

Dess–Martin periodinane mediated synthesis of thioesters from aldehydes

Sunita B. Bandgar, B. P. Bandgar,* B. L. Korbadi and S. S. Sawant

Organic Chemistry Research Laboratory, School of Chemical Sciences, Swami Ramanand Teerth Marathwada University, Nanded 431 606, India

Received 30 July 2006; revised 29 November 2006; accepted 7 December 2006

Abstract—Dess–Martin periodinane (DMP) mediated efficient synthesis of thioesters from the corresponding aldehydes under mild conditions is described.

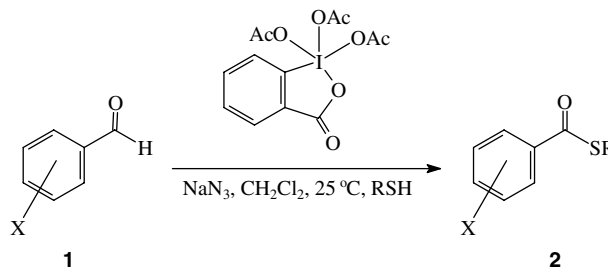
© 2007 Elsevier Ltd. All rights reserved.

The driving force for the development of new methodologies in organic synthesis has been the need for simple and efficient strategies to obtain complex products. Thioesters are activated carboxylic acid derivatives, which exhibit acylating properties similar to those of acid anhydrides¹ and are important functional groups in organic synthesis.² Biologically active thioesters play central roles in living cells serving as essential metabolic intermediates due to their ability to act as excellent intermediates for acyl group transfer reactions. In addition, biosynthesis of polyketides and nonribosomal polypeptides is achieved via thioester intermediates of fatty acids and amino acids.³

Thioesters are usually prepared by condensation of a thiol and an acid chloride and they have widespread applications in synthetic chemistry as precursors to aldehydes, ketones, acids, esters, lactones, amides, lactams and heterocycles.⁴ Surprisingly, in view of the diverse chemistry this functional group offers, it has attracted scant interest from combinatorial chemists.⁵ Due to the importance of thioesters, various chemical and enzymatic methods have been developed for their synthesis directly from carboxylic acids⁶ or acid chlorides.⁷ The conversion of alkyl halides to thioesters using potassium thioacetate is well reported in the literature.⁸ More recently, it has been reported that the combination of the water-soluble radical initiator, 2,2'-azobis[2-(2-imidazolizolyl)propane dihydrochloride (VA-044), and

the surfactant, cetyltrimethyl ammonium bromide (CTAB), was found to be the most suitable condition for the effective and direct synthesis of useful active thioesters (pentafluorophenyl thioesters) from the corresponding aldehydes in water.⁹

In recent years, hypervalent iodine reagents have occupied an important place in the reactions of natural and synthetic organic chemistry because of their potential applications in the construction of carbon–carbon and carbon–heteroatom bonds.¹⁰ One of the most significant advances in the field, discovery of the Dess–Martin periodinane (DMP) reagent,¹¹ opened the door to a mild oxidation procedure allowing alcohols to be converted to the corresponding carbonyl compounds. Its widespread use over the past decade attests to its benign nature and its ability to succeed under difficult oxidation circumstances. DMP is an oxidizing agent that overcomes many of the disadvantages associated with oxidative methods developed so far. As a part of our ongoing



Scheme 1.

Keywords: Dess–Martin periodinane (DMP); Thioester; Aldehyde.

* Corresponding author. Fax: +91 2462 229245; e-mail: bandgar_bp@yahoo.com

Table 1. Synthesis of thioesters from aldehydes, sodium azide and thiols using Dess–Martin periodinane

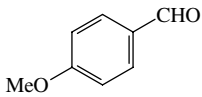
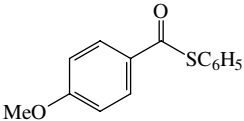
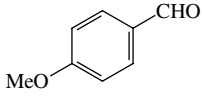
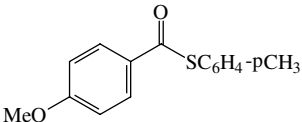
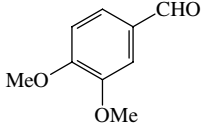
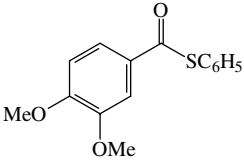
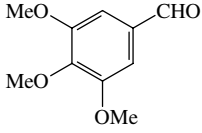
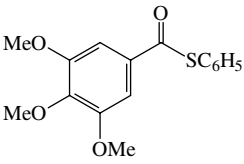
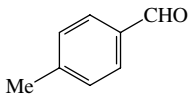
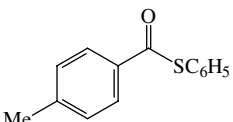
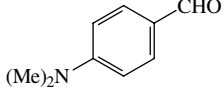
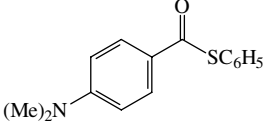
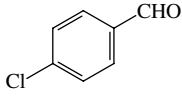
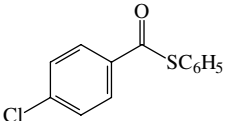
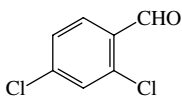
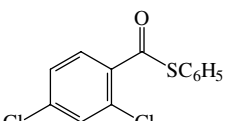
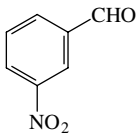
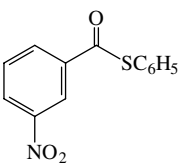
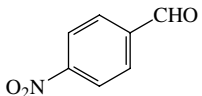
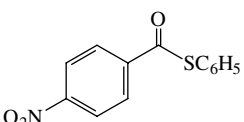
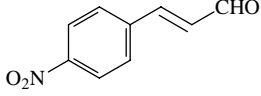
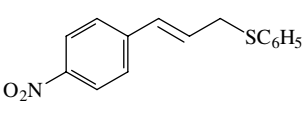
Entry	Aldehyde 1	Thioester 2	Time (h)	Yield ^{a,b} (%)
1			2.75	75
2			2.75	74
3			0.50	94
4			0.5	95
5			1.0	97
6			1.8	92
7			2.2	87
8			3.5	85
9			3.2	72
10			3.2	70
11			2.2	60

Table 1 (continued)

Entry	Aldehyde 1	Thioester 2	Time (h)	Yield ^{a,b} (%)
12			2.5	70
13			3.1	75
14			3.1	70
15			4.1	80
16			2.1	85

^a Yields of isolated pure products.

^b The products were characterized by IR, ¹H NMR and mass spectroscopies and by elemental analysis.

program on the development of novel methods in organic synthesis under mild conditions,¹² we describe a new efficient and practical route for the one-step conversion of aldehydes into the corresponding thioesters using Dess–Martin periodinane and sodium azide in dichloromethane at 25 °C in high yield under mild conditions (Scheme 1).

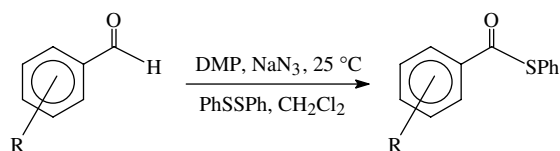
To the best of our knowledge, the applicability of DMP in the synthesis of thioesters from aldehydes has not been reported. Attempts to prepare thioesters using DMP without any additive or with NaBr or KBr or I₂ as an additive furnished very poor yields (5–10%). The best results were obtained using DMP and NaN₃ in dichloromethane. To explore the generality and scope of this methodology, diverse aldehydes were studied to illustrate this novel and general method for the synthesis of thioesters and the results are summarized in Table 1. It is important to note that aldehydes possessing electron-donating groups furnished excellent yields of the corresponding thioesters in short reaction times (Table 1, entries 1–6), whereas aldehydes with electron-withdrawing substituents resulted in comparatively low yields and required longer times (Table 1, entries 7–12). Dialdehydes as well as aliphatic aldehydes were also converted smoothly to the corresponding thioesters in good yields (Table 1, entries 12 and 16). Heterocyclic aldehydes were transformed into the corresponding thioesters in good yields under these mild and neutral conditions; this can be problematic under acidic conditions (Table 1, entries 13–15).

Reaction of sodium azide with DMP furnished the azido derivative, which reacted with the aldehyde to form an azido-hydrin intermediate. This intermediate on further oxidation resulted in an acyl azide, which on nucleophilic substitution with the thiol furnished the corresponding thioester. In order to support the nucleophilic activation mechanism, we thought that NaCN might be a better activator than NaN₃ because cyanide is known as a good nucleophile as well as a good leaving group. When we performed the reaction with NaCN and thiophenol with 3,4-dimethoxy benzaldehyde, the corresponding thioester was formed in low yield (40%) and required a longer reaction time (6 h). Therefore, we have selected NaN₃ as an additive for the synthesis of thioesters (Table 1).

A successful attempt was made to prepare thioesters from the corresponding aldehydes using Dess–Martin periodinane (DMP), NaN₃ and diphenyldisulfide in dichloromethane (Scheme 2). Excellent yields of the corresponding thioesters were obtained in a short reaction time.

In conclusion, the mild reaction conditions, simple work-up, short reaction time and good to excellent yields are important features of this novel methodology as compared to other reported methods.

In a typical experimental procedure, *p*-methoxybenzaldehyde (1.0 mmol) was treated with Dess–Martin periodinane (6 mmol), sodium azide (6.5 mmol) and



R	Time (h)	Yield (%)
H	1.5	80
Me	1.0	90
OMe	1.0	92
Cl	2.5	85
NO ₂	2.5	88

Scheme 2.

thiophenol (1 mmol) in CH₂Cl₂ (10 ml) at 0 °C. Then the reaction mixture was stirred at 25 °C for 2.75 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was washed with H₂O (3 × 5 ml) and extracted with CH₂Cl₂ (2 × 10 ml). The combined organic layer was dried over anhydrous Na₂SO₄ and the solvent was removed under vacuum to afford the crude product, which was purified by column chromatography on silica gel (petroleum ether–ethyl acetate = 9:1) to furnish phenyl *p*-methoxyphenyl thioester (95%).

Compound **2a**, IR: 780, 820, 1030, 1600, 1730, 2930 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 3.80 (s, 3H, OMe), 6.9 (d, 2H, *J* = 8 Hz, ArH), 7.50 (m, 5H, ArH), 8.00 (d, 2H, *J* = 8 Hz, ArH). Anal. Calcd for C₁₄H₁₂O₂S: C, 68.82; H, 4.95; S, 13.12. Found: C, 68.74; H, 5.02; S, 13.05.

Acknowledgement

B.P.B. thanks CSIR, New Delhi, for financial assistance (Project No. 1/2023/05/EMR-II) and B.L.K. thanks CSIR, New Delhi, for a Junior Research Fellowship.

References and notes

- (a) Ugava, A.; Sonod, N. *Comp. Org. Funct. Group Transform.* **1995**, *5*, 231; (b) Voss, J. *Comp. Org. Synth.* **1991**, *6*, 435; (c) Bauer, W.; Kuhlein, K. *Methoden Org. Chem. (Houben-Weyl)* **1985**, *E5*, 832; (d) Barrett, G. C. In *Organic Compounds of Sulphur, Selenium, Tellurium*; Hogg, D. R., Ed.; RSC: London, 1981; Vol. 6, p 13; (e) Voss, J. In *The Chemistry of Acid Derivatives*; Patai, S., Ed.; Wiley: Chichester, 1979; Suppl. B, p 1021; (f) Jansson, M. In *The Chemistry of Carboxylic Acids and Esters*; Patai, S., Ed.; Wiley: Chichester, 1969; p 705.
- (a) Bublitz, D. E. *J. Org. Chem.* **1967**, *32*, 1630–1631; (b) Wolfform, M. L.; Karabinos, J. V. *J. Am. Chem. Soc.* **1946**, *68*, 742–745; (c) Nagao, Y.; Kawabata, K.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1978**, 330; (d) Savrda, J.; Veyrat, D. H. *Tetrahedron Lett.* **1968**, *9*, 6253–6254; (e) Liu, H. J.; Lai, H. K. *Tetrahedron Lett.* **1979**, *20*, 1193–1196; (f) Corey, E. J.; Bhattachaya, S. *Tetrahedron Lett.* **1977**, *18*, 3919–3922; (g) Ernest, I.; Gostell, J.; Greengrass, C. W.; Howlick, W.; Jackman, D. E.; Pfaendler, H. R.; Woodward, R. B. *J. Am. Chem. Soc.* **1978**, *100*, 8214–8222; (h) Mukaiyama, T.; Araki, M.; Takei, H. *J. Am. Chem. Soc.* **1973**, *95*, 4763–4765; (i) Lloyd, K.; Young, G. T. *J. Chem. Soc.* **1971**, *93*, 2890–2895; (j) Nicolau, K. C. *Tetrahedron* **1977**, *33*, 683–686; (k) Masamune, S.; Carcoran, J. W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 585–607; (l) Back, T. C. *Tetrahedron* **1977**, *33*, 3041–3059.
- Keating, T. A.; Walsh, C. T. *Curr. Opin. Chem. Biol.* **1999**, *3*, 598–599.
- (a) Evans, D. A.; Dart, M. J.; Duffy, J. L.; Yang, M. G. *J. Am. Chem. Soc.* **1996**, *118*, 4322–4343; (b) Paz, M. M.; Corra, J. F.; Cabca, M. I.; Sardina, F. J. *Tetrahedron Lett.* **1996**, *37*, 9259–9262; (c) Um, P. J.; Drucckhammer, D. G. *J. Am. Chem. Soc.* **1998**, *120*, 5605–5610; (d) Agarwal, V. K.; Thomas, A.; Schade, S. *Tetrahedron* **1997**, *53*, 16213–16228; (e) Yang, W., II; Romo, D. *Tetrahedron* **1997**, *53*, 16471–16488; (f) Mizumo, M.; Muramoto, I.; Kawakami, T.; Soike, M.; Aimoto, S.; Hanoda, K.; Inazu, T. *Tetrahedron Lett.* **1998**, *39*, 55–58; (g) White, J. D.; Kim, T. S.; Nambu, M. *J. Am. Chem. Soc.* **1997**, *119*, 103–111.
- (a) Canne, L. E.; Walker, S. M.; Kent, S. B., II. *Tetrahedron Lett.* **1996**, *36*, 1217–1220; (b) Kobayashi, S.; Iilachiya, I.; Suzuki, S.; Moriwaki, M. *Tetrahedron Lett.* **1996**, *37*, 2809–2812; (c) Kobayashi, S.; Ichiya, I.; Yasuda, M. *Tetrahedron Lett.* **1996**, *37*, 5569–5572.
- (a) Pelter, A.; Levitt, T.; Smith, K. *J. Chem. Soc., Chem. Commun.* **1969**, 435; (b) Liu, H.; Sabesan, S. I. *Can. J. Chem.* **1985**, *63*, 2645–2648; (c) Grieco, P. A.; Ycoyama, Y.; Williams, E. *J. Org. Chem.* **1978**, *43*, 1283–1285; (d) Yamada, S.; Yokuyama, Y.; Shioiri, T. *J. Org. Chem.* **1974**, *39*, 3302–3303; (e) Cohen, T.; Gapinski, R. E. *Tetrahedron Lett.* **1978**, *45*, 4319–4321; (f) Ravi, D.; Ram Rao, N.; Reddy, G. S.; Sucheta, K.; Rao, V. J. *Synlett* **1994**, 856.
- (a) Meshram, H. M.; Reddy, G. S.; Bindu, K. H.; Yadav, J. S. *Synlett* **1998**, 877–878; (b) Reibig, H. U.; Scherer, B. *Tetrahedron Lett.* **1980**, *21*, 4259–4262; (c) Padwa, A.; Coasts, S. J.; Hadjarapoglou, L. *Heterocycles* **1994**, *39*, 219–223; (d) Shaha, S. T. A.; Shan, K. M.; Heinrich, A. M.; Voelter, W. *Tetrahedron Lett.* **2002**, *43*, 8281–8283.
- Zheng, T.; Burkart, M.; Richrdson, D. E. *Tetrahedron Lett.* **1999**, *40*, 603–606.
- Nambu, H.; Hata, K.; Motsugi, M.; Kita, Y. *Chem. Eur. J.* **2005**, *11*, 719–727.
- (a) Varvoglis, A. *Hypervalent Iodine in Organic Synthesis*; Academic Press: San Diego, 1997; p 256; (b) Nicolaou, K. C.; Baran, P. S.; Zong, Y.-L.; Sugita, K. *J. Am. Chem. Soc.* **2002**, *124*, 2212–2220.
- (a) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155–4156; (b) Dess, D. B.; Martin, J. C. *J. Am. Chem. Soc.* **1991**, *113*, 7277–7287; (c) Chaudhari, S. S.; Akamanchi, K. G. *Tetrahedron Lett.* **1998**, *39*, 3209–3212; (d) Boss, D. S.; Reddy, A. V. N. *Tetrahedron Lett.* **2003**, *44*, 3543–3545.
- (a) Bandgar, B. P.; Patil, A. V. *Tetrahedron Lett.* **2005**, *46*, 7627–7630; (b) Das, B.; Holla, H.; Mahoder, G.; Venkateswarlu, K.; Bandgar, B. P. *Synthesis* **2005**, *10*, 1572–1574; (c) Bandgar, B. P.; Sawant, S. S. *Synth. Commun.* **2006**, *36*, 859–864; (d) Bandgar, B. P.; Kamble, V. T.; Kulkarni, A. *Aust. J. Chem.* **2005**, *58*, 602–605; (e) Bandgar, B. P.; Bettigeri, S. V.; Phopse, J. *Tetrahedron Lett.* **2004**, *45*, 6959–6962; (f) Bandgar, B. P.; Bettigiri, S. V.; Phopse, J. *Org. Lett.* **2004**, *6*, 2105–2108.