

## Potassium carbonate: a highly efficient catalyst for the acylation of alcohols, phenols and thiols under mild conditions

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### Abstract

A general, mild and efficient protocol has been developed for the synthesis of esters and thioesters. The process has been taking place using tetra *n*-butylammonium iodide (TBAI) as a phase-transfer catalyst and in the presence of potassium carbonate (K<sub>2</sub>CO<sub>3</sub>). A wide range of esters and thioesters was prepared in high yields and suitable times by the treatment of alcohols, phenols and thiols with acetic anhydride. Acylation reactions of a number of alcohols, phenols and thiols with acetic anhydride demonstrated that potassium carbonate is a convenient and efficient catalyst for the synthesis of esters and thioesters. This is a mild, general and practical procedure for the synthesis of esters and thioesters in high yields and suitable times.

**Keywords:** Acylation, esters, thioesters, tetra *n*-butylammonium iodide, potassium carbonate, acetic anhydride.

### Introduction

Esters and thioesters have a long history [3-4]. Generally, acylation of alcohols and with a wide variety of uses as key intermediates in organic synthesis [1-2]. Several esters and thioesters derivatives have been extensively used in production of food supplements, fragrance and cosmetic materials

thiols (both aliphatic and aromatic) is carried out with acid anhydrides in the presence of tertiary amines such as triethylamine and pyridine [5]. Moreover, these classes of chemicals, esters and thioesters, can be

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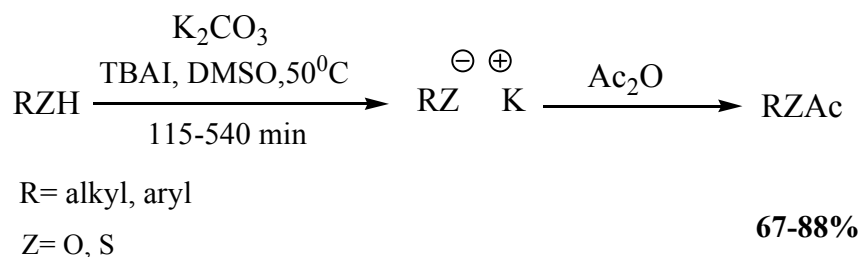
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prepared by the reaction of anhydrides or acyl halides with disulfides in the presence of various promoting agents, such as InI [6] and Zn/AlCl<sub>3</sub> [7]. In addition, other catalysts such as ruthenium (III) chloride [8], ionic liquids [9], magnesium bromide [10], indium trihalides [11] and CsF–Celite have also been utilized to achieve the acylated products of alcohols, phenols and thiols [12-13]. However, most of these protocols have some limitations such as: use of very strong basic catalyst, low yields, high temperature and longer reaction time [5,8,13,14]. But, it is important to find a

new, simple, useful and environmentally friendly method for the preparation of esters and thioesters.

More recently, a new, practical and convenient method was described for the preparation of ethers using K<sub>2</sub>CO<sub>3</sub> [15]. In development of our research in the utility of K<sub>2</sub>CO<sub>3</sub>, we wish to describe a practical, simple and efficient method for the acylation of alcohols, phenols and thiols. The results showed that our procedure overcomes different limitations which often occur during the preparation of esters and thioesters (Scheme 1).



**Scheme 1.**

## Experimental

### General

Chemicals were purchased from commercial suppliers and were used without further purification. Yields refer to isolated products. Melting points were determined by an electro thermal 9100 apparatus and presented without any further correction. The IR spectra were obtained on a FT-IR Hartman-Bomen spectrophotometer on KBr disks, or

neat. The <sup>1</sup>H NMR (400 MHz) and <sup>13</sup>C NMR (100 MHz) spectra were characterized by Bruker Avance NMR spectrometer in CDCl<sub>3</sub> solution. The progress of the reaction was monitored by TLC. All products are known and can be characterized by comparing their physical and spectral data with those of the authentic samples.

### General procedure for the synthesis of esters and thioesters:

A mixture of alcohols or thiols (1.5 or 1 mmol), TBAI (1 mmol) and DMSO (5 mL) was stirred under reflux conditions at 50 °C in the presence of K<sub>2</sub>CO<sub>3</sub> (1 mmol) for the appropriate times. Then, acetic anhydride (1 or 1.5 mmol) was added to the reaction mixtures to perform the corresponding esters or thioesters. The progress of reaction was monitored by TLC (*n*-hexane/EtOAc). After completion of the reaction, the solvent which was evaporated to give esters and thioesters was purified by preparative TLC (silica gel, eluent *n*-hexane/EtOAc). After the completion of the reaction, pure esters and thioesters were obtained (Tables 3 and 4).

### Selected spectral data

**Benzyl acetate (Table 3, entry 1):**Yield: 88%, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ= 2.17 (3H, *s*, CH<sub>3</sub>), 5.19 (2H, *s*, CH<sub>2</sub>), 7.25-7.35 (5H, *m*, ArH). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 22, 65.4, 126.9, 128.5, 128.9, 138.7, 170.4 ppm.

**Phenyl acetate (Table 1, entry 9):**Yield: 80%, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ= 2.08 (3H, *s*, COCH<sub>3</sub>), 7.24-7.54 (5H, *m*, ArH) . <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 20.1, 113.8, 129.3, 130.7, 159.2, 170.5 ppm.

### Benzyl thioacetate, (Table 2, entry1):

Yield: 85%, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ= 2.27 (3H, *s*, CH<sub>3</sub>), 4.2 (2H, *s*, CH<sub>2</sub>), 7.27 (1H, *t*, <sup>3</sup>J<sub>HH</sub>=7.2Hz, ArH) 7.35(2H, *t*, ArH), 7.53 (2H, *q*, ArH). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 31.2, 43.6, 126.7, 127.3, 128.5, 139.9, 198.3 ppm.

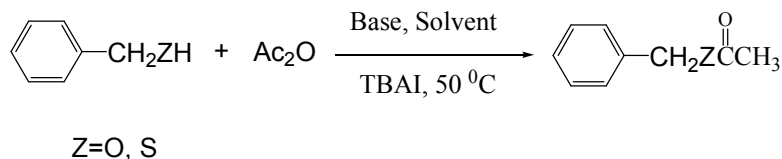
### 4-Methoxybenzylthioacetate (Table 2, entry2):

Yield: 85%, <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ= 2.02 (3H, *s*, CH<sub>3</sub>), 3.4 (2H, *s*, OCH<sub>3</sub>), 4.71 (2H, *s*, CH<sub>2</sub>S), 7.1 (2H, *d*, J= 8, ArH), 7.4 (2H, *d*, J= 8, ArH). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ= 15.3, 55.3, 65.4, 113.8, 129.3, 130.7, 159.1, 196.7 ppm.

### Result and discussion

To evaluate the effect of various factors on this system, we studied several variables to optimize the reaction condition. Initially, we have chosen the synthesis benzyl acetate and benzyl thioacetate at 50 °C as a model reaction for the optimization of various parameters. In order to reach our aim, we studied the influence of various bases and solvents on the reaction course . The results are demonstrated in Table 1 (all reactions accomplished at 50 °C) (Scheme 2).



**Scheme 2.****Table 1.** Synthesis of benzyl acetate and benzyl thioacetate using various bases and solvents<sup>a</sup>

Entry	Base	Solvent	Ester		Thioester	
			Time (min)	Yield (%) <sup>b</sup>	Time (min)	Yield (%) <sup>b</sup>
1	K <sub>3</sub> PO <sub>4</sub>	Toluene	440	54	460	55
2	Na <sub>2</sub> CO <sub>3</sub>	Toluene	310	80	320	80
3	Li <sub>2</sub> CO <sub>3</sub>	Toluene	370	61	400	60
4	t-BuOK	Toluene	590	36	560	31
5	LDA	Toluene	480	42	500	41
6	Triethylamine	Toluene	510	41	500	40
7	K <sub>2</sub> CO <sub>3</sub>	Toluene	300	84	310	83
8	KOH	Toluene	470	32	520	41
9	Na <sub>2</sub> CO <sub>3</sub>	CH <sub>3</sub> CN	160	81	180	80
10	K <sub>2</sub> CO <sub>3</sub>	CH <sub>3</sub> CN	155	84	160	83
11	Na <sub>2</sub> CO <sub>3</sub>	DMSO	155	82	160	83
12	K <sub>2</sub> CO <sub>3</sub>	DMSO	140	86 *	145	85 *
13	Na <sub>2</sub> CO <sub>3</sub>	DMF	150	82	155	82
14	K <sub>2</sub> CO <sub>3</sub>	DMF	150	84	170	83
15	K <sub>2</sub> CO <sub>3</sub>	Toluene	250	83	265	83
16	K <sub>2</sub> CO <sub>3</sub>	NMP	200	81	190	82
17	K <sub>2</sub> CO <sub>3</sub>	1,4-Dioxane	310	80	330	80
18	K <sub>2</sub> CO <sub>3</sub>	Toluene	280	82	290	81

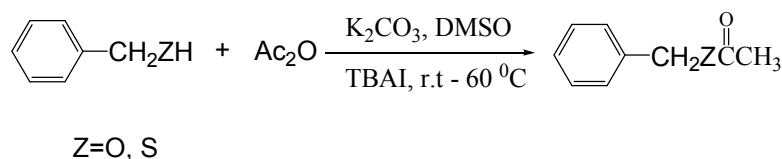
<sup>a</sup> Molar ratio of benzyl alcohol/acetic anhydride was 1.5/1 and benzyl mercaptane/acetic anhydride was 1/1.5. The reactions run in the presence of tetra *n*-butylammonium iodide (TBAI) (1 mmol) as phase-transfer catalyst, various bases and solvents at 50 °C and under reflux condition.

<sup>b</sup> Isolated yields.

First, 8 various bases were used for the synthesis benzyl acetate and benzyl thioacetate in toluene at 50 °C (Table 1, entries 1-8). As can be seen, among K<sub>3</sub>PO<sub>4</sub>, Li<sub>2</sub>CO<sub>3</sub>, t-BuOK, triethylamine, KOH, LDA, K<sub>2</sub>CO<sub>3</sub> and Na<sub>2</sub>CO<sub>3</sub>, the best results were obtained using K<sub>2</sub>CO<sub>3</sub> and Na<sub>2</sub>CO<sub>3</sub>. In order to select a better base for carrying out the reaction, We investigated the effect of K<sub>2</sub>CO<sub>3</sub> and Na<sub>2</sub>CO<sub>3</sub> on the model reactions in the presence of polar aprotic solvents.

As it is evident from Table 1, the reaction was highly effective with polar aprotic solvents such as CH<sub>3</sub>CN, DMSO and DMF (Table 1, entries 9-14). The best result was obtained when we used K<sub>2</sub>CO<sub>3</sub> as our base in the presence of DMSO as solvent (Table 1 entry 12). We also studied the modal reaction in the presence of K<sub>2</sub>CO<sub>3</sub> in other polar solvents such as 1,4-dioxane, NMP and toluene (table 1, entries 15-18). Therefore, the best results were obtained when we used K<sub>2</sub>CO<sub>3</sub> as base and

DMSO as solvent. After selection of base and solvent, we studied synthesis of benzyl acetate and benzyl thioacetate at various temperatures with the purpose of temperature optimization. The results are demonstrated in Table 2 (Scheme 3).



**Scheme 3.**

**Table 2.** Synthesis of benzyl acetate and benzyl thioacetate at various temperatures in the presence of  $K_2CO_3$ <sup>a</sup>

Entry	Temperature (°C)	Ester		Thioester	
		Time (min)	Yield (%) <sup>b</sup>	Time (min)	Yield (%) <sup>b</sup>
1	r.t	550	71	580	70
2	30	480	79	500	75
3	35	390	82	400	82
4	40	140	86	145	85
5	50	115	88*	125	85*
6	60	115	86*	125	84*

<sup>a</sup> Molar ratio of benzyl alcohol/ acetic anhydride/  $K_2CO_3$ / TBAI was 1.5/1/1/1 in the presence of DMSO (5 ml). Molar ratio of benzyl mercaptan/ acetic anhydride/  $K_2CO_3$ / TBAI was 1/1.5/1/1 in the presence of DMSO (5 ml).

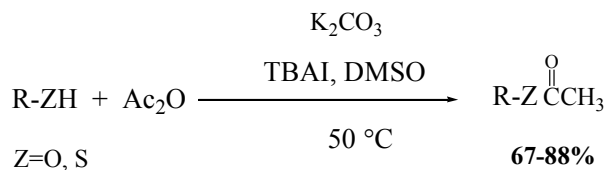
<sup>b</sup> Isolated yields.

As can be seen in Table 2, the rate and efficiency of reactions depend on temperature. The progress of the reaction at room temperature did not give satisfactory results (Table 2, entry 1), rising the temperature, the rate and efficiency of reaction become better (Table 2, entries 2-5). By arising the temperature up to 60 °C, it was observed that yield of reaction has decreased (Table 2, entry 6). The ideal temperature for the reaction was found to be 50 °C (Table 2, entry 5). Therefore, we decided to use tetra *n*-butylammonium iodide (TBAI) as phase-transfer catalyst,  $K_2CO_3$  as base and DMSO as solvent at 50 °C for the preparation of derivatives of esters and thioesters (Scheme 4).

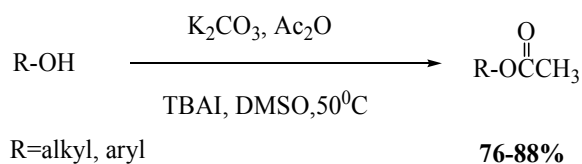
The procedure is very general and wide range of aliphatic and aromatics alcohols and thiols easily react with acetic anhydride in order to prepare their correspondence (Scheme 5).

As demonstrated in Table 1, the best results were obtained from treatment of benzyl alcohols and its derivatives with acetic anhy-

drude (Table 3, entries 1-6). Esters prepared from reaction of aliphatic alcohols with acetic anhydride (Table 3, entries 7-8) give relatively high yields. Also, the corresponding ester produced from treatment of phenol with acetic anhydride (Table 3, entry 9) in very good yields.

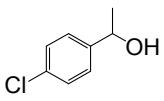
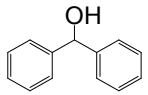


**Scheme 4.**



**Scheme 5.**

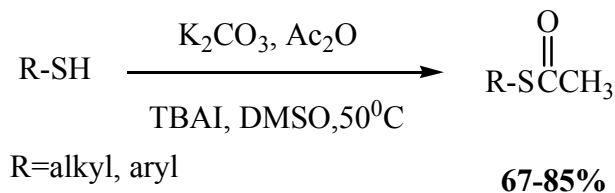
**Table 3.** Acylation of alkyl and aryl alcohols using acetic anhydride in the presence of  $\text{K}_2\text{CO}_3$  <sup>a</sup>

Entry	ROH	Time(min)	Yield <sup>b</sup> %
1	PhCH <sub>2</sub> OH	115	88
2	4- NO <sub>2</sub> C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OH	110	87
3	4- FC <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OH	120	87
4	4- BrC <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OH	125	88
5	4-OCH <sub>3</sub> C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OH	125	86
6	4- CH <sub>3</sub> C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> OH	140	85
7		390	83
8		440	76
9	C <sub>6</sub> H <sub>5</sub> OH	150	80

<sup>a</sup>All the products are known compounds and were characterized by comparison of their NMR spectral data and physical properties with those reported in the literature [5,16,17].

<sup>b</sup> isolated yields.

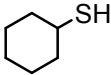
On the other hand, thioesters are versatile compounds and drugs[1]. Therefore, we de- and valuable intermediates in organic synthe- cided the synthesis of thioesters under these sis and are integral part of numerous natural conditions (Scheme 6).



**Scheme 6.**

Under the optimized reaction condition, were acylated successfully. The results are various derivatives of thioesters prepared in summarized in Table 3 (entries 2-6) and table high yields and their results have been 4 (entries 2-3). Acylation of alcohols (both revealed in Table 4 (entries1-7 ). Different aliphatic and aromatic) (Table 3) was phenols, benzyl alcohols and thiols with elec- performed faster than thiols ( Table 4). tro-donating and electron-withdraing groups

**Table 4.** Acylation of alkyl thiols and aryl thiols using acetic anhydride in the presence of  $\text{K}_2\text{CO}_3$  <sup>a</sup>

Entry	RSH	Time(min)	Yield <sup>b</sup> %
1	PhCH <sub>2</sub> SH	125	85
2	4-OCH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> SH	145	85
3	4-ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> SH	150	84
4		540	74
5	CH <sub>3</sub> CH <sub>2</sub> SH	190	67
6	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> SH	200	73
7	C <sub>6</sub> H <sub>5</sub> SH	180	79

<sup>a</sup> All the products are known compounds and were characterized by comparison of their NMR spectral data and physical properties with those reported in the literature [5,8, 16-18].

<sup>b</sup> isolated yields.



## Conclusion

In conclusion, we extended the utility of Potassium carbonate as an efficient, non-corrosive, inexpensive and environmentally friendly catalyst for the preparation of esters and thioesters. Primary alcohols and thiols reacted several times faster than secondary alcohols and thiols. Acylation reactions of a

number of alcohols, phenols and thiols with acetic anhydride demonstrated that Potassium carbonate is a convenient and efficient catalyst for the synthesis of esters and thioesters. In this way, we described a simple, mild and efficient method for the synthesis of esters and thioesters in good yields within suitable times.

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