A novel efficient sulfenylation method using quinone mono-*O,S*-acetals under mild conditions

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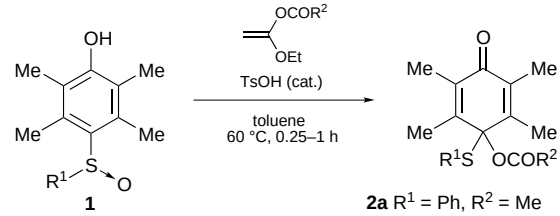
A novel method for sulfenylation induced by aromatization of quinone mono-*O,S*-acetals is described.

It is important to introduce sulfur effectively into organic compounds, as many biologically active compounds contain sulfur functions.[1] Although many methods for sulfenylation have been reported to date,[2] a mild sulfenylation reaction under neutral conditions is not readily available. Under these circumstances, we report here a novel sulfenylation reaction using quinone mono-*O,S*-acetals which gives high yields under almost neutral conditions.

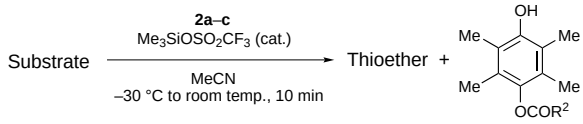
We have already reported that various quinone mono-*O,S*-acetals **2**, which are intermediates in aromatic Pummerer rearrangement, could be isolated easily in high yields.[3] These compounds readily aromatize by reaction with various nucleophiles, giving sulfenylation products. Therefore, we examined



2a R^1 = Ph, R^2 = Me 70%
b R^1 = Ph, R^2 = CH_2Cl 87%
c R^1 = Me, R^2 = Me 86%

Scheme 1

Table 1 Sulfenylation by quinone mono-*O,S*-acetals **2a**–**c**



3a R^2 = Me
b R^2 = CH_2Cl

Entry	Substrate	*O,S*-Acetals	Thioethers	Yield (%)[a]
1	**4a** *n* = 0	**2a**	**5a** *n* = 0, R^1 = Ph	98
2	**4a** *n* = 0	**2b**	**5a** *n* = 0, R^1 = Ph	99
3	**4a** *n* = 0	**2c**	**5b** *n* = 0, R^1 = Me	94
4	**4b** *n* = 1	**2b**	**5c** *n* = 1, R^1 = Ph	95
5	**6a** R^3 = H, R^4 = OMe	**2b**	**7a**	99
6	**6b** R^3 = Me, R^4 = OMe	**2b**	**7b**	100
7	**6c** R^3 = Ph, R^4 = OMe	**2b**	**7c**	98
8	**6d** R^3 = OMe, R^4 = OMe	**2b**	**7d**	99
9	**6e** R^3 = H, R^4 = Ph	**2b**	**7e**	96
10	**8a** R^5 = H, R^6 = OMe, R^7 = OMe, R^8 = OMe	**2b**	**9a**	99
11	**8b** R^5 = OMe, R^6 = H, R^7 = OMe, R^8 = OMe	**2b**	**9b**	99
12	**8c** R^5 = Me, R^6 = H, R^7 = OMe, R^8 = OMe	**2b**	**9c**	99
13	**8d** R^5 = Me, R^6 = H, R^7 = OMe, R^8 = Me	**2b**	**9d**	67[b]
14	**8e** R^5 = H, R^6 = H, R^7 = NMe_2, R^8 = H	**2b**	**9e**	64[b]
15	**10a** R^9 = H, R^{10} = Me	**2b**	**11a**	99
16	**10b** R^9 = OMe, R^{10} = Me	**2b**	**11b**	99
17	**10c** R^9 = H, R^{10} = Ph	**2b**	**11c**	94

[a] Yields refer to pure isolated products by column chromatography; phenol derivatives **3a** or **3b** were almost quantitatively formed as by-products in all cases.
[b] Diphenyl disulfide was formed as a by-product.

the possibility that **2** might act as an effective reagent for the sulfenylation of various nucleophiles under mild conditions. The starting quinone mono-*O*,*S*-acetals **2a–c** were prepared by Pummerer reaction of the corresponding sulfoxide **1** with 1-ethoxyvinyl esters.[4] A higher yield was obtained with **2b** and **2c** than **2a** (Scheme 1).[3]

First we examined the ability of quinone mono-*O*,*S*-acetals **2a–c** for sulfenylation by the use of cyclic silyl enol ethers **4a**,**b** and found that **2a–c** were excellent sulfenylating reagents which gave the target thioethers in quantitative yields (Table 1, entries 1–4).† The generality of this sulfenylation reaction was confirmed using various acyclic silyl enol ethers **6a–e** with **2b** (Table 1, entries 5–9). This sulfenylating reagent also reacted easily with electron-rich aromatic compounds such as **8a–e** and heteroaromatic compounds **10a–c**, and the corresponding thioethers were obtained by direct sulfenylation (Table 1, entries 10–17). These sulfenylation reactions were completed within 10 min at −30 °C to room temperature under nearly neutral conditions, giving thioether derivatives in almost quantitative yields. In addition, as a side product, the hydroquinone derivative **3** was easily removed by treatment with weak aqueous alkali.

In conclusion, we have succeeded in developing novel sulfenylating reagents by taking advantage of activation on the sulfur atom based on aromatization. These reagents might be applied to the synthesis of biologically active substances having sulfur functions and labile functions that are sensitive to basic or acidic conditions.

Footnotes

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† Typical procedure: a mixture of **4** (1 mmol), **2a–c** (1 mmol) and $Me_3SiOSO_2CF_3$ (cat.) in MeCN (5 ml) was stirred at room temperature under a positive atmosphere of dry nitrogen. After 10 min, the mixture was concentrated *in vacuo*. Purification by column chromatography on silica gel (eluent: AcOEt–hexane = 1 : 5) gave **5a–c** in 94–99% yield.

References

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