The synthesis and hydrolysis of dimethyl acetals catalyzed by sulfated metal oxides. An efficient method for protecting carbonyl groups

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Sulfated metal oxides including SO_4^{2-}/ZrO_2, SO_4^{2-}/TiO_2, SO_4^{2-}/HfO_2, SO_4^{2-}/Fe_2O_3, SO_4^{2-}/SnO_2, and SO_4^{2-}/Al_2O_3 were highly efficient catalysts for the reaction of aldehydes and ketones with trimethyl orthoformate producing dimethyl acetals under mild reaction conditions. At room temperature, dimethyl acetal yields of 83–100% were obtained for the five carbonyl compounds chosen. These mesoporous solid acids also effectively catalyzed the hydrolysis of dimethyl acetal to regenerate the original carbonyl compounds in aqueous acetone. They not only provided an effective method for synthesizing dimethyl acetals of larger molecular size but also acted as a versatile catalyst for protecting and deprotecting carbonyl groups during organic synthesis.

KEY WORDS: sulfated; trimethyl orthoformate; dimethyl acetal; carbonyl; hydrolysis

1. Introduction

Recently, sulfated metal oxides (SMO) have been the focus of intensive research worldwide due to their high efficiencies in catalyzing the hydroisomerization of paraffins [1–4]. These SMO include sulfated oxides of ZrO_2, TiO_2, Fe_2O_3, SnO_2, Al_2O_3, HfO_2, and SiO_2 [5]. They were mesoporous materials containing both Brønsted and Lewis acid sites. Although SMO displayed a stronger acidity than other solid acids such as zeolite, Nafion-H, and heteropolyacid, most of their applications were limited to petrochemistry [6]. Compared with other solid acids, very few investigations have been reported thus far on the application of SMO in the synthetic organic chemistry, and their potentials in this field have not yet been fully explored.

In this paper, we want to report a highly efficient method for the synthesis of dimethyl acetals from ketones and aldehydes at room temperature utilizing the SMO as catalysts. Trimethyl orthoformate was used as the acetalization reagent. The reaction is depicted as

$$\begin{aligned} &R_1R_2C{=}O + HC(OCH_3)_3 \\ &\quad \rightarrow R_1R_2C(OCH_3)_2 + HCOOCH_3 \qquad (1) \end{aligned}$$

Catalysts reported for this reaction included sulfuric acid [7], *p*-toluenesulfonic acid [8], montmorillonite clay [9], iron (III) chloride [10], sulfonic acidic resins [11,12], and zeolites [13,14].

While some of these catalysts did have their own merits, they had drawbacks such as the low yield, corrosive catalyst, separation requiring tedious aqueous workup, reagent requiring pre-adsorption, or steric restriction imposed by the molecular size. We had found that SMO were excellent catalysts for this reaction under mild reaction conditions. At room temperature, the catalyzed reaction could achieve a minimum of 83% of dimethyl acetal yield for all the carbonyl compounds tested. Interestingly, we found that SMO were also effective in catalyzing the hydrolysis of dimethyl acetals to regenerate the starting ketones and aldehydes.

Since dimethyl acetals displayed a higher stability toward strong bases, $LiAlH_4$, and Grignard reagent than their parent carbonyl compounds, SMO provided a convenient catalytic route for protecting and deprotecting the carbonyl groups during the organic synthesis. It should be noted that methyl and ethyl acetals, particularly of *n*-octanal and *n*-decenal, have widespread applications in perfume and flavor industries [15].

2. Experimental

2.1. Catalyst preparation

The sulfated metal oxides were prepared according to the method reported in the literature [5]. Except for SO_4^{2-}/Al_2O_3, all the SMO were prepared by immersing the proper metal hydroxides into a sulfuric acid solution. The mixture was filtered, dried, and calcined at a proper temperature. The metal hydroxides were obtained by precipitating their metal salt solutions with aqueous ammonia (29.5%) to a final pH. The calcination temperatures and the final pH of the precipitating solution are listed in table 1. The surface area for SO_4^{2-}/ZrO_2 calcined at 625 °C was 95 $m^2\,g^{-1}$ and that for SO_4^{2-}/TiO_2 was 85 $m^2\,g^{-1}$. The metal salts

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Table 1
Synthesis of dimethyl acetals using SMO catalysts in CCl_4.[a]

Catalyst	Calcination temp. (°C)/pH	Dimethyl acetal yield (%)
SO_4^{2-}/ZrO_2	625/9.0	100
SO_4^{2-}/TiO_2	525/9.0	100
SO_4^{2-}/SnO_2	550/9.5	95
SO_4^{2-}/HfO_2	700/9.0	100
SO_4^{2-}/Fe_2O_3	500/8.0	99
SO_4^{2-}/Al_2O_3	550	90
HY	400	15
HM	400	63
Blank rexn.[b]	–	0

[a] Reaction took place at ambient temperature and for 30 min using 0.5 g of catalyst, 15 mmol of cyclohexanone, 55 mmol of trimethyl orthoformate, and 20 ml of CCl_4.

[b] No catalyst was used.

used were $ZrOCl_2 \cdot 8H_2O$, $Ti[OCH(CH_3)_2]_4$, $SnCl_4 \cdot 5H_2O$, $Fe(NO_3)_3 \cdot 9H_2O$, and $HfCl_4$. Sulfated alumina was prepared by immersing γ-Al_2O_3 in 1.60 M sulfuric acid solution followed by calcining at 550 °C. HY ($SiO_2/Al_2O_3 = 5.2$) and H-mordenite ($SiO_2/Al_2O_3 = 12$) were prepared by an ion-exchange method: 10 g of sodium form of molecular sieves were treated with 100 ml of 1.0 M of HCl at 90 °C and the procedure was repeated three times. The material after ion-exchange was filtered and rinsed with deionized water until free from Cl^- ions. They were then dried at 100 °C overnight and calcined at 400 °C for 3 h.

2.2. Catalytic activity test and TPD/NH_3 experiments

To synthesize the dimethyl acetal, 15 mmol of ketone or aldehyde were mixed with 55 mmol of trimethyl orthoformate in 20 ml of solvent. This mixture was added to 0.50 g of SMO contained in a flask under nitrogen atmosphere and reacted with stirring for a specific amount of time at room temperature. At the end of the reaction, the mixture was separated from the solid catalyst by filtration. The filtrate was analyzed by GC using an internal standard method. The hydrolysis of dimethyl acetal was performed in aqueous acetone (H_2O : acetone = 1 : 20 volume ratio) in a similar manner.

Temperature-programmed desorption (TPD) experiments using ammonia as adsorbate and TCD as detector were performed on some of the catalysts to compare their acidity. Before introducing NH_3, 0.2 g of catalyst was dried at 350 °C for 1.0 h in a 20 v/v % O_2/He mixture flowing at a rate of 45 ml min^{-1}. The adsorption step was conducted at 100 °C using flowing NH_3 of 30 ml min^{-1} for 20 min. After adsorption, the gas flow was switched to 30 ml min^{-1} of He for 20 min to flush out the excess NH_3. The reactor temperature then was raised to 800 °C at a rate of 10 °C min^{-1} in flowing He of 45 ml min^{-1}. The TPD spectrum of HM had been corrected for water desorbed at temperatures higher than 400 °C by subtracting a blank spectrum without using NH_3.

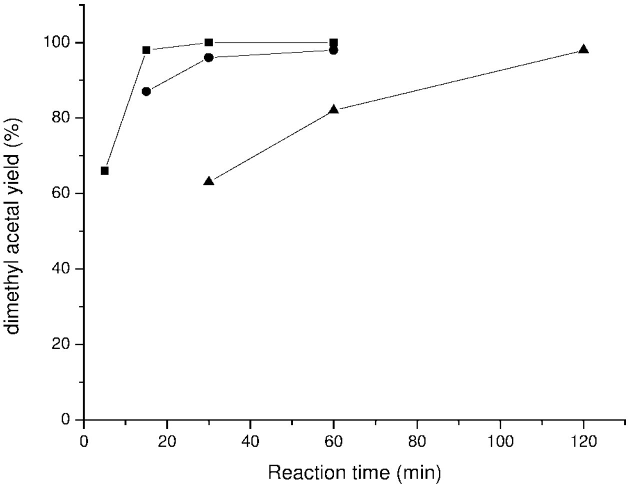


Figure 1. Effect of the amount of catalyst on dimethyl acetal yield of cyclohexanone at room temperature (●) 0.50 g SO_4^{2-}/ZrO_2, (■) 0.15 g SO_4^{2-}/ZrO_2, and (▲) 0.5 g HM.

3. Results and discussion

The efficiency of SMO to form dimethyl acetal was demonstrated by the reaction of cyclohexanone with trimethyl orthoformate over SO_4^{2-}/ZrO_2. The results are depicted in figure 1. As clearly shown in figure 1, at room temperature a quantitative transformation of cyclohexanone in CCl_4 was achieved in 30 min over 0.50 g of SO_4^{2-}/ZrO_2. When the amount of SO_4^{2-}/ZrO_2 was reduced to 0.15 g, an acetal yield of 96% could still be obtained. The reaction was highly selective. Except for a small amount of methanol, dimethyl acetal and methyl formate were the only products observed. There was no detectable dimethyl acetal in the absence of the catalyst. Such high catalytic activity and selectivity are comparable to those of sulfonic acidic resins and K-10 montmorillonite clay [9,11,12], but superior to those of HY and MCM-41 molecular sieves [13,14].

The yields of dimethyl acetal of cyclohexanone over other SMO were also screened (table 1). HY and H-mordenite (HM) zeolites were tested to compare their catalytic effectiveness with SMO in the reaction. Table 1 indicates that in addition to SO_4^{2-}/ZrO_2, other SMO were also very active and selective in producing the dimethyl acetal from cyclohexanone. For example, a dimethyl acetal of 100% was obtained over the more active SO_4^{2-}/TiO_2, but even for the least active SO_4^{2-}/Al_2O_3, a 90% dimethyl acetal yield could still be achieved at room temperature in 30 min. Interestingly, under the same reaction conditions the dimethyl acetal yields of HM and HY were only 63 and 15%, respectively. Nonetheless, after a reaction period of 120 min, an acetal yield of 98% could be achieved over the HM catalyst (figure 1). Furthermore, it is interesting to note that SO_4^{2-}/Fe_2O_3 could achieve a comparable acetal yield (99%) as those of SO_4^{2-}/TiO_2 and SO_4^{2-}/ZrO_2. The former was known to be much less acidic than the latter two catalysts [5].

TPD experiments were performed on SO_4^{2-}/TiO_2, SO_4^{2-}/Fe_2O_3, and HM in order to reveal the distribution of the

Table 2
The distribution of the strength and the number of acid sites in the catalysts.

Catalyst	Desorption temperature and amount					
	Strong acid sites		Medium-strong acid sites		Weak acid sites	
	Peak temp./range (K)	Amount (μmol g^{-1})	Peak temp./range (K)	Amount (μmol g^{-1})	Peak temp./range (K)	Amount (μmol g^{-1})
SO_4^{2-}/TiO_2	808/723–843	50	– /543–723	51	475/373–543	42
SO_4^{2-}/Fe_2O_3	713/623–793	85	– /543–623	23	475/373–543	35
HM	852/683–1073	93	– / 543–683	24	472/373–543	51

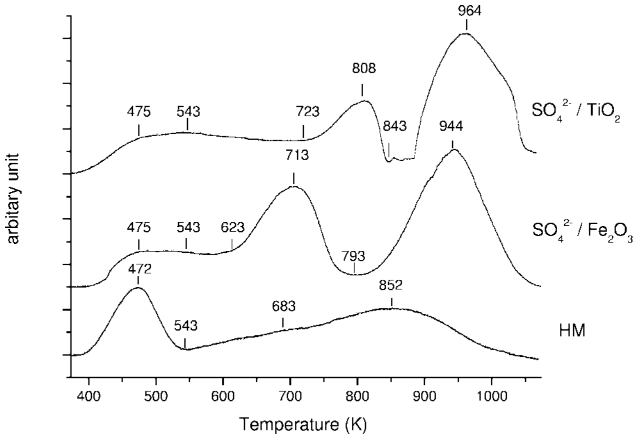


Figure 2. The distribution of the number and the strength of acid sites in the catalysts measured by TPD/NH_3; (a) SO_4^{2-}/TiO_2, (b) SO_4^{2-}/Fe_2O_3, and (c) HM catalysts.

Table 3
Synthesis[a] and hydrolysis[b] of dimethyl acetals catalyzed over SO_4^{2-}/ZrO_2.

Carbonyl compound	Dimethyl acetal yield (%)	Yield of carbonyl compounds upon hydrolysis (%)
Cyclohexanone	100	100 (0.5 h)
Heptanal	100	89 (5 h)[c]
Benzaldehyde	98	96 (3 h)
Acetophenone	83 (24 h)	100 (3 h)
Phenylacetaldehyde	88	60 (24 h)[c]

[a] Reaction took place at ambient temperature unless specified and for 30 min using 0.5 g of SO_4^{2-}/ZrO_2, 15 mmol of carbonyl compound, 55 mmol of trimethyl orthoformate, and 20 ml of CCl_4.

[b] Reaction took place at ambient unless specified and for an indicated amount of time using 0.15 g of SO_4^{2-}/ZrO_2, 14 mmol of dimethyl acetal, and 40 ml of aqueous acetone.

[c] Reaction took place at 50 °C.

strength and the number of the acid sites in these catalysts. The results are summarized in figure 2 and table 2. The high temperature peak at 964 K for SO_4^{2-}/TiO_2 and that at 944 K for SO_4^{2-}/Fe_2O_3 were due to the decomposition of SO_4^{2-} in these catalysts since they were also observed in the absence of NH_3. In addition to the decomposition peak, a well-defined peak at 808 K and an asymmetric peak at 475 K were observed for SO_4^{2-}/TiO_2. The former was attributed to the desorption of NH_3 from the strong acid sites and the latter from the weakly adsorbed NH_3. In between these two peaks, there was a plateau area (543–723 K) which was attributed to the desorption of NH_3 from the medium-strong acid sites.

A similar distribution of acid sites was found in SO_4^{2-}/Fe_2O_3, albeit that the NH_3 desorption peak of strong acid sites in SO_4^{2-}/Fe_2O_3 was located at 713 K and the plateau area (543–623 K) arising from the medium-strong acid site was smaller. Surprisingly, HM displayed a NH_3 desorption peak at a much higher temperature, 852 K, and its medium-strong acid sites appeared as a left shoulder of the high peak (543–683 K). TPD results indicated that the order of the acid strength is HM $>$ SO_4^{2-}/TiO_2 $>$ SO_4^{2-}/Fe_2O_3.

Since the less acidic SO_4^{2-}/Fe_2O_3 was as active as the more acidic SO_4^{2-}/TiO_2 in this reaction, it was reasonable to postulate that both the strong and medium-strong acid sites in SMO were the active sites for the reaction. This hypothesis is supported by the data in table 2: Although SO_4^{2-}/TiO_2 had stronger acid sites than SO_4^{2-}/Fe_2O_3, the sum of the number of medium-strong and strong acid sites was about the same in both catalysts (101 μmol g^{-1} vs. 108 μmol g^{-1}). Therefore, SO_4^{2-}/Fe_2O_3 was able to achieve the same level of product yield as SO_4^{2-}/TiO_2 if medium-strong acid sites were also acidic enough to catalyze the reaction. Such assumption was further supported by what was observed with a MCM-41 catalyst [13]. It was reported that the more acidic Si–OH–Al as well as the weakly acidic silanol group in MCM-41 could catalyze the acetalization reaction.

According to TPD results, HM was the most acidic catalyst and had the highest number of strong plus medium-strong acid sites (117 μmol g^{-1}) among the three catalysts. However, it produced a lower acetal yield for the first 30 min (figure 1). As pointed out by Corma, the pore diffusion limitation imposed by the larger molecular size of the reactant played an important role during the acetalization reaction using zeolite catalyst [13,14]. Therefore, only the fraction of acid sites on the outer surface of HM was available to reactants, and a higher product yield could only be achieved at a longer reaction period. SMO are mesoporous materials [5] and the effect of the pore diffusion was not as critical as in the case of zeolite.

The reactivies of other carbonyl compounds such as 2-heptanone, benzaldehyde, acetophenone, and phenylacetaldehyde were examined for the reaction and the resulting dimethyl acetal yields were exceptional. A minimum acetal yield of 83% could be achieved for these compounds (table 3). The lower reactivity of acetophenone might be due to the formation of a stable cation species (see below). Since one of our goals is to provide a method for protecting the

Table 4
Synthesis of dimethyl acetals in different solvents.[a]

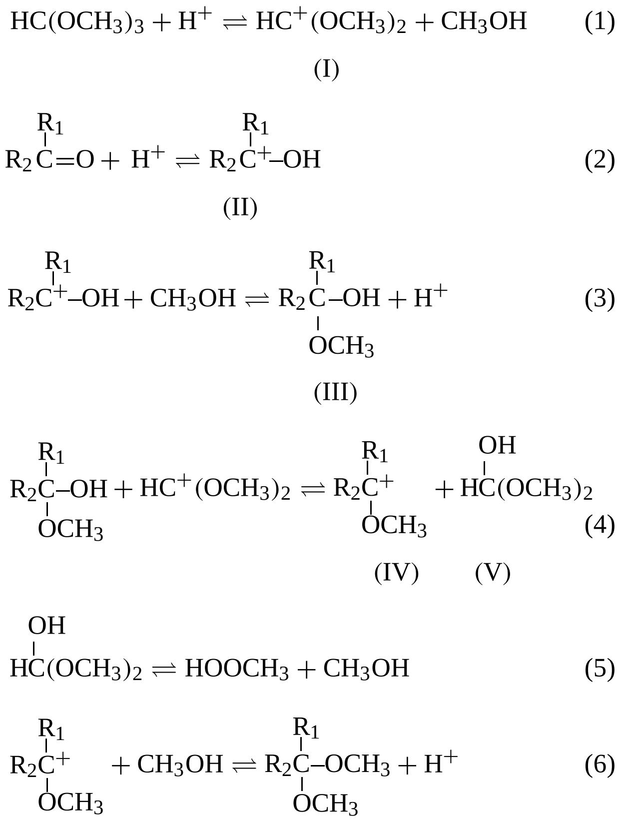
Solvent	Dimethyl acetal yield (%)
Carbon tetrachloride	100
Chloroform	100
Toluene	97
Acetonitrile	90

[a] Reaction took place at ambient temperature and for 30 min using 0.5 g of catalyst, 15 mmol of cyclohexanone, 55 mmol of trimethyl orthoformate, and 20 ml of CCl_4.

carbonyl group, it is important to survey the catalytic performance of SMO in different solvents. The data in table 4 indicate that the dimethyl acetal yields of cyclohexanone remained high in the four solvents chosen. However, the yield dropped from 100% in CCl_4 and $CHCl_3$ to a lower value of 90% in acetonitrile. Acetonitrile has the largest dipole moment among these solvents and its π-electron is easily polarized. It was probably competing with carbonyl compounds for the acid sites in SMO through its π-electrons.

There was no appreciable degree of catalyst deactivation. We had reused a 0.5 g of the SO_4^{2-}/ZrO_2 sample three times to prepare the dimethyl acetal of cyclohexanone, and the product yields after 30 min of the reaction were 98, 99, and 99%, respectively. However, the catalyst did turn to a light yellow color after the first use, but the color change did not seem to impair the efficiency of SMO. The used catalyst was calcined at 500 °C for 3 h to regenerate the catalyst. The calcined SO_4^{2-}/ZrO_2 regained its original white color and could still maintain a dimethyl acetal yield of 99%. In fact, no catalyst deactivation was suggested by the data in figure 1, 0.5 g of SO_4^{2-}/ZrO_2 could achieve a 98% yield in 15 min, but it only took 30 min to achieve a 96% yield using 0.15 g of SO_4^{2-}/ZrO_2 (less than 1/3 amount).

A modified reaction mechanism for the formation of dimethyl acetals over SMO was proposed as shown in scheme 1 [8]. In this mechanism, the carbonyl compound and trimethyl orthoformate are first protonated by a Brønsted acid site and produced species (I), (II), and methanol. Species (II) and methanol then combine to form a hemiacetal, (III). The hemiacetal can be dehydrated by an acid site to produce an enol ether, which was one of the products reported for MCM-41 or Amberlyst-15 resin catalysts [11,13]. In another reaction route, the hemiacetal can react with (I) to form a oxocarbocation (IV) and a neutral species (V). The latter decomposes to form methyl formate. The former reacts with methanol to form the dimethyl acetal. Step (2) is believed to be the rate-limiting step. According to this scheme, the lower reactivity of acetophenone is probably due to the slow formation oxocarbocation (IV) in step (4). The bulkiness of the hemiacetal (III) of acetophenone might prevent the also bulky $HC^+(OCH_3)_2$ from attacking its carbonyl carbon and the rate-limiting step is shifted from step (2) to step (4). Recently, the protonation of hemiacetal of acetophenone was shown to be partially or wholly rate limiting during the hydrolysis of the symmetrical dimethyl and diethyl acetals of acetophenone (see below) [16].



$$\underset{(I)}{HC(OCH_3)_3 + H^+ \rightleftharpoons HC^+(OCH_3)_2 + CH_3OH} \tag{1}$$

$$R_2\overset{R_1}{C}{=}O + H^+ \rightleftharpoons \underset{(II)}{R_2\overset{R_1}{C^+}\text{–}OH} \tag{2}$$

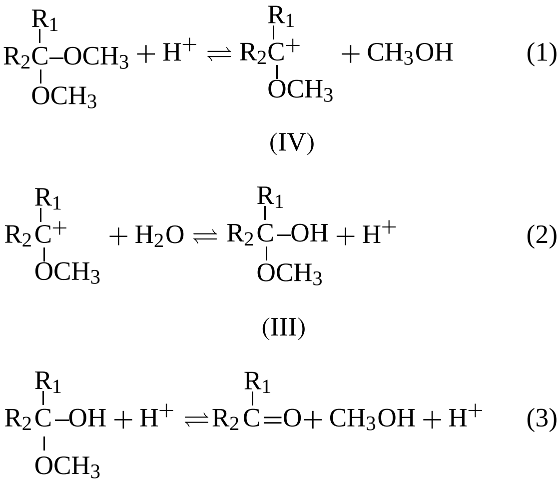
$$R_2\overset{R_1}{C^+}\text{–}OH + CH_3OH \rightleftharpoons \underset{(III)}{R_2\underset{OCH_3}{\overset{R_1}{C}}\text{–}OH} + H^+ \tag{3}$$

$$R_2\underset{OCH_3}{\overset{R_1}{C}}\text{–}OH + HC^+(OCH_3)_2 \rightleftharpoons \underset{(IV)}{R_2\underset{OCH_3}{\overset{R_1}{C^+}}} + \underset{(V)}{\overset{OH}{HC}(OCH_3)_2} \tag{4}$$

$$\overset{OH}{HC}(OCH_3)_2 \rightleftharpoons HOOCH_3 + CH_3OH \tag{5}$$

$$R_2\underset{OCH_3}{\overset{R_1}{C^+}} + CH_3OH \rightleftharpoons R_2\underset{OCH_3}{\overset{R_1}{C}}\text{–}OCH_3 + H^+ \tag{6}$$

Scheme 1. A proposed reaction mechanism for the formation of dimethyl acetals from the reaction between carbonyl compounds and trimethyl orthoformate over SMO catalysts.



$$R_2\underset{OCH_3}{\overset{R_1}{C}}\text{–}OCH_3 + H^+ \rightleftharpoons \underset{(IV)}{R_2\underset{OCH_3}{\overset{R_1}{C^+}}} + CH_3OH \tag{1}$$

$$R_2\underset{OCH_3}{\overset{R_1}{C^+}} + H_2O \rightleftharpoons \underset{(III)}{R_2\underset{OCH_3}{\overset{R_1}{C}}\text{–}OH} + H^+ \tag{2}$$

$$R_2\underset{OCH_3}{\overset{R_1}{C}}\text{–}OH + H^+ \rightleftharpoons R_2\overset{R_1}{C}{=}O + CH_3OH + H^+ \tag{3}$$

Scheme 2. A proposed reaction mechanism for the hydrolysis of dimethyl acetals to regenerate carbonyl compounds in aqueous acetone over SMO catalysts.

We had also studied the cleavage of dimethyl acetal using SMO as catalysts. In aqueous acetone, the SMO-catalyzed hydrolysis reaction was able to produce carbonyl yields between 60 and 100% under relatively mild reaction conditions (table 3). A three-step reaction mechanism was generally accepted for this acid-catalyzed reaction [17,18]. The mechanism is depicted in scheme 2, in which the protonation of dimethyl acetal to produce the oxocarbocation (IV) (step (1)) is regarded as the rate-limiting step. Our results were consistent with the proposed mechanism in that the hydrolysis rates of benzaldehyde and acetophenone were appreciably higher than those of heptanal and phenylacetaldehyde. The former two compounds were able to form much more stable oxocarbocations (IV) whose positive charge could easily be delocalized through the benzene ring [19]. Furthermore, it was observed that the direct conjugation of a double bond with the reaction carbon center increased the rate of acetal hydrolysis by one order of magnitude [20].

4. Conclusions

Mesoporous sulfated metal oxides can effectively catalyze the reaction between carbonyl compounds and trimethyl orthoformate producing dimethyl acetals at room temperature. They also catalyze the hydrolysis of dimethyl acetal to regenerate the parent carbonyl compounds. These mesoporous solid acids not only provide an excellent synthetic route to manufacture dimethyl acetals of larger molecular size but also acted as versatile catalysts in protecting and deprotecting carbonyl groups during organic synthesis.

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References

[1] M. Hino and K. Arata, J. Chem. Soc. Chem. Commun. (1980) 851.
[2] T. Hosoi, T. Shimidzu, S. Itoh, S. Baba, H. Takaoka, T. Imai and N. Yokoyama, Prepr. Am. Chem. Soc. Div. Pet. Chem. 33 (1988) 562.
[3] E. Iglesia, S.L. Sole and G.M. Kramer, J. Catal. 144 (1993) 238.
[4] R.A. Keogh, D. Sparks, J. Hu, I. Wender, J.W. Tierney, W. Wang and B.H. Davis, Energy Fuels 8 (1994) 755.
[5] K. Arata, Appl. Catal. A 146 (1996) 3.
[6] G.D. Yadav and J.J. Nair, Micropor. Mesopor. Mater. 33 (1999) 1.
[7] E. Schwenk, G. Fleischer and B. Whitman, J. Am. Chem. Soc. 60 (1938) 1702.
[8] C.A. MacKinzie and J.H. Stocker, J. Org. Chem. 20 (1955) 1695.
[9] E.C. Taylor and C.S. Chiang, Synthesis (1977) 467.
[10] J. Bornstein, S.F. Bedell, P.E. Drummond and C.F. Kosoloski, J. Am. Chem. Soc. 78 (1956) 83.
[11] S.A. Patwardhan and S. Dev, Synthesis (1974) 348.
[12] G.A. Olah, S.C. Narang, D. Meidar and G.F. Salem, Synthesis (1981) 282.
[13] M.J. Climent, A. Corma, S. Iborra, M.C. Navarro and J. Primo, J. Catal. 161 (1996) 783.
[14] A. Corma, M. Climent, H. Carcia and J. Primo, Appl. Catal. 59 (1990) 333.
[15] S. Arctander, *Perfumary and Flavor Chemicals*, Vols. I, II (Allured Publishing, New York, 1969).
[16] R.A. McClland and P.-E. Sorensen, Acta Chem. Scand. 44 (1990) 1082.
[17] T.H. Fife, Acc. Chem. Res. 5(1972) 264.
[18] E.H. Cordes and H.G. Bull, Chem. Rev. 74 (1974) 581.
[19] J. Toullec and M. El-Alaoui, J. Org. Chem. 50 (1985) 4928.
[20] J.L. Jensen and R. Siegel, J. Org. Chem. 53 (1988) 6105.