

SHORT
COMMUNICATIONS

Reductive Selenation of Aliphatic Ketones to Dialkyl Diselenides with Se–CO–H₂O under Atmospheric Pressure*

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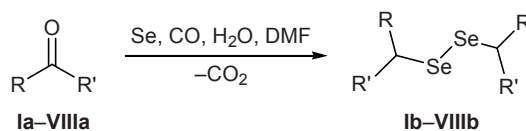
Organoselenium compounds have received considerable attention as useful synthetic reagents and intermediates in organic synthesis. Among them, dialkyl diselenides are frequently used as starting materials and reagents in functional group transformations [1]. Many methods have been reported so far for the synthesis of dialkyl selenides. For example, most common methods involve the reaction of metal diselenides with alkyl halides [2], dimerization with selenocyanates [3–5], and oxidation of selenols [6] or selenolates [7]. In addition, dialkyl diselenides can be prepared by the reaction of carbonyl compounds with hydrogen selenide in the presence of triethylamine in anhydrous pyridine [8], sodium hydrogen selenide in the presence of amine and sodium tetrahydridoborate in ethanol [9], and elemental selenium and sodium tetrahydridoborate in the presence of amine in EtOH [10] or in the absence of amine in DMF–EtOH (2:1) [11]. Though all these methods have their merits they suffer from disadvantages such as using strong reducing agents and highly toxic gas, harsh reaction conditions, and complicated manipulations. Sonoda has also reported that elemental selenium can be readily reduced with carbon(II) oxide and water in the presence of a base to produce hydrogen selenide which was successfully applied to the synthesis of dialkyl diselenides from both aliphatic aldehydes and ketones. However, the process required fairly high pressure (3.0 MPa), high temperature (120°C), and long reaction time (24 h) [12].

We recently developed a new reduction system in which hydrogen selenide (H₂Se) is formed *in situ* from elemental selenium, carbon monoxide, and water in

DMF under atmospheric pressure in the absence of a base. In this system, aromatic and aliphatic aldehydes can be reduced and selenated to the corresponding organic diselenides [13]. Herein we report on a convenient synthesis of dialkyl diselenides from aliphatic ketones with Se–CO–H₂O in DMF in moderate to good yields under atmospheric pressure without a base.

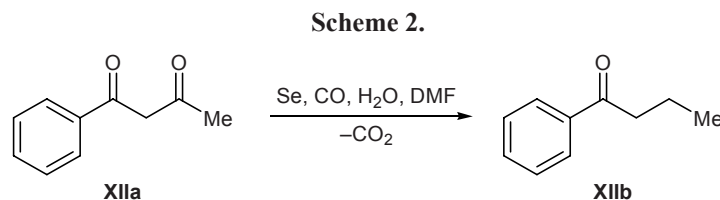
When cyclohexanone (**Ia**, 2.5 mmol) was reacted with 1 equiv of selenium (2.5 mmol), carbon(II) oxide (bubbling), and water (2 ml) in DMF (20 ml) at 90°C for 7 h, the reductive selenation of **Ia** efficiently proceeded to give bis(cyclohexyl) diselenide (**Ib**) in 74% yield (Scheme 1). Table shows the results of the reductive selenation of various ketones with the system Se–CO–H₂O in DMF under atmospheric pressure without a base. The reaction temperatures varied, depending on the boiling point of the initial ketone. Reductive selenation of cyclohexanone and cyclopentanone gave the corresponding diselenides in good yields (see table). Under the same conditions, the reactions with methyl ethyl ketone (**IIIa**) and diethyl ketone (**IVa**) gave the corresponding diselenides **IIIb** and **IVb** in slightly lower yields (48 and 42%, respectively). Obviously, lower steric hindrances in the substrate molecule favor increased yield of the target diselenide.

Scheme 1.



I, RR' = (CH₂)₅; **II**, RR' = (CH₂)₄; **III**, R = Me, R' = Et; **IV**, R = R' = Et; **V**, R = Me, R' = Pr; **VI**, R = Me, R' = C₆H₁₃; **VII**, R = Et, R' = Bu; **VIII**, R = Me, R' = C₉H₁₉.

* The text was submitted by the authors in English.



Long-chain aliphatic ketones **VIa–VIIIa** were also studied, and the corresponding diselenides **VIb–VIIIb** were obtained in moderate to good yields. Aromatic ketones, such as *p*-chloroacetophenone (**IXa**), acetophenone (**Xa**), and 1,3-diphenylpropane-2-one (**XIa**) failed to undergo reductive selenation even on prolonged heating (10 h); presumably, the reason is steric hindrance created by the phenyl ring. We also made an attempt to effect reductive selenation of diketones; the reaction with 1-phenylbutane-1,3-dione (**XIIa**) as an example led to the formation of the reduction product of one carbonyl group, 1-phenylbutan-1-one (**XIIb**) [14] (Scheme 2). According to the ^1H NMR data (CDCl_3), the purity of the isolated diselenides was up to 95%, while unidentified impurities amounted to about ~5% [15].

General procedure for the synthesis of organic diselenides. A 100-ml three-necked flask was charged

with 2.5 mmol of an aliphatic ketone, 2.5 mmol of selenium, 2 ml of water, 20 ml of DMF, and a magnetic stirring bar. Carbon(II) oxide was bubbled through the mixture under vigorous stirring at 90°C over a period of 8–10 h. When the reaction was complete, carbon(II) oxide supply was terminated, and the resulting mixture was stirred for 30 min at room temperature on exposure to air, 20 ml of water was added, and the mixture was extracted with diethyl ether (3×40 ml). The combined extracts were dried over anhydrous MgSO_4 , filtered, and evaporated under reduced pressure to leave a yellow oil which was purified by column chromatography on silica gel or thin-layer chromatography to give the pure product. All the products were identified by ^1H NMR and/or comparison with authentic samples.

Thus we have developed a convenient method for the synthesis of dialkyl diselenides from aliphatic

Reductive selenation of aliphatic ketones to dialkyl diselenides and NMR spectra of the products

Substrate no.	Product no.	Reaction time, h	Yield, ^a %	NMR spectra, δ , δ_{C} ppm	
				^1H	^{13}C
Ia	Ib [12]	7	74	3.01–3.05 m (2H), 2.06–2.16 m (4H), 1.25–1.76 m (16H)	44.12, 35.30, 27.67, 26.36
IIa	IIb [12]	7	60	3.50–3.52 m (2H), 2.00–2.02 m (4H), 1.24–1.73 m (8H)	43.30, 35.38, 25.61
IIIa	IIIb [11]	9	48	2.99–3.04 m (2H), 1.71–1.77 q (4H), 1.43–1.44 d (6H), 0.98–1.01 t (3H)	42.27, 31.15, 22.84, 13.15
IVa	IVb [11]	9	42	2.83–2.86 m (2H), 1.75–1.82 q (8H), 0.97–1.00 t (12H)	51.27, 30.40, 12.91
Va	Vb [11]	7	64	3.06–3.09 m (2H), 1.69–1.42 m (10H), 0.90–0.94 q (4H), 0.86–0.87 t (6H)	40.80, 30.44, 23.35, 21.89, 14.83
VIa	VIb [15]	8	73	3.03–3.10 m (2H), 1.50–1.71 m (6H), 1.44–1.29 m (20H), 0.87–0.90 t (6H)	40.50, 38.64, 32.49, 29.79, 28.67, 23.44, 23.35, 14.80
VIIa	VIIb [16]	8	69	2.89 m (2H), 1.66–1.79 m (8H), 1.26–1.34 m (14H), 0.91–1.00 t (6H)	49.37, 35.78, 30.67, 29.29, 23.26, 14.75, 12.8
VIIIa	VIIIb [12]	7	61	3.05–3.11 m (2H), 1.72–1.83 m (6H), 1.70–1.44 m (12H), 0.90–0.87 t (6H)	41.70, 30.82, 26.70, 23.20, 14.82, 12.76
XIIa	XIIb [14]	10	40	7.97–7.95 m (2H), 7.56–7.52 m (1H), 7.53–7.47 m (2H), 2.96–2.92 t (2H), 1.77–1.72 m (2H), 1.00–0.97 t (3H)	

^a Isolated product.

ketones under atmospheric pressure in the absence of a base. Further work is now in progress to extend this methodology to unsymmetrical diselenides.

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