SHORT PAPER

A convenient one-pot synthesis of thiol esters from disulfides using a Zn/AICl₃ system[†] Barahman Movassagh,* Moslem M. Lakouraj* and Zahra Fadaei

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A novel synthetic procedure for the direct preparation of thiol esters from various disulfides and symmetrical anhydrides using a Zn/AlCl₃ system is described.

Keywords: thiol esters, disulfides, Zn/AlCl₃

Thiol esters show higher reactivity and selectivity toward nucleophiles than their oxygen analogues. They play important roles in biological system as acyl coenzyme A, and S-acetyl dihydrolipoic acid.¹ Thiol esters are used as mild acyl transfer reagents,² as intermediates in the synthesis of ketones³ and for asymmetric aldol reactions,⁴ and in the preparation of macrocyclic lactones.⁵ Masamune *et al.*⁶ have described the activation of phenyl thiol esters by transition metal ions in the preparation of these macrocycliclactones. The growing importance of thiol esters in organic synthesis has stimulated the recent extensive research toward improved methods for their preparation.⁷ Recently, Meshram and coworkers⁷ⁿ condensed acyl chlorides with thiols using activated zinc to prepare thiol esters.

We have recently reported the synthesis of organic sulfides from disulfides using a Zn/AlCl₃ system in aqueous media.⁸ Here we wish to report the transformation of disulfides into the corresponding thiol esters, which involves treatment of variety of disulfides and different carboxylic acid anhydrides with this system in dry dimethylformamide (DMF) at 65°C (Scheme 1).

Results are summarised in Table 1. Thiol esters prepared from aryl disulfides need shorter reaction times and generally give higher yields than those produced from alkyl disulfides. In the case of the aromatic carboxylic and anhydride (benzoic anhydride) a longer reaction time is required (entries 3, 6, and 9, Table 1) which is due to its lower reactivity towards nucleophiles compared to aliphatic carboxylic acid anhydrides. Reducing the molar ratios of aluminum chloride to disulfide (from 6.0 to 4.0) and carboxylic acid anhydride to disulfide (from 3.0 to 2.0) did not lead to completion of the reaction. The presence of aluminum chloride is essential and in the absence of this Lewis acid the reaction either goes more slowly with a lower yield or does not proceed at all. The most efficient organic solvent seems to be DMF.

$$RSSR + (R'CO)_2 O \xrightarrow{Zn/AlCl_3} R'COSR$$
(1) (2) (3)

Scheme 1

In conclusion, the thiol ester synthesis described above is a valuble alternative in all processes where direct transformation of a carboxylic acid to the corresponding thiol ester is not required. This methodology offers several advantages such as the availability of the starting materials, simple reaction work-up, and avoidance of the use of the very toxic reagents such as heavy metal thiolates or phenyl dichlorophosphate.

Experimental

General procedure: The carboxylic acid anhydride (1.5 mmol) and the disulfide (0.5 mmol) were added to a well stirred suspension of finely ground anhydrous aluminum chloride (3.0 mmol) and zinc powder (2.0 mmol) in DMF (10 ml) at room temperature. The reaction mixture was warmed at 65°C for an appropriate time (Table 1) during which the zinc powder was completely consumed. When the reaction was complete, DMF was evaporated *in vacuo*, and ethyl ether (15 ml) was added to the residue, washed with 10% NaHCO₃ (2 × 15 ml), water (2 × 15 ml), dried (MgSO₄) and concentrated. Column chromatography on silica gel (petroleum ether: CCl₄, 1:1) afforded the pure product.

 Table 1
 Thiol esters (3) from disulfides (1) and carboxylic and anhydrides (2)

Entry	R	R'	Reaction time/h	Thiol ester yields/%	Ref.
1	Ph	CH2	4	80 ^a	9
2	Ph	CH ₃ CH ₂	5	82 ^a	9
3	Ph	Ph 1	13	82 ^a	9
4	p-CIC ₆ H ₄	CH	5	79 ^a	10
5	, p-CIC ₆ H₄	CH ₃ CH ₂	5	91 ^a	9
6	, p-CIC _e H ⁴	Ph í	15	76 ^a	11
7	, p-MeČ _e Ĥ₄	CH	5	90 ^a	12
8	p-MeC ₆ H₄	CH ₃ CH ₂	5.5	83ª	9
9	p-MeC ₆ H₄	Ph í	15	92 ^a	12
10	PhCH ₂ [*]	CH₂	6	78ª	7b
11	n-C ₈ H ₁₇	CH ² CH,	12	75 ^a	13
12	$n-C_{4}^{\circ}H_{9}^{\prime\prime}$	CH ²	10	74 ^b	14
13	$n-C_4^4H_9^9$	CH, CH,	10	70 ^b	13

^aYield of pure, isolated product. ^bYield is based on GC analysis.

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[†] This is a Short Paper, there is therefore no corresponding material in

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References

- 1 (a) T.C. Bruice, Organic Sulfur Compounds, N. Kharasch (ed.), Pergamon press, New York and London, 1961, Vol. 1, chapt 35; (b) T.C. Bruice and S.J. Benkovic, Bioorganic Mechanism, Benjamin Inc., New York and Amesterdam, 1966, Vol. 1, chapt 3.
- 2 J. Mukaiyama, M. Araki and H. Takei, J. Am. Chem. Soc., 1973, **95**, 4763.
- 3 (a) G. McGarvey, J. Am. Chem. Soc., 1986, 108, 4943; (b) R. Corow and P. Portoghese, J. Org. Chem., 1986, 51, 938.
- 4 (a) S. Kobayashi, H. Uchiro, Y. Fujishita, I. Shiina and T. Mukaiyama, J. Am. Chem. Soc., 1991, 113, 4247; (b) K.H. Suh and D.J. Choo, Tetrahedron Lett., 1995, 36, 6109.
- 5 T. J. Buch, *Tetrahedron*, 1977, 33, 3041.
 6 S. Masamune, Y. Hayase, W. Schilling, W. K. Chan and G.S. Bates, J. Am. Chem. Soc., 1977, 99, 6756, and references cited therein.
- 7 (a) F. Isao, T. Naomi. and H. Shizunobu, Chem. Express, 1989, 4, 337; (b) J.Y. Gauthier, F. Bourdon and N. Young, Tetrahedron Lett., 1986, 27, 15; (c) P. Giovanni, N. Marino, G. Giacomo and

F. Marcos, Tetrahedron, 1989, 45, 7411; (d) Y.V. Gulevich, N.A. Bumagin and Z.P. Beletskaya, Zh. Org. Khim., 1988, 24, 2126; (e) B. Ramon, G. Jordi and V. Jaume, Synthesis, 1989, 4, 305; (f) A. Shlomo and A. Howard, Organometallics, 1986, 5, 596; (g) C. Cardellicchio, V. Fiandanese, G. Marchese and L. Ronzini, Tetrahedron Lett., 1985, 26, 3595; (h) A. Saeed and I. Javed, ibid, 1986, 27, 3791; (i) R.P. Hatch and S.M. Weinreb, J. Org. Chem., 1977, 42, 3960; (j) K. Sucheta, G.S. Reddy, D. Ravi and N.R. Rao, Tetrahedron Lett., 1994, 35, 4415; (k) X. Jia, Y. Zhang and X. Zhou, *ibid*, 1994, 35, 8833; (l) A.L. Braga, O.E.D. Rodrigues, E.D. Avila and C.C. Silveira, ibid, 1998, 39, 3395; (m) H.-J. Liu and S. I. Sabesan, Can. J. Chem., 1980, 58, 2645; (n) H.M. Meshram, G.S. Reddy, K.H. Bindu and J.S. Yadav, Synlett, 1998, 877.

- 8 B. Movassagh, M.M. Lakouraj and Z. Fadaei, J. Chem. Res. (S), 2000, 350.
- 9 H.-U. Reissig and B. Scherer, Tetrahedron Lett., 1980, 21, 4259. 10 T. Mukaiyama, M. Miyashita and I. Shiina, Chem. Lett., 1992,
- 1747
- 11 G.H. Berezin and G.H. Harris, U.S. Pat. 3219679, 1965; C. A., 1966, **64**, 8098a.
- 12 J. Morgenstern and R. Mayer, Z. Chem., 1968, 8, 146.
- 13 T. Takido, K. Sato, T. Nakazawa and M. Seno, Sulfur Lett., 1995, 19, 67.
- 14 L.H. Noda, S.A. Kuby and H.A. Lardy, J. Am. Chem. Soc., 1953, 75.913.