

Selective synthesis of 3-isopropylindole over modified HY zeolites

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Abstract

The vapor-phase alkylation of indole with 2-propanol was carried out over HZSM-5 (30), HY, CuHY, CrHY, LaHY and CeHY zeolites at 300 °C with 0.5 h⁻¹ weight hourly space velocity. The catalytic activity with respect to the yield of 3-isopropylindole followed the order: HZSM-5 (30) < CuHY < HY < CrHY < LaHY < CeHY. The various reaction parameters like effect of temperature, weight hourly space velocity and time on stream have been studied. The maximum yield of 3-isopropylindole of 40.0% at a conversion of 63.0% indole was obtained over 3 wt% CeHY zeolite at 300 °C with 0.5 h⁻¹ weight hourly space velocity. The catalysts are characterized by XRD, BET surface area and STPD of ammonia. © 2001 Elsevier Science B.V. All rights reserved.

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1. Introduction

One of the foremost challenges currently faced by the chemical industry is the need for alternative production technologies that are cleaner, safer and more environmentally friendly. Processes should be efficient in both energy and raw material consumption and produce minimum waste. The usage of conventional homogeneous acid catalysts such as H₂SO₄, BF₃, HF, AlCl₃, FeCl₃ etc., has several disadvantages like high corrosion, tedious workup

procedure, need for stoichiometric quantities, found to give undesirable side products and they are not reusable. To overcome these difficulties, several heterogeneous acid catalysts were introduced from time to time, which include clays, amorphous silica–alumina, mixed oxides and crystalline zeolites. Among solid acid catalysts, zeolites are extensively used on a large scale for the oil refining, petrochemical and chemical industries. Zeolites are continuously finding applications in various fields of science and replacing the traditional Lewis acid catalysts as well as amorphous solid catalysts due to their high acidity, thermal stability, shape selectivity and ease of separation [1–5]. Zeolite catalyzed alkylation of heterocyclic compounds is important because of the alkylated heterocyclic compounds which are widely used as intermediates for many

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organic processes [3,6–8]. Indole and its derivatives are extensively used as intermediates in the synthesis of anti-inflammatory agents, antibiotics and dyes [9–11]. They have also shown biological action as an antidiuretic, stimulant, hypertensive, muscle relaxant, respiratory inhibitor (inhibits the respiration in cancer cells), heart stimulant, tuberculo-stat, and plant growth regulators [12].

Botta et al. [13] reported N-alkylation of indole with *n*-propanol and isopropanol in the presence of aluminum alkoxide and Raney nickel catalyst. Bourak and Gallo [14] have reported N-alkylation of indole with benzyl halide in the presence of NaOH and a catalyst like Bu₄NHSO₄ (quaternary ammonium catalyst) under phase transfer conditions. Traditionally indole is C-alkylated by alcohols in the presence of sodium or potassium alkoxide [15]. C-alkylation of indole was reported with electron deficient olefins and epoxides under the influence of Yb(OTf)₃, a Lewis acid to yield 3-alkylated indole [16]. However these reactions are performed in homogeneous catalysis mode and they suffer from catalyst recovery and end up with tedious workup procedures. In this context, it is worthwhile mentioning that zeolites are found to be excellent catalysts for many alkylation and acylation reactions due to their high acidity, thermal stability and shape selectivity. Recently, we have reported alkylation of indole with methanol over modified HY zeolites [17]. We are now reporting here for the first time, the vapor-phase alkylation of indole with 2-propanol over zeolite catalysts.

2. Experimental

The HZSM-5 (30) zeolite was supplied by Conteka (Sweden), and HY (2.6) zeolite from PQ

Corporation (USA). The catalyst powder was pelletized, crushed and sieved into 2 mm sized granules. Required amount of metal nitrate in aqueous medium was taken onto the sized catalyst to modify the surface by impregnation technique followed by calcination in air at 400 °C for 4 h.

The vapor-phase alkylation reaction was carried out using a continuous fixed bed Pyrex glass reactor with 20 mm internal diameter. The 4 g of the catalyst was used in the form of granules and placed in the middle of the reactor. The reactor was placed inside a temperature-controlled furnace with a thermocouple placed at the center of the catalyst bed for measuring the reaction temperature. The indole and 2-propanol in the 1:6 mole ratio was used as a feed. The need for an excess of 2-propanol is because of the side reactions. It is also due to the fact that the indole system contains π -electronic cloud and its activation appears to be easier than 2-propanol thus demanding higher ratios of the alkylating agent. The reaction mixture was fed from the top using a B. Brown (Germany) syringe pump. The product was collected through an ice-cold water condenser and analyzed by gas chromatography (HP-6890 series) using HP-1 capillary column and products were confirmed by GC-MS and NMR spectroscopy. The product distribution at different time intervals is given in respective tables.

3. Results and discussion

Acidity of the zeolites and modified zeolites was measured by the method of stepwise temperature programmed desorption of ammonia, as reported earlier [18], and the values of the zeolites are given in Table 1. The rare earth metal cation-modified

Table 1
Acidity and surface area of the zeolite catalysts used for alkylation of indole

S. No.	Catalyst	Acidity (mmol g ⁻¹)			Total acidity (mmol g ⁻¹)	Surface area (m ² g ⁻¹)
		150–250 °C	250–350 °C	350–450 °C		
1	HZSM-5 (30)	0.30	0.13	0.10	0.53	427.3
2	HY	0.42	0.19	0.09	0.70	457.2
3	CrHY	0.35	0.15	0.07	0.57	411.4
4	CuHY	0.32	0.16	0.08	0.56	393.8
5	CeHY	0.48	0.23	0.20	0.91	405.3
6	LaHY	0.48	0.27	0.22	0.97	355.7

zeolites exhibit slightly higher acidity than those of parent zeolites [6,18]. The strength of acidity observed decreased in the order of LaHY \geq CeHY > HY > CrHY \geq CuHY > HZSM-5 (30). The X-ray diffraction patterns of the modified zeolites also indicate that the crystallinity was not affected on modification. The surface areas of the modified and unmodified zeolites were measured by N₂ adsorption at 77 K (BET method). The surface areas of the zeolite catalysts are found to be decreasing on metal ion modification and their values are shown in Table 1.

The vapor-phase alkylation of indole with 2-propanol was carried out over HZSM-5 (30), HY, CuHY, CrHY, LaHY and CeHY zeolites at 300 °C with 0.5 h⁻¹ weight hourly space velocity (WHSV) and the results are shown in Table 2. The catalytic activity with respect to the yield of 3-isopropylindole followed the order: HZSM-5 (30) < CuHY < HY < CrHY < LaHY < CeHY. The low catalytic activity of HZSM-5 than HY may be attributed to its lower pore size (5.4 Å) through which the product 3-isopropylindole cannot diffuse out. The pore size of the catalyst must be accessible to reactant and product molecules in order to take part in the reaction.

As it is evident from the literature, the rare earth like La and Ce-modified zeolites are active for alkylation and acylation reactions [18–20]. In

view of this we have modified the HY zeolite with La and Ce (Table 2). The yield of 3-isopropylindole obtained over La and Ce-modified HY zeolite was 36.7% and 40.0%, respectively (Table 2). The maximum yield of 40.0% of 3-isopropylindole with 63.0% conversion of indole was obtained over 3 wt% Ce-modified HY zeolite. The low catalytic activity of Cu and Cr-modified HY zeolites may be due to low acidity. Earlier reports also suggested that rare earth metal cation modified HY zeolites were active for the alkylation and acylation reactions due to their high acidity [18–20]. The high acidity of La and Ce-modified HY zeolite can be attributed to the coordinating ability of La and Ce with water to generate Brnsted acid sites by dissociation [19,20]. It is known that Brnsted and Lewis acid sites are generated during the calcination of the catalyst. Brnsted sites on the catalyst are generated by the dissociation of water molecules and Lewis acid sites are generated by the dehydroxylation of hydroxyl groups at higher temperature [20]. The acid sites of medium strength of either Brnsted or Lewis sites that retain pyridine/ammonia around 300 °C are active for selective alkylation of indole to 3-isopropylindole; this was demonstrated in our previous paper on methylation of indole [17]. The present data on acidity and catalytic activity of the zeolites for 3-isopropylindole formation are very much in cor-

Table 2
Alkylation of indole with 2-propanol over various catalysts

S. No.	Catalyst	TOS (h)	Conversion of indole (%)	Yield (wt%)		
				3-Isopropylindole	1-Isopropylindole	Others
1	HZSM-5 (30)	1	17.8	10.6	0.2	7.0
		4	6.3	4.4	0.1	1.9
2	HY	1	74.8	27.6	5.3	41.9
		4	40.0	13.2	1.0	25.8
3	CeHY	1	75.9	34.9	3.4	37.6
		4	63.0	40.0	1.9	21.1
4	LaHY	1	75.2	30.5	3.6	41.1
		4	60.0	36.7	1.3	22.0
5	CrHY	1	68.9	27.8	2.9	38.2
		4	32.9	19.7	1.2	12.0
6	CuHY	1	41.6	22.4	2.6	16.6
		4	29.4	12.6	0.9	15.9

Amount of metal on modified zeolites = 3 wt%; reaction temperature = 300 °C; indole:2-propanol = 1:6 (mole ratio); WHSV = 0.5 h⁻¹; TOS = time on stream; others = di- and polyalkylindoles.

Table 3

Effect of reaction temperature on alkylation of indole with 2-propanol over 3 wt% CeHY zeolite

S. No.	Temperature (°C)	TOS (h)	Conversion of indole (%)	Yield (wt%)		
				3-Isopropylindole	1-Isopropylindole	Others
1	250	4	72.7	24.4	3.3	45.0
2	300	1	75.9	34.9	3.4	37.6
		4	63.0	40.0	1.9	21.1
3	350	1	78.3	31.7	2.6	44.0
		4	52.0	37.8	1.5	12.7
4	400	1	57.9	28.5	2.1	27.3
		4	48.0	28.0	3.1	16.9

Indole:2-propanol = 1:6 (mole ratio); WHSV = 0.5 h⁻¹; TOS = time on stream; others = di- and polyalkylindoles.

relation with our earlier observations on alkylation of quinoline [6,8]. The effect of various reaction parameters such as temperature, WHSV and product distribution with time on stream has been studied.

The effect of temperature on the isopropylation of indole was studied in the range 200–400 °C at 0.5 h⁻¹ WHSV and the results are shown in Table 3. The maximum yield of 3-isopropylindole was obtained at 300 °C temperature. Below 250 °C temperature the alkylation activity is very low. At temperatures above 300 °C the catalytic activity is decreasing and this may be due to the availability of strong acid sites at high reaction temperatures

[18–21], which enhances the formation of poly-alkylated indoles resulting in the pore blockage. The decrease in activity may also be due to the coke formation.

The reaction was carried out over 1, 3, 5 and 10 wt% Ce-modified HY zeolite and the results are shown in Fig. 1. The 3 wt% Ce-modified HY zeolite was found to be more active for the alkylation of indole to 3-isopropylindole. Further increase in the wt% of Ce decreased the catalytic activity and selectivity.

The effect of WHSV on the alkylation of indole with 2-propanol was studied from 0.25–1 h⁻¹ and the results are shown in Fig. 2. The maximum yield

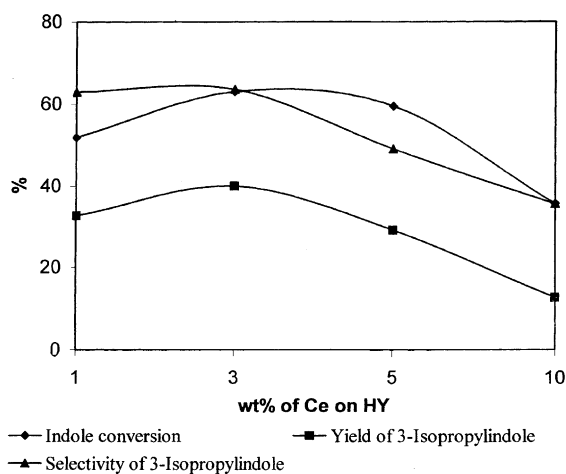


Fig. 1. Effect wt% of Ce over HY zeolite on the alkylation of indole with 2-propanol. Reaction temperature = 300 °C; indole:2-propanol = 1:6 (mole ratio); WHSV = 0.5 h⁻¹; time on stream = 4 h.

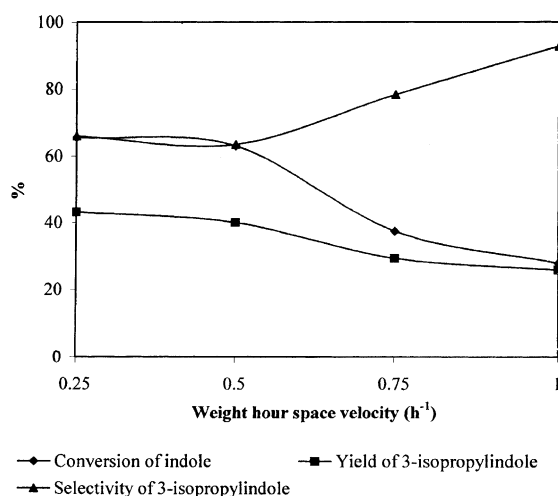


Fig. 2. Effect of WSHV on the alkylation of indole with 2-propanol. Catalysts = 3 wt% CeHY; reaction temperature = 300 °C; indole:2-propanol = 1:6 (mole ratio); time on stream = 4 h.

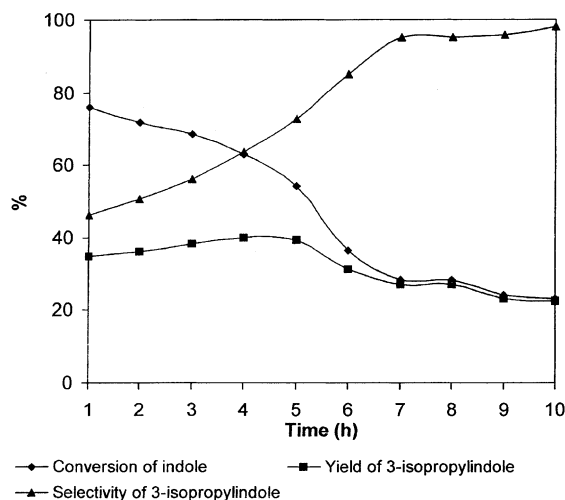
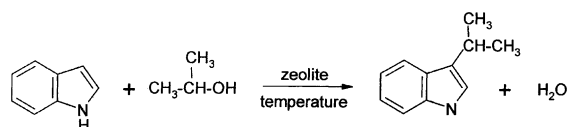


Fig. 3. Effect of time on stream on alkylation of indole with 2-propanol. Catalysts = 3 wt% CeHY; reaction temperature = 300 °C; indole:2-propanol = 1:6 (mole ratio); WHSV = 0.5 h⁻¹.

of 3-isopropylindole was obtained at 0.25 h⁻¹ WHSV. The catalytic activity decreased with the increase of weight hourly space velocity and this may be due to the decrease in contact time between the reactant and the catalyst.

The effect of time on stream on the alkylation of indole was studied at 300 °C and 0.5 h⁻¹ WHSV for a 10 h duration run and the results are shown in Fig. 3. The catalytic activity decreased with time on stream. It is due to the formation of coke on the catalyst with time on stream. On the other hand the selectivity of 3-isopropylindole is increasing with time. This selectivity towards 3-isopropylindole formation may be due to coke-induced selectivity, which also may reduce the intersection and/or pore diameter through which the polyalkylated products could not diffuse out [22,23].

Generally acid catalyzed alkylation by using alcohol as alkylating agent takes place via carbo-



Scheme 1.

nium ion formation and the alkylation follows electrophilic substitution reaction mechanism. Indole undergoes electrophilic substitution at third position of indole ring (Scheme 1). Although pyrrole undergoes electrophilic substitution at position 2, the indole forms mainly 3-substituted products [10,11]. This orientation of the substitution may be attributed to the higher electron density on position 3, due to the delocalization of nitrogen doublet on this position, since substitution is electrophilic. It is also due to the fact that the transition state of 3-substituted indole is more stable due to the benzenoid structure whereas in the transition state of 2-substituted product the benzenoid system is disrupted. Thus formed 3-alkyl indole may be further alkylated to give di- and poly alkylated indoles.

4. Conclusions

In conclusion, rare earth metal cation-modified HY zeolites are active for the alkylation of indole to produce 3-isopropylindole. The modification by rare earth metal cations increases the acidity of HY zeolite and in turn the catalytic activity. The maximum yield of 40.0% of 3-isopropylindole with 63.0% conversion of indole was obtained over 3 wt% Ce-modified HY zeolite at 300 °C.

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