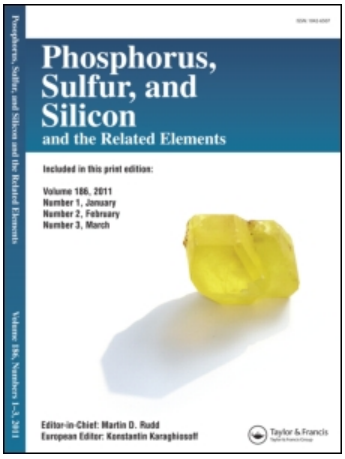

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Solvent-Free Acetylation of Thiols Under Catalysis of $MgBr_2 \cdot OEt_2$

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SOLVENT-FREE ACETYLATION OF THIOLS UNDER CATALYSIS OF $MgBr_2 \cdot OEt_2$

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Solvent-free protection of aromatic and aliphatic thiols with acetic anhydride was performed at room temperature under trace quantities of magnesium bromide ethyl etherate, affording rapid formation of various thiol esters in excellent yields.

Keywords Acylation; catalysis; magnesium bromide ethyl etherate; solvent-free reaction; thiol esters

Thiol esters constitute an important class of organic compounds due to their bioorganic applications.[1] In addition they are key synthetic precursors in the preparation of heterocyclic compounds,[2] acyl radicals,[3] asymmetric aldol products,[4] and various ketones.[5] Among available methods for the preparation of thiol esters,[6] direct acylation of thiols with acetic anhydride or acetyl chloride is very common. This preparation is traditionally carried out in the presence of amine bases or protic acids. Recent developments include the use of various Lewis acids such as niobium(V) chloride,[7] pyridine/alumina in combination with microwave irradiation,[8] acetonyltriphenylphosphonium bromide,[9] ruthenium(III) chloride,[10] copper-based reagents,[11] and aluminum dodecatungstophosphate.[12] However, many of these procedures usually require the use of environmentally unsafe conditions, demand application of expensive or commercially unavailable reagents, or involve the use an additional stimulant.

Recently, we released a self-promoted chemoselective acylation of amines and thiols in the presence of no extra catalyst or additive.[13] However, protection of thiols was limited to aromatic substrates and took relatively longer reaction time periods. Based on our previous experience on the use of magnesium bromide ethyl etherate ($MgBr_2 \cdot OEt_2$) as an efficient Lewis acid to catalyze various organic transformations under mild conditions,[14] we envisioned that the acetylation of thiols could be boosted by using trace quantities of the catalyst. As a result, we report in this article a facile and room-temperature transformation of thiols to their corresponding acylated derivatives under very mild conditions (Scheme 1).

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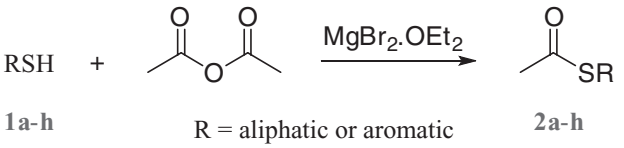
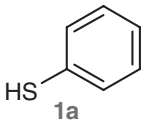
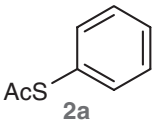
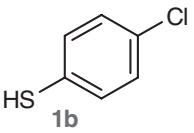
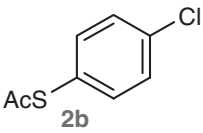
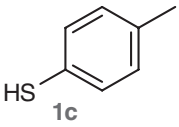
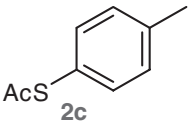
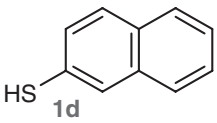
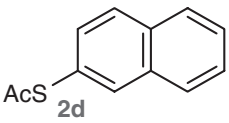
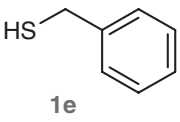
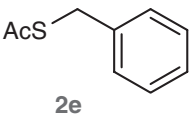
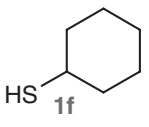
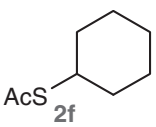
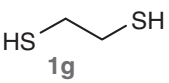
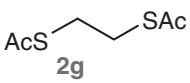
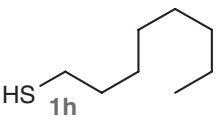
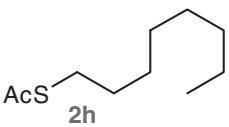


Scheme 1

Table I $MgBr_2.OEt_2$-catalyzed acetylation of various thiols with Ac_2O

Entry	Thiol	Thiol ester	M_P (°C) found/reported	Yield %[a]
1	 1a	 2a	oil/oil[6c]	98
2	 1b	 2b	33–34/38–39[6c]	90
3	 1c	 2c	oil/oil[6c]	82
4	 1d	 2d	48–49/50–51[1b]	96
5	 1e	 2e	oil/oil[6f]	86
6	 1f	 2f	oil/oil[6f]	86
7	 1g	 2g	65–67/68–69[11b]	88[b]
8	 1h	 2h	oil/oil[6f]	86

[a]Isolated yields.
[b]Two equivalents of Ac_2O.

Results for the acetylation of various aliphatic and aromatic thiols are summarized in Table I. The synthesis of *S*-phenyl ethanethioate (entry 1) represents the typical procedure for solvent-free magnesium bromide ethyl etherate–catalyzed conversion of different thiols to their respective acetyl protected derivatives. An equimolar mixture of acetic anhydride and thiophenol in the presence of 4 mol% of the catalyst yields complete formation of the product **2a** in less than 1 h at room temperature under solventless conditions. The generality of the methodology is demonstrated by reacting other thiols with acetic anhydride under similar conditions. The course of the reactions were monitored by TLC and GC, products were easily separated in good yields from the reaction mixtures by simple aqueous workup, and the identity of the products was confirmed by comparing their spectroscopic data with those of known samples.

TYPICAL PROCEDURE

A mixture of acetic anhydride (5.1 mmol), a thiol (5.0 mmol), and magnesium bromide ethyl etherate (0.2 mmol, 4 mol%) was stirred in a flask at room temperature. The course of the reaction was monitored by TLC, and complete disappearance of the starting thiol was observed within 1 h. The mixture was dissolved in ether (20 mL) and washed twice by water (25 mL portions). The organic phase was dried over sodium sulfate, the volatile portion was removed at reduced pressure, and the product was isolated in good purity. All products are known, and their spectral and physical data are compared with those existing in the literature.

Selected Spectral Data

***S*-4-Chlorophenyl ethanethioate (2b).** ^{1}H NMR ($CDCl_3$): δ 2.34 (s, 3H), 7.29 (s, 4H); MS: *m*/*z* (%) 186 (60) [M^+], 144 (100), 108 (36); IR (KBr): cm^{-1} 2929, 1713, 1092.

***S*-Naphthalen-2-yl ethanethioate (2d).** ^{1}H NMR ($CDCl_3$): δ 2.45 (s, 3H), 7.62–8.00 (m, 7H); MS: *m*/*z* (%) 202 (30) [M^+], 160 (100), 115 (24); IR (KBr): cm^{-1} 3050, 1699, 1117.

***S*-Benzyl ethanethioate (2e).** ^{1}H NMR ($CDCl_3$): δ 2.29 (s, 3H), 4.08 (s, 2H), 7.24 (s, 5H); MS: *m*/*z* (%) 166 (33) [M^+], 123 (26), 91 (100); IR (KBr): cm^{-1} 3030, 1694, 1133.

***S,S′*-Ethane-1,2-diyl diethanethioate (2g).** ^{1}H NMR ($CDCl_3$): δ 2.45 (s, 6H), 2.96 (s, 4H); MS: *m*/*z* (%) 178 (13) [M^+], 119 (100), 103 (48); IR (KBr): cm^{-1} 1693, 1142.

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