Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters
Tetrahedron Letters 47 (2006) 4771–4774

Facile preparation of bis(thiocarbonyl)disulfides via elimination

Wolfgang G. Weber, James B. McLeary* and Ron D. Sanderson

UNESCO Associated Centre for Macromolecules and Materials, Department of Chemistry and Polymer Science, University of Stellenbosch, Private Bag X1, Matieland 7602, South Africa

Received 1 February 2006; revised 3 April 2006; accepted 10 April 2006
Available online 19 May 2006

Abstract—A robust facile synthetic preparation of bis(thiocarbonyl)disulfides is presented. The route follows an elimination mechanism rather than the more common oxidation. Addition of *p*-tosyl chloride to a thiocarbonyl thiolate results in the elimination of the chloride by the trithiocarbonate anion and subsequent elimination of the tosyl leaving group (by a second thiocarbonyl thiolate). The side products of the reaction are bis(4-methylphenyl)disulfone and tosylate salts/acids.

1. Introduction

The use of thiocarbonyl thio compounds in free radical polymerization as agents that allow control of the molecular weight and polydispersity of polymers is now widespread.[1,2] The process is referred to as Reversible Addition Fragmentation chain Transfer or RAFT mediated polymerization.[3] The use of disulfides prepared via oxidation by iodine systems is quite common,[4,5] and these materials also provide a simple route for the synthesis of RAFT agents with tertiary leaving groups by reaction with azo compounds that form tertiary radicals upon decomposition.[6,7]

The use of trithiocarbonate disulfides[8,9] has been more restricted and only a few examples have been reported in the literature, all of which use anhydrous conditions for their preparation. The primary reason for most failures to prepare disulfides is the sensitivity of the oxidation reaction to impurities and specific conditions. The use of a more robust method to produce disulfides would be a welcome addition to the synthetic pathways currently being used for the production of these compounds. The literature suggests that the use of sulfonyl chlorides to react with thiolates and then eliminate in a single step to form disulfides is a route that could provide higher yields and might prove simpler to implement.[10,11]

The reaction commences by the presumed formation of the reactive thio-tosylate intermediate **X**,[11–14] which could not be isolated. Water (*p*-tosyl chloride added as solid) or water/dichloromethane was used as a solvent. The yields were slightly better when using an organic co-solvent with slow addition. *p*-Tosyl chloride was added in a half molar ratio to the thio compound. Increasing this amount did not increase the yield of product **1a** significantly. The unhydrolyzed excess *p*-tosyl chloride can be recovered.

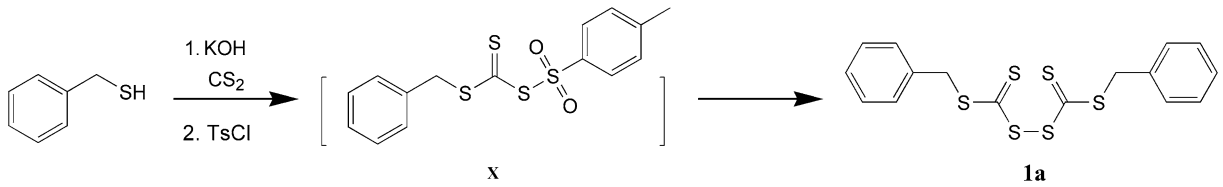
Efforts to isolate **X** by slow addition of potassium alkyltrithiocarbonate to an excess of cooled *p*-tosyl chloride in CH_2Cl_2 also led only to disulfide products (Scheme 1).

Two pathways can be considered for the decomposition of intermediate **X**, both of which form disulfide **1** and disulfone **2**.[11] The first is based on the disproportionation of **X** to **1** and **2** without the formation of a sulfinate salt. The second possible pathway involves the nucleophilic attack of the trithiocarbonate anion on intermediate **X** and the formation of **1** and the sulfinate salt. The salt subsequently reacts with *p*-tosyl chloride to form **2** and KCl. This mechanism is supported by the isolation of potassium sulfinate due to insufficient *p*-tosyl chloride (only half a mole used), and yields above 50%. The free 4-methylphenyl sulfinic acid is unstable in the presence of mineral acids (Scheme 2).

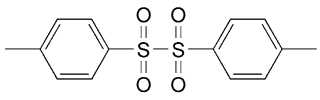
The disulfone **2** was recovered predominantly from the organic phase, while 4-methylphenyl sulfinic and sulfonic acids as well as other salts were isolated from the aqueous layer. The by-products in the case of dithiocarbonates **1e**–**h** are under investigation.[10]

* Corresponding author. Tel.: +27 (21) 808 4553/3986; fax: +27 (21) 808 4967; e-mail: jmcleary@sun.ac.za

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.04.031



Scheme 1. The elimination of a toluenesulfinate leaving group to provide a disulfide.



2

Scheme 2. Disulfone side product **2**.

The reaction is suitable for a wide range of starting materials, including Grignard-derived dithio species, and can be used with xanthic, dithiocarbamic and trithiocarbonic species. Reactions where iodine oxidation generally provides poor results were found to provide significantly improved yields of disulfides using this process.

2. Experimental

2.1. Method A1

2.1.1. Bis(dodecylsulfanyl thiocarbonyl)disulfide 1b.[9] 1-Dodecanthiol (10.1 g, 50 mmol) was added dropwise to a solution of potassium hydroxide (3.65 g, 65 mmol) in 40 ml water, followed by 0.2 g of Aliquat 336 and carbon disulfide (3.8 g, 50 mmol) in one portion. The resulting solution was vigorously stirred at room temperature for 30 min and cooled to −5 °C. *p*-Tosyl chloride (5.0 g, 26 mmol) was added in portions over 5 min and stirring was continued for another hour. Afterwards the mixture was stirred for 10 min at 45 °C. The oily orange product, which solidifies on cooling, was washed with water (2 × 50 ml) and recrystallized from acetone. The resulting yellow solid was washed with 10 ml of ice cold pentane and dried under vacuum.

Yellow oil/crystals, mp 33–35 °C (acetone), 11.2 g (81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 3.30 (t, $J = 7.4$ Hz, 4H, CH_2), 1.69 (q, 4H, CH_2), 1.43–1.20 (m, 36H, CH_2), 0.88 (t, $J = 7.0$ Hz, 6H, CH_3);[8,9] ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 221.51 (C=S), 38.32, 31.91, 29.62, 29.61, 29.54, 29.42, 29.34, 29.08, 28.93, 22.68, 14.11; MS (EI^+) *m/e*: 554 (M^+, 5), 477, 446, 434, 413, 402 (92), 277, 245, 235, 201, 76 (100), 71.

2.2. Method A2

2.2.1. Bis(benzylsulfanyl thiocarbonyl)disulfide 1a. A solution of potassium benzyl trithiocarbonate was prepared analogously to method A1 from benzyl mercaptan (12.4 g, 100 mmol), potassium hydroxide (7.3 g, 130 mmol), Aliquat 336 (0.2 g) and carbon disulfide (7.6 g, 100 mmol) in 30 ml of water (Table 1). *p*-Tosyl chloride (9.6 g, 50 mmol) and 0.2 g Aliquat 336 were dissolved in 100 ml of dichloromethane, then stirred and cooled to −5 °C. The trithiocarbonate solution was added dropwise over 1 h to the *p*-tosyl chloride solution. Stirring was continued for another 30 min at −5 °C, then for a further hour at room temperature and the layers, separated. The aqueous layer was extracted with dichloromethane (2 × 30 ml). The combined organic phases were successively washed with aqueous $NaHCO_3$, water and saturated sodium chloride solution and then dried over magnesium sulfate. The solvent was removed under vacuum and the yellow solid washed with pentane and recrystallized from acetone. The resulting crystals were washed with pentane and dried under vacuum.

Yellow crystals, mp 94–95 °C (acetone), 16.0 g (80%); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.32–7.29 (m, 10H, Ar), 4.50 (s, 4H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 220.75 (C=S), 134.07, 129.51, 128.98, 128.26, 42.96; MS (EI^+) *m/e*: 398 (M^+, 5), 366, 322, 290, 246 (93), 213, 212, 181, 168, 123, 91 (100), 77 (100).

2.2.2. Bis(*n*-butylsulfanyl thiocarbonyl)disulfide 1c. Purification was done by column chromatography on silica gel with hexane.

Yellow oil, 10.15 g (62%); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 3.28 (t, $J = 7.4$ Hz, 4H, CH_2), 1.65 (m, 4H, CH_2), 1.39 (m, 4H, CH_2), 0.89 (t, $J = 7.4$ Hz, 6H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 221.96 (C=S), 37.88, 29.24, 21.90, 13.32 IR (neat): 1050 cm^{-1} (C=S); MS (EI^+) *m/e*: 330 (M^+, 7), 286, 254, 178, 165, 133, 122, 91, 76 (40), 57 (100).

2.2.3. *O*-Ethyl xanthogen disulfide 1d.[15] Purification by column chromatography on silica gel with hexane /chloroform (4:1) as solvent.

Yellow oil/crystals, mp 32 °C (ethanol), 9.3 g (77%); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.68 (q, $J = 7.1$ Hz, 4H, CH_2), 1.40 (t, $J = 7.1$ Hz, 6H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 207.91 (C=S), 71.56 (CH_2), 13.37 (CH_3); IR (neat): 1021 cm^{-1} (C=S).

2.3. Method B1

2.3.1. Bis(phenyl thiocarbonyl)disulfide 1e.[16] Dry THF (40 ml), a small crystal of iodine and magnesium turnings (2.45 g, 100 mmol) were stirred at room temperature. 2 ml of a solution prepared by dissolving 15.7 g bromobenzene in 40 ml THF. After the reaction had started, the remainder of the bromobenzene solution was added dropwise at such a speed so as to keep

the temperature below 40 °C. Stirring was continued until the magnesium had been consumed. The flask containing the Grignard solution was then placed into a cooling bath (ice/water), and carbon disulfide (7.6 g, 100 mmol) was added dropwise. The internal temperature rose and the solution turned red. Stirring was continued at room temperature for 1 h and the reaction then cooled down again to 0 °C. A solution of *p*-tosyl chloride (9.5 g, 50 mmol) in 40 ml of dry THF was added dropwise over 30 min. The colour changed from red to purple. The solution was stirred for another hour at room temperature and then the solvent was removed under reduced pressure and the residue kept overnight in a freezer. The solidified material was washed repeatedly with water and recrystallized from acetone or acetonitrile. Purplish-red crystals, mp 92–93 °C (acetone), 8.4 g (55%). The mother liquor contained further product (4.5 g), which could be purified by column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.10 (d, $J = 8.2$ Hz, 4H, H-2/6), 7.62 (t, 2H, H-4), 7.46 (t, 4H, H-3/5); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 220.13 (C=S), 143.98 (C-1), 133.32 (C-4), 128.85 (C-2), 127.76 (C-3).

2.3.2. Bis(4-methoxyphenyl thiocarbonyl)disulfide 1f.[16] Red crystals, mp 156–158 °C (acetonitrile), 13.4 g (73%); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.19 (d, $J = 9.0$ Hz, 4H, H-2/6), 6.93 (d, $J = 9.0$ Hz, 4H, H-3/5), 3.88 (s, 6H, CH_3O–); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 218.14 (C=S), 164.58 (C-4), 137.24 (C-1), 130.25 (C-2), 114.03 (C-3), 55.57 (CH_3O–).

2.3.3. Bis(4-fluorophenyl thiocarbonyl)disulfide 1g.[15] Purification was done by column chromatography on silica gel with chloroform as solvent.

Red solid, 10.1 g (59%); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.16–8.12 (m, 4H, H-2/6), 7.16–7.12 (m, 4H, H-3/5); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 217.32 (C=S), 165.20 (C-4), 139.84 (C-1), 130.06 (C-2), 115.78 (C-3).

2.3.4. Bis(dimethyl thiocarbamyl)disulfide 1i. White crystals, mp 155–156 °C (ethanol), 18.4 g (77%); MS: 240 (M^+). A sample of commercially available **1i** (tetramethylthiuram disulfide, [137-26-8], Aldrich) was used as reference.

2.3.5. Bis(4-methylphenyl) disulfone 2.[17–19] White crystals, mp 221–222 °C (acetone); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.87–7.81 (m, 4H, Ar), 7.45–7.40 (m, 4H, Ar), 2.48 (s, 6H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 148.31, 131.67, 130.53, 128.27, 21.82.

For comparison purposes **2** was independently synthesized by reaction of *p*-tosyl chloride with sodium 4-methylphenyl sulfinate.

2.4. Method B2

2.4.1. Bis(2-thienyl thiocarbonyl)disulfide 1h. A Grignard solution, prepared from 2-bromothiophene (16.3 g, 100 mmol) and magnesium turnings (4.85 g, 200 mmol) in 80 ml of THF at 30 °C, was stirred for 30 min after dropwise addition of the bromide and then decanted into a new flask. The residual metal was washed with 20 ml of THF and the solvent combined with the Grignard solution. After cooling to room temperature, 145 mg (1 mmol) of copper(I) bromide and carbon disulfide (10.65 g, 140 mmol) were added. The temperature rose to 40 °C and the solution turned red. The reaction mixture was warmed to 50 °C for 30 min to allow the reaction to reach completion.[20]

The solution was cooled to 0 °C and *p*-tosyl chloride (9.6 g, 50 mmol) in 40 ml of THF was added dropwise over 45 min after which the reaction mixture was stirred for another hour. The colour changed to brown and a solid precipitated. The solution was concentrated to 30–40 ml and the solids were filtered off. Recrystallization was carried out twice, firstly from acetonitrile and secondly from chloroform.

Red crystals, mp 129–131 °C (decomposition, acetonitrile), 9.7 g (61%); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.04 (dd, $J = 4.0$, 1.1 Hz, 2H, H-5), 7.77 (dd, $J = 5.1$, 1.1 Hz, 2H, H-3), 7.21 (t, $J = 5.1$, 4.0 Hz, 2H, H-4); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 205.63 (C=S), 149.98 (C-2), 137.07 (C-4), 129.21/128.71 (C-3/5).

The structure of **1h** was further confirmed by X-ray analysis. Crystallographic data (excluding structure factors) for the structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 601487. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

The preparation of disulfide **1h** by oxidation of the free 2-thiophenecarbodithioic acid with DMSO or its potassium salt with I_2/KI solution resulted in crude yields of only 5% and 12%, respectively.

Table 1. Synthesis of compounds **1a**–**i**

R–CS–S–S–CS–R	R	Method	% Yield[a]
1a	$C_6H_5CH_2S$	A1/A2	70/80
1b	$C_{12}H_{25}S$	A1	81
1c	*n*-C_4H_9S	A1	61
1d	H_5C_2O	A2	77
1e	C_6H_5	B1	55
1f	4-$(H_3CO)C_6H_4$	B1	73
1g	4-FC_6H_4	B1	59
1h	C_4H_3S	B2	61
1i	$(CH_3)_2N$	A2	77

All products provided satisfactory spectroscopic data.
[a] Yield for recrystallized products.

3. Conclusions

The synthesis of bis(thiocarbonyl)disulfides following the presented protocol is efficient and results in satisfactory yields of the desired products. Purification of the products

is easily achieved and their use in further reactions or directly in polymerizations is convenient as a result.

Acknowledgements

The authors acknowledge the financial support of MONDI business paper (SA) and the National Research Foundation (NRF) of South Africa. Gareth Lloyd is acknowledged for the crystal structure analysis of novel disulfides.

References and notes

1. Moad, G.; Rizzardo, E.; Thang, S. H. *Aust. J. Chem.* **2005**, *58*, 379–410.
2. Moad, G.; Chiefari, J.; Chong, B. Y.; Krstina, J.; Mayadunne, R. T.; Postma, A.; Rizzardo, E.; Thang, S. H. *Polym. Int.* **2000**, *49*, 993–1001.
3. Chiefari, J.; Chong, Y. K. B.; Ercole, F.; Krstina, J.; Jeffery, J.; Le, T. P. T.; Mayadunne, R. T. A.; Meijs, G. F.; Moad, C. L.; Moad, G.; Rizzardo, E.; Thang, S. H. *Macromolecules* **1998**, *31*, 5559–5562.
4. Vosloo, J. J.; De Wet-Roos, D.; Tonge, M. P.; Sanderson, R. D. *Macromolecules* **2002**, *35*, 4894–4902.
5. Sprong, E.; De Wet-Roos, D.; Tonge, M. P.; Sanderson, R. D. *J. Polym. Sci. Part A: Polym. Chem.* **2003**, *41*, 223–235.
6. Thang, S. H.; Chong, Y. K. B.; Mayadunne, R. T. A.; Moad, G.; Rizzardo, E. *Tetrahedron Lett.* **1999**, *40*, 2435–2438.
7. Bouhadir, G.; Legrand, N.; Quiclet-Sire, B.; Zard, S. Z. *Tetrahedron Lett.* **1999**, *40*, 277–280.
8. Farnham, W. B. PCT Int. Appl. WO 2005113493, A1 20051201; CAN 144:22642, AN 2005:1260607.
9. Moad, G.; Chong, Y. K.; Postma, A.; Rizzardo, E.; Thang, S. H. *Polymer* **2005**, *46*, 8458–8468.
10. Kato, S.; Kato, T.; Kataoka, T.; Mizuta, M. *Int. J. Sulfur Chem.* **1972**, *8*, 437–440.
11. Bulmer, G.; Mann, F. G. *J. Chem. Soc.* **1945**, 680–686.
12. Hansen, H. C.; Senning, A. *J. Chem. Soc., Chem. Comm.* **1979**, 1135–1136.
13. Senning, A. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 941–942.
14. Hansen, H. C.; Senning, A. *J. Am. Chem. Soc.* **1967**, *89*, 692–693.
15. Shi, L.; Chapman, T. M.; Beckman, E. J. *Macromolecules* **2003**, *36*, 2563–2567.
16. Benaglia, M.; Rizzardo, E.; Alberti, A.; Guerra, M. *Macromolecules* **2005**, *38*, 3129–3140.
17. Lin, Y.; Zhang, Y. *Tetrahedron Lett.* **2003**, *44*, 4291–4294.
18. Bartmann, E. A. *Synthesis* **1993**, 490–496.
19. Lalonde, R. T.; Tsai, A. I.-M.; Wong, C. *J. Org. Chem.* **1976**, *41*, 2514–2520.
20. Wakefield, B. J. *Organomagnesium Methods in Organic Synthesis*; Academic Press, 1995; p 149 and literature cited therein.