

# **$\alpha$ -Arylchalcogenation of Aldehydes and Ketones with Diaryl Dichalcogenides Promoted by $K_3PO_4$**

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## **Abstract:**

A new catalytic method for direct  $\alpha$ -arylchalcogenation reaction of aldehydes and ketones has been developed. When various aldehydes and ketones were allowed to react with diaryl dichalcogenides in the presence of  $K_3PO_4$ , under mild reaction condition, the corresponding  $\alpha$ -phenylseleno- and  $\alpha$ -arylthio aldehydes and ketones were obtained in good to high yields.

## **Keywords:**

$\alpha$ -Arylchalcogenation; Diaryl dichalcogenides; Aldehydes; Ketones;  $K_3PO_4$

## **1. Introduction**

Due to wide synthetic utility of  $\alpha$ -phenylseleno carbonyl compounds [1-5], and  $\alpha$ -sulfenyl ketones [6-9], much effort has been devoted to accomplish the synthesis of these compounds. For example,  $\alpha$ -phenylseleno aldehydes and ketones can be converted into the corresponding synthetically useful  $\alpha,\beta$ -unsaturated carbonyl compounds through selenoxide elimination reactions [10-12]. In addition, these compounds can be transformed into other important organic intermediates such as amines [13],  $\alpha$ -amino acids [14], allylic alcohols [15], aziridines [16], and  $\alpha$ -hydroxy esters [17].

Several procedures have been developed for the preparation of  $\alpha$ -phenylseleno aldehydes and ketones, including: (i) reaction of electrophilic organoselenium reagents such as  $PhSeX$  ( $X = Br, Cl$ ),  $N$ -(phenyl-seleno)phthalimide (NPSP),  $PhSeX_3$ ,  $PhSeO_2CCF_3$  with aldehydes, ketone enolates or enolate derivatives [18-23], (ii) nucleophilic reaction of phenylselenolates with  $\alpha$ -halo aldehydes or ketones [24-26], and (iii) insertion of elemental selenium into zinc carbon bond [27]. The most common method for  $\alpha$ -sulfenylation of ketones involve the reaction of enolates [28-33] with various sulfenylating reagents such as  $MeSSMe$ ,  $PhSSPh$ ,  $PhSCl$ , methylmethanthiosulfate ( $MeSSO_2Me$ ),  $N$ -phenylthiocaprolactam, or  $N$ -(phenylthio)phthalimide.  $N$ -Chlorosuccinimide (NCS) has also been introduced for  $\alpha$ -

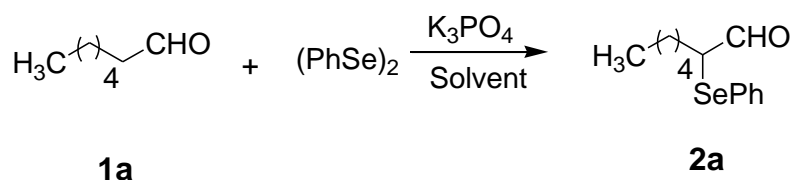
sulfenylation of ketones with aromatic thiols [34]. However, various drawbacks, such as employment of air and moisture sensitive and expensive reagents or poisonous transition metal catalysts, use of very low temperature ( $-78\text{ }^{\circ}\text{C}$ ), low yields, laborious manipulation, and multistep reaction encountered in the reported methodologies necessitate the development of a more efficient and convenient method.

Recently, we reported a simple and very efficient procedure for  $\alpha$ -phenylselenenylation of aldehydes and ketones from the corresponding aldehydes or ketones and diphenyl diselenide in the presence of  $\text{KF}/\text{Al}_2\text{O}_3$  [35]. In the same year, similar reaction utilizing  $\text{Cs}_2\text{CO}_3$ , as catalyst, was reported by Nishiyama and co-workers [36]; however, this catalyst was largely successful on ketones, and complex reaction mixtures was observed for aldehydes. Driven by our continuing interest on the  $\text{K}_3\text{PO}_4$ -mediated reactions [37,38] and with the aim to expand its application, we want to present herein its utility in the synthesis of  $\alpha$ -arylchalcogeno aldehydes and ketones by reaction of various aldehydes and ketones with diaryl dichalcogenides.

Tripotassium phosphate continues to attract much attention from organic chemists due to the versatility of use in synthetic chemistry; it is cheap, non-toxic, and a strong inorganic base ( $\text{pK}_a$  12.32 for the conjugate acid), used as an alternative non-nucleophilic base in several reaction [39-42].

## 2. Results and discussion

The model reaction of *n*-heptanal (**1a**) with diphenyl diselenide was carried out at various reaction conditions under an aerobic atmosphere in the presence of  $\text{K}_3\text{PO}_4$  (Scheme 1). The results are listed in Table 1. It was found that the



Scheme 1

reaction proceeded quantitatively with a molar ratio of diselenide:*n*-heptanal:  $\text{K}_3\text{PO}_4$  = 1: 3: 1.5 in dimethyl sulfoxide (DMSO) at  $40\text{ }^{\circ}\text{C}$  (Table 1, entry 6). When diphenyl diselenide was

treated with 2, 1 and 5 equivalent amounts of **1a** at 40 °C for 4 h, **2a** were obtained in lower yields (Table 1, entries 7-9). It is interesting to note that when higher (2 mmol) or lower (1, 0.7, 0.5, and 0.25 mmol) concentration of K<sub>3</sub>PO<sub>4</sub> were used, the yields of **2a** dropped (Table 1, entries 10-14). The effect of reaction temperature was also checked; lower temperatures (25 and 35 °C) gave poorer results (Table 1, entries 15 and 16), while higher temperature (50 °C) had no effect on the isolated yield (Table 1, entry 17).

**Table 1** Optimization of reaction conditions

Entry	Solvent	<i>n</i> -heptanal(mmol)	K <sub>3</sub> PO <sub>4</sub> (mmol)	Condition	Yield <sup>a</sup> (%)
1	THF	3	1.5	40 °C/4 h	N.R.
2	DMF	3	1.5	40 °C/4 h	70
3	CH <sub>3</sub> CN	3	1.5	40 °C/4 h	61
4	EtOH	3	1.5	40 °C/4 h	N.R.
5	DME <sup>b</sup>	3	1.5	40 °C/4 h	42
6	DMSO	3	1.5	40 °C/4 h	78
7	DMSO	2	1.5	40 °C/4 h	69
8	DMSO	1	1.5	40 °C/4 h	63
9	DMSO	5	1.5	40 °C/4 h	77
10	DMSO	3	2	40 °C/4 h	46
11	DMSO	3	1	40 °C/4 h	71
12	DMSO	3	0.7	40 °C/4 h	69
13	DMSO	3	0.5	40 °C/4 h	41
14	DMSO	3	0.25	40 °C/4 h	32
15	DMSO	3	1.5	25 °C/4 h	53
16	DMSO	3	1.5	35 °C/4 h	64
17	DMSO	3	1.5	50 °C/4 h	78

<sup>a</sup> Isolated yields; <sup>b</sup> 1,2-Dimethoxyethane.

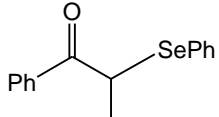
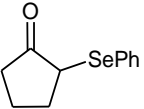
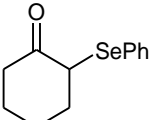
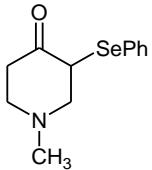
After optimization, a variety of other aldehydes and ketones were shown to undergo the reaction smoothly, giving the desired  $\alpha$ -phenylselenated product in good to high yields (Scheme 2). The results are summarized in Table 2.



Scheme 2

**Table 2**  $\text{K}_3\text{PO}_4$ -mediated  $\alpha$ -phenylselenation reactions of aldehydes and ketones.

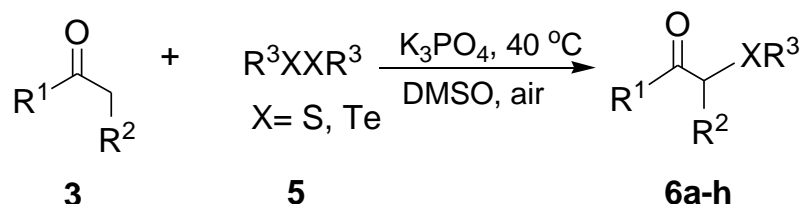
Entry	Product		Time(h)	Yield <sup>a</sup> (%) [Ref]
1		<b>4a</b>	3.5	81 [27]
2		<b>4b</b>	6	61 [27]
3		<b>4c</b>	3	82 [27]
4		<b>4d</b>	4	64 [27]
5		<b>4e</b>	5	72 [27]
6		<b>4f</b>	6	62 [27]
7		<b>4g</b>	6	56 [27]
8		<b>4h</b>	6	73 [27]
9		<b>4i</b>	24	82 [27]
10		<b>4j</b>	20	84 [27]
11		<b>4k</b>	20	82 [27]

12		<b>4l</b>	20	80 [27]
13		<b>4m</b>	28	64 [27]
14		<b>4n</b>	24	62 [27]
15		<b>4o</b>	18	74 [27]

<sup>a</sup> Isolated yields.

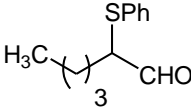
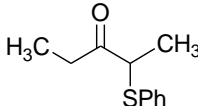
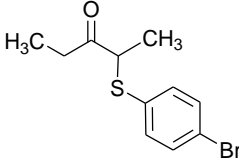
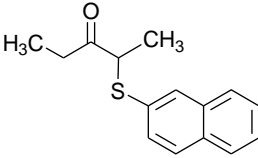
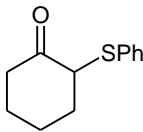
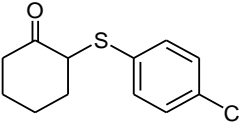
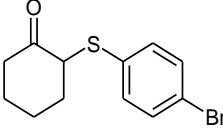
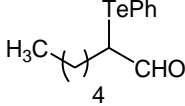
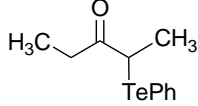
All products were fully characterized by spectroscopic methods (IR, <sup>1</sup>H and <sup>13</sup>C NMR) and compared with authentic spectra. Interestingly, neither condensation adducts nor double  $\alpha$ -phenylselenenylated products were detected in the course of these reactions. The treatment of aldehydes with diphenyl diselenide afforded the corresponding  $\alpha$ -phenylselenated product **4a-h** in 56-82% yields (Table 2, entries 1-8). When  $\alpha$ -phenylselenenylation reactions of various ketones with diphenyl diselenide were examined, longer reaction times were observed giving the corresponding mono  $\alpha$ -phenylselenyl ketones **4i-o** in 62-84% yields (Table 2, entries 9-15).

Encouraged by these results, the scope of this methodology was extended to  $K_3PO_4$ -mediated reaction of carbonyl compounds with diphenyl ditelluride and various disulfides (Scheme 3, Table 3). As in the case of diphenyl diselenide, disulfides can also react smoothly with



Scheme 3

**Table 3** K<sub>3</sub>PO<sub>4</sub>-mediated  $\alpha$ -aryltelluration and  $\alpha$ -phenyltelluration of aldehydes and ketones

Entry	Product	Time(h)	Yield <sup>a</sup> (%) [Ref]	
1		<b>6a</b>	3	63 [33]
2		<b>6b</b>	20	86 [34]
3		<b>6c</b>	18	85 [34]
4		<b>6d</b>	20	85 [34]
5		<b>6e</b>	22	61 [34]
6		<b>6f</b>	18	63 [34]
7		<b>6g</b>	20	64 [34]
8		<b>6h</b>	24	N.R.
9		<b>6i</b>	24	N.R.

<sup>a</sup> Isolated yields.

different aldehyde and ketones under the same reaction conditions. It was observed that ketones require longer reaction times to afford the respective  $\alpha$ -aryltio derivatives **6b-g**

(Table 3, entries 2-7). We also noted that the reaction yields were slightly lower when cyclic ketone, cyclohexanone, was used. However, under the same conditions, the treatment of *n*-heptanal and 3-pentanone with diphenyl ditelluride did not produce the expected  $\alpha$ -phenyltelluro derivatives **6h** and **6i** even after 24 h.

### 3. Conclusion

In conclusion, we have developed a new convenient and efficient protocol for  $\alpha$ -arylchalcogenation of aldehydes and ketones with diaryl dichalcogenides in the presence of  $K_3PO_4$  under mild reaction conditions with good to high yields. This process represents a suitable option to existing methods.

### 4. Experimental

#### *General procedure*

To a stirred solution of aldehyde or ketone (3.0 mmol) and anhydrous  $K_3PO_4$  (1.5 mmol) in dry DMSO (2 cm<sup>3</sup>), diaryl dichalcogenide (1.0 mmol) was added. Stirring of the resulting reaction mixture was continued at 40 °C for the appropriate time (Tables 2 and 3). After the reaction was complete (monitored by TLC) the mixture was filtered and the solid,  $K_3PO_4$ , was washed thoroughly with EtOAc (25 cm<sup>3</sup>). The filtrate was washed with water (2 × 20 cm<sup>3</sup>) and dried over anhydrous  $MgSO_4$ . The solvent was evaporated to give the crude product which was purified by preparative TLC (silica gel, eluent *n*-hexane:EtOAc = 10:1). Excess diaryl dichalcogenides were recovered in high purity. All compounds were characterized by IR, <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy. (**4a**): Yellow oil; IR (neat):  $\bar{\nu} = 1709\text{ cm}^{-1}$ ; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 0.89$  (t,  $J = 6.6$  Hz, 3H), 1.28-1.33 (m, 4H), 1.43-1.72 (m, 4H), 3.57-3.63 (m, 1H), 7.25-7.34 (m, 3H), 7.49-7.58 (m, 2H), 9.39 (d,  $J = 3.7$  Hz, 1H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 14.3, 22.9, 28.0, 28.1, 31.6, 53.2, 126.4, 129.32, 129.33, 136.0, 193.3$  ppm. (**4b**): Orange oil; IR (neat):  $\bar{\nu} = 1707\text{ cm}^{-1}$ ; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 1.09$  (t,  $J = 7.4$  Hz, 3H), 1.64-1.77 (m, 1H), 1.82-1.94 (m, 1H), 3.54 (dt,  $J = 7.4, 3.4$  Hz, 1H), 7.27-7.33 (m, 3H), 7.51-7.59 (m, 2H), 9.43 (d,  $J = 3.4$  Hz, 1H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 12.6, 21.1, 54.7, 125.9, 128.8, 129.2, 135.9, 193.1$  ppm. (**4c**): Pale yellow oil; IR (neat):  $\bar{\nu} = 1709\text{ cm}^{-1}$ ; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta = 0.95$  (t,  $J = 7.3$  Hz, 3H), 1.38-1.61 (m, 2H), 1.62-1.69 (m, 1H), 1.70-1.87 (m, 1H), 3.62 (dt,  $J = 7.4, 3.7$  Hz, 1H), 7.23-7.38 (m, 3H), 7.48-7.55 (m, 2H), 9.39 (d,  $J = 3.7$  Hz, 1H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta = 13.7, 21.2, 29.7, 52.6, 126.0, 128.8, 129.2, 135.8, 193.0$  ppm. (**4h**): Yellow oil; IR (neat):  $\bar{\nu} = 1704\text{ cm}^{-1}$ ; <sup>1</sup>H

NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.02 (dd,  $J$  = 11.2, 6.6 Hz, 1H), 3.36 (dd,  $J$  = 11.2, 8.0 Hz, 1H), 3.91 (ddd,  $J$  = 8.0, 6.6, 4.0 Hz, 1H), 7.19-7.40 (m, 8H) 7.48-7.53 (m, 2H), 9.50 (d,  $J$  = 4.0 Hz, 1H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 28.2, 45.3, 126.4, 128.9, 129.0, 129.4, 131.5, 134.5, 138.0, 194.7 ppm. **(4j)**: Yellow oil; IR (neat):  $\bar{\nu}$  = 1702 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.09 (t,  $J$  = 7.3 Hz, 3H), 1.49 (d,  $J$  = 7.0, 3H), 2.50 (dq,  $J$  = 17.3, 7.3 Hz, 1H), 2.79 (dq,  $J$  = 17.3, 7.3, 1H), 3.82 (q,  $J$  = 7.0 Hz, 1H), 7.25-7.36 (m, 3H), 7.49-7.56 (m, 2H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.4, 16.5, 33.0, 45.1, 127.1, 128.7, 128.9, 135.9, 207.7 ppm. **(4l)**: Pale orange oil; IR (neat):  $\bar{\nu}$  = 1673 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.65 (d,  $J$  = 6.8 Hz, 3H), 4.69 (q,  $J$  = 6.8, 1H), 7.22-7.60 (m, 8H), 7.87 (d,  $J$  = 7.3, 2H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 17.7, 39.7, 128.7, 128.9, 129.0, 129.3, 132.9, 133.1, 136.7, 137.0, 196.3 ppm. **(4m)**: Yellow oil; IR (neat):  $\bar{\nu}$  = 1730 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.92-2.04 (m, 4H), 2.27-2.32 (m, 2H), 3.74-3.77 (m, 1H), 7.44-7.62 (m, 3H), 7.94 (dd,  $J$  = 6.5, 1.5 Hz, 2H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 20.0, 29.6, 35.6, 45.7, 127.4, 128.0, 128.6, 134.4, 211.0 ppm. **(4o)**: Orange oil; IR (neat):  $\bar{\nu}$  = 1709 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 2.15-2.19 (m, 1H), 2.24 (s, 3H), 2.46-2.49 (m, 1H), 2.80-2.90 (m, 2H), 3.17-3.21 (m, 1H), 3.30-3.36 (m, 1H), 3.80 (brs, 1H), 7.16-7.33 (m, 3H), 7.55-7.60 (m, 2H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 37.1, 45.8, 50.2, 55.6, 61.5, 128.6, 129.7, 129.9, 136.9, 205.5 ppm. **(6a)**: Yellow oil; IR (neat):  $\bar{\nu}$  = 1722 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.90 (t,  $J$  = 7.5 Hz, 3H), 1.40-1.49 (m, 4H), 1.50-1.52 (m, 1H), 1.80-1.89 (m, 1H), 3.33 (dt,  $J$  = 7.5, 2.7 Hz, 1H), 7.25-7.35 (m, 3H), 7.44 (d,  $J$  = 6.9 Hz, 2H), 9.40 (d,  $J$  = 4.2 Hz, 1H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 14.7, 23.1, 29.7, 31.8, 56.7, 127.4, 129.2, 129.6, 136.9, 196.0 ppm. **(6e)**: Pale yellow oil; IR (neat):  $\bar{\nu}$  = 1712 cm<sup>-1</sup>; <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta$  = 1.49-1.78 (m, 3H), 1.95-2.06 (m, 1H), 2.38-2.45 (m, 2H), 2.51- 2.60 (m, 1H), 3.25-3.35 (m, 1H), 4.22-4.23 (m, 1H), 7.23-7.41 (m, 3H), 7.51 (d,  $J$  = 7.9 Hz, 2H) ppm; <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta$  = 25.1, 29.3, 36.1, 40.5, 55.5, 130.3, 130.4, 131.0, 136.0, 209.3 ppm.

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