Journal of Molecular Liquids 172 (2012) 136–139

Contents lists available at SciVerse ScienceDirect

Journal of Molecular Liquids

journal homepage: www.elsevier.com/locate/molliq

Short Communication

A novel L-asparaginyl Amido ethyl methyl imidazolium bromide catalyst for heterogeneous epoxidation of α, β-unsaturated ketones

Parasuraman Karthikeyan, Aswar Sachin Arunrao, Muskawar Prashant Narayan, Sythana Suresh Kumar, S. Senthil Kumar, Pundlik Rambhau Bhagat *

Organic Chemistry Division, School of Advanced Sciences, VIT University, Vellore,-632 014, India

ARTICLE INFO

Article history:
Received 23 September 2011
Received in revised form 26 March 2012
Accepted 21 May 2012
Available online 2 June 2012

Keywords:
Epoxidation
Ionic liquid
Amino acid
Room temperature

ABSTRACT

In the present work, a class of imidazolium based ionic liquid coupled with asparagine system was employed for asymmetric epoxidation. The heterogeneous catalyst exhibited excellent activity for epoxidation of α, β-unsaturated ketones, affording the corresponding epoxy ketones in the presence of hydrogen peroxide. The catalyst was easily recovered from the reaction mixture and reused for five consecutive runs.

1. Introduction

The development of efficient methods for the asymmetric epoxidation of α, β-unsaturated ketones is an important goal in organic synthesis, since optically active epoxy ketones are among the most versatile building block and intermediate for the synthesis of many natural products or biologically active compounds [1]. Over several decades of development, a number of valuable catalytic methodologies have been established for efficient asymmetric epoxidation induction [2], mainly involving the use of chiral metal peroxides [3], asymmetric phase transfer catalysts [4], poly amino acid catalysts [5], chiral dioxiranes [6] or other organo catalysts [7].

Ionic liquid coupled with amino acid has been extensively studied due to its many advantages including operational simplicity, highly effective catalytic and recyclability [8]. However many types of ionic liquid have been applied to the asymmetric epoxidation and fine tuning of the reaction conditions with various oxidants has been performed. To date, imidazolium based ionic liquids have been most widely used for synthesis of epoxides by several groups including S. Chandrasekhar [9], C. Freire [10], S. Tangestaninejad [11], W. A. Herrmann [12], D. Yin [13], Anil Kumar [14], P. A.Z. Suareza, [15], C-G Xia [16] and S. Liu [17]. From the above open literature, there was no report of ionic liquid coupled with asparagine amino acid in the asymmetric epoxidation of α, β-unsaturated ketones (Fig. 1). Herein, we have reported the asymmetric epoxidation of α, β-unsaturated ketones using L-asparaginyl amido ethyl methyl imidazolium bromide [L-Aaemim] Br (Scheme 1).

2. Experimental section

2.1. Materials and methods

The ^{1}H-NMR spectrum was recorded on a Bruker 500 using $CDCl_3$/DMSO-d_6 as the solvent. Enantiomeric excesses were determined by HPLC analysis on an Agilent 1100 using Chiralpak® OD-H or OJ-H columns with racemic epoxides as standards. Column chromatography was performed on silica gel (200–300 mesh). Analytical thin-layer chromatography (TLC) was carried out on precoated silica gel GF-254 plates. All solvents and chemicals were commercially available and used without further purification unless otherwise stated.

2.2. Preparation of [L-Aaemim] Br ionic liquid

A mixture of Boc-Asparagine (2.42 g, 11.0 mmol) and triethyl amine (2.23 g, 22.0 mmol) in DMF was cooled in an ice-bath. The 1-(2-aminoethyl)-3-methylimidazolium bromide [Aemim] Br (2.05 g, 10.0 mmol) was added and agitation continued at ambient temperature for 24 h. After, the completion of the reaction, the mixture was exacted with ether and poured to water. The unreacted Boc-asparagine was removed by centrifugation. The aq. layer was concentrated using rotary evaporator and ionic liquid was dried under vacuum 70 °C 6 h [18].

The BOC-[L-Aaemim] Br was deprotected using 50% TFA in dichloromethane (5 mL) for 1 h at ambient temperature. After evaporation of solvent from the mixture, TFA salts were removed by triturating the

---

* Corresponding author. Tel.: +91 9047289073; fax: +91 416 2240411.
E-mail address: drprbhagat111@gmail.com (P.R. Bhagat).

0167-7322/$ – see front matter © 2012 Elsevier B.V. All rights reserved.
doi:10.1016/j.molliq.2012.05.016

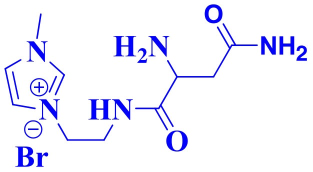


Fig. 1. L-asparaginyl amido ethyl methyl imidazolium bromide [L-Aaemim] Br.

residue with 5 mL of methanol (saturated with ammonia). The resulting mixture was concentrated using rotary evaporator and ionic liquid was dried under vacuum 80 °C 3 h.

General procedure for epoxidation of α, β-unsaturated ketones using [L-Aaemim] Br: A 25 mL flask was charged with L-asparaginyl amido ethyl methyl imidazolium bromide (0.05 mmol), unsaturated ketones (0.04 mol), DMF (5 ml), hydrogen peroxide (30%, 11 ml, 0.1 mol) and NaOH (0.01 mmol) was stirred for 12 h at ambient temperature. After completion of the reaction, the product was extracted with ether (3 × 5 mL). The combined ether extracts were concentrated on a rotary evaporator and the crude product was purified by column chromatography on silica gel to get the desired product.

3. Result and discussion

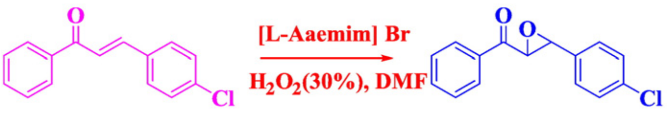
Initially epoxidation reaction was carried out in the presence of different bases without using any catalyst and solvent. It was found that no product formed even after 24 h [Table 1, entry 1–6]. Next, epoxidation was carried out in the presence of Na_2CO_3, $NaHCO_3$ using [L-Aaemim] Br as a catalyst, in DMF for different intervals. It was noted that no product formation in the presence of weak bases [Table 1, entry 7–10]. There was appreciable yield of epoxide when the reaction was conceded in the presence of [L-Aaemim] Br and NaOH at room temperature for 12 h [Table 1, entry 11]. Finally, effect of reaction time to the yield of the product was studied at room temperature for the same concentration of [L-Aaemim] Br ionic liquid. Almost similar yield was obtained when increasing the catalyst loading and duration [Table 1, entries 12 and 14].

To understand the capacity of this catalyst, we studied the epoxidation of various α, β-unsaturated ketones under the optimized condition and the results are summarized in Table 2.

As is obvious from Table 2, besides *E*-chalcone (Table 2, entry 1), substituted *E*-chalcones are also good substrates for this reaction. For example, *E*-4-methoxychalcone yielded the desired product in a 90% yield (Table 2, entry 2). Similarly, the epoxide of *E*-2-hydroxychalcone and *E*-2-chorochalocone was obtained in 88 and 87% yield (Table 2, entry 3 and 4). An excellent yield (90%) was also obtained for the product of *E*-4-chlorochalcone (Table 2, entry 5).

Further, potential of catalyst was studied for epoxidation of chromones (Table 2, entry 6). The electron repelling and electron donating groups of chromone was also successfully epoxidized, and the product was obtained in an excellent yield (Table 2, entries 7 and 8). A good yield was also obtained for the product of isoflavone and substituted isoflavones (Table 2, entry 9 and 10). The formation of all the products was confirmed by ^{1}HNMR spectra. The melting points were comparable with the reported compounds.

Reusability of the catalyst was investigated by the model reaction under optimized condition. The catalyst [L-Aaemim] Br was recovered from aq. layer by removing the water using rotary evaporator and drying under vacuum for 3 h. As shown in Table 3, the [L-Aaemim] Br ionic liquid could be reused at least five successive runs for the synthesis of epoxide without significant loss of activity. The yields that remained around 84–90% clearly illustrate the reusability of the catalyst.



Scheme 1. Synthesis of epoxide from α, β-unsaturated ketone using [L-Aaemim] Br.

Table 1
Optimization of (3-(4-chlorophenyl) oxiran-2-yl)(phenyl) methanone using [L-Aaemim] Br.

S. No	Catalyst	Base	Time (h)	Yield (%)
1	NIL	Na_2CO_3	12	–
2	NIL	Na_2CO_3	24	–
3	NIL	$NaHCO_3$	12	–
4	NIL	$NaHCO_3$	24	–
5	NIL	NaOH	12	–
6	NIL	NaOH	24	–
7	[L-Aaemim] Br	Na_2CO_3	12	–
8	[L-Aaemim] Br	Na_2CO_3	24	–
9	[L-Aaemim] Br	$NaHCO_3$	12	–
10	[L-Aaemim] Br	$NaHCO_3$	24	–
11	[L-Aaemim] Br	NaOH	12	90
12	[L-Aaemim] Br	NaOH	14	90
13	[L-Aaemim] Br	NaOH	18	91
14	[L-Aaemim] Br	NaOH	24	92

Reaction condition: 0.04 mole (3-(4-chlorophenyl) oxiran-2-yl)(phenyl) methanone, 30% H_2O_2 (11 ml, 0. 1 mol), DMF (5 ml), [L-Aaemim] Br (0.05 mmol), ambient temperature.

The spectroscopic data for [L-Aaemim] Br; ^{1}H-NMR (500 MHz, DMSO-d_6): δ 3.8(s, 3 H), 7.9(d, 1 H), 7.6(d, 1 H), 8.4(s,1 H), 4.9(t, 2 H), 3.2(t, 2 H) ,8.2(s, 1 H), 4.1(t, 1 H), 7.3(s,2 H), 2.3(t, 2 H), 5.4(s,2 H). ^{13}C-NMR: 36.53, 130.28, 131.77, 136.39, 56.82, 21.28, 176.89, 54.98, 23.61, 177.32.

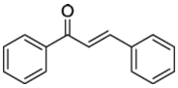
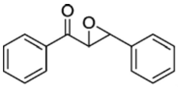
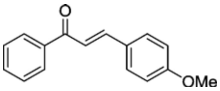
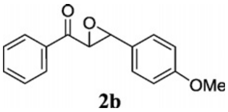
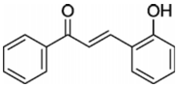
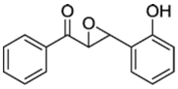
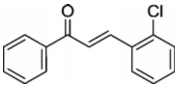
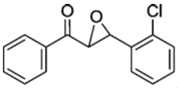
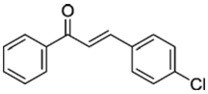
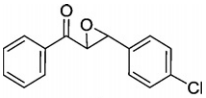
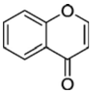
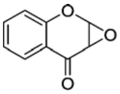
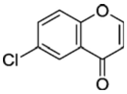
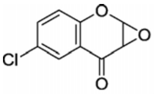
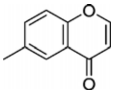
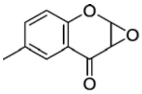
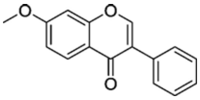
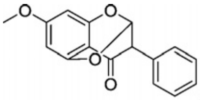
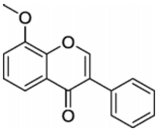
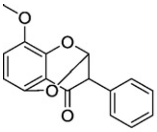
The spectroscopic data were consistent with those reported in the literature [18–21].

2a: White solid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.08 (d, 1 H), 4.30 (d, 1 H), 7.44–7.37 (m, 5 H), 7.51–7.47 (m, 2 H), 7.64–7.60 (m, 1 H), 8.01 (dd, 2 H).
2b: White solid, ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.87(s, 3 H), 4.07(d, 1 H), 4.26–4.25(d, 1 H), 6.96–6.94 (m, 2 H), 7.41–7.36(m, 5 H), 8.02–8.00(d, 2 H).
2c: White solid, ^{1}H-NMR (500 MHz, $CDCl_3$): δ 4.20 (d, 1 H), 4.42 (d, 1 H), 5.42 (s, 1 H), 7.32 (m, 2 H), 7.40–7.42 (m, 2 H), 7.55–7.58 (m, 2 H), 7.63 (m, 1 H), 8.05–8.02 (m, 2 H).
2d: White solid, ^{1}H-NMR (500 MHz, $CDCl_3$): δ 4.17 (d, 1 H), 4.41 (d, 1 H), 7.34–7.31 (m, 2 H), 7.41–7.39 (m, 2 H), 7.53–7.49 (m, 2 H), 7.63 (m, 1 H), 8.07–8.05 (m, 2 H).
2e: White solid, ^{1}H-NMR (500 MHz, $CDCl_3$): δ 4.04 (s, 1 H), 4.25 (d, 1 H), 7.28 (d, 2 H), 7.34 (d, 2 H), 7.47 (t, 2 H), 7.60 (dd, 1 H), 7.97 (d, 2 H).
2f: Yellow solid, ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.72 (d, 1 H), 5.75 (d, 1 H), 7.20–7.14 (m, 2 H), 7.54–7.50 (m, 1 H), 7.83 (dd, 1 H).
2g: Yellow solid, ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.70 (d, 1 H), 5.64 (d, 1 H), 7.07 (d, 1 H), 7.50–7.48 (m, 1 H), 7.80 (d, 1 H).
2h: Yellow solid, ^{1}H-NMR (500 MHz, $CDCl_3$): δ 2.33 (s, 3 H), 3.70 (d, 1 H), 5.60 (d, 1 H), 6.92 (d, 1 H), 7.35–7.32 (m, 1 H), 7.65 (d, 1 H).
2i: White solid, ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.85 (s, 3 H), 5.49 (s, 1 H), 6.50 (d, 1 H), 6.75 (dd, 1 H), 7.45–7.40 (m, 5 H), 7.92 (d, 1 H).
2j: Colorless oil, ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.80 (s, 3 H), 5.45 (s, 1 H), 7.06 (d, 1 H), 7.40–7.37 (m, 7 H).

4. Conclusion

We have developed a simple and efficient protocol for the epoxidation of α, β-unsaturated ketones in the presence of [L-Aaemim] Br catalyst. The method merits attention due to the simplicity of the experimental procedure, the reduced waste production and the

Table 2
Epoxidation of various α, β-unsaturated ketones using [L-Aaemim] Br.

Entry	Reactant	Product	Yield[a] (%)	ee[b] (%)	Melting point (°C)	
					Found	Literature value
1		 2a	93	89	88–90	88–90 [19]
2		 **2b**	95	90	55–57	55–58 [19]
3		 2c	92	88	90–93	90–91 [20]
4		 2d	88	87	65–67	65–68 [20]
5		 2e	90	90	48–49	49–51 [21]
6		 2f	94	90	63–65	65–66 [22]
7		 2g	90	85	90–92	92–94 [22]
8		 2h	87	80	78–80	80–82 [22]
9		 2i	82	[c]	122–124	121–123 [22]
10		 2j	89	[c]	Oil	Oil

Reaction condition: 0.04 mole α, β-unsaturated ketones, 30% H_2O_2 (11 ml, 0.1 mol), DMF (5 ml), 0.05 mmol of [L-Aaemim] Br, room temperature.

[a] The yield of isolated epoxide.

[b] Determined by chiral HPLC.

[c] Not determined by chiral HPLC.

good yields in short reaction time. The present methodology utilizes chalcones of aldehyde with both electron repelling and electron donating groups with moderate to good yields of the epoxides obtained under very mild reaction condition. The procedure is operationally simple and the [L-Aaemim] Br could be easily recovered and reused for the next cycle. Further exploration on the potential application of other unsaturated compound is on underway in this laboratory.

Table 3
Recycling of [L-Aaemim] Br system for the (3-(4-chlorophenyl) oxiran-2-yl) (phenyl) methanone.

Run	Time (h)	Yield (%)
1	12	90
2	12	90
3	12	88
4	12	86
5	12	84

Acknowledgments

We gratefully acknowledge the management of VIT University for providing required facilities and SAIF (IITM) for providing the spectral data.

References

[1] R. Bernini, E. Mincione, A. Coratti, G. Fabrizib, G. Battistuzzib, Tettrahedron: Asymmetry 12 (2001) 2359.

[2] Q.-H. Xia, H.Q. Ge, C.P. Ye, Z.M. Liu, K.X. Su, Chemical Reviews 105 (2005) 1603.

[3] D. Enders, J. Zhu, G. Raabe, Angewandte Chemie, International Edition 35 (1996) 1725.

[4] S. Arai, H. Tsuge, T. Shioiri, Tetrahedron Letters 39 (1998) 7563.

[5] S. Juliá, J. Masana, J.C. Vega, Angewandte Chemie, International Edition 19 (1980) 929.

[6] Y. Shi, Accounts of Chemical Research 37 (2004) 488.

[7] M. Marigo, J. Franzén, T.B. Poulsen, W. Zhuang, K.A. Jørgensen, Journal of the American Chemical Society 127 (2005) 6964.

[8] P.T. Anastas, J.C. Warner, Green Chemistry, Theory and Practice, Oxford University, Oxford, 1998.

[9] S. Chandrasekhar, Ch. Narasihmulu, V. Jagadeshwar, K. Venkatram Reddy, Tetrahedron Letters 44 (2003) 3629.
[10] J. Teixeira, A.R. Silva, L.C. Branco, C.A.M. Afonso, C. Freire, Inorganica Chimica Acta 363 (2010) 3321.
[11] S. Tangestaninejad, M. Moghadam, V. Mirkhani, I. M-Baltork, R. Hajian, Inorganic Chemistry Communication 13 (2010) 1501.
[12] D. Betz, W.A. Herrmann, F.E. Kuhn, Journal of Organometallic Chemistry 694 (2009) 3320.
[13] R. Tan, D. Yin, N. Yu, Y. Jin, H. Zhao, D. Yin, Journal of Catalysis 255 (2008) 287–295.
[14] A. Kumar, Catalysis Communications 8 (2007) 913.
[15] W.S.D. Silv, A.A.M. Lapis, P.A.Z. Suarez, B.A.D. Neto, Journal of Molecular Catalysis B: Enzymatic 68 (2011) 98.
[16] Z. Li, C.-G. Xia, Tetrahedron Letters 44 (2003) 2069.
[17] L.-L. Lou, K. Yu, F. Ding, W. Zhou, X. Peng, S. Liu, Tetrahedron Letters 47 (2006) 6513.
[18] S.-D. Yang, L.-Y. Wu, Z.-Y. Yan, Z.-L. Pan, Y.-M. Liang, Journal of Molecular Catalysis A: Chemical 268 (2007) 107.
[19] T. Ooi, D. Ohara, M. Tamura, K. Maruoka, Journal of the American Chemical Society 126 (2004) 6844.
[20] V. Aggarwal, G. Hynd, W. Picoul, J.-L. Vasse, Journal of the American Chemical Society 124 (2002) 9964.
[21] Y. Wang, J. Ye, X. Liang, Advanced Synthesis Catalysis 349 (2007) 1033.
[22] R. Bernini, E. Mincione, A. Coratti, G. Fabrizi, G. Battistuzzi, Tetrahedron 60 (2004) 967–971.