An efficient synthesis of α,β-unsaturated thiol esters

Xiaoxia Wang*, Xuefei Zou and Jingxing Du

Zhejiang Key Laboratory for Reactive Chemistry on Solid Surfaces, College of Chemistry and Life Sciences, Zhejiang Normal University, Jinhua, 321004, P.R. China

α,β-Unsaturated thiol esters were synthesised conveniently from samarium thiolates and α,β-unsaturated *N*-acylbenzotriazoles under mild conditions with good to excellent yields.

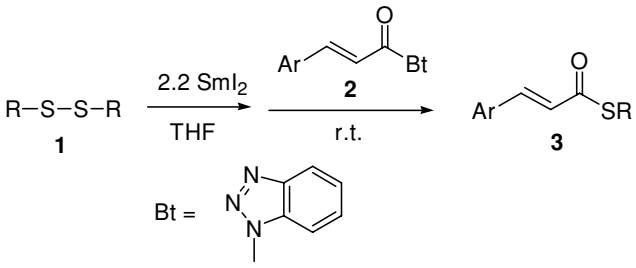
Keywords: α,β-Unsaturated *N*-acylbenzotriazoles, samarium thiolates, α,β-unsaturated thiol esters

Thiol esters are a class of important intermediates in organic synthesis.[1] Among a variety of methods for the preparation of them, acylation of thiols with an activated acyl derivatives are common and generally an additional catalyst is required for the process.[2] Acylation of thiolates resulting from the *in situ* reductive cleavage of disufides or thiocyanates seems to be advantageous[3] thanks to no extra catalysts required, neutral conditions and avoidance of the unpleasant odors of thiols. Though various methods for the preparation of thiol esters were available, documents regarding general syntheses of α,β-unsaturated thiol esters are rare. The attack of aryl thiolates on six-membered rings of isopropylidene malonate derivatives could afford α,β-unsaturated thiol esters in moderate to good yields.[4] Here we report that samarium thiolates react with α,β-unsaturated *N*-acylbenzotriazoles readily and afford a convenient and high-yielding method for the preparation of α,β-unsaturated thiol esters.

α,β-Unsaturated *N*-acylbenzotriazoles, a special kind of acylbenzotriazloes recently developed by Katritzky's group, were readily available from α,β-unsaturated acids and *N*-(1-methanesulfonyl)benzotriazole.[5] Samarium thiolates were reported to undergo 1,4-Michael addition with α,β-unsaturated esters.[6a] However, our investigation here find that other than 1,4-addition, samarium thiolates undergo exclusively neucleophilic substitution with α,β-unsaturated *N*-acylbenzotriazoles with the benzotriazole anion as a good leaving group. The reaction is so neat that it offers a facile and efficient synthesis of α,β-unsaturated thiol esters (Scheme 1).

Tentatively, α,β-unsaturated *N*-acylbenzotriazoles and disufides were added to the SmI_2-THF solution simultaneously, but a complex mixture was obtained. Bearing in mind that *N*-acylbenzotriazoles are unstable towards samarium iodide,[6b] the experimental procedure was modified as follows: first the disulfide was added, which reacted with samarium diiodide to produce the corresponding samarium thiolates.[3a-c] The resulting samarium thiolates were then treated with α,β-unsaturated *N*-acylbenzotriazoles so as to complete the reaction. All the thiol esters synthesised by this method are listed in Table 1.

Both aliphatic disufides and aromatic disufides were used as the substrates. As a whole, aromatic disufides are more reactive towards samarium diiodide. Aromatic disufides with an electron-withdrawing group (Table 1, entry 10) could be reduced to the samarium thiolates more quickly (within 10 min.) than those with an electron-donating group (Table 1, entry 1-5, 4–6 h required). In contrast, it took usually more than 8 h for the complete reductive cleavage of aliphatic disufides and dibenzyl disulfide to afford the corresponding samarium thiolates at room temperature. It should be noted that no matter which kind of samarium thiolates were formed, subsequent acylation with α,β-unsaturated *N*-acylbenzotriazoles could be completed within 30 min. under mild conditions and no extra catalysts such as bases are needed for the acylation process. It can be concluded from Table 1 that samarium aryl thiolates



Scheme 1

afford higher yields of α,β-unsaturated thiol esters than alkyl and benzyl thiolates.

Heterocyclic α,β-unsaturated *N*-acylbenzotriazoles such as **2e** worked as well as *N*-cinnamoyl benzotriazoles in the present study and the expected furylacryl thiol esters (**3h** and **3j**) were obtained in good yields.

N-Acylbenzotriazoles have been applied extensively to *N*-acylation,[7a,5] *O*-acylation[7b] and even to *C*-acylation[7c-e] in organic syntheses. Very recently, it was found that *S*-acylation with *N*-acylbenzotriazole of the thiols in the presence of triethyl amine was also very successful.[2e] However, investigation involving the application of α,β-unsaturated *N*-acylbenzotriazoles remains to be explored. Our research found that other than 1,4-addtition, samarium thiolates substitute the benzotriazolyl group in α,β-unsaturated *N*-acylbenzotriazoles exclusively, thus providing a facile and high efficient method for the synthesis of α,β-unsaturated thiol esters. The cleanness, high yields and ready access to the starting materials make the method attractive.

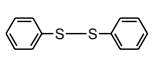
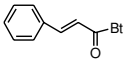
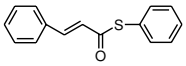
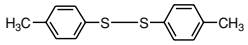
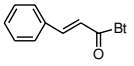
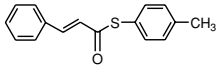
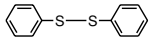
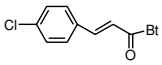
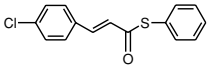
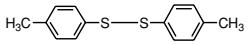
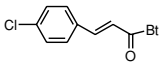
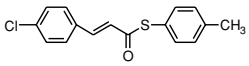
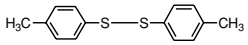
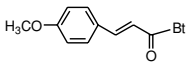
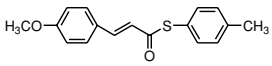
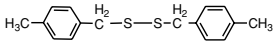
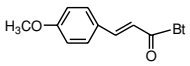
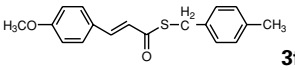
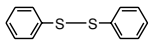
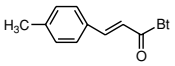
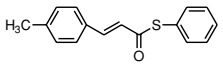
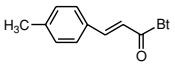
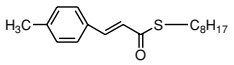
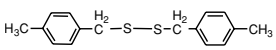
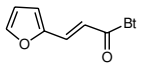
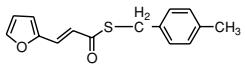
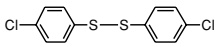
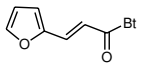
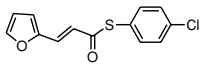
Experimental

Tetrahydrofuran was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points are uncorrected. ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded on a Bruker AV400 NMR instrument as $CDCl_3$ solutions using TMS as internal standard. Chemical shifts (δ) are reported in ppm and coupling constants *J* is given in Hz. IR spectra were recorded using KBr disks with a NEXUS 670 FTIR spectrometer. Mass spectra were recorded on a HP 5989B MS spectrometer. Elemental analyses were performed on a Vario-ELIII instrument.

General procedure for the preparation of α,β-*unsaturated thiol esters*: Disufides (0.5 mmol) in anhydrous THF (1 ml) was added first by syringe to the solution of SmI_2 (1.1 mmol) in dry THF (10 ml) at room temperature under nitrogen atmosphere. α,β-Unsaturated *N*-acylbenzotriazoles (1.0 mmol) in anhydrous THF (2 ml) was added when the blue colour of samarium diiodide faded (indicating the samarium diiodide having been consumed out). After completion of the acylation (about 30 min, monitored by TLC), 0.1 N of hydrochloric acid (3 ml) was added followed by extraction with ethyl ether (3 × 30 ml). The combined extracts were washed successively with 10% Na_2CO_3 and saturated brine, and dried over anhydrous $NaSO_4$. The solvent removed under reduced pressure and the residue frequently recrystallised from ethanol to afford the pure thiol esters. Otherwise, purification was done by preparative TLC on silica gel (ethyl acetate/cyclohexane 1:6 as eluent).

* Correspondent. E-mail: wangxxzj@163.com

Table 1 Syntheses of thiol esters from α,β-unsaturated *N*-acylbenzotriazoles and disulfides mediated by samarium diiodide

Entry	Disulfides	α,β-Unsaturated *N*–acylbenzotriazoles		Products		Yields[a]/%
1			**2a**		**3a**	93
2			**2a**		**3b**	91
3			**2b**		**3c**	95
4			**2b**		**3d**	91
5			**2c**		**3e**	85
6			**2c**		**3f**	78
7			**2d**		**3g**	90
8	C_8H_{17}–S–S–C_8H_{17}		**2d**		**3h**	76
9			**2e**		**3i**	71
10			**2e**		**3j**	89

[a]Isolated yields based on the disufides.

3a: M.p. 79–81°C (lit.[4] 78–80°C). ν_{max}(KBr)/cm^{-1}: 3065, 2932, 1684, 1614, 1448. δ_H($CDCl_3$): 7.68 (1H, d, *J* = 16.0 Hz), 7.56–7.58 (2H, m), 7.41–7.51 (8H, m), 6.79 (1H, d, *J* 16.0 Hz).

3b: M.p. 74–76°C (lit.[8] 76–77°C). ν_{max}(KBr)/cm^{-1}: 3058, 3032, 2922, 2853, 1676, 1648, 1618. δ_H($CDCl_3$): 7.66 (1H, d, *J* = 16.0 Hz), 7.24–7.57 (9H, m), 6.78 (1H, d, *J* = 16.0 Hz), 2.39 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 188.5, 148.8, 141.4, 139.8, 134.6, 134.1, 130.7, 130.1, 129.2, 129.1, 124.1, 21.4.

3c: M.p. 112–113°C (lit.[4] 109–111°C). ν_{max}(KBr)/cm^{-1}: 2926, 2853, 1660, 1614, 1560. δ_H($CDCl_3$): 7.62 (1H, d, *J* = 16.0 Hz), 7.37–7.50 (9H, m), 6.76(1H,d, *J* = 16.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): 187.8, 140.0, 136.7, 134.6, 132.5, 129.7, 129.6, 129.3, 129.3, 127.4, 124.6.

3d: M.p. 132–134°C. ν_{max}(KBr)/cm^{-1}: 2926, 2859, 1698, 1653, 1612, 1561. δ_H($CDCl_3$): 7.69 (1H, d, *J* = 16.0 Hz), 7.24–7.62 (8H, m), 6.75(1H, d, *J* = 16.0 Hz), 2.40(3H,s). ^{13}C NMR (100 MHz, $CDCl_3$): 188.3, 147.2, 139.8, 136.7, 134.5, 132.6, 130.1, 129.7, 129.6, 129.3, 124.6, 21.4. *m/z* (%):289 (M^++1, 1.51), 288 (M^+, 0.44), 254 (0.84), 165 (100), 167 (35.09), 137 (18.98), 139 (6.22), 123 (5.93), 102 (27.91) Anal. Calcd. for $C_{16}H_{13}ClOS$: C, 66.54; H, 4.54; S, 11.10. Found C, 66.69; H, 4.56; S, 11.05%.

3e: M.p. 112–113°C. (lit.[9] 109–110°C). ν_{max}(KBr)/cm^{-1}: 3012, 2972, 2939, 2846, 1669, 1590, 1510. δ_H($CDCl_3$): 7.63 (1H, d, *J* = 16.0 Hz), 7.52 (2H, d, *J* = 6.8 Hz), 7.36 (2H, d, *J* = 6.8 Hz), 7.23–7.26 (2H, m), 6.92 (2H, d, *J* = 6.8 Hz), 6.66 (1H, d, *J* = 16.0 Hz),3.85 (3H,s), 2.39 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 188.2, 161.8, 141.1, 139.3, 134.6, 130.3, 130.0, 126.8, 121.8, 117.9, 114.5, 55.4, 21.3.

3f: M.p. 78–80°C. ν_{max}(KBr)/cm^{-1}: 3051, 3030, 3018, 2946, 2926, 2853, 1654, 1596, 1510. δ_H($CDCl_3$): 7.59 (1H, d, *J* = 16.0 Hz), 7.47 (2H, d, *J* = 8.0 Hz), 7023 (2H, d, *J* = 7.6 Hz), 7.11 (2H, d, *J* = 7.6 Hz), 7.11 (2H, d, *J* = 7.6 Hz), 6.89 (2H, d, *J* = 8.0 Hz), 6.59 (1H d, *J* = 16.0 Hz), 4.21 (2H, s), 3.83 (3H, s,),2.31 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 189.2, 161.7, 140.6, 137.0, 134.7, 130.2, 129.3, 128.8, 126.7, 122.3, 114.4, 55.4, 32.9, 21.2. *m/z* (%): 299 (M^++1, 0.22), 298 (M^+, 0.43), 161 (100), 133 (20.13), 105 (14.34). Anal. Calcd. for $C_{18}H_{18}O_2S$: C, 72.45; H, 6.08; S, 10.75 Found C, 72.28; H, 6.11; S, 10.71%.

3g: M.p. 98–99°C. ν_{max}(KBr)/cm^{-1}: 3032, 2926, 2853, 1682, 1655, 1601. δ_H($CDCl_3$): 7.66 (1H, d, *J* = 16.0 Hz), 7.43–7.49 (7H, m), 7.20–-7.25 (2H, m), 6.75 (1H, d, *J* = 16.0 Hz), 2.38 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 188.0, 141.6, 141.4, 134.7, 131.3, 129.8, 129.4, 129.3, 128.6, 127.7, 123.1, 21.6. *m/z* (%):255 (M^++1, 0.36), 145 (100), 117 (30.53), 115 (30.79), 109 (5.12), 91 (20.75). Anal. Calcd. for $C_{16}H_{14}OS$: C, 75.55; H, 5.55; S, 12.61 Found C, 75.27; H, 5.57; S, 12.56%.

3h: M.p. 30–32°C. ν_{max}(KBr)/cm^{-1}: 3065, 3018, 2954, 2922, 2851, 1657, 1605, 1511. δ_H($CDCl_3$): 7.58 (1H, d, *J* = 16.0 Hz), 7.43 (2H, d, *J* = 7.6 Hz), 7.18 (2H, d, *J* = 7.6 Hz), 6.67 (1H, d, *J* = 16.0 Hz), 3.00 (2H, t, *J* = 7.2 Hz), 2.36 (3H, s), 1.59–1.66 (2H, m), 1.27–1.39 (10H, m), 0.87 (3H, t, *J* = 6.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): 190.0, 141.0, 140.2, 131.4, 129.7, 128.4, 124.1, 31.8, 29.6, 29.2, 29.2, 29.0, 28.9, 22.6, 21.5, 14.1. *m/z* (%): 291 (M^++1, 0.15), 290 (M^+, .3.70), 145 (100), 117 (18.32), 115 (16.59). Anal. Calcd. for $C_{18}H_{26}OS$: C, 74.43; H, 9.02; S, 11.04 Found C, 74.19;H, 9.05; S, 11.00%.

3i: M.p. 52–54°C. ν_{max}(KBr)/cm^{-1}: 3131, 3051, 3038, 2919, 2860, 1667, 1611, 1551. δ_H($CDCl_3$): 7.47 (1H, s), 7.37 (1H, d, *J* = 15.6 Hz), 7.22 (2H, d, *J* = 8.0 Hz), 7.11 (2H, d, *J* = 8.0 Hz), 6.65 (1H, d, *J* = 4.0 Hz), 6.59 (1H, d, *J* = 15.6 Hz), 6.46–6.47 (1H, m), 4.21 (2H s), 2.31 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): 188.1, 150.6. 145.1, 137.0, 134.6, 129.4, 128.8, 126.8, 122.1, 116.2, 112.6, 33.0, 21.2. *m/z* (%): 259 (M^++1, 0.46), 258 (M^+, 2.24), 137 (1.15), 121 (100), 105 (12.20) ,93 (5.48), 65 (31.63). Anal. Calcd. for $C_{15}H_{14}O_2S$: C, 69.74; H, 5.46; S, 12.41 Found C, 69.99; H,5.48; S, 12.35%.

3j: M.p. 90–92°C. ν_{max}(KBr)/cm^{-1}: 3131, 2925, 2859, 1677, 1624, 1560. δ_H($CDCl_3$): 7.53 (1H, s), 7.39–7.43 (5H, m), 6.72 (1H, d, *J* = 3.2 Hz), 6.67 (1H, d, *J* = 15.6 Hz), 6.50–6.52 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$): 187.1, 150.5, 145.4, 135.8, 129.5, 127.8, 126.2, 121.2, 116.9, 112.8. *m/z* (%): 264 (M^+, 0.11), 143 (1.73), 145 (0.64), 121 (100), 93 (7.87), 65 (49.46). Anal. Calcd. for $C_{13}H_9ClO_2S$: C, 58.98; H, 3.43; S, 12.11 Found C, 58.77; H,3.44; S, 12.07%.

We are grateful to the Education Foundation of Zhejiang Province (Project No.20040847).

Received 19 May 2005; accepted 13 July 2005
Paper 05/3257

References

1 For example: (a) P. Blakskjær, B. Høj; D. Riber and T. Skrydstrup, *J. Am. Chem. Soc.,* 2003, **125**, 4030; (b) G.J. McGarvey, J.M. Williams, R.N. Hiner, Y. Matsubara and T. Oh, *J. Am. Chem. Soc.,* 1986; **108**, 4943; (c) Y. Hayashi, T. Itoh and T. Fukuyama, *Org. Lett,*. 2003, **5**, 2235; (d) T. Shimizu and M. Seki, *Tetrahedron Lett*., 2002, **43**, 1039.

2 (a) H.-U. Reißig and B. Scherer, *Tetrahedron Lett.*, 1980, **21**, 4259; (b) M.R. Detty and G.P. Wood, *J. Org. Chem*., 1980, **45**, 80; (c) H.M. Meshram, G. Sudershan Reddy, K.H. Bindu and J.S. Yadav, *Synlett*., 1998, 877; (d) S.T.A. Shah, K.M. Khan, A.M. Heinrich and W. Voelter, *Tetrahedron Lett.*, 2002*,* **43**, 8281; (e) A.R. Katritzky, A.A. Shestopalov and K. Suzuki, *Synthesis*, 2004, 1806.

3 (a) X. Jia, Y. Zhang and X. Zhou, *Tetrahedron Lett*., 1994, **35**, 8833; (b) X. Jia, Y. Zhang and X. Zhou, *Synth. Commun.,* 1994, **24**, 387; (c) F.D. Toste, F. LaRonde and I.W.J. Still, *Tetrahedron Lett*., 1995, **36**, 2949; (d) B.C. Ranu and T. Mandal, *J. Org. Chem.*, 2004**, 69**, 5793.

4 W. Bao and Y. Zhang, *Synth. Commun*., 1995, **25**, 143.

5 A.R. Katritzky, M. Wang and S. Zhang, *Arkivoc*, 2001, **ix,** 19. (www.arkat-usa.org).

6 (a) H.J. Jiang and Y.M. Zhang, *Chin. Chem. Lett*., 1999, **10**, 7; (b) X. Wang and Y. Zhang, *Tetrahedron Lett.,* 2002, **43**, 5431.

7 (a) A.R. Katritzky, H.Y. He and K. Suzuki, *J. Org. Chem*., 2000, **65**, 8210; (b) A.R. Katritzky, A. Pastor and M.V. Voronkov, *J. Heterocycl. Chem*., 1999, **36**, 777; (c) A.R. Katritzky and A. Pastor, *J. Org. Chem.,* 2000, **65**, 3679; (d) A.R. Katritzky, K. Suzuki, K.S. Singh and H.-Y. He, *J. Org. Chem*., 2003, **68**; 5720; (e) A.R. Katritzky, A.A.A. Abdel-Fattah, M. Wang, *J. Org. Chem.,* 2003, **68**, 4932.

8 T. Manimaran, T.K. Thiruvengadam and V.T. Ramakrishnan, *Synthesis*. 1975, 739.

9 T. Manimaran and V.T. Ramakrishnan, *Indian J. Chem. Sect. B.,* 1979, **18B**, 324.