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Efficient and Convenient Deprotection of Thiocarbonyl to Carbonyl Compounds Using 3-Carboxypyridinium and 2,2′-Bipyridinium Chlorochromates in Solution, Dry Media, and under Microwave Irradiation

Iraj Mohammadpoor-Baltork*, **Hamid Reza Memarian**, and **Kiumars Bahrami**

Department of Chemistry, Isfahan University, Isfahan 81746-73441, Iran

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Summary. A synthetic utility of 3-carboxypyridinium (*CPCC*) and 2,2′-bipyridinium (*BPCC*) chlorochromates in deprotection reactions is reported. Different types of thioamides, thioureas, thiono esters, and thioketones are deprotected to their corresponding carbonyl compounds with these reagents in good to excellent yields. The reactions were carried out in solution, under solvent-free conditions, and under microwave irradiation. The results show that with both reagents the rates of the reactions and the yields are usually highest under microwave irradiation.

Keywords. Chlorochromates; Deprotection; Thiocarbonyl compounds; Carbonyl compounds.

Introduction

Protection and deprotection of functional groups is of importance in organic synthesis. The conversion of thiocarbonyls to their corresponding carbonyl compounds is an important chemical transformation. Several methods and reagents, such as bromate and iodate solutions [1], dimethyl selenoxide [2], sodium peroxide [3], diaryl selenoxide [4], *t*-butyl hypochlorite [5], benzeneseleninic anhydride [6], $NOBF_4$ [7], thiophosgene [8], tetrabutylammonium hydrogensulfate/NaOH [9], dimethyl sulfoxide/iodine [10], soft NO^+ species [11], *m*-chloroperbenzoic acid [12], trifluoroacetic anhydride [13], manganese dioxide [14], diaryl telluroxide [15], clay supported ferric nitrate [16], *N*-nitrosamines [17], *p*-nitrobenzaldehyde/

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* Corresponding author. E-mail: Imbaltork@sci.ui.ac.ir

TMSOTf [18], 2-nitrobenzenesulfonyl chloride/potassium superoxide [19], clayfen or clayan/MW [20], and *Caro*'s acid supported on silica-gel [21] have been reported for this purpose. However, some of these methods are not suitable for deprotection of primary thioamides, and some of the others also show limitations such as long reaction times, low yields of the products, the use of expensive reagents, and tedious work-up.

We have recently reported bismuth(III) nitrate pentahydrate and oxone as convenient reagents for the deprotection of thioamides and thioureas [22]. However, bismuth(III) nitrate pentahydrate was not effective for the conversion of thiono esters and thioketones to their corresponding esters and ketones. With oxone thiono esters are converted to their esters while thioketones remained intact. In continuation of our research in this area, we were interested to find an efficient method for the deprotection of all the above mentioned thiocarbonyl compounds. In this respect, we wish to report, that 3-carboxypyridinium (*CPCC*) and 2,2′-bipyridinium (*BPCC*) chlorochromates are able to transform thiocarbonyls to their carbonyl compounds efficiently under different reaction conditions.

Results and Discussion

Deprotection Reactions with CPCC

3-Carboxypyridinium chlorochromate (*CPCC*) is an inexpensive and easily prepared reagent. Several synthetically useful organic transformations such as cleavage of the carbon-nitrogen double bonds [23], oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers [24], and oxidation of 1,4-dihydropyridines [25] have been previously reported.

In this paper, at first the deprotection of thioamides, thioureas, thiono esters, and thioketones with *CPCC* was investigated using refluxing acetonitrile. As shown in Table 1, **1a**–**1z**, **1a′**–**1l′** were reacted with 2 molar equivalents of the reagent to afford the corresponding carbonyl compounds **2a**–**2z**, **2a′**–**2l′** in 68–97% yields within 2–120 min. The deprotection of these thiocarbonyl compounds was also performed under solvent-free conditions with 2.5 molar equivalents of the reagent. Under these conditions, the carbonyl compounds were obtained in 60–95% yields within 3–40 min. It is important to note that grinding is necessary for the reactions to proceed in high yields. The reactions without grinding resulted in low yields, 15–25%, even on heating. Finally, the transformation of thiocarbonyls to their carbonyl compounds was investigated under microwave irradiation. The deprotection was carried out in the presence of 2 molar equivalents of *CPCC* with reaction periods ranging between 1–20 min and the pure products were obtained in 80–98% yields. Under microwave irradiation, acetonitrile was used for homogenization of the reaction mixture. The polar character of this solvent also seems to increase the reaction temperature, so the reaction is completed in a short time [26]. The results show that the rate of the reactions and the yields are usually higher under microwave irradiation compared to solution and solvent-free reactions (Scheme 1).

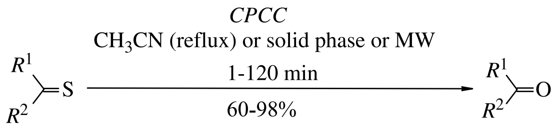
Table 1. Conversion of thiocarbonyl to carbonyl group with *CPCC*

Substrate	Product	Yield/%[a] (t/min)			$\bar{\nu}$/cm^{-1}	Mp or bp [31]
		Solution	Solid-phase	MW		
1a	**2a**	94 (7)	93 (15)	95 (2)	3340, 3168, 1680	82
1b	**2b**	93 (10)	92 (15)	95 (2)	3440, 3350, 1682	131–132
1c	**2c**	91 (5)	93 (15)	93 (2)	3415, 3245, 1685	95
1d	**2d**	94 (10)	92 (15)	98 (2)	3420, 3315, 1658	145–146
1e	**2e**	91 (3)	91 (13)	96 (2)	3326, 1648	238–239
1f	**2f**	93 (30)	91 (20)	94 (5)	3385, 3190, 1665	>320
1g	**2g**	93 (2)	92 (12)	94 (1)	3312, 1662	154–156
1h	**2h**	93 (3)	90 (7)	96 (8)	3330, 1650	163
1i	**2i**	96 (5)	92 (5)	97 (5)	3312, 1638	105–106
1j	**2j**	94 (10)	90 (15)	94 (6)	3424, 1650	60–61
1k	**2k**	96 (10)	94 (20)	97 (7)	3240,1648	143
1l	**2l**	92 (10)	95 (10)	95 (6)	3324, 1645	153
1m	**2m**	96 (15)	93 (5)	96 (5)	3310, 1647	157–158
1n	**2n**	97 (20)	93 (10)	97 (6)	3325, 1644	202–203
1o	**2o**	91 (30)	92 (30)	93 (13)	3330, 1657	198–199
1p	**2p**	95 (5)	92 (10)	96 (5)	3340, 1648	145
1q	**2q**	90 (70)	90 (20)	92 (12)	3320, 1650	211–212
1r	**2r**	94 (10)	92 (20)	94 (10)	3300, 1645	146–148
1s	**2s**	92 (50)	90 (40)	94 (10)	3285, 1646	153–155
1t	**2t**	95 (70)	90 (40)	95 (12)	3285, 1655	159–160
1u	**2u**	96 (35)	93 (30)	96 (7)	3376, 1658	130–131
1v	**2v**	96 (15)	91 (10)	96 (3)	3248, 1640	171–173
1w	**2w**	96 (2)	91 (3)	96 (2)	3312, 1667	168
1x	**2x**	90 (2)	90 (3)	93 (2)	3405, 1680	215–216
1y	**2y**	91 (40)	91 (25)	95 (13)	3280, 1651	232
1z	**2z**	96 (30)	90 (25)	96 (10)	3320, 1644	238–240
1a′	**2a′**	85 (75)	70 (30)	97 (10)	1650	101–103
1b′	**2b′**	90 (20)	92 (20)	92 (3)	3210, 1750, 1714	247
1c′	**2c′**	70 (120)	60 (35)	80 (20)	1646	106–107
1d′	**2d′**	70 (120)	60 (30)	96 (15)	1637	127–130
1e′	**2e′**	68 (120)	60 (35)	97 (15)	1638	89–90
1f′	**2f′**	91 (10)	90 (10)	92 (2)	1720	210–212/760
1g′	**2g′**	90 (10)	90 (10)	92 (2)	1725	196–197/760
1h′	**2h′**	96 (15)	92 (20)	96 (2)	1653	75–77
1i′	**2i′**	86 (40)	85 (35)	97 (12)	1650	136–137
1j′	**2j′**	90 (20)	90 (15)	93 (2)	1650	49
1k′	**2k′**	85 (25)	87 (25)	96 (2)	1660	41–43
1l′	**2l′**	90 (10)	90 (15)	94 (2)	1715	82–84

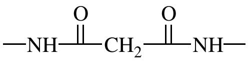
[a] Isolated yields

Deprotection Reactions with BPCC

2,2′-Bipyridinium chlorochromate (*BPCC*) is a commercially available oxidizing agent and has been used for the oxidation of different organic compounds [27, 28].



1a-1z, 1a′-1l′ **2a-2z, 2a′-2l′**

1, 2	R^1	R^2	**1, 2**	R^1	R^2
a	*Me*	NH_2	**v**	1-NaphthylNH	4-*Me*C_6H_4
b	NH_2	NH_2	**w**	4-BrC_6H_4NH	*Me*
c	NH_2	$NHNH_2$	**x**	4-$NO_2C_6H_4$NH	*Me*
d	NH_2	NHPh	**y**	3,5-$(NO_2)_2C_6H_3$	NH*Ph*
e	*Ph*NH	NH*Ph*	**z**	3,5-$(NO_2)_2C_6H_3$	2-*Me*C_6H_4NH
f	$H_2NC{=}S$	NH_2	**a′**	*Me*	*Me*N*Ph*
g	*Ph*N=N	NHNH*Ph*	**b′**	 $-NH-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-NH-$	
h	*Ph*NH	*Ph*			
i	*Ph*CH_2NH	*Ph*			
j	2-*Me*OC_6H_4NH	*Ph*	**c′**	4-$NO_2C_6H_4$	*Me*N*Ph*
k	2-*Me*C_6H_4NH	*Ph*	**d′**	3,5-$(NO_2)_2C_6H_3$	N(*Me*)$_2$
l	4-*Me*OC_6H_4NH	*Ph*	**e′**	3,5-$(NO_2)_2C_6H_3$	N(*Et*)$_2$
m	4-*Me*C_6H_4NH	*Ph*	**f′**	*Ph*	O*Et*
n	4-BrC_6H_4NH	*Ph*	**g′**	*Ph*	O*Me*
o	4-$NO_2C_6H_4$NH	*Ph*	**h′**	4-ClC_6H_4	*Ph*
p	4-*Me*C_6H_4	NH*Ph*	**i′**	4-$NO_2C_6H_4$	*Ph*
q	4-$NO_2C_6H_4$	NH*Ph*	**j′**	*Ph*	*Ph*
r	2-*Me*OC_6H_4NH	4-$NO_2C_6H_4$	**k′**	2-Pyridyl	*Ph*
s	2-*Me*C_6H_4NH	4-$NO_2C_6H_4$	**l′**	$2-C_6H_4-2-C_6H_4$	
t	2-ClC_6H_4NH	4-$NO_2C_6H_4$			
u	4-*Me*C_6H_4NH	2-ClC_6H_4			

Scheme 1

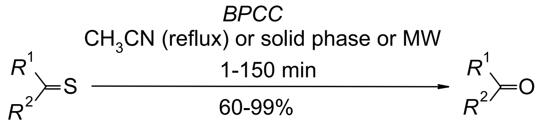
As with *CPCC*, the deprotection reactions with this reagent were investigated in solution, under solvent-free conditions, and under microwave irradiation. The treatment of a variety of thioamides, thioureas, thiono esters and thioketones **1a**–**1z**, **1a**′–**1l**′ with 2.5 molar equivalents of *BPCC* in refluxing acetonitrile afforded the corresponding carbonyl compounds **2a**–**2z**, **2a**′–**2l**′ in 68–98% yields within 2–150 min (Table 2). Under solvent-free conditions these reactions proceeded within 2–40 min in the presence of 3 molar equivalents of the reagent, and the corresponding carbonyl compounds were obtained in 60–95% yields. The deprotection was also carried out under microwave irradiation in the presence of 2.5 molar equivalents of *BPCC* and the pure carbonyl compounds were obtained in 80–99% yields after 1–20 min (Scheme 2). Under microwave irradiation, as with *CPCC* the reaction times are shorter and the yields are higher.

Table 2. Conversion of thiocarbonyl to carbonyl group with *BPCC*

Substrate	Product	Yield/%[a] (*t*/min)		
		Solution	Solid-phase	MW
1a	**2a**	94 (10)	93 (15)	94 (2)
1b	**2b**	94 (10)	93 (15)	94 (2)
1c	**2c**	93 (5)	91 (13)	95 (3)
1d	**2d**	93 (10)	90 (15)	95 (2)
1e	**2e**	90 (5)	89 (13)	95 (2)
1f	**2f**	93 (30)	92 (20)	94 (5)
1g	**2g**	92 (2)	92 (2)	93 (1)
1h	**2h**	90 (3)	91 (5)	95 (9)
1i	**2i**	96 (7)	93 (5)	96 (5)
1j	**2j**	92 (15)	90 (12)	92 (6)
1k	**2k**	95 (15)	94 (25)	95 (7)
1l	**2l**	92 (15)	91 (10)	94 (7)
1m	**2m**	98 (20)	95 (10)	99 (7)
1n	**2n**	95 (20)	93 (5)	95 (7)
1o	**2o**	93 (35)	90 (30)	93 (12)
1p	**2p**	92 (5)	92 (10)	98 (5)
1q	**2q**	91 (90)	93 (30)	94 (12)
1r	**2r**	92 (10)	93 (15)	94 (10)
1s	**2s**	94 (60)	90 (35)	92 (10)
1t	**2t**	93 (75)	91 (40)	93 (14)
1u	**2u**	95 (40)	92 (30)	95 (7)
1v	**2v**	90 (5)	95 (5)	96 (3)
1w	**2w**	96 (2)	93 (5)	96 (3)
1x	**2x**	91 (2)	90 (3)	93 (3)
1y	**2y**	92 (50)	90 (15)	92 (10)
1z	**2z**	97 (30)	90 (25)	93 (10)
1a′	**2a′**	86 (150)	85 (30)	93 (10)
1b′	**2b′**	92 (25)	93 (15)	93 (2)
1c′	**2c′**	70 (120)	63 (30)	80 (20)
1d′	**2d′**	70 (120)	60 (30)	98 (15)
1e′	**2e′**	68 (120)	60 (35)	98 (15)
1f′	**2f′**	92 (10)	90 (10)	93 (3)
1g′	**2g′**	91 (10)	91 (10)	91 (3)
1h′	**2h′**	94 (20)	94 (20)	96 (3)
1i′	**2i′**	80 (40)	85 (35)	94 (12)
1j′	**2j′**	92 (20)	91 (15)	97 (3)
1k′	**2k′**	85 (30)	85 (20)	92 (3)
1l′	**2l′**	90 (15)	92 (15)	93 (3)

[a] Isolated yields

In order to show the advantage of 2,2′-bipyridinium chlorochromate (*BPCC*) over pyridinium chlorochromate (*PCC*), we compared the results obtained for some of the reactions using these two reagents. It was found that in comparison with pyridinium chlorochromate, the yields of the reactions are considerably higher with 2,2′-bipyridinium chlorochromate (Table 3).



1a-1z, 1a′-11′ **2a-2z, 2a′-21′**

Scheme 2

Table 3. Comparison of some of the results obtained with *BPCC* and *PCC*

Substrate	Product	*BPCC*:Yield/%[a] (*t*/min)			*PCC*:Yield/%[a] (*t*/min)		
		Solution	Solid-phase	MW	Solution	Solid-phase	MW
1j	**2j**	92 (15)	90 (12)	92 (6)	55 (40)	30 (12)	75 (6)
1p	**2p**	92 (5)	92 (10)	98 (5)	62 (40)	32 (10)	81 (5)
1s	**2s**	94 (60)	90 (35)	92 (10)	63 (60)	35 (35)	60 (10)

[a] Isolated yields

Varma et al. have also reported the deprotection of thioketones under microwave irradiation [20]. Although, in one case (compound **1j**′) the results of the present work are comparable to that of *Varma et al.*, this similarity may be expected for other thioketones too. However, in this work we have investigated the deprotection of other thiocarbonyl compounds including thioamides, thioureas, and thiono esters.

In conclusion, in this study a new and efficient procedure for the deprotection of thioamides, thioureas, thiono esters, and thioketonens is described. The method offers several advantages including high yields of the products, short reaction times, and experimental simplicity, which makes it a useful and attractive process for this transformation.

Experimental

The thiocarbonyl compounds are either commercially available or were prepared as following: thioamides from the reaction of the corresponding amides with P_4S_{10} [29]; thiono esters and thioketones from the reaction of the corresponding carbonyl compounds with *Lawesson*'s reagent [30]. Yields refer to isolated products. All of the products were characterized by comparison of their physical and spectral data with those of authentic samples. *CPCC* and *BPCC* were prepared according to the reported procedures [23, 27].

General Procedure for the Conversion of Thiocarbonyls to Carbonyl Compounds in Acetonitrile

In a 50 cm^3 round-bottomed flask a solution of 1 mmol of thiocarbonyl compound in 10 cm^3 of CH_3CN was treated with 2 mmol of *CPCC* or 2.5 mmol of *BPCC* and the reaction mixture was stirred under reflux for the time indicated in Tables 1 and 2. The progress of the reaction was monitored by TLC (CCl_4:EtOAc = 4:1). The reaction mixture was filtered and the solid material was washed with 15 cm^3 of CH_3CN. The filtrate was evaporated and the crude product was either recrystallized from *Et*OH/H_2O or purified by chromatography on silica gel to afford the pure product (Tables 1 and 2).

General Procedure for the Conversion of Thiocarbonyls to Carbonyl Compounds under Solvent-free Conditions

A mixture of 1 mmol of substrate and 2.5 mmol of *CPCC* or 3 mmol of *BPCC* in a mortar was prepared. The mixture was ground with a pestle for the length of time according to Tables 1 and 2. The progress of the reaction was monitored by TLC. The mixture was extracted with CH_2Cl_2. Evaporation of the solvent followed by recrystallization from *Et*OH/H_2O or chromatography on silica-gel afforded the pure product (Tables 1 and 2).

General Procedure for the Conversion of Thiocarbonyls to Carbonyl Compounds under Microwave Irradiation

Thiocarbonyl compound (1 mmol) and 2 mmol of *CPCC* or 2.5 mmol of *BPCC* were mixed and then 0.5 cm^3 of CH_3CN were added. The mixture was subjected to microwave irradiation at 900 W for the appropriate time according to Tables 1 and 2. After completion of the reaction (TLC), the mixture was extracted with CH_2Cl_2. The solvent was evaporated and the crude product was either recrystallized from *Et*OH/H_2O or subjected to chromatography on silica-gel to afford the pure product (Tables 1 and 2).

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