Short Communication

CSIRO PUBLISHING

Aust. J. Chem. **2008**, *61*, 1006–1010

www.publish.csiro.au/journals/ajc

Convenient and Efficient Synthesis of Thiol Esters using Zinc Oxide as a Heterogeneous and Eco-Friendly Catalyst

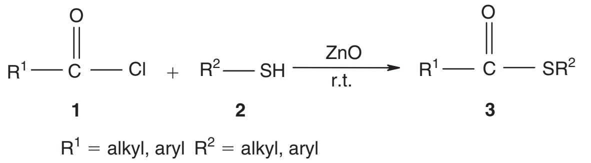
Babasaheb Pandurang Bandgar,[A,B] *Parmeshwar Eknath More,*[A]
Vinod Tribhuvannathji Kamble,[A] *and Sanjay Suresh Sawant*[A]

[A]Organic Chemistry Research Laboratory, School of Chemical Sciences, Swami Ramanand Teerth Marathwada University, Vishnupuri, Nanded-431606 MS, India.
[B]Corresponding author. Email: bandgar_bp@yahoo.com

A catalytic method was developed to synthesize thiol esters from the reaction of acyl chlorides and thiols using zinc oxide as a catalyst under solvent-free conditions at room temperature. Mild reaction conditions, short reaction time, excellent yields of products and recyclability of the catalyst are noteworthy features of this methodology.

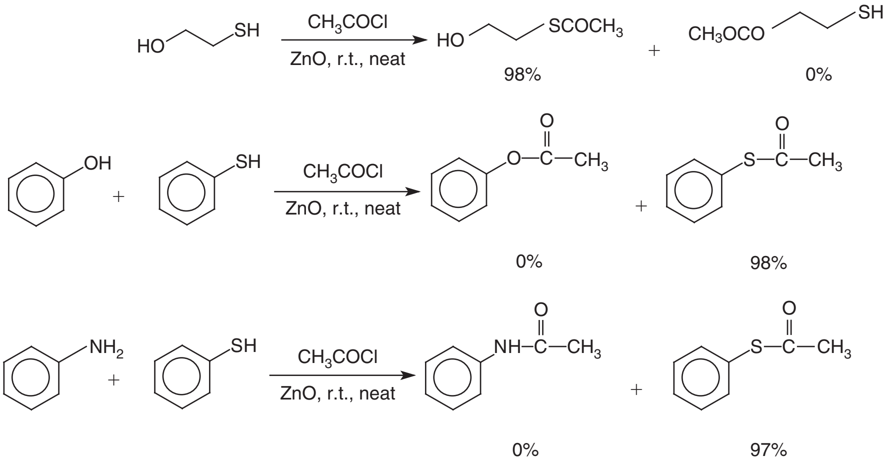
Manuscript received: 12 May 2008.
Final version: 4 August 2008.

Thiol esters are used in the formation of carbon–carbon bonds and other functionalities. In addition, they show higher reactivity and selectivity towards nucleophiles than the corresponding oxygen analogue, which makes them the universal acylation reagents in biochemical processes. These compounds were traditionally synthesized from the reaction of carboxylic acids and thiols.[1] A problem associated with this synthetic method is that the reaction requires essentially the activation of an acid. A variety of activating agents such as trisalkylthioborane,[1a] phenyl dichlorophosphonate,[1b] tri-*n*-butylphosphine,[1c] diethyl phosphorocyanidate[1d] and triphenylphosphine *N*-bromo succiniamide/*N*-iodo succiniamide,[1e] and phosgene[1f] have been reported for this purpose. Preparation of thiol esters from the reaction of amides and thiols using aluminium thiophenoxide or boron thiophenoxide are also reported in the literature.[1g] Some other methods using *N*-methylbenzene thiazolium trifluoromethane sulfonate,[2a] zinc[2b] and thallium[2c,2d] and tin[2e] or copper mercaptides[2f] proceed through the intermediacy of an acid chloride.[2f,2g] All these reported methods have one or other disadvantage, such as the use of expensive reagents,[1b–1d,2a,2f] tedious workup procedures,[1a–1f,2a,2f] toxic or hazardous reagents,[1e,1f] and sometimes difficult isolation of intermediates.[1e] In recent years, cyanuric chloride,[3a] and Dess–Martin periodinane[3b] have been reported to catalyze this reaction.



Scheme 1.

Organic chemists continue to explore novel synthetic methods involving new reagents and catalysts to carry out chemical



Scheme 2.

10.1071/CH08202 0004-9425/08/121006

transformations. One of these novel synthetic methods is to carry out reactions on the surface of solids. Organic reactions were found to occur efficiently and selectively on the surface of solids.[4] Even in the absence of new chemistry, a surface reaction may be more desirable than a solution counterpart, because the reaction is more convenient to run, or a high yield of product is attained. Reactions on surfaces of solids have some advantages, such as: (i) easy isolation of products; (ii) high yields of products and suppression of by-product formation; and (iii) improved selectivity of catalyst.

In recent years, zinc oxide has gained much interest in the synthesis of nitriles from aldoximes,[5] the Beckmann rearrangement,[6] Friedel–Crafts acylation,[7] and the acylation of alcohols, phenols, and amines.[8] Herein, we describe a new, simple, and effective procedure for the synthesis of thiol esters from acid chlorides and thiols in the presence of zinc oxide as a heterogeneous catalyst under solvent-free condition (Scheme 1).

A mixture of acid chloride, thiol and zinc oxide was stirred at room temperature. Although the reactions were monitored by TLC, visual monitoring was possible for these reactions: immediately after the addition of the catalyst to the mixture of the acid chloride and thiol, yellow or brown colour started developing, indicating the progress of the reaction. After completion of the reaction (TLC), dichloromethane was added to the reaction mixture and the catalyst was filtered off. The dichloromethane extract was washed with an aqueous sodium bicarbonate solution and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure furnished the desired products in excellent yields. The results are presented in Table 1.

The methodology was found to be general, as both aliphatic as well as aromatic acid chlorides smoothly reacted with aliphatic and aromatic thiols, resulting in the formation of the corresponding thiol esters in excellent yields in a short reaction time. The reactions were remarkably clean and no chromatographic separation was necessary to get pure products. It is indeed gratifying to note that acylation occurred exclusively at the sulfur and not on the ring carbon atom. It is also interesting to mention that the reaction conditions are mild enough not to induce any dealkylation of an ether residue (entry o, Table 1). The dicarboxylic acid chloride also smoothly converted to the corresponding dithiol ester (entry k, Table 1) using two equivalents of thiol. However, this conversion took a comparatively longer time (45 min).

The superiority of this protocol can be clearly visualized in the preparation of thiol esters when both the reactants were aromatic, furnishing excellent yields of products in a short reaction time (4–45 min) in the presence of zinc oxide as a catalyst without any activation. In this connection, it should be mentioned that the literature-reported method[2b] using a stoichiometric amount of activated zinc required a longer reaction time (240–300 min).

The feasibility of the reusability and recycling of the zinc oxide was examined through a series of sequential reactions of benzoyl choride and thiocresol as a model reaction. In a typical reaction, the catalyst was recovered by simple filtration from the reaction mixture and reused for three cycles. The reaction proceeded smoothly with a yield of 96–90% and this result shows that the catalyst does not lose its activity even after three runs (Table 2, entries 1–3).

Further, we investigated the possible chemoselectivity of zinc oxide-mediated acylation reactions by running the competitive acetylation of alcohols, phenols, amines, and thiols at room temperature over 25 min. It was found that thiols were acylated selectively in the presence of alcohols, phenols, and amines (Scheme 2). The reactions were monitored by TLC. The reaction temperature is an important factor for chemoselectivity and the best temperature was approximately room temperature.

We have developed a novel, simple, and highly efficient protocol for the acylation of thiols to furnish thiol esters using non-toxic and inexpensive zinc oxide as a catalyst under solvent-free conditions. The advantages of this environmentally benign and efficient protocol include: simple reaction set-up not requiring specialized equipment, no requirement to activate the catalyst, mild reaction conditions, excellent yields of products, short reaction times, and high chemoselectivity.

Experimental

Melting points were measured using a Buchi R-535 apparatus. IR spectra were recorded on a Bomem MB Fourier transform (FT)-IR spectrometer. ^{1}H NMR spectra were recorded on a Varian Gemini-300 spectrometer. The catalyst (zinc oxide) was purchased from Sigma–Aldrich and used without any activation.

General Experimental Procedure

To a stirred mixture of acid chloride (1 mmol) and zinc oxide powder (0.5 mmol), thiol (1 mmol) was added. The yellow-brown colour developed immediately and became dark with the progress of the reaction. Stirring was continued up to completion of the reaction (TLC). After addition of dichloromethane (10 mL), zinc oxide was filtered off, and washed with dichloromethane (3 × 5 mL). The dichloromethane extract was washed with aqueous sodium bicarbonate and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure furnished practically pure product.

3a: $\nu_{\max}$(KBr)/cm^{-1} 894, 1200, 1666, 2916, 3059. δ_H ($CDCl_3$, 300 MHz) 7.28–7.62 (m, 10H).

3b: $\nu_{\max}$(KBr)/cm^{-1} 645, 897, 1204, 1668, 2916, 3070. δ_H ($CDCl_3$, 300 MHz) 3.39 (s, 3H), 7.22–7.57 (m, 5H), 8.00 (d, *J* 72, 2H), 8.10 (d, *J* 7.2, 2H).

3c: $\nu_{\max}$(KBr)/cm^{-1} 645, 897, 1204, 1668, 2916, 3070. δ_H ($CDCl_3$, 300 MHz) 1.58 (s, 9H), 7.30–7.68 (m, 5H).

3d: $\nu_{\max}$(KBr)/cm^{-1} 620, 805, 929, 1473, 1695, 2930, 2966. δ_H ($CDCl_3$, 300 MHz) 1.60 (s, 9H), 2.42 (s, 3H), 7.99 (d, *J* 7.4, 2H), 8.09 (d, *J* 7.4, 2H).

3e: $\nu_{\max}$(neat)/cm^{-1} 620, 746, 1354, 1439, 1709, 2928, 3062. δ_H ($CDCl_3$, 300 MHz) 2.40 (s, 3H), 7.28–7.76 (m, 5H).

3f: $\nu_{\max}$(neat)/cm^{-1} 615, 746, 1114, 1478, 1708, 3061. δ_H ($CDCl_3$, 300 MHz) 2.38 (s, 3H, $COCH_3$), 3.41 (s, 3H), 7.97 (d, *J* 7.2, 2H), 8.01 (d, *J* 7.2, 2H).

3g: $\nu_{\max}$(neat)/cm^{-1} 670, 895, 1605, 1680, 2900, 3029. δ_H ($CDCl_3$, 300 MHz) 7.21 (s, 5H, ArH), 7.40 (s, 5H, ArH), 7.50 (d, 1H, *J* 16.2, =CH), 7.62 (d, 1H, *J* 16.2, =CH).

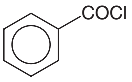
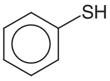
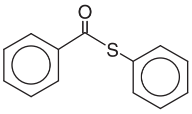
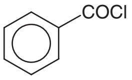
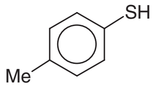
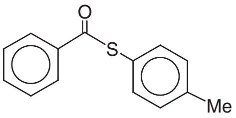
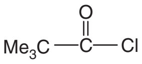
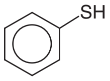
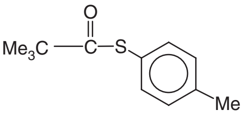
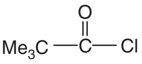
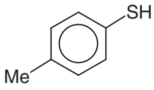
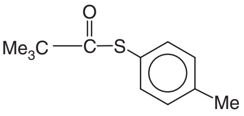
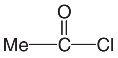
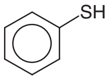
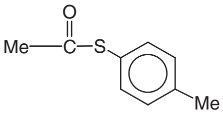
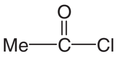
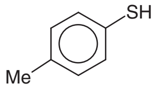
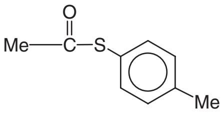
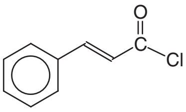
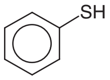
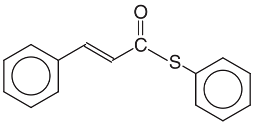
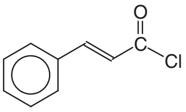
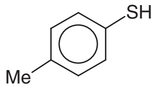
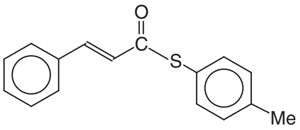
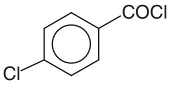
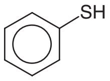
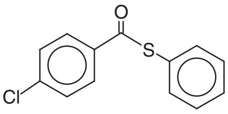
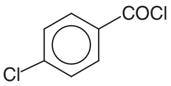
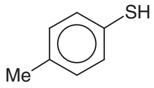
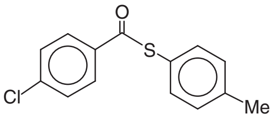
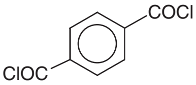
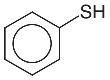
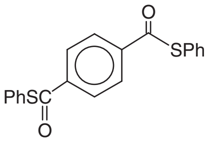
3h: $\nu_{\max}$(neat)/cm^{-1} 690, 880, 1609, 1675, 2917, 3060. δ_H ($CDCl_3$, 300 MHz) 2.30 (s, 3H, Ar–CH_3), 7.10 (s, 5H, Ar–H), 7.40 (d, 1H, *J* 15.5, =CH), 7.55 (d, 1H, *J* 15.5, =CH), 7.85 (d, 2H, *J* 7.4, ArH), 7.90 (d, 2H, *J* 7.4, ArH).

3i: $\nu_{\max}$(KBr)/cm^{-1} 720, 916, 1171, 1588, 1665, 2970, 3035. δ_H ($CDCl_3$, 300 MHz) 7.03–7.52 (m, 5H), 7.90 (d, *J* 8.5, 2H), 8.02 (d, *J* 8.5, 2H).

3j: $\nu_{\max}$(KBr)/cm^{-1} 740, 925, 1170, 1603, 1670, 2960, 3040. δ_H ($CDCl_3$, 300 MHz) 2.30 (s, 3H, $ArCH_3$), 7.69 (d, *J* 8.5, 2H), 7.76 (d, *J* 8.5, 2H), 7.95 (d, *J* 7.4, 2H), 8.01 (d, *J* 7.4, 2H).

3k: $\nu_{\max}$(KBr)/cm^{-1} 751, 845, 1240, 1669, 1690, 2930, 3061. δ_H ($CDCl_3$, 300 MHz) 7.21–7.54 (s, 10H, ArH), 7.85 (s, 4H, ArH).

Table 1. Zinc oxide-catalyzed synthesis of thiol esters under solvent-free conditions

Entry	Acid chloride	Thiol	Product	Time [min]	Yield [%]	mp [°C]
a				05	94	56–58
b				05	96	64
c				07	96	33–35
d				15	91	38
e				07	97	Oil
f				03	93	Oil
g				30	87	Semi-solid
h				30	89	Oil
i				35	81	69
j				30	82	48
k				45	90	58–60

(*Continued*)

Table 1. (Continued)

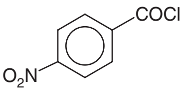
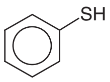
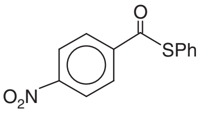
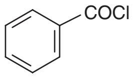
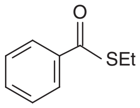
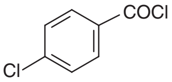
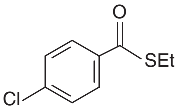
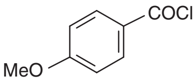
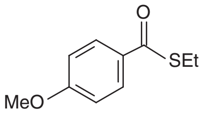
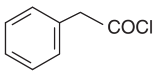
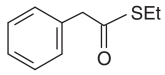
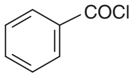
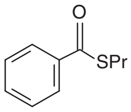
Entry	Acid chloride	Thiol	Product	Time [min]	Yield [%]	mp [°C]
l				30	80	98
m		EtSH		15	89	Oil
n		EtSH		25	90	Semi-solid
o		EtSH		25	90	Semi-solid
p		EtSH		30	90	76
q	Me_3CCOCl	EtSH	$Me_3CCOSEt$	4	76	Oil
r		*n*-PrSH		10	86	Semi-solid

Table 2. Reuse studies of zinc oxide for the reaction *o*-benzoyl chloride with thiocresol

No. of uses	Reaction time [min]	Yield[A]
1	10	96
2	15	92
3	20	90

[A] Yield of pure isolated products.

3l: ν_{max}(KBr)/cm^{-1} 742, 850, 1220, 1670, 2918, 3062. δ_H ($CDCl_3$, 300 MHz) 7.31–7.58 (m, 5H, ArH), 7.92 (d, *J* 7.0, 2H), 8.03 (d, *J* 7.0, 2H).

3m: ν_{max}(neat)/cm^{-1} 690, 913, 1208, 1448, 1663, 2929, 3062. δ_H ($CDCl_3$, 300 MHz) 1.35 (t, *J* 7.4, 3H), 3.08 (q, *J* 7.4, 2H), 7.41–7.56 (m, 5H, ArH).

3n: ν_{max}(KBr)/cm^{-1} 836, 916, 1171, 1588, 1665, 2970, 3029. δ_H ($CDCl_3$, 300 MHz) 3.09 (q, *J* 7.4, 4H), 7.39 (t, *J* 7.4, 3H), 7.40 (d, *J* 8.1, 2H), 8.12 (d, *J* 8.1, 2H).

3o: ν_{max}(KBr)/cm^{-1} 803, 910, 1140, 1475, 1668, 2916, 3060. δ_H ($CDCl_3$, 300 MHz) 1.32 (t, *J* 7.5, 3H), 3.04 (q, *J* 7.2, 2H), 3.82 (s, 3H), 7.95 (d, *J* 7.0, 2H), 8.06 (d, *J* 7.0, 2H).

3p: ν_{max}(KBr)/cm^{-1} 759, 1259, 1600, 1688, 2966, 3030. δ_H ($CDCl_3$, 300 MHz) 1.27 (t, *J* 7.5, 3H), 2.98 (q, *J* 7.5, 2H), 3.82 (s, 2H), 7.45–7.61 (m, 5H, ArH).

3q: ν_{max}(neat)/cm^{-1} 689, 914, 1206, 1448, 1695, 2964, 3067. δ_H ($CDCl_3$, 300 MHz) 1.04 (t, *J* 7.5, 3H), 1.98 (s, 9H), 2.01 (q, *J* 7.5, 2H).

3r: ν_{max}(neat)/cm^{-1} 688, 1175, 1448, 1581, 1689, 2964, 3062. δ_H ($CDCl_3$, 300 MHz) 1.02 (t, *J* 7.4, 3H), 1.66–1.72 (m, 2H), 3.04 (t, *J* 7.3, 2H), 7.40–7.55 (m, 5H, ArH).

Acknowledgement

The authors thank Council of Scientific and Industrial Research, New Delhi, for financial assistance (project no. 1/2023/05/EMR-II), and P. E. More thanks University Grant Commission, New Delhi for a teaching fellowship and S. P. Mahila College, Baramati, for sanctioning study leave.

References

[1] (a) A. Pelter, T. Levitt, K. Smith, *J. Chem. Soc. Chem. Commun.* **1969**, 435.
(b) H. Liu, S. I. Sabesan, *Can. J. Chem.* **1985**, *63*, 2645.
(c) P. A. Grieco, Y. Yokoyama, E. Williams, *J. Org. Chem.* **1978**, *43*, 1283. doi:10.1021/JO00400A048
(d) S. Yamada, Y. Yokoyama, T. Shioiri, *J. Org. Chem.* **1974**, *39*, 3302. doi:10.1021/JO00936A038
(e) K. Sucheta, G. C. R. Reddy, D. Ravi, N. Rama Rao, *Tetrahedron Lett.* **1994**, *35*, 4415. doi:10.1016/S0040-4039(00)73371-5
(f) D. Ravi, N. Rama Rao, G. S. R. Reddy, K. Sucheta, V. J. Rao, *Synlett* **1994**, 856. doi:10.1055/S-1994-23031
(g) T. Cohen, R. E. Gapinski, *Tetrahedron Lett.* **1978**, *19*, 4319. doi:10.1016/S0040-4039(01)95213-X

[2] (a) F. Souto-Bachiller, G. S. Bates, S. Musamune, *J. Chem. Soc. Chem. Commun.* **1976**, 719. doi:10.1039/C39760000719
(b) H. M. Meshram, S. G. Reddy, H. Bindu, J. S. Yadav, *Synlett* **1998**, 877. doi:10.1055/S-1998-1797
(c) S. Masamune, S. Kamata, W. Schilling, *J. Am. Chem. Soc.* **1975**, *97*, 3515. doi:10.1021/JA00845A039
(d) M. R. Detty, G. P. Wood, *J. Org. Chem.* **1980**, *45*, 80. doi:10.1021/JO01289A018
(e) D. N. Harpp, T. Aida, T. H. Cham, *Tetrahedron Lett.* **1979**, *20*, 2853. doi:10.1016/S0040-4039(01)86433-9
(f) H. U. Reibig, B. Scherer, *Tetrahedron Lett.* **1980**, *26*, 4259.
(g) A. Padwa, S. J. Coats, L. Hadjiarapoglou, *Heterocycles* **1994**, *39*, 219.

[3] (a) B. P. Bandgar, S. S. Pandit, *J. Sulfur Chem.* **2004**, *25*, 343.
(b) S. B. Bandgar, B. P. Bandgar, B. L. Korbad, S. S. Sawant, *Tetrahedron Lett.* **2007**, *48*, 1287. doi:10.1016/J.TETLET.2006.12.024

[4] F. Toda, *Acc. Chem. Res.* **1995**, *28*, 480. doi:10.1021/AR00060A003

[5] M. H. Sarvari, *Synthesis* **2005**, 787. doi:10.1055/S-2005-861826

[6] H. Sharghi, M. H. Sarvari, *Synthesis* **2002**, 1057. doi:10.1055/S-2002-31964

[7] M. H. Sarvari, H. Sharghi, *J. Org. Chem.* **2004**, *69*, 6953. doi:10.1021/JO0494477

[8] M. H. Sarvari, H. Sharghi, *Tetrahedron* **2005**, *61*, 10903. doi:10.1016/J.TET.2005.09.002