Tetrahedron Letters, Vol. 34, No. 5, pp. 873-876, 1993
Printed in Great Britain

0040-4039/93 $6.00 + .00
Pergamon Press Ltd

Bis(trimethylsilyl)sulfide based Thionation of Carbonyl Compounds: Synthesis of Thioketones.

Alessandro Degl'Innocenti*[a], Antonella Capperucci*[b], Alessandro Mordini[c], Gianna Reginato[c], Alfredo Ricci[c,d] and Francesca Cerreta[b].

[a]Dipartimento di Chimica, Via N. Sauro 85, 85100 Potenza, Italy. [b]Dipartimento di Chimica Organica Ugo Schiff and [c]Centro C.N.R. sulla Chimica e la Struttura dei Composti Eterociclici, Via G. Capponi 9, 50121 Firenze, Italy. [d]Dipartimento di Chimica Organica, Viale Risorgimento 4, 40136 Bologna, Italy.

Abstract: A wide range of thioketones may be conveniently obtained by silyl triflate promoted bis(trimethylsilyl)sulfide thionation of ketones.

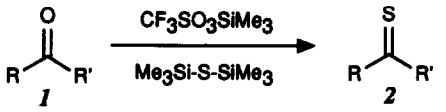
The interest in thiocarbonyl containing molecules has recently seen an increasing growth due to interesting applications of this group in the synthesis of complex natural products[1].

Many methods for the synthesis of thioketones have appeared in the literature, ranging from photochemical to thermolytic techniques[2], the most synthetically useful being those based on the direct conversion of carbonyl derivatives into the corresponding thiono derivatives[2,3]. Anyway, unless sterically or electronically stabilized, these compounds show a great tendency to oligomerize or polymerize. More recently some other methodologies have been developed[4] for the synthesis of such highly reactive compounds, thus demonstrating the still present need to find milder conditions for their generation.

We recently reported a novel $CoCl_2.6H_2O$ or $CF_3SO_3SiMe_3$ induced thionation of aldehydes with bis(trimethylsilyl)sulfide[5] that allows the synthesis and the "in situ" trapping of those elusive compounds such as thioaldehydes. While $CoCl_2.6H_2O$ proved ineffective to induce the bis(trimethylsilyl)sulfide based thionation of ketones, trimethylsilyltriflate has been able to promote the thionation of some ketones.

We want to report in this communication on the development of this new thionation procedure, that affords, in mild conditions, a general synthesis of a wide range of thioketones, including aliphatic and α,β-unsaturated compounds.

Relevant results are summmarized in the Table.



Scheme 1

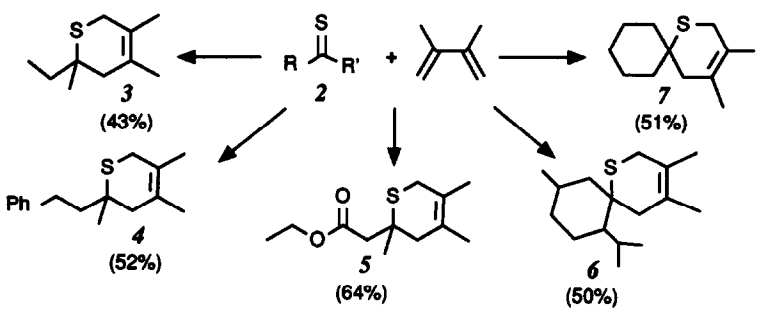
Treatment, as an example, of a solution of 2-adamantanone ***1h*** (100 mg, 0.67 mmol) and bis(trimethylsilyl)sulfide (238.5 mg, 1.34 mmol) in 2.8 mL of CH_3CN with $CF_3SO_3SiMe_3$ (29.5 mg, 0.13 mmol) under stirring at room temperature for 8 h affords, after $NaHCO_3$ work up, 2-adamantanethione ***2h*** in 68% yield[6].

Outstanding features of this reactivity are the very mild reaction conditions, which allow the synthesis of a wide range of thioketones, and the possibility of minimizing side reactions through a strict control of the stoichiometry of the thionating agent, $Me_3Si\text{-}S\text{-}SiMe_3$.

Acetonitrile proved to be the most efficient solvent, even though the reaction can be equally performed in methylene chloride, albeit with a relevant slowing of the reaction rate.

As expected when thionating the more reactive and less hindered ketones ***1a-c***, ***1f*** only their oligomers can be obtained, while compounds ***1d***, ***1e***, ***1g***, ***1h*** and ***1i*** smoothly afforded the isolation of the thioketones. In this context the synthesis of thiomenthone ***2i*** should be noted. To the best of our knowledge this particular compound has always been observed in its enethiol form[7]. Thanks to the mildness of the present methodology, this compound is obtained as a 1 : 1 mixture of thioketone : enethiol[8].

Noteworthy, in the present conditions thioketones obtained may be trapped "in situ" as the corresponding cycloadducts. Thus for istance ketones ***1b, d, f, g, i***, when reacted with $(Me_3Si)_2S$ in the presence of 2,3-dimethyl-1,3-butadiene, afford the corresponding functionalized dihydrothiopyrans[9] (Scheme 2).

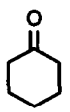
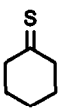
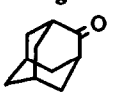
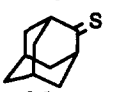
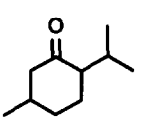
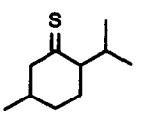
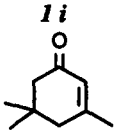
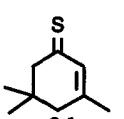
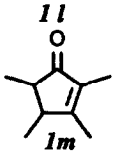
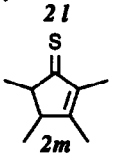
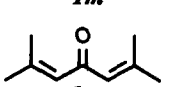
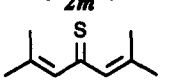


Scheme 2

The synthesis of the cycloadduct ***5*** outlines the chemoselectivity of the present methodology, which allows the selective thionation of the keto functionality in the presence of the ester group, as shown in Scheme 2.

Finally this procedure even allows the synthesis of α,β-unsaturated thioketones, a class of compounds still not readily accessible[10]. As shown by ketones ***1l-n*** in the Table, in this case, as already observed by

Table. Synthesis of Thioketones

Ketone	Product [a]	Conditions	Yield (%)[b]
CH_3COCH_3 *1a*	CH_3CSCH_3 *2a*	1 h	88 [c]
$CH_3COC_2H_5$ *1b*	$CH_3CSC_2H_5$ *2b*	2 h	85 [c]
$(CH_3)_2CHCOCH_3$ *1c*	$(CH_3)_2CHCSCH_3$ *2c*	2 h	76 [c]
$CH_3COCH_2CH_2Ph$ *1d*	$CH_3CSCH_2CH_2Ph$ *2d*	2 h	60 [d]
$(CH_3)_3CCOCH_3$ *1e*	$(CH_3)_3CCSCH_3$ *2e*	6 h	54
 *1f*	 *2f*	9 h	61 [c]
$C_2H_5OCOCH_2COCH_3$ *1g*	$C_2H_5OCOCH_2CSCH_3$ *2g*	10 h	57
 *1h*	 *2h*	8 h	68
 *1i*	 *2i*	12 h	40 [e]
 *1l*	 *2l*	23 h	48
 *1m*	 *2m*	24 h	47
 *1n*	 *2n*	22 h	51 [f]

[a] All compounds showed spectroscopical data consistent with the assigned structure. [b] Yields of isolated material. [c] Isolated as the trimer. [d] 20% of the trimer was isolated. [e] 40% of the enethiol as well as 10% of di- 3-(menth-3-ene)sulfide were isolated. ^{13}C NMR (C=S) δ 264 ppm. [f] 20% of 2,6-dimethyl-2-hepten-6-thiol-4-one was detected.

Metzner et Vialle[10], the β-position of the enone must be sterically hindered to avoid the formation of the corresponding Michael adduct, thus evidencing a limitation of this procedure.

In conclusion this new thionation procedure compares well to the ones already reported in the literature and, for the mild conditions employed, can be the methodology of choice for rather sensitive substrates.

REFERENCES AND NOTES.

1. Ireland, R.E.; Brown, F.R.,Jr. *J. Org. Chem.* **1980**, *45*, 1868. Vedejs, E.; Reid, J.G. *J. Org. Chem.* **1987**, *52*, 4269. Vedejs, E.; Fedde, C.L.; Schwartz, C.E. *J. Am. Chem. Soc.*, **1984**, *106*, 4617.
2. Nader, R.G.; Kaloustian, M.K. *Tetrahedron Lett.* **1979**, 1477. Duus, F. in *Comprehensive Organic Chemistry*; Jones, D. Neville, Ed.; Pergamon Press: Oxford, 1979. Klages, C.P.; Voss, J. *Chem. Ber.* **1980**, *113*, 2255.
3. Mrani, M. *J. Am. Chem. Soc.* **1982**, *104*, 3104. Cava, M.P.; Levinson, M.I. *Tetrahedron*, **1985**, *41*, 5061.
4. Schaumann, E.; Winter-Extra, S.; Ruther, G. *J. Org. Chem.* **1990**, *55*, 4200. Sato, R.; Satoh, S.-i. *Synthesis* **1991**, 785.
5. Capperucci, A.; Degl'Innocenti, A.; Ricci, A.; Mordini, A.; Reginato, G. *J. Org. Chem.* **1991**, *56*, 7363 and references cited therein.
6. GC/MS: m/z (%) 166 (M^+, 100), 133 (46), 125 (39), 124 (49), 97 (37), 91 (96), 79 (88), 77 (80), 71 (89), 65 (49), 53 (55), 51 (48). ^{13}C NMR δ: C=S 271 ppm.
7. Paquer, D.; Vialle, J. *Bull. Soc. Chim. Fr.* **1969**, 3595. Paquer, D.; Morin, L.; Vazeux, M.; Andrieu, C.G. *Recl. Trav. Chim. Pays-Bas*, **1981**, *100*, 52.
8. Determined by GC/MS analysis.
9. Typical procedure: a solution of ethylacetoacetate ***1g*** (100 mg, 0.77 mmol), bis(trimethylsilyl)sulfide (274 mg, 1.54 mmol) and 2,3-dimethyl-1,3-butadiene (190 mg, 2.30 mmol) in 3 mL of CH_3CN is treated with $CF_3SO_3SiMe_3$(34 mg, 0.15 mmol) and stirred for 16 h. After $NaHCO_3$ work up and TLC purification (petroleum ether/ethyl acetate 10:1) 113 mg of the corresponding cycloadduct *5* are obtained (64% yield). GC/MS: m/z (%) 228 (M^+, 70), 141 (44), 140 (50), 139 (49), 125 (78), 121 (100), 113 (36), 107 (48), 79 (23), 67 (25), 59 (37), 55 (25), 53 (29). ^1H NMR δ (ppm): 1.25 (t, 3H, J= 7.2 Hz), 1.42 (s, 3H), 1.66 (bs, 3H), 1.73 (bs, 3H), 2.23-2.27 (m, 2H), 2.52 (A part of an AB system, 1H, J= 13.7 Hz), 2.61 (B part of an AB system, 1H, J= 13.7 Hz), 2.95 (A part of an AB system, 1H, J= 17 Hz), 3.22 (B part of an AB system, 1H, J= 17 Hz), 4.19 (q, 2H, J= 7.2Hz).
10. Metzner, P.; Vialle, J. *Bull. Soc. Chim. Fr.* **1972**, 3138 and references cited therein. Saito, T.; Nagashima, T.; Motoki, S. *J. Chem. Soc., Chem. Commun.* **1990**, 1665.

(Received in UK 16 November 1992)