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Liquid phase acetylation of thioanisole with acetic anhydride to 4-(methylthio) acetophenone (4-MTAP) using H-beta catalyst

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Abstract

Acetylation of thioanisole (TA) with acetic anhydride (AA) to give *p*-(methylthio) acetophenone (4-MTAP) has been investigated using different solid acid catalysts such as H-Y, H-ZSM-5, H-mordenite and H-beta in liquid phase conditions. The reaction is studied in the temperature range 80–180 °C in a pressure reactor under nitrogen atmosphere. Among the catalysts tested, H-beta is found to be more active and shape selective than other zeolite catalysts. The conversion of TA (32 mol%) with a turnover frequency, TOF, 30.6 (10^{-4} s^{-1} mol^{-1} Al) gave exclusively 4-MTAP (99.9%) and the other *o*-(methylthio) acetophenone (2-MTAP) over H-beta at 150 °C after 2 h. Acidity and structural features of zeolites play an important role in the conversion and product distribution in acetylation of TA. The effect of AA/TA molar ratio, catalyst concentration and reaction temperature have been optimized to get higher conversion of TA and product selectivity. Efficient utility of AA has been established in the reaction. H-beta catalyst has been reused in few cycles after regeneration by washing with ethyl acetate followed by calcination at 500 °C for 4 h without loss in its activity.

Keywords: Acetylation; Thioanisole; H-beta; 4-(methylthio) acetophenone

1. Introduction

Friedel-crafts acylation and alkylation are the most useful reactions for introducing functional substituents to aromatic rings [1] and applied to industrial production of pharmaceuticals, agricultural chemicals, plastics, liquid crystals, etc. [2]. Sulfur containing aromatic ketones are potential intermediates for the synthesis of industrially useful compounds such as vioxx (refecoxible) [3–6]. These reactions were originally performed using more than stoichiometric amounts of Lewis acids such as aluminum trichloride because the Lewis acids are consumed by co-ordination with the produced aromatic ketones. Ring acylation of aromatic thioethers has been carried out in the presence of varieties of catalysts including anhydrous hydrogen fluoride [7] and rare earth metal trifluromethanesulfonates [8]. Unfortunately, the use of such conventional catalysts and their waste after aqueous work-up procedures often causes serious environmental problems. The use of recoverable and regenerable solid acid catalysts such as zeolites can overcome many problems of conventional catalysts providing eco-friendly routes for industrial applications. The use of solid acid catalysts like zeolites, clays, Nafion-H, etc. is gaining importance in the manufacture of fine chemicals and chemical intermediates [9–13].

It has been found that zeolite beta; a wide pore high silica aluminosilicate [14] has potential technological applications in petrochemical processes and in the synthesis of many organic intermediates. Besides the structural characteristics [15–17], higher thermal and acid

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treatment stability, higher strength associated with acid centers and hydrophobicity make zeolite beta a potential industrial catalyst for various hydrocarbon conversion reactions. Though, zeolite catalysts were found to be active in the acylation of aromatics, their use in the acetylation of thioanisole has not been reported in the literature. So, we report in this paper our results on the liquid phase acetylation of thioanisole with acetic anhydride over H-beta.

2. Experimental

2.1. Materials

Thioanisole and acetic anhydride of AR grade were purchased from Merck, UK and S.D. Fine Chemicals Ltd., Mumbai, respectively. All the above materials were used as received in the acetylation experiment. The SiO_2/Al_2O_3 (SAR) ratio and crystallite sizes of zeolites, H-beta (30 and 0.5 μm), H-ZSM-5 (100 and 0.6 μm) and H-Y (6 and 1.0 μm) recovered by calcination of NH_4-Y in air at 550 °C for 8h were provided by CPP-NCL, Pune. H-Mordenite (SAR-20 and 1.0 μm) was obtained from PQ Zeolites BV., The Netherlands. All catalysts used in the reaction were in the powder form.

2.2. Characterization

The SiO_2/Al_2O_3 ratio of various zeolites were estimated by atomic absorption methods (AAS-Hitachi Model Z-8000). The surface area of the samples was measured by nitrogen BET method using an area meter by Omnisorb 100 CX (Coulter, USA). X-ray powder diffraction (XRD) was carried out on a Rigaku D-Max/III-VC model using the Cu Kα radiation and was used to evaluate the peak positions of various zeolite samples. The crystallite size and morphology of the zeolite catalysts were estimated by Leica Stereoscan-440 scanning electron microscope (SEM). Acidity of the zeolite catalysts was measured by the temperature-programmed desorption (TPD) of ammonia.

2.3. Procedure for catalytic experiments

Zeolite catalysts were thermally activated at 500 °C for 4 h and cooled to room temperature prior to their use in the acetylation reaction. In a typical experiment, known amounts of equimolar (0.08 mol) quantities of thioanisole and acetic anhydride along with catalyst (0.9 g, 5 wt% of total reaction mixture) were placed in 50 ml Parr autoclave. The reactor was pressurized with N_2 (200 psig) and heated to 150 °C for 2 h under constant stirring. At the end of 2 h, the autoclave was cooled to room temperature and pressure released. A sample of reaction mixture was centrifuged and analyzed for its contents by HP 5890 gas chromatograph equipped with a fused megabore column SE-52, HP-5 (cross-linked 5% PhMe silicone), 30 m length, 0.53 mm ID, 0.3 μm film thickness and a FID detector. Conversion and product selectivities were calculated from gas chromatographic analysis. The authenticities of acetylated products were confirmed by GCMS (Shimadzu QP 5000) and GC-IR (Shimadzu FTIR).

3. Results and discussion

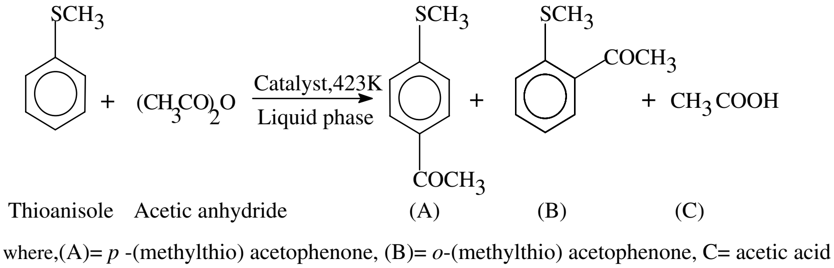
Liquid phase acetylation of thioanisole with acetic anhydride catalyzed by H-beta gave acetylated products *p*-(methylthio) acetophenone (4-MTAP) as the major product and *o*-(methylthio) acetophenone (2-MTAP) as a minor product as shown in the reaction Scheme 1.

3.1. Catalyst characterization

The physicochemical properties of the catalysts used in the acetylation of thioanisole for SiO_2/Al_2O_3 ratios, surface area (m^2/g), total acidity (mmol/g) and crystallite size (μm) are presented in Table 1.

3.2. Catalytic activity of various zeolites

The catalytic activities of H-beta, H-Y, H-mordenite and H-ZSM-5, in the acetylation of thioanisole by acetic anhydride carried out at 150 °C are presented in Table 2. It is seen that all the catalysts readily form 4-MTAP as



where,(A)= *p* -(methylthio) acetophenone, (B)= *o*-(methylthio) acetophenone, C= acetic acid

Scheme 1.

Table 1
Physicochemical properties of the catalysts

Catalyst	SiO_2/Al_2O_3[a] (molar ratio)	Surface area[b] (m^2/g)	Acidity[c] (mmol/g)	Crystallite[d] size (μm)
H-beta	30	540	0.94	0.5
H-Y	6	530	2.25	1.0
H-mordenite	20	490	0.72	1.0
H-ZSM-5	100	364	0.82	0.6

[a] Measured by atomic absorption.
[b] Measured by N_2 adsorption.
[c] Measured by TPD of ammonia.
[d] Measured by scanning electron microscope.

the major product with small amount of 2-MTAP in 2 h. In the presence of catalyst, acetic anhydride forms the acetyl carbocation, which attacks on TA at *ortho*- and *para*-positions to give an isomeric mixture of the products.

In acetylation of TA, H-beta was found to be the most active catalyst in comparison with other zeolites H-Y, H-mordenite and H-ZSM-5 under the reaction conditions studied. H-beta having three-dimensional pore systems with straight channels of ca. 7.3 × 6.5 Å and tortuous channel of 5.5 × 5.5 Å [15] with more strong and medium acid sites gave higher conversion of TA. Even though, H-Y has the highest acidity (Table 1), being large pore and weaker acid sites, gave less conversion of TA. Similarly, the poor activity of H-ZSM-5 might be explained on the basis of its smaller pore size (5.4 × 5.6 and 5.1 × 5.5 Å) compared with the larger size of the products. While, H-mordenite is having one-dimensional pore with elliptical channels, 6.5 × 7.0 Å [18] also has poor activity. The catalysts showed the decreasing order of activity after 2 h of reaction time in acetylation of TA with AA: H-beta > H-Y > H-mordenite > H-ZSM-5.

3.3. Time on stream data (H-beta)

In order to investigate the effect of contact time on the conversion of TA or rate of TA conversion (TOF) and product selectivity, the acetylation of TA was carried out for 10 h with H-beta with catalyst weight = 0.9 g (5 wt% of the reaction mixture), reaction mixture = 18 g, AA:TA) molar ratio = 1 and 150 °C and the results are shown in Fig. 1. The conversion of TA increased linearly up to 2 h and progressively reached a steady state with a marginal increase in the conversion (34.1 mol%) at the end of 10 h. The steady state conversion of TA after 4 h is due to strong adsorption of di- and tri-acetylated thioanisole products causing pore blockage, which could not be analyzed as these were entrapped in the zeolite micropores [12]. While, the rate of reaction (bar graph Fig. 1) decreased continuously as a function of time. However, the selectivity to 4-MTAP remained unchanged (>99.9%) in acetylation of thioanisole by acetic anhydride. Therefore, to get higher conversion of TA, carrying out the reaction for shorter time has been found to be ideal to achieve desired results.

3.4. Influence of catalyst concentration

To know the effect of H-beta catalyst concentration on the conversion of TA or TOF and products distribution in the acetylation of TA, the reaction was

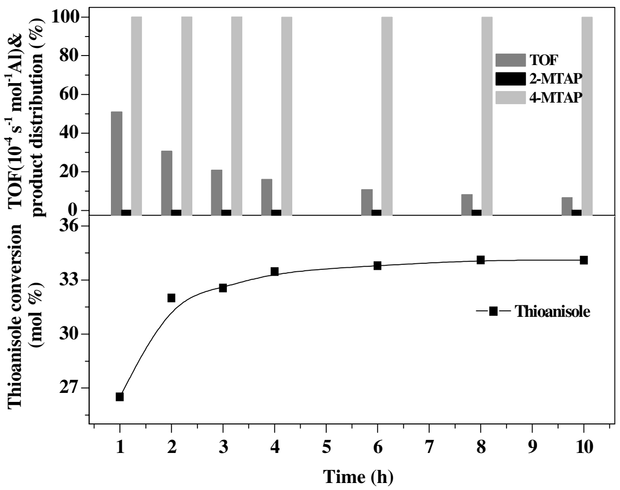


Fig. 1. Time on stream study. Conditions: catalyst = H-beta, catalyst weight = 0.9 g (5 wt% of the reaction mixture), weight of reaction mixture = 18 g, temperature = 150 °C, (AA/TA) molar ratio = 1.

Table 2
Acetylation of thioanisole[a]

Catalyst	Thioanisole conversion (mol%)	TOF[b] (10^{-4} s^{-1} mol^{-1} Al)	Product distribution[c] (%)		4-MTAP/2-MTAP
			2-MTAP	4-MTAP	
H-beta	32	30.6	0.1	99.9	≈100
H-Y	8.5	2.0	3.8	96.2	25.3
H-mordenite	5.5	3.6	1.4	98.6	70.4
H-ZSM-5	1.2	3.7	0.3	99.7	≈100

[a] Reaction conditions: catalyst/acetic anhydride (wt/wt) = 0.11; reaction temperature = 423 K; thioanisole/$(CH_3CO)_2O$ (molar ratio) = 1; thioanisole = 0.08 mol; reaction time = 2 h.
[b] TOF is given as mole of thioanisole transformed per second per mole of Al^{3+}.
[c] 2-MTAP = 2-methylthio acetophenone; 4-MTAP = 4-methylthio acetophenone.

conducted by varying the catalyst concentration in the range 2.5–10 wt% of total reaction mixture (18 g), keeping constant molar ratio of AA:TA as 1, 150 °C and 2 h. The results are shown in Fig. 2 as a conversion or TOF of TA as a function of catalyst concentration. It is seen from the bar graph that the conversion of TA increased from 26 to 41 mol% linearly in 2 h, with no change in the product distribution, 4-MTAP (>99.9%), while, TOF decreased continuously with increase in catalyst concentration.

3.5. Influence of reaction temperature

The effect of reaction temperature on acetylation of TA by AA was studied by varying the temperature from 80 to 180 °C with catalyst (5 wt% of total reaction mixture), AA/TA molar ratio = 1 and 2 h. The results are shown in Fig. 3. As the temperature is increased from 80 to 180 °C, both the conversion of TA and TOF increased without change in the selectivity for major product (4-MTAP > 99.9%). The highest conversion of TA at 180 °C was 34 mol% after 2 h and the reaction is less sensitive to temperature.

3.6. Influence of substrate molar ratio

The influence of acetic anhydride to thioanisole (AA:TA) molar ratio on the conversion of TA or TOF and product distribution are presented in Fig. 4. The AA:TA mole ratio was changed from 0.3 to 3, keeping other quantities same. As AA:TA molar ratio is increased from 0.3 to 1, conversion of TA or TOF sharply increased up to molar ratio 1, after this, a slow and steady increase was observed with the highest selectivity for 4-MTAP (>99.9%).

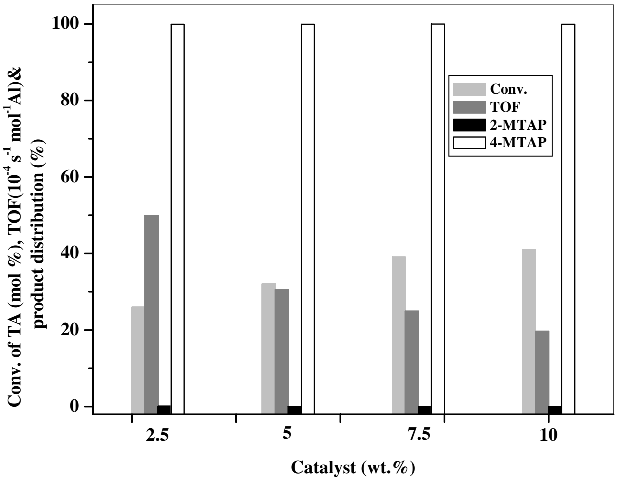


Fig. 2. Effect of catalyst concentration. Conditions: catalyst = H-beta, weight of the reaction mixture = 18 g, temperature = 150 °C, (AA/TA) molar ratio = 1, time = 2 h.

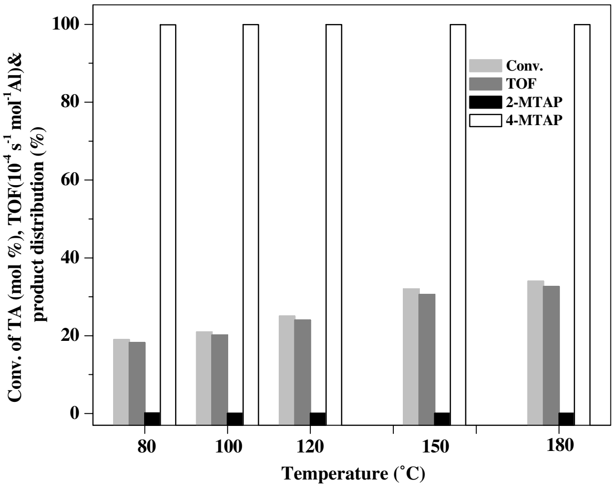


Fig. 3. Effect of reaction temperature. Conditions: catalyst = H-beta, catalyst weight = 0.9 g (5 wt% of the reaction mixture), weight of the reaction mixture = 18 g, (AA/TA) molar ratio = 1, time = 2 h.

3.7. Catalyst recycling

H-beta catalyst was reused by separating the catalyst from reaction mixture by filtration, washing with ethyl acetate and calcining at 500 °C for 4 h in air before use in the fresh experiment. The results on recycling of H-beta in the acetylation of thioanisole by acetic anhydride are presented in Table 3. Thus, the recovered zeolite after each reaction was characterized for its crystallinity by XRD, which showed downward trend in crystallinity of H-beta after each cycle. The conversion of TA and selectivity for 4-MTAP decreased marginally when H-beta was recycled in the acetylation reaction. The loss of Al and a decrease in the crystallinity of zeolite H-beta were attributed to the decrease in

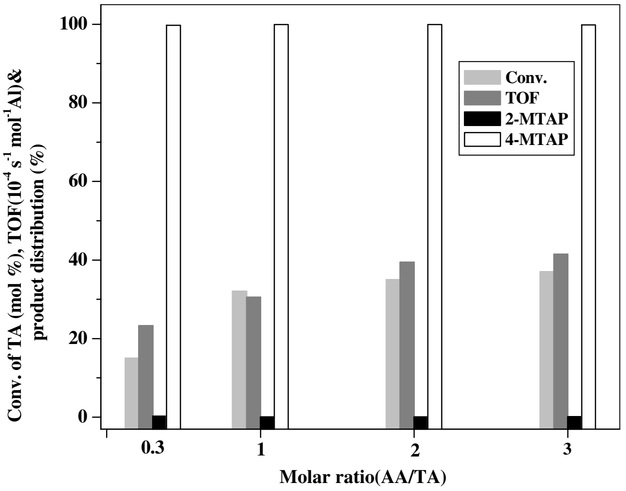


Fig. 4. Effect of acetic anhydride to thioanisole molar ratio. Conditions: catalyst = H-beta, catalyst weight = 0.9 g (5 wt% of the reaction mixture), weight of the reaction mixture = 18 g, temperature = 150 °C, time = 2 h.

Table 3
Catalyst recycling[a]

Cycle	Thioanisole conversion (mol%)	Product distribution[b] (%)		4-MTAP/2-MTAP	H-beta crystallinity (%)
		2-MTAP	4-MTAP		
Fresh	32	0.1	99.9	≈100	100
First recycle	29.9	0.9	99.1	≈100	100
Second recycle	27.8	0.1	99.9	≈100	91.7

[a] Reaction conditions: catalyst/acetic anhydride (wt/wt) = 0.11; reaction temperature = 423 K; thioanisole/$(CH_3CO)_2O$ (molar ratio) = 1; thioanisole = 0.08 mol; reaction time = 2 h.

[b] 2-MTAP = 2-methylthio acetophenone; 4-MTAP = 4- methylthio acetophenone.

catalytic activity after each cycle, which is in agreement with the observation made on acetylation of anisole using zeolite catalysts [12].

3.8. Efficiency of acetic anhydride utilization

In few runs of acetylation of thioanisole, we checked the mass balance after the reaction by estimating the amounts of moles of thioanisole, acetic anhydride, acetylated products and acetic acid in the reaction mixture. It was found that the mass balance between reactants and products were very well matched with the stoichiometry of the reaction. Also, the nitrogen gas used (for pressurizing the reactor to keep the reactants in liquid phase conditions) for efficient interaction of the reactants with catalyst was analyzed for decomposed gaseous products of acetic anhydride such as, CO_2. Our analysis did not show any of the gaseous products in the nitrogen released after the reaction. The above observations confirmed the efficient use of acetic anhydride in acetylating thioanisole under the reaction conditions studied.

4. Conclusions

Acetylation of thioanisole with acetic anhydride was carried over H-beta in liquid phase conditions under nitrogen pressure. H-beta showed good activity and shape selectivity to 4-MTAP (99.9%) with a maximum conversion of thioanisole (41 mol%) at 150 °C, equimolar ratio of AA to TA and catalyst (10 wt% of reaction mixture). When, the mass of the catalyst was doubled and the temperature was increased from 150 to 180 °C, we did not see significant enhancement in the conversion of TA. This could be due to the deactivation of catalyst and product inhibition [12,13]. The above catalyst is recyclable, cost effective and environmental friendly in the liquid phase acetylation of thioanisole by acetic anhydride and efficient use of acetic anhydride has been established in the reaction.

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