Liquid-phase cyclization of (phenylthio)acetaldehyde diethylacetal to benzo[*b*]thiophene over Zn^{2+} ion-exchanged zeolite BEA

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Cyclization of (phenylthio)acetaldehyde diethylacetal was examined in 1,2-dichloroethane and chlorobenzene solvents in the presence of H-beta zeolite and Zn^{2+} ion-exchanged beta zeolite under reflux conditions. Zn^{2+} ion-exchanged beta zeolite showed better activity than its H-form counterpart owing to its higher Lewis acidity. The cyclization proceeds via two different pathways. At lower temperature the reaction proceeds predominantly via a pathway in which deacetalization of the reactant occurs first and then the resulting aldehyde cyclizes to benzo[*b*]thiophene.

KEY WORDS: benzo[*b*]thiophene; cyclization; zeolite; H-beta; ion-exchange; deacetalization.

1. Introduction

Benzo[*b*]thiophene and its derivatives are important heterocyclics which find use in pharmaceuticals, pesticides and in general organic synthesis [1,2]. Sulphur-containing crude petroleum is the main source of these compounds. However, separation of these compounds from crude petroleum is a tedious process and hence the demand for these compounds is mainly met by synthetic methods. One of the methods followed for the synthesis of these compounds is cyclization of the corresponding (arylthio)-acetaldehyde diethylacetal or dimethylacetal in the presence of polyphosphoric acid [3–5]. The main problem associated with this method is the low yields due to acid-catalyzed side reactions which lead complex mixture of by-products [6–8]. Another serious problem is the handling and disposal of the acid residues, which pose an environmental threat. Hence there is a clear need for a new, efficient and ecofriendly catalyst. Clark *et al.* [9] reported the cyclization of (phenylthio)acetaldehyde diethylacetal in the presence of K-10 clay impregnated with $ZnCl_2$ in both liquid- and vapor-phase conditions. They were able to achieve a good yield only in vapor-phase conditions, which requires temperatures as high as 300 °C, vacuum, and specialized apparatus to carry out the reaction. Further, a high catalyst to reagent ratio (10–15) is required for effective cyclization [9].

In recent years, the use of zeolites, the so-called microreactors, in the manufacture of fine chemicals and chemical intermediates has attracted increasing interest owing to the special features such as shape selectivity, controlled variability, thermal stability and above all reusability and ecofriendly nature, the characters most sought after in green chemistry [10]. In the present study, we attempted the cyclization of (phenylthio)acetaldehyde diethylacetal in the presence of beta zeolites, keeping in mind the ecofriendly nature of the zeolites and their restricted pore system, which can limit the unwanted polymerized byproducts. We report here a successful and relatively simple method for the cyclization of (phenylthio)acetaldehyde diethylacetal in the liquid phase which requires temperatures as low as 90 °C and a catalyst to reagent ratio as low as 0.4.

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2. Experimental

2.1. Materials

Na form beta zeolite (Si/Al = 15) was obtained from Süd-Chemie (India) and converted into the H-form by repeated ion exchange with 1 M ammonium nitrate solution at 80 °C and subsequent calcination of the resulting filtered material in air at 550 °C. This product is abbreviated as HB. The Zn^{2+} ion-exchanged zeolite (ZnB) was obtained by stirring HB with 0.1 N zinc acetate solution (15 ml per gram of catalyst) at 80 °C (repeated three times) and subsequent filtration and calcination in air at 550 °C. The *in situ* DRIFT spectra were recorded in a Nicolet Avatar 360 FTIR spectrophotometer equipped with a high-temperature vacuum chamber. About 10 mg of the powdered catalyst sample were dehydrated at 500 °C under vacuum (10^{-5} mbar) and then cooled to room temperature. Pyridine was adsorbed at the same temperature and allowed to equilibrate. The catalyst was then evacuated at 200 °C under vacuum (10^{-5} mbar) for 30 min. The sample was then cooled to room temperature and the spectrum was recorded. (Phenylthio)acetaldehyde diethylacetal (PTADEA) was prepared following the method reported by Tilak [3].

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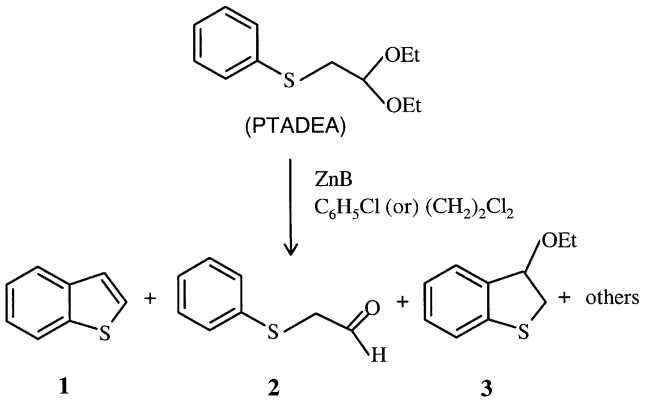
2.2. Cyclization procedure

Cyclization was carried out in a 50 ml double-necked, round-bottomed flask fitted with a reflux condenser and equipped with a magnetic stirrer. The flask was heated by means of an oil-bath fitted with a temperature controller. In the typical cyclization procedure, to the refluxing solution of (phenylthio)acetaldehyde diethylacetal (500 mg, 2.2 mol) in 15 ml of solvent, the catalyst (activated at 300 °C for 3 h) was added and heating was continued. Aliquots were withdrawn periodically and analysed by gas chromatography (Shimadzu GC 17A, DB-5 capillary column, 30 m × 0.25 mm i.d. × 0.25 μm film thickness). The products were also identified by GC–MS (Perkin-Elmer Auto System XL gas chromatograph (Perkin-Elmer Elite series PE-5 capillary column, 30 m × 0.25 mm i.d. × 1 μm film thickness) connected to a Turbo mass spectrometer).



Scheme 1.

3. Results and discussion

The major products in the cyclization process were benzo[*b*]thiophene (**1**), thiophenylacetaldehyde (**2**), 2,3-dihydro-3-ethoxybenzo[*b*]thiophene (**3**) and others (diphenyl disulphide and unidentified by-products) (scheme 1). The results of cyclization of PTADEA are summarized in table 1. The reaction in 1,2-dichloroethane requires a slightly higher amount of catalyst and a longer reaction time. The decrease in concentration of **2** and **3** with increase in reaction time (figures 1 and 2) and catalyst amount, as shown in figure 3, reveals that the products **2** and **3** are the intermediates

Table 1
Results of cyclization of PTADA

Catalyst	Catalyst to PTADEA ratio	Solvent	Temperature (°C)	Time (h)	Conversion of PTADEA (%)	Product yield (%)			
						1	**2**	**3**	Others
ZnB	0.4	$(CH_2)_2Cl_2$	90	4	100	89	6.5	–	4.5
	0.3	C_6H_5Cl	135	1	100	87	–	3.5	9.5
	0.4	CH_2Cl_2	45	2	40	4	30	2	4
HB	0.4	$(CH_2)_2Cl_2$	90	4	85	27	51.5	3.5	3
	0.3	C_6H_5Cl	135	1	98	43.5	6	40.5	8

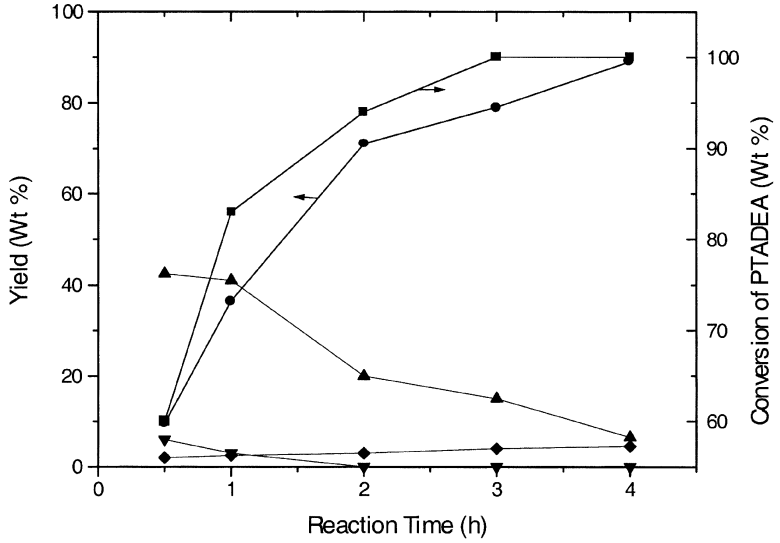


Figure 1. Conversion and product yields as a function of reaction time in 1,2-dichloroethane over ZnB catalyst. Catalyst weight, 150 mg; temperature, 85 °C. ■, Conversion of PTADEA; ●, **1**; ▲, **2**; ▼, **3**; ◆, others.

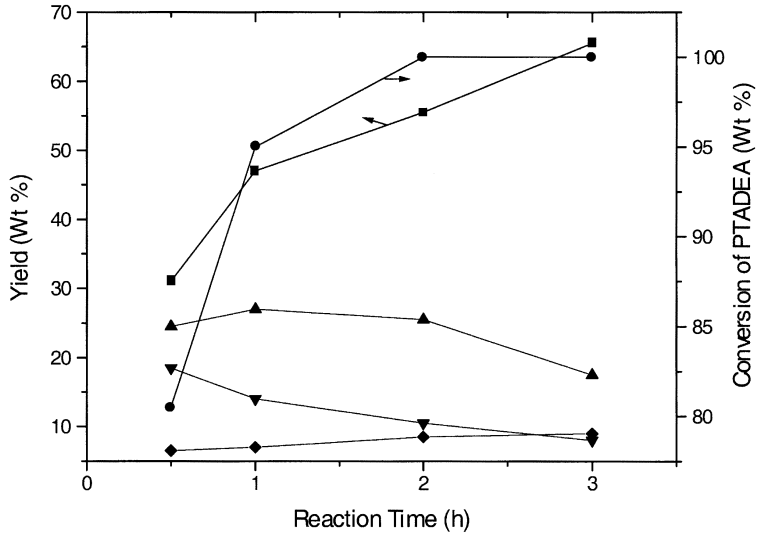


Figure 2. Conversion and product yields as a function of reaction time in chlorobenzene over ZnB catalyst. Catalyst weight, 50 mg; temperature, 135 °C. ■, Conversion of PTADEA; ●, **1**; ▲, **2**; ▼, **3**; ◆, others.

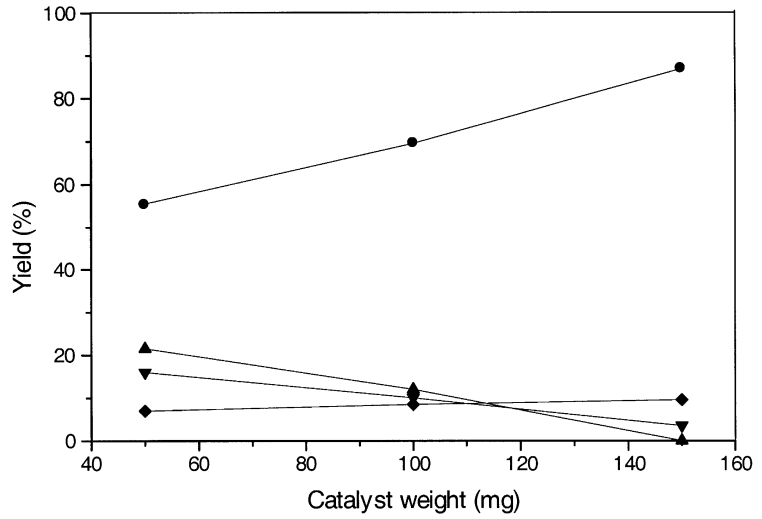
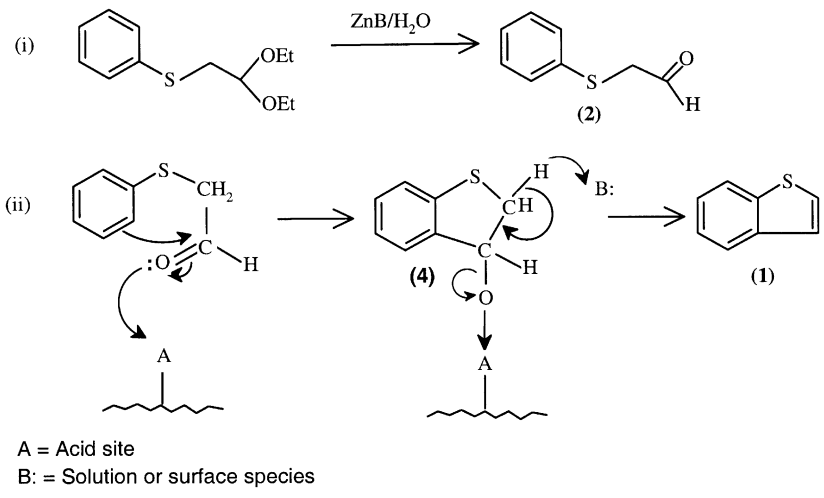
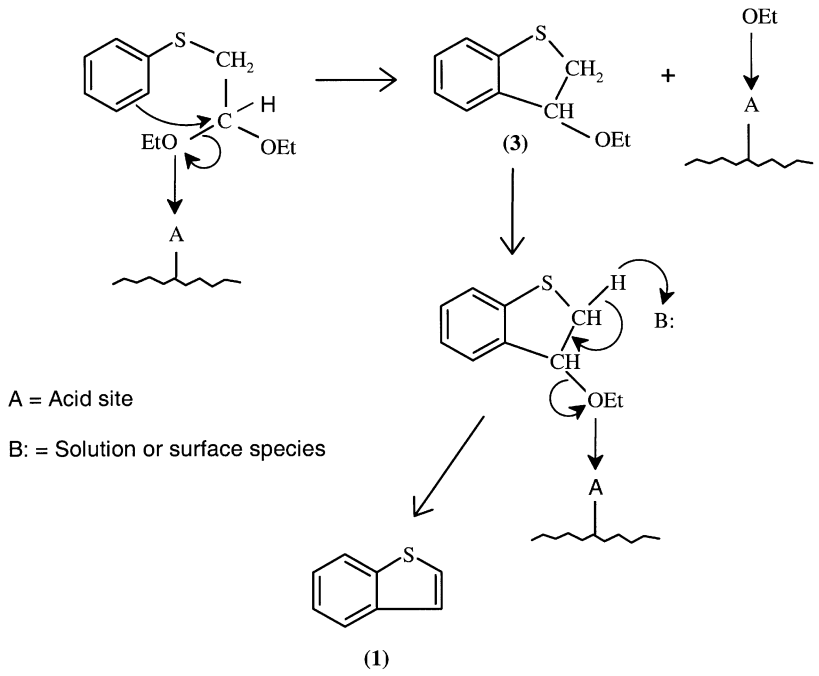


Figure 3. Effect of catalyst weight (ZnB) on product yields. Solvent, C_6H_5Cl; temperature, 135 °C; reaction time, 1 h. ●, **1**; ▲, **2**; ▼, **3**; ◆, others.



Scheme 2.



Scheme 3.

formed in the reaction which yields benzo[*b*]thiophene by different pathways. On comparing figures 1 and 2, it was observed that the yield of **2** is higher in 1,2-dichloroethane than in chlorobenzene. A similar trend was observed when the reaction was carried out in dichloromethane at even lower temperature (table 1). From the experimental results, it is obvious that on going from lower to higher temperature the yield of **3** increases. Based on these observations, it is suggested that at lower temperature deacetalization that yields the aldehyde **2** is favored over cyclization that yields the ether **3**. Considering these facts, it is proposed that at lower temperature the cyclization proceeds predominantly via a pathway (scheme 2) in which first the PTADEA undergoes deacetalization in the presence of acid sites and water present in the catalyst to give the aldehyde **2** and in the second step the carbonyl oxygen coordinates with the acid sites to give the intermediate **4**, which further gives rise to benzo[*b*]thiophene. The small amount of 2,3-dihydro-3-hydroxybenzo[*b*]thiophene observed in the GC–MS analysis confirms this mechanism. At higher temperature both deacetalization and cyclization are possible. Hence the reaction proceeds *via* both of the pathways as shown in schemes 2 and 3. The formation of diphenyl disulphide is due to the intermolecular attack of one reactant molecule over the other as suggested by Clark *et al*. [9].

The *in situ* DRIFT spectra of pyridine-adsorbed catalysts are presented in figure 4. It can be seen that in the spectrum of ZnB there is an increase in the intensity

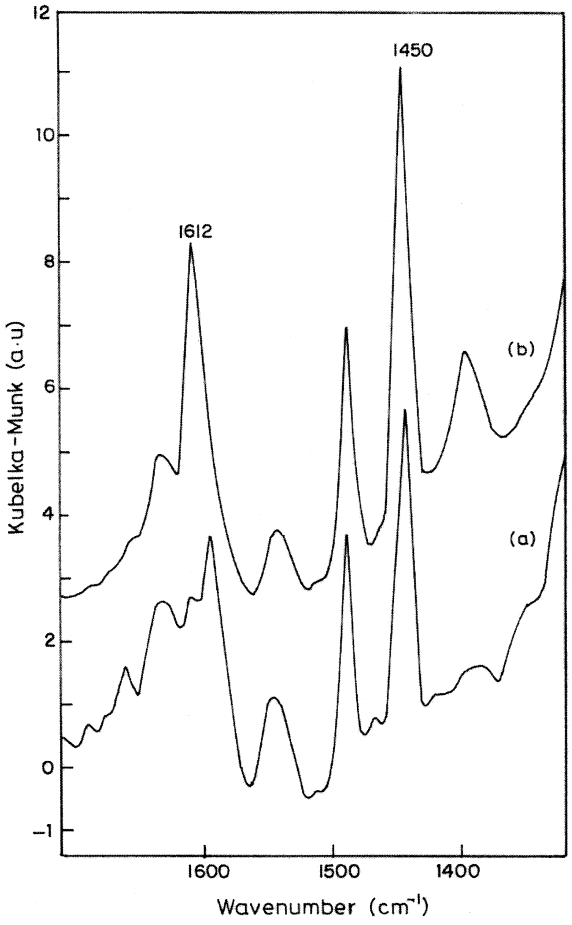


Figure 4. *In situ* DRIFT spectra of pyridine-adsorbed catalysts: (a) HB and (b) ZnB.

of the peaks at 1450 and 1612 cm^{-1}, which correspond to coordinately bound pyridine Lewis acid sites [11,12]. Lewis acidity of the catalysts was calculated from the absorbance value of the peak at 1450 cm^{-1} using an extinction coefficient (ε) of 1.5×10^6 cm^{-1} per mol, and it was found to be 0.227 mmol/g for HB and 0.437 mmol/g for ZnB [13,14]. This increase in Lewis acidity reveals that new Lewis acid sites are created upon Zn^{2+} ion exchange in the parent zeolite. These newly generated Lewis acid sites may be responsible for the enhanced catalytic activity of the ZnB catalyst compared with the parent HB catalyst. After the end of the reaction the catalyst was filtered, washed with acetone, and regenerated at 500 °C in the presence of moisture-free air and reused. The catalytic activity of the catalyst was found to be retained even after three recycles.

4. Conclusion

Zn^{2+} ion-exchanged beta zeolite could be a viable, economical and ecofriendly alternative to polyphosphoric acid catalysts in the synthesis of benzo[*b*]thiophene *via* cyclization of (phenylthio)acetaldehyde diethylacetal in the liquid phase.

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