

Efficient Reductive Selenation of Aromatic Aldehydes to Symmetrical Diselenides with Se/CO/H₂O under Atmospheric Pressure

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Abstract: An efficient method for the synthesis of symmetrical diselenides is described. Reductive selenation of aromatic and heterocyclic aromatic aldehydes (ArCHO) with Se/CO/H₂O in DMF afforded diselenides (ArCH₂SeSeCH₂-Ar) in yields up to 94% under atmospheric pressure without use of a base.

Organic diselenides, as useful synthetic reagents and intermediates, play an important role in organoselenium chemistry because they are stable, easily handled, and reactive enough to produce electrophilic, nucleophilic, and radicophilic species.¹ General routes to organic diselenides involve reactions of metal diselenides with alkyl halides,² dimerization with seleno-cyanates,^{3–5} and oxidation of selenols⁶ or selenolates.⁷ Carbonyl compounds have also been used for this purpose. Both Margolis⁸ and Cohen⁹ reported that treatment of carbonyl compounds with hydrogen selenide generated from the reaction of Al₂Se₃ and water gave diselenides in the presence of organic base triethylamine. Diselenides were also syn-

TABLE 1. Reductive Selenation of Benzaldehyde (1a) to Dibenzyl Diselenide (1b)

entry ^a	solvent	temp (°C)	H ₂ O (mL)	yield (%) ^b
1	THF	60	2	
2	1,4-dioxane	95	2	
3	CH ₃ CN	75	2	
4	EtOH	75	2	
5	DMAC ^c	95	2	
6	DMSO	95	2	15
7	FP ^d	95	2	65
8	DMF	23	2	
9	DMF	60	2	67
10	DMF	80	2	85
11	DMF	95	2	94
12	DMF	95	0	
13	DMF	95	1	60
14	DMF	95	4	94

^a Reaction conditions: benzaldehyde, 2.5 mmol; Se, 2.5 mmol; bubbling CO, 0.1 MPa; solvent, 20 mL; 7.0 h. ^b Isolated yield of **1b**. ^c DMAC = *N,N*-dimethylacetamide. ^d FP = 1-formylpiperidine.


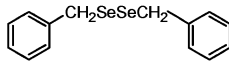
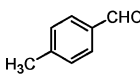
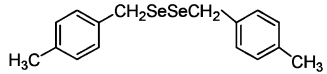

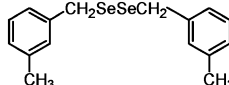

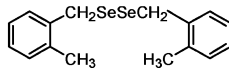
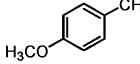
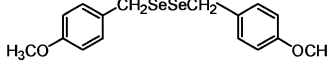

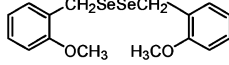
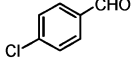
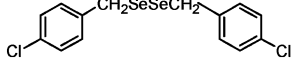
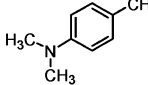
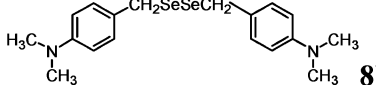


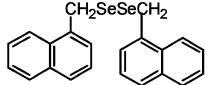
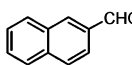
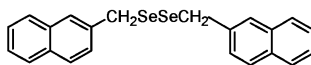

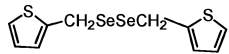

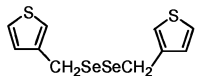

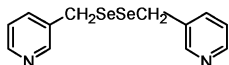
thesized from the reactions of aldehydes with sodium hydrogen selenide in the presence of an amine and sodium borohydride.¹⁰ Huang et al. reported that aldehydes reacted with elemental selenium and sodium borohydride to afford dibenzyl diselenides in the absence of an amine.¹¹ However, most of the known methods for preparation of diselenides suffer from disadvantages such as use of strong reducing agents and highly toxic gas, harsh reaction conditions, low yields, or complicated manipulations. Sonoda et al. discovered that elemental selenium can be readily reduced by carbon monoxide and water in the presence of base to produce hydrogen selenide, which was successfully applied to the synthesis of aliphatic diselenides from both aliphatic ketones and aldehydes¹² or from alkyl chlorides and acyl chlorides,¹³ respectively. Although Sonoda's method is relatively convenient and can be easily manipulated,^{12,13} the process is subject to relatively high pressure of CO (0.5–3.0 MPa), high temperature (120 °C), and long reaction times (e.g., 24 h), and when aromatic ketones ArC(=O)R' were used as the substrates, only reduction products ArCH₂R' instead of diselenides were obtained.¹⁴

In the course of our ongoing studies on selenium-catalyzed reductive carbonylation of nitroaromatic compounds with carbon monoxide,¹⁵ we have developed new

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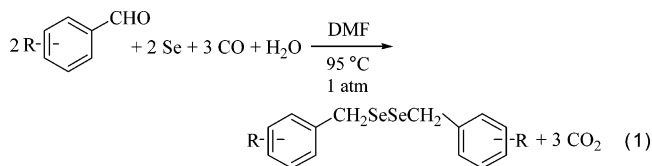
TABLE 2. Reductive Selenation of Aromatic and Heterocyclic Aromatic Aldehydes to Symmetrical Diselenides

entry ^a	aldehyde (ArCHO)	diselenide (ArCH ₂ SeSeCH ₂ Ar)	mp (°C)	reaction time (h)	yield (%) ^b
1	 1a	 1b	92-93 (90-91 ¹⁸)	7	94
2	 2a	 2b	58-59 (61-62 ^{10b})	9	92
3	 3a	 3b	Yellow liquid	7	89
4	 4a	 4b	80-81 (86-86.5 ^{2c})	11	80
5	 5a	 5b	72-73 (72 ⁹)	7	87
6	 6a	 6b	66-67 (- ¹⁹)	11	81
7	 7a	 7b	73-75 (76 ⁹)	9	36
8	 8a	 8b	102-104	12	45
9	 9a	no reaction		12	
10	 10a	 10b	102-103 (102 ⁹)	11	90
11	 11a	 11b	137-138 (134-135 ^{10b})	9	92
12	 12a	 12b	Yellow liquid	9	85
13	 13a	 13b	94-96	7	89
14	 14a	 14b	77-79	9	92

^a Reaction conditions: aldehyde, 2.5 mmol; Se, 2.5 mmol; bubbling CO, 0.1 MPa; water, 2 mL; DMF, 20 mL; 95 °C. ^b Isolated yield.

applications of the Se/CO/H₂O/DMF system from which dinitroaromatics can be reduced to mononitroanilines under atmospheric pressure.¹⁶ Keeping this result in mind, we investigated reactions of aromatic aldehydes with stoichiometric selenium under similar conditions and surprisingly found that these reactions led to symmetrical diselenides in the absence of base in excellent yields (eq 1). Herein we report a novel and efficient

synthesis of symmetrical diselenides from aromatic and heterocyclic aromatic aldehydes with Se/CO/H₂O in DMF under atmospheric pressure without use of a base.



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TABLE 3. Reductive Selenation of Aliphatic Aldehydes to Symmetrical Diselenides

entry ^a	aldehyde (RCHO)	diselenide (RCH ₂ SeSeCH ₂ R)	mp (°C)	reaction temp (°C)	yield (%) ^b
1	ⁿ PrCHO 15a	ⁿ PrCH ₂ SeSeCH ₂ ⁿ Pr 15b	yellow liquid ^{4a}	60	54
2	ⁿ BuCHO 16a	ⁿ BuCH ₂ SeSeCH ₂ ⁿ Bu 16b	yellow liquid ¹¹	70	72
3	ⁿ BuCHO 17a	ⁿ BuCH ₂ SeSeCH ₂ ⁿ Bu 17b	yellow liquid ¹¹	60	85
4	ⁿ C ₇ H ₁₅ CHO 18a	CH ₃ (CH ₂) ₇ SeSe(CH ₂) ₇ CH ₃ 18b	yellow liquid ¹⁸	80	87
5	ⁿ C ₁₁ H ₂₃ CHO 19a	CH ₃ (CH ₂) ₁₁ SeSe(CH ₂) ₁₁ CH ₃ 19b	29–31 (29.5–30.5) ^{10b}	80	80
6	PhCH ₂ CHO 20a	PhCH ₂ CH ₂ SeSeCH ₂ CH ₂ Ph 20b	yellow liquid ^{2c}	90	84

^a Reaction conditions: aldehyde, 2.5 mmol; Se, 2.5 mmol; bubbling CO, 0.1 MPa; water, 2 mL; DMF, 20 mL; 8 h. ^b Isolated yield.

Benzaldehyde (**1a**) was treated with equivalent selenium and carbon monoxide (bubbling) in the presence of water in DMF at 95 °C for 7 h. Reductive selenation of **1a** efficiently proceeded to give dibenzyl diselenide (**1b**) in 94% yield (Table 1, entry 11). No reduction product such as benzyl alcohol or toluene was detected from the reaction mixture, although photochemical reactions of ketones or aldehydes with hydrogen selenide afforded alcohols.¹⁷ At atmospheric pressure reaction parameters of **1a** were examined (Table 1). When aprotic solvents such as THF, 1,4-dioxane, CH₃CN, EtOH, and DMAC (*N,N*-dimethylacetamide) were used as the reaction solvents at elevated temperatures, no reductive selenation of **1a** occurred (Table 1, entries 1–5, respectively). The reaction proceeded to some extent in DMSO and 1-formylpiperidine (Table 1, entries 6 and 7, respectively). When DMF (*N,N*-dimethylformide) was used as the reduction solvent, dibenzyl diselenide was formed in moderate yields at elevated temperatures (Table 1, entries 9 and 10). At 95 °C dibenzyl diselenide was formed in 94% yield (Table 1, entry 11). It is noteworthy that reductive selenation of **1a** did not proceed in DMF at ambient temperature (Table 1, entry 8). The presence of water remarkably affected formation and yields of the diselenide product. The reaction did not proceed without water and increasing the amount of water obviously improved the yield of dibenzyl diselenide, but a large excess of water is not necessary for the reaction (Table 1, entries 11–14).

In a fashion similar to the synthesis of dibenzyl diselenide, reductive selenation of aromatic and heterocyclic aromatic aldehydes was investigated, and the results are summarized in Table 2. It is noteworthy that aromatic ketones cannot undergo the same type of reactions under the conditions as stated in Table 1. Diselenide products were obtained in very good yields (80–94%) (Table 2, entries 1–6). Increasing steric hindrance on the phenyl rings of the substrates obviously decreased yields of the products; poor yields (36–45%) of the intended products were obtained. Somehow, salicylaldehyde was unchanged under the reaction conditions (Table 2, entry 9), but 1- and 2-naphthaldehydes gave the corresponding diselenides in 90% and 92% yields, respectively (Table 2, entries 10 and 11). Heterocyclic aromatic aldehydes, i.e., 2- and 3-thiophenecarboxaldehydes, and 3-pyridinecarboxaldehyde were also efficiently transformed to their corresponding diselenides in good yields (85%–92%) (Table 2, entries 12–14).

Reductive selenation of aliphatic aldehydes (**15a–20a**) was also investigated under the conditions as stated in

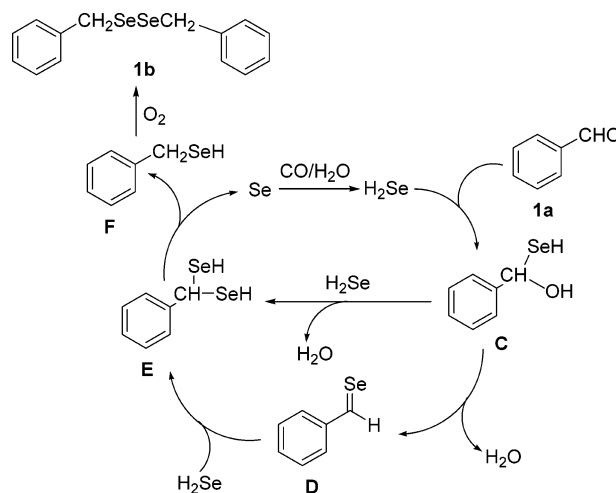
**FIGURE 1.** Proposed pathway to dibenzyl diselenide (**1b**).

Table 3. Reaction temperatures varied upon the boiling points of aliphatic aldehydes. Complete conversions were achieved for aliphatic aldehydes over a period of 8 h, and diselenide products (**15b–20b**) were obtained in moderate yields (54–87%) after workup (Table 3). Dibutyl diselenide was isolated in 54% yield (Table 3, entry 1), whereas only 45% yield was reached under 30 atm CO for the same reaction.¹² However, reduction of butyl selenocyanate with LiEt₃BH gave dibutyl diselenide in 97% yield.^{4a} The reactions of valeraldehyde and isovaleraldehyde afforded their corresponding diselenide products in 72% and 85% yields, respectively (Table 3, entries 2 and 3), which demonstrated efficiency much lower than that of reactions of the aldehydes with Na₂Se₂/NaHSe.¹¹ Long-chain aldehydes, i.e., octyl aldehyde and dodecyl aldehyde, afforded the diselenide products in 87% and 80% yields (Table 3, entries 4 and 5), which are not comparable with the best results for synthesizing the same diselenides using other procedures.^{2c,18} Proton NMR determination in CDCl₃ revealed a purity of ≤95% for the diselenide products and ~5% unknown impurities. It is noteworthy that it is difficult to purify the diselenide products to be >95% purity by repeated column chromatography or TLC on silica gel at ambient temperature in air. It appears that the corresponding diselenides from aliphatic aldehydes are less stable than their analogues from aromatic aldehydes.

Although the mechanism for formation of diselenide has not been clarified, it is likely that the reductive

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selenation of aromatic aldehydes may involve formation of selenol **F** by nucleophilic attack of H_2Se formed in situ to the carbonyl carbon atom of an aldehyde (Figure 1). Initially generated 2-hydroxylselenol **C** may be converted to diselenol **E** via an intermediate **D**, and further decomposition of **E** affords selenol **F**. Air-oxidation of **F** gives diselenide **1b** as the product.

In summary, we have developed an efficient synthetic method for symmetrical diselenides from aromatic aldehydes and less efficiency has been observed for aliphatic aldehydes. Further studies regarding the systematic extension of the method to synthesis of unsymmetrical diselenides (R_1SeSeR_2) with mixed aldehydes are underway.

Experimental Section

A typical synthetic procedure for symmetrical diselenides was carried out as follows. A 100-mL three-necked flask was charged with aldehyde (2.5 mmol), selenium (2.5 mmol), water (2 mL), and DMF (20 mL). Carbon monoxide was introduced and

bubbled into the reaction mixture with vigorous stirring at 95 °C for the given time. The reaction was monitored by TLC determination. After the reaction was complete, CO bubbling was stopped and the resultant mixture was stirred in air at ambient temperature for 30 min. Next, 20 mL of water was added, and the mixture was extracted with diethyl ether (3×40 mL). The organic phase was dried over anhydrous MgSO_4 and filtered, and the volatiles were evaporated under reduced pressure to afford the crude product. Further purification by column chromatography on silica gel or recrystallization gave the pure product. All products were identified by NMR and/or comparison with the authentic samples.

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Supporting Information Available: NMR spectral data for new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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