Ytterbium(III) Triflate-Catalyzed Conversion of Carbonyl Compounds into 1,3-Oxathiolanes in Ionic Liquids

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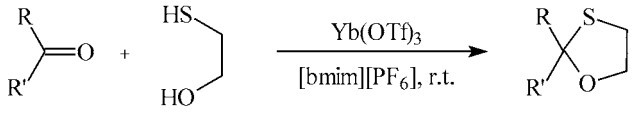
Abstract: The reaction of carbonyl compounds with 2-mercaptoethanol to prepare 1,3-oxathiolanes has been successfully carried out in ionic liquids using ytterbium(III) triflate as a catalyst. Yields of the products are high and the catalyst can be easily recovered and reused in this reaction.

Key words: carbonyl compounds, 1,3-oxathiolanes, ionic liquid, ytterbium(III) triflate

The protection and deprotection of carbonyl compounds is of great importance in organic synthesis.[1] 1,3-Oxathiolanes have been recognized as useful protecting groups of carbonyls due to their easy introduction and more stability towards acidic media as compared to *O*,*O*-acetals and easier removal than the corresponding *S*,*S*-acetals and can be utilized as acyl equivalents for C-C bond formation.[2] Various methods have been reported for their preparation[3,4] but many of these methods have drawbacks such as long reaction times,[5] use of expensive catalysts,[6] harsh reaction conditions,[7] and relatively low yields of the oxathiolanes.[8] Furthermore in most of the methods the catalyst cannot be recovered.

Lanthanide triflates are versatile Lewis acids and they have been employed in a number of organic reactions.[9] Ytterbium(III) triflate $Yb(OTf)_3$ was first used by Forsberg et al.[10] and since then it has found a wide utility in organic synthesis especially in deprotection of acetates,[11] Michael and Diels–Alder reactions,[12] aldol-Grob reaction,[13] imino ene reaction,[14] detritylation,[15] electrophilic substitution and cyclization,[16] and isomerization of glycidic esters.[17]

Ionic liquids, particularly those based on the 1,3-dialkylimidazolium cation have gained considerable interest as reaction media in recent years,[18] often permitting easier catalyst recycling.[19] Recently, lanthanide triflates immobilized in ionic liquids have been used as efficient and recyclable catalysts for different organic reactions[20] but, to the best of our knowledge, there is no report on the formation of 1,3-oxathiolanes catalyzed by $Yb(OTf)_3$ immobilized in ionic liquids. In this letter we wish to report the conversion of different carbonyl compounds to 1,3-oxathiolanes with 2-mercaptoethanol using $Yb(OTf)_3$ in ionic liquid at room temperature (Scheme 1).



Scheme 1

The reaction of various aliphatic, aromatic and heterocyclic carbonyl compounds (1.0 equiv) with 2-mercaptoethanol (1.5 equiv) in the presence of $Yb(OTf)_3$ (0.01–0.05 equiv) in [bmim][PF_6] at room temperature gave the corresponding 1,3-oxathiolanes (Table 1). Carbonyl compounds with electron-withdrawing groups such as fluoro (entry 4, Table 1) and nitro (entry 5, Table 1) gave higher yields of corresponding 1,3-oxathiolanes compared with carbonyl compounds with electron-donating groups (entry 3, Table 1). The reaction of aldehydes was faster compared with ketones and 95% of 2-phenyl-1,3-oxathiolane was obtained as compared to 20% of 2-phenyl-2-methyl-1,3-oxathiolane after one hour of reaction of 2-mercaptoethanol with benzaldehyde and acetophenone, respectively. The reaction of 4-nitrobenzaldehyde (1.0 equiv) with 2-mercaptoethanol (1.5 equiv) in the presence of a catalytic amount of $Yb(OTf)_3$ (0.01 equiv) was compared in [bmim][Br], [bmim][BF_4] and [bmim][PF_6] and best activity of catalyst was observed in [bmim][PF_6] (entry 5, Table 1). A very small amount of $Yb(OTf)_3$ (0.01–0.05 equiv) is required for the preparation of 1,3-oxathiolanes unlike other Lewis acid-catalyzed methods which utilize stoichiometric amounts of catalyst and require higher temperatures. Furthermore, no dehydrating agent is required under these conditions and the products can be easily separated by extraction with varying ratios of hexane–EtOAc leaving behind the catalyst immobilized in the ionic liquid. Recycling experiments of the recovered ionic liquid containing catalyst were carried out for the reaction of 4-nitrobenzaldehyde and 2-mercaptoethanol and it was observed that the catalyst could be reused for four cycles without noticeable reduction in activity.

In conclusion we have developed an efficient and mild procedure for the preparation of 1,3-oxathiolanes by the reaction of carbonyl compounds with 2-mercaptoethanol catalyzed by ytterbium(III) triflate in ionic liquids. The method offers advantages as compared to other Lewis acid-catalyzed reactions as tedious procedures to remove water from the solvent; substrates and catalyst are not necessary. Furthermore, the catalyst immobilized in ionic liquid can be recycled and reused several times without any loss in activity.

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Table 1 $Yb(OTf)_3$-Catalyzed Conversion of Carbonyl Compounds into 1,3-Oxathiolanes in [bmim][PF_6][21,22]

Entry	R	R′	Substrate/$Yb(OTf)_3$/ $HOCH_2CH_2SH$	Time (h)	Yield (%)[a]
1	Ph	H	1:0.01:1.5	1	95
2	4-$CH_3C_6H_4$	H	1:0.01:1.5	1	90
3	4-$CH_3OC_6H_4$	H	1:0.01:1.5	1	86
4	4-FC_6H_4	H	1:0.01:1.5	1	95
5	4-$NO_2C_6H_4$	H	1:0.01:1.5	1	98
6	$CH{=}CHC_6H_5$	H	1:0.01:1.5	1	88
7	Citronellal	–	1:0.01:1.5	2	89
8	$CH_3(CH_2)_8CH_2$	H	1:0.02:1.5	4	86
9	Piperonal	–	1:0.01:1.5	2	84
10	2-Furfuralcarboxaldehyde	–	1:0.02:1.5	3	82
11	3-Pyridinecarboxaldehyde	–	1:0.02:1.5	3	80
12	4-Methylmaino-3-nitrobenzaldehyde	–	1:0.01:1.5	3	78
13	C_6H_5	CH_3	1:0.05:1.5	5	82
14	Cyclohexanone	–	1:0.01:1.5	1	87
15	Tetralone	–	1:0.01:1.5	1	83
16	$CH_3(CH_2)_5CH_2$	CH_3	1:0.05:1.5	8	80
17	C_6H_5	C_6H_5	1:0.05:1.5	20	72

[a] Isolated yield.
[b] Yield of oxathiolane was 86% in [bmim][Br] and 88% in [bmim][BF_4] after 1 h.

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(21) **Representative Experimental Procedure for the Reaction of 4-Nitrobenzaldehyde with 2-Mercaptoethanol:** To a mixture of 4-nitrobenzaldehyde (151 mg, 1 mmol) and $Yb(OTf)_3$ (6.2 mg, 0.01 mmol) in [bmim][PF_6] (3 mL) was added 2-mercaptoethanol (117 mg, 1.5 mmol) and the contents were stirred at r.t. for about 1 h. The product was extracted with a mixture of hexane–EtOAc (1:1 v/v, 3 × 10 mL) and this organic extract was washed with 10% $NaHCO_3$ solution and then with H_2O. The organic layer was dried over anhyd Na_2SO_4 and concentrated under reduced pressure to yield 2-(4-nitrobenzyl)-1,3-oxathiolane in 98% yield. The products were characterized by ^{1}H NMR spectroscopic data and CHN analysis.

(22) **Data of Selected Oxathiolanes**:

2-(4-Methylphenyl)-1,3-oxathiolane (2): Anal. Calcd for $C_{10}H_{12}OS$: C, 66.66; H, 6.68; S, 17.77. Found: C, 66.48; H, 6.72; S, 17.54. ^{1}H NMR (300 MHz, $CDCl_3$, TMS): δ = 7.17 (2 H, d, *J* = 8 Hz), 6.99 (2 H, d, *J* = 8 Hz), 5.17 (1 H, s), 4.26–4.28 (1 H, m), 3.84–3.88 (1 H, m), 3.22–3.25 (1 H, m), 3.02–3.06 (1 H, m), 2.13 (3 H, s).

2-(3,4-Methylenedeoxyphenyl)-1,3-oxathiolane (9): Anal. Calcd for $C_{10}H_{10}O_3S$: C, 57.14; H, 4.76; S, 15.23. Found: C, 57.45; H, 4.57; S, 15.37. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.64 (1 H, d, *J* = 9 Hz), 6.59 (1 H, s,), 5.90 (2 H, s), 5.17 (1 H, s), 4.30–4.32 (1 H, m), 3.90–3.94 (1 H, m), 3.24–3.29 (1 H, m), 3.12–3.16 (1 H, m).

2-(2-Furyl)-1,3-oxathiolane (10): Anal. Calcd for $C_7H_8O_2S$: C, 53.80; H, 5.12; S, 20.50. Found: C, 53.61; H, 5.25; S, 20.68. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.30, (1 H, d, *J* = 8 Hz), 6.25 (1 H, m), 6.19 (1 H, d, *J* = 8 Hz), 5.40 (1 H, s), 4.20–4.22 (1 H, m), 3.70–3.74 (1 H, m), 3.12–3.18 (1 H, m), 2.90–2.96 (1 H, m).

2-(3-Pyridyl)-1,3-oxathiolane (11): Anal. Calcd for C_8H_9OSN: C, 57.48; H, 5.38; N, 8.30; S, 19.16. Found: C, 57.32; H, 5.18; N, 8.45; S, 19.05. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.70 (1 H, s, *J* = 8, 7 Hz), 8.55 (1 H, dd, *J* = 8, 3 Hz), 7.90 (1 H, dd, *J* = 8, 3 Hz), 7.42 (1 H, dd, *J* = 8, 7 Hz), 5.17 (1 H, s), 4.40–4.42 (1 H, m), 3.92–3.96 (1 H, m), 3.30–3.36 (1 H, m), 3.22–3.26 (1 H, m).

2-(4-Methylamino-3-nitrophenyl)-1,3-oxathiolane (12): Anal. Calcd for $C_{10}H_{12}O_3N_2S$: C, 50.12; H, 5.00; N, 11.66; S, 13.33. Found: C, 50.38; H, 5.16; N, 11.48; S, 13.20. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98 (1 H, d, *J* = 3 Hz), 7.57 (1 H, dd, *J* = 9, 3 Hz), 7.52 (1 H, d, *J* = 9 Hz), 6.05 (1 H, s), 4.52 (1 H, m), 4.00 (1 H, m), 3.24 (2 H, m).

2-Methyl-2-phenyl-1,3-oxathiolane (13): Anal. Calcd for $C_{10}H_{12}OS$: C, 66.66; H, 6.66; S, 17.77. Found: C, 66.45; H, 6.43; S, 17.90. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.08–7.18 (3 H, m), 7.21 (2 H, m), 4.10–4.14 (1 H, m), 3.82 (1 H, m), 3.10 (2 H, m), 1.83 (3 H, s).

Cyclohexyl-1,3-oxathiolane (14): Anal. Calcd for $C_8H_{14}OS$: C, 60.75; H, 8.86; S, 20.25. Found: C, 60.58; H, 8.42; S, 20.45. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.42 (1 H, m), 4.17 (2 H, t, *J* = 11.4 Hz), 3.80–3.86 (1 H, m), 3.24 (1 H, m), 3.10 (1 H, m), 3.03 (2 H, t, *J* = 11.4 Hz), 1.82 (6 H, m), 1.50 (4 H, m).

2-Tetralonyl-1,3-oxathiolane (15): Anal. Calcd for $C_{12}H_{14}OS$: C, 69.90; H, 6.79; S, 15.53. Found: C, 69.78; H, 6.64; S, 15.42. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.93–7.24 (4 H, m), 4.53–4.55 (1 H, m), 3.70–3.74 (1 H, m,), 3.29–3.34 (1 H, m), 3.18–3.20 (1 H, m), 2.85 (2 H, t, *J* = 11 Hz), 2.06 (2 H, t, *J* = 11 Hz), 1.60 (2 H, m).

2-Phenyl-2-phenyl-1,3-oxathiolane (17): Anal. Calcd for $C_{15}H_{14}OS$: C, 74.38; H, 5.78; S, 13.22. Found: C, 74.1; H, 5.64; S, 13.12. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.19–7.28 (6 H, m), 7.30–7.38 (4 H, m), 4.42–4.44 (1 H, m), 3.80–3.84 (1 H, m), 3.34–3.39 (1 H, m), 3.16 (1 H, m).