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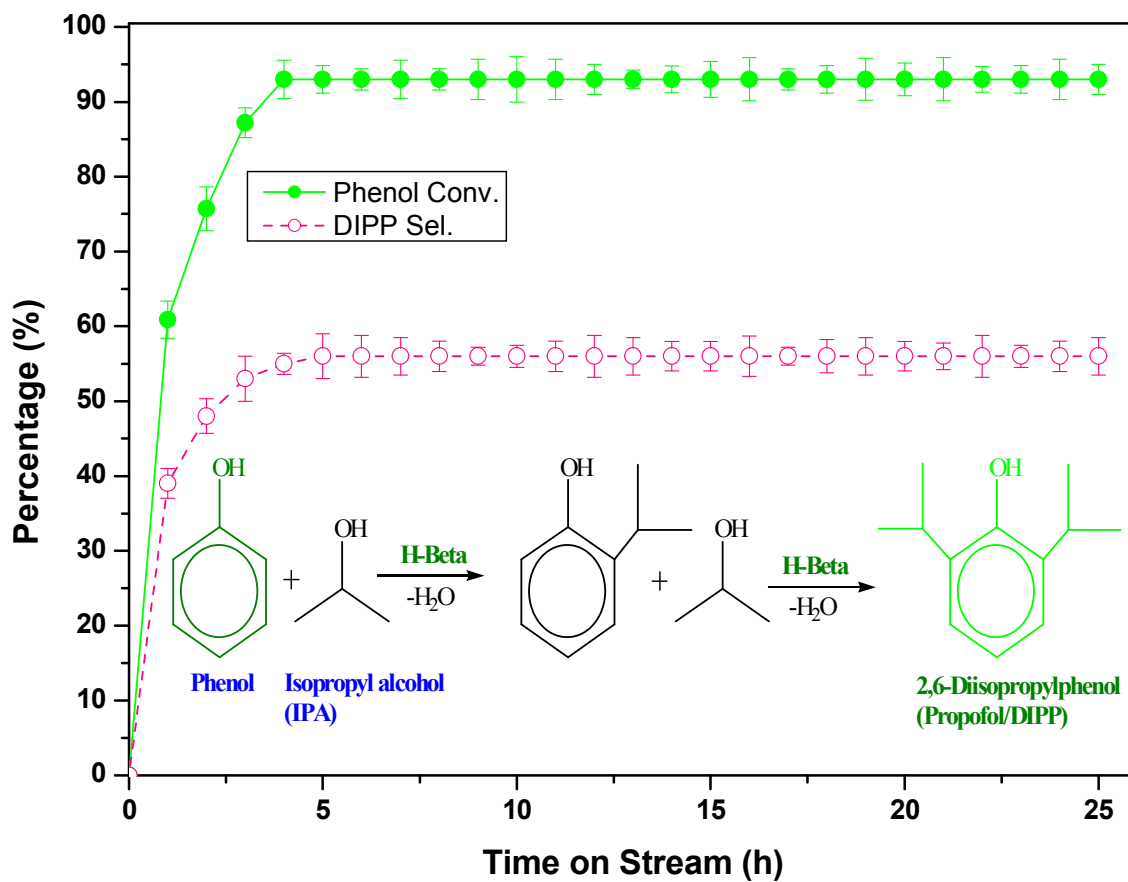


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H-Beta exhibited 94% phenol conversion & 56% propofol (DIPP) selectivity with 25h stability, which is far better than reported.

**Selective Synthesis of Propofol (2, 6-Diisopropylphenol) an Intravenous Anesthetic Drug by Isopropylation of Phenol over H-Beta and H-Mordenite**

**Kakasaheb Y. Nandiwale and Vijay V. Bokade\***

Catalysis and Inorganic Chemistry Division, CSIR - National Chemical Laboratory, Pune-411008, India.

\*Correspondence to:

Dr. Vijay V. Bokade,

Catalysis and Inorganic Chemistry Division,

CSIR - National Chemical Laboratory,

Pune-411008, India.

Ph; +91-20-25902458, Fax; +91-20-25902634

E-mail: [yv.bokade@ncl.res.in](mailto:yv.bokade@ncl.res.in)

## Abstract

Propofol (2,6-diisopropylphenol/DIPP) is the world's most widely used intravenous general anesthetic, is typically synthesized by isopropylation of phenol over an acid catalyst. It is highly demanding to stabilize bio-oil containing phenolic compounds. The isopropylation of such phenol (a model compound representing species in bio-oils) is one of the options to stabilize the bio-oil and convert into valuable products. For the first time, H-Beta and H-Mordenite catalysed vapour phase isopropylation of phenol with isopropyl alcohol (IPA) was studied to selectively synthesize DIPP.

The optimization of various operating parameters such as molar ratio (phenol: IPA), weight hourly space velocity (WHSV), reaction temperature and time on stream were performed. H-Beta (94% phenol conv. & 56% DIPP sel.) was found to be a potential and most active catalyst than H-Mordenite (68% phenol conv. & 43% DIPP sel.) at optimized process parameters. Kinetic model is proposed to probe into the intricate reaction kinetics and validated ( $R^2 > 0.98$ ) with the experimental results.

H-Beta catalyst was observed to be stable for more than 25 h, with 94% phenol conversion and 56% selectivity towards DIPP at optimized process parameters. The phenol conversion and DIPP selectivity obtained in present study is higher than those reported so far. The activation energy obtained for isopropylation of phenol with IPA over H-Beta is calculated to be  $25.39 \text{ kJ mol}^{-1}$ .

**Keywords:** Propofol (2,6-diisopropylphenol), Isopropylation, Bio-oil, H-Beta, Kinetic model.

## 1 Introduction

Recently, processing of renewable raw materials from ligno-cellulosic biomass into value added chemicals and fuels have gained much attention of researchers.<sup>1-3</sup> The bio-oils obtained by fast pyrolysis of lignin are highly viscous, very corrosive and have low heating value, hence requires upgrading to be applicable as fuel.<sup>4</sup> In order to improve these qualities, hydro-deoxygenation processes which increase the H/C molar ratio and decrease the O/C molar ratio have been utilized.<sup>5</sup> However, due to difficulties in complete removal of oxygen, the phenolic compounds often exist in the final bio-oil composition. An alkylation has been used to further improve bio-oils by enhancing their H/C ratios.<sup>3,6</sup> An alkylated phenols obtained from bio-oil could serve as useful chemicals for industrial application.

In addition, isopropylation of this phenol (a model compound representing species in bio-oils) would be green process to produce industrially important isopropylphenol (IPP). IPP finds extensive applications in flavouring agents, adhesives, agricultural chemicals and pharmaceuticals.<sup>3,7-15</sup> In particular, isopropylation of phenol with isopropyl alcohol (IPA) also produce 2,6-diisopropylphenol (DIPP/propofol), a very important drug.<sup>9-12</sup> Propofol (DIPP) is the world's most widely used intravenous general anaesthetic.<sup>16</sup> It is the active ingredient in Diprivan. Furthermore, the isopropyl group on the ring can be subjected to make phenol carboxylic acids and esters, opening up new avenues for many synthetic routes. In this work, we have evaluated isopropylation of phenol, a model compound representing species in bio-oils with IPA catalysed by H-Beta and H-Mordenite zeolites, aiming to selective synthesis of propofol.

To the best of our knowledge, open literature on the isopropylation of phenol to propofol is very limited.<sup>3, 7-15</sup> Wei *et al.*,<sup>13</sup> reported 61% phenol conversion and 70% IPP selectivity over MCM-49 at optimized reaction conditions. Wang *et al.*,<sup>14</sup> reported the use of hierarchical

structured ZSM-5 zeolite of c-axis-oriented nano-rods in a continuous alkylation of phenol with isopropanol. They obtained maximum phenol conversion of 58% and maximum yield of 40% IPP over NZ160-08 catalyst.<sup>13</sup> Recently, Wang *et al.*,<sup>15</sup> used modified SAPO-11 zeolites as catalysts for an alkylation of phenol with IPA and reported 55% phenol conversion and 77% selectivity towards IPP. All these reports leads to the formation of IPP not DIPP.<sup>13-15</sup> There are very few reports on the synthesis of DIPP.<sup>3,7-12</sup> Xu *et al.*,<sup>3</sup> have used various types of zeolites such as Y, BEA, MOR, ZSM-5, TNU-9 and ZSM-11 for gas phase alkylation of phenol with propylene. Alkylation of phenol with propylene have been reported over H- $\beta$ , USY and Cs<sup>+</sup> exchanged HZSM.<sup>7,8</sup> Vapour phase alkylation of phenol with isopropyl acetate have been performed over Zn-Al-MCM-41, Al-MCM-41 and Fe-Al-MCM-41 catalysts.<sup>9,10</sup> Isopropylation of phenol with IPA have been reported over 20% (w/w) Cs<sub>2.5</sub>H<sub>0.5</sub>PW<sub>12</sub>O<sub>40</sub>/K-10,<sup>11</sup> and Al<sub>3</sub>O<sub>3</sub> catalyst.<sup>12</sup> All the literature leads to less phenol conversion and DIPP selectivity, more catalyst deactivation, less catalyst stability etc.

In view of above literature,<sup>3,7-15</sup> there is no report on use of H-Beta and H-Mordenite catalysts for vapour phase isopropylation of phenol using IPA as an alkylating agent to selective synthesis of DIPP (Table 1). The use of heterogeneous solid acid catalysts may be a very promising way for the synthesis of propofol in view of their activity, selectivity, re-usability and the increasing demand for eco and environmentally harmonized routes in the chemical industry.

Thus, we are presenting for the first time the use of H-Beta and H-Mordenite for vapour phase isopropylation of phenol (a model compound representing species in bio-oils) with IPA as an alkylating agent. The present study involves optimization of process parameters such as molar ratio (phenol:IPA), weight hourly space velocity (WHSV), reaction temperature and time on

stream in order to achieve higher phenol conversion and selectivity towards propofol (DIPP). The kinetic model is also proposed and validated with experimental data.

## 2 Results and discussion

### 2.1 Catalyst performance

X-ray diffraction patterns of synthesized catalysts H-Beta and H-Mordenite have shown the characteristic peaks of zeolite with no contribution due to other crystalline or amorphous phases (Fig. 1).<sup>17,18</sup> The characteristic peaks of H-Beta were appeared in the  $2\theta$  range of 6.44-9.44, 19.32-24.42, 26.30-27.52, 32.72-34.16 and 42.84-44.82 confirmed the fully crystalline pure H-Beta zeolitic phase (Fig. 1).<sup>17</sup> Characteristic fingerprints of H-Mordenite were observed in the  $2\theta$  range of 9.42-9.85, 13.5-14.01, 15.21-15.74, 19.14-20.13, 21.83-22.32, 25.28-26.75, 27.01-28.71, 30.42-31.41, 35.11-36.07, 43.92-44.93 and 47.61-49.59 which confirmed phase purity and crystallinity.<sup>18</sup> The obtained XRD patterns were well agreement with reported literature.<sup>17,18</sup> Initially, isopropylation of phenol over thermal, H-Beta and H-Mordenite were carried out at reaction conditions: molar ratio (phenol: IPA) of 1:2, WHSV of  $4 \text{ h}^{-1}$  and reaction temperature of 473 K. All the experiments were performed in triplicate and have 3% error as depicted in relevant figures by error bars. The time courses of the phenol conversion and selectivity towards DIPP are shown as Fig. 2. The phenol conversion obtained at 240 min was in the trend of H-Beta (62%) > H-Mordenite (54%) > Thermal (22%). Higher surface area and higher micropore volume ( $V_{\text{micro}}$ ) along with much smaller crystal size may be the decisive reasons for higher activity of H-Beta as compared to H-Mordenite (Table 2). In addition, selectivity towards DIPP over H-Beta (46%) was higher than H-Mordenite (30%) which is attributed to higher pore size of H-Beta (7.5 Å) than H-Mordenite (6.5 Å). Hence, the detailed optimization of process parameters was carried out for isopropylation of phenol with IPA over H-Beta to maximize the

phenol conversion and DIPP selectivity. The comparative performance of H-Mordenite at optimized process parameters is also discussed later.

## 2.2 Optimization of process parameters

### 2.2.1 Effect of molar ratio

Isopropylation of phenol with IPA was carried out by varying the molar ratio of phenol to IPA from 1:2 to 1:6 over H-Beta to assess its effect on the catalytic activity and selectivity. All the experiments were conducted in kinetically controlled regime. The following hypotheses were used for the reaction: the rate of an alkylation is not controlled by dehydration rate and reaction follows adsorption of phenol and IPA on two different sites, which is discussed later. The time courses of the phenol conversion and selectivity towards DIPP over H-Beta catalyst at different molar ratio are shown as Fig. 3. The phenol conversion and selectivity towards DIPP increased with increase in molar ratio from 1:2 to 1:4. The maximum value of phenol conversion (72%) and selectivity towards DIPP (50%) was obtained at molar ratio (phenol: IPA) of 1:4 and reaction time of 240 min. This may be because at the lower concentration of phenol more active sites of catalyst would be available for the surface adsorption of IPA, which in turn results in quantitatively large formation of propylene and diisopropyl ether (DIPE) to react with phenol and also favours formation of DIPP.<sup>9-12</sup> However, above 1:4 (phenol: IPP), the phenol conversion (73%) and selectivity towards DIPP (51%) was marginally increased. Hence, the optimal phenol to IPA molar ratio of 1:4 was used in further experiments.

### 2.2.2 Effect of weight hourly space velocity (WHSV)

Influence of WHSV (2 to 6 h<sup>-1</sup>) on phenol conversion and selectivity towards DIPP over H-Beta was investigated (Fig. 4). The phenol conversion was observed to be decreased from 72 to 62%, with increase in WHSV from 4 to 6 h<sup>-1</sup>. This decrease in phenol conversion with



increase in WHSV may be due to less contact time. With increase in WHSV ( $4-6 \text{ h}^{-1}$ ), the DIPP selectivity was also observed to be decreased from 50 to 46% (Fig. 4). This decrease in DIPP selectivity with increase in WHSV may be due to the less external surface reaction and decrease in formation of propylene and DIPE, due to less contact time. However, the marginal variation in phenol conversion (74-72%) and DIPP selectivity (52-50%) was observed with increase in WHSV from  $2 \text{ h}^{-1}$  to  $4 \text{ h}^{-1}$ . This implies, above WHSV of  $2 \text{ h}^{-1}$  the phenol conversion and DIPP selectivity were not influenced by interphase limitations (external diffusion).<sup>19</sup> Hence WHSV of  $2 \text{ h}^{-1}$  with maximum phenol conversion (74%) and selectivity towards DIPP (52%) was used in further experiments.

The effect of particle size on the rate of reaction was studied by varying catalyst particle size from  $35 \mu\text{m}$  to  $355 \mu\text{m}$ . It has been revealed that, the phenol conversion and DIPP selectivity remains constant below an average catalyst particle size of  $82.5 \mu\text{m}$ . This proved there were no external diffusional and internal diffusional resistances below an average catalyst particle size of  $82.5 \mu\text{m}$ .<sup>20</sup> Hence this particle size ( $82.5 \mu\text{m}$ ) of catalyst was used in all experiments. This ensured that all the experiments were performed under chemical reaction kinetic control.

### 2.2.3 Effect of reaction temperature

The influence of reaction temperature is very essential, as kinetic parameters such as rate of reaction and activation energy are directly dependent on variation in temperature. Fig. 5 depicts the effect of temperature on the conversion and selectivity of the isopropylation reaction of phenol with IPA as an alkylating agent over H-Beta. The steady rise in the phenol conversion profile with rise in temperature from 453 to 533 K was observed. The H-Beta catalyst was observed to be stable in this temperature range. The phenol conversion was found to be increased

from 66 to 93% with rise in temperature from 453 to 533 K. This may be due to rise in temperature accelerates the rate of reaction. The selectivity towards DIPP was also observed to be increased from 52 to 56% with increase in temperature from 473 to 533 K. The increase in DIPP selectivity suggests that its own rate of an alkylation was much higher than the rate of formation of isopropylphenol from direct alkylation of phenol and from the rearrangement of isopropyl phenyl ether. Further rise in temperature from 553 to 573 K, the phenol conversion was found to be decreased from 93% to 66%. The obtained decline in conversion of phenol conversion at higher temperature may be attributed to deisopropylation of isopropyl phenol (the product) into lower hydrocarbons and phenol.<sup>11</sup> Selectivity of DIPP was observed to be decreased with increase in temperature above 533 K. Hence, the temperature of 533 K was chosen as an optimum parameter and used in further experiments. The optimum process parameters for isopropylation phenol were molar ratio (phenol: IPA) of 1:4, WHSV of 2 h<sup>-1</sup> and temperature of 533 K. The comparative performance of H-Mordenite was also evaluated at optimized process parameters. The maximum phenol conversion of 68% and DIPP selectivity of 43% was obtained over H-Mordenite.

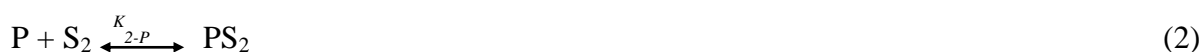
#### **2.2.4 Effect of time on stream (TOS) and stability of catalyst**

The stability of H-Beta catalyst in isopropylation of phenol with IPA as an alkylating agent was evaluated at optimized process parameters: molar ratio (phenol: IPA) of 1:4, WHSV of 2 h<sup>-1</sup> and temperature of 533 K. The catalyst was observed to stable for more than 25 h, with stable phenol conversion of 93% and selectivity towards DIPP of 56% (Fig. 6). This may be due to the vapour phase isopropylation reaction delay the coke formation on catalyst surface. After 25 h, the conversion of phenol was observed to be decreased to 87%. The catalyst was regenerated in situ by calcination at 823 K for 5 h in presence of air to remove the organic coke

deposited on active sites. The regenerated catalyst was observed to be regained its catalytic activity at 93% phenol conversion and 56% DIPP selectivity.

### 2.3 Kinetic modeling and estimation of kinetic parameters

Model built on the hypothesis of two catalytic sites S1 and S2 is proposed.<sup>11</sup> In the studied temperature range (453-533 K), an alkylation rate was not monitored by the rate of dehydration, but the reaction mechanism involved dual sites mechanism includes adsorption of reactants on two different sites and then surface reaction of adsorbed reactant species to give desired product. In the present case, the isopropylation of phenol (*P*) adsorbed on site S2 with IPA (*I*) adsorbed on adjacent site S1, to give the 2,6-diisopropylphenol (propofol) desired product (*D*) and water (*W*), which is formed due to the surface reaction as shown below:



The site balance is given as follows,

$$C_T - S_1 = C_V - S_1 + C_I - S_1 + C_W - S_1 \quad (4)$$

$$C_T - S_2 = C_V - S_2 + C_P - S_2 + C_D - S_2 \quad (5)$$

The following adsorption equilibriums for different species hold:



Thus rate of reaction of phenol is,

$$-r_P = \frac{k_{SR}C_T - S_1C_T - S_2K_1 - IC_IK_2 - PC_P}{(1 + K_1 - IC_I + K_1 - WC_W + K_1 - EC_E)(1 + K_PC_P + K_D - SC_D)} \quad (8)$$

With weak adsorption of all species, it gives the following:

$$-r_P = k_P w C_I C_P \quad (9)$$

$$\text{Where, } k_P = k_{SR} C_T - S_1 C_T - S_2 K_1 - I K_2 - P \quad (10)$$

Writing in terms of conversion and further integration results in,

$$\ln \frac{(M - X_P)}{M(1 - X_P)} = (M - 1) k_P w C_{P0} t \quad (11)$$

Where,  $M$  is molar ratio (phenol: IPA),  $X_P$  is fractional conversion of phenol,  $k_p$  is rate constant of isopropylation of phenol,  $w$  is weight of catalyst,  $C_{P0}$  is initial concentration of phenol and  $t$  is reaction time.

Eq. (11) is an expression of a second-order reaction. The reaction rate constants at different temperatures can be obtained from linear plot of  $\ln((M-X_P)/M(1-X_P))$  vs  $(M-1)C_{P0}t$ . Fig. 7 shows a linear relationship between  $\ln((M-X_P)/M(1-X_P))$  and  $(M-1)C_{P0}t$ . at different reaction temperatures (453-533 K). Both reaction rate constants and  $R^2$  values of trend lines at different reaction temperature were obtained by linear regression ( $R^2 > 0.98$ ), using the software OriginPro70 (Table 3). The rate constant was found to be increased with the increase of reaction temperature. Besides, the straight line the plots, fitted well with the experimental data (Fig. 7). This is a clear indication that the developed kinetic model is valid for this reaction.

To consider the effect of reaction temperature on the kinetic model, the Arrhenius equation can be listed as:

$$k_P = A \exp\left(-\frac{E_a}{RT}\right) \quad (12)$$

Where  $R$ = gas constant ( $8.314 \text{ J mol}^{-1} \text{ K}^{-1}$ ).

The plots of  $\ln k_p$  can be used as a function of the reciprocal temperature,

$$\ln k_p = \left(-\frac{E_a}{RT}\right) + \ln A \quad (13)$$

The plot of  $\ln k_p$  vs.  $1/T$  for isopropylation of phenol with IPA over H-Beta is represented by a straight line (Fig. 8). Both the pre-exponential factor ( $A$ ) and activation energy ( $E_a$ ) were obtained by linear regression ( $R^2 > 0.99$ ), using the software OriginPro70. The activation energy ( $E_a$ ) and pre-exponential factor ( $A$ ) for isopropylation of phenol with IPA over H-Beta were  $25.39 \text{ kJ mol}^{-1}$  and  $1.4375 \text{ L min}^{-1} \text{ mol}^{-1}$  respectively. This implies that the isopropylation reaction was in kinetic regime owing to the high activation energy.

## 2.4 Merits of present method

Xu *et al.*,<sup>3</sup> reported gas phase alkylation of phenol with propylene over various zeolites such as Y, BEA, MOR, ZSM-5, TNU-9 and ZSM-11 and obtained phenol conversion of 2-10% and selectivity towards DIPP of <5%. Wang *et al.*,<sup>7</sup> studied C alkylation of phenol with propylene over H- $\beta$  and USY and obtained phenol conversion of 80% and 71% and selectivity towards DIPP of 30% and 31%, respectively. They have also reported the vapour phase alkylation of phenol with propylene using HZSM5 by varying the Si/Al ratio and introducing Cs<sup>+</sup> sites via ion exchange Cs<sup>+</sup> and reported 50% decrease in the original selectivity.<sup>8</sup> Savidha *et al.*,<sup>9,10</sup> reported the vapour phase alkylation of phenol with isopropyl acetate catalysed by Zn–Al–MCM-41, Fe–Al–MCM-41 and Al–MCM-41. They obtained maximum phenol conversion of 76.8% and 13% selectivity towards DIPP over Fe-Al-MCM-41 (50) catalyst.<sup>9,10</sup> Yadav and Salgaonkar reported isopropylation of phenol with IPA over 20% (w/w) Cs<sub>2.5</sub>H<sub>0.5</sub>PW<sub>12</sub>O<sub>40</sub>/K-10 in batch process and obtained the maximum phenol conversion of 50% with selectivity towards DIPP of 16%.<sup>11</sup> Klemm and Taylor reported 100% phenol conversion with 52% DIPP selectivity over Al<sub>3</sub>O<sub>3</sub> catalyst.<sup>12</sup>

Table 1, describes the merits of the present method. All the reported literature presented in Table 1, have some limitations in terms of its lower activity value, less catalyst stability and use of an alkylating agent such as propylene or isopropyl acetate which leads to fast deactivation by coking. In order to eliminate these limitations the use of IPA as an alkylating agent and improved version of catalyst will be advantageous. The present study was carried out using IPA as an alkylating agent in continuous vapour phase over H-Mordenite and H-Beta, which is not reported so far. In this context, the present method of using H-Mordenite and H-Beta for the synthesis of propofol (2,6-isopropyl phenol/DIPP) by isopropylation of phenol (a model compound representing species in bio-oils) with IPA offers greener methodology with potential advantages with respect to higher phenol conversion of 94% and selectivity towards propofol of 56% over H-Beta which is much higher than the reported at milder operating parameters.<sup>3,7-15</sup> The maximum phenol conversion of 68% and DIPP selectivity of 43% was obtained over H-Mordenite at optimized process parameters. H-Beta catalyst was also observed to be highly active and stable for 25 h. This study demonstrates principles of green chemistry such as safe synthetic method, reusable heterogeneous catalyst, ambient operating parameters and minimized material diversity (high selectivity of desired product).<sup>20</sup> This study provides an efficient catalytic process to stabilize the bio-oil containing phenolic compounds and to synthesize more valuable products such as propofol. The scale up work is on-going and will be considered in future publication. This study open an avenue for the development of eco-friendly catalytic process to the selective synthesis of propofol (DIPP), a most widely used intravenous general anaesthetic.

### 3 Conclusions

Selective synthesis of propofol (2,6-isopropyl phenol/DIPP) by isopropylation of phenol using isopropyl alcohol (IPA) as an alkylating agent over zeolites such as H-Beta and H-Mordenite were carried out, probably for the first time. H-Beta was observed to be optimum catalyst over H-Mordenite. The maximum phenol conversion of 94% with 56% selectivity towards propofol was achieved over H-Beta, which is far better than reported. H-Beta catalyst was also observed to be highly active and stable for 25 h. The second order kinetic model is proposed and validated with experimental data with  $R^2 > 0.98$ . The activation energy is calculated to be  $25.39 \text{ kJ mol}^{-1}$ . This implies that the isopropylation reaction is kinetically controlled owing to the high activation energy. Thus, isopropylation of phenol (a model compound representing species in bio-oils) over H-Beta can be considered as an environmental benign catalytic process to stabilize the bio-oil and make products that are more valuable. This study opens an avenue for the development of eco-friendly catalytic process for the selective synthesis of propofol.

## 4 Experimental section

### 4.1 Materials

Phenol and isopropyl alcohol (IPA) were obtained from E. Merck Ltd., Mumbai, India. All reagents used were of analytical quality and used as it is.

### 4.2 Catalyst synthesis and characterization

The protonic forms of zeolite catalysts H-Beta and H-Mordenite with Si/Al ratio of 10 were synthesized according to the reported procedures.<sup>17,18</sup> The crystallinity and the phase purity of synthesized samples were confirmed by powder X-ray diffraction (XRD) patterns using an X-ray diffractometer (Rigaku Miniflex, Tokyo, Japan). The XRD patterns were recorded on X-ray diffractometer (P Analytical PXRD system, Model X-Pert PRO-1712) using  $\text{CuK}\alpha$  radiation at a

scanning rate of  $0.0671 \text{ s}^{-1}$  in the  $2\theta$  ranging from  $5$  to  $60^\circ$  (Fig. 1). Specific surface area and the micropore volume ( $V_{\text{micro}}$ ) of catalysts were obtained from nitrogen adsorption-desorption isotherms measured in an SA 3100 analyser (Beckman Coulter, CA, USA). The adsorption was carried out at  $77 \text{ K}$  overnight under nitrogen with a residual vapour pressure of  $0.3 \text{ Pa}$ . Temperature-programmed ammonia desorption (TPAD) was used to determine total acidity of all synthesized samples (Table 2). TPAD was performed using a Micromeritics AutoChem 2910 (Norcross, GA, USA). The  $0.5 \text{ g}$  of sample was loaded and activated at  $873 \text{ K}$  in a quartz cell, in presence of  $\text{He}$  flow ( $20 \text{ mL min}^{-1}$ ) for  $2 \text{ h}$ . Pre-saturation was accomplished by passing  $10\%$  ammonia in  $\text{He}$  for  $1 \text{ h}$  at ambient temperature ( $303 \text{ K}$ ). Then the sample was flushed with helium for  $1 \text{ h}$  at  $323 \text{ K}$  to remove excess ammonia. The adsorbed ammonia was desorbed in helium flow ( $30 \text{ mL min}^{-1}$ ) with a heating rate of  $10 \text{ K min}^{-1}$  as a function of temperature from  $323$  to  $773 \text{ K}$ . Thermal conductive detectors (TCD) detected the desorbed ammonia.

### 4.3 Catalyst evaluation and analysis

Isopropylation of phenol with IPA over protonic forms of H-Beta and H-Mordenite zeolite samples were carried out in a continuous, down-flow, fixed bed reactor SS316 ( $40 \text{ cm}$  length  $\times$   $2 \text{ cm}$  internal diameter) at atmospheric pressure. The amount of  $1.0 \text{ g}$  ( $2 \text{ cm}$  height) of  $10$ – $20$  mesh granules of self-bonded catalyst was loaded in the reactor. Prior to reaction, the activation of catalysts were done at  $723 \text{ K}$  for  $8 \text{ h}$  in air to drive off adsorbed hydrocarbon and moisture, if any. Reactants (phenol and IPA) were fed through a syringe pump (ISCO, USA) into the reactor at the desired reaction temperature. The analysis of products was done by Shimadzu gas chromatograph (Model GC 15A), coupled with an Apiezone L (B.P. 1/1) column, by a flame ionization detector. The column used was of  $0.0032 \text{ m i.d.} \times 50 \text{ m}$  length. The conversion of phenol and selectivity towards propofol (DIPP) as a function of time on stream over H/Beta



catalysts was investigated at temperature of 453-573 K with weight hourly space velocity (WHSV) of 2-6 h<sup>-1</sup> and feed (phenol:IPA) molar ratios of 1:2 to 1:6.

Phenol conversion was calculated according to Eq. (14):

$$\text{Phenol Conversion} = \frac{\text{Phenol in feed} - \text{Phenol in product}}{\text{Phenol in feed}} \times 100 \quad (14)$$

Product selectivity was calculated according to Eq. (15):

$$\text{Selectivity} = \frac{\text{Product concentration}}{\text{Phenol reacted}} \times 100 \quad (15)$$

### Nomenclature

<i>A</i>	Pre-exponential factor (L min <sup>-1</sup> mol <sup>-1</sup> )
<i>C<sub>i</sub></i>	Concentration of species <i>i</i> (mol L <sup>-1</sup> )
<i>C<sub>T</sub></i>	Concentration of total sites of catalyst (mol L <sup>-1</sup> )
<i>C<sub>V</sub></i>	Concentration of vacant sites of catalyst (mol L <sup>-1</sup> )
<i>D</i>	2, 6-Diisopropylphenol/DIPP/propofol
<i>E</i>	Diisopropyl ether/DIPE
<i>E<sub>a</sub></i>	Activation energy (J mol <sup>-1</sup> )
<i>I</i>	IPA/Isopropyl alcohol
<i>i-j</i>	Species ' <i>j</i> ' adsorbed on site ' <i>i</i> '
IPP	Isopropylphenol
<i>K</i>	Adsorption/reaction rate constant
<i>k<sub>p</sub></i>	Reaction rate constants of isopropylation of phenol (g mol <sup>-1</sup> min <sup>-1</sup> )
<i>M</i>	Molar ratio (phenol:IPA)
<i>P</i>	Phenol
<i>S</i>	Vacant catalyst sites
SR	Surface reaction
<i>t</i>	Time (min)

$T$	Temperature (K)
$T-S_i$	Total sites $S$ of type ' $i$ '
$V-S_i$	Vacant sites $S$ of type ' $i$ '
$w$	Weight of catalyst (g)
$W$	Water
$X_p$	Fractional conversion of phenol

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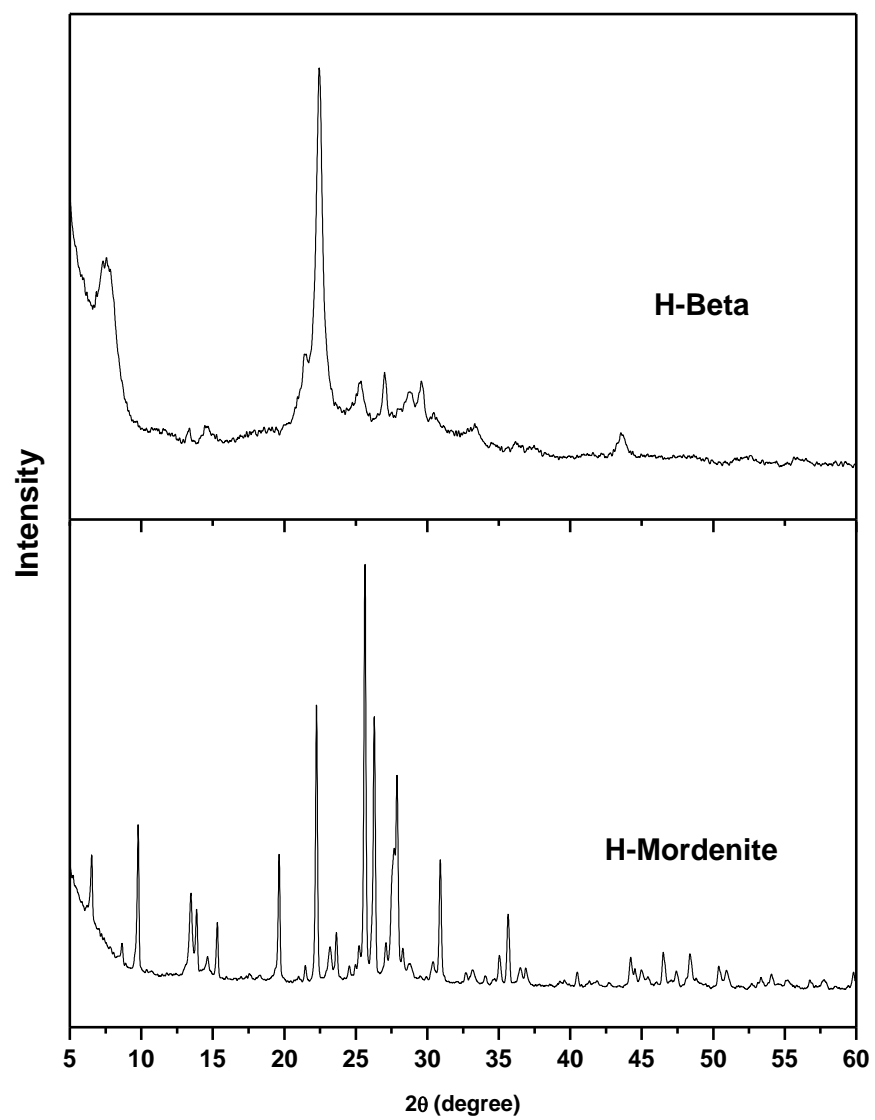
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**Figure captions**

- Fig. 1** X-ray diffraction patterns of H-Beta and H-Mordenite
- Fig. 2** Isopropylation of phenol with IPA over Thermal, H-Beta and H-Mordenite at reaction conditions: weight of catalyst 1 g; molar ratio (phenol: IPA) of 1:2; WHSV of  $4 \text{ h}^{-1}$  and reaction temperature of 473 K.
- Fig. 3** Effect of molar ratio on isopropylation of phenol with IPA over H-Beta at reaction conditions: weight of catalyst 1 g; WHSV of  $4 \text{ h}^{-1}$  and reaction temperature of 473 K.
- Fig. 4** Effect of WHSV on isopropylation of phenol with IPA over H-Beta at reaction conditions: weight of catalyst 1 g; molar ratio (phenol: IPA) of 1:4; and reaction temperature of 473 K.
- Fig. 5** Effect of reaction temperature and time on isopropylation of phenol with IPA over H-Beta at reaction conditions: weight of catalyst 1 g; molar ratio (phenol: IPA) of 1:4; WHSV of  $2 \text{ h}^{-1}$ .
- Fig. 6** Time on stream study of isopropylation of phenol with IPA over H-Beta at reaction conditions: weight of catalyst 1 g; molar ratio (phenol: IPA) of 1:4; WHSV of  $2 \text{ h}^{-1}$  and reaction temperature of 533 K.
- Fig. 7** Kinetic model plot of isopropylation of phenol with IPA over H-Beta to obtain the reaction rate constants at different temperatures.
- Fig. 8** Arrhenius plot of isopropylation of phenol with IPA over H-Beta to obtain activation energy and pre-exponential factor.

**Fig. 1**

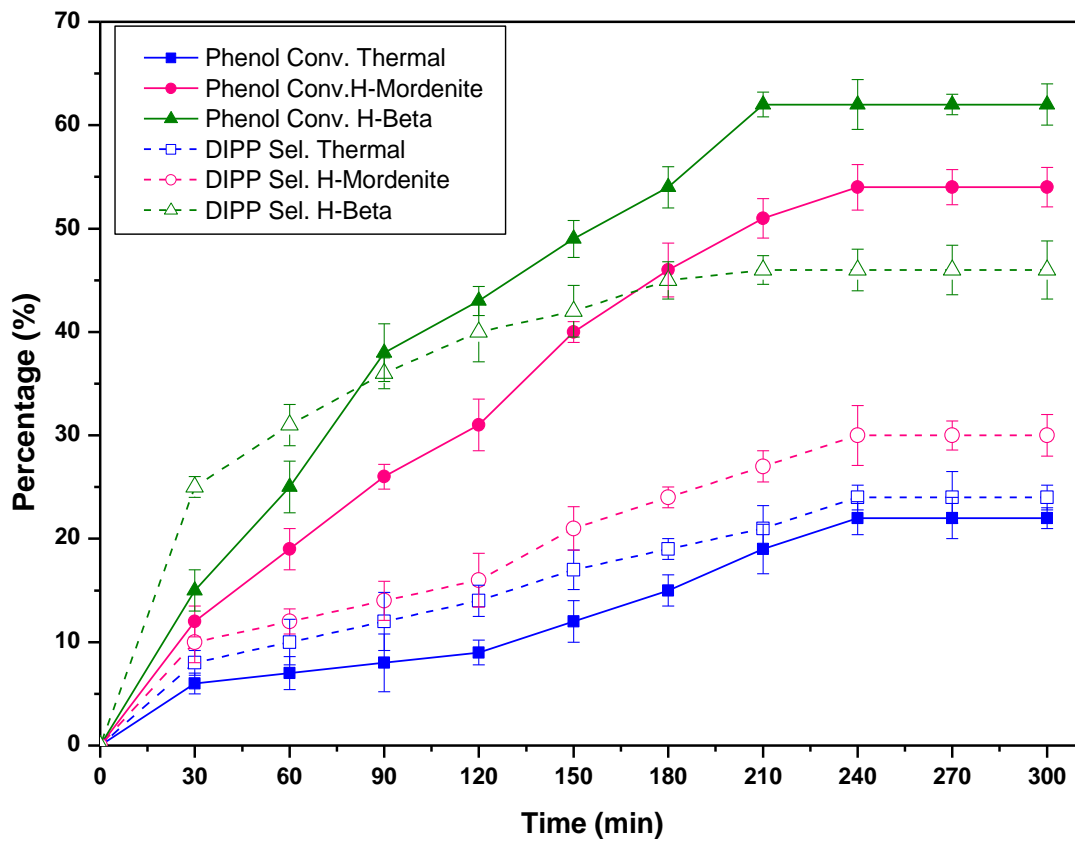


Fig. 2

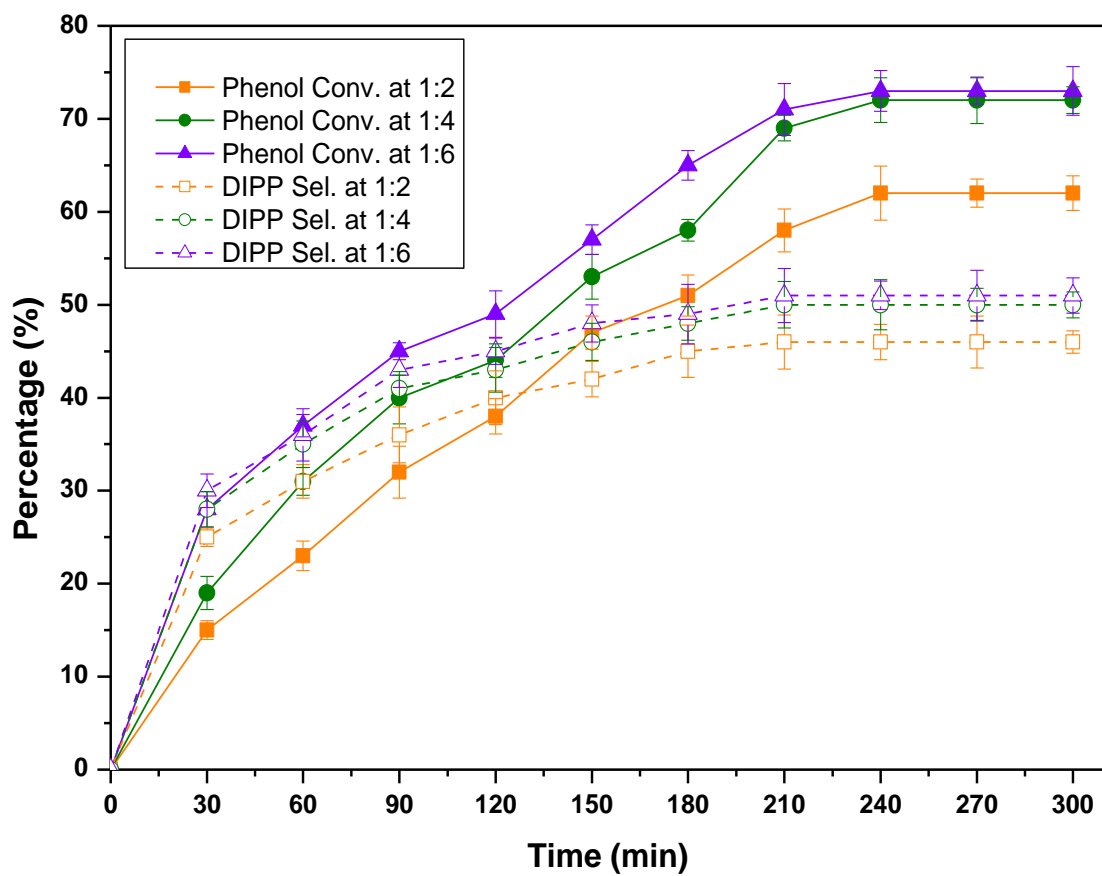


Fig. 3

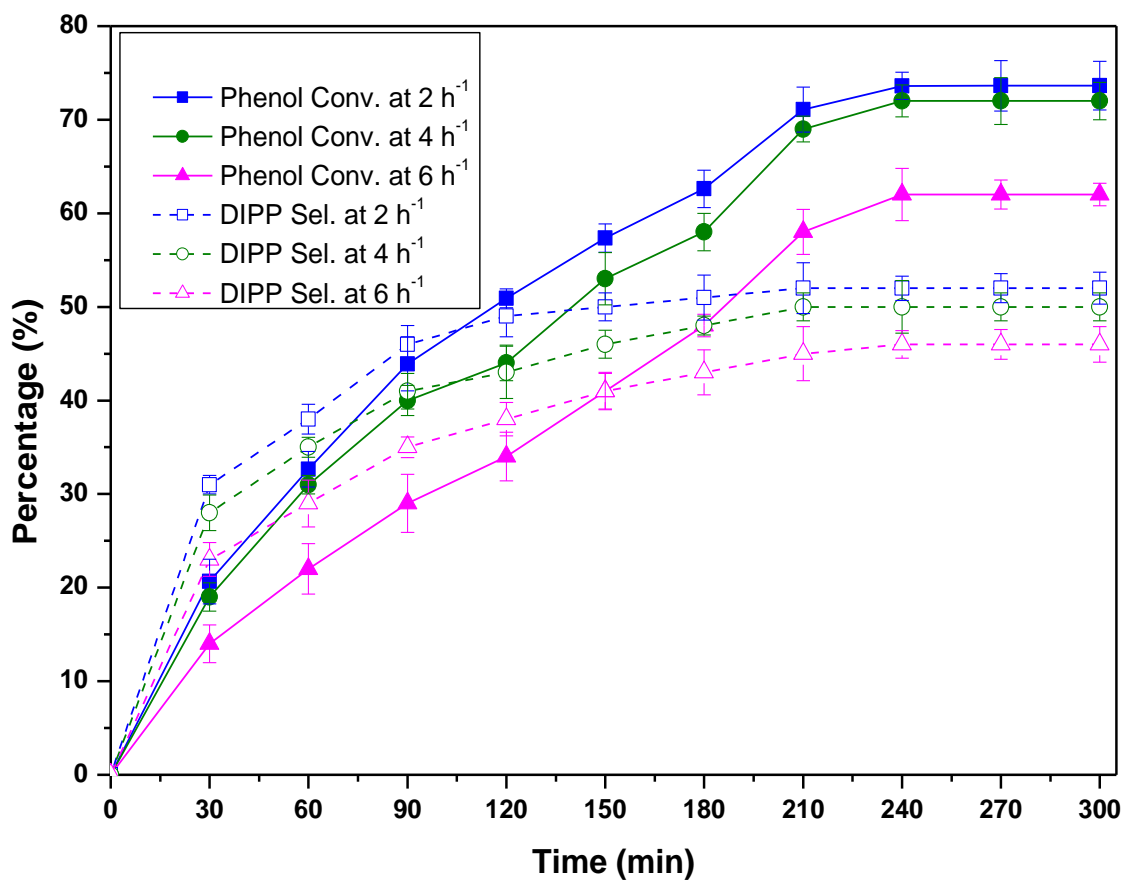


Fig. 4



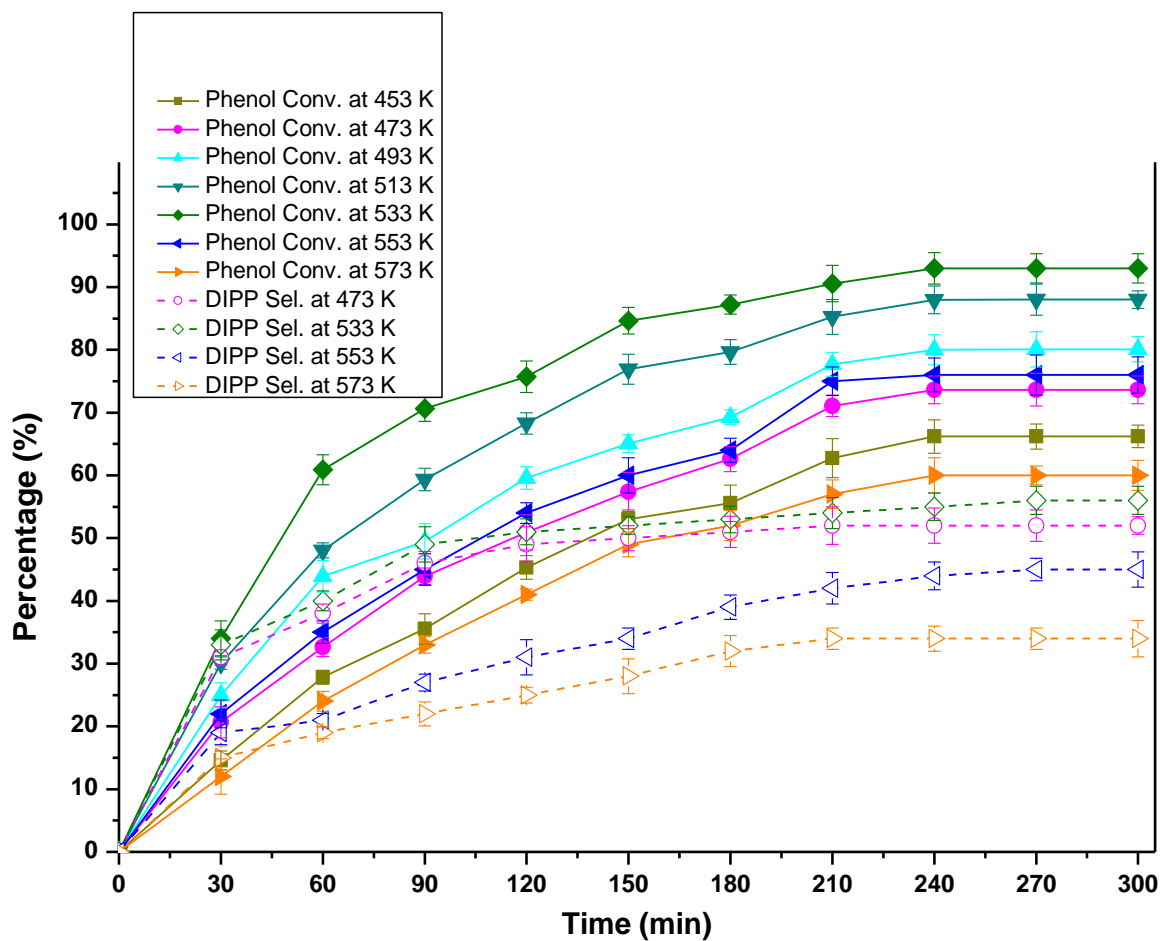


Fig. 5

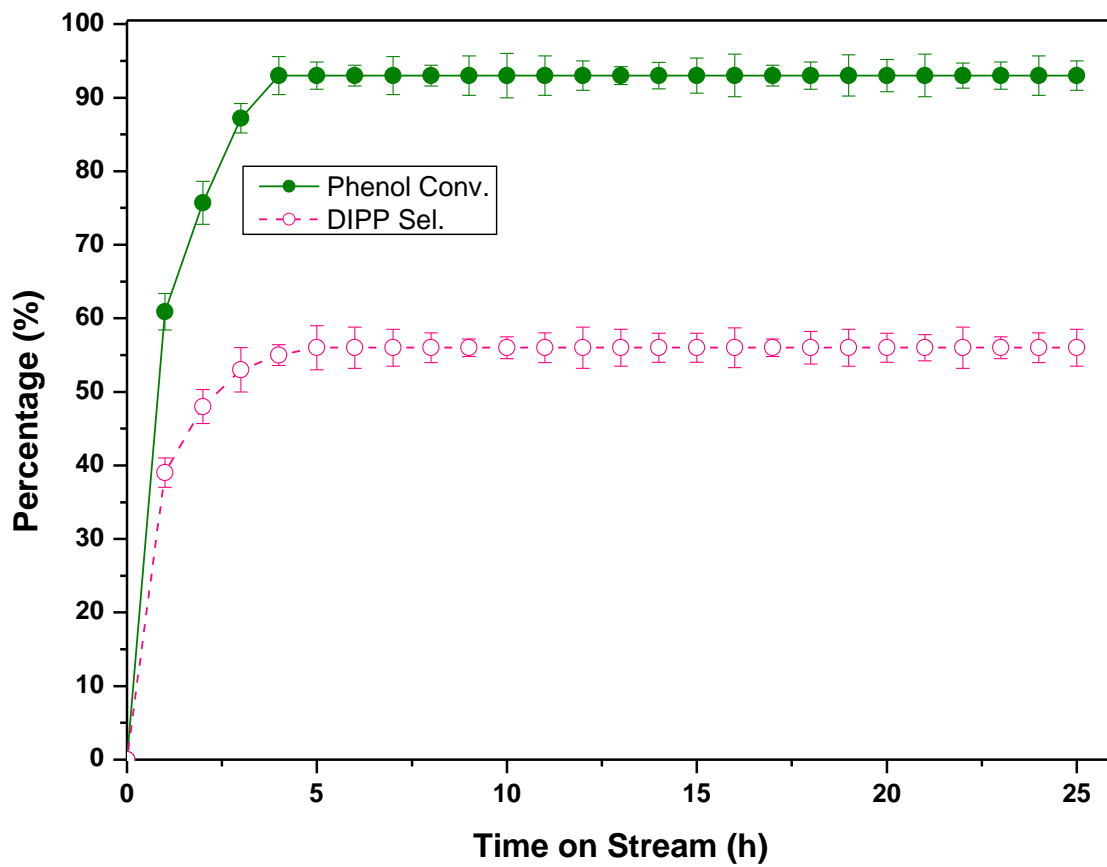


Fig. 6

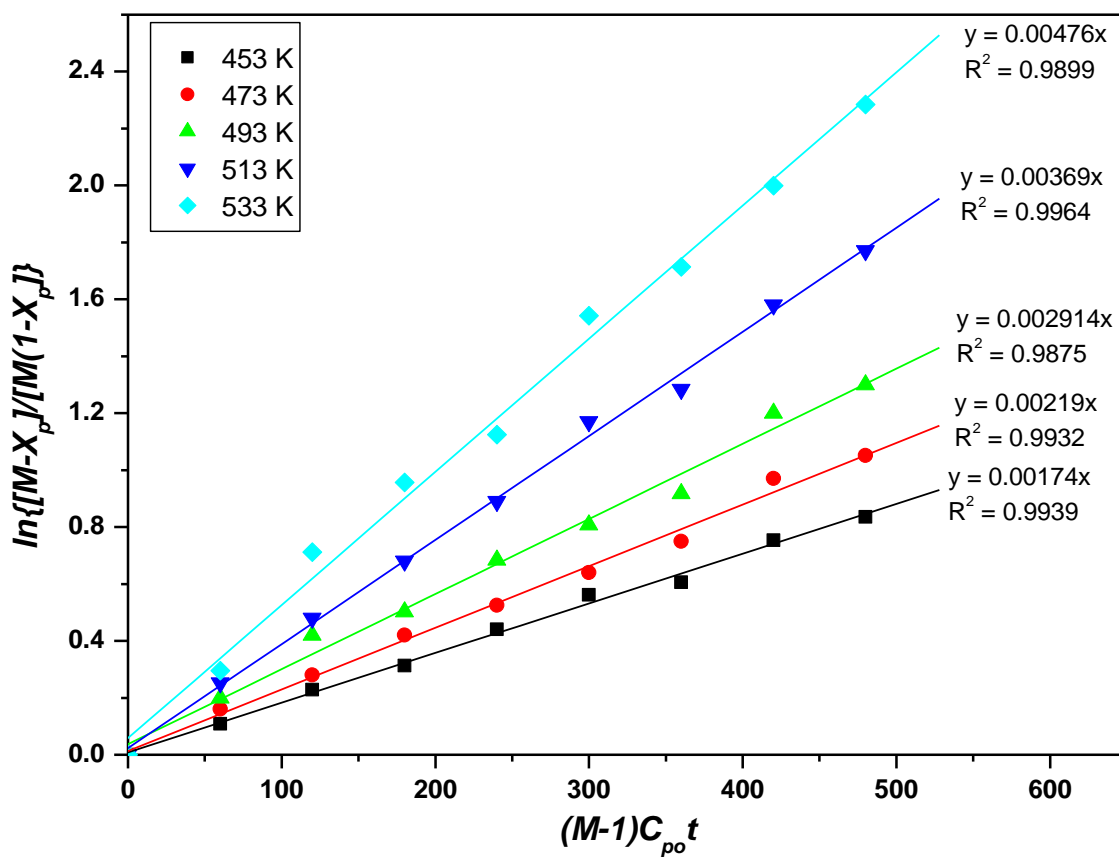


Fig. 7

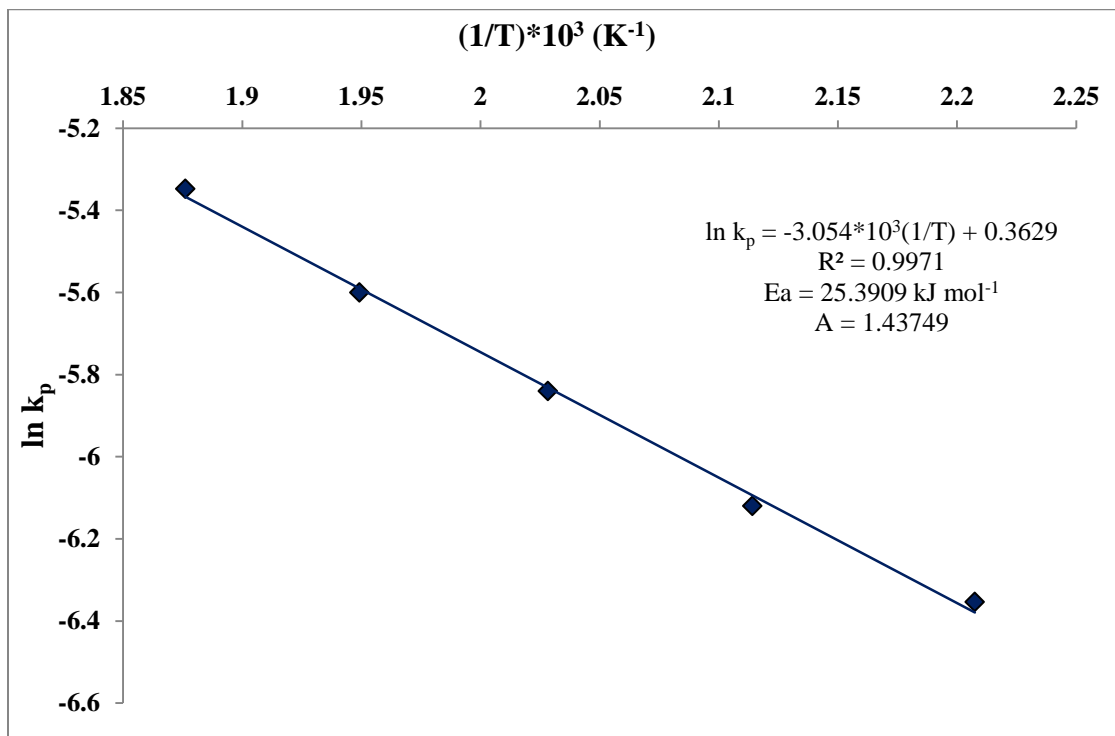


Fig. 8

**Table 1** Comparative isopropylation of phenol with various alkylating agents over different catalysts.

Substrate	Alkylating agent	Process	Catalyst	Phenol Conversion	Propofol/DIPP Selectivity	Reference
Phenol	Propylene	Continuous	zeolites (Y, BEA, MOR, ZSM-5, TNU-9 and ZSM-11)	2-10%	<5%	Xu <i>et al.</i> , <sup>3</sup>
Phenol	Propylene	Continuous	H-β	80%	30%	Wang <i>et al.</i> , <sup>7</sup>
Phenol	Propylene	Continuous	H-USY	71%	31%	Wang <i>et al.</i> , <sup>7</sup>
Phenol	Isopropyl acetate	Continuous	Fe-Al-MCM-41 (50)	76.8%	13%	Savidha <i>et al.</i> , <sup>9</sup>
Phenol	IPA	Batch	Cs <sub>2.5</sub> H <sub>0.5</sub> PW <sub>12</sub> O <sub>40</sub> /K-10	50%	16%	Yadav & Salgaonkar, <sup>11</sup>
Phenol	IPA	Continuous	Al <sub>2</sub> O <sub>3</sub>	100%	52%	Klemm & Taylor, <sup>12</sup>
Phenol	IPA	Continuous	H-Mordenite	68%	43%	Present case
Phenol	IPA	Continuous	H-Beta	94%	56%	Present case

**Table 2** Physico-chemical properties of catalysts

<b>Catalyst</b>	<b>Si/Al (bulk)</b>	<b>BET surface area (m<sup>2</sup> g<sup>-1</sup>)</b>	<b>Crystal size (μm)</b>	<b>V<sub>micro</sub> (cc N<sub>2</sub> g<sup>-1</sup>)</b>	<b>Total acidity (mmol g<sup>-1</sup>)</b>
H-Beta	10	535	0.2-0.3	0.221	0.51
H-Mordenite	10	426	1-2	0.188	1.28

**Table 3** Reaction rate constants ( $k_p$ ) and  $R^2$  values of trend lines for isopropylation of phenol with IPA over H-Beta at different temperature.

Temperature (K)	453	473	493	513	533
$k_p \cdot 10^{-3} (\text{L g}^{-1} \text{min}^{-1})$	1.74	2.19	2.91	3.69	4.76
$R^2$	0.9939	0.9932	0.9875	0.9964	0.9899