

Experimental and theoretical analysis of Friedel–Crafts acylation of thioanisole to 4-(methylthio)acetophenone using solid acids

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Abstract

4-(Methylthio)acetophenone is an important drug intermediate used for the synthesis of Vioxx (Rofecoxib), an NSAID, which has selective COX-2 inhibition. It is typically produced on industrial scale by Friedel–Crafts acylation using homogeneous corrosive and polluting acid catalysts such as aluminium chloride in more than stoichiometric amounts with acetyl chloride as the acylating agent. This process creates pollution problems related to the disposal of catalyst and treatment of acidic effluent and needs to be replaced by a green process. In the current work, a simple process was developed based on the use of heterogeneous catalysts. The activities of 20% w/w $\text{Cs}_{2.5}\text{H}_{0.5}\text{P}_{12}\text{W}_{40}/\text{K}-10$ clay, Amberlyst-15, Indion-190 and Indion-130 were studied in the acylation of thioanisole with acetic anhydride to prepare 4-(methylthio)acetophenone. Amberlyst-15, a cation exchange resin, was found to be the best catalyst. The effects of various parameters were studied using this catalyst. Dynamic adsorption studies were performed independently to get adsorption equilibrium constants for the reactants and products. A theoretical model was developed to account for kinetics and mechanism and the various constants were evaluated from the experimental data. Simulations were performed to validate the model against experimental data and there was an excellent agreement between theory and experiment.

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1. Introduction

Aromatic thioketones are employed as intermediates for the production of pharmaceuticals, agrochemicals, UV cure photo-initiators, polymers and dyestuffs [1]. For instance, 4-mercaptoacetophenone is a precursor for the manufacture of 4-mercaptostyrene acetate and its polymers [2,3] and 4'-(methylthio)-2-methylpropiofenone is an intermediate for UV cure photoinitiator [4]. Amongst these thioketones, 4-(methylthio)acetophenone is a very important drug intermediate used for the synthesis of Vioxx (Rofecoxib), an NSAID, which has selective COX-2 inhibition. 4-(Methylthio) acetophenone is typically synthesized by the acylation of thioanisole with aluminium chloride in

stoichiometric amounts with acetyl chloride as the acylating agent. This process is beset with pollution problems related to the disposal of catalyst and treatment of acidic effluent and needs to be replaced by a green process.

The preparation of thioketones is a typical Friedel–Crafts acylation reaction. Generally the synthesis of aromatic ketones is achieved by the use of Lewis acids (AlCl_3 , FeCl_3 , BF_3 , ZnCl_2 , TiCl_4 , ZrCl_4) or Brønsted acids (polyphosphoric acid, H_2SO_4 and HF) as homogeneous catalysts [5]. Several commercial Friedel–Crafts acylations use AlCl_3 as a catalyst and these processes require 2 equiv. of AlCl_3 per mol of product. AlCl_3 is not a recyclable catalyst and is associated with tremendous disposal and environmental problems. HF is used many times as a recyclable solvent-cum catalyst but it is beleaguered with corrosion and hazard. The use of zeolites in Friedel–Crafts alkylation in refinery processes is well known but they have limitations for organic synthesis in other industries [6]. Acylation of substituted aromatics with solid acids are quite challenging and sulfur containing

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Nomenclature

| | |
|----------------------------------|---|
| <i>A</i> | thioanisole |
| <i>B</i> | acetic anhydride |
| C_{I_0} | initial concentration of <i>I</i> th species |
| C_{IS} | Surface concentration of <i>I</i> th species (mol/g-cat) |
| $C_{I_{in}}$ | initial concentration of <i>I</i> th species (mol/cm ³) |
| $C_{I_{fin}}$ | final concentration of <i>I</i> th species (mol/cm ³) |
| <i>I</i> | <i>I</i> th species |
| k_{SR} | forward reaction rate constant for surface reaction between A and B (cm ⁶ s/mol s g-cat) |
| k_{SR}' | reverse reaction rate constant for surface reaction between M and P (cm ⁶ /mol s g-cat) |
| $K_{AS}, K_{BS}, K_{MS}, K_{PS}$ | adsorption equilibrium constants for species A, B, M, and P |
| K_{SR} | surface reaction rate constant for reaction of adsorbed A with adsorbed B |
| <i>M</i> | 4-methylthioacetophenone |
| M_R | initial molar ratio of concentration of B to that of A |
| <i>P</i> | acetic acid |
| $-r_A, -r_B$ | rate of reaction of A, B (mol/cm ³ s) |
| <i>S</i> | vacant site |
| <i>w</i> | catalyst loading per unit volume of liquid phase (g/cm ³) |
| X_A | fractional conversion of A |
| <i>Subscript</i> | |
| 0 | initial condition |

substrates are difficult to acylate using solid acids. Besides, aromatic ethers are known to deactivate the catalyst. For instance, with aromatic ethers such as anisole and veratrole, zeolites are deactivated rapidly [7,8]. Heteropoly acids supported on hexagonal mesoporous silica (HMS) are quite robust catalysts for acylation [9] whereas ion exchange resins were found to deactivate in acylation of diphenyl oxide [10]. There is no report on acylation of thioanisole using heterogeneous catalysts including kinetic modeling and thus the current work was undertaken.

Our laboratory has been pursuing the development of new ecofriendly acid catalysts for several industrially relevant reactions including process kinetics and reactor design. It was found that cation exchange resins possess several advantages, as Brønsted acids, over other solid acids and their performance was evaluated in low temperature liquid phase reactions. Catalysis by cation exchange resins has been reviewed periodically [11–13]. The activities and selectivities of different solid acids such as clays and modified clays [14–17], zeolites [15,18], sulfated zirconia [19–29], heteropoly acids (HPA)/K10 clay [30–38], Cs-modified HPA (Cs_{2.5}H_{0.5}P₁₂W₄₀)/K10 clay [39–42] and metal halides [18,33–34], UDCaT series of catalysts [43–47]

and ion exchange resins [48–55] have been evaluated in our laboratory for developing green acylation, alkylation, condensation, cyclization, esterification, etherification, isomerisation, oligomerisation, and nitration. Deactivation of ion exchange resins has also been studied and modeled for industrial acylation [10] and alkylations [56–57].

The current work is concerned with the process development and kinetic aspects of synthesis of 4-(methylthio)acetophenone from thioanisole and acetic anhydride. Although sulfur containing molecules are known to deactivate acid catalysts, ion exchange resins are more robust to deactivation and the studies were focused mainly on use of cation exchange resins in the synthesis of 4-(methylthio)acetophenone. The use of partially substituted heteropolyacids in supported form was also considered.

2. Experimental

2.1. Chemicals and catalysis

The following chemicals and catalysts were procured from firms of repute and used without further purification: Thioanisole (Spectrochem, India), acetic anhydride (AR grade; s.d. Fine Chem. Pvt. Ltd., Mumbai, India), K-10 clay (Aldrich, USA), cation exchange resins such as Indion-190, Indion-130 (Ion Exchange (India) Ltd, Mumbai), Amberlyst-15 (Rohm and Haas, USA). Heteropolyacids were obtained from M/s. s.d. Fine Chemicals Pvt Ltd. 20% w/w Cs_{2.5}H_{0.5}PW₁₂O₄₀/K10 (abbreviated as Cs-DTP/K-10) was synthesized as per the procedure developed in this laboratory [38–42]. The catalyst properties are summarized in Table 1.

2.2. Reaction procedure

The reaction was carried out in a Parr autoclave of 100 mL capacity with an internal diameter of 0.05 m. The temperature was maintained at $\pm 1^\circ\text{C}$ of the desired value with the help of an in-built proportional–integral–derivative (PID) controller. A standard four bladed pitched turbine impeller was employed for agitation. In a typical experiment, 0.025 mol thioanisole, 0.075 mol acetic anhydride, 30 mL ethylene dichloride and 4.0 g of the particular catalyst were charged to the autoclave. The total liquid phase volume of the reaction mixture was 40.03 mL. The reaction mass was allowed to reach the desired temperature which was 70 °C in the control experiments. Agitation was then commenced at a known speed. Clear samples were withdrawn periodically for analysis.

2.3. Adsorption experiments

Analysis of experimental data had suggested that it would be necessary to study adsorption of different species from liquid phase. The adsorption of reactants and products on the best catalyst was studied. The adsorption studies were performed by taking the catalyst with a given substrate

Table 1
Characteristics of catalysts used in this work

| # | Catalyst | Source | Surface area (m ² /g) | Pore volume (cm ³ /g) | Average pore diameter (nm) | Nature of acidity | H ⁺ exchange capacity (mequiv./g) |
|---|---|------------------------|----------------------------------|----------------------------------|----------------------------|-------------------|--|
| 1 | Sulfated zirconia | This work | 100 | 0.115 | 2.8 | Lewis + Brønsted | ND |
| 2 | K-10 clay | Fluka | 230 | 0.36 | 6.4 | Lewis + Brønsted | 0.35 |
| 3 | 20% w/w Cs _{2.5} H _{0.5} PW ₁₂ O ₄₀ /K-10 | This work | 207 | 0.29 | 5.8 | Brønsted + Lewis | ND |
| 4 | Indion-130 | Ion Exchange India Ltd | 48 | 0.35 | 20 | Brønsted | 4.8 |
| 5 | Indion-190 | Ion Exchange India Ltd | 50 | 0.37 | 28 | Brønsted | 4.7 |
| 6 | Amberlyst-15 | Rohm & Haas | 53 | 0.30 | 30 | Brønsted | 4.7 |

such as thioanisole, 4-(methylthio)acetophenone, acetic anhydride and acetic acid in ethylene dichloride. A mixture of thioanisole and 4-(methylthio)acetophenone in ethylene dichloride along with catalyst was also used for the adsorption studies at 70 °C. The assembly used for the adsorption experiments consisted of a flat-bottomed cylindrical glass vessel of 100 mL capacity equipped with four baffles, a pitched-turbine stirrer and a condenser. The assembly was kept in a thermostatic oil bath at the desired temperature and mechanically agitated with an electric motor. Table 2 lists the conditions used for the adsorption studies. The mass was allowed to reach 70 °C and agitation was then commenced at 600 rpm. Clear samples were withdrawn periodically for analysis. The adsorbed quantity was found at each interval. The experiments were continued until there was no more adsorption of the substrate.

2.4. Method of analysis

2.4.1. Reaction mixture

Analysis of the reaction mixture was performed by gas chromatography (GC) (Chemito model 8510) by using FID using 2 m × 1/8 in. i.d., SS column packed with 10% OV-17 on Chromosorb WHP. The quantification data was done through calibration using synthetic mixtures.

2.4.2. Adsorption studies

The amount of free adsorbate in the liquid phase was found by G.C. in the case of thioanisole, 4-(methylthio)anisole and acetic anhydride using the method given above.

Acetic acid analysis was performed by HPLC (A Knauer, model K-501: 63614) with the UV detector (A Knauer, model

K-2501: 62964) by using mobile phase acetonitrile: water (60:40) and flow rate 0.7 mL/min at λ_{max} 220 nm. The quantification data was done by standard calibration method.

2.5. Identification and isolation of product

The G.C. analysis showed that a major product of 4-(methylthio) acetophenone (98.4%) and the minor product of 2-(methylthio) acetophenone (1.6%) were produced for conversion levels up to 50%. At the end of the reaction, the catalyst was filtered off and the filtrate was subjected to vacuum distillation. The solvent ethylene dichloride, acetic acid, unreacted thioanisole were all removed and the residue remaining in the bottoms was purified by crystallization using ethanol. Pale yellow crystals of 4-(methylthio)acetophenone were dried. Confirmation of the desired product was done by I.R., ¹H NMR, GC-MS and melting point: 80 °C (Reported mp 80–81 °C).

3. Results and discussion

3.1. Reaction scheme

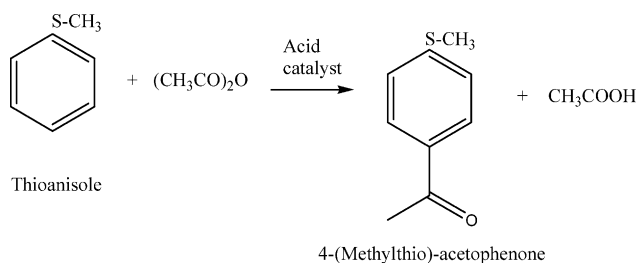


Table 2
Adsorption of components on Amberlyst-15

| No. | Thioanisole (mL) | 4-Methyl thioanisole (mL) | Acetic acid (mL) | Acetic anhyd. | Time (h) | Catal. loading (g) | Total volume (mL) |
|---------------------------------|------------------|---------------------------|------------------|------------------|----------|--------------------|-------------------|
| Individual component adsorption | | | | | | | |
| 1. | 1.5 (0.0125 mol) | – | – | – | 4 | 3.15 | 31.5 |
| 2. | – | 2.0 (0.0125 mol) | – | – | 4 | 3.2 | 32.0 |
| 3. | – | – | 1.5 (0.026 mol) | – | 2 | 3.15 | 31.5 |
| 4. | – | – | – | 7.08 (0.075 mol) | 2 | 4.0 | 37.08 |
| Adsorption from mixture | | | | | | | |
| 5. | 2.0(0.0125 mol) | – | – | 4 | 3.15 | 33.5 | |

Solvent: ethylene dichloride: 30 mL, temperature: 70 °C.

3.2. Catalyst screening

There are no reports on the acylation of thioanisole with solid acids as catalysts. Sulfur containing organic molecules are known catalyst poisons due to strong adsorption and thioethers are obviously difficult substituents for acylation. Besides acylation of aromatic ethers has proved to be challenging and zeolites get deactivated in liquid phase reactions [6–10]. Thioanisole and the acylated thioanisole are bulky molecules. Thus, the nature of acidity of catalyst, its pore size and surface area, solvent, mole ratio of reagents, and temperature will affect the rate of reaction and selectivity in acylation of thioanisole. Catalysts with pore sizes in mesoporous range with minimum loss in activity over a long period will be attractive. We have worked with sulfated zirconia, acid treated clays, heteropolyacids (HPA) supported on clay, pillared clays and ion exchange resins. In our laboratory, we have developed a nano-sized Cs-DTP/K10 catalyst, with very interesting properties for acylation reactions [38–42] and had found ion exchange resins robust in acylations of aromatic ethers in comparison with sulfated zirconia [10]. Therefore catalysts with different acidities and pore size distribution were selected (Table 1).

A 0.1 g/cm^3 loading of catalyst, based on the organic volume of the reaction mixture was employed at a mole ratio of thioanisole to acetic anhydride of 1:3 at 70°C and 600 rpm, in the control experiment. A speed of 600 rpm was sufficient to ensure the elimination of external mass transfer resistance, which is discussed later.

At the operating conditions, sulfated zirconia and K10 clay did not show any noticeable activity. These catalysts have wide pore size distributions with some pores in mesoregion and also contain both Lewis and Brønsted sites. Thus, both nature of acidity and its accessibility to reacting molecules were unfavourable for the current studies. It appeared that supported heteropoly acids with more Brønsted acidity than Lewis acidity could work. Both 20% w/w DTP/K-10 and 20% Cs-DTP/K-10 having variable Lewis and Brønsted acids also did not show any activity. There was no reaction with Cs-DTP/K-10 at 70°C and even when the temperature was raised to 140°C , a conversion of only 2.9% was obtained. It suggested that Cs-DTP/K-10 was strongly poisoned by one of the products/reactants and a separate study was required on adsorption.

The clays and supported clays have low proton exchange capacity and thus were not active. Sulfated zirconia, having both Lewis and Brønsted acids, also gets totally poisoned and has a wide pore size distribution with major pores in mesoregion. Thus, catalysts with pores in mesoporous region and having only Brønsted acidity were considered. Only the cation exchange resin catalysts, which contain Brønsted sites, were effective. The catalyst activity was in the following order under otherwise similar conditions (Fig. 1):

Amberlyst-15 (max). > Indion-190 > Indion-130
> 20% w/w Cs – DTP/K – 10 and S – ZrO₂ (nil)

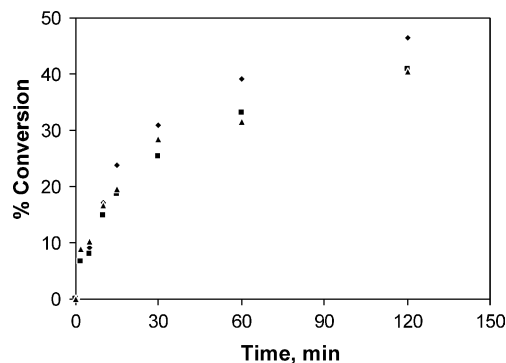


Fig. 1. Efficacy of various catalysts. Thioanisole: 0.025 mol, acetic anhydride: 0.075 mol, ethylene dichloride: 30 mL, temperature: 70°C , catalyst loading: 0.1 g/cm^3 , speed of agitation: 600 rpm, particle size: $500\text{--}600 \mu\text{m}$. (●) Amberlyst-15; (■) Indion-190; (▲) Indion-130 (No activity for K10, Cs-DTP/K10, S-ZrO₂).

In spite of their very close ion exchange capacities, Amberlyst-15 shows maximum conversion (Fig. 1) since it has bigger pores and more surface area. The selectivity to the desired product at the end of the experiment was over 98% in all cases. The second isomer in a small quantity was noticed only after 90 min with Amberlyst-15.

Further experiments were conducted with Amberlyst-15 as the catalyst, where only one parameter was varied at a time keeping all other parameters constant.

3.3. Effect of speed of agitation

The effect of speed of agitation was studied in the range of 600–1000 rpm at a catalyst loading 0.1 g/cm^3 at 70°C . The mole ratio of thioanisole to acetic anhydride was kept 1:3. There was no change in conversion beyond 600 rpm. There was insignificant attrition even at 1000 rpm. A theoretical calculation was also done to assess the effect of mass transfer and it was found that the rates of external mass transfer to particle surface were orders of magnitude higher at 600 rpm in comparison with the observed rate of reaction. Thus, 600 rpm was chosen as the appropriate speed for all further experiments (Fig. 2).

3.4. Effect of catalyst loading

In the absence of external mass transfer resistance, the rate of reaction is directly proportional to catalyst loading based on the entire liquid phase volume. The catalyst loading was varied over a range $0.05\text{--}0.25 \text{ g/cm}^3$ on the basis of the total volume of the reaction mixture under otherwise similar conditions. The conversion of thioanisole increased with increasing catalyst loading which was obviously due to the proportional increase in the number of active sites. Further reactions were carried out with 0.1 g/cm^3 catalyst loading used in the standard experiment (Fig. 3).

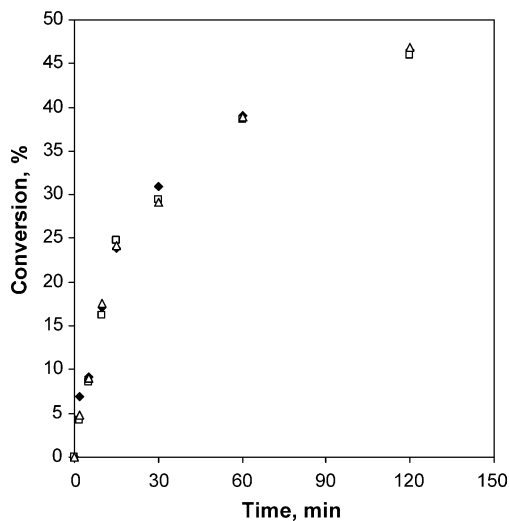


Fig. 2. Effect of speed of agitation. Thioanisole: 0.025 mol, acetic anhydride: 0.075 mol, ethylene dichloride: 30 mL, temperature: 70 °C, catalyst loading: 0.1 g/cm³, particle size: 500–600 μm. (◆) 600 rpm; (□) 800 rpm; (Δ) 1000 rpm.

3.5. Effect of particle size

There is a variation in particle sizes of commercial resins. The resins are supplied water wet in the form of spherical beads having a particle diameter between 0.30 and 1.2 mm. The particles were also ground and then sieved to cover a much wide range. Particle sizes were measured by image analysis using a Tracor Northern image analyzer. Thus, six particle sizes were chosen in ranges of 850–1200, 700–850, 600–700, 500–600, 100–250 and <50 μm. The effect of particle size on conversion was studied with a catalyst loading 0.1 g/cm³ for a mole ratio of thioanisole to acetic anhydride of 1:3 at 70 °C. For particles in the ranges of 500–600, 100–250 μm and less than 50 μm, there was no variation in conversions. For size range 850–1200 μm, there was a reduction in conversion (Fig. 4). Thus, there was no

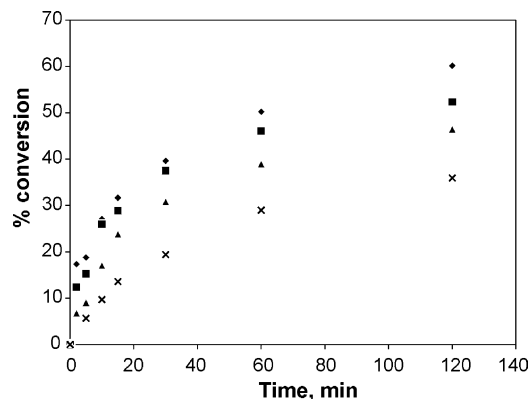


Fig. 3. Effect of catalyst loading on conversion of thioanisole. Thioanisole: 0.025 mol, acetic anhydride: 0.075 mol, ethylene dichloride: 30 mL, temperature: 70 °C, speed of agitation: 600 rpm, particle size: 500–600 μm. (×) 0.05 g/cm³; (▲) 0.1 g/cm³; (■) 0.20 g/cm³; (◆) 0.25 g/cm³.

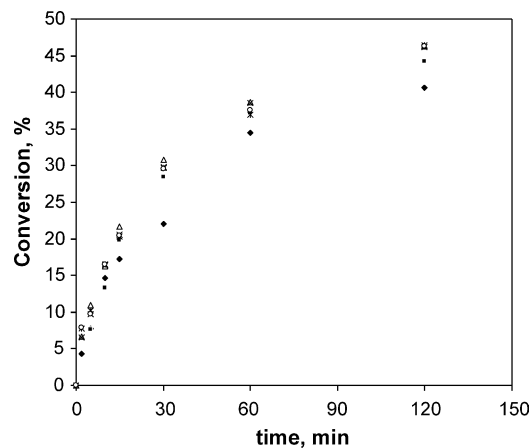


Fig. 4. Effect of particle size on conversion of thioanisole. Thioanisole: 0.025 mol, acetic anhydride: 0.075 mol, ethylene dichloride: 30 mL, temperature: 70 °C, catalyst loading: 0.1 g/cm³, speed of agitation: 600 rpm. (○) <50 μm; (□) 100–250 μm; (×) 500–600 μm; (Δ) 600–700 μm; (■) 700–800 μm; (◆) 1000–1200 μm.

intraparticle diffusion resistance below 500–600 μm range which was used in all further experiments. The Weisz–Prater criterion was used earlier to show absence of intra-particle diffusion resistance.

3.6. Effect of mole ratio

The effect of mole ratio of thioanisole to acetic anhydride was studied at 1:1, 1:2, 1:3, 1:4 and 1:5 with a catalyst loading 0.1 g/cm³ at 70 °C. It was observed that at 1:1 mol ratio, there was hardly any conversion (2.9%) and as the concentration of acetic anhydride was increased from 7.07×10^{-4} mol/cm³ (1:1) to 1.87×10^{-3} mol/cm³ (1:3 mol ratio), by keeping the same moles of thioanisole, the conversion increased substantially to 47%. There was no further increase in conversion when mole ratio was increased from 1:3 to 1:5 (Fig. 5). This suggests that thioanisole or the product is strongly adsorbed and there is a competitive adsorption of acetic anhydride with

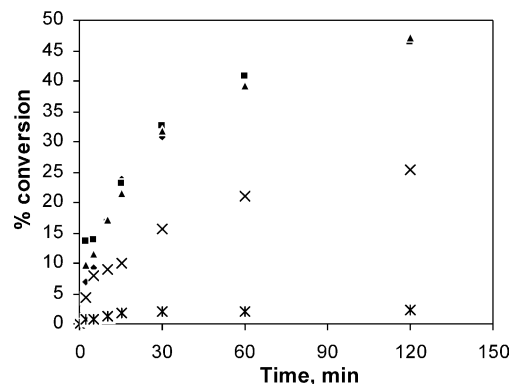


Fig. 5. Effect of mole ratio of thioanisole to acetic anhydride. Ethylene dichloride: 30 mL, temperature: 70 °C, catalyst loading: 0.1 g/cm³, speed of agitation: 600 rpm, particle size: 500–600 μm. (●) 1:3; (■) 1:4; (▲) 1:5; (×) 1:2; (*) 1:1.

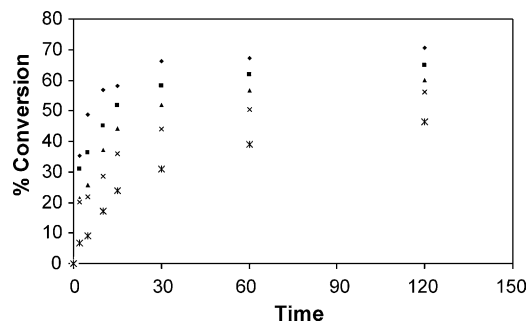


Fig. 6. Effect of temperature. Thioanisole: 0.025 mol, acetic anhydride: 0.075 mol, ethylene dichloride: 30 mL, catalyst loading: 0.1 g/cm³, speed of agitation: 600 rpm, particle size: 500–600 μm. (◆) 120 °C; (■) 100 °C; (▲) 90 °C; (x) 80 °C; (*) 70 °C.

thioanisole and or the product. Adsorption of acetic anhydride is essential to generate carbocations for the reaction to proceed. Adsorption of thioanisole is reduced and many sites are occupied by acetic anhydride. Therefore, further kinetic parameters studied with the mole ratio of thioanisole to acetic anhydride of 1:3.

3.7. Effect of temperature

The effect of temperature on conversion was studied in the range of 70–120 °C under otherwise similar conditions (Fig. 6). It was observed that the conversion increased with temperature. This would suggest a kinetically controlled mechanism. The initial rates of acylation were calculated at different temperatures and the Arrhenius plots have made to determine the energy of activation. It was found to be 11.8 kcal/mol, which is an indication of the overall rate being controlled by intrinsic kinetics.

3.8. Effect of catalyst reusability

The reusability test determines the structural fidelity as also suitability of the catalyst on large scale (Fig. 7). The

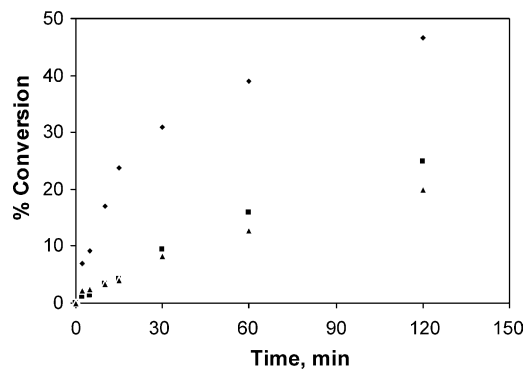


Fig. 7. Effect of catalyst reusability. Thioanisole: 0.025 mol, acetic anhydride: 0.075 mol, ethylene dichloride: 30 mL, temperature: 70 °C, catalyst loading: 0.1 g/cm³, speed of agitation: 600 rpm, particle size: 500–600 μm. (◆) fresh; (■) first use; (▲) second use.

reusability of the catalyst was studied by using the same catalyst, which was filtered twice and refluxed with methanol in order to remove any adsorbed material from the catalyst surface and pores. It was dried at 100 °C after every use. The first reuse was without any make-up catalyst and thus, there was a decrease in final conversion. There was loss of catalyst due to attrition during filtration. In the second reuse, the catalyst loss was made-up. The conversion had dropped. In subsequent run catalyst quantity was made up to find that the drop in conversion was marginal. Fig. 8 shows the pore structure of virgin catalyst (Fig. 8a), and used catalyst. After first use, the product is deposited inside the pore space at a few crucial junctions (Fig. 8b). If no washing is done then the activity of the catalyst is lost considerably since the molecules of reactants are not able to diffuse and some networks are inaccessible. However, the product can be washed off the sites by using a solvent. Thus, some product is leached out and the pore space becomes free, as shown in Fig. 8c. But still the available pore space is less than that of the virgin catalyst and some catalyst activity is lost due to this permanent deposition of product molecules on catalytic sites. Thus, the pore structure is modified on first use,

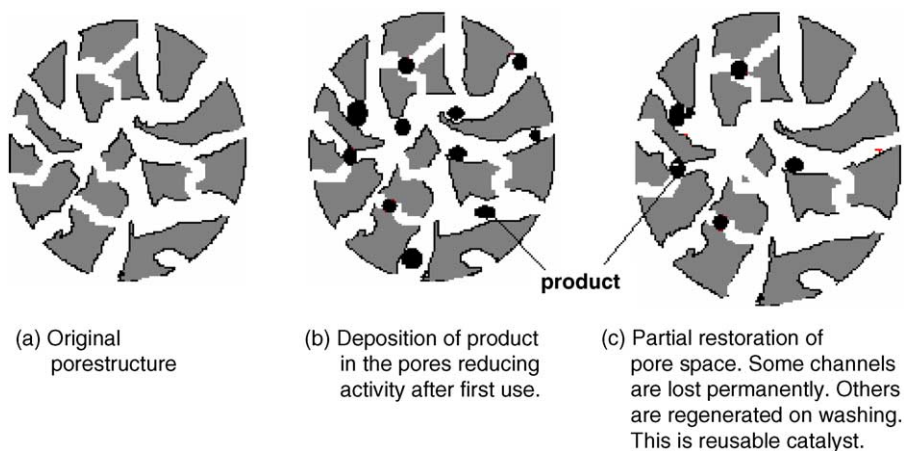


Fig. 8. Catalyst pore structure: virgin catalyst and used catalyst.

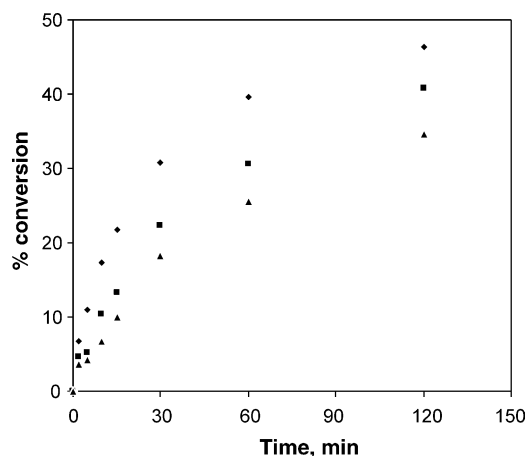


Fig. 9. Effect of addition of acetic acid at the start of reaction. Ethylene dichloride: 30 mL, temperature: 70 °C, catalyst loading: 0.1 g/cm³, speed of agitation: 600 rpm, particle size: 500–600 μm. (◆) 0.0 mol; (■) 0.0173 mol; (▲) 0.0347 mol.

which is the accessible for regeneration without any loss. Fig. 8c is thus then actual structure retained in subsequent 4 runs.

3.9. Effect of acetic acid

Effect of acetic acid on the conversion of thioanisole was studied at two different concentrations of 1.041×10^{-4} and 0.520×10^{-4} mol/cm³ of acetic acid with 0.1 g/cm³ of catalyst. The mole ratio of thioanisole to acetic anhydride was maintained 1:3 at 70 °C (Fig. 9). It was observed that the conversion had decreased drastically as the initial acetic acid concentration in the reaction mixture was increased. The formation of carbocation from acetic anhydride results into acetic acid as co-product and thus the reverse reaction predominates and the effective concentration of the carbocation decreases. Acetic acid does not poison the catalyst sites and is an acylating species with strong acids wherein the carbocation is formed due to dehydration of acetic acid

leading to the formation of acetic anhydride in situ [58]. Thus, it appeared that there was a contribution of the reverse reaction.

3.10. Adsorption studies

The above kinetic experiments suggested that there was a need to study the adsorption of various species on Amberlyst-15 at the reaction conditions. Thus, experiments were conducted at different initial concentrations of thioanisole (reactant) and 4-methylthioacetophenone (product) independently without taking any acetic anhydride. A mixture of thioanisole and 4-methylthioacetophenone was also chosen to find out the adsorption of these compounds (Table 2). Figs. 10 and 11 show the individual adsorptions and adsorption from the mixture. The calculation of the adsorption constant was done as per the procedure given by Ramachandran and Chaudhari [59]:

$$K'_I = \frac{1}{w[(C_{I_{in}}/C_{I_{fn}}) - 1]}, \quad K_I = \frac{K'_I}{(C_{I_{in}} - C_{I_{fn}})/w} \quad (1)$$

where *I* is the species A, B, M, P, *C*_{I_{in}} the initial concentration of *I*, and *C*_{I_{fn}} the final concentration.

The adsorption constant *K*_A for thioanisole was 2.9422×10^5 cm³/mol and 2.3515×10^5 cm³/mol for separate and mixture whereas that for 4-(methylthio)acetophenone (*K*_M) was 2.9863×10^5 mol/cm³ and 3.2645×10^5 mol/cm³ indicating that both these species are strongly adsorbed and that the adsorption constants are nearly the same in the mixture.

Fig. 11 shows the plot for adsorption of acetic anhydride and acetic acid. The adsorption constants for acetic anhydride (*K*_B) and acetic acid (*K*_P) on the contrary were 0.2014×10^5 and 0.8413×10^5 cm³/mol, respectively. This would mean that both the reactant and product being sulfur compounds act as inhibitor and therefore the use of excess acetic anhydride only avoids this inhibition up to a certain concentration. It also helps in washing of product molecules from the pore space. This is one of the reasons as to why the conversions

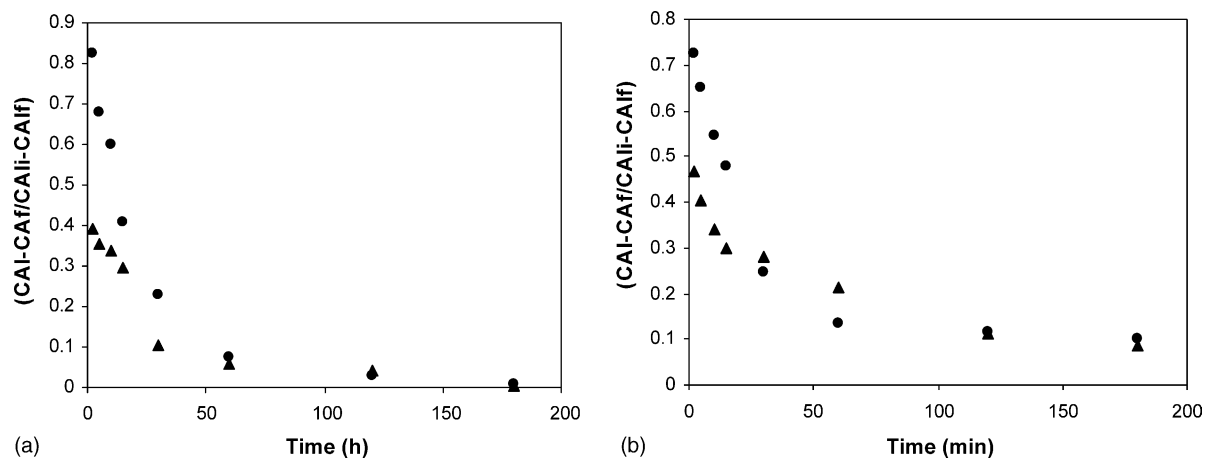


Fig. 10. Adsorption study of thioanisole and 4-methylthioacetophenone. (a) Thioanisole; (b) 4-Methylthioacetophenone; (▲) separate; (●) mixture $K' = 6.242$ cm³/g; (▲) separate; (●) mixture $K' = 7.139$ cm³/g.

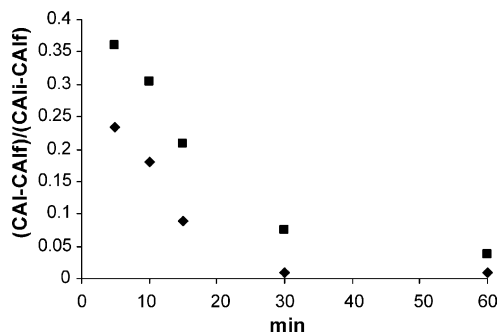


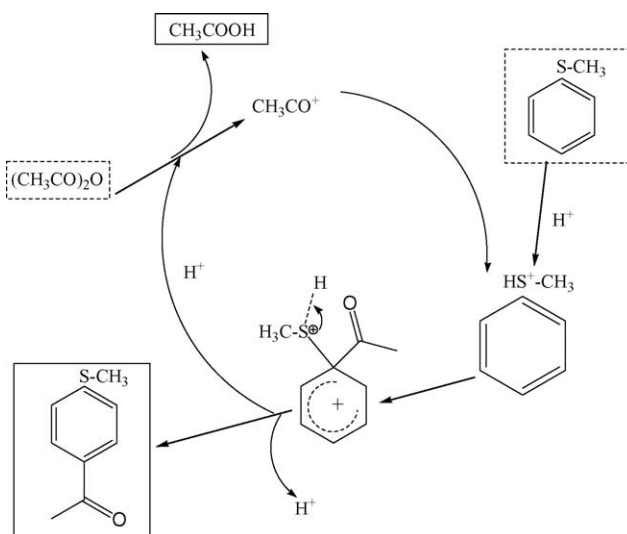
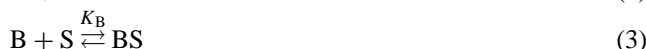
Fig. 11. Adsorption study of acetic acid and acetic anhydride. (■) Acetic anhydride $K_1' = 4.695 \text{ cm}^3/\text{g}$; (◆) acetic acid, $K_1' = 9.498 \text{ cm}^3/\text{g}$.

were limited to 47% even at 1:3–1:5 mole ratio of thioanisole to acetic anhydride.

3.11. Mechanism and kinetics

The above studies can now be used to develop a mechanistic model for the reaction. In the first instance, the power law model was tried and found to be inadequate. Hence, the dynamic experiments were performed to study the effect of adsorption of reactants and products independently. The mechanism follows with the formation of carbocations which attacking on *o/p* position of thioanisole to give the maximum of 4-methylthioacetophenone. Scheme 1 gives the typical catalytic cycle.

According to this model, there is a competitive adsorption of thioanisole (A), acetic anhydride (B), 4-methylthioacetophenone (M) and acetic acid (P) on the Brønsted sites (S):



Scheme 1. Catalytic cycle for acylation of thioanisole according to the LHHW mechanism.

A Langmuir Hinselwood Hougen–Watson (LHHW) type of model leads to the following:



The rate of reaction of A or B ($\text{mol}/\text{cm}^3 \text{ s}$) is given by

$$-r_A = -r_B = k_{SR}C_{AS}C_{BS} - k_{SR'}C_{MS}C_{PS} \quad (7)$$

where k_{SR} and $k_{SR'}$ are the forward and reverse reaction rate constants.

The total site balance is

$$\begin{aligned} C_T &= C_S + C_{AS} + C_{BS} + C_{MS} + C_{PS} \\ &= C_S + K_A C_A + K_B C_B + K_M C_M + K_P C_P \end{aligned} \quad (8)$$

$$\therefore C_S = \frac{C_T}{1 + K_A C_A + K_B C_B + K_M C_M + K_P C_P} \quad (9)$$

Putting all these terms in the rate equation, and writing in terms of X_A , fractional conversion of A, and the mol ratio $MR = C_{B_0}/C_{A_0}$ and replacing C_T by w (catalyst loading in g/cm^3), without loss of generality.

Therefore, the overall rate of reaction of thioanisole is given by

$$\frac{-dC_{A_0}}{dt} = C_{A_0} \frac{dX_A}{dt} = \frac{k_{SR} w \left[C_{A_0}(1 - X_A)C_{A_0}(MR - X_A) - \left(\frac{C_{A_0}^2 X_A^2}{K_{SR}} \right) \right]}{\left[1 + K_A C_{A_0}(1 - X_A) + K_B C_{A_0}(MR - X_A) + K_M C_{A_0} X_A + K_P C_{A_0} X_A \right]^2} \quad (11)$$

Thus, the following equation is derived:

$$\frac{dX_A}{dt} = \frac{\left(\frac{k_{SR} w}{C_{A_0}} \right) \left[(1 - X_A)(MR - X_A) - \left(\frac{X_A^2}{K_{SR}} \right) \right]}{\left[\left(\frac{1}{C_{A_0}} \right) + K_A(1 - X_A) + K_B(MR - X_A) + K_M X_A + K_P X_A \right]^2} \quad (12)$$

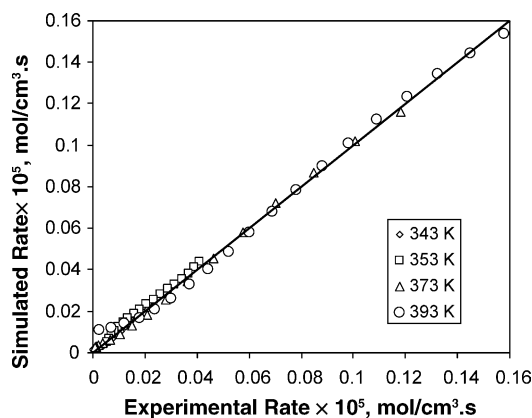


Fig. 12. Parity plot of experimental and simulated rates.

Table 3
Rate constants and adsorption constants at different temperatures

| Constant | 343 K | 353 K | 373 K | 393 K |
|---|--------------------|--------------------|--------------------|--------------------|
| k_{SR} ($\text{cm}^6/\text{mol g-cat s}$) | 1.99 | 2.46 | 3.22 | 6.53 |
| K_{SR} | 0.0458 | 0.1228 | 0.2767 | 0.4479 |
| K_A (cm^3/mol) | 8.54×10^4 | 5.00×10^4 | 4.07×10^4 | 1.75×10^5 |
| K_B (cm^3/mol) | 5.86×10^4 | 5.32×10^4 | 3.47×10^4 | 1.54×10^3 |
| K_M (cm^3/mol) | 5.78×10^4 | 2.43×10^4 | 2.42×10^4 | 1.10×10^5 |
| K_P (cm^3/mol) | 5.78×10^4 | 2.43×10^4 | 2.42×10^4 | 1.00×10^4 |

The experimental equilibrium constants were used for fitting the above equation with the help of Polymath 5.1 software. The effect of acetic acid concentration was also considered in the model and simulations were performed. Several data points are used, which considered effects of different variables such as catalyst loading, concentrations and temperature. The data points at different temperatures were shown by different symbols. The model was found to be well fitted in other cases also as shown in the parity plot (Fig. 12). Since the data were well represented by experiments, we tried to fit the data at other temperatures by simulation. In this case, the equilibrium constants were also evaluated using the data. The best fit values obtained for other temperatures as well (Table 3). Further, the experimental values of adsorption equilibrium constants obtained as 70°C are in close agreement. Further, the trends of equilibrium constants and rate constants as functions of temperature are also appropriate. The calculated values of rates are plotted against experimental values in Fig. 12 to show that the developed model is valid.

4. Conclusions

4-(Methylthio)acetophenone is an important drug intermediate which is typically produced by Friedel–Crafts acylation on industrial scale by using homogeneous corrosive and polluting acid catalysts. In the current work, a simple process was developed based on the use of heterogeneous catalysts. The activity of various catalysts such as 20% w/w Cs-DTP/K-

10, Amberlyst-15, Indion-190 and Indion-130 were studied for the acylation of thioanisole with acetic anhydride to prepare 4-(methylthio)acetophenone. Amberlyst-15 was found to be the best catalyst. The effects of various parameters were studied using this catalyst and also dynamic adsorption studies were performed to get adsorption equilibrium constants for the reactants and products. A LHHW type of model was built to account for the rate. The various constants were evaluated from the experimental data. The simulated and experimental values of rates and conversions are in excellent agreement.

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