

# Facile synthesis of bis(indolyl)methanes using polyindole salt as reusable catalyst

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Received 16 July 2005; received in revised form 18 July 2005; accepted 26 July 2005

Available online 8 September 2005

## Abstract

Polyindole salt was used as an efficient catalyst for the synthesis of bis(indolyl)methanes for the first time and afford excellent yield in room temperature. Furthermore, after completion of reaction the catalyst could be easily recovered and can be reused.  
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**Keywords:** Polyindole salt; Solid acid catalyst; Reusable catalyst; Bis(indolyl)methane

## 1. Introduction

Indole derivatives are found abundantly in variety of natural plants and exhibit various physiological properties and are potentially bioactive compounds. Therefore, there is a great deal of interest in the synthesis of this class of compounds. Several methods have been reported in the literature for the synthesis of bis(indolyl)methanes using protic acids [1] and Lewis acids [2,3]. Many Lewis acids like trifluoroboron etherate and aluminium chloride promote this type of reaction but they generate harmful wastes, which pose environmental problems. Many Lewis acids are deactivated or sometimes decomposed by nitrogen-containing reactants. Even when the desired reactions proceed, more than stoichiometric amounts of Lewis acids are required because they are trapped by nitrogen [4]. Solid acid catalyst like zeolite is also used for bis(indolyl)methane synthesis, but it needs very high temperature for reactivation [5]. Recently, we reported polyaniline-based solid acid catalysts for the synthesis of bis(indolyl)methanes [6,7]. The above mentioned catalysts are having their own advantages and disadvantages but it is always interesting to develop a new catalyst with desirable features such as efficient, recyclable and ecofriendly catalyst for the organic transformation.

In the present investigation, we report the polyindole salt as an efficient polymer-based solid acid catalyst for the preparation of bis(indolyl)methanes. Polyindole is an electroactive polymer which can be obtained either by anodic or by chemical oxidation of indole [8,9]. However, only little investigation has been made on chemically synthesized polyindole. This polymer and its derivative appear to be good candidates for applications in various domains like electronics, electrocatalysis, pharmacology and it can be used as models for certain biopolymers like melanines [10]. As far as our knowledge is concerned, polyindole salt is used as catalyst for the first time in organic transformation.

## 2. Experimental

### 2.1. Materials

Indole, FeCl<sub>3</sub> and aldehydes (purchased from E. Merck, India and also CDH, India) were used without further purification. Solvents were purified as per reported procedure.

### 2.2. Synthetic procedures

#### 2.2.1. Procedure for preparation of polyindole solid acid catalyst

In a typical experiment, 8.5 mmol of indole was dissolved in 50 ml chloroform; to this solution, 34.2 mmol of FeCl<sub>3</sub> was

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added. The reaction mass was kept under constant stirring at room temperature for 12 h under  $N_2$  atmosphere. At the end of the reaction, 100 ml of acetone was added and the separated solid was filtered and washed with acetone until the filtrate became colorless. The solid was dried at  $90^\circ C$  until a constant mass.

### 2.2.2. Procedure for synthesis of bis(indolyl)methanes

In a typical reaction procedure, indole (8 mmol), aldehyde (4 mmol) and polyindole salt catalyst (20 wt.% with respect to indole) in methanol solvent (40 ml) was stirred in a round-bottomed flask at room temperature for 3 h. The conversion of the reaction was monitored by TLC. Catalyst was separated by filtration and washed with acetone, filtrate was evaporated under vacuum. The product was isolated by two methods: (a) treating with hexane, and (b) preparative column with ethyl acetate and hexane mixture (20:80).

## 2.3. Characterization

### 2.3.1. Resistance measurement

Polyindole sample was pressed into disks of 16 mm diameter and ca. 2-mm thickness under a pressure of 400 MPa. Resistance measurement of the pellet was carried out on a four probe connected to a Keithley digital multimeter (Model-2010). Resistance was calculated based on the average of at least three pairs of consistent readings at different points on the pressed pellet.

### 2.3.2. Pellet density

Polyindole sample in the form of pellet was obtained by subjecting the sample to a pressure of 400 MPa. Pellet density was measured from mass per unit volume of the pressed pellet.

### 2.3.3. Infrared spectrum

The polyindole sample was mixed with KBr powder and compressed into pellet, wherein the polyindole powder was evenly dispersed. Fourier transform infrared spectrum was recorded using GC-FT-IR spectrometer (Model 670 Thermo Nicolet Nexus, USA spectra).

### 2.3.4. X-ray diffraction pattern

Wide angle X-ray diffraction (XRD) pattern for the polyindole powder sample was obtained using a Siemens/D-5000 X-ray diffractometer using  $Cu K\alpha$  radiation of wave length  $1.54 \text{ \AA}$  and continuous scan speed of  $0.045^\circ \text{ min}^{-1}$ .

### 2.3.5. Elemental analysis

The content of elements in the polyindole sample was determined using Elementor Vario EC Germany elemental analyzer. The value of percentage of carbon, hydrogen and nitrogen observed for polyindole salt was 59.0, 2.7 and 7.3%, respectively.

### 2.3.6. Scanning electron microscopy

A morphology study of polyindole sample was carried out using Hitachi S520 scanning electron microscope instrument operating at 10 kV. The sample was mounted on a double-sided adhesive carbon disk and sputter-coated with a thin layer of gold to prevent sample-charging problem.

### 2.3.7. Thermo gravimetric analysis

Thermo gravimetric analysis (TGA) of polyindole sample was carried out from  $25$  to  $900^\circ C$  under nitrogen atmosphere at a heating rate of  $10^\circ C \text{ min}^{-1}$  using 851<sup>e</sup>, Mettler Toledo, Switzerland.

### 2.3.8. Differential scanning calorimetry

Differential scanning calorimetry (DSC) analysis of polyindole sample was carried out from  $-20$  to  $300^\circ C$  under nitrogen atmosphere at a heating rate of  $10^\circ C \text{ min}^{-1}$  using DSC 821<sup>e</sup>, Mettler Toledo, Switzerland.

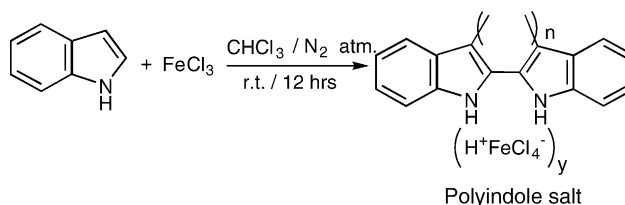
## 3. Results and discussion

### 3.1. Polyindole salt preparation and characterization

Polyindole salt can be prepared easily with useful catalytic properties such as easy recovery, reusability and activity. Polyindole was prepared by chemical oxidation of indole by ferric chloride in  $CHCl_3$  (Scheme 1).

This process yielded 70% polyindole with respect to the weight of indole used in the reaction. The polyindole salt was characterized by infrared (IR), XRD, TGA, DSC, scanning electron microscopy (SEM) techniques, C, H, N, S analysis, conductivity and pellet density measurements. Pellet density and conductivity of the polyindole salt were found to be  $1.1 \text{ g/cm}^3$  and  $1.7 \times 10^{-5} \text{ S/cm}$ , respectively.

Infrared spectrum of polyindole salt is shown in Fig. 1. The important characteristic bands of polyindole salts are: a band around  $3430 \text{ cm}^{-1}$  is assigned to the stretching frequency of N-H bond. A peak observed at  $1600 \text{ cm}^{-1}$  with the shoulder at  $1570 \text{ cm}^{-1}$  is attributed to aromatic bond in benzene ring. The band at  $1370 \text{ cm}^{-1}$  is assigned for C=N stretching. The band located at  $1215 \text{ cm}^{-1}$  reveals the quinonic form of the doped state. A peak located at  $765 \text{ cm}^{-1}$  is assigned to the out of plane deformation of the C-H bond. The infrared spectrum of polyindole salt is similar to the spectrum reported by Talbi et al. in which they have studied vibrational properties



Scheme 1.

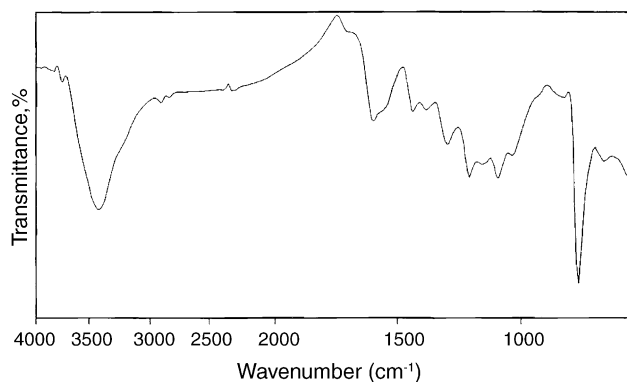


Fig. 1. Infrared spectrum of polyindole salt.

and structural studies of doped and dedoped polyindole by FT-IR, Raman and EEL spectroscopic techniques [11]. X-ray diffraction pattern of polyindole salt was recorded and it shows amorphous nature (Fig. 2). The scanning electron micrograph of polyindole salt shows irregular morphology (Fig. 3).

Thermo gravimetric analysis of polyindole salt (Fig. 4) shows two-step weight loss behaviour. First step weight loss (4% upto 110 °C) is due to the loss of moisture trapped in the polymer. The second step weight loss from 110 °C may be due to initial degradation of polymer and dopant present in the polymer followed by degradation of polymer chain. DSC thermogram (Fig. 5) shows that the polymer material is having  $T_g$  around 110 °C and an exotherm around 170 °C may be due to thermal degradation of the polymer chain.

### 3.2. Polyindole salt as catalyst in the synthesis of bis(indolyl)methanes

There was no appreciable reaction when indole was allowed to react with benzaldehyde in the absence of catalyst in methanol. However, indole (1.7 mmol) was reacted with benzaldehyde (0.849 mmol) in 5 ml methanol using 20 wt.% of polyindole salt with respect to indole leads to the corresponding 1H,1'H-3,3'-phenylmethanediyl-bis-indole in 3 h (98%).

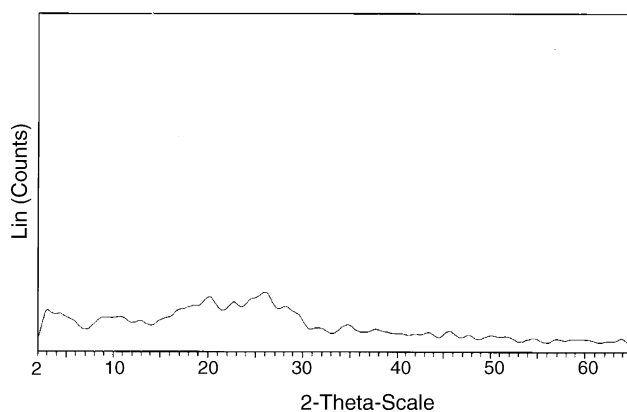


Fig. 2. XRD spectrum of polyindole salt.

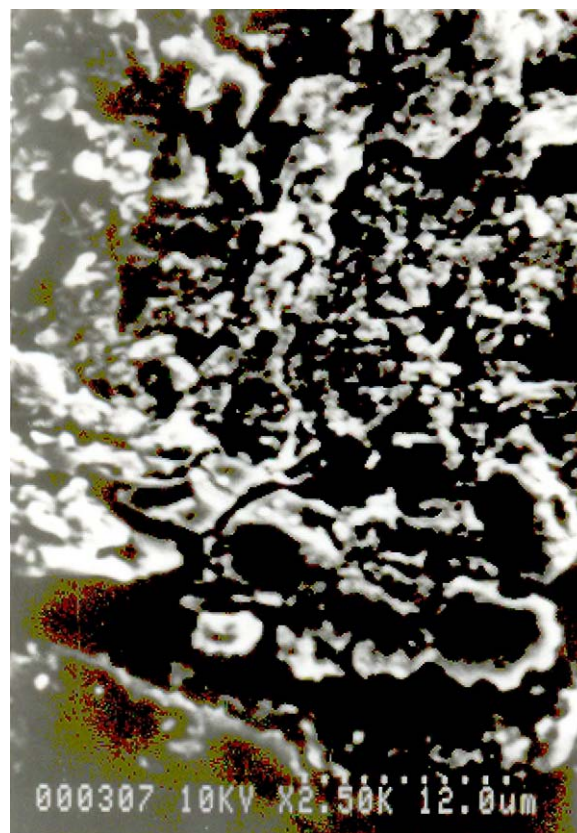
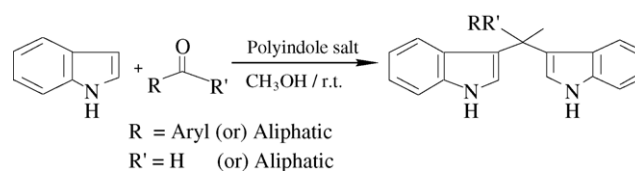


Fig. 3. SEM picture of polyindole salt.



Likewise, several aromatic, aliphatic aldehydes and aliphatic ketone reacted with indole under similar conditions to afford the products. The effect of electron deficiency and the nature of the substituents on the aromatic ring of aldehyde

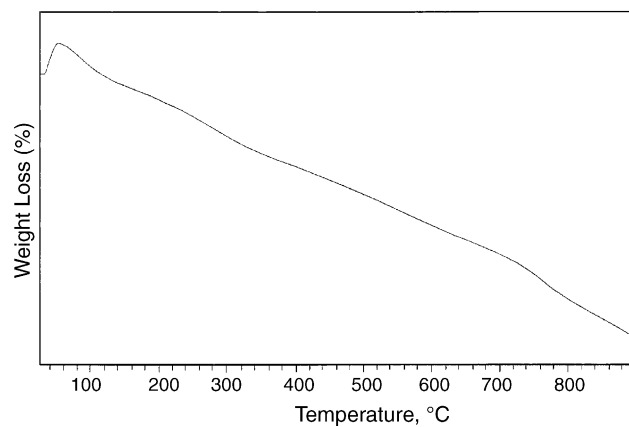
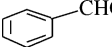
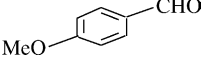
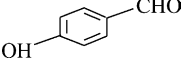
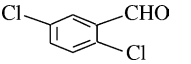
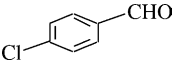
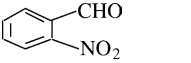
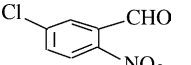
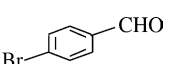
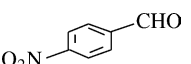
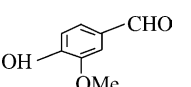
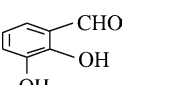
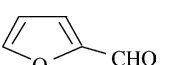
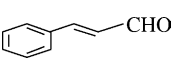
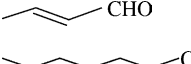
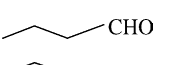

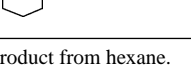
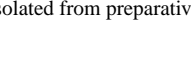


Fig. 4. TGA spectrum of polyindole salt.

Table 1  
Synthesis of bis(indolyl)methanes using polyindole salt as catalyst

Entry	Aldehyde or ketone	Time (h)	Yield (%)
1		3.0	98 <sup>a</sup>
2		0.25	98 <sup>a</sup>
3		0.5	98 <sup>b</sup>
4		4.0	36 <sup>a</sup>
5		0.75	97 <sup>b</sup>
6		4.0	97 <sup>b</sup>
7		4.0	99 <sup>b</sup>
8		0.5	98 <sup>b</sup>
9		4.0	98 <sup>b</sup>
10		0.5	97 <sup>b</sup>
11		1.0	97 <sup>a</sup>
12		0.5	98 <sup>b</sup>
13		1.0	97 <sup>b</sup>
14		0.75	98 <sup>b</sup>
15		4.0	5 <sup>a</sup>
16		4.0	73 <sup>a</sup>
17		4.0	21 <sup>a</sup>
18		4.0	42 <sup>a</sup>

<sup>a</sup> Isolated product from hexane.

<sup>b</sup> Product isolated from preparative column (EtOAc–hexane mixture).

showed some effect on this conversion. It is seen that chloro and nitro substituted aldehydes (Table 1, entries 4, 6, 7 and 9) required longer reaction time to produce comparable yield than their electron-donating counterparts. This is in harmony with the rules of electrophilic aromatic substitution. Aldehydes like 4-methoxy benzaldehyde and 4-hydroxy-3-methoxy benzaldehyde (Table 1, entries 2 and 10) reacted rapidly with indole to furnish the product. Aliphatic aldehyde (Table 1, entries 15–18) gives moderate yield compared to aromatic

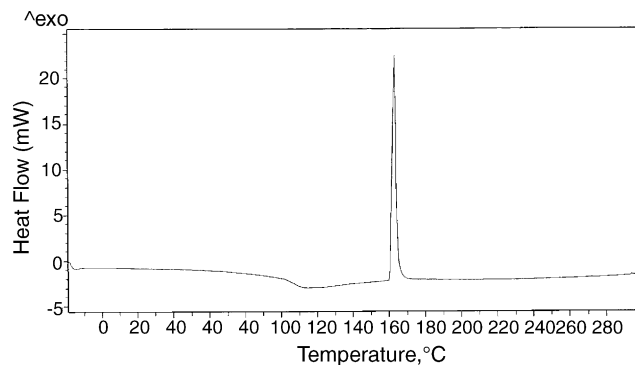


Fig. 5. DSC spectrum of polyindole salt.

Table 2  
Reusability of polyindole salt

Entry	Number of recycle	Time (h)	Yield (%)
1	Fresh	0.25	98
2	1	0.25	98
3	2	1	98
4	3	2	98
5	4	2	98
6	5	2	97

aldehyde. The results summarized in Table 1 clearly indicate the scope of the reaction with respect to various substituted aldehydes on polyindole catalyst.

Billaud et al. synthesized polyindole by chemical oxidation with  $\text{FeCl}_3$  and reported the presence of  $\text{FeCl}_4^-$  species in the polymer [9]. The presence of  $\text{H}^+\text{FeCl}_4^-$  in the polyindole salt acts as solid acid catalyst in the reaction between indole and aldehydes.

The feasibility of reusability of the catalyst was also examined by treating indole with 4-methoxy benzaldehyde in the presence of 20 wt.% of the catalyst with respect to indole in methanol as solvent for five consecutive reactions. The reactions proceed smoothly with increase in reaction time and furnished the yield between 97 and 98% and this result indicates that the catalyst can be reused (Table 2).

#### 4. Conclusion

In summary, polyindole was prepared by chemical oxidation of indole with  $\text{FeCl}_3$ . The polyindole salt was used as polymer-based solid acid catalyst in the synthesis of bis(indolyl)methane. The salient features of the catalyst are simple preparation, easy separation, reusability and excellent activity.

#### Acknowledgement

Support of this research by CSIR network project (CMM-0010) is gratefully acknowledged.

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