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Selenonium ionic liquid as an efficient catalyst for the synthesis of thioacetals under solvent-free conditions

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Abstract

Acidic ionic liquid butyl ethyl phenyl selenonium tetrafluoroborate, [BEPSe]BF_4, was successfully employed as a catalyst for the synthesis of several dithioacetals in the absence of a solvent. The method is general and selectively afforded thioacetals derived from aldehydes and ketones in good yields.

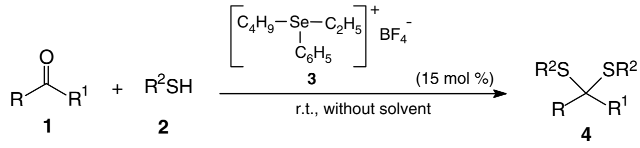
Keywords: Thioacetals; Selenonium salts; Solvent-free conditions

The protection of carbonyl compounds as thioacetals has attracted great interest in organic synthesis,[1] especially due to their versatility, since they can also be used as nucleophilic acylating agents,[1c,d] masked methylene functions,[1e] and in the asymmetric synthesis of homoallylic thioethers.[1f] A number of methods for the dithioacetalization of carbonyl compounds have been described, including the use protic or Lewis acids in the presence of organic solvents[1a] and solid-supported Lewis acids under solvent-free conditions.[1b,2] On the other hand, room-temperature ionic liquids are receiving much attention in organic chemistry as reaction solvents and catalysts.[3] Product isolation or catalyst recycling is very easy in ionic liquids and in some cases, rate accelerations and/or selectivity improvements are also observed. Recently, the preparation of dithioacetals starting from aldehydes was described using $BMIMBF_4$ at room temperature as solvent,[4a] while molten TBAB (110 °C) was used as a catalyst in the transthioacetalization of acetals.[4b]

Our major research goal has been the development of new methods for the preparation and synthetic applications of organochalcogenium compounds[5] and the development of new cleaner protocols for classical reactions.[6,7] In continuation to our studies on the development of new protocols under solvent-free conditions, we wish to report here the use of a new Se-based ionic liquid, phenyl butyl methyl selenonium tetrafluoroborate ([BEPSe]BF_4, **3**),[7] as catalyst in the preparation of dithioacetals from aldehydes and ketones (Scheme 1, Table 1).[8]

Accordingly, when benzaldehyde (**1a**; 1.0 mmol) was treated with phenylthiol (**2a**; 2.2 mmol) in presence of [BEPSe]BF_4 (15 mol %) at room temperature, benzaldehyde dithiophenylacetal (**4a**) was obtained in 83% yield after 2.5 h (Table 1, entry 1).

When the same reaction was performed in the presence of a smaller amount of [BEPSe]BF_4 (5 mol %), an incomplete consumption of starting materials, even after stirring for 24 h was observed. The use of a larger amount of **3** (25 mol %) has not significantly increased the yield of **4a**.



Scheme 1.

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Table 1
Conversion of aldehydes and ketones to thioacetals **4**

Entry	R	R^1	Thiol (**2**)	Product (**4**)	Time (h)	Yield[a] (%)
1	C_6H_5	H	C_6H_5SH **2a**	**4a**	2.5	83
2	C_6H_5	H	*p*-$ClC_6H_4CH_2SH$ **2b**	**4b**	2.0	97
3	C_6H_5	H	$C_6H_5CH_2SH$ **2c**	**4c**	2.5	75
4	C_3H_7	H	C_6H_5SH **2a**	**4d**	3.5	58
5	C_4H_9	H	C_6H_5SH **2a**	**4e**	3.5	66
6	C_4H_9	H	$C_6H_5CH_2SH$ **2c**	**4f**	2.5	78
7	(*E*/*Z*)-$Me_2C{=}CHCH_2CH_2C(Me){=}CH$	H	C_6H_5SH **2a**	**4g**	1.5	83
8	CH_3	CH_3	$C_6H_5CH_2SH$ **2c**	**4h**	4.5	46
9	CH_3	CH_3	*p*-$ClC_6H_4CH_2SH$ **2b**	**4i**	5.0	44
10	2-Tetralone		*p*-$ClC_6H_4CH_2SH$ **2b**	**4j**	5.5	25
11	2-Tetralone		$C_6H_5CH_2SH$ **2c**	**4k**	4.0	65
12	2-Tetralone		$CH_3(CH_2)_{11}SH$ **2d**	**4l**	2.5	80
13	$-CH_2CH_2CH_2CH_2CH_2CH_2-$		$C_6H_5CH_2SH$ **2c**	**4m**	5.0	58
14	C_6H_5	C_6H_5	C_6H_5SH **2a**	**4n**	24	7
15	C_6H_5	H	$HSCH_2CH_2SH$ **2e**[b]	**4o**	3	96
16	$-CH_2CH_2CH_2CH_2CH_2CH_2-$		$HSCH_2CH_2SH$ **2e**[b]	**4p**	5	88

[a] Yields of pure products isolated by column chromatography (hexanes) and identified by mass spectrometry, ^1H and ^{13}C NMR.[1,2]

[b] 1.0 equiv of 1,2-ethanedithiol was used.

The experimental procedure is very easy, and a complete conversion of starting materials to products was observed after stirring for a few hours at room temperature. The efficiency of the method can be clearly visualized by the reaction of benzaldehyde (**1a**) with 4-chlorobenzylthiol (**2b**) affording the respective dithioacetal **4b** in almost quantitative yield (Table 1, entry 2). The scope of our methodology was successfully expanded to other aromatic and aliphatic aldehydes and thiols (Table 1, entries 3–7). The present thioacetalization procedure is also applicable to aliphatic ketones (Table 1, entries 8–14), affording the respective dithioacetals in reasonable yields, except for the condensation of benzophenone with phenylthiol (**2a**, entry 14). On the other hand, the Se-ionic liquid **3** can also be used in the selective protection of the α,β-unsaturated aldehyde citral as the respective dithioacetal **4g**, without the formation of the Michael-adduct (Table 1, entry 7). Besides, when 1,2-ethanedithiol (**2e**, 1 equiv) was employed, the preparation of 1,3-dithiolanes was possible in good yields (Table 1, entries 15 and 16).

As the preparation of thioacetals from aldehydes is kinetically favorable, as shown in Table 1, we investigated the ability to chemoselectively protect an aldehyde in the presence of a ketone under our best conditions. Thus, when an equimolar mixture of benzaldehyde and cyclohexanone was allowed to react with benzenemethanethiol (**2c**) in the presence of a catalytic amount of $[BEPSe]BF_4$, the thioacetal derived from benzaldehyde (**4c**) was obtained almost exclusively (73% yield) with a little amount of the protected ketone **4m** (3% yield) after 5 h.

In conclusion, we presented here an easy and general method for the selective conversion of aromatic, aliphatic, α,β-unsaturated aldehydes and ketones to their corresponding dithioacetals. This method consists in low consumption of solvent, mild reaction conditions, good yields, and use of catalytic amount of ionic liquid with non-aqueous work-up.

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8. *General procedure for the synthesis of thioacetals*: To a mixture of benzaldehyde (**1a**, 0.106 g; 1 mmol) and phenylthiol (**2a**, 0.242 g; 2.2 mmol), $[\mathrm{BEPSe}]\mathrm{BF}_4$[7] (**3**, 0.049 g, 15 mol %) was added and the solution stirred at room temperature for 2.5 h. The crude product was purified by column chromatography over silica gel (SiO_2) eluting with hexanes, yielding product **4a** (0.256 g, 83%) as a light yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ (ppm) 7.32–7.40 (m, 6H); 7.20–7.27 (m, 9H); 5.42 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ (ppm) 133.8, 130.0, 129.5, 128.3, 78.5, 78.4, 78.0, 61.3.[1f]