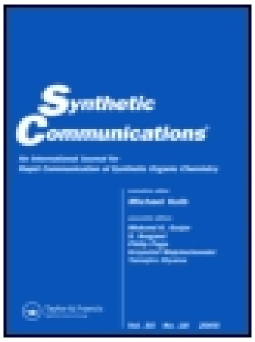

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Highly regioselective O-allylation of phenol derivatives using MMZ$_{Cu(I)Y}$ catalyst

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ABSTRACT

A clean and effective method has been developed for the regioselective of O-allylation of phenol derivatives using a recyclable Cu(I)-exchanged multi-size porous material. Ease of preparation of catalyst through simple solid-state exchange and its compatibility in producing excellent amount of O-allylated products and a plausible mechanistic pathway for the regioselectivity are highlighted. This reported procedure is not requiring any external stabilizing ligand for Cu(I) species and further purification of products.

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KEYWORDS
MMZ$_{Cu(I)Y}$; O-allylation; regioselectivity

GRAPHICAL ABSTRACT

Where X = H, p–Br, p–$COCH_3$, O–CHO, O–$COCH_3$, O–Cl, p–Cl, Ph, Py, heterobicyclic (3 examples).

Introduction

Allylation of functional moieties always receives much attention in synthetic organic chemistry since the external double bond finds scope for further derivatization like ring closer leads to the formation of heterobicyclic system such as chromones and coumarones[1], hydrogenation, radical substitution reaction, click reaction[2], epoxidation, Claisen Rearrangement[3], 1,3-hydrogen shift, [3,3]-sigma tropic rearrangement[4] and polymerization reactions[5], as an educt for Suzuki–Miyaura coupling reaction, protecting groups for alcohols[6] and also as the accelerators for rubber vulcanization, explosives, lubricant oils, gasoline anti-corrosive additives[7], etc. These allylic ethers also find many pharmaceutical applications which involve as a protected intermediate in the

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synthesis of diclofenac, a non-steroidal anti-inflammatory, dicycloxygenase inhibitor, and as precursors for the benzo-fused coumarins having anti-tumor activity[8].

However, the synthesis of allyl phenyl ethers is always a very challenging task because of achieving regioselectivity. The traditional methods for the synthesis of allyl ethers normally require strongly basic metal alkoxide anion, highly active alkyl species, and a stoichiometric amount of coupling agents such as DEAD and triphenylphosphine[9]. In addition, to activate the allyl alcohol, either the use of ligands, supporting agent, additives, or elevated temperatures are also necessary due to its less reactivity. There are other few reports also available which includes metal complexes like Ru[10], Pd[11], Ir[12], Mo(II)[13], In[14], Au[15], Rh[16] for the allylation of phenolic compounds. Recently, nanoferrites[17], lead composite[18], PTC[19], cyclodextrins[20] are also reported. However, most of the reported procedures involve both C- and O-allylation by the use of expensive ligands for the complex formation, toxic solvents, limited substrate scope, strong base, harsh reaction conditions, non-recyclable catalyst, and poor selectivity.

Our recent report on allylation of dicarbonyl compounds[21] using hierarchically architectured $\text{MMZ}_{\text{Cu(I)Y}}$ prompted us to extend the study of the allylation of functional moieties like OH groups as the reported catalytic system can influence the outcome of product selectivity. Moreover, the catalyst reserves its own advantages like functional tolerance, tunable acidity, basicity and pore sizes, recycling nature with same impact on product distribution, easy separation, etc.

Consequently, this challenging task on achieving a selective allylation by the use of simple and affordable method led us to explore this study by the use of a $\text{MMZ}_{\text{Cu(I)Y}}$ catalyst and interesting results are discussed here.

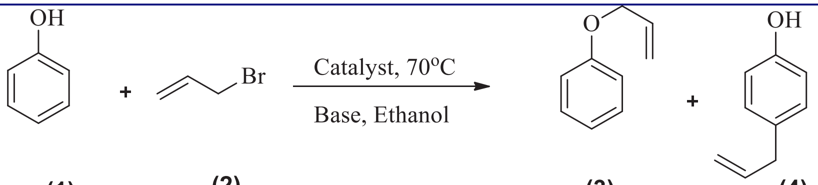
Results and discussion

The optimization study of screening of catalysts and solvents is performed in which phenol and allylbromide are used as model substrates and results are summarized in Tables 1 and 2.

Either the presence of catalyst or base alone has not produced any significant result. Similarly, there is no reaction with Na-exchanged zeolite (entry 1). However, KY has produced considerable amount of allylated product but with no selectivity (entry 2). Both O- and C-allylation occurred in other cases also like with LiY and CsY (entries 4 and 5). To check the influence of Bronsted acidity, we employed HY zeolite (entry 3), but the yield is poor when compared with other cations. It is due to the acidic sites present in HY prevents the formation of phenolate ion to attack by the allylating agent.

However, transition metals enhance the product yield with good selectivity towards O-allylation by the expense of C-allylated product. Our recent research on the exploration of multi-size porous material MMZ with various cations for fine selectivity prompted us to employ them in the present study also. MMZ_{NiY} and $\text{MMZ}_{\text{Cu(II)Y}}$ have produced 91% and 80% of allylation (entries 6 and 7), however, with considerable amount of C-allylation also. Surprisingly, the Cu(I)Y zeolite has produced an excellent amount of O-allylation selectively with a trace amount of C-allylation (entry 8). In fact, this interesting result further incited us to employ $\text{MMZ}_{\text{Cu(I)Y}}$ and which produced only O-allylation (entry 9) with almost same amount of yield. We have also examined the

Table 1. Screening of catalysts for the regioselective O-allylation.[a]



(1) (2) (3) (4)

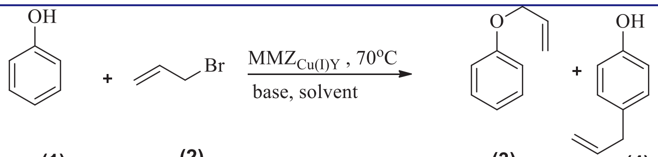
Entry	Catalyst	Time	Yield[b] (%) (3)	Yield[b] (%) (4)
1.	NaY	24	–	–
2.	KY	24	48	27
3.	HY	10	20	–[c]
4.	LiY	24	40	21
5.	CsY	24	45	26
6.	MMZ_{NiY}	10	67	24
7.	$MMZ_{Cu(II)Y}$	10	72	8
8.	Cu(I)Y	10	91	2
9.	$MMZ_{Cu(I)Y}$	10	89	–

[a] Reaction conditions: Stirred the mixture of Phenol (1 mmol), allyl bromide (1 mmol), catalyst (100 mg), ethanol (3 mL), K_2CO_3 (1 mmol) at 70 °C for the reaction time as specified in the table.

[b] Isolated yields.

[c] Trace amount of C-allylated product also noted (confirmed by GC-MS).

Table 2. Optimization of the solvent.[a]



(1) (2) (3) (4)

Entry	Solvent	Polarity[26]	Yield[b] (%) (3)	Yield[b] (%) (4)
1.	$CHCl_3$	0.259	25	7
2.	DMF	0.386	11	–
3.	DMSO	0.444	45	28
4.	ACN	0.46	21	3
5.	CH_3CH_2OH	0.654	89	–
6.	CH_3OH	0.762	67	9

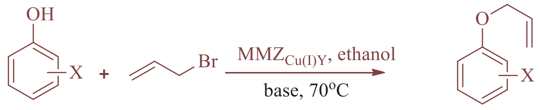
[a] Reaction conditions: stirred the slurry containing Phenol (1 mmol), allyl bromide (1 mmol), $MMZ_{Cu(I)Y}$ (100 mg), solvent (3 mL), K_2CO_3 (1 mmol) at 70 °C for 10 hr.

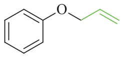
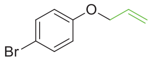
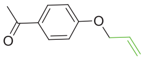
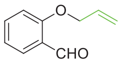
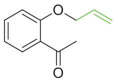
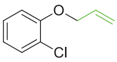
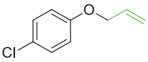
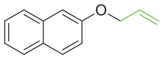
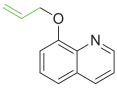
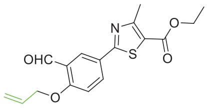
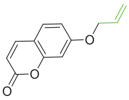
[b] Isolated yields.

recycling of $MMZ_{Cu(I)Y}$ to see its efficiency which afforded the same yield even after two time usage.

Solvents having high polarity influence the reaction to good extend as evident from its scaling range if above 0.5, particularly methanol and ethanol are found to be more suitable for the present study. Comparing methanol, ethanol produces a very clean reaction without any by products at 70 °C. To check the functional tolerance of $MMZ_{Cu(I)Y}$ catalyst, various substituted phenolic compounds are also employed and the results are presented in Table 3. The reaction finds faster with all substituents as evident from the

Table 3. O-Allylation of different phenolic compounds using MMZ$_{Cu(I)Y}$.[a]

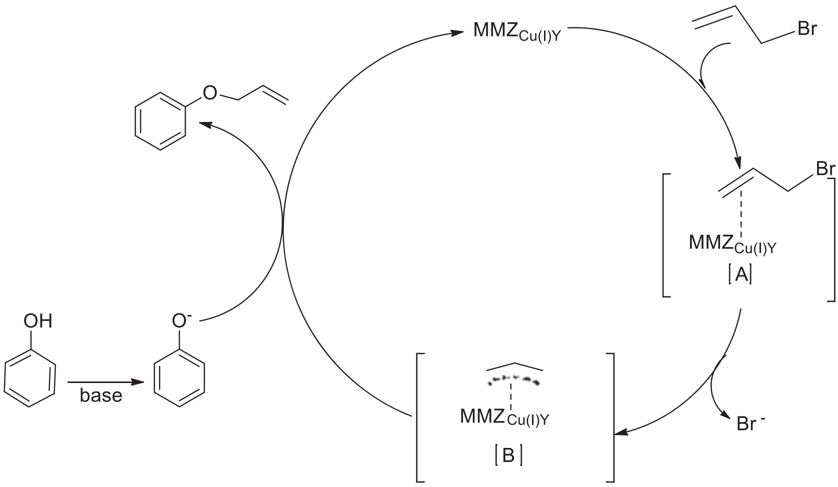


(3 A)  89%	(3 B)  94%	(3 C)  92%
(3 D)  87%	(3 E)  89%	(3 F)  93%
(3 G)  92%	(3 H)  76%	(3 I)  84%
(3 J)  97%	(3 K)  80 %	

[a]Reaction conditions: stirred the slurry containing Phenolic compounds (1 mmol), allyl bromide (1 mmol), MMZ$_{Cu(I)Y}$ (100 mg), solvent (3 mL), K_2CO_3 (1 mmol) at 70 °C for 10 hr.

observed yields 76–97%. In most of the cases, the reaction is not required any further purification technique since it piped out exclusively O-allylated products.

Generally, para substituents are giving better yields than ortho substituents under the present experimental conditions. There is no difficulty at all to allylate even for bulkier phenolic compounds like p-substituted thiazole phenolic compounds and 7-hydroxycoumarin (entries 10 and 11). In such cases, we believe that the mesopores present in MMZ$_{Cu(I)Y}$ allows to mobilize the bulkier molecules easily to reach the active sites present in catalyst and pipes out the O-allylated products.



Scheme 1. Proposed mechanism for the regioselective O-allylation catalyzed by $MMZ_{Cu(I)Y}$.

The mechanistic pathway passes through the oxidative addition of allyl bromide to Cu(I) sites [A] in MMZ occurs in a γ-selective manner following S_N2' mechanism with anti-stereochemistry, giving π-allyl complex [B] by expelling the leaving group bromide. Meanwhile, the simpler base K_2CO_3 yields phenolate ion which undergoes a nucleophilic attack at the metal center followed by reductive elimination gives selectively O-allylated product in excellent yields.

Conclusions

In summary, we have developed a simple procedure for a clean regioselective O-allylation of phenol derivatives by a one pot strategy promoted by an inexpensive, reusable, nontoxic, and environmentally benign catalytic system of $MMZ_{Cu(I)Y}$ material. The other advantages of this procedure are no need of external stabilizing ligand for Cu^I metal ion, use of a simple base, shorter reaction time and excellent regioselectivity with higher yield.

Experimental section

Synthesis and characterization of hierarchical nanoporous material ($MMZ_{Cu(I)Y}$)

MMZ_Y zeolite was synthesized from the commercially available NH_4-Y zeolite according to the procedure Ryoo et al. reported[22]. A mixture of CuCl (500 mg) and MMZ_Y (1 g) was grounded well by pestle and mortar; it was heated in flowing nitrogen atmosphere at a heating rate of 10 °C/min. The ion-exchange of Cu(I) in solid CuCl with H^+ in MMZ_Y zeolite occurred at over 300 °C and the maximum ion-exchange rate was reached at 340 °C with the consequent release of HCl gas[23]. The rate of ion-exchange was determined using H/D titration method[24]. After the preparation was over, the $MMZ_{Cu(I)Y}$ was kept under vacuum. The as-prepared catalyst was characterized using SEM, TEM, EDAX, and powder XRD analysis[25].

General procedure for the selective synthesis of O-allyl phenolic derivatives (3a–i) using $MMZ_{Cu(I)Y}$

100 mg of $MMZ_{Cu(I)Y}$ was taken in a reaction tube containing ethanol (3 mL) as a solvent and K_2CO_3 (1 mmol) as base. A mixture of equimolar (1 mmol) phenol (1a) and allylbromide (2a) was added simultaneously to the reaction tube. The reaction mixture was allowed to stir for 10 hr at 70 °C, and the proceedings of the reaction were constantly monitored by TLC. After 10 hr, products were extracted from $MMZ_{Cu(I)Y}$ using excess amount of solvent. The organic layer was separated, dried, and concentrated in vacuo and the residue was subjected to column chromatography over silica gel [60–120 mesh, petether:ethylacetate, (8:2)]. The isolated products were characterized by ^1H and ^{13}C-NMR spectra on Bruker Instrument (300 MHz and 75 MHz, respectively) in $CDCl_3$. GC-MS spectrum recorded in Agilent GC 7820 A and MS 5977E Model using DB-5 Column and the new products also by HR-MS spectrums.

Full experimental details, ^1H and ^{13}C-NMR spectra of all new compounds can be found via the "Supplementary Content" section of this article's webpage.

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