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Synthesis of Thiolesters from Thioacetylenes

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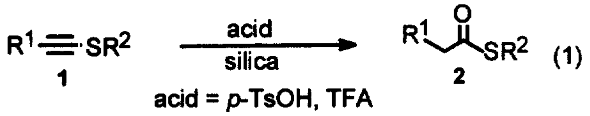
Abstract : Thiolesters were conveniently prepared in good yields by reacting thioacetylenes with *p*-toluenesulfonic or trifluoracetic acid in dichloromethane in the presence of silica

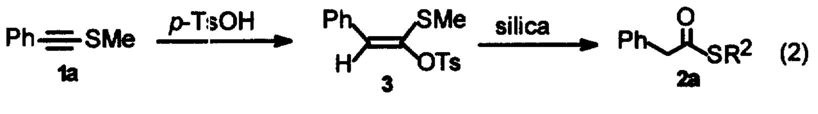
Keywords: Thiolesters; Thioalkynes; Hydrolysis; Sulfides

Thiolesters are important intermediates in organic synthesis. They have been used as mild acyl transfer reagents,[1] as intermediates in the synthesis of ketones[2] and for asymmetric aldol reactions.[3] Recently, application of this functional group has expanded into the synthesis of proteins by chemical ligation of benzyl thiolesters[4] as well as a latent carboxylic acid in the macrolactonization applicable to the dilactonic pyrrolizidine alkaloids.[5] In spite of the growing interest in new organic transformations of these compounds, preparative methods available for their synthesis are still limited, with the few exceptions,[6] of those based on conventional methodology (i. e. formal substitution at the carbonyl carbon of carboxylic acids and their derivatives or addition to nitriles).[7] Herein we describe our results on the preparation of thiolesters 2 based on a very convenient procedure,[8] the addition of *p*-toluenesulfonic acid (*p*-TsOH) or trifluoroacetic acid (TFA) to a dichloromethane suspension of thioacetylenes 1 and silica with its natural water content (Eq. 1).



The reactions described here are performed very easily by simply mixing all reagents at 40 °C. The thiolesters are obtained in good yields (Table 1). This procedure is especially useful because the starting thioacetylenes are readily available by various efficient methods.[9] The study of the reaction of 1-(methylthio)-2-phenylethyne **1a** with various acids was undertaken in dichloromethane. *p*-TsOH and TFA proved to be equally effective acids, both providing the thiolester in 86% yield. With other acids such as $ClSO_3H$, $HClO_4$, or HCl, **2a** was obtained in 85%, 80% and 80% yields, respectively. In acetic acid no reaction was observed. The reaction does not proceed satisfactorily in the absence of silica.

The reactions can be monitored by NMR, and the two stages of the process (Eq. 2) can be observed. For example, 1-(methylthio)-2-phenyletyne **1a** within 10 min of the addition of *p*-TsOH showed no methyl signal attributable to the starting alkynyl sulfide [expected signal at δ ($CDCl_3$) 2.33], but a new signal at δ 6.49 as singlete and a weak signal at δ 3.79 as singlet. We assign the former to the vinylic sulfide 3 and the latter to thiolester **2a**. The signal due to **2a** gradually increases in intensity at the expense of the signals representing the vinylic sulfide 3.



The present procedure nicely complements other methods, offering several advantages such as the

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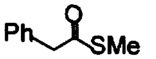
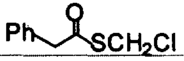
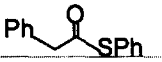
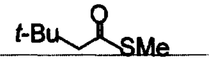
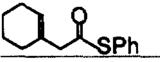
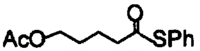
greater availability of the starting material, compatibility with various functional groups, and avoidance of the use of the very toxic reagents such as heavy metal thiolates or phenyl dichlorophosphate. Most important, isolation of pure material is easily achieved.

Table 1: Synthesis of thiolesters by reaction of thioacetylenes with acids, according to the Eq. 1.

Thioacetylenes 1	Thiolester 2	Acid	Time (h)	Yield[a,b] (%)
$Ph-\equiv-SMe$		TFA	2	86
		p-TsOH	10	86
		$ClSO_3H$	6	85
		$HClO_4$	140	80
		HCl	15	80
		AcOH	140	-
$Ph-\equiv-SBu$-t		TFA	96	81
		p-TsOH	140	70
$Ph-\equiv-SCH_2Cl$		TFA	20	86
		p-TsOH	24	70
$Ph-\equiv-SPh$		TFA	15	80
		p-TsOH	24	75
t-$Bu-\equiv-SMe$		TFA	16	85
		p-TsOH	12	75
		TFA	25	85
		p-TsOH	30	87
		p-TsOH	30	51

a) Refer to isolated yields by column chromatography; b) All thiolesters prepared exhibit spectral properties (^1H NMR, ^{13}C NMR, IR and GC/Ms) according with the assigned structures.

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References and Notes

1. Mukaiyama, T.; Araki, M.; Takei, H. *J. Am. Chem. Soc.* **1973**, *95*, 4763.
2. (a) McGarvey, G. et al. *J. Am. Chem,. Soc.* **1986**, *108*, 4943.
   (b) Conrow, R.; Portoghese, P. *J. Org. Chem.* **1986**, *51*, 938.
3. (a) Kobayashi, S.; Uchiro, H.; Fujishita, Y.; Shiina, I.; Mukaiyama, T. *J. Am. Chem. Soc.* **1991**, *113*, 4247.
   (b) Suh, K-H.; Choo, D-J. *Tetrahedron Lett.* **1995**, *36*, 6109.
4. Baca, M.; Muir, T.; Schnolzer, M.; Kent, S. *J. Am. Chem. Soc.* **1995**, *117*, 1881.
5. Chou, W-C.; Fang, J-M. *J. Org. Chem.* **1996**, *61*, 1473.
6. (a) Barrett, A. G. M.; Grabcski, G. G.; Russell, M. A. *J. Org. Chem.* **1986**, *51*, 1012.
   (b) Uemura, S.; Takahashi, H.; Ohe, K.; Sugita, N. *J. Organomet. Chem.* **1989**, *361*, 63.
   (c) Khumtaveeporn, K.; Alper, H. *J. Org. Chem.* **1994**, *59*, 1414.
   (d) Inoue, T.; Takanobu, T.; Kambe, A; Ogawa, A.; Ryu, I.; Sonoda, N. *J. Org. Chem.* **1994**, *59*, 5824.
7. (a) Spessard, G. O.; Masamune, S.; Chan, W. K. *Org. Synth., Coll. Vol VII* **1990**, 81 and 87.
   (b)Adamczyk, M.; Fishpaugh, J. R. *Tetrahedron Lett.* **1996**, *37*, 4305.
8. Typical Procedure for thiolester **2a**: To a round flask was added 1-(methylthio)-2-phenyletyne **1a** (0.148 g; 1 mmol), 5 mL of dichloromethane, p-TsOH (0.19 g; 1.1 mmol) and 1 g of silica. The resulting suspension was heated at 40 °C. After 10 h, 5.0 mL of dichoromethane was added and the silica removed by filtration. The solvent was removed and the residue was purified by column chromatography over silica eluting with hexane to give 0.143 g (86 %). ^1H NMR (200 MHz, $CDCl_3$): δ ppm 2.25 (s, 3H); 3.80 (s, 2H); 7.24-7.32 (m, 5H); m/z (CG/MS): 166 (13%, M^+), 138, 119, 91(100%); IR (neat) ν (C=O) 1670 cm^{-1}.
9. (a) Braga, A. L.; Reckziegel, A.; Menezes, P. H.; Silveira, C. C. *Tetrahedron Lett*, **1993**, *34*, 8041.
   (b) Brandsma, L. *Preparative Acetylenic Chemistry*; Elsevier: Amsterdam, **1988**, pp. 129-141.