Synthesis of dimethyl acetal of ketones: design of solid acid catalysts for one-pot acetalization reaction

Bejoy Thomas, Sreedharan Prathapan, Sankaran Sugunan *

Department of Applied Chemistry, Cochin University of Science and Technology, Kochi 682 022, Kerala, India

Abstract

The synthesis of dimethyl acetals of carbonyl compounds such as cyclohexanone, acetophenone, and benzophenone has success-fully been carried out by the reaction between ketones and methanol using different solid acid catalysts. The strong influence of the textural properties of the catalysts such as acid amount and adsorption properties (surface area and pore volume) determine the catalytic activity. The molecular size of the reactants and products determine the acetalization ability of a particular ketone. The hydrophobicity of the various rare earth exchanged Mg Y zeolites, K-10 montmorillonite clay, and cerium exchanged montmoril-lonite (which shows maximum activity) is more determinant than the number of active sites present on the catalyst. The optimum number of acidic sites as well as dehydrating ability of Ce^{3+}-montmorillonite and K-10 montmorillonite clays and various rare earth exchanged Mg–Y zeolites seem to work well in shifting the equilibrium to the product side.
© 2004 Elsevier Inc. All rights reserved.

Keywords: Acetalization; Dimethyl acetal; hydrophobicity; Ce-montmorillonite; K-10 montmorillonite; Rare earth exchanged MgFAU-Y zeolites

1. Introduction

The title reaction is many times a requirement to pro-tect carbonyl groups specifically during the manipulation of multifunctional organic molecules since dimethyl ace-tals display higher stability towards strong bases, Grig-nard reagent, lithium aluminium hydride, strong oxidants, and esterification reagents than their parent carbonyl compounds [1]. 1,2-Diacetals are efficient pro-tecting groups for vicinal 1,2-diol units in carbohydrates [2,3]. In particular, protection of monosaccharide units as cyclohexane 1,2-diacetals (CDA) offers rapid access to important building blocks for oligosaccharide synthesis [3–5]. Grice and co-workers reported the preparation, structure, derivatization and NMR data of cyclohexane 1,2-diacetal protected carbohydrates [6,7]. Zeolites,

clays, sulphated metal oxides, and mesoporous materials provide a convenient catalytic route for protecting the carbonyl groups during organic synthesis.

Besides the interest of acetals as protecting groups, many of them have found direct applications as fra-grances [8,9], in cosmetics [9], food and beverage addi-tives [10,11], pharmaceuticals [12], in the synthesis of enantiometrically pure compounds [13,14], and polymer chemistry [15]. The methyl and ethyl acetals of n-octanal and n-decanal, for example, find widespread applications in perfume and flavour industries [16]. Sometimes, several acetals named as 'potential fragrances' are introduced into the different formulations and, at the time of contact with the skin, the products are hydrolysed and odorous compounds are released. The conversion of a carbonyl compound to its acetal alters its vapour pressure, solubil-ity and aroma characteristics, and often results in flavour attenuation. For example, the propylenedioxy derivative of vanillin is commonly used as a vanilla flavour since it causes flavour attenuation [17].

The most general method for the synthesis of acetals is to react carbonyl compounds with an alcohol or an orthoester in the presence of acid catalysts. The commonly used acid catalysts include corrosive protic acids such as HCl, H_2SO_4 and Lewis acids such as $ZnCl_2$ and $FeCl_3$ [18,19]. Homogeneous acid catalysts ranging from $Mg(ClO_4)_2$[20], p-toluenesulphonic acid [21], and a series of cationic diphosphine Lewis acidic complexes of Pt(II), Pd(II), and Rh(III) [22,23], etc. have also been employed successfully for the generation of acetals. Gorla and Venanzi have described the basic structural requirements to achieve high activity of the catalysts [24]. However, acetalisation procedures mentioned above require expensive reagents, tedious work-up procedure, and neutralization of the strongly acidic media leading to the production of harmful wastes. Hence, these methods suffer limitations derived from high E-factors and low atom utilization as the catalysts are irreversibly lost. Furthermore, the formation of dimethyl acetals in homogeneous phase is often carried out by using trimethyl orthoformate as the reagent. Though methanol is more desirable for this reaction, many kinds of by-products are often produced when methanol/acid system is employed.

The choice of the catalyst is of prime importance in these environmentally conscious days. Green chemistry demands the replacement of highly corrosive, hazardous and polluting acid catalysts with eco-friendly and renewable solid acid catalysts. Environmentally benign solid acid catalysts such as SO_4^{2-}/ZrO_2, SO_4^{2-}/TiO_2 [25], Ce-exchanged montmorillonite [26], acidic zeolites [27–29], mesoporous silica [30], and siliceous mesoporous material [31,32] have also been reported to be active for the acetalization reactions. In this paper, a simple, efficient, and highly eco-friendly protocol is described for the chemoselective acetalization of three ketones namely, cyclohexanone, acetophenone, and benzophenone at ambient temperatures utilizing rare earth exchanged $(Ce^{3+}, La^{3+}, RE^{3+})$ MgFAU-Y zeolites, K-10 montmorillonite, and cerium-exchanged montmorillonite as catalysts.

2. Materials and instrumentation

Magnesium exchanged zeolite was prepared by ion exchange of H–Y (Sud-Chemie India Ltd. Si/Al = 1.5) at room temperature with 0.1 M $MgCl_2$ solution (0.05 mole of $MgCl_2$/g of zeolite) for three times. Rare earth exchanged Mg-Y zeolites were obtained by contacting Mg-Y with a 0.5 M nitrate solution of the metal (0.025 mole of nitrate/g of zeolite, obtained from Indian Rare Earths Ltd. Udyogamandal, Kerala) at 353 K for 24 h. All the samples were calcined after each exchange at temperatures from 423 to 773 K, and at 773 K for 5 h with a heating rate of 12 K/min with a constant air

blowing over the sample (60 mL/min). K-10 montmorillonite clay (Si/Al ratio 2.7) was procured from Aldrich Chemical Company. Ce-mont was prepared by treating K-10 montmorillonite with cerium nitrate hexahydrate (obtained from Indian Rare Earths Ltd., Udyogmandal, Kerala; 0.025 mole nitrate per gram clay) in aqueous acetone for 24 h [33,34].

The chemical composition of the rare earth exchanged Mg-Y zeolites were determined by EDX using a JEO JSM-840 A (Oxford make model 16211 with a resolution of 1.3 eV). Samples were prepared by dusting the zeolite powder onto a double-sided carbon tape mounted on a metal stub. It was then sputter coated with a thin film of gold to reduce charging effects and a minimization procedure was adopted to calculate the exact metal ion concentration. The crystalline nature of the materials was established by X-ray diffraction studies performed using a Rigaku D-max C X-ray diffractometer with Ni-filtered $CuK\alpha$ radiation ($\lambda = 1.5406$ Å) in an angular range 2θ from 5° to 50°. Infrared spectra were recorded using a Nicolet Impact 400FT IR spectrometer in the range 400–4000 cm^{-1}. BET surface area and pore volume measurements were performed using a Micromeritics Gemini surface area analyzer using N_2 adsorption technique at liquid nitrogen temperature. Acid structural properties were estimated using temperature programmed desorption (TPD) of ammonia with conventional equipment.

2.1. Reaction procedure

Cyclohexanone, acetophenone, and benzophenone purchased from Aldrich Chemical Company, USA and commercial-grade methanol (available from SD Fine Chemicals, India) were used as received. One-pot acetalization reactions of carbonyl compounds were carried out in a 50 mL glass batch reactor equipped with a magnetic stirrer, thermometer, water condenser and temperature controller. All the experiments were performed under gentle nitrogen flow. In a typical run, 10 mL of a 1:10 mixture of ketone and methanol was stirred with 250 mg of pre-activated catalysts (773 K) for 10 h under a slow stream of moisture-free nitrogen. Samples were withdrawn every 2 h and at the end of the reaction (after 10 h) and were analyzed with a Chemito GC1000 gas chromatograph equipped with a SE-30 capillary column (oven temperature 353–503 K, injector temperature 373 K, detector temperature 373 K). The products were further analyzed by GCMS using a Shimadzu-5050 instrument provided with a 30 m HP-30 capillary column of cross linked 5% phenylmethylsilicone. The detector voltage was 1 kV. The m/z values and relative intensity (%) are indicated for the significant peaks. (Conditions: column temperature was adjusted between 323 and 533 K with a heating rate of 10 K/min, injector and detector 513 and 563 K respectively.)

3. Results and discussion

3.1. Physicochemical properties

A detailed study of the characterization of the present catalyst systems has been already reported elsewhere [35,36]. The unit cell composition of various rare earth exchanged Mg–Y zeolites is depicted in Table 1. Rare earth exchange at 353 K does not change the crystalline nature of the zeolite. The parent and different rare earth exchanged zeolites crystallizes into cubic crystal system. Major shift in the framework vibrational bands is due to the strain in the framework in presence of bulky and heavily charged residual (Mg^{2+}) and counter (Ce^{3+}, La^{3+} and RE^{3+}) cations in the extra-framework cation locations (REMg–Y is a mixed rare earth exchanged zeolite with La^{3+} as the main counter cation and small amounts of Ce^{3+}, Pr^{3+} and Nd^{3+}, etc.). The major framework band shifts are presented in Table 1. In the hydroxyl region (3000–4000 cm^{-1}), a broad band is observed around 3450 cm^{-1} in all the samples, which is assigned to ν_{OH} of Si–O–H. Generally SiOH groups cause a band at/or around 3740 cm^{-1}. The large shift of the Si–O–H band to lower wave numbers is due to the possibility of hydrogen bonding of internal SiOH groups. Due to the in plane bending $\{\delta_{OH}(H_2O)\}$ of hydroxyl groups, a band around 1630 cm^{-1} is observed.

The surface area (S_{BET}) and the micro pore volume (V_{micro}) are presented in Table 2. Surface area and pore volume increase invariably on exchange with rare earth cations. The increase of surface area might be due to the decrease in the crystallite size and improvement in the microporous nature on exchange with the rare earth metal ions. K-10 montmorillonite clay is a layered aluminosilicate with a dioctahedral layer sandwiched between two tetrahedral layers. Unlike any other zeolites used, this does not have a regular pore structure [37]. The structure of the clay is constituted of both micropores and mesopores. The amount of mesopores is lesser when compared to the amount of micropores. This explains its

reduced surface area and pore volume when compared to zeolites (Table 2). However, the average pore size is greater than that of zeolites (>1.0 nm).

The acid structural properties of the samples were determined by thermodesorption of chemisorbed ammonia (NH_3 TPD). The method provides general information on the number and distribution of acid strength of the active sites. The amounts of ammonia desorbed were formally divided into three temperature ranges to denote three types of acid sites: (1) weak acid sites ranging from 373 to 473 K, (2) moderate acid strength, ranging from 473 to 673 K, and (3) high acid strength, ranging from 673 to 873 K as shown in Table 2. Ammonia desorption from acid sites occurred mainly at relatively low temperatures region (373–473 K) for HFAU-Y zeolites. Rare earth exchange invariably enhances the total acid amount of the zeolites. The major enhancement appears to be in the medium acid range portion (473–673 K). Lock and co-workers reported that desorption of ammonia in the moderate temperature range is due to potential Brönsted acid sites (BAS) [38]. This supports the generation of BAS through the hydrolysis of rare earth cations during temperature treatment. However, in these zeolites also the major amount of ammonia desorption is in the weak acid (373–473 K) region, which is physisorbed plus BAS. K-10 montmorillonite clay is rather weakly acidic (0.92 mmol/g) and the cumulative acid amount increases slightly on cerium exchange (1.02 mmol/g). In general, ammonia TPD studies shows that zeolites are far more acidic compared to clay.

3.2. Acetalization of ketones

Acetal or ketal formation is a reversible reaction, which proceeds by a two-step mechanism. Their formation is strongly affected by electronic and steric factors. The first step is the formation of hemiacetal, followed by the removal of a molecule of water (Scheme 1). Formation of a cation from the protonated hemiacetal is the

Table 1
Unit cell compositions and major infrared induced framework band shifts of pure HFAU-Y, binder free Mg Y, and different rare earth exchanged Mg-Y zeolites

Zeolite	Chemical composition[a]	Assymetric stretch (cm^{-1}) EL or IT[b]	Symmetric stretch (cm^{-1}) EL or IT[b]	Double ring[c] (cm^{-1})	T O bend[d] (cm^{-1})
H–Y	$H_{76.5}Al_{76.5}Si_{115.5}O_{384}$	1050	771	570	457
Mg–Y	$Mg_{18.29}Al_{76.58}Si_{115.42}O_{384}$	1067	777	579	466
CeMg–Y	$Ce_{11.38}Mg_{17.74}Al_{75.62}Si_{116.38}O_{384}$	1087	787	580	472
LaMg–Y	$La_{13.08}Mg_{18.51}Al_{76.25}Si_{115.75}O_{384}$	1100	782	578	472
REMg Y[e]	$La_{9.98}Ce_{2.52}Pr_{4.21}Nd_{4.91}Mg_{13.68}Al_{75.78}Si_{116.22}O_{384}$	1084	783	580	473

[a] As determined by energy dispersive X-ray analysis.
[b] EL, external linkage; IT, internal tetrahedral.
[c] D6R double ring units.
[d] T = Si, Al.
[e] REMg Y is a mixed rare earth exchanged zeolite with La^{3+} as the main counter cation and small amounts of Ce^{3+}, Pr^{3+} and Nd3$^+$, etc.

Table 2

Acid strength distribution and surface area and pore volume measurements of parent, different rare earth exchanged Mg–Y zeolites, K-10 montmorillonite and Ce-mont clays

Catalyst	Ammonia desorbed in the stipulated temperature ranges (K) in mmol/g				Textural properties		
	W[a,b]	M[b]	S[b]	Total acid amount	BET surface area (m²/g)	Langmuir surface area (m²/g)	Pore volume[c] (cm³/g)
H–Y	0.69	0.41	0.33	1.43	398	593	0.266
Mg–Y	0.60	0.51	0.18	1.29	301	438	0.252
CeMg–Y	1.21	0.63	0.44	2.28	497	728	0.312
LaMg–Y	0.71	0.43	0.28	1.42	455	681	0.294
REMg–Y	0.94	0.76	0.31	2.01	471	707	0.306
K-10-mont	0.55	0.24	0.13	0.92	183	304	0.204
Ce-mont	0.56	0.28	0.18	1.02	198	321	0.207

[a] The ammonia desorbed in the temperature range 373–473 K might contain small amounts of physisorbed ammonia too.

[b] W, M, and S stand for weak (373–473 K), medium (474–673 K), and strong (674–873 K) acidic sites.

[c] Total pore volume measured at 0.9976 P/P_0.

rate determining the step of acetalization reactions. However, the protonation of hemiacetal is also a slow step and the reaction medium has to be sufficiently acidic to promote efficient protonation of hemiacetal. Also, the reaction medium must be polar enough to stabilize of the cation intermediate formed from hemiacetal.

Scheme 1 envisages the mechanism of the acetal formation of ketones over zeolite catalyst by taking cyclohexanone as a typical example. In the mechanism presented below, cyclohexanone is first protonated by the Brönsted acid sites (H^+ ions of the catalyst) to produce the intermediate 2 which then combine with methanol to form the hemiacetal 4. Protonation of 4 leads to intermediate 5 which undergoes subsequent dehydration to give 6. Reaction of 6 with a molecule of methanol gives intermediate 7. Removal of a proton from 7 leads to the formation of the acetal 8.

We have used four classes of solid acid catalyst in this work for ketone acetalizations. They include; (1) rare earth exchanged Mg–Y zeolites, (2) K-10 montmorillonite clay, (3) cerium exchanged montmorillonite clay, and

(4) silica. Three ketones with different molecular size; cyclohexanone, acetophenone, and benzophenone were reacted with methanol to produce the corresponding dimethylacetals. The results of the studies are illustrated in Table 3.

Acetalization was studied both in presence of solid acid catalysts and without catalysts. Zeolites and clay are acidic enough to initiate acetalization reaction at moderate temperatures. However, from the reaction mechanism, it appears that the reaction proceeds with the formation of very bulky intermediates and a microporous material like zeolite may be less reactive in comparison to a mesoporous material. From this point of view, a study of materials with different pore topologies such as clays and zeolites for carrying out the synthesis of ketals of cyclohexanone, acetophenone, and benzophenone was undertaken. In all the cases only the corresponding ketal was obtained in the reaction mixture even after 10 h of reaction time.

In general, clays are found to be the more active catalyst with all ketones. Cerium exchanged montmorillonite clay is much more active compared to pure K-10
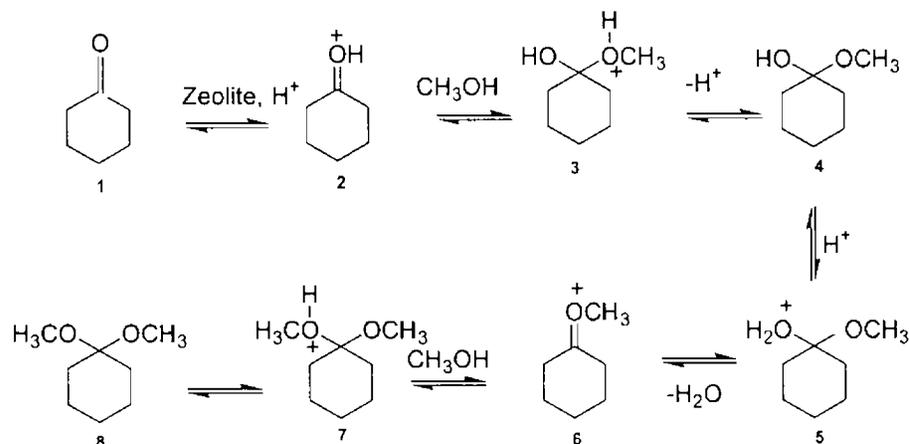
Scheme 1. General reaction mechanism for acetalization of ketones catalyzed by solid acid catalysts.

Table 3

Results obtained in the acetalization of cyclohexanone, acetophenone, and benzophenone with methanol over different solid acid catalysts

| Catalyst | Percentage conversion of ketones | | | | | |
| | Cyclohexanone[a] | | Acetophenone[b] | | Benzophenone[b] | |
	2 h	10 h	2 h	10 h	2 h	10 h
H–Y	43.6	49.9	4.4	7.6	1.2	2.4
Mg-Y	42.0	48.2	3.1	4.5	<1	1.3
CeMg–Y	69.8	75.1	11.5	18.7	2.3	4.8
LaMg–Y	56.5	62.3	7.2	9.9	1.8	3.3
REMg Y	59.0	64.7	8.3	11.3	1.9	3.7
K-10-mont	71.7	88.2	13.8	21.2	2.8	5.8
Ce-mont	78.9	96.8	21.2	28.6	4.1	7.2
SiO$_2$[c]	0	0	<1	1.2	0	0
None[d]	0	0	0	0	0	0
Filtrate[e]	0	0	0	0	0	0

Experimental conditions: Ketone:methanol molar ratio, 1:10; reaction temperature, ambient temperatures; catalyst amount, 250 mg; gentle flow of dry nitrogen.

[a] Reactions were carried out at room temperature under atmospheric pressure.

[b] Reactions were carried out at ambient temperature (353 K) and atmospheric pressure.

[c] SiO$_2$ was prepared by the acidification of an aqueous solution of sodium silicate followed by washing and calcinations at 773 K.

[d] Without catalyst.

[e] After the reaction over CeMg–Y zeolite, the catalyst was removed by filtration and the filtrate obtained was used to examine the catalytic activity of the possible dissolved components of the catalyst.

clay. Pure H–Y, binder free Mg–Y or various as-exchanged rare earth zeolites exhibit lower reactivity (Table 3) compared to the mesoporous clays. Among different zeolites, CeMg–Y is found to be the most active (69.8% vs 42% for Mg–Y zeolite) towards the acetalization reactions and Mg–Y the least. Silica exhibits negligible activity for the reaction. There was no predominant increase in the percentage conversion with reaction time. Among different ketones, cyclohexanone shows maximum conversion to the corresponding acetal; whereas benzophenone the least. Ce-mont shows a conversion of 78.9% in 2 h with cyclohexanone, 21.2% with acetophenone and 4.1% with benzophenone whereas; with CeMg–Y it is 69.8%, 11.5%, and 2.9% respectively. No conversion was observed while blank run (without catalyst).

We shall now consider the difference in activity of zeolites and clays towards acetalization reaction. Table 2 shows that zeolites are far more acidic compared to K-10 clays. If we consider the acid structural properties (see Table 2), zeolites must be far more active than clay. According to TPD studies, CeMg–Y was the most acidic and had the highest number of acid sites (2.28 mmol/g) among the catalysts. However, CeMg–Y zeolite produced only a small amount of acetal in 2 h (Table 3). K-10 clay has an acid amount far inferior (cumulative; 0.92 mmol/g) to any as-exchanged zeolite. However, it produces more acetal with any of the ketone than CeMg–Y. The catalytically active sites involved in the reaction were thought to be bridging hydroxyl groups, which must be related to the presence of tetrahedrally coordinated aluminium in the structure. The bridging hydroxyl groups present in much larger amounts in

zeolites than clays and must have much higher intrinsic activity than clays which have weaker acid sites related to silanol groups [31]. Thus, it is not only the acidic structure of the catalysts which determine the acetalization ability to a greater extent. The activity of catalyst towards the acetalization reaction does not require strong acidic sites [31]. As pointed out by Corma and co-workers the pore diffusion limitation imposed by larger molecular sizes (0.75, 1.03 and 1.19 nm respectively for cyclohexanone, acetophenone and benzophenone; as determined by the energy minimization program) of the reactant played an important role during the acetalization reaction using zeolite catalysts [27,28].

Based on the above arguments, it appears that rather than the acid structural properties, the diffusional properties of the catalytic systems are the deciding factor in the acetalization reaction of ketones. H–Y has a 3-D interconnecting pore systems with super cages of 1.18 nm connected by circular 12-ring 0.74 nm windows [39]. Montmorillonite clay is a layered alumino-silicate with a dioctahedral layer sandwiched between two tetrahedral layers. The average pore size is greater than zeolites (>1.0 nm). SiO$_2$ does not have a regular pore structure. As pointed earlier the pore diffusion limitation induced by the molecular size of the reactant played an important role during the acetalization reaction using zeolite catalyst [27,28]. Therefore only a fraction of the acid sites on the outer surface of the zeolites are available for reactants and practically higher product yield could only be attained by performing the reaction for long time (69.8% in 2 h and 75.1% in 10 h). K-10 clay and Ce-mont are mesoporous materials and the effect of pore diffusion is not as critical as in the case of

zeolites. This explains the comparative low (conversion range from 56.5% to 69.8% in 2 h with cyclohexanone for different rare earth Mg–Y zeolites) activity of as-exchanged rare earth zeolites than low acidic mesoporous K-10 montmorillonite clay (conversion is 71.7% in 2 h). The bigger pore size of clays over zeolites promotes the rate of diffusion of the bulky products through the channels.

Now, we shall consider the variation of activity in different zeolites. Comparing H–Y and various rare earth zeolites, the yield of acetal on rare earth zeolites is much more than pure H–Y. HFAU-Y zeolite produces 43.6%, 4.4% and 1.2% acetal with cyclohexanone, acetophenone and benzophenone respectively whereas, the as-exchanged CeMg–Y produce 69.8%, 11.5% and 2.9% of respective acetals. This enhancement in catalytic activity could be explained in terms of improvement in textural and structural properties (see Table 3). Enhancement in the total pore volume could provide a better diffusional pathway for the bulky acetals. The enhanced formation of acetal over rare earth exchanged zeolites could also be explained as follows. In general, rare earth exchanged zeolites possess much more amounts of weak plus medium acid sites (see Table 2) and an assembly of these weak acid sites may act as an effective/strong acid site. A reasonable hypothesis is that all the surface hydroxyl groups on the pore wall of the zeolite point to the center of each pore, and thus they could work as a group. Such an assembly might induce efficient catalysis despite the low acidity of each OH group [27,29,30]. In the case of zeolites, the surface hydroxyl groups provide most of the weak acid sites.

Cerium exchanged materials; both CeMg–Y and Ce-mont produce comparatively larger amounts of acetals than other rare earth exchanged zeolites and K-10 montmorillonite clay. Tateiwa and co-workers reported the acetalization of carbonyl compounds with methanol in presence of different cation exchanged montmorillonite clay (M^{n+}-mont; M^{n+} = Ce^{3+}, Zr^{4+}, Fe^{3+}, Al^{3+}, Zn^{3+}, H^+, and Na^+) [26]. They proposed that in the case of Ce-mont the carbonyl oxygen presumably coordinates to Ce^{3+} cation in the interlayer space as well as to an aluminium atom (Lewis acid site) in the framework clay facilitating active adsorption of ketones [26,40]. Ce-mont was found to be the most effective catalysts for the substrate-selective acetalization. The high catalytic activity of K-10 clay and Ce-mont (Table 3) are comparable to those of sulphonic acid resins [41,42]. RENa-Y zeolite yields comparatively larger amounts of acetal (59.0%, 8.3% and 1.9% respectively with cyclohexanone, acetophenone and benzophenone) with all ketones than LaMg–Y. Presence of small amounts of cerium (see Table 1) might be the reason for the enhanced production of acetal over REMg–Y. It is worth noting that, in the case of cyanosilation and Mukaiyama aldol reaction, the carbonyl group was activated by a strong Brönsted

acid site induced by exchangeable cations (Fe^{3+} and Al^{3+}) in the interlayer space. The optimum number of acidic sites as well as dehydrating ability of CeMg–Y zeolite and Ce-mont clay drive the equilibrium of the reaction towards the acetal side with near complete conversion of some carbonyl compounds. Also, a Ce^{3+} ion acts as a Lewis acid site and activates the carbonyl group by coordination, in the order of 1 kJ/mol [26].

We have checked the complete heterogeneity of the reaction. After the reaction over a typical catalyst (CeMg–Y zeolite for acetalization of cyclohexanone in the present study), the catalyst was removed by filtration and the filtrate obtained was used to examine the catalytic activity of the possible dissolved components of the catalyst. The filtrate was further subjected to acetalization reaction for 2 h. No noticeable conversion of ketone to acetal was observed.

3.3. Effect of reaction time

Acetalization of cyclohexanone was measured over CeMg–Y, K-10 montmorillonite clay, and Ce-mont clay as a function of reaction time. No product other than acetal was detected by careful GC and GC-MS analysis of the reaction mixture even after 50 h of reaction. The effect of reaction time on acetal formation is shown in Fig. 1. The reaction reached equilibrium within 60 min, and the yield of acetal was 66.7% with CeMg–Y zeolite. Once the reaction attains equilibrium in 1 h (66.7% in 1 h), there is slight increase in the formation of acetal over CeMg–Y zeolite (80.5% in 50 h). On the other hand, K-10 montmorillonite and Ce-mont, while having
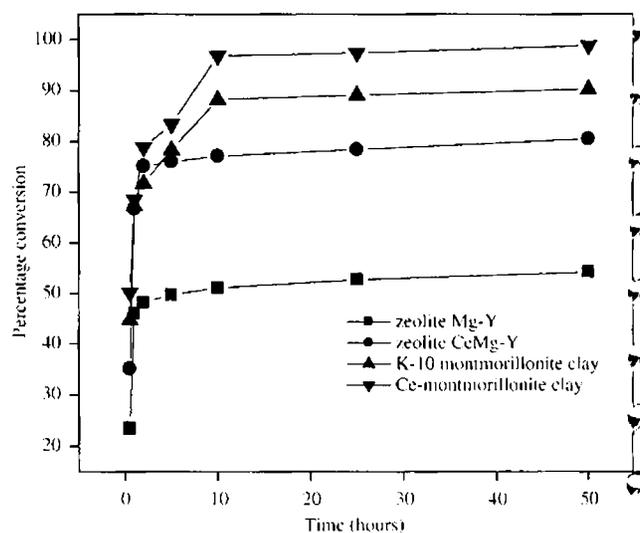

Fig. 1. Effect of reaction time on the formation of 1,1-dimethoxycyclohexane with methanol over Mg Y, CeMg–Y zeolites, K-10 montmorillonite, and Ce-mont clays. Experimental conditions: Cyclohexanone: methanol molar ratio, 1:10; reaction temperature and pressure, room temperature under atmospheric pressure; catalyst amount, 250 mg; gentle flow of dry nitrogen.

slightly higher initial activities (67.3% and 69.8% respectively in 1 h), can achieve a final larger conversion (90.2% and 98.8% in 50 h). This is due to major deactivation of the zeolite catalyst. Bulky reaction products and intermediates formed can adsorb in zeolite-Y blocking the pores and/or the active sites leading to a loss of catalytic activity. The adsorption of products on the large pores of K-10 and Ce-mont (>1.0 nm) clays are only to a limited extent and hence we observe an increase in the yield of dimethoxycyclohexane with time (limited deactivation compared with zeolites).

We have observed that deactivated catalysts can be partially regenerated by solvent extraction to remove most of the bulky products. Thus, the spent catalysts (CeMg–Y zeolite, K-10 mont and Ce-mont) were subjected to continuous solid–liquid extraction with dichloromethane several times. These as-extracted samples show less than 50% of activity for the reaction. These samples were then regenerated by activating at 773 K for 5 h under constant flow of nitrogen (60 mL/h). Repeated use of the catalyst for a third time showed no substantial loss of activity. CeMg–Y produces 66.3% acetal in 1 h, K-10 montmorillonite 67.1% and Ce-mont 68.8%. The catalyst deactivation studies indicate that while zeolites and K-10 clay have slightly different initial activity, zeolites deactivate much more rapidly than K-10 clay owing to the larger adsorption and lower diffusion rates of the products in the microporous structure.
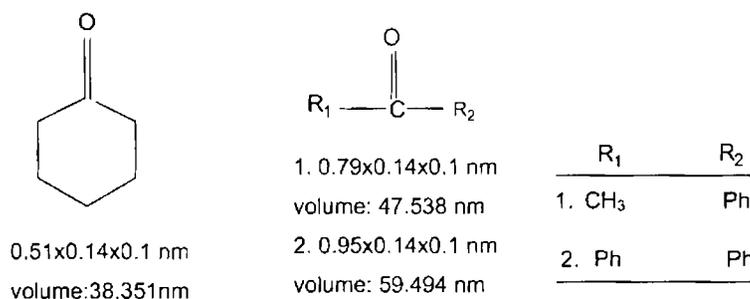
3.4. Effect of molecular size of ketones

The diffusion of the reactants through a given pore size is a factor of the molecular size of the ketones. The reactivity of the ketones decreases in the order cyclohexanone > acetophenone > benzophenone (Table 3). The difference in the acetalization activity among different ketones could be correlated to their molecular sizes and volumes. The molecular size and volume of the different reactants have been measured using a molecular docking simulation and are presented in Scheme 2. We have employed the molecular modeling program CERIUS2 (MSI, USA) using COMPASS force field calculation for molecular size determination.

Scheme 2 depicts the molecular sizes of the ketones examined by us and their corresponding volumes.

In the case of cyclohexanone; the distance between oxygen and the most distant hydrogen is 0.51 nm; the van der Waals radius of oxygen is 0.14, and that of hydrogen is 0.1 nm leading to an effective end-to-end distance of 0.75 nm. Its volume is estimated at 38.351 nm^3. Applying similar strategy, the molecular sizes of acetophenone and benzophenone were found to be 1.03 nm (volume 43.578 nm^3) and 1.19 nm (volume 59.494 nm^3). It is seen from the above molecular size and volume calculations that both follow the order cyclohexanone < acetophenone < benzophenone. The efficiency of acetalization of the three ketones over different solid acid catalysts follows the reverse order.

Tateiwa et al. reported that the adsorption of acetophenone to the interlayer space of Ce-mont clay is very low and no peaks were observed from the FT-IR spectra from compounds even after prolonged treatment [26]. The rate determination step of acetalization is the formation of a cation from the protonated hemiacetal. Lin and co-workers proposed that the bulkiness of hemiacetal of acetophenone might prevent the also bulky CH$^+$ (OCH$_3$) from attacking its carbonyl carbon shifting the rate determining step during the acetalyzation with trimethoxy orthoformate [25]. Hence, we conclude that the comparative low activity of acetophenone and benzophenone might be due to two reasons: (1) The bulkiness of hemiacetals might prevent the attack of the CH$_3$ OH on the carbonyl carbon atom there by effecting a change in the rate-determining step. (2) The electron withdrawing power of phenyl group (1 for acetophenone and 2 for benzophenone) in these compounds reduces the easy release of the pair of electron on the carbonyl carbon during the reaction. But we cannot overemphasize the role of molecular size on reactivity since it is known that cyclohexanone is more reactive towards nucleophiles than both acetophenone and benzophenone (taken in that order) [43]. Studies addressed towards the extension of this protocol to other types of substituted ketones are currently under investigation to examine the exact reason for the difference in the reactivity. These preliminary results, in principle, afford an

O
‖
(cyclohexanone structure)

0.51x0.14x0.1 nm
volume:38.351nm

O
‖
R₁ —— C —— R₂

1. 0.79x0.14x0.1 nm
volume: 47.538 nm

2. 0.95x0.14x0.1 nm
volume: 59.494 nm

	R₁	R₂
1.	CH₃	Ph
2.	Ph	Ph

Scheme 2. Molecular sizes and the corresponding volumes of different ketones.

attractive alternative for the protection of carbonyl compounds.

4. Conclusion

Microporous rare earth exchanged Mg–Y zeolites and mesoporous K-10 montmorillonite and Ce-mont clays can effectively catalyze the reaction between carbonyl compounds and methanol producing dimethyl acetal at ambient temperatures. CeMg–Y zeolite, K-10 clay, and Ce-mont clay were revealed to be the most efficient catalysts for the reaction. The characteristic features of Ce-mont are its proper acid amount and drying ability which drive the acetalization reaction equilibrium in favor of acetal side. Also, Ce^{3+} cation acts as a Lewis acid site and activates the carbonyl group by coordination, on the order of 1 kJ/mol. Cyclohexanone reacted smoothly in methanol at room temperature with solid acid catalysts. On the other hand, aromatic ketones, namely acetophenone and benzophenone reacted only at high temperature, but with a much lower conversion. The acetalization activity follow the order cyclohexanone > acetophenone > benzophenone. Hence, when reactants with molecular size greater then 0.75 nm (cyclohexanone; 0.75 nm) are used, geometrical constraints do not allow the reactants to diffuse inside the pores of the zeolites and only the external surfaces of these materials become available for the reactants. We have developed a mild, efficient and environmentally benign protocol for the preparation of acetals of carbonyl compounds using heterogeneous catalysts. The method developed by us does not involve additives and the catalysts can be recycled without loss of activity. Removal of water is not warranted in these reactions.

References

[1] T.W. Green, P.G.M. Wuts, Protective Groups on Organic Synthesis, vol. 4, 2nd ed., Wiley, New York, 1991, p. 212.

[2] P. Grice, S.V. Ley, J. Pietruszka, H.W.M. Priepke, Angew. Chem. Int. Ed. Engl. 35 (1996) 197.

[3] S.V. Ley, R. Downham, P.J. Edwards, J.E. Innes, M. Woods, Contmp. Org. Synth. 2 (1995) 365.

[4] S.V. Ley, H.W.M. Priepke, S.L. Warriner, Angew. Chem. Int. Ed. Engl. 33 (1994) 2290.

[5] S.V. Ley, H.W.M. Priepke, Angew. Chem. Int. Ed. Engl. 33 (1994) 2292.

[6] P. Grice, S.V. Ley, J. Pietruszka, H.W.M. Priepke, S.L. Warriner, J. Chem. Soc., Perkin Trans. 1 (1997) 351.

[7] P. Grice, S.V. Ley, J. Pietruszka, H.W.M. Priepke, E.P.E. Walther, Synlett (1995) 781.

[8] M.J. Climent, A. Velty, A. Corma, Green Chem. 4 (2002) 565.

[9] K. Bauer, D. Garbe, H. Surburg, Common Fragrances and Flavour Materials, 2nd ed., VCH, New York, 1990.

[10] D.M. Clode, Chem. Rev. 79 (1979) 224.

[11] S.V. Ley, H.W.M. Priepke, Angew. Chem. 106 (1994) 2412.

[12] K. Bruns, J. Conard, A. Steigel, Tetrahedran 35 (1979) 2523.

[13] M.-K. Cheung, N.L. Douglas, B. Hinzen, S.V. Ley, X. Pannecoucke, Synlett (1997) 257.

[14] K. Narasaka, M. Inone, T. Yamada, J. Sugiomori, N. Iwasawa, Chem. Lett. (1987) 2409.

[15] A.J. Elliot, 1,3-Dioxalane Polymers in Comprehensive Heterocyclic Polymers1,3-Dioxalane Polymers in Comprehensive Heterocyclic Polymers, vol. 6, Pergamon Press, Oxford, UK, 1984.

[16] S. ArctanderPerfumary and Flavour Chemicals, vols. I and II, Allured Publishing, New York, 1969.

[17] G.A. BurdockFenaroli's Handbook of Flavour Ingradients, vol. 2, CRC, New York, 1995.

[18] T.W. Greene, Protective groups in Organic Synthesis, Wiley-Interscience, New York, 1981, p. 178.

[19] J. Bornstein, S.F. Bedell, P.E. Drummond, C.F. Kosoloki, J. Am. Chem. Soc. 78 (1956) 83.

[20] G. Strukul, Top. Catal. 19 (1) (2002) 33.

[21] C.A. McKinzie, J.H. Stocker, J. Org. Chem. 20 (1955) 1695.

[22] M. Cataldo, F. Neiddu, R. Gavagnin, F. Pinna, G. Strukul, J. Mol. Catal. A: Chem. 142 (1999) 305.

[23] E. Neiddu, M. Cataldo, F. Pinna, G. Strukul, Tetrahedran Lett. 40 (1999) 6987.

[24] F. Gorla, L.M. Venanzi, Helv. Chim. Acta. 73 (1990) 690.

[25] C.-H. Lin, S.D. Lin, Y.-H. Yang, T.-P. Lin, Catal. Lett. 73 (2-4) (2001) 121.

[26] J. Tateiwa, H. Hiriuchi, S. Uemura, J. Org. Chem. 60 (1995) 4043.

[27] A. Corma, M.J. Climent, H. Garcia, J. Primo, Appl. Catal. A: Gen. 59 (1990) 333.

[28] R. Ballini, G. Bosica, B. Frullanti, R. Maggi, G. Sartori, F. Schroer, Tetrahedron Lett. 39 (1998) 1615.

[29] F. Algarre, A. Corma, H. Garcia, J. Primo, Appl. Catal. A: Gen. 128 (1995) 119.

[30] M. Iwamoto, Y. Tanaka, N. Sawamura, S. Namba, J. Am. Chem. Soc. 125 (43) (2003) 13033.

[31] M.J. Climent, A. Corma, S. Iborra, M.C. Navarro, J. Primo, J. Catal. 161 (1996) 783.

[32] Y. Tanaka, N. Sawamura, M. Iwamoto, Tetrahedron Lett. 39 (1998) 9457.

[33] J. Tateiwa, H. Horiuchi, H. Hashimoto, T. Yamauchi, S. Uemura, J. Org. Chem. 59 (1994) 5901.

[34] J. Tateiwa, H. Horiuchi, S. Uemura, Bull. Chem. Soc. Jpn. 67 (1994) 2883.

[35] B. Thomas, S. Sugunan, Micropor. Mesopor. Mater. 72 (2004) 227.

[36] B. Thomas, S. Sugunan, Indian J. Chem. A 43 (2004) 2503.

[37] A.V. Ramaswamy, Sci. Tech. Chim. Ind. (2000) 1.

[38] B.M. Lok, B.K. Marcus, C.L. Angell, Zeolites 6 (1986) 185.

[39] W.H. Baur, Am. Mineral. 49 (1964) 697.

[40] K. Higuchi, M. Onaka, Y. Izumi, Bull. Chem. Soc. Jpn. 66 (1993) 2016.

[41] G.A. Olah, S.C. Narang, D. Meidar, G.F. Salem, Synthesis (1981) 282.

[42] S.A. Patwardhan, S. Dev, Synthesis (1974) 348.

[43] C.D. Gutsche, The Chemistry of Carbonyl Compounds, Prentice-Hall of India (P) Ltd., New Delhi, 1975, p. 71.