

HY Zeolite Catalyzed One-Pot Synthesis of 2,3-Dihydro-2,2-dimethylbenzofurans from Aryl Methallyl Ethers[†]

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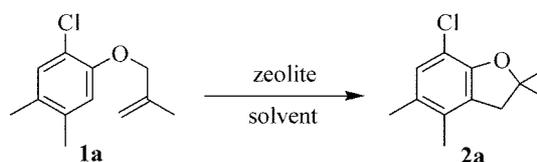
Zeolites, heterogeneous catalysts, have been widely utilized as catalysts in the petroleum refining and chemical industries¹ as well as in the preparation of fine chemicals² by use of their characteristic properties such as highly acidic and basic nature, high thermal stability and specific shape selectivity. Main advantages of acidic zeolites over homogeneous acid catalysts can be offered by replacing corrosive and polluting acid catalysts with more environmentally friendly zeolites.

The development of one-pot reaction has been of great interest in organic synthesis because this methodology provides easy access to highly complex molecules from relatively simple reagents under economically favorable reaction conditions. Thus, the combination of the one-pot strategy with the use of environmentally friendly zeolite catalysts becomes a powerful means of preparation for specific target compounds to minimize pollutants and to reduce production cost.³

As part of a program aimed at achieving simple and environmentally compatible synthetic methodologies, we have investigated the catalytic activity of zeolites for organic syntheses. Herein we report the synthetic utility of zeolites as a catalyst for a one-pot Claisen rearrangement-cyclization reaction of the aryl methallyl ethers (**1**) to give the corresponding 2,3-dihydrobenzofuran derivatives (**2**). The 2,3-dihydrobenzofuran derivatives are important intermediates in medicinal and agricultural chemistry.⁴ Their preparation generally consists of Claisen rearrangement of allyl aryl ethers to the corresponding 2-allylphenols and the subsequent cyclization of the 2-allylphenols to dihydrobenzofurans in the presence of strong acids.⁵ Recently, one-pot syntheses of dihydrobenzofurans were reported through a tandem Claisen rearrangement-cyclization reaction of allyl aryl ethers using Lewis acid such as ZnCl₂,⁶ AlCl₃,⁷ MgCl₂,⁸ and Mo(CO)₆.⁹

As an initial attempt to find an optimal reaction condition, a variety of experimental conditions were examined for 2-chloro-4,5-dimethylphenyl methallyl ether (**1a**) by changing catalyst, reaction temperature and catalyst/substrate ratio (Table 1). It was found that more acidic HY zeolite is the best choice of catalyst for the preparation of the dihydro-

Table 1. Claisen rearrangement-cyclization of aryl methallyl ether (**1a**) to the corresponding dihydrobenzofuran (**2a**) under various reaction conditions



Entry	Zeolite		Reaction Condition		Yield (%) ^d
	Type	Wt % ^a	Temp. (°C)	Time (h)	
1	HY	100	25 ^b	72	0
2	HY	100	50 ^b	72	56
3	HY	100	83 ^b	2	68
4	HY	100	130 ^c	0.5	83
5	HY	30	130 ^c	12	34
6	HY	50	130 ^c	7	68
7	NaY	100	130 ^c	7	0
8	CaY	100	130 ^c	7	14
9	LaY	100	130 ^c	7	32

^aAmount of catalyst used. 100 wt% means that the substrate:catalyst weight ratio is 1 : 1. ^b1,2-Dichloroethane was used as solvent. ^cThe reaction was carried out in refluxing chlorobenzene. ^dIsolated yields of **2a**.

benzofuran (**2a**) compared with NaY, CaY and LaY zeolites (entry 4, 7-9). Since the number and strength of acid site in zeolite increases with metal cation exchanged in the order of Na⁺ < Ca²⁺ < La³⁺, the increase in the yield of **2a** according to this order suggests that acid sites on zeolite work as active sites for this reaction.¹⁰ As usual in the catalytic reaction, the increase of the reaction temperature accelerated the conversion of the substrate (entry 1-4, Table 1). The use of 100 wt% of HY zeolite provided the dihydrobenzofuran **2a** in 83% yield within 30 min in chlorobenzene at reflux (entry 4, Table 1), whereas the yields of **2a** were low to medium at below 83 °C (entry 1-3, Table 1). The reaction was also dependent upon the amount of HY zeolite (entry 4-6, Table 1). The best yield of **2a** was obtained when the reaction was carried out in refluxing chlorobenzene using 100 wt% of HY zeolite.

Employing this optimized reaction condition, we examined the tandem Claisen rearrangement-cyclization of various methallyl aryl ethers (**1a-h**) and the results are summarized in Table 2. Although the conversion of methallyl aryl ethers was very high (>90%) and no 2-allylphenol intermediate

[†]This paper is dedicated to Professor Yong Hae Kim at KAIST on the occasion of his 65th anniversary.

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Table 2. HY zeolite catalyzed Claisen rearrangement-cyclization of aryl methallyl ethers (**1**) to the corresponding dihydrobenzofurans (**2**)^a

Entry	Substrate	R	Reaction Time (h)	Yield (%) ^b	Product Distribution ^c	
					2	3
1	1a	2-Cl-4,5-Me ₂	0.5	96 (83)	86	14
2	1b	3,4,5-Me ₃	0.5	93 (80)	86	14
3	1c	3,5-Me ₂	0.5	97 (81)	84	16
4	1d	2,3,5-Me ₃	1	94 (45)	48	52
5	1e	2,5-Me ₂	2	76 (36)	47	55
6	1f	4-Me	1.5	91 (59)	65	35
7	1g	4-OMe	3	89 (49)	55	45
8	1h	2-Cl	6	55 (30) ^d	35	29

^a100 Wt% of zeolite was used. ^bYield of isolated product mixture (**2** + **3**). The yields of isolated pure **2** are given in parentheses. ^cDetermined based on the yield of each isolated pure product. ^dStarting material was recovered in 30% yield.

was detected regardless of substituents, dihydrobenzofuran **2** was produced in medium to high yields accompanied by the formation of phenol derivatives **3** which came from cleavage of the starting materials. This observation indicates that the Claisen rearrangement into the 2-allylphenol competes with the acid-catalyzed etheral bond cleavage of the allyl aryl ether.

The substituents of the aromatic ring affected the yields as well as the distribution of products. The reaction of methallyl aryl ethers (**1a-g**) substituted with electron-donating groups provided high conversion in a short reaction time (entry 1-7, Table 2), while the reaction of ether **1h** substituted with an electron-withdrawing group resulted in low conversion (55%) together with the low yield (30%) of the dihydrobenzofuran (**2h**). The yield of desired dihydrobenzofuran **2** was found to be increased as the number of electron-donating substituents on the aromatic ring increased. Thus, in the case of aryl methallyl ethers substituted with two or three methyl groups, the higher yields of **2** were obtained (entry 1-3, Table 2).

The reactions of **1d** and **1e** having the electron-donating substituents gave high conversions similarly to those of **1b** and **1c**, respectively, but the yields of the dihydrobenzofurans (**2d** and **2e**) were low. The significant decrease in the yields of **2d** and **2e** is probably due to a steric hindrance caused by the *ortho* methyl substituent on the aromatic ring, resulting in slow Claisen rearrangement into the 2-allylphenol intermediate. The accelerated cleavage of the allyl ether bond by HY zeolite caused the enhanced yields of the corresponding phenols (**3d** and **3e**).

In summary, we have demonstrated that HY zeolite promoted the tandem Claisen rearrangement-cyclization reaction of methallyl aryl ethers to the corresponding 2,2-dimethyl-2,3-dihydrobenzofurans in medium to good yields.

The reaction is favored by electron-donating substituents on the aromatic ring. The suggested procedure using zeolite catalysts is clean and the workup procedure is simple. Furthermore, the recovered zeolites can be regenerated simply by calcinating at 500 °C in air stream. The suggested synthetic technology based on environmentally friendly zeolite catalysts, therefore, could replace the conventional corrosive and polluting acid catalysts in the one-pot synthesis of the 2,3-dihydrobenzofurans.

Experimental Section

Prior to use HY zeolite (Tosoh Co.) was activated by heating at 550 °C for 6 h. CaY and NaY zeolites were prepared by metal cation exchange on HY zeolite according to the known method¹¹ and activated before use by heating at 550 °C for 8 h. Methallyl aryl ethers (**1a-h**) were prepared from the corresponding phenols and chloroalkenes according to the reported method.⁷

General procedure for the synthesis of 2,3-dihydrobenzofurans (2a-h) over zeolite catalysts. A heterogeneous mixture of allyl aryl ether (200 mg) and zeolite (200 mg) in chlorobenzene (15 mL) was heated at reflux. The progress of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was cooled to room temperature and filtered. The filtered catalyst was washed with MeOH (20 mL × 3). The combined filtrate was concentrated under reduced pressure and the residue was purified by column chromatography with silica gel (*n*-hexane/EtOAc = 20/1). All the products were characterized by comparison of their ¹H NMR spectral data with the reported ones.^{7,12,13}

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