

Short communication

Amberlist-15 as heterogeneous reusable catalyst for regioselective ring opening of epoxides with amines under mild conditions

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Abstract

Oxiranes undergo rapid ring-opening reaction with amines catalyzed by Amberlist-15 under mild reaction conditions. The reactions were carried out at room temperature to afford the corresponding β -amino alcohols in excellent yields and high regioselectivity. The catalyst was recovered and reused further without loss of activity.

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Keywords: Epoxides; Amines; Amberlist-15; 2-Amino alcohols

1. Introduction

2-Amino alcohols are versatile intermediates for the synthesis of various biologically active natural products, unnatural amino acids, β -blockers, insecticidal agents, chiral auxiliaries and oxazolines [1]. One of the most straightforward synthetic approaches for the preparation of β -amino alcohols involves the heating of an epoxide with an excess of amines at elevated temperature [2]. Since some functional groups are sensitive to high temperature, a variety of activators such as alkali metal halides [3], metal perchlorates [4], metal triflates [5], Bu_3P , ionic liquids and hexafluoro-2-propanol [6] have been developed for this conversion. However, many of these methods involve the use of expensive and stoichiometric amounts of reagents, suffer from poor regioselectivity and also require extended reaction times. Therefore, the development of a new and efficient protocol for this transformation under mild and more convenient conditions is still needed. A macro reticular sulfonic acid based polystyrene cation exchange resin, Amberlist-15 is an inexpensive and commercially available catalyst and which is very familiar for various organic transformations in the literature. In recent years, heterogeneous catalysts are gaining much importance due to their interesting reactivity as well as economic and ecological point of view [7].

2. Results and discussion



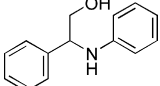


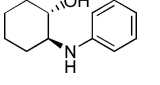


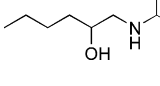

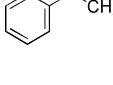
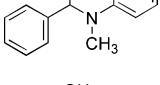

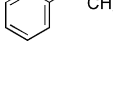
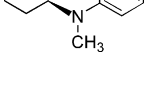

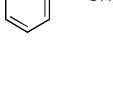
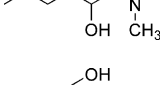

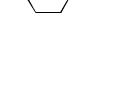
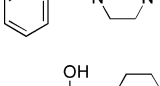
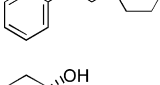

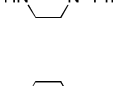
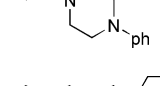

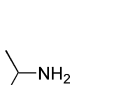
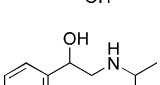


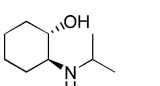


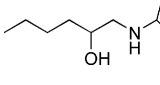


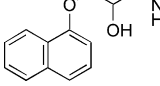



As part of our ongoing program towards the development of new synthetic methodologies, we report herein our results on regioselective ring opening of various oxiranes with a variety of amines using the catalyst Amberlist-15 under mild reaction conditions (Scheme 1).

In a typical experiment, styrene oxide (2 mmol) and aniline (2 mmol) were stirred in presence of Amberlist-15 at room temperature in dichloromethane to obtain the corresponding β -amino alcohol in 92% yield (entry **a**). The reaction was completed within 2 h and the epoxide opening took place in a regioselective manner with the attack of nucleophile at benzylic position. Only a single product was obtained from the reaction of styrene oxide with aromatic and benzyl amines (entries **a** and **d**). The structure of the products was confirmed by their ^1H NMR spectrum. The mass spectrum of these compounds showed a fragment of $M^+ - 31$ due to the loss of CH_2OH . In case of sterically hindered alicyclic amine such as *N*-phenyl piperazine (entry **g**), the product was obtained as a mixture of regioisomers in a ratio of 3:2, arising from the attack of nucleophile at benzylic as well as at terminal position. However, in case of isopropyl amine and styrene oxide, the product was obtained as a single isomer resulting from the terminal attack of the nucleophile (entry **j**). The product thus obtained was identified by its ^1H NMR spectrum that showed a doublet of doublet at δ 4.80 for benzylic proton. In a similar manner, glycidyl aryl ethers (entry **m**), alicyclic oxiranes and aliphatic alkyl oxiranes (entries **c**, **f**,

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Table 1
Amberlist-15 catalyzed regioselective ring opening of epoxides

Entry	Substrate	Amine	Product ^a	Reaction time (h)	Yield ^b (%)
a				2.0	92
b				2.5	89
c				3.0	86
d				2.0	90
e				3.5	88
f				3.5	87
g			 	2.5	90
h				3.0	88
i				3.5	86
j				3.0	89
k				3.5	86
l				4.0	85
m				3.0	87

^a All products were characterized by ¹H NMR, IR and mass spectroscopy.

^b Isolated and unoptimized yield.



Scheme 1.

i, and **l**) reacted smoothly with aromatic, aliphatic and alicyclic amines to afford the corresponding β -amino alcohols in very good yields with high regioselectivity. In these cases, the epoxide opening took place in regioselective manner preferentially by terminal attack of the nucleophile. In these reactions also, the product was obtained as a single isomer and the structure of which was confirmed by their ^1H NMR spectrum. Furthermore, cycloalkyl epoxide such as cyclohexene oxide reacted smoothly in a $\text{S}_{\text{N}}2$ fashion with different substituted aromatic, benzylic and aliphatic amines to afford the corresponding β -amino alcohols (entries **b**, **e**, **h**, and **k**) in excellent yields. The stereochemistry of the ring opening products was found to be *trans* from the coupling constants of the ring protons in ^1H NMR spectrum. In general, all the reactions were completed with in 2–4 h and the obtained yields also in very good to excellent (85–92%). The catalyst Amberlist-15 was conveniently removed by simple filtration from the reaction mixture. The recovered catalyst showed almost equal efficiency in consecutive three cycles for the same conversion without loss of activity. All the reactions were carried out at room temperature in methylene dichloride as the solvent.

3. Conclusion

In conclusion, the present methodology describes a simple, convenient and efficient procedure for the regioselective ring opening of various epoxides with a variety of amines using Amberlist-15. The notable features of this procedure are mild reaction conditions, excellent regioselectivity, cleaner reactions, improved yields, enhanced reaction rates, reusability of the catalyst and simplicity in operation, which makes it a useful and attractive process for the synthesis of β -amino alcohols.

4. Experimental

4.1. General methods

IR spectra were recorded on a Perkin-Elmer FT-IR 240-c spectro-photometer. ^1H NMR spectra were recorded on Gemini-200 spectrometer in CDCl_3 using TMS as internal standard. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70 eV. The spectroscopic data of products was compared with the data reported in the literature.

4.2. General procedure

To a mixture of epoxide (2 mmol) and amine (2 mmol) in dichloromethane (10 ml) was added Amberlist-15 (100 mg) and

the resulting mixture was stirred at room temperature for a specified period (Table 1). The progress of the reaction was monitored by TLC. After complete conversion of the starting material, as indicated by TLC, the reaction mixture was diluted with methylene dichloride (20 ml) and washed twice with water followed by brine solution. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to obtain the crude product, which was purified by column chromatography (silicagel 60–120 mesh) using ethyl acetate and *n*-hexane (3:7) to afford the pure β -amino alcohol.

4.3. Spectral data for selected compounds

2-(Phenylamino)-2-phenylethanol (**a**): IR (KBr): ν 3341, 3267, 3047, 3051, 2972, 2847, 1605, 1543, 1511, 1438, 1361, 1310, 1232, 1128, 1045, 1005, 986, 878, 746 cm^{-1} . ^1H NMR (CDCl_3): δ 3.78 (dd, 1H, $J=5.0, 10.5$ Hz), 3.90 (dd, 1H, $J=4.0, 10.5$ Hz), 4.55 (dd, 1H, $J=6.5, 10.8$ Hz), 6.40 (d, 2H, $J=7.5$ Hz), 6.80 (t, 1H, $J=7.8$ Hz), 6.95 (d, 2H, $J=8.0$ Hz), 7.35–7.45 (m, 5H). EIMS: m/z (%): 213 (M^+ 25), 195 (18), 185 (10), 107 (100), 91 (35), 77 (28), 57 (40).

trans-2-(Phenylamino)-cyclohexanol (**b**): IR (KBr): ν 3358, 3269, 3047, 2938, 2856, 1605, 1571, 1508, 1450, 1318, 1241, 1126, 1065, 1012, 985, 863, 742 cm^{-1} . ^1H NMR (CDCl_3): δ 1.05–1.40 (m, 4H), 1.48 (brs, 1H, OH), 2.15–2.25 (m, 2H), 2.80–2.90 (m, 2H), 3.20 (ddd, 1H, $J=3.5, 10.0, 10.0$ Hz), 3.40 (ddd, 1H, $J=4.0, 10.0, 10.0$ Hz), 3.80 (brs, 1H), 6.80–7.10 (m, 5H). EIMS: m/z (%): 191 (M^+ 20), 174 (15), 114 (45), 92 (22), 82 (10), 77 (100), 63 (10), 51 (20), 43 (25).

2-(*N,N*-Phenyl, methylamino)-2-phenylethanol (**d**): IR (KBr): ν 3407, 3059, 3028, 2884, 2815, 1598, 1504, 1450, 1378, 1320, 1202, 1109, 1065, 1032, 995, 902, 843, 750, 696 cm^{-1} . ^1H NMR (CDCl_3): δ 1.45 (brs, 1H, OH), 2.70 (s, 3H), 4.10 (t, 2H, $J=7.5$ Hz), 5.10 (t, 1H, $J=7.5$ Hz), 6.80 (t, 1H, $J=7.5$ Hz), 6.90 (d, 2H, $J=7.5$ Hz), 7.07–7.18 (m, 2H), 7.25–7.35 (m, 5H). EIMS: m/z (%): 227 (M^+ 16), 202 (100), 185 (15), 169 (10), 156 (18), 133 (10), 121 (15), 105 (20), 95 (22), 79 (35), 63 (10), 52 (20).

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