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$H_2O_2/SOCl_2$: a useful reagent system for the conversion of thiocarbonyls to carbonyl compounds

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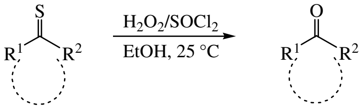
ABSTRACT

The $H_2O_2/SOCl_2$ reagent system has been used as a new and efficient reagent for deprotection of thiocarbonyls to carbonyl compounds. The salient features of this protocol are short reaction times, good chemoselectivity, clean reaction profiles, and simple work-up that preclude the use of toxic solvents.

1. Introduction

Evolution of clean and environmentally benign chemical processes using less hazardous catalysts has become a primary goal in synthetic organic chemistry. The formation of amide bonds constitutes a widely used process for both synthetic organic chemists and biologists. Amide linkages are present in many biologically active molecules and key natural products and hence, a variety of methods for the synthesis of this functionality have been developed to date.[1–15] However, the different reagents used for this conversion have varying degree of success as well as limitations due to side reactions. To circumvent these problems, alternative strategies toward the preparation of amides have been explored for years.

As part of our continuing studies on the use of hydrogen peroxide in organic synthesis.[16] We now wish to report a reasonably simple and efficient method to desulfurise thiocarbonyls to their oxo analogues using H_2O_2 in the presence of $SOCl_2$ in excellent yields (Scheme 1).

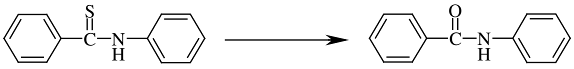


Scheme 1.

2. Results and discussion

Among various solvents like acetonitrile, ethanol, chloroform, diethyl ether and THF used for this transformation, ethanol and acetonitrile were the solvents of choice as best results were obtained with them. To optimize the reaction conditions, the reaction of *N*-phenyl benzothiomide was selected as model to examine the effects of different amount of H_2O_2 and $SOCl_2$ in ethanol at room temperature. As shown in Table 1, the use of $SOCl_2$ is essential for the success of the reaction because H_2O_2 oxidizes thioamides rather slowly. Furthermore, $SOCl_2$ is effective agent only in the presence of H_2O_2. The best result (98% yield) was obtained by carrying out the reaction with 1:2:1 mol ratios of thioamide, H_2O_2 and $SOCl_2$ for 1 min.

Table 1
Effect of increasing amount of $SOCl_2$ on oxidation of *N*-phenyl benzothiomide using H_2O_2[a]



Entry	$SOCl_2$	H_2O_2	Yield[b] %
1	0	4	20
2	0.6	3	65
3	0.8	2	76
4	1	2	98
5	1	0	10

[a] Reaction conditions: the reactions were performed with *N*-phenyl benzothiomide (1 mmol) for 1 min, at 25 °C.
[b] Isolated yields.

Using the optimized reaction conditions, the reactions of various thioamides were investigated. All the reactions proceeded smoothly and fast to give the corresponding amides in excellent yields (Table 2).

Most importantly, thioamides carrying either electron-donating or electron-withdrawing substituents reacted very well to give the corresponding amides in excellent yields with high purity (monitored by ^1H NMR spectroscopy). Meanwhile, the protocol is fairly

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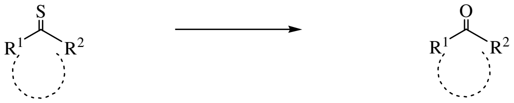
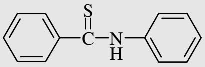
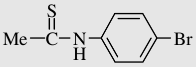
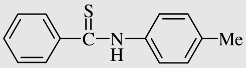
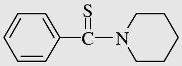
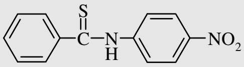
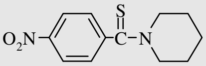
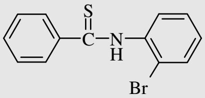
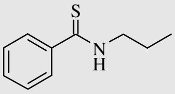
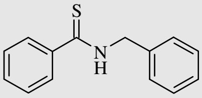
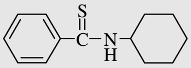
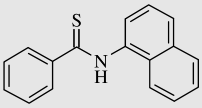
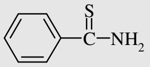
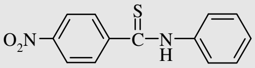
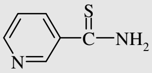
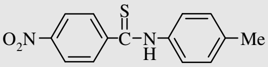
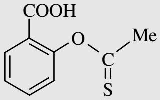
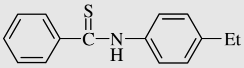
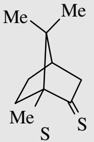
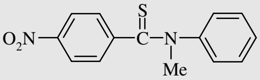
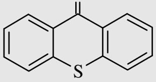
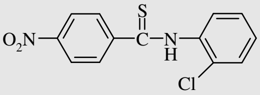
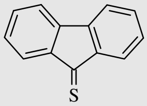
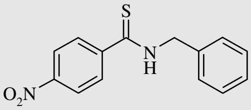
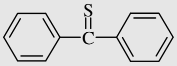
Table 2
Desulfurization of thiocarbonyls using $H_2O_2/SOCl_2$ reagent system[a]

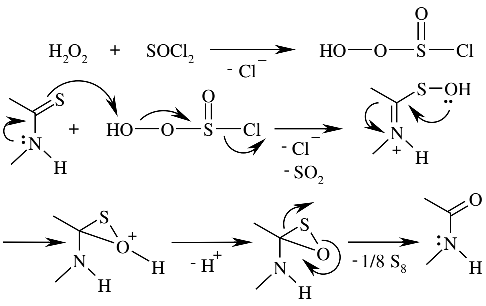


Entry	Thiocarbonyl	Yield[b] % (t/min)	Mp (lit.)[Ref]/°C	Entry	Thiocarbonyl	Yield[b] % (t/min)	Mp (lit.)[Ref]/°C
1		98 (1)	163 (163)[4]	13		94 (1)	165–167 (168)[4]
2		94 (1)	158–159 (157–158)[4]	14		97 (1)	138–140 (140)[7b]
3		96 (1)	195 (198–199)[4]	15		97 (1)	121 (122–125)[7b]
4		93 (2)	112–115 (116)[17a]	16		95 (2)	83 (83–84)[7d]
5		97 (1)	103 (105–106)[7c]	17		94 (1)	144 (147)[21]
6		93 (2)	163 (164–165)[18]	18		95 (1)	127 (129)[12]
7		95 (1)	208 (211–212)[4]	19		94 (1)	129 (126)[12]
8		96 (1)	200–202 (201–203)[1]	20		95 (1)	133 (135)[17b]
9		94 (2)	149 (150–151)[19]	21		95 (1)	181 (180–182)[12]
10		94 (2)	105 (106–107)[4]	22		97 (2)	209 (213)[6]
11		96 (1)	157–158 (159–160)[4]	23		93 (2)	80 (84)[12]
12		96 (1)	139–140 (140–143)[20]	24		94 (2)	48–49 (49)[12]

[a] The products were characterized by comparison of their spectroscopic and physical data with authentic samples synthesized by reported procedures.
[b] Yields refer to pure isolated products.

general and several functionalities including nitro, carboxyl, sulfur and halide do survive during the course of the reaction. As shown in Table 2, *N*,*N*-disubstituted thioamide worked well without the formation of any side product and afforded the desired product in 94% yield (entry 10). Primary, secondary and tertiary thioamides undergo this reaction with equal efficiency. For example, benzamide is produced in 95% yield, *N*-phenyl benzamide in 98% yield and *N*-methyl-4-nitro-*N*-phenylbenzamide in 94% yield.

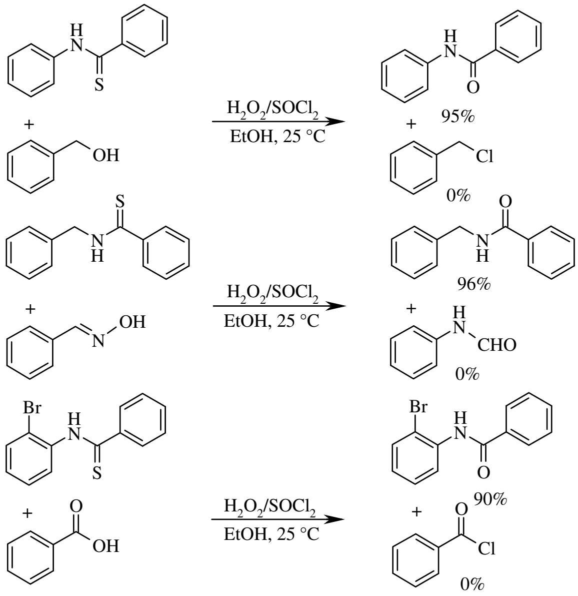
The possible mechanism for this reaction is outlined in Scheme 2. It is acceptable to assume that the nucleophilic attack of H_2O_2 on $SOCl_2$ makes oxygen atom more electrophilic. Therefore, the mechanism proceeds probably through a cyclic intermediate that undergoes sulfur extrusion.



Scheme 2. Proposed mechanism for the desulfurization of thioamides.

Thioketones and a thioester, under similar conditions for thioamides, also underwent the reaction, affording the corresponding products in excellent yields (Table 2, entries 20–24).

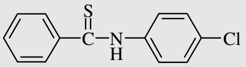
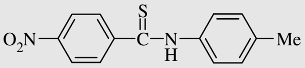
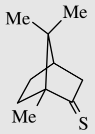
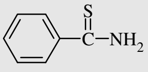
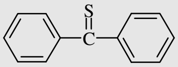
In order to evaluate the selectivity of this reagent system, we studied the desulfurization of thioamides in the presence of alcohol, oxime and acid. The results are depicted in Scheme 3.



Scheme 3. Reagents and conditions: molar ratio of substrates to H_2O_2 to $SOCl_2$ (1:1:2:1), EtOH, 25 °C.

A comparison of the efficiency of this method with selected previously methods is collected in Table 3. As can be seen, our method is simpler, more efficient, and uses no toxic solvents.

Table 3
Comparison of desulfurization of thiocarbonyls by the $H_2O_2/SOCl_2$ reagent system with some of those reported in the literature

Entry	Thiocarbonyl	Conditions	Time	Yield (%)
1		$H_2O_2/SOCl_2$/EtOH/rt	3 min	98
2		Caro's acid/SiO_2 /CH_3CN/40 °C[5]	5 h	61
3		$H_2O_2/SOCl_2$/EtOH/rt	1 min	96
4		Oxone/$MgSO_4$/ball milling/rt[1]	90 min	78
5		$H_2O_2/SOCl_2$/EtOH/rt	1 min	95
6		$NOBF_4/CH_2Cl_2$/rt[12]	3 h	88
7		$(4\text{-}MeOC_6H_4)_2$ Te=O[a]/$CHCl_3$/rt[22]	Mixture of products	
8		$H_2O_2/SOCl_2$/EtOH/rt	1 min	95
9		t-BuOK/I_2/t-BuOH/ reflux[14]	40 h	90
10		$NOBF_4/CH_2Cl_2$/rt[12]	8 h	76
11		$H_2O_2/SOCl_2$/EtOH/rt	2 min	94
12		Clyfen/MW[23]	1.5 min	60

[a] Bis(p-methoxyphenyl) telluroxide.

3. Conclusion

In conclusion, $H_2O_2/SOCl_2$ is an efficient reagent system for the conversion of thiocarbonyls to carbonyl compounds. The advantages are high chemoselectivity, environmentally efficient, excellent yields, fast reaction, low cost, and operation at room temperature. This methodology also overcomes the formation of unwanted by-products, and the use of hazardous solvents, thus, we believe that the present methodology could be an important addition to the existing methodologies.

4. Experimental

4.1. General remark

The thiocarbonyl compounds are either commercially available or were prepared as follows: thioamides from the reaction of the corresponding amides with P_4S_{10},[24] thioketones and thioester from the reaction of the corresponding carbonyl compounds with Lawesson's reagent.[25] Melting points were determined in a capillary tube. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker-200 NMR spectrometer using TMS as internal standard.

4.2. General procedure for deprotection of thioamides to amides

A mixture of thiocarbonyl comopund (2 mmol), H_2O_2 (30%, 4 mmol, 0.4 mL) and $SOCl_2$ (2 mmol, 0.14 mL) was stirred in EtOH at 25 °C for an appropriate time (Table 2). A yellow solid, (elemental sulfur, mp 120 °C) immediately precipitated. After completion of the reaction as indicated by TLC, the reaction mixture was filtered to give elemental sulfur. The filtrate was poured into water (10 mL), extracted with ethyl acetate (4×5 mL) and the extract dried with anhydrous $MgSO_4$. The filtrate was evaporated under vacuum to afford the analytically pure product (Table 2).

All of products are known compounds and characterized easily by comparison with authentic samples (^1H NMR, ^{13}C NMR, mp).

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.06.110.

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