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ORIGINAL PAPER

α-Organylchalcogenation of aldehydes and ketones with diorganyl dichalcogenides promoted by K_3PO_4

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Abstract A new catalytic method for direct α-organylchalcogenation of aldehydes and ketones has been developed. When various aldehydes and ketones were allowed to react with diorganyl dichalcogenides in the presence of K_3PO_4, under mild reaction conditions, the corresponding α-organylseleno and α-arylthio aldehydes and ketones were obtained in good to high yields.

Keywords α-Organylchalcogenation · Diorganyl dichalcogenides · Aldehydes · Ketones · K_3PO_4

Introduction

Owing to the wide synthetic utility of α-organylseleno carbonyl compounds [1–5] and α-sulfenyl ketones [6–9], much effort has been devoted to their syntheses. For example, α-phenylseleno aldehydes and ketones can be converted into the corresponding synthetically useful α,β-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], α-amino acids [14], allylic alcohols [15], aziridines [16], and α-hydroxy esters [17].

Several procedures have been developed for the preparation of α-phenylseleno aldehydes and ketones, including (1) the reaction of electrophilic organoselenium reagents, such as PhSeX (X = Br, Cl), *N*-(phenylseleno)phthalimide (NPSP), $PhSeX_3$, $PhSeO_2CCF_3$ with aldehydes, ketone enolates, or enolate derivatives [18–23]; (2) the nucleophilic reaction of phenylselenolates with α-halo aldehydes or ketones [24–26]; and (3) the insertion of elemental selenium into zinc–carbon bonds [27]. The most common method for α-sulfenylation of ketones involves 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 α-sulfenylation of ketones with aromatic thiols [34]. However, various drawbacks, such as the employment of air- and moisture-sensitive and expensive reagents or poisonous transition metal catalysts, the use of very low temperature (−78 °C), low yields, laborious manipulation, and multistep reactions 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 α-phenylselenenylation of aldehydes and ketones from the corresponding aldehydes or ketones and diphenyl diselenide in the presence of KF/Al_2O_3 [35]. In the same year, 2-phenylseleno aldehydes and ketones were selectively obtained from diphenyl diselenide using KF/Al_2O_3 and PEG-400 [36]. A similar reaction, utilizing Cs_2CO_3 as catalyst, was reported by Nishiyama and co-workers [37]; however, this catalyst was largely successful on ketones, but complex reaction mixtures were observed for aldehydes. Driven by our continuing interest in the K_3PO_4-mediated reactions [38, 39] and with the aim to expand its application, herein we present its utility in the

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synthesis of α-organylchalcogeno aldehydes and ketones by the reaction of various aldehydes and ketones with symmetrical diorganyl dichalcogenides. Symmetrical dichalcogenides (RXXR, X = Te, Se, S) are versatile synthetic reagents [40, 41].

Tripotassium phosphate continues to attract much attention from organic chemists because of its versatility in synthetic chemistry: it is cheap, non-toxic, a strong inorganic base ($pK_a = 12.32$ for the conjugate acid), and it is used as an alternative non-nucleophilic base in several reactions [42–45].

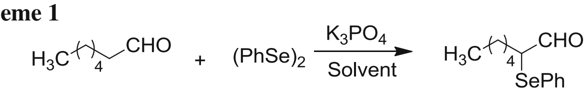
Results and discussion

The model reaction of *n*-heptanal (**1a**) with diphenyl diselenide was carried out under various reaction conditions in an aerobic atmosphere in the presence of K_3PO_4 (Scheme 1). The results are listed in Table 1. The reaction proceeded quantitatively with a molar ratio of diselenide/*n*-heptanal/K_3PO_4 = 1:3:1.5 in dimethyl sulfoxide (DMSO) at 40 °C (Table 1, entry 6). When diphenyl diselenide was treated with 2, 1, and 5 equivalents of **1a** at 40 °C for 4 h, **2a** was 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) concentrations of K_3PO_4 were used, the yields of **2a** dropped (Table 1, entries 10–14). The effect of the reaction temperature was also checked; lower temperatures (25 and 35 °C) gave poorer results (Table 1, entries 15 and 16) whereas higher temperature (50 °C) had no effect on the isolated yield (Table 1, entry 17).

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

All products were fully characterized by spectroscopic methods (IR, ^{1}H and ^{13}C NMR) and compared with authentic spectra. Interestingly, neither condensation adducts nor double α-organylselenenylated products were detected in the course of these reactions. The treatment of aldehydes with diphenyl diselenide afforded the corresponding α-phenylselenenylated products **4a–4h** in 56–82 % yields (Table 2, entries 1–8). When α-phenylselenenylation reactions of various ketones with diorganyl diselenide were examined, longer reaction times were observed, giving the corresponding mono α-phenyl/alkylselenyl ketones **4i–4q** in 37–84 % yields (Table 2, entries 9–17).

Scheme 1



1a **2a**

Table 1 Optimization of reaction conditions

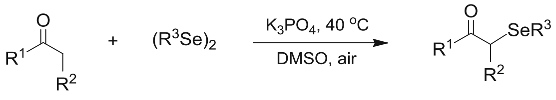
Entry	Solvent	*n*-Heptanal/ mmol	K_3PO_4/ mmol	Conditions	Yield[a]/ %
1	THF	3	1.5	40 °C/4 h	NR
2	DMF	3	1.5	40 °C/4 h	70
3	CH_3CN	3	1.5	40 °C/4 h	61
4	EtOH	3	1.5	40 °C/4 h	NR
5	DME	3	1.5	40 °C/4 h	42
6	DMSO	3	1.5	40 °C/4 h	78
7	DMSO	2	1.5	40 °C/4 h	69
8	DMSO	1	1.5	40 °C/4 h	63
9	DMSO	5	1.5	40 °C/4 h	77
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

Reaction conditions: *n*-heptanal, diphenyl diselenide, K_3PO_4, 2 cm^3 solvent, air atmosphere

DME 1,2-dimethoxyethane, *NR* no reaction

[a] Isolated yields

Scheme 2

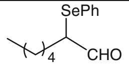
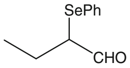
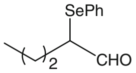
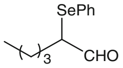
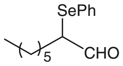
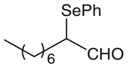
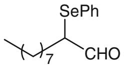
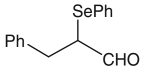
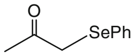
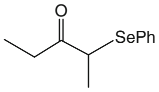
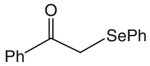
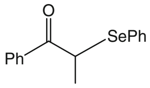
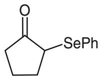
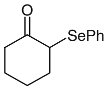
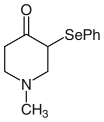
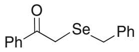
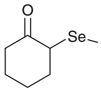


3 **4a-4q**

R^1= H, alkyl, Ph R^3= Ph, alkyl
R^2= H, alkyl

Encouraged by these results, we extended the scope of this methodology to K_3PO_4-mediated reaction of carbonyl compounds with diphenyl ditelluride and various disulfides (Scheme 3; Table 3). As in the case of diorganyl diselenide, disulfides can also react smoothly with different aldehydes and ketones under the same reaction conditions. It was observed that ketones require longer reaction times to afford the respective α-arylthio derivatives **6b–6g** (Table 3, entries 2–7). We also noted that the reaction yields were slightly lower when a cyclic ketone, cyclohexanone, was used. However, under the same reaction conditions, the treatment of *n*-heptanal and 3-pentanone with diphenyl ditelluride did not produce the expected α-phenyltelluro derivatives even after 24 h.

Table 2 K_3PO_4-mediated α-organylselenation reactions of aldehydes and ketones

Entry	Product		Time /h	Yield[a] /%	Ref.
1		**4a**	3.5	81	[20]
2		**4b**	6	61	[20]
3		**4c**	3	82	[20]
4		**4d**	4	64	[20]
5		**4e**	5	72	[20]
6		**4f**	6	62	[20]
7		**4g**	6	56	[20]
8		**4h**	6	73	[20]
9		**4i**	24	82	[20]
10		**4j**	20	84	[20]
11		**4k**	20	82	[20]
12		**4l**	20	80	[35]
13		**4m**	28	64	[20]
14		**4n**	24	62	[20]
15		**4o**	18	74	[20]
16		**4p**	28	54	[46]
17		**4q**	72	37	[47]

Reaction conditions: aldehyde or ketone (3.0 mmol), diorganyl dichalcogenide (1.0 mmol), K_3PO_4 (1.5 mmol), in 2 cm^3 dry DMSO at 40 °C

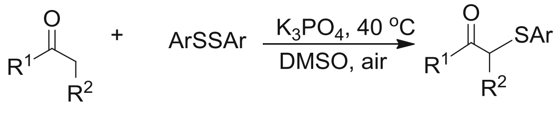
[a] Isolated yields

In conclusion, we have developed a new convenient and efficient protocol for α-organylchalcogenation of aldehydes and ketones with symmetrical diorganyl dichalcogenides in the presence of K_3PO_4 under mild reaction conditions with good to high yields. This process represents a suitable alternative to existing methods.

Experimental

Chemicals were purchased from Merck chemical company. Yields refer to the isolated products. ^{1}H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded using a Bruker AQS-300 Avance spectrometer. IR spectra were obtained using an ABB FTLA 2000 instrument. Analytical thin-layer chromatography (TLC) was carried out on precoated plates (silica gel 60 F_{254}). Preparative TLC was performed on TLC glass plates (20 × 20 cm) using silica gel 60 $PF_{254+366}$ as adsorbent.

Scheme 3

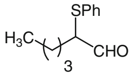
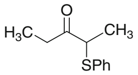
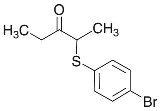
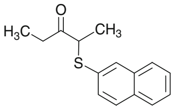
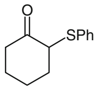
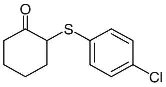
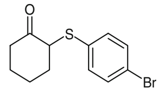


3 **5** **6a-6g**

General procedure

To a stirred solution of aldehyde or ketone (3.0 mmol) and anhydrous K_3PO_4 (1.5 mmol) in 2 cm^3 dry DMSO, diorganyl dichalcogenide (1.0 mmol) was added. Stirring of the resulting reaction mixture was continued at 40 °C for an appropriate time (Tables 2, 3). After the reaction was complete (monitored by TLC), the mixture was filtered and the solid, K_3PO_4, was washed thoroughly with 25 cm^3 EtOAc. The filtrate was washed with water (2 × 20 cm^3) 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 diorganyl dichalcogenides were recovered in high purity. All compounds were characterized by IR, ^{1}H and ^{13}C NMR spectroscopy.

Table 3 K_3PO_4-mediated α-arylthiolation of aldehydes and ketones

Entry	Product		Time /h	Yield[a] /%	Ref.
1		**6a**	3	63	[33]
2		**6b**	20	86	[34]
3		**6c**	18	85	[34]
4		**6d**	20	85	[34]
5		**6e**	22	61	[34]
6		**6f**	18	63	[34]
7		**6g**	20	64	[34]

Reaction conditions: aldehyde or ketone (3.0 mmol), diaryl disulfide (1.0 mmol), K_3PO_4 (1.5 mmol), 2 cm^3 dry DMSO at 40 °C

[a] Isolated yields

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