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Amberlyst-15 as a new and reusable catalyst for regioselective ring-opening reactions of epoxides to β -alkoxy alcohols

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ABSTRACT

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1. Introduction

Epoxides are versatile and important intermediates in organic synthesis and undergo ring-opening reactions to give β -substituted alcohols with a variety of nucleophilic species [1-4]. The opening of epoxides with alcohols is an important transformation in the synthesis of β -alkoxy alcohols, which are valuable organic solvents, versatile synthons, and intermediates [5-7]. Previous attempts to achieve the alcoholysis of epoxides under basic or acidic conditions resulted in polymerization and low regioselectivity because of the need of high temperature [8]. Various activators have been employed to accomplish this transformations including Lewis acids such as FeCl₃ [9], Cu(BF₄)₂·nH₂O [10], InCl₃ [11], Mg(HSO₄)₂ [12], and heterogeneous catalysts like polymer supported ferric chloride [13], and AlPW₁₂O₄₀ [14]. Recently, the use of many triflates and perchlorates has been reported, e.g. Yb(OTf)₃ [15], TiCl₃(OTf) [16], Al(OTf)₃ [17], and Fe(ClO₄)₃ [18]. Other catalysts such as bis(cyclopentadienyl)zirconium dichloride [19], K₅[CoW₁₂O₄₀]·3H₂O [20], CBr₄ [21] and tin(IV)porphyrinato trifluoromethanesulfonate [22] have been used for the alcoholysis of epoxides. Although there are currently a number of methods available, they have one or more disadvantages, such as long reaction time, high reaction temperature, and low selectivity. Perchlorates are explosive and triflates are expensive. Many catalysts need special conditions for their preparation. Thus, the development of new catalytic methods is highly desirable.

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Amberlyst-15 serves as an inexpensive, effective, and environmental friendly heterogeneous catalyst for

the regioselective ring-opening of epoxides by primary, secondary and tertiary alcohols, resulted in the

formation of β -alkoxy alcohols in 40–95% yields under ultrasound irradiation.

In recent years, heterogeneous catalysts have attracted much attention as catalysts for various organic transformations as well as process related to fine-chemical synthesis [23-25]. In this regard, Amberlyst-15 possesses unique properties such as environmental compatibility, nontoxic, reusability, non-corrosive, chemical and physical stability and can be used over a prolonged period. Owing to the numerous advantages associated with this cheap and no hazardous catalyst, Amberlyst-15 has been explored as a powerful catalyst for various organic reactions such as conversion of THP ethers into acetates [26], the glycosylation with disarmed glycosyl trichloroacetimidate donors [27]. Michael [28] and aza-Michael reactions [29], the synthesis of allyl amides [30], α -hydroxy phosphonates [31], 2,3-unsaturated glycosides [32], quinolines [33], α-aminophosphonates [34], 14-substituted-14Hdibenzo[*a*,*j*]xanthenes [35], 1,8-dioxo-octahydroxanthenes and 1,8-dioxo-decahydroacridines [36]. In parallel, ultrasound has increasingly been used in organic synthesis in the last three decades. A large number of organic reactions can be carried out in higher yields, shorter reaction time and milder conditions under ultrasound irradiation [37]. In continuation of our previous work on the applications of cheap and ecofriendly materials as catalysts for development of new synthetic methodologies [38-43], we herein report a mild and highly efficient procedure for the synthesis of

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Scheme 1. The reaction of epoxides with alcohols catalyzed by Amberlyst-15.

 β -alkoxy alcohols using Amberlyst-15 as a catalyst under ultrasound irradiation (Scheme 1).

2. Experimental

Sonication was performed in a KQ-250E ultrasonic clearer with a frequency of 40 kHz. Melting points were determined on X-4 apparatus and are uncorrected. IR spectra were obtained using Shimadzu FTIR-8900 spectrometer. ¹H NMR spectra were recorded with a Varain Mercury Plus 400 spectrometer using TMS as internal standard. Elemental analyses were performed on Vario EL III CHNOS elemental analyzer.

2.1. General synthetic procedure for synthesis of β -alkoxy alcohols (Table 1)

To a solution of the epoxide (1 mmol) in alcohol (5 mL), Amberlyst-15 (100 mg) was added and the reaction mixture was irradiated in the water bath of the ultrasonic cleaner for a period as indicated in Table 1 during which time the temperature of the reaction mixture attained 24–28 °C. After completion of the reaction (followed by TLC or GC), the catalyst was separated by filtration and washed with ether. The combined organics were dried over anhydrous Na₂SO₄ and solvent was removed under reduced pressure. The crude mixture was purified by column chromatography (hexane–ethyl acetate, 8:2) to provide pure compound.

2.2. Characterization of some compounds

2.2.1. 2-Methoxy-2-phenylethanol (3a)

Colorless liquid; IR (KBr): 3255, 3072, 2836, 1615, 1582, 1450, 1340, 1218, 1146, 1062, 945, 835 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ (ppm): 2.37 (br s, 1H), 3.31 (s, 3H), 3.60 (dd, *J* = 12.0, 4.0 Hz, 1H), 3.68 (dd, *J* = 12.0, 8.8 Hz, 1H), 4.32 (dd, *J* = 8.8, 4.0 Hz, 1H), 7.29–7.38 (m, 5H); Anal. Calcd for C₉H₁₂O₂: C, 71.03; H, 7.95. Found: C, 69.88; H, 7.76.

2.2.2. 2-(4-Chlorophenyl)-2-methoxyethanol (3f)

Colorless liquid; IR (KBr): 3421, 2987, 2827, 1596, 1577, 1488, 1406, 1348, 1245, 1188, 1112, 1066, 1014, 866, 827 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ (ppm): 2.48 (br s, 1H), 3.14 (s, 3H), 3.37 (dd, *J* = 11.6, 4.8 Hz, 1H), 3.49 (dd, *J* = 11.6, 6.4 Hz, 1H), 4.17 (dd, *J* = 6.4, 4.8 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H); Anal. Calcd for C₉H₁₁ClO₂: C, 57.92; H, 5.94. Found: C, 58.08; H, 6.12.

2.2.3. 2-Anthracen-9-yl-2-methoxyethanol (3j)

Yellow solid; m.p. $131-132 \degree$ C; IR (KBr): 3411, 2985, 2927, 1521, 1448, 1400, 1319, 1247, 1184, 1105, 1043, 956, 887, 730, 626 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ (ppm): 2.62 (br s, 1H), 3.31 (s, 3H), 3.83–3.87 (m, 1H), 4.43 (dd, *J* = 12.0, 9.6 Hz, 1H), 5.94 (dd, *J* = 9.6, 4.0 Hz, 1H), 7.46–7.53 (m, 6H), 8.02 (d, *J* = 8.0 Hz, 2H), 8.45 (s, 1H); Anal. Calcd for C₁₇H₁₆O₂: C, 80.93; H, 6.39. Found: C, 80.78; H, 6.56.

2.2.4. 2-Anthracen-9-yl-2-ethoxyethanol (3k)

Yellow solid; m.p. 96–97 °C; IR (KBr): 3421. 2976, 2973, 1676, 1624, 1591, 1400, 1332, 1284, 1170, 1107, 887, 729, 694 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ (ppm): 1.19 (t, *J* = 7.2 Hz, 3H), 2.36 (br s,

1H), 3.37-3.50 (m, 2H), 3.84 (dd, J = 11.6, 4.0 Hz, 1H), 4.42 (dd, J = 9.6, 11.6 Hz, 1H), 6.03 (dd, J = 9.6, 4.0 Hz, 1H), 7.45-7.57 (m, 6H), 8.02 (d, J = 7.2 Hz, 2H), 8.44 (s, 1H); Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.30; H, 6.62.

2.2.5. 2-Anthracen-9-yl-2-isopropoxyethano (31)

Yellow solid; m.p. 135–137 °C; IR (KBr): 3421, 1622, 1521, 1386, 1367, 1340, 1271, 1172, 1157, 1091, 1055, 964, 889, 731 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ (ppm): 1.00 (d, *J*=6.4 Hz, 3H), 1.25 (d, *J*=6.0 Hz, 3H), 2.26 (br s, 1H), 3.53–3.59 (m, 1H), 3.81 (dd, *J*=11.6, 4.0 Hz, 1H), 4.39 (dd, *J*=9.6, 11.6 Hz, 1H), 6.13 (dd, *J*=9.6, 4.0 Hz, 1H), 7.46–7.57 (m, 4H), 8.02–8.08 (m, 2H), 8.36–8.47 (m, 2H), 9.12 (s, 1H); Anal. Calcd for C₁₉H₂₀O₂: C, 81.40; H, 7.19. Found: C, 81.58; H, 7.02.

2.2.6. 1-(2-Methoxyethoxy)-3-phenoxypropan-2-ol (3q)

Colorless liquid; IR (KBr): 3415, 2925, 2879, 1598, 1458, 1400, 1292, 1245, 1136, 1107, 1043, 995, 756, 692 cm^{-1} ; ¹H NMR (400 MHz, CDCl₃): δ (ppm): 3.01 (br s, 1H), 3.37 (s, 3H), 3.54 (t, *J* = 4.8, 2H), 3.60–3.74 (m, 4H), 4.01 (d, *J* = 5.2, 2H), 4.15–4.21 (m, 1H), 6.89–6.95 (m, 3H), 7.24–7.29 (m, 2H); Anal. Calcd for C₁₂H₁₈O₄: C, 63.70; H, 8.02. Found: C, 63.45; H, 8.30.

3. Results and discussion

To find the optimum conditions for the alcoholysis of epoxides, a mixture of phenyl glycidyl ether (1 mmol) and methanol (5 ml) was stirred in the presence of Amberlyst-15 (100 mg) at 24 °C. This reaction proceeded well and produced 1-methoxy-3-phenoxy-2propanol (Table 1, 3m) as a predominant product along with only a trace amount of its regioisomer, 2-methoxy-3-phenoxy-propan-1ol. Next, we optimized the quantity of the catalyst for this reaction. We noted that although the product could be formed by the use of very small quantities of catalyst (20 mg/mmol of substrate), the best result, in terms of yield and reaction time, was obtained using a 100 mg/mmol ratio at 24 °C. When the same reaction was performed under sonication in an ultrasonic bath at room temperature (24–28 °C), the reaction was strikingly shortened to 50 min from 2.5 h. So, it is apparent that the reaction could be efficiently promoted by ultrasound irradiation. It should be mentioned when the reaction was carried out in the absence of catalyst for 1 h under ultrasonic irradiation, no product was formed and only the starting materials were collected.

Using the optimized reaction conditions, we investigated the scope of ring-opening reaction of various 1,2-epoxides with different alcohols and the results are summarized in Table 1. The reaction appears to be generally applicable, in all cases the reaction proceeded smoothly at room temperature (24-28 °C) under ultrasonication to give the desired products in 40-95% yields. In general, among the alcohols tested for this reaction, methanol gave the best yield. As the alkyl group of alcohol becomes bulkier, the yield of the ring-opening reaction gradually decreases. The styrene oxide and substituted styrene oxide (1a-1i), the reaction occurred at the more hindered carbon atom of the epoxide ring since the benzylic cation is more stabilized than the primary carbocation, thus giving rise to the formation of 2-alkoxy-2-phenylethanols (3a-3i) with essentially high regioselectivity. In a similar fashion, glycidyl aryl ethers (1m-1r) afforded the corresponding β -hydroxy ethers (**3m–3r**) in a regioselective manner with preferential attack at the less hindered carbon centre. In the case of alkyl oxiranes (3s-3u), the reactions are regioselective with an attack of alcohol at the terminal position. On the other hand, the reaction of cyclohexene oxide (1v-1y) with alcohols generated *trans*-hydroxy ethers in high yield signifying that the ring opening completely took place via a trans-stereospecific pathway.

Table 1

Amberlyst-15 catalyzes the synthesis of β -alkoxy alcohols under ultrasonication.	
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Entry	Epoxide	Alcohol	Product	Time (min)	Yield (%) ^a	References for known compound
a		MeOH	OMe	20	95(2) ^b	[9]
Ь		EtOH	OEtOH	30	95	[9]
c		i-PrOH	O/-Pr OH	90	85(4) ^b	[9]
d		t-BuOH	Of-Bu OH	120	60(5) ^b	[9]
e		MeOCH ₂ CH ₂ OH	OCH ₂ CH ₂ OMe OH	120	85(3) ^b	[13]
f	CI CI	MeOH	CI OMe	30	95	[11]
g	CI CI	EtOH	OEt OH	45	90	[11]
h	CI CI	i-PrOH	CI OH	90	65	[11]
i	CI CI	t-BuOH	CI Ot-Bu	180	50(3) ^b	[11]
j		МеОН	MeO OH	25	95	
k		EtOH	EtO OH	45	90	
1		i-PrOH	i-Pro OH	60	85	
m	C ^ ^	MeOH	OH OMe	50	95 (3) ^b	[9]

Entry	Epoxide	Alcohol	Product	Time (min)	Yield (%) ^a	References for known compound
n		EtOH	OH OEt	120	85	[11]
0		i-PrOH	OH Oi-Pr	180	75	[9]
р		t-BuOH	OH Ot-Bu	210	40 ^c (4) ^b	[9]
q		MeOCH ₂ CH ₂ OH	OH OCH ₂ CH ₂ OMe	60	85	
r	Me	MeOH	OH OMe Me	60	90	[44]
s	ci,	МеОН	CIOMe	30	90(5) ^b	[9]
t	ci	EtOH		60	86	[9]
u	ci,	i-PrOH	CIOi-Pr	120	80	[9]
v	$\bigcirc \diamond \diamond$	МеОН	OMe ,OH	30	90	[9]
w	\bigcirc	EtOH	OEt ,OH	60	88	[9]
x	\bigcirc	i-PrOH	O/-Pr	90	85	[9]
у	$\bigcirc \bigcirc \bigcirc$	t-BuOH	Ot-Bu	180	50	[9]

Table 1 (Continued)

^a Isolated yield after column chromatography.

^b Yields in parentheses refer to the other regioisomer determined by GC.

^c 53% of unreacted **1p** was recovered.

The likely role of Amberlyst-15 is to act as a Brönsted acid in this case for the activation of epoxide and render the epoxide more susceptible to nucleophilic attack by alcohols. It is noteworthy that the workup involves simple filtration, and the catalyst could be recycled after washing with ether and air drying. The recovered catalyst was recycled consecutively three times to produce the desired products with little variation of their yields.

4. Conclusion

In summary, Amberlyst-15 has been demonstrated to be an efficient catalyst for the synthesis of β -alkoxy alcohols by regioselective ring-opening reactions of epoxides under ultrasound irradiation. The mildness, simple experimental procedures, enhanced rates, improved yields and reusability of catalyst are the advantages of the present protocol.

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