ARTICLE IN PRESS

Journal of Molecular Liquids xxx (2014) xxx-xxx



Contents lists available at ScienceDirect

Journal of Molecular Liquids



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

Facile protection of carbonyl compounds as oxathiolanes and thioacetals promoted by PEG₁₀₀₀-based dicationic acidic ionic liquid as

³ chemoselective and recyclable catalyst

Q1 Yi-Ming Ren^{*}, Juan-Juan Shao, Zhi-Chuan Wu, Shuai Zhang, Ting-Xian Tao

5 Department of Biochemical Engineering, Anhui Polytechnic University, Wuhu, Anhui 241000, China

6 ARTICLE INFO

Article history:
Received 19 March 2014
Received in revised form 16 April 2014
Accepted 22 April 2014
Available online xxxx

12 Keywords:

- 13 Ionic liquids24 Poly(ethylene glycol)
- 15 Thermoregulated
- 16 Oxathioacetalization
- 17 Thioacetalization
- 18 Recyclable
- 20
- 29
- 31 1. Introduction

Protection of carbonyl groups plays an important role during multi-32 step syntheses in organic, medicinal, carbohydrate, and drug design 33 chemistry [1]. Among these, oxathioacetals and dithioacetals are impor-34 tant because they are considered more stable than the corresponding O, 35 O-acetals under acidic conditions and are also useful in organic synthe-36 37 sis as acyl carbanion equivalents in C-C bond forming reactions [2]. A 38 large number of methods have been developed for the protection of carbonyl compounds as oxathiolanes and thioacetals [3–7]. However, 39 developments in this area demand further searches for better catalysts 40 that could be superior to the existing ones with regard to environmental 41 42 compatibility, efficiency, chemoselectivity, operational simplicity, toxicity, handling and recyclability. In this respect, we are interested in intro-43 ducing better catalysts for oxathioacetalization and thioacetalization of 44 45 carbonyl compounds.

Ionic liquids (ILs), as environmental friendly reaction media or catalysts, have attracted increasing attention because of their particular properties, for example negligible vapor pressure, wide liquid range, and high thermal stability, making them a greener alternative to volatile organic solvents [8–11]. Among the numerous ILs developed, recyclable ones were figured as the most important research targets. Unfortunately, ILs showed more or less solubility in commonly used molecular solvents,

E-mail address: yimingren@ahpu.edu.cn (Y.-M. Ren).

http://dx.doi.org/10.1016/j.molliq.2014.04.020 0167-7322/© 2014 Published by Elsevier B.V.

ABSTRACT

Efficient oxathioacetalization and thioacetalization of carbonyl compounds have been achieved in high yields 19 employing PEG₁₀₀₀-based dicationic acidic ionic liquid as a catalyst. The PEG ionic liquid and toluene have the 20 advantages of both homogeneous and heterogeneous phases at different temperatures (biphasic conditions at 21 lower temperatures and monophasic at higher temperatures) with the ease of product as well as catalyst 22 separation. Recycling studies have shown that the ionic liquid can be readily recovered and reused several 23 times without significant loss of activity. In addition, by using this catalyst, high chemoselective protection of 24 carbonyl compounds has been achieved. 25

© 2014 Published by Elsevier B.V.

69

70

which caused inconvenience for product separation and catalyst recov-53 ery, especially in homogeneous catalysis. Recently, poly(ethylene glycol) 54 linked dicationic neutral ionic liquids (PEG-DILs) [12,13] and poly(ethyl-55 ene glycol) linked dicationic acidic ionic liquids (PEG-DAILs) (Scheme 1) 56 have been explored as a powerful catalyst for various organic transforma-57 tions [14–21]. The PEG-D(A)ILs and toluene have the advantages of 58 both homogeneous and heterogeneous phases at different temperatures 59 (biphasic conditions at lower temperatures and monophasic at higher 60 temperatures) with the ease of product as well as catalyst separation 61 [12,14]. 62

To the best of our knowledge, there is no report on the application of 63 PEG₁₀₀₀-DAIL as Lewis acid catalysts for the preparation of oxathioacetals 64 and dithioacetals. In this paper, we report herein a simple and efficient 65 procedure for oxathioacetalization and thioacetalization of carbonyl 66 compounds using PEG₁₀₀₀-DAIL as an effective and reusable catalyst 67 (Scheme 2). 68

2. Experimental and methods

2.1. Materials and methods

IR spectra were recorded on a Bomem MB154S infrared analyzer. ¹H 71 NMR was recorded with Bruker Advance RX300. ESI-MS was recorded 72 on a Thermo Finnigan Trace TSQ. The PEG₁₀₀₀-DAIL was prepared by 73 the procedure given in the literature [14]. All the other chemicals and 74 reagents are obtained from commercial resource. Commercially 75

^{*} Corresponding author. Tel.: +86 553 2871254.

ARTICLE IN PRESS

Y.-M. Ren et al. / Journal of Molecular Liquids xxx (2014) xxx-xxx



Scheme 1. Poly(ethylene glycol) linked dicationic ionic liquids.

available reagents were used without further purification. Products are
all known compounds and were identified by comparing their physical

and spectra data with those reported in the literature.

79 2.2. Typical procedure for the protection of carbonyl groups catalyzed by
80 PEG₁₀₀₀-DAIL

A solution of carbonyl compound (2 mmol) and 2-mercaptoethanol 81 (or ethane-1,2-dithiol) (2.2 mmol) in toluene (1 mL) were added to **O**3 PEG₁₀₀₀-DAIL (1 mL) at room temperature. Then the mixture was 83 stirred at 80 °C for the specified time and monitored by TLC. After the 84 reaction, the mixture was cooled at room temperature, the upper tolu-85 86 ene that contained the expected product was separated by decantation. The toluene was evaporated and the pure products were obtained via pu-87 rification through a short silica-gel column. The bottom phase was the 88 PEG₁₀₀₀-DAIL that contained the produced water. The PEG₁₀₀₀-DAIL was 89 reused after the removal of water under reduced pressure. 04

91 3. Results and discussion

To choose the appropriate reaction temperature in this heterocyclization reaction, we examined the protection of benzaldehyde as a model compound with 2-mercaptoethanol using PEG₁₀₀₀-DAIL as catalyst in toluene at different temperatures (Table 1). The reaction temperature had a great influence on the reaction. A low yield was obtained and a long reaction time was needed when the reaction was processed at



Scheme 2. Conversion of carbonyl compounds to oxathiolanes and dithioacetals catalyzed by PEG_{1000} -DAIL.

room temperature (Table 1, entry 1). However, in the absence of toluene, 98 the reaction could be completed within 45 min with high yield (93%) at 99 room temperature (Table 1, entry 2) because the catalyst PEG₁₀₀₀-DAIL 100 and toluene (contain the reaction substrates benzaldehyde and 2- 101 mercaptoethanol) form a heterogeneous phase at room temperature, 102 which results in the catalyst not having a good contact with reaction **Q6** substrates. Increasing the reaction temperature could remarkably 104 enhance both reaction yield and rate, perhaps because PEG₁₀₀₀-DAIL 105 and toluene could form a homogeneous phase at high temperature. 106 The results showed that the appreciable temperature was 80 °C. And 107 the yield was not increased when higher temperature was employed 108 (Table 1, entries 8 and 9).

Under the optimized reaction conditions, we investigated the reac- 110 tion of carbonyl compounds with 2-mercaptoethanol or ethane-1,2- 111 dithiol (Table 2). It was found that both aromatic and aliphatic alde- 112 hydes reacted efficiently with 2-mercaptoethanol or ethane-1,2-dithiol 113 promoted by PEG_{1000} -DAIL. Table 2 showed the aromatic aldehydes, 114 having different substituents such as chloro, nitro, methoxy, methyl, 115 were converted to the corresponding oxathioacetals and dithioacetals 116 in high yields. Application of this method was then extended for the 117 protection of ketones of different structures. The corresponding products were formed, although time required for the completion of the reaction was found to be longer (Table 2, entries 11–14, 22, 23). 120

Entry	T (°C)	t (min)	Yield (%)
1	r.t.	120	51
2	r.t.	45	93 ^b
3	40	120	59
4	50	120	72
5	60	55	92
6	70	30	91
7	80	8	93
8	90	8	94
9	100	8	93

^b Without toluene.

Table 1

t1.1 t1.2

t1.15

Y.-M. Ren et al. / Journal of Molecular Liquids xxx (2014) xxx-xxx

Table 2 t2.1

t2.2 Conversion of carbonyl compounds to oxathiolanes and dithioacetals catalyzed by PEG1000-DAIL. t2.3

t2.4	Entry	Carbonyl compounds	Х	t (min)	Yield (%) ^a
t2.5	1	Benzaldehyde	0	8	93, 93, 93, 92, 92, 91, 90 ^b
t2.6	2	4-Methoxy-benzaldehyde	0	6	94
t2.7	3	4-Methyl-benzaldehyde	0	8	92
t2.8	4	2-Methyl-benzaldehyde	0	10	90
t2.9	5	4-Nitro-benzaldehyde	0	15	90
t2.10	6	2-Nitro-benzaldehyde	0	18	88
t2.11	7	4-Chloro-benzaldehyde	0	10	92
t2.12	8	2-Chloro-benzaldehyde	0	12	89
t2.13	9	Butanal	0	8	91
t2.14	10	Heptanal	0	8	90
t2.15	11	Cyclopentanone	0	80	92
t2.16	12	Cyclohexanone	0	80	90
t2.17	13	Acetophenone	0	120	89
t2.18	14	Benzophenone	0	150	90
t2.19	15	Benzaldehyde	S	8	92
t2.20	16	4-Methoxy-benzaldehyde	S	7	95
t2.21	17	4-Methyl-benzaldehyde	S	7	93
t2.22	18	4-Nitro-benzaldehyde	S	16	88
t2.23	19	4-Chloro-benzaldehyde	S	12	91
t2.24	20	Butanal	S	10	92
t2.25	21	Heptanal	S	10	90
t2.26	22	Cyclohexanone	S	80	91
t2.27	23	Acetophenone	S	120	87

Isolated vields +2.28

t2.29 The PEG₁₀₀₀-DAIL was run for seven consecutive cycles.

PEG₁₀₀₀-DAIL.



Scheme 3. Chemoselective reactions of carbonyl groups with ethane-1,2-dithiol.

The differences of reactivities of the aldehydes and ketones suggest 121 that this method can be used for the selective protection of these groups, 122and the high chemoselectivity of the method has also been demonstrated 123 by a competitive reaction between the acetal of an aldehyde and a 124 125 ketone. For instance, when an equimolar mixture of benzaldehyde and acetophenone was allowed to react with ethane-1,2-dithiol using 126 PEG₁₀₀₀-DAIL as catalyst in toluene, only the 2-phenyl-1,3-oxathiolane 127128was obtained, acetophenone was recovered quantitatively (Scheme 3). This indicates that the presented protocol is potentially applicable 129130for the chemoselective protection of aldehydes to the corresponding 183

oxathioacetals and dithioacetals in the presence of ketone functions in 131 multi-functional compounds.

In addition, the PEG₁₀₀₀-DAIL could be typically recovered and 133 reused for subsequent reactions with no appreciable decrease in yield 134 and reaction rates (Table 1, entry 1). The recycling process involved 135 the upper layer of toluene containing products and was removed by 136 decantation, and the under layer of PEG₁₀₀₀-DAIL was concentrated to 137 remove generated water under reduced pressure. Fresh substrates 138 were then recharged to the residual PEG₁₀₀₀-DAIL, and the mixture 139 was heated to react once again, and only 4.0% loss of weight was ob- 140 served after recycling 7 times. 141

4. Conclusions

142

In conclusion, we have developed a simple, novel and effective meth- 143 od for the protection of carbonyl compounds catalyzed by PEG₁₀₀₀-DAIL. 144 The advantages of the present reaction are the elimination of the metals, 145 short reaction times, high chemoselectivity, operational simplicity and 146 good yields of products. Simple reaction conditions, good thermoregulat- 147 ed biphasic behavior of PEG₁₀₀₀-DAIL and facile manipulations in the 148 isolation of the product are the attractive features of this methodology. 149 Moreover, the excellent recyclability of the PEG₁₀₀₀-DAIL makes 150 this procedure cleaner, which is a good example of green chemistry 151 technology. 152

Acknowledgments

153

157

161

169

170

171

172

173

174

175

176

177

178

179

180

181

182

The project is sponsored by the Anhui University for Young Elite 07 Talents (No. 2013RZR002ZD) and the National Innovation Program for 155 University Students (Nos. 201210363036 and 201310363065). 156

References

- P.G. Wuts, T.W. Greene, Greene's Protective Groups in Organic Synthesis, 4th ed. 158 Wiley, New York, 2007 159160
- A. Kamal, G. Chouhan, K. Ahmed, Tetrahedron Lett, 43 (2002) 6947.
- H. Alinezhad, F. Fallahi, Chin. Chem. Lett. 23 (2012) 927.
- G. Perin, L.G. Mello, C.S. Radatz, L. Savegnago, D. Alves, R.J. Jacob, E.J. Lenardão, 162 Tetrahedron Lett. 51 (2010) 4354. 163 164
- H. Flink, T. Putkonen, A. Sipos, R. Jokela, Tetrahedron 66 (2010) 887.
- M. Rahimizadeh, T. Bazazan, A. Shiri, M. Bakavoli, H. Hassani, Chin. Chem. Lett. 22 165 [6] (2011) 435. 166
- [7] S. Madabhushi, K.K.R. Mallu, N. Chinthala, C.R. Beeram, V.S. Vangipuram, Tetrahedron 167 Lett. 53 (2012) 697 168
- C. Jing, Y. Bing, RSC Adv. 3 (2013) 20077.
- S. Riyaza, A. Indrasenaa, A. Naidua, P. Dubeya, Synth. Commun. 44 (2014) 368.
- A.R. Hajipour, F. Rafiee, Org. Prep. Proced. Int. 42 (2010) 285 [10]
- [11] T. Chang, L. He, L. Bian, H. Han, M. Yuan, X. Gao, RSC Adv. 4 (2014) 727.
- Y.M. Ren, C. Cai, Tetrahedron Lett. 49 (2008) 7110. [12]
- Y.M. Ren, C. Cai, Synth. Commun. 40 (2010) 1670.
- H. Zhi, C. Lü, Q. Zhang, J. Luo, Chem. Commun. (2009) 2878. 14
- Y.L. Hu, Q. Ge, Y. He, M. Lu, ChemCatChem 2 (2010) 392.
- Y.L. Hu, M. Lu, Q. Ge, P.C. Wang, T.T. Lu, J. Ind. Eng. Chem. 16 (2010) 615.
- J. Luo, Q. Zhang, Monatsh. Chem. 142 (2011) 923. [17]
- D. Fang, J. Yang, C. Jiao, Catal. Sci. Technol. 1 (2011) 243. 18]
- Y.L. Hu, H. Jiang, J. Zhu, M. Lu, New J. Chem. 35 (2011) 292. [19]
- H. Lu, L. Sun, D. Wu, Y. Gao, Y. Shi, Q. Xue, Chin. J Inorg. Chem. 32 (2012) 1880.
- [21] Y. Wang, H. Zhi, J. Luo, J. Mol. Catal. A Chem. 379 (2013) 46