied from 22–42% with 92–94% selectivity of 2-methylpentenal using various alkali ion exchanged zeolites without any thermal treatment or activation, which are known to be weak bases. On the activation of ion-exchanged zeolites at 450 °C for 4 h, the conversion of propanal decreased with increase in the selectivity of 2-methylpentenal.
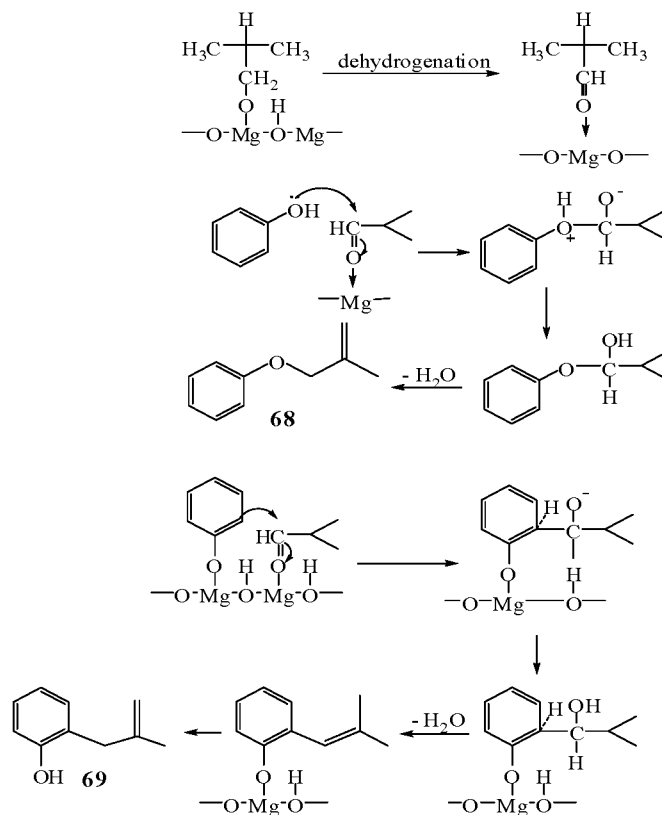

Scheme 41. A plausible mechanism for the formation of butenyl phenols

Meanwhile, conversion of propanal was found to be 42% with 97% selectivity of 2-methylpentenal using neutral alumina without activation. The conversion increased up to 46% with neutral alumina activated at 450 °C for 4 h. The conversion of propanal strongly depends on the amount of impregnated KOH on the neutral alumina.

Meanwhile, Srivastava *et al.* [36], Sharma *et al.* [34], Patel *et al.* [38] used synthetic talc, magnesium organo silicates (MOSs), as a solid base catalyst for self condensation of propanal (proposed reaction as Scheme 44). Catalytic activity of MOSs (MOS1, MOS2 and MOS3) for self-condensation of propanal was showed in Table 11. Conversion of propanal by synthetic talc increased with the increasing amount of amine functionali-
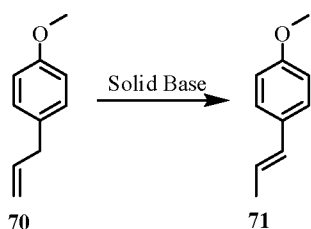
Scheme 42. Isomerization of 1-methoxy-4-(2-propen-1-yl) benzene to 1-methoxy-4-(1-propen-1-yl) benzene
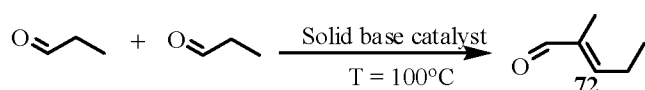
Scheme 43. Aldol condensation of propanal.
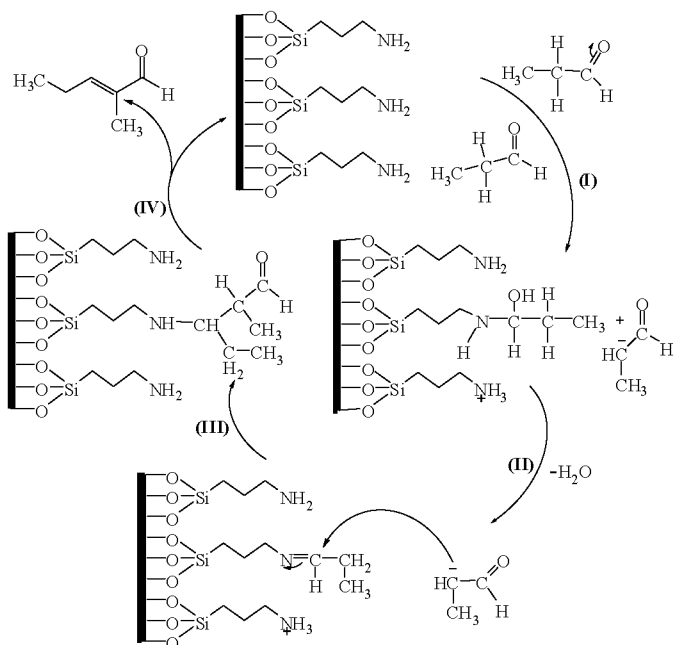
Scheme 44. Proposed reaction mechanism for self-condensation of propanal [38]

Table 10. Conversion and selectivity data for isomerization of 1-methoxy-4-(2-propen-1-yl) benzene using impregnated KOH on alumina

Catalysts	Time (h)	Conversion (wt%)	Selectivity (wt%)
10%KOH/alumina [a;b]	10	97	79
10%KOH/alumina [a;c]	5	95	79
KOH [b]	10	99	76
10%KOH/alumina [b;d]	10	81	78
20%KOH/alumina [b;d]	10	55	74
30%KOH/alumina [b;d]	10	39	36
40%KOH/alumina [b;d]	10	21	13
50%KOH/alumina [b;d]	10	16	11

Reaction temperature 491 K (refluxing), weight of 2 = 5 g, weight of tetradecane = 0.05 g. a. Without calcination, used after drying at 383 K to remove water. b. Weight of catalyst=1 g. c. Weight of catalyst=0.5 g. d. Used after calcination at 673 K for 4 h.

Table 11. Effect of functional groups on conversion and selectivity for self-condensation of propanal[a]

Entry	Catalyst	% Conversion	% Selectivity		
			2-Methyl pentenal	3-Hydroxy-2-methyl pentanal	C$_9$ products
1	MOS1	24	98	2	-
2	MOS2	65	95	-	5
3	MOS3	70	82	14	4
4	Natural Talc	32	99	-	1
5	Without Catalyst	4	75	25	-

[a] Reaction conditions: propanal = 1.25 g, catalyst = 0.1 g, temperature = 100 °C, solvent (toluene) = 5 mL, time = 10 h

ties in MOS. For diamine-functionalized catalysts (MOS3), conversion of propanal increased to 70% [38].

4. Conclusion

Synthesis of fragrances by acid-base reaction can be conducted by heterogeneous catalysts. All researchers have the same view in the use of a heterogeneous catalyst, especially based on environmental safety considerations, simplifying methods in product separation, and its possibility to be reused.

In the fragrance synthesis, acid heterogeneous catalysts are commonly used compared with base heterogeneous catalysts. Solid heteropolyacids are more widely used as non-zeolitic heterogeneous catalysts in synthesis of fragrance, while zeolite Y, zeolite b, and ZSM-5 are usually used as zeolitic heterogeneous catalysts. Hydrotalcites are the most used as base heterogeneous catalysts.

Heterogeneous acid catalysts for preparation of fragrances are usually applied in acetalization, esterification, isomerization, and rearrangement reactions, while heterogeneous base catalysts are applied in the condensation, alkylation, and isomerization reactions.

Developing and engineering heterogeneous acid catalysts and testing catalytic in synthesis of fragrances still need to do.

Acknowledgment

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