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Hβ zeolite: An Efficient and Reusable Catalyst for Ring-Opening of Epoxides with Amines Under Microwave Irradiation

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Abstract A solvent-free protocol for the synthesis of β-amino alcohols (Yield, up to 94%) is demonstrated by the ring-opening reactions of *meso* and terminal epoxides with aromatic amines using Hβ zeolite as catalyst under microwave irradiation. The catalytic system is 80 times faster than the reaction conducted at *RT* with six times catalyst recyclability.

Keywords Hβ zeolite · Epoxides ring-opening · β-Amino alcohols · Microwave irradiation · Amones

1 Introduction

The epoxide ring opening with amine is an important area of research because β-amino alcohols have a wide application in the synthesis of a vast range of biologically active natural and synthetic products [1, 2], unnatural amino acids [3] and chiral auxiliaries [4]. The classical and widely used strategy for the synthesis of β-amino alcohols is the direct aminolysis of epoxides with an excess of amine at elevated temperature. However, under these conditions less reactive epoxides or sluggish amines react slowly, and thermally sensitive functional groups undergo undesirable side reactions [5]. Therefore, the development of new methods for the nucleophilic ring-opening of epoxides that work under mild conditions is of great importance. In this direction various Lewis acid promoters viz., metal halides [6–9], metal triflates [10–13], metal alkoxides [14], metal amides and triflamide [15–17], transition metal salts [18], hexafluoro-2-propanol under reflux (HFIP) [19], ionic liquid [20], zirconium sulfophenyl phosphonate [21], sulphated zirconia [22], silica [23], alumina/modified alumina [24, 25] and montmorillonite clay were used as catalysts at room temperature/microwave irradiation [26] in the presence/absence of a solvent [27]. The reactions proceed smoothly to give the β-aminoalcohol in good to excellent yields. However, some of these methods suffer from disadvantages such as the use of expensive or air-sensitive reagents, extended reaction time, tedious work-up procedures, or utilization of limited range of amines. Therefore, the introduction of new and efficient methods is still in demand.

Microwave heating becomes currently popular in recent years [28–30] largely due to the dramatic reduction in reaction time, increased energy efficiency, higher product yields for a wide range of synthetic transformations [23, 26–33]. As a part of our research program to develop green chemistry for various organic transformations under solvent-free conditions [34–36], we have earlier used NaY zeolite as efficient recyclable catalyst for epoxide ring opening reaction at RT giving moderate to high yields and good regioselectivity in 6–10 h [34]. Herein, we are reporting the microwave-assisted and solvent-free protocol for the synthesis of β-amino alcohols from the reactions of aromatic amines with various *meso* and terminal epoxides using Hβ zeolite as recyclable catalyst. Excellent yield of β-amino alcohols (up to 94%) was achieved in 2.5 min (80 times faster than reaction conducted at RT) with the advantage of catalyst recyclability.

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2 Experimental

2.1 Materials and Methods

Zeolites, NaY, Naβ, Hβ (M/S. Zeocat, Uetikon, Switzerland), cyclohexene oxide, cyclopentene oxide, cyclooctene oxide, 1-propene oxide, 1-hexene oxide, 1-octene oxide, 1-decene oxide, 1-dodecene oxide, epichlorohydrin, styrene oxide, 1-butoxy-2,3-epoxypropane, 1-isobutoxy-2,3-epoxypropane, 1,2-epoxy-3-phenoxy propane, glycidyl 4-chloro phenyl ether and anilines 2-Meo- , 4-Meo- , 4-Me- , 2-Cl- , 4-Cl- , 2-NO_2- and 4-NO_2-anilines (Aldrich, USA) were used as received. Sineo Mas-II Microwave synthesis workstation was used as Microwave reactor. Microanalysis of the products was carried out on a Perkin Elmer CHN Analyzer 2400. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ (Bruker F113V 500 and 125 MHz).

2.2 Typical Experimental Procedure

In a 25 ml long neck round bottom flask epoxide, (2 mmol), amine (2 mmol), zeolites (25 mg,) were taken and mixed. The reaction was carried out under microwave irradiation for 3 min at 70 °C, 900 W. The progress of the reaction was checked on TLC using hexane/ethyl acetate (8/2) as mobile phase until the epoxide was fully consumed. The reaction mixture was then treated with 10 ml of diethyl ether and the catalyst was filtered, washed with additional 5 ml of diethyl ether and dried at 350 °C for 3 h before further use. The filtrate was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash column chromatography using hexane–ethyl acetate as mobile phase (80:20). The recovered catalyst was used six times for ring opening of cyclohexene oxide with aniline with retention of activity.

2.2.1 The Spectral Data for Some of the Selected Compounds

2.2.1.1 2-(Phenylamino)-Cyclopentanol (Table 2, Entry 1) ^{1}H ($CDCl_3$, 500 MHz) $\delta = 1.33$–1.40 (m, 1H), 1.57–1.81 (m, 3H), 1.91–1.97 (m, 1H), 2.20–2.27 (m, 1H), 2.80 (brs, 1H), 3.55–3.57 (m, 1H), 3.99–4.01 (m, 1H), 6.63–6.71 (m, 3H), 7.14–7.17 (m, 2H) ppm. ^{13}C ($CDCl_3$, 125 MHz) $\delta = 21.01$, 31.15, 32.79, 62.11, 76.88, 78.17, 113.46, 117.60, 129.33, 147.80 ppm.

2.2.1.2 2-(4-Methoxyphenylamino)Cyclohexanol (Table 2, Entry 5) ^{1}H ($CDCl_3$, 500 MHz) $\delta = 0.99$–1.01 (m, 1H), 1.26–1.38 (m, 4H), 1.68–1.76 (m, 2H), 2.08–2.10 (m, 2H), 2.23 (s, 3H), 2.88 (brs, 1H), 3.03–3.07 (m, 1H), 3.28–3.33 (m, 1H), 6.62 (m, 2H), 6.99 (m, 2H) ppm. ^{13}C ($CDCl_3$, 125 MHz) $\delta = 20.43$, 24.33, 25.10, 31.59, 33.16, 60.69, 74.49, 114.80, 127.77, 129.84, 145.45 ppm.

2.2.1.3 1-(Phenylamino)-Butan-2-ol (Table 3, Entry 2) ^{1}H ($CDCl_3$, 500 MHz) $\delta = 0.97$ (t, $J = 7.5$, 3H), 1.50–1.56 (m, 2H), 2.72 (brs, 1H), 2.92–3.01 (m, 1H), 3.20–3.23 (m, 1H), 3.35–3.50 (m, 1H), 3.68–3.37 (m, 1H), 6.61–6.73 (m, 3H), 7.15–7.18 (m, 2H) ppm. ^{13}C ($CDCl_3$, 125 MHz) $\delta = 10.66$, 27.99, 49.88, 71.66, 113.36, 117.89, 129.41, 148.36 ppm.

2.2.1.4 1-(Phenylamino)decan-2-ol (Table 3, Entry 5) ^{1}H ($CDCl_3$, 500 MHz) $\delta = 0.88$ (t, $J = 5.5$, 3H), 1.24 (m, 12H), 1.49–1.52 (m, 2H), 2.40 (brs, 1H), 2.96–3.00 (m, 1H), 3.23–3.26 (m, 1H), 3.45–3.51 (m, 1H), 3.81–3.82 (m, 1H), 6.63–6.72 (m, 3H), 7.15–7.19 (m, 2H) ppm.

2.2.1.5 1-Chloro-3-(Phenylamino)Propan-2-ol (Table 3, Entry 7) ^{1}H ($CDCl_3$, 500 MHz) $\delta = 3.15$–3.21 (m, 3H), 3.31–3.34 (m, 1H), 3.53–3.64 (m, 2H), 4.00 (m, 3H), 6.62–6.76 (m, 3H), 7.17 (m, 2H) ppm. ^{13}C ($CDCl_3$, 125 MHz) $\delta = 47.17$, 47.67, 69.86, 113.40, 118.33, 129.44, 147.78 ppm.

2.2.1.6 1-Butoxy-3-(Phenylamino)-Propane-2-ol (Table 3, Entry 8) ^{1}H ($CDCl_3$, 500 MHz) $\delta = 0.93$ (t, $J = 7.5$ Hz, 3H), 1.36–1.40 (m, 2H), 1.55–1.60 (m, 2H), 2.62 (brs, 1H), 3.12–3.16 (m, 1H), 3.16–3.31 (m, 2H), 3.44–3.55 (m, 4H), 4.01–4.02 (m, 1H), 6.63–6.71 (m, 3H), 7.15–7.19 (m, 2H) ppm. ^{13}C ($CDCl_3$, 125 MHz) $\delta = 13.93$, 19.32, 31.71, 46.79, 71.45, 72.92, 113.19, 117.76, 129.28, 129.39, 148.31 ppm.

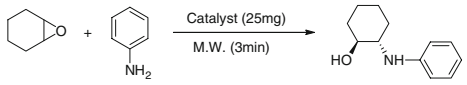
2.2.1.7 1-Isobutoxy-3-(Phenylamino)Propan-2-ol (Table 3, Entry 9) ^{1}H ($CDCl_3$, 500 MHz) $\delta = 0.92$ (d, $J = 6$ Hz, 6H), 1.88 (m, 1H), 2.66 (brs, 1H), 3.12–3.16 (m, 2H), 3.22–3.31 (m, 2H), 3.44–3.48 (m, 2H), 3.51–3.53 (m, 1H), 4.00(m, 1H), 6.63–6.71 (m, 3H), 7.15–7.18 (m, 2H) ppm. ^{13}C ($CDCl_3$, 125 MHz) $\delta = 19.36$, 28.04, 46.85, 69.08, 73.16, 113.20, 117.75, 129.29, 148.32 ppm.

2.2.1.8 1-Phenoxy-3-(Phenylamino)Propan-2-ol (Table 3, Entry 10) ^{1}H ($CDCl_3$, 500 MHz) $\delta = 2.96$ (brs, 1H), 3.27–3.31 (m, 1H), 3.42–3.45 (m, 1H), 4.01–4.08 (m, 3H), 4.24–4.27 (m, 1H), 6.69–6.79 (m, 3H), 6.94–7.02 (m, 3H), 7.22–7.34(m, 4H) ppm. ^{13}C ($CDCl_3$, 125 MHz) $\delta = 46.69$, 68.83, 70.07, 113.37, 114.60, 118.11, 121.37, 129.40, 129.65, 148.10, 158.44 ppm.

3 Results and Discussion

Initially, the solvent-free ring opening reaction of cyclohexene oxide as representative substrate was carried out

Table 1 Data for ring opening of cyclohexene oxide with aniline as a model substrate under microwave irradiation[a]



Entry	Zeolite	Temp. (°C)	MW (W)	Time (min)	Yield (%)[b]
1	Hβ	60	900	3	82
2	Hβ	70	900	3	91
3	Hβ	80	900	3	92
4	Hβ	70	500	3	69
5	Hβ	70	700	3	81
6	NaY	70	900	3	80
7	Naβ	70	900	3	52
8	Hβ	RT	900	240[c]	85
9	Hβ	70	900	90[d]	87
10	–	70	900	3	ND

[a] Cyclohexene oxide (0.20 ml, 2 mmol), aniline (0.19 ml, 2 mmol), zeolite (25 mg) under MW

[b] Isolated yield

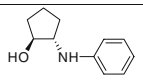
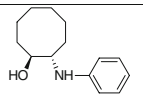
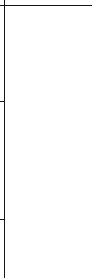
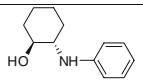
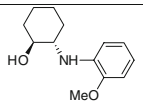
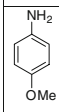
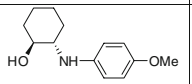
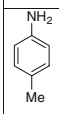
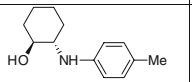
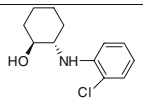
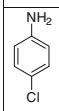
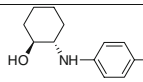
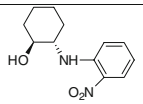
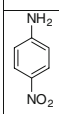
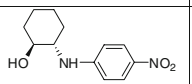
[c] Reaction was carried out at RT

[d] Reaction was carried out at 70 °C oil bath heating

with aniline as the representative nucleophile under microwave (MW) irradiation by varying the temperature from 60 to 80 °C and microwave output from (500 to 900 W) using Hβ, zeolites as catalysts (entries 1–5). Results as shown in Table 1 reveal that the 70 °C temperature and 900 W output of MW irradiation was the optimum reaction condition (entry 2). Under this optimum condition Naβ and NaY zeolites were also used as catalyst for the same reaction (Entries 6, 7). The results obtained have indicated that among the three zeolites tested, the Hβ zeolite gave the best catalytic activity in terms of product yields (entry 2) within 3 min. When the same reaction was carried out at room temperature 85% isolated yield of the product was achieved in 4 h (entry 8) while at 70 °C, 87% isolated yield was obtained in 1.5 h. (entry 9). Furthermore, conducting the same reaction in the absence of Hβ zeolite under MW there was no product formation (entry 10), signifying that the catalyst is necessary for the reaction to proceed.

Under the optimized reaction condition (as per Table 1 entry 2), cyclopentene oxide and cyclooctene oxide were allowed to react with aniline as nucleophile that produced amino alcohols in 89 and 88% yield, respectively (Table 2, entries 1, 2). In order to evaluate the effect of electronic and steric influence of the nucleophile, cyclohexene oxide was used as representative substrate for the ring opening reaction with various substituted anilines viz., 2-Meo-, 4-Meo-, 4-Me-, 2-Cl-, 4-Cl-, 2-NO_2- and 4-NO_2-anilines. The data thus obtained revealed that the *para* substituted

Table 2 Ring opening of cyclohexene oxide with various amines in the presence of Hβ zeolite under MW irradiation[a]

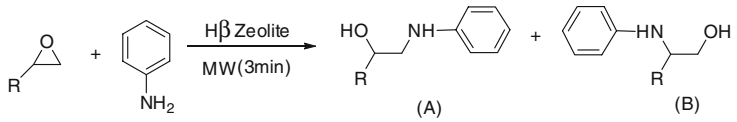
Entry	Epoxide	Amine	Product	Yield (%)[b]
1				89
2				88
3				91
4				83
5				93
6				94
7				80
8				89
9				No product formation
10				No product formation

[a] Cyclohexene oxide (0.20 ml, 2 mmol), amine (0.19 ml, 2 mmol), Hβ zeolite (25 mg) at 70 °C, 900 W, 3 min MW irradiation

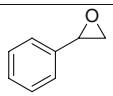
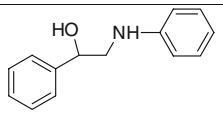
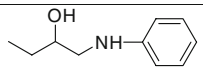
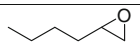
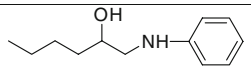
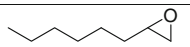
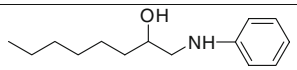
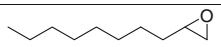
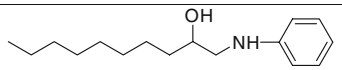
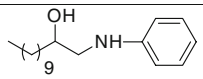
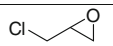
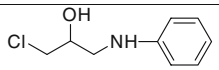
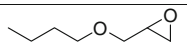
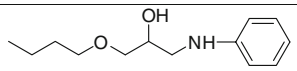
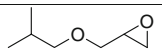
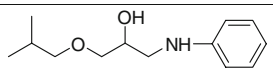
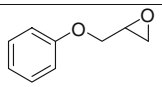
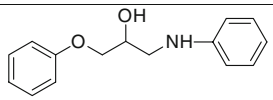
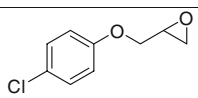
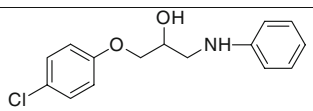
[b] Isolated yield

anilines (Table 2; entries 5, 6, 8) with electron donating groups yielded more product than *ortho* substituted anilines (Table 2, entries 4, 7). However, in the case of anilines having electron withdrawing nitro group on *ortho* or *para* position the ring opening reaction with cyclohexene oxide does not commence (entries 9, 10).The structure of β-amino alcohols was determined on the basis of proton coupling constant in the ^{1}H NMR spectrum. For example, in ^{1}H NMR (500 MHz) of 2-(4-chlorophenylamino)cyclohexanol two signals appeared at δ 3.05 (ddd, J = 12.5 Hz,

Table 3 Ring opening of various epoxides with aniline in the presence of Hβ zeolite[a] under microwave irradiation



1 R = C_6H_5
2 R = CH_3CH_2
3 R = $CH_3(CH_2)_2CH_2$
4 R = $CH_3(CH_2)_4CH_2$
5 R = $CH_3(CH_2)_6CH_2$
6 R = $CH_3(CH_2)_8CH_2$
7 R = $ClCH_2$
8 R = $CH_3(CH_2)_3OCH_2$
9 R = $(CH_3)_2CHCH_2OCH_2$
10 R = $C_6H_5OCH_2$
11 R = $ClC_6H_4OCH_2$

Entry	Epoxide	Product	Yield (%)[b]	**A:B** [d]
1			88	74:26
2			90	74:26
3			91	70:30
4			92	44:56
5			93	45:55
6			90	40:60
7[c]			89	40:60
8			91	45:55
9			92	42:58
10			89	34:66
11			93	38:62

[a] Oxide (2 mmol), aniline (2 mmol), Hβ zeolite (25 mg) at 70 °C, 900 W, MW (3 min) irradiation

[b] Isolated yield

[c] One minute MW irradiation

[d] Regioisomeric ratio was determined by ^{1}H NMR analysis

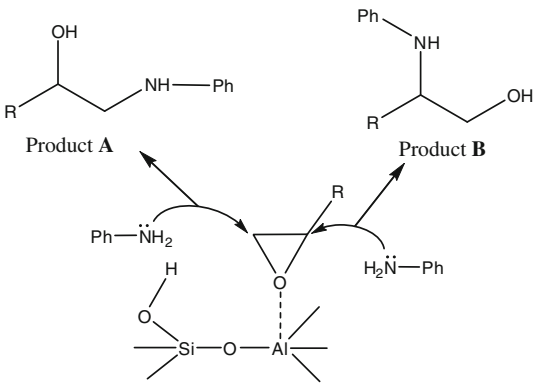
8.5 Hz, 4 Hz) and δ 3.32 (ddd, J = 13.5 Hz, 9.5 Hz, 4 Hz) for the CHNH and CHOH protons, respectively, which are indicative of *trans* stereochemistry of β-amino alcohols in agreement with earlier reports [19, 21, 37].

To asses the regioselectivity the above protocol with various terminal epoxides viz., styrene oxide, 1-propene oxide, 1-hexene oxide, 1-octene oxide, 1-decene oxide, 1-dodecene oxide, epichlorohydrin, 1-butoxy-2,3-

epoxypropane, 1-isobutoxy-2,3-epoxypropane, 1,2-epoxy-3-phenoxy propane, 1,2-epoxy-3-(4-chlorophenoxy) propane was tested for the ring opening reaction with aniline as nucleophile and the results are shown in Table 3. Overall excellent yields of β-amino alcohols (85–91%) were obtained within 3 min under MW irradiation in all the cases. However, the regioselectivity for the secondary alcohol (product **A**) was highest as compared to terminal alcohol (product **B**) for styrene and propene oxides (**A:B**::74:26). In the case of terminal alkene oxide the regioselectivity for the product **B** increases with increase in chain length. Highest selectivity for the product **B** was achieved for dodecene oxide (Table 3, entry 6) so was the case with the ring opening of epichlorohydrin (entry 7). In the case of alkoxy oxides the regioselectivity for the product **B** was higher for branched alkoxy oxide (Table 3, entry 9) than for the respective straight chain oxide (entry 8). On the other hand, the formation of the product **B** was preferred with the substrate 1,2-epoxy-3-phenoxy propane (Table 3, entry, 10) than with substrate 1,2-epoxy-3-(4-chlorophenoxy) propane.

In order to evaluate the recycling capability of the catalyst Hβ, the ring opening of cyclohexene oxide as representative substrate with aniline was carried out. After the completion of the catalytic reaction, 10 ml of diethyl ether was added to the reaction mixture and filtered. The recovered catalyst was further washed with an additional 5 ml portion of diethyl ether and dried for 3 h at 350 °C before reuse. The reactivity of the recovered catalyst was retained in the subsequent six test runs under identical reaction conditions.

On the basis of product formation, a plausible mechanism of the reaction involved the activation of epoxide through the weak interaction between the oxygen atom of epoxide and Lewis acidic sites (Al) of the zeolites to make it susceptible to nucleophilic attack by nitrogen atom of aniline either on terminal carbon to produce product **A** or on internal carbon to give the product **B** (Scheme 1).



Scheme 1 Proposed catalytic cycle for the ring opening of epoxide

4 Conclusion

In conclusion a very simple, efficient and eco-friendly protocol for the synthesis of β-amino alcohols using easily commercially available Hβ zeolite as a catalyst under microwave irradiation in solvent free condition has been developed. An excellent yield of β-amino alcohol has been achieved (94%) within 3 min. The catalytic system is 80 times faster than the reaction conducted at *RT* with the added advantage of six times catalyst recyclability. Terminal epoxides such as styrene oxide and propene oxide preferably produce secondary alcohols in excess while, long chain alkene oxides and alkoxy oxides preferentially produce terminal alcohols in excess.

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