Catal Lett (2008) 125:396–400
DOI 10.1007/s10562-008-9575-5

Synthesis of a Novel Strong Brønsted Acidic Ionic Liquid and its Catalytic Activities for the Oxathioacetalization

Xuezheng Liang · Shan Gao · Jianguo Yang · Mingyuan He

Received: 16 April 2008 / Accepted: 7 July 2008 / Published online: 25 July 2008

Abstract The novel efficient procedure has been developed for the oxathioacetalization of carbonyl compounds and 2-mercaptoethanol at room temperature under solvent-free condition. The results showed that the novel multi-SO_3H functionalized ionic liquid was very efficient for the reactions with the good to excellent yields in short time. Operational simplicity, without need of any solvent, room temperature, low cost of the catalyst used, high yields, applicability to large-scale reactions, reusability and chemoselectivity are the key features of this methodology.

Keywords Oxathioacetalization · Efficient · Catalysis · Chemoselective

1 Introduction

Acetalization is commonly utilized as a protecting method for carbonyl groups in multi-step syntheses of man-made complex organic molecules or natural products [1–3]. Among various acetals, O/S-acetals are the most important from the protection aspect. S/S-acetals are quite stable in different acidic conditions and their removal as protecting groups is not a straightforward task that needs harsh reaction conditions using toxic heavy metals such as Hg^{2+}. In contrast, O/O-acetals are very sensitive towards acids and their manipulation in acidic media requires strict precautions [4]. The considerable stability in acidic conditions rather than O/O-acetals and the ease of removal in comparison with S/S acetals, make O/S-acetals good choice to be used as protecting tools in organic synthesis. O/S-acetals and ketals are generally prepared in the presence of acid catalysts [5]. The commonly used catalysts are protonic acids, Lewis acids, transitional metal complexes including TMSOTf, $ZrCl_4$, $LiBF_4$, $HClO_4$, $Sc(OTf)_3$, $In(OTf)_3$, PTSA, BF_3–OEt_2, $ZnCl_2$, TMSCl–NaI, $AlCl_3$, $TiCl_4$, $LaCl_3$, $LiClO_4/Et_2O$ (LPDE) and $TaCl_5$–SiO_2 [6–21]. Although some of these methods have convenient protocols with good to high yields, majority of these methods suffer at least from one of the following drawbacks: reaction under oxidizing conditions, use of halogenated solvents, high temperature, long reaction time, moisture sensitivity of the catalyst, high cost and high toxicity. The well-documented application of solid catalysts and solvent-free reactions are safety, economy, high yields, easy workup procedure and short reaction time. Aiming to these advantages, we developed a solvent-free protocol for the oxathioacetalization of carbonyl compounds using a novel acidic ionic liquid. The novel multi-SO_3H functionalized ionic liquid has been synthesized for the oxathioacetalization of carbonyl compounds and 2-mercaptoethanol (Scheme 1). The results showed that the novel catalyst showed very high activity for the reactions with the average yields over 90% in short time even at room temperature. A comparative study showed that the novel catalyst owned much higher activity than other catalysts with the additional advantage of reusability.

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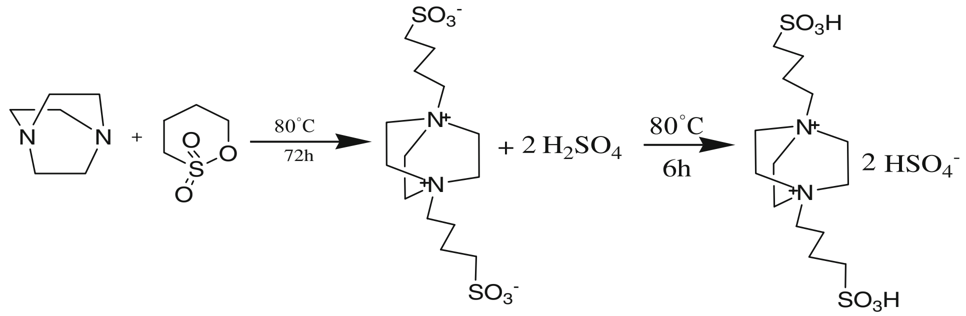


Scheme 1 The synthetic route of the novel ionic liquid

2 Experimental

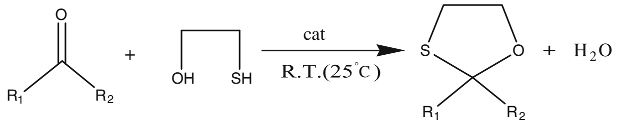
All organic reagents were commercial products of the highest purity available (>98%) and used for the reaction without further purification. Cyclohexanone, *p*-chlorobenzaldehyde, *o*-chlorobenzaldehyde, *o*-methoxybenzaldehyde, *p*-methoxybenzaldehyde, *p*-nitrobenzaldehye, butanone, propionaldehyde, 2-furaldehyde, cinnamaldehyde, mercaptoethanol, *n*-butyraldehyde, *iso*-butyraldehyde, cyclopentanone, benzaldehyde were purchased from Shanghai Chemicals Co. *n*-Valeraldehyde was obtained from Fluck.

2.1 Synthesis of the Catalyst

The procedure for synthesizing the novel IL: Triethylenediamine (11.6 g, 0.1 mol) and 1,4-butane sulfonate (58.4 g, 0.4 mol) were mixed with toluene (50 ml) and stirred magnetically for 72 h at 80 °C. Then, a white solid zwitterion was formed. The white solid zwitterion was filtrated and washed repeatedly with ether. After dried in vacuum (110 °C, 0.01 Torr), the white solid zwitterion was obtained in good yield (>90%). A stoichiometric amount of sulfuric acid was added to the above obtained zwitterion and the mixture was stirred for 6 h at 80 °C to form the ionic liquid. The IL phase was then washed repeatedly with toluene and ether to remove non-ionic residues, and dried in vacuum (110 °C, 0.01 Torr). The product was formed quantitatively and in high purity as assessed by mass balance and ^{1}H NMR and sufficient purity as assessed by a Varian DRX-400 NMR spectroscopy. Spectroscopic data for the zwitterions—^{1}H NMR (400 MHz, D_2O, TMS): δ 1.423 (m, 2H), 1.584 (m, 2H), 2.593 (t, J = 7.6 Hz, 2H), 3.463 (t, J = 7.8 Hz, 6H), 3.964 (t, J = 7.6 Hz, 2H). ^{13}CNMR (100 MHz, D_2O, TMS): δ 21.180, 21.879, 50.368, 51.914, 52.193. The spectroscopic data for the IL ^{1}H NMR (400 MHz, D_2O, TMS): δ 1.323 (m, 2H), 1.483 (m, 2H), 2.503 (t, J = 7.6 Hz, 2H), 3.263 (t, J = 7.8 Hz, 6H), 3.874 (t, J = 7.6 Hz, 2H).

2.2 The Oxathioacetalization of Carbonyl Compounds

The oxathioacetals were synthesized from the oxathioacetalization of carbonyl compounds and mercaptoethanol.



Scheme 2 The reaction equation

In the typical procedure (Scheme 2): Into a mixture of carbonyl compound (30 mmol) and 2-mercaptoethanol (30 mmol) is added the catalyst (60 mg) at room temperature and left for stirring at the same temperature. The reaction was monitored by GC analysis. After completion of the reaction, the catalyst was recovered by filtering off and washing with acetone, then dried in an oven at 453 K for about 1 h and the filtrate was distilled directly to get the pure product 1,3-oxathiolane derivatives under reduced pressure.

2.3 The Spectroscopic Data for Products

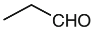
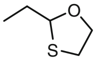
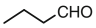
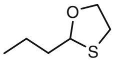
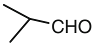
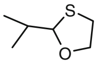
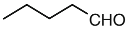
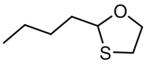
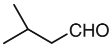
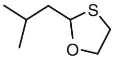
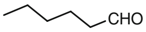
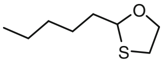
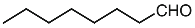
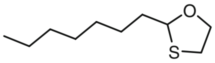
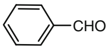
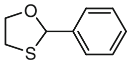
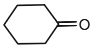
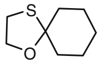
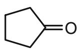
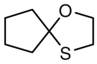
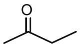
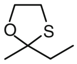
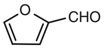
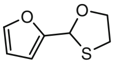
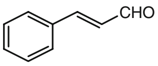
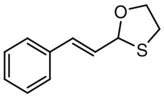
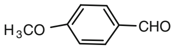
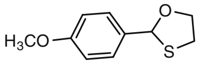
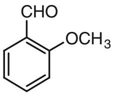
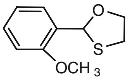
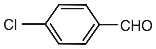
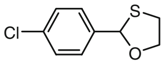
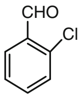
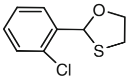
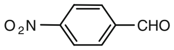
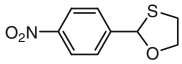
Table 1. Entry 8: IR (KBr) 2869, 1492, 1454, 1265, 1230, 1195, 1062, 1018, 972 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.15–3.31 (m, 2H), 3.90–3.98 (m, 1H), 4.49–4.55 (m, 1H), 6.06 (s, 1H), 7.29–7.41 (m, 3H), 7.45–7.49 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.9, 71.8, 86.9, 126.5, 128.3, 128.5, 139.1.

Table 1. Entry 9: Colorless liquid, b.p. 85 °C/5 mm; IR (neat) 1449, 1270, 1239, 1145, 1075, 686 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 1.32–1.52 (m, 4H), 1.74–1.89 (m, 6H), 3.00 (t, 2H, J = 5.8 Hz), 4.14 (t, 2H, J = 5.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.83 (2C), 25.02, 32.86, 39.94 (2C), 69.46, 96.49. Anal. Calcd for C8H14OS: C, 60.72; H, 8.92; S, 20.26%. Found: C, 60.53; H, 8.98; S, 20.08%.

Table 1. Entry 10: Colorless liquid, b.p. 70 °C/5 mm; IR (neat) 1439, 1323, 1264, 1159, 1070 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.55–1.74 (m, 4H), 1.91–2.05 (m, 4H), 3.06 (t, 2H, J = 5.8 Hz), 4.05 (t, 2H, J = 5.9 Hz); ^{13}C NMR (100 MHz) δ 23.90 (2C), 33.66, 40.92 (2C), 69.74, 100.43. Anal. Calcd for $C_7H_{12}OS$: C, 58.29; H, 8.39; S, 22.23%. Found: C, 58.08; H, 8.33; S, 22.15%.

Table 1. Entry 13: Colorless liquid, 125 °C/1 mm; IR (neat) 1496, 1445, 1268, 1200, 1059, 968, 754 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.88–2.93 (m, 1H), 2.95–2.98

Table 1 Preparation of various oxathioacetals from the corresponding carbonyl compounds

Entry	Substrate	Product	Reaction time/min	Yield/%[a, b]
1			15	99.1
2			25	98.4
3			35	97.6
4			45	96.3
5			50	95.5
6			60	95.3
7			65	93.5
8			20	97.3
9			85	93.2
10			95	91.8
11			120	85.8
12			75	93.4
13			50	93.3
14			35	94.4
15			45	92.5
16			20	96.3
17			30	95.7
18			20	98.5

[a] All reactions were taken at R.T. (25 °C) conditions: carbonyl compounds: 20 mmol; 2-mercaptoethanol: 24 mmol; catalyst: 60 mg

[b] Isolated yield

(m, 1H), 3.89–3.92 (m, 1H), 4.46–4.51 (m, 1H), 5.69 (d, 1H, J = 7.5 Hz), 6.27 (d, 1H, J = 7.5 Hz, J = 15.8 Hz,), 6.60 (d, 1H, J = 11.5 Hz), 7.41 (m, 5H). Anal. Calcd for C11H12OS: C, 68.71; H, 6.29; S, 16.68%. Found: C, 64.55; H, 6.35; S, 16.53%.

Table 1. Entry 14: Colorless liquid, 135 °C/1 mm; IR (neat) 1613, 1516, 1260, 1175, 1029, 830 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.18–3.20 (m, 1H), 3.26–3.30 (m, 1H), 3.80 (s, 3H), 3.87–3.94 (m, 1H), 4.49–4.54 (m, 1H), 5.99 (s, 1H), 6.87 (d, 2H, J = 8.6 Hz), 7.40 (d, 2H,

Table 2 The comparison of different catalyst

Entry	Catalyst	Catalyst amount/mg	Reaction time/min	Yield/%[a,b]
1	Novel IL	60	20	97.3
2	$ZrCl_4$	60	65	90.5
3	$HClO_4$	60	40	92.5
4	PTSA	120	50	86.5
5	BF_3–OEt_2	200	120	91.5
6	$ZnCl_2$	180	180	89.9
7	$AlCl_3$	75	90	90.7
8	$TiCl_4$	75	75	92.3
9	$LaCl_3$	100	125	88.7
10	$Sc(OTf)_3$	120	95	82.8

[a] All reactions were taken at R.T. (25 °C) conditions: benzaldehyde: 20 mmol; 2-mercaptoethanol: 24 mmol

[b] Isolated yield

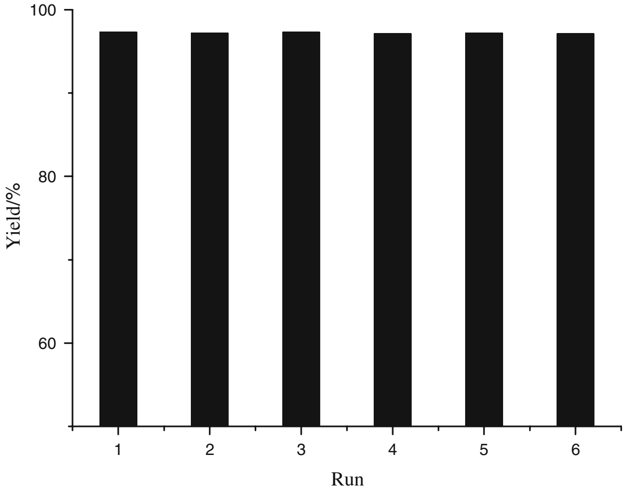


Fig. 1 The reuse of the catalyst

J = 8.6 Hz). Anal. Calcd for C10H12O2S: C, 61.20; H, 6.16; S, 16.34%. Found: C, 60.97; H, 6.22; S, 16.10%.

Table 1. Entry 16: Colorless liquid, 125 °C/5 mm; IR (neat) 1598, 1496, 1414, 1209, 1091, 1015 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.10–3.23 (m, 2H), 3.82–3.92 (m, 1H), 4.41–4.54 (m, 1H), 5.94 (s, 1H), 7.30 (d, 2H, J = 8.6 Hz), 7.44 (d, 2H, J = 8.4 Hz). Anal. Calcd for C9H9ClOS: C, 53.86; H, 4.52; S, 15.98%. Found: C, 53.63; H, 4.59; S, 15.77%.

Table 1. Entry 18: mp 78 °C; IR (KBr) 1603, 1526, 1347, 1070, 866, 717 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.21–3.30 (m, 2H), 3.99–4.06 (m, 1H), 4.52–4.58 (m, 1H), 6.13 (s, 1H), 7.60 (d, 2H, J = 8.7 Hz), 8.21 (d, 2H, J = 8.7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.08, 72.39, 85.33, 123.69 (3C), 127.12, 146.95, 147.7. Anal. Calcd for C9H9NO3S: C, 51.17; H, 4.29; N, 6.63; S, 15.18%. Found: C, 51.29; H, 4.22; N, 6.52; S, 15.00%.

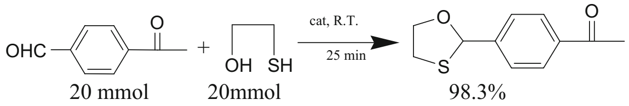
3 Result and Discussion

3.1 The Oxathioacetalization of Carbonyl Compounds and Mercaptoethanol

A wide variety of carbonyl compounds was successfully transformed to the corresponding oxathioacetals using the novel ionic liquid under solvent-free condition (Scheme 2). The results in Table 1 clearly demonstrate that the catalyst is efficient with almost quantitative conversion and exclusive selectivity for most reactions. Aliphatic aldehydes transformed to the corresponding acetals smoothly under the reaction conditions (entries 1–7). Aromatic aldehydes, such as *p*-chlorobenzaldehyde, *p*-methoxybenzaldehyde, *p*-nitrobenzaldehye could also be oxathioacetalized to afford the corresponding 1,3-oxathiolanes with 96.3%, 94.4% and 98.5% yields respectively (entries 14–18). Cinnamaldehyde was converted to the corresponding products in high yield (93.3%) without any damage of the double bond (entry 13). The ketalization reactions were also examined over the system. The linear chain ketones butanone can also be converted to the corresponding ketals in moderate yield (entry 11). Cyclohexanone and cyclopentanone were also worked well, but the reactivity of cyclopentanone seems to be slightly lower than that of cyclohexanone (entries 9 and 10). The reactions were also very efficient for the heterocyclic compounds. 2-Furaldehyde was successfully oxathioacetalized with the conversion of 93.4% (entry 12), further expanding the generality of this catalytic system to heterocyclic aromatic aldehydes. In our system, many acid-labile substrates such as 4-methoxybenzaldehyde, cinnamaldehyde, all worked well (entries 13–15). These results indicated the usefulness of the novel catalyst for the reactions and the reaction conditions are mild and not sufficiently acidic to cause side-reactions.

3.2 The Comparative Study on the Catalytic Activities of Different Catalysts

A comparative study on the catalytic activities of the novel catalyst with the reported catalysts was carried out using benzaldehyde as a model substrate (Table 2). From this study it can be concluded that the novel catalyst has much higher activity than others, furthermore it has the additional advantage of reusability. It clearly shows that the novel catalyst should be considered as one of the best choices for the economically convenient, user-friendly catalyst and for the reactions.



Scheme 3 The chemoselectivity of the catalyst

3.3 The Reuse of the Catalyst

One property of the novel catalyst is the heterogeneous catalytic process. Thus, recovery of the catalyst is very convenient. After reactions, the reaction mixture was extracted with ethyl acetate–ethyl ether = 1:1 and the lower phase, the ionic liquid, could be reused without any disposal. The recovered activities were investigated through the reaction of benzaldehyde and 2-mercaptoethanol carefully (Fig. 1). The yields and the sample composition remained unchanged even after the catalyst had been recycled for a sixth time.

3.4 The Chemoselectivity of the Catalyst

The chemoselective protection of aldehyde group in the presence of a ketone can also be achieved by using the novel ionic liquid in good yield under identical conditions because of the reactivity difference between aldehyde and ketone, as depicted in Scheme 3. This result indicated that the present protocol could be applicable to the chemoselective protection of aldehydes in the presence of ketones.

4 Conclusion

In conclusion, a novel efficient procedure has been developed for 1,3-oxathiolane derivatives formation from carbonyl compounds and 2-mercaptoethanol. Operational simplicity, without need of any solvent, room temperature, low cost of the catalyst used, high yields, excellent chemoselectivity, applicability to large-scale reactions are the key features of this methodology.

Acknowledgment This work was supported by National Key Project of Scientific and Technical Supporting Programs Funded by Ministry of Science & Technology of China (No. 2006BAE03B06), Shanghai Leading Academic Discipline Project, Project Number: B409 and Shanghai International Cooperation of Science and Technology Project, Project Number: 06SR07101.

References

1. Anastas PT, Kirchhoff MM (2002) Acc Chem Res 35:685
2. DeSimone JM (2002) Science 297:799
3. Harton B (1999) Nature 400:797
4. Batool A, Sedigheh T, Mozaffar A, Elham S (2006) J Porphyrins Phthalocyanines 10:167
5. Habib F, Nasser I, Abbas Ali J, Reza JM (2006) J Mol Catal A Chem 247:14
6. Khan AT, Parvin T, Choudhury LH (2006) Synthesis 2497
7. Chandrasekhar S, Jaya Prakash S, Shyamsunder T, Ramachandar T (2005) Synth Commun 35:3127
8. Ghanashyam B, Nabajyoti B (2006) Chem Lett 35:542
9. Bandgar BP, Kamble VT, Kulkarni A (2005) Aust J Chem 58:607
10. Kumar A, Jain N, Rana S, Chauhan SMS (2004) Synlett 2785
11. Aoyama T, Takido T, Kodomari M (2004) Synlett 2307
12. Khan AT, Sahu PR, Majee A (2005) J Mol Catal A Chem 226:207
13. Gogoi S, Borah JC, Barua NC (2004) Synlett 1592
14. Rana KK, Guin C, Jana S, Roy SC (2003) Tetrahedron Lett 44:8597
15. Kamal A, Chouhan G, Ahmed K (2002) Tetrahedron Lett 43:6947
16. Kazahaya K, Hamada N, Ito S, Sato T (2002) Synlett 1535
17. Mondal E, Sahu PR, Khan AT (2002) Synlett 463
18. Battaglia L, Pinna F, Strukul G (2001) Can J Chem 79:621
19. Perio B, Hamelin J (2000) Green Chem 2:252
20. Ravindranathan T, Chavan SP, Dantale SW (1995) Tetrahedron Lett 36:2285
21. Bergmann ED, Lavie D, Pinchas S (1951) J Am Chem Soc 73:5662