Chemoselective O- versus C-alkylation of substituted phenols with cyclohexene over mesoporous ZSM-5

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A R T I C L E   I N F O

Article history:
Received 5 September 2013
Received in revised form 4 December 2013
Accepted 20 December 2013
Available online 28 December 2013

Keywords:
Chemoselective
Alkylation
Mesoporous ZSM-5
Mesoporosity
Substituted phenols

A B S T R A C T

Chemoselective O- versus C-alkylation of substituted phenols such as phenol, p-cresol, and guaiacol with cyclohexene were investigated over various ZSM-5 catalysts with different degree of mesoporosity and external acidity such as mesoporous ZSM-5 synthesized by microwave induced assembly via electrostatic interaction between sulfonic acid, functionalized or non-functionalized ZSM-5 nanozeolites and counter cationic surfactant, and hydrothermal synthesized microporous ZSM-5 with or without sulfonic acid functionalization and surfactant. The selectivity of O- and C-alkylated products varied with different degree of mesoporosity. The selectivity of C-alkylated products increased with increasing mesopore volume and external acid sites, whereas that of O-alkylated product decreased. The mesoporous ZSM-5 synthesized under microwave via sulfonic acid functionalization showed not only the highest mesoporosity and external acid sites but also the best catalytic activity and selectivity of C-alkylated products, whereas the other ZSM-5 catalysts mainly produced O-alkylated products due to diffusion limitation of bulky product.

1. Introduction

The catalytic alkylation of substituted phenols with cyclohexene [1] or various alcohols such as cyclohexanol [2], methanol [3–8], ethanol [9], n-propanol [10], n-butanol [10], and tert-butanol [11] are one of the most important industrial organic reactions. These reactions yield both O- and C-alkylated products having commercial utility. The O-alkylated products are promising perfumery compound [1], whereas the C-alkylated products are used as important intermediates in the preparation of dyestuffs, drugs, printing inks, wire enamels, rubber chemicals, petroleum additives, polymer additives, resins and so on [12]. Hence, the selective production of each alkylated products is quite challenging in these reaction processes.

These chemoselective alkylation processes have been normally catalyzed by mineral acids such as AlCl3, H2SO4, HF, and BF3 which give rise to many technological and environmental problems such as equipment corrosion, industrial hazard, difficult separation, and catalyst recovery [13,14]. Moreover these homogenous catalysts show poor selectivity in such organic reactions. Hence, the replacement of these mineral acids with environmental-friendly solid acid catalysts is one of major demand for industrial green process. Several alternative heterogeneous acid catalysts such as cationic ion exchange resins [1], silica-supported BF3 [13], styrene divinylbenzene sulfonic resins (Amberlyst 15™ and Amberlyst 36™) [14,15], various Starbon supported acids [16], dodecatungstophosphoric acid supported K-10 clay [17], sulphonic acid treated hexagonal mesoporous silica [17], and zeolites (H-Y, ZSM-5, H-FER and H-hmordemrite) [2,18] have been used in selective alkylation reactions of phenol with cyclohexene or cyclohexanol. p-Toluenesulfonic acid (p-TSA) treated clays and cation-exchange resins have been also used as acid catalysts in alkylation of guaiacol [12] and p-cresol [19], respectively. From the prior works, it can be stated that the selective formation of O- and C-alkylated products is affected by several parameters such as temperature, alkylation agent, solvent, pore size, and nature of active sites in catalyst [20]. Recent studies by Yadav et al. on chemoselective alkylation of guaiacol [20] and p-cresol [21] with cyclohexene over sulphated zirconia revealed that existence of Lewis acid sites inside the mesopores were required to selectively yield desired bulky O-alkylated product. As per reports, large pore size of catalysts is contributing to ring alkylation whereas narrow pore size favors O-alkylation [17,18]. Earlier report by Prins et al. [22] mentioned that the alkylation mainly occurred in the mesoporous parts of zeolites due to diffusion limitation of bulky molecules. Moreover, the selectivity was mainly affected by the acidity [23]. Based on these reports we can deduce that both mesoporosity and external acid sites of catalysts play an important role.
on activity and selectivity in such chemoselective alkylation reactions.

Mesoporous zeolites containing both crystalline micropores and developed intracrystalline mesopores have attracted much attention in various alkylation reactions [24–31], which exhibited enhanced catalytic activity and remarkable change of product selectivity due to improved accessibility to and/or from active sites in micropores through the mesopores [32–36]. Recently, we reported the novel method for synthesis of mesoporous ZSM-5 by microwave induced assembly via electrostatic interaction between anionic sulfonic acid functionalized ZSM-5 nanoparticles and counter cationic surfactant (Cetylttrimethylammonium bromide: CTAB) [37]. This mesoporous ZSM-5 showed not only remarkably improved catalytic activity in aromatic benzylations but also much higher selectivity of desired monobenzylation aromatic compared with microporous ZSM-5, which was due to enhanced intracrystalline mesoporosity and external acid sites. Moreover, the selectivity of desired monobenzylation aromatic increased with increase in mesoporosity was observed [38].

In continuation to our earlier studies on aforementioned zeolitic catalyst, in the current study, we investigated the effect of mesoporosity and external acid sites on the catalytic activity and selectivity of O- and C-alkylated products in the chemoselective alkylation of phenol with cyclohexene as an alkyllating agent over ZSM-5 catalysts with different degree of mesoporosity as such Meso ZSM-5 (SO3H-CTAB)-MW, Meso ZSM-5 (CTAB)-MW (mesoporous ZSM-5 were synthesized by assembly via electrostatic interaction between sulfonic functionalized or non-functionalized ZSM-5 nanozelites and counter cationic surfactant under microwave), ZSM-5 (SO3H-CTAB)-HT, and ZSM-5 (HT) (hydrothermal synthesis with or without sulfonic acid functionalization and surfactant). Moreover, the effects of mole ratio of phenol to cyclohexene, reaction temperature and time, catalyst loading, substituent on phenol, and recyclability have also been investigated.

2. Experiment

2.1. Chemicals and catalysts

Phenol, p-cresol, guaiacol, cyclohexene, tetraethyl orthosilicate (TEOS, 98%), and aluminum isopropoxide (AIP) were purchased from Sigma–Aldrich Co. Ltd. Tetrapropylammonium hydroxide (TPOH, 20 – 25%), 3-mercaptotripropylthoxysilane (MPTES) and cetylttrimethylammonium bromide (CTAB) were obtained from Tokyo Chemical Industry Co. Ltd. (TCI). Hydrogen peroxide (H2O2, 30% in the water) was procured from Duksan Company (Korea).

The ZSM-5 catalysts with different degree of mesoporosity such as Meso ZSM-5 (SO3H-CTAB)-MW, Meso ZSM-5 (CTAB)-MW, ZSM-5 (SO3H-CTAB)-HT, and ZSM-5 (HT) were prepared according to established procedures reported in Ref. [37]. Prior to reaction all the catalysts were pretreated at 450 °C for 2 h.

2.2. Catalysts characterization

All the catalysts were characterized by powder X-ray diffraction (XRD), N2 adsorption and desorption isotherms (BET surface area and external surface area were calculated from the linear part of the BET plot and p–plot, respectively. The amount adsorbed at the relative pressure (P/P0) of 0.99 was used to evaluate the total pore volume, temperature-programmed desorption (TPD) of NH3, chemisorption of 2,6-di-tert-butylypyridine, and the details were published recently by our group [38]. Molecular size of products in Scheme 2A was estimated by geometry optimizations which were calculated using the local density approximation (LDA) with the Vosko–Wilk–Nusair (VWN) functional implemented in the DMOL3 software package Material Studio 6.0 from Accelrys.

2.3. Catalytic tests

All the experiments were carried out in a 25 mL single-necked flask equipped with reflux condenser. The mole ratio of phenol, p-cresol, and guaiacol with cyclohexene was 5:1. In a typical reaction, an 1 ml solution containing 9.41 mmol of phenol and 1.88 mmol of cyclohexene were placed into the reactor. The 0.05 g/ml of catalyst was loaded with respect to total volume of the reaction mixture. The reaction was carried out at 80 °C for 4 h. Small amounts of clear liquid reaction mixture was analyzed by using a gas chromatograph (Agilent Technologies, GC6890 N) equipped with a flame ionization detector (FID) and a capillary column (HP 5% silicone gum, 0.25 mm i.d. with 30 m long). The products were also confirmed by GC–MS (Agilent Technologies GC 6890 N, and MS5975).

3. Results and discussion

3.1. Porosity and acidity of catalyst

All the obtained ZSM-5 catalysts such as Meso ZSM-5 (SO3H-CTAB)-MW, Meso ZSM-5 (CTAB)-MW, ZSM-5 (SO3H-CTAB)-HT, and ZSM-5 (HT) showed typical crystalline structure of MFI in wide-angle XRD patterns. In low-angle XRD patterns, the meso ZSM-5 (SO3H-CTAB)-MW exhibited remarkably higher intensity of the diffraction peak at 2θ = 1–3° which was an evidence for the presence of mesopore arrays compared with meso ZSM-5 (CTAB)-MW. Whereas there was no distinct peak observed in case of ZSM-5 (SO3H-CTAB)-HT which was similar to microporous ZSM-5 (HT) [38]. These results coincided with the N2 adsorption–desorption isotherms and physical properties which are summarized in Table S1. The three types of pores such as micropores (<2 nm), uniform mesopores (2.7 nm), and intercrystalline mesopores (~12 nm) were observed from the N2 adsorption–desorption isotherm and pore size distribution of meso ZSM-5 (SO3H-CTAB)-MW [37,38]. The forced closure at relative pressure of 0.45 was due to tensile strength effect which was in consonance with earlier reports [39–41]. The BET surface area, external surface area, and mesopore volume of meso ZSM-5 (SO3H-CTAB)-MW were 529, 400 m2/g and 0.75 cm3/g, respectively, which were much higher than those of other catalysts due to enhanced mesoporosity.

The number of strong acid sites and external acid sites were measured by NH3 TPD and chemisorptions of 2,6-di-tert-butylypyridine, respectively as shown in Table S1. The strong acid sites of meso ZSM-5 (SO3H-CTAB)-MW (0.32 mmol/g) were only 8% less than the ZSM-5 (HT) (0.46 mmol/g). This was approximately similar which indicated that the meso ZSM-5 (SO3H-CTAB)-MW was prepared without significantly sacrificing acidity [42]. Moreover, the external acid sites increased with the increasing of mesoporosity were confirmed.

3.2. Chemoselective alkylation of substituted phenols with cyclohexene

Chemoselective alkylation of phenol, p-cresol, and guaiacol with cyclohexene are presented in Scheme 1. These reactions mainly produce both O- and C-alkylated products. The O-alkylated products are cyclohexylphenylether, 1-cyclohexyloxy-4-methylenebenzen, and 1-cyclohexyloxy-2-methylenebenzen; the C-alkylated products are O- and p-cyclohexylphenol, 2-cyclohexyl-p-cresol and o- and m- and p-cyclohexyl guaiacol, respectively [14,19,20]. Moreover, several parallel reactions can be occurred such as cyclohexene oligomerization (to form cyclohexyl
cyclohexene and/or cyclohexenylbicyclohexane), rearrangement and/or isomerisation of O- and C-alkylated products (to form di-alkylated products) [14]. The effects of several parameters on selective production of O- and C-alkylated products are described in detail as below:

3.2.1. Effect of mole ratio of phenol to cyclohexene

The mole ratio of phenol to cyclohexene was varied from 1:3 to 5:1 in chemoselective alkylation of phenol with cyclohexene over meso ZSM-5 (SO$_3$H-CTAB)-MW in order to access its effect on the catalytic activity and selectivity. As summarized in Table 1, the conversion of phenol decreased with increasing mole ratio of phenol to cyclohexene, whereas the selectivity of monoalkylated products (O- and C-alkylated products) increased from 41.8 to 100%. The low selectivity at lower mole ratio (1:3 and 1:1) was due to a fast formation of cyclohexene oligomerization products like cyclohexyl cyclohexene and cyclohexenylbicyclohexane. The selectivity of O-alkylated products was 44.0% in a mole ratio of 5:1 which was slightly lower than that of 3:1 (45.6%), it was because that the O-alkylated products (cyclohexylphenylether) further isomerised to C-alkylated products [14]. The selectivity of C-alkylated products reached a maximum of 56.0% at mole ratio of 5:1. Thus, all the subsequent reactions were investigated with a mole ratio of 5:1.

3.2.2. Effect of reaction temperature and time

The chemoselective alkylation of phenol with cyclohexene over meso ZSM-5 (SO$_3$H-CTAB)-MW was investigated in the temperature range of 60–100 °C (Fig. 1). The conversion of phenol and cyclohexene were found to increase remarkably with an increase in temperature from 60 to 80 °C, further increase in temperature to 100 °C had no significant effect on the conversion of both reactants. The selectivity of C-alkylated products increased with

![Scheme 1](image-url)
increasing reaction temperature, whereas that of O-alkylated products decreased. This result indicated that the alkylation reaction was of higher activation energy than the etherification [1] and the O-alkylated products as an intermediate further isomerised to C-alkylated products at high temperature [18]. The effect of reaction time from 15 to 240 min was carried out through the same reaction over meso ZSM-5 (SO3H-CTAB)-MW at 80 °C as shown in Fig. 2. The conversion of both reactants remarkably increased from 30 to 60 min, and then increased gradually with increasing reaction time. Selectivity of O- and C-alkylated products depicted similar trend with the effect of reaction temperature. Moreover, the selectivity of C-alkylated products was higher than that of O-alkylated products after certain longer reaction time (240 min). Hence further investigations were carried for reaction time of 4 h.

### 3.2.3. Effect of catalyst loading

Fig. 3 showed the effect of catalyst loading on the catalytic conversion and selectivity over meso ZSM-5 (SO3H-CTAB)-MW at 80 °C for 4 h. The catalyst amount was varied over a range of 0.01–0.1 g/ml on the basis of total volume of reaction mixture. The conversion of both phenol and cyclohexene increased with increase in catalyst loading, which was due to the proportional increase in the number of active sites [43]. The same trend of selectivity with effect of reaction temperature and time was observed. The selectivity of C-alkylated products was higher than that of O-alkylated products with catalyst loading more than 0.05 g/ml; it indicated the more active sites favor to form more C-alkylated products. Hence, all the further experiments were performed by using 0.05 g/ml loading of catalyst.

### Table 1

Catalytic performance of meso ZSM-5 (SO3H-CTAB)-MW in chemoselective O- versus C-alkylation of phenol with cyclohexene as a function of various mole ratio of phenol to cyclohexene.

<table>
<thead>
<tr>
<th>Mole ratio of phenol to cyclohexene</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cyclohexene</td>
<td>Phenol</td>
</tr>
<tr>
<td>1:3</td>
<td>95.6</td>
<td>96.9</td>
</tr>
<tr>
<td>1:1</td>
<td>94.4</td>
<td>81.4</td>
</tr>
<tr>
<td>3:1</td>
<td>92.6</td>
<td>30.1</td>
</tr>
<tr>
<td>5:1</td>
<td>92.5</td>
<td>18.3</td>
</tr>
</tbody>
</table>

* Reaction condition: total reactor volume = 1 ml; catalyst = 0.05 g/ml; reaction temperature = 80 °C; stirring speed = 800 rpm; reaction time = 4 h.

### 3.2.4. Effect of substituent on phenol

Chemoselective alkylation of phenol, p-cresol, and guaiacol with cyclohexene over meso ZSM-5 (SO3H-CTAB)-MW were investigated in order to demonstrate the effect of substituent on phenol (Fig. 4A and B). As illustrated in Fig. 4A, the conversion of p-cresol was higher than that of phenol which was mainly due to ring activation by electron donating effects (≈CH3 > ≈H) [38]. Whereas the conversion of guaiacol was little lower than those of phenol and p-cresol due to its larger molecular size which caused less accessibility to active sites compared with the others. The selectivity of C-alkylated products was higher than that of O-alkylated products in case of all substituted phenols as shown in Fig. 4B. The selectivity for C-alkylated products among the three substrates was the highest in case of guaiacol whereas the least in case of phenol, which was attributed to ring activation effect by electron donating substituent (≈OCH3 > ≈CH3 > ≈H).

### 3.2.5. Effect of catalyst mesoporosity and acidity

Various ZSM-5 catalysts with different mesoporosity such as meso ZSM-5 (SO3H-CTAB)-MW, meso ZSM-5 (CTAB)-MW, ZSM-5 (SO3H-CTAB)-HT, and ZSM-5 (HT) were used as catalysts in phenol alkylation with cyclohexene to examine the effect of mesoporosity and external acid sites on catalytic activity and selectivity (Table 2). The conversion of both phenol and cyclohexene were in the following order: meso ZSM-5 (SO3H-CTAB)-MW > meso ZSM-5 (CTAB)-MW > ZSM-5 (SO3H-CTAB)-HT > ZSM-5 (HT). The meso ZSM-5 (SO3H-CTAB)-MW with the highest external surface area and mesopore volume (Table S1) showed the best catalytic activity which was much higher than that of ZSM-5 (HT). Moreover, the meso ZSM-5 (SO3H-CTAB)-MW mainly produced bulky C-alkylated products.
Table 2
Chemoselective O- versus C-alkylation of phenol with cyclohexene over various ZSM-5 catalysts.

<table>
<thead>
<tr>
<th>Catalysts</th>
<th>Conversion (%)</th>
<th>Selectivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cyclohexene</td>
<td>Phenol</td>
</tr>
<tr>
<td>Meso ZSM-5 (SO₃H-CTAB)-MW</td>
<td>92.5</td>
<td>18.3</td>
</tr>
<tr>
<td>Meso ZSM-5 (CTAB)-MW</td>
<td>63.0</td>
<td>12.5</td>
</tr>
<tr>
<td>ZSM-5 (SO₃H-CTAB)-HT</td>
<td>32.1</td>
<td>6.3</td>
</tr>
<tr>
<td>ZSM-5 (HT)</td>
<td>26.0</td>
<td>5.0</td>
</tr>
</tbody>
</table>

* Reaction condition: phenol: cyclohexene = 5:1; total reactor volume = 1 ml; catalyst = 0.05 g/ml; reaction temperature = 80 °C; stirring speed = 800 rpm; reaction time = 4 h.

Fig. 4. (A) Conversion and (B) selectivity in chemoselective O- versus C-alkylation of phenol with cyclohexene, p-cresol and guaiacol with cyclohexene over meso ZSM-5 (SO₃H-CTAB)-MW.

Scheme 2. Correlation between catalytic activity and selectivity and (A) mesoporosity and external acidity, (B) diffusion of reactants and products.
products whereas O-alkylated products were mainly formed in case of the other ZSM-5 catalysts. It indicated that the presence of enhanced mesoporosity significantly improved the accessibility of both reactants and products to and/or from active sites. As shown in Scheme 2A, both the reactants phenol (kinetic diameter: ca. 0.66 nm [44]) and cyclohexene (kinetic diameter: ca. 0.58 nm [45]) have less diffusivity in the ZSM-5 micropore channels (0.51 × 0.55 and 0.53 × 0.56 nm) thereby limiting the accessibility due to larger molecular size. Hence the alkylation was mainly occurred inside of the mesopores and micro pore mouths. Furthermore, the C-alkylated products (0.97 × 0.58 nm) were difficult to pass through the micropore channels due to diffusion limitation whereas the O-alkylated products (1.00 × 0.53 nm) were able to go through the micropores. According to previous reports [30,38,46], the selectivity of alkylation products was found to be mainly affected by the external acid sites due to diffusional limitation of bulky molecule. The external acid sites were affected by mesopore generation which increased with increase in external surface area and mesopore volume as shown in Table S1 and Scheme 2B. The selectivity of C-alkylated products increased with increasing external acid sites whereas that of O-alkylated products decreased, which inferred that the improved mesoporosity and external acid sites enhanced the accessibility and preferentially form bulky C-alkylated products. These observations revealed that the mesoporosity and external acid sites play a significant role on product distribution.

3.2.6. Effect of reusability

The reusability of meso ZSM-5 (SO₃H-CTAB)-MW as heterogeneous catalysts was investigated for three runs (Table 3). The catalysts were filtered, washed with methanol, dried at 120 °C and calcined at 550 °C for 5 h after each reaction. The conversion of phenol and cyclohexene were 18.3 and 93.8%, respectively, which did not decreased considerably even after reusing two times. The selectivity of O-alkylated products increased slightly, it seemed that the O-alkylated products did not isomerised further under less active sites due to loss of catalyst amount during recycle. These results indicated that the meso ZSM-5 (SO₃H-CTAB)-MW can be reused without significant loss of catalytic activity and selectivity.

4. Conclusion

Chemoselective alkylation of phenol with cyclohexene was successfully investigated over various ZSM-5 catalysts with different mesoporosity to study the effect of mesoporosity and external acid sites on catalytic activity and selectivity. The meso ZSM-5 (SO₃H-CTAB)-MW with the highest mesoporosity and external acid sites preferred to form C-alkylated products whereas O-alkylated products were mainly formed in case of microporous ZSM-5 due to diffusion limitation. The selectivity of C-alkylated products increased with increasing external acid sites which were affected by improved mesoporosity. It inferred that the presence of mesopore remarkably enhanced the accessibility of bulky C-alkylated products to/from active sites. Controllable mesoporosity play an important role on product distribution in chemoselective alkylation reaction. The selectivity of C-alkylated products increased with increase in reaction temperature, time, catalyst loading and mole ratio of phenol to cyclohexene. The meso ZSM-5 (SO₃H-CTAB)-MW is promising heterogeneous catalysts which can be reused for three cycles without significant loss of activity.

Acknowledgements

This work was supported by the National Research Foundation of Korea [NRF] grant funded by the Korea government [MSIP] [No. 20090083525] and Inha University.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.apcata.2013.12.025.

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