Journal of Sulfur Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713926081

A novel and direct synthesis of thiolesters using cyanuric chloride under mild conditions

B. P. Bandgar[a]; S. S. Pandit[b]
[a] Organic Chemistry Research Laboratory, School of Chemical Sciences, Swami Ramanand Teerth Marathwada University, Nanded, (M.S), India [b] P.G. Department of Chemistry, Padmashri Vikhe Patil College, Ahmednagar, (M.S), India

To cite this Article Bandgar, B. P. and Pandit, S. S.(2004) 'A novel and direct synthesis of thiolesters using cyanuric chloride under mild conditions', Journal of Sulfur Chemistry, 25: 5, 343 — 346
To link to this Article: DOI: 10.1080/17415990412331317928
URL: http://dx.doi.org/10.1080/17415990412331317928

J. Sulfur Chemistry
Vol. 25, No. 5, October 2004, 343–346

Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

A novel and direct synthesis of thiolesters using cyanuric chloride under mild conditions

B. P. BANDGAR*,† and S. S. PANDIT‡

†Organic Chemistry Research Laboratory, School of Chemical Sciences, Swami Ramanand Teerth Marathwada University, Vishnupuri, Nanded, 431606 (M.S) India
‡P.G. Department of Chemistry, Padmashri Vikhe Patil College, Pravaranagar (Loni. Kd.) Tal. Rahata. Dist. Ahmednagar, 413713 (M.S) India

(*Received 12 April 2004; in final form 28 August 2004*)

A direct synthesis of thiolester from carboxylic acids and thiols under mild conditions using cyanuric chloride as an inexpensive and readily available reagent is described.

Keywords: Cyanuric chloride; Carboxylic acid; Thiols; Thiolester; Mild conditions

1. Introduction

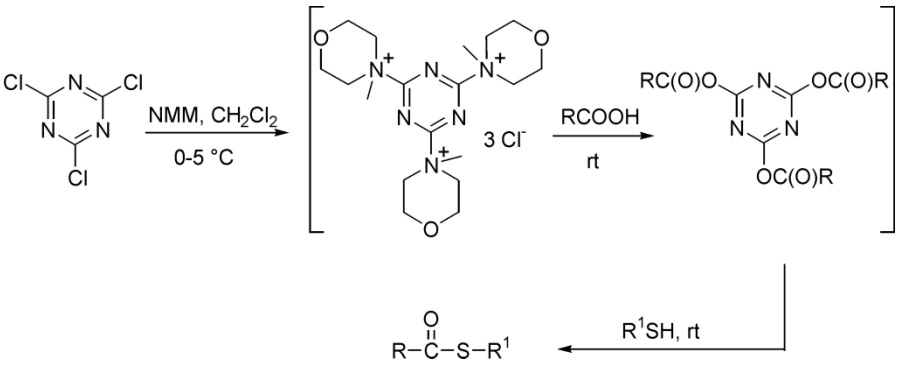
The thiolester, an important functional group in organic synthesis [1], is used to prepare carbon–carbon bonds and numerous other functionalities. Thiolesters are activated carboxylic acid derivatives, which exhibit acylating properties similar to those of acid anhydride [2]. Resin bound thiolesters are used as "traceless" linkers in solid phase synthesis [3]. In general, thiolesters have found widespread application in synthetic chemistry as precursors to aldehydes, ketones, acids, esters, lactones, amides, and heterocycles [4].

Thiolesters are usually prepared by condensation of a thiol and an acid chloride. Various improved methods have been developed for their direct preparation from carboxylic acids [5]. This protocol in effect requires activation of the acid. There are numerous activating agents, including trialkylthioborane [5a], phenyldichlorophosphonate [5b], tri-n-butylphosphine [5c], diethyl phosphorocyanidate or diethyl phosphorazidate [5d]. Amides have also been converted into thiolesters using aluminium thiophenoxide or boron thiophenoxide [5e]. Recently, phosgene [5f] was also used for the preparation of thiolesters. These existing reagents are very expensive and procedures require tedious work up or, occasionally, the isolation of intermediates. Therefore, there remains reason to search for a new and inexpensive reagent. Some of the methods using NBS [6a], Zn [6b] and *N*-methylbenzene thiazolium trifluoromethanesulfonate [6c] proceed through the intermediacy of an acid chloride [6d, 6e], involving use of

* Corresponding author. E-mail: bandgar_bp@yahoo.com

J. Sulfur Chemistry
ISSN 1741-5993 print; ISSN 1741-6000 online © 2004 Taylor & Francis Ltd
http://www.tandf.co.uk/journals
DOI: 10.1080/17415990412331317928

the aggressive reagent $SOCl_2$. We report here the use of 2,4,6-trichloro-1,3,5-triazine for the direct conversion of carboxylic acids into the corresponding thiolester under mild conditions (scheme 1).



SCHEME 1

2. Results and discussion

Our strategy involves enhancement of the reactivity of the carbonyl group of the acid moiety using 2,4,6-trichloro-1,3,5-triazine (cyanuric chloride). The carboxylic acid was first allowed to react with 2,4,6-trichloro-1,3,5-triazine in dichloromethane in the presence of *N*-methylmorpholine; the hydrogen chloride generated is absorbed by the amine. The resulting reaction mixture containing activated carboxylic acid was further treated with aliphatic as well as aromatic thiols at room temperature to afford the corresponding thiolester in good to excellent yields. The results are summarized in table 1. The methodology is general as aliphatic, aromatic,

Table 1. Cyanuric chloride mediated synthesis of thiolesters from carboxylic acids and thiols.

Entry	Carboxylic acid	Thiol	Product	Time (min)	Yield (%)[a,b]	Ref.[c]
1	PhCOOH	PhSH	PhC(O)SPh	30	93	5
2	p-Cl[C_6H_4]COOH	PhSH	p-Cl[C_6H_4]C(O)SPh	270	89	5
3	*p*-NO_2[C_6H_4]COOH	PhSH	*p*-NO_2[C_6H_4]C(O)SPh	360	75	7
4	2,4-Cl_2[C_6H_3]COOH	PhSH	2,4-Cl_2[C_6H_3]C(O)SPh	360	75	7
5	*p*-Me[C_6H_4]COOH	*p*-Me[C_6H_4]COOH	*p*-Me[C_6H_4]C(O)S[C_6H_4]*p*-Me	30	84	5
6	PhCH=CHCOOH	PhSH	PhCH=CHC(O)SPh	30	90	3
7	$PhCH_2COOH$	PhSH	$PhCH_2C(O)SPh$	40	86	7
8	$PhOCH_2COOH$	PhSH	$PhOCH_2C(O)SPh$	100	80	7
9	*o*-[C_6H_4]$(COOH)_2$	PhSH	*o*-[C_6H_4]$(C(O)SPh)_2$	30	79	7
10	*m*-[C_6H_4]$(COOH)_2$	PhSH	*m*-[C_6H_4]$(C(O)SPh)_2$	30	76	7
11	*p*-[C_6H_4]$(COOH)_2$	PhSH	*p*-[C_6H_4]$(C(O)SPh)_2$	30	80	7
12	PhCH(OH)COOH	PhSH	PhCH(OH)C(O)SPh	55	88	—[d]
13	PhCOOH	$CH_3(CH_2)_3SH$	$PhC(O)S(CH_2)_3CH_3$	45	79	5
14	PhCOOH	$PhCH_2SH$	$PhC(O)SCH_2Ph$	45	89	7
15	$CH_3(CH_2)_6COOH$	PhSH	$CH_3(CH_2)_6C(O)SPh$	55	87	5
16	3-[C_5H_5N]COOH	$CH_3(CH_2)_3SH$	3-[C_5H_5N]$C(O)S(CH_2)_3CH_3$	80	84	7

[a] Yield of isolated product. [b]Products characterized by comparison of their mp or bp with authentic samples. [c]Published physical and spectral properties. [d]Spectroscopic data for **12** is given in the Experimental section.

heterocyclic and dicarboxylic acids are smoothly converted into the corresponding thiolester using alkyl and aryl thiols.

Our method is superior to other methods because the carboxylic acid group can be converted directly into the thiolester at room temperature without converting the carboxylic acid into an acyl chloride. Importantly, cyanuric chloride is a safe, inexpensive and readily available reagent in comparison with some of the reported reagents.

In conclusion, a convenient and straightforward general protocol has been developed to convert various carboxylic acids directly into the corresponding thiolester under mild conditions. All chemicals used are commercially available and inexpensive.

3. Experimental

General procedure: To a solution of cyanuric chloride (3 mmol) in dichloromethane (30 ml), *N*-methylmorpholine (10 mmol) was added at 0–5 °C under continuous stirring. A white suspension was formed and to this reaction mixture a solution of mandelic acid (9 mmol) in dichloromethane (10 mL) was added. After 3 hours the reaction mixture was filtered through Celite® and to this filtrate a solution of thiophenol (9 mmol) was added at room temperature with constant stirring. After completion of the reaction (TLC), the mixture was washed with $NaHCO_3$ (10%, 2 × 10 mL) and then with water (2 × 10 mL). The organic layer was dried with anhydrous Na_2SO_4 and removal of the solvent under reduced pressure furnished the crude product, which was further purified by column chromatography (light petroleum).

12: mp 98 °C, IR (KBr) (cm^{-1}): 746, 836, 907, 1011, 1107, 1207, 1397, 1438, 1695, 3260; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 3.8 (s, 1H, OH); 4.6 (s, 1H, CH); 7.24–8.1 (m, 10H, Ar-H); Analysis, calcd. (%) for $C_{14}H_{12}O_2S$ (244.227): C, 68.85; H, 4.91; S, 13.12. Found (%): C, 67.98; H, 5.21; S, 13.52.

Acknowledgment

S. S. P. thanks U. G. C. for a teacher fellowship under the FIP scheme

References

[1] (a) Bach, T. G., 1977, *Tetrahedron*, **33**, 3041. (b) Masamune, S. and Corcoran, J. W., 1977, *Angew. Chem., Int. Ed. Engl.*, **16**, 585. (c) Nicolaou, K. C., 1977, *Tetrahedron*, **33**, 683. (d) Lloyd, K. and Young, G. T., 1971, *J. Chem. Soc.*, **93**, 2890. (e) Mukaiyama, T., Araki, M. and Takei, H., 1973, *J. Am. Chem. Soc*, **95**, 4763. (f) Ernes, I., Gostell, J., Greengrass, C. W., Howlick, W., Jackman, D. E., Pfaendler, H. R. and Woodward, R. B., 1978, *J. Am. Chem. Soc.* **100**, 8214. (g) Corey, E. J. and Bhattacharya, S., 1977, *Tetrahedron Lett.*, **18**, 3919. (h) Liu, H. J. and Lai, H. K., 1979, *Terahedron Lett.*, **20**, 1193. (i) Savrda, J. and Veyrat, D. H., 1968, *Tetrahedron Lett.*, **9**, 6253. (j) Naguo, Y., Kawabata, K. and Fujita, E., 1978, *J. Chem. Soc., Chem. Commun.*, 330. (k) Wolfform, M. I. and Karabinos, J. V., 1946, *J. Am. Chem. Soc.*, **68**, 742. (l) Bublitz, D. E., 1967, *J. Org. Chem.*, **32**, 1630.

[2] (a) Voss, J., 1991, *J. Comp. Org. Synth.*, **6**, 435. (b) Barrett, G. C., 1981, in Organic Compounds of sulfur, selenium and tellurium, Hogg, D. R. (Ed.) (London: Royal Society of Chemistry), volume 6, p. 13.

[3] (a) May, P. J., Bradley, M., Harrowven, D. C. and Pallin, D., 2000, *Tetrahedron Lett.,* **41**, 1627. (b) Masamune, S., Hayase, Y., Schillina, W., Chan, W. K. and Bates, G. S., 1977, *J. Am. Chem. Soc.*, **99**, 6756 and references cited therein. (c) Corey, E. J. and Beames, D. J., 1973, *J. Am. Chem. Soc.*, **95**, 5829.

[4] For some more recent examples of their use in synthesis, see (a) Evans, D. A., Dart, M. J., Duffy, J. L. and Yang, M. G., 1996, *J. Am. Chem. Soc.*, **118**, 4322. (b) Paz, M. M., Correa, J. F., Cabeza, M. I. and Sardina, F. J., 1996, *Tetrahedron Lett.*, **37**, 9259. (c) Aggarwal, V. K., Thomas, A. and Schade, S., 1997, *Tetrahedron*, **53**, 16213. (d) Yang, H. W., Zhao, C. X. and Ramo, D., 1997, *Tetrahedron*, **53**, 16471. (e) White, J. D., Kim, T. S. and Namsbu, M., 1997, *J. Am. Chem. Soc.*, **119**, 103.

[5] (a) Pelter, A., Levitt, T. and Smith, K., 1969, *J. Chem. Soc., Chem., Commun.*, 435. (b) Liu, H. and Sabesan, S. I., 1985, *Can. J. Chem.*, **63**, 2645. (c) Grieco, P. A., Yokoyama, Y. and Williams, E., 1978, *J. Org. Chem.*, **43**, 1283. (d) Yamada, S., Yokoyama, Y. and Shioiri, T., 1974, *J. Org. Chem.*, **39**, 3302. (e) Cohen, T. and Gapinski, R. E., 1978, *Tetrahedron Lett.*, **45**, 4319. (f) Ravi, D., Rama Rao, N., Reddy, G. S. R., Sucheta, K. and Rao, V. J., 1994, *Synlett*, 856.

[6] (a) Sucheta, K., Reddy, G. S. R., Ravi, D. and Rama Rao, N., 1994, *Tetrahedron Lett.*, **35**, 4416. (b) Meshram, H. M., Reddy, G. S., Bindu, K. H. and Yadav, J. S., 1998, *Synlett*, 877. (c) Bachiller, F. S., Bates, G. S. and Masamune, S. J., 1976, *J. Chem. Soc., Chem. Commun.*, 719. (d) ReiBig, H. U. and Scherer, B., 1980, *Tetrahedron Lett.*, **21**, 4253. (e) Padwa, A., Coates, S. J. and Hadjiarapoglou, L., 1994, *Heterocycles*, **39**, 219.

[7] (a) Bruice, T. C., 1961, in Organic sulfur compounds, Kharasch, N. (Ed.) (New York and London: Pergamon Press), chapter 35. (b) Bruice, T. C. and Benkovic, S. J., 1966, in Bioorganic mechanisms (Benjamin: New York), volume 1, chapter 3. (c) Bodanszky, M. and Ondetti, M. A., 1966, Peptide synthesis (Interscience: New York), chapter VI.