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Conversion of Bis(*o*-nitrophenyl)diselenides to Heterocycles Containing Selenium and Nitrogen with the Aid of Samarium Diiodide

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ABSTRACT: *Treatment of bis(o-nitrophenyl)diselenides with SmI_2 led to simultaneous reduction of nitro groups and reductive cleavage of Se—Se bonds as well as to the formation of the intermediates* **2**. *The intermediates* **2** *were "living" double-anions formed in situ, and reacted readily with ω-bromoketones and α-bromocarboxylic acid derivatives to afford the desired 2H-1,4-benzoselenazines and 2H-1,4-benzoselenazin-3(4H)-ones, respectively, in moderate to high yields and under mild conditions.* © 2002 Wiley Periodicals, Inc. Heteroatom Chem 13:302–306, 2002; Published online in Wiley Interscience (www.interscience.wiley.com). DOI 10.1002/hc.10034

INTRODUCTION

Organoselenium compounds have received considerable attention as useful synthetic reagents and intermediates in organic synthesis [1]. A number of synthetic methods have been introduced to prepare organoselenium derivatives [2] such as selenides and selenoesters. However, relatively few studies on synthesis of heterocycles containing selenium have been reported [3].

As a powerful and versatile single electron reductant, samarium diiodide (SmI_2) has been applied widely in synthetic chemistry [4]. Its use in synthesis has been especially advantageous for promoting C—C bond formation reactions, ring-closure reactions, and regio-controlled reactions difficult to accomplish by other existing methodologies. Recently we reported that the nitro group and S—S bond in bis(*o*-nitrophenyl)disulfides could be reduced and cleaved simultaneously by SmI_2, leading to the formation of a "living" intermediate (samarium nitride and sulfide). The active species could react readily with many kinds of electrophilic reagents (such as aldehydes, ketones, α,β-unsaturated ketones, and ω-bromoketones) to produce heterocycles containing nitrogen and sulfur [5]. Compared with the S—S bond, the Se—Se bond is more easily cleaved by SmI_2, and so we studied whether the nitro group and the Se—Se bond in bis(*o*-nitrophenyl)diselenides can be reduced and cleaved simultaneously by SmI_2.

RESULTS AND DISCUSSION

When 0.5 equivalent of bis(*o*-nitrophenyl)diselenides **1** were added to a solution of seven equivalents of SmI_2 at room temperature under a nitrogen

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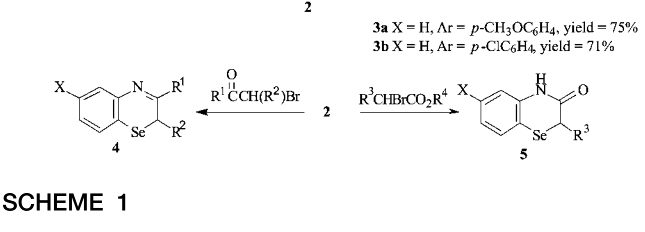
atmosphere, the deep blue color of SmI_2 changed to a brown-red color. The above appearance showed that nitro groups and Se—Se bonds were simultaneously reduced by SmI_2. According to the literature [5,6], we considered that an intermediate **2** could be generated in situ during the reduction procedure. Then, many kinds of electrophilic reagents were tested to react with these species **2**. It was found in our experiments, unlike the case of bis(*o*-nitrophenyl)disulfides that we have reported [5], that no ring-closure reactions took place between these species **2** and aldehydes (or ketones or α,β-unsaturated ketones) under similar reaction conditions. As for aromatic aldehydes, only bis(2-*N*-(arylmethylidene)aminophenyl)diselenides **3** were obtained.

Fortunately, we found that the species **2** could react smoothly with ω-bromoketones and α-halocarboxylic derivatives to afford the corresponding 2*H*-1,4-benzoselenazines **4** and 2*H*-1,4-benzoselenazin-3(4*H*)-ones **5**, respectively, in moderate to good yield. To our knowledge, compounds **4** and **5** are unknown in the literature (Scheme 1).

According to the data presented in Tables 1 and 2, when the intermediates **2** were protonated by adding MeOH, the simple reduction products, *o*-aminoselenophenols, were obtained; if this were followed by adding the above-mentioned electrophilic reagents under similar conditions, no further reaction would take place and no products **4** and **5** would be detected. These experimental results brought us to the conclusion that the intermediates **2** are highly reactive species.



SCHEME 1

TABLE 1 Synthesis of 2*H*-1,4-Benzoselenazines Promoted by SmI_2

Entry	*X*	*R^1*	*R^2*	*Time (h)*	*Yield (%)*[a]
4a	H	C_6H_5	H	2	68, 0[b]
4b	H	p-MeC_6H_4	H	2	58
4c	H	p-ClC_6H_4	H	4	77
4d	H	p-BrC_6H_4	H	4	73
4e	H	C_6H_5	Me	2	58
4f	H	CH_3	H	12	40
4g	Cl	C_6H_5	H	2	67
4h	Cl	p-ClC_6H_4	H	4	77, 0[b]
4i	Cl	p-$MeOC_6H_4$	H	4	54

[a] Yield of crude product based on bis(*o*-nitrophenyl)diselenides.
[b] MeOH was added to the solution of the intermediate **2**, followed by reaction with ω-bromoketones.

The compounds **3a,b, 4a–i**, and **5a–g** were purified by preparative thin-layer chromatography (TLC) on silical gel and fully characterized by IR, ^{1}H NMR, and MS spectroscopy. The IR spectrum of products **3** exhibited a middle strong absorption band at ~1620 cm^{-1} (C=N) while that of products **4** appeared at ~1650 cm^{-1} (C=N); as for the IR spectrum of products **5**, the characteristic absorption of the carboxy group appeared at ~1660 cm^{-1} (CONH). The ^{1}H NMR spectra of the products **3** showed a singlet peak because of the CH=N proton at $\delta_H \sim 8.25$, apart from the usual peaks in the aromatic region; while that of the products **4** (except for entry 4f) exhibited a two-proton singlet peak because of $SeCH_2$ protons at $\delta_H \sim 3.0$. Mass spectra of all the products **4** showed that the cyclic benzoselenazole ions derived from the fragmentation and skeletal rearrangement of the molecular ions were the main spectral features, while that of the products **5** exhibited that the molecular ions were major.

In summary, the simultaneous reduction of nitro groups and Se—Se bonds in bis(*o*-nitrophenyl)diselenides induced by SmI_2 were studied and the results provide a new and simple synthesis of 2*H*-1,4-benzoselenazines and 2*H*-1,4-benzoselenazin-3(4*H*)-ones.

EXPERIMENTAL

Melting points were obtained on an electrothermal melting point apparatus and were uncorrected. Infrared spectra were recorded on a Bruker Vector 22 spectrometer using KBr pellets or a thin film with maximun absorption indicated in cm^{-1}. ^{1}H

TABLE 2 Synthesis of 2*H*-1,4-Benzoselenazin-3(4*H*)-ones Promoted by SmI_2

Entry	*X*	*$R^3CHBrCO_2R^4$*	*T (°C)*	*Time (h)*	*Yield (%)*[a]
5a	H	$BrCH_2CO_2Et$	r.t.	2	83, 0[b]
5b	H	$CH_3CH(Br)CO_2H$	40	3	79
5c	H	$(CH_3)_2CHCH(Br)CO_2H$	60	4	71, 0[b]
5d	H	$C_6H_5CH(Br)CO_2Me$	60	4	65
5e	Cl	$BrCH_2CO_2Et$	r.t.	2	89
5f	Cl	$CH_3CH(Br)CO_2H$	40	3	81
5g	Cl	$(CH_3)_2CHCH(Br)CO_2H$	60	4	75

[a] Yield of crude product based on bis(*o*-nitrophenyl)diselenides.
[b] MeOH (0.2 ml) was added after the formation of the intermediates **2** and *o*-aminoselenophenols were obtained. In this case, no products **5** could be detected.

NMR spectra were recorded on a Bruker AC-80 spectrometer using $CDCl_3$ solutions. *J* values are in Hz. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Mass spectra were recorded on an HP 5989B MS spectrometer. Microanalyses were carried out on a Carlo Erba EA 1110 instrument.

Tetrahydrofuran (THF) was distilled from sodium-benzophenone immediately prior to use. All organic compounds, such as aldehydes, ketones, and acid chlorides or anhydrides, were commercially available and were used without further purification. α-Bromoketones and α-bromocarboxylic acid derivatives were prepared by known procedures. All reactions were performed in a Schlenk-type glass apparatus under a nitrogen atmosphere.

Formation of the Intermediates **2** *Promoted by* SmI_2

Samarium powder (1.05 g, 7 mmol, 99.9%) was placed in a well-dried three-necked round-bottom flask containing a magnetic stirrer bar. The flask was flushed with nitrogen several times. Tetrahydrofuran (30 ml) was added through a rubber septum by a syringe. Iodine (1.75 g, 7 mmol) was added to the flask and the mixture was stirred at room temperature until the solution became deep blue and homogeneous (1–2 h). The solution of SmI_2 was now ready for subsequent use. To the solution of SmI_2 was added bis(*o*-nitrophenyl)diselenide **1** (0.202 g, 0.5 mmol) in THF (3 ml) by using syringe at room temperature under a nitrogen atmosphere. The deep blue solution gradually became brown-red within 0.5 h, which showed that the nitro groups were reduced and the Se—Se bonds were reductively cleaved by SmI_2; the intermediates **2** had been generated.

Reactions of the Intermediates **2** *with Aldehydes or α-Bromoketones*

Each aldehyde (or α-bromoketone, 1.1 mmol) in THF (1 ml) was added to the solution of the intermediates **2** by syringe. After having been stirred for a given time (Scheme 1 and Table 1, the reaction was monitored by TLC), the reaction mixture was treated with dilute hydrochloric acid (0.1 mol/l, 3 ml) and the mixture was extracted with ether (3 × 30 ml). The combined organic extracts were washed with saturated aqueous $Na_2S_2O_3$ (15 ml), saturated aqueous NaCl (15 ml), and then dried over anhydrous $MgSO_4$. After evaporation of the solvent under reduced pressure, the crude product was purified by preparative TLC on silica gel using ethyl acetate/cyclohexane (1:7) as eluant.

Reactions of the Intermediates **2** *with α-Bromocarboxylic Acid Derivatives*

The preparation of the intermediates **2** is the same as described previously. α-Bromocarboxylic acid derivatives (1.1 mmol) in THF (1 ml) were then added by a syringe and the mixtures were stirred for a given time (Table 2). The crude products were isolated as before and purified by preparative TLC on silica gel using ethyl acetate/cyclohexane (1:4) as eluant.

DATA OF PRODUCTS

3a, Bis(2-N-(4′-methoxyphenylmethylidene)aminophenyl)diselenide: yellow crystal, mp 131–133°C. ν_{max}: 2925, 1623, 1565, 1250, 990, 830, 780 cm^{-1}. δ_H: 8.23 (2H, s), 7.80–6.87 (16H, m), 3.73 (6H, s). *m/z* (%): 290 ($^{80}Se - M^+/2$, 100), 210 (24), 157 (21), 77 (59). Anal. Calcd. for $C_{28}H_{24}N_2o_2Se_2$: C, 58.15; H, 4.18; N, 4.84. Found: C, 57.93; H, 4.27; N, 4.77%.

3b, Bis(2-N-(4′-chlorophenylmethylidene)aminophenyl)diselenide: light yellow crystal, mp 165–167°C. ν_{max}: 2925, 1620, 1550, 970, 840, 790 cm^{-1}. δ_H: 8.25 (2H, s), 7.87–6.92 (16H, m). *m/z* (%): 294 ($^{80}Se—M^+/2$, 100), 214 (30), 157 (85), 139 (12), 137 (38). Anal. Calcd. for $C_{26}H_{18}Cl_2N_2Se_2$: C, 53.19; H, 3.09; N, 4.77. Found: C, 53.33; H, 2.95; N, 4.63%.

4a, 3-Phenyl-2H-1,4-benzoselenazine: light yellow crystal, mp 61–63°C. ν_{max}: 2930, 1650, 1475 cm^{-1}. δ_H: 7.42–6.87 (9H, m), 3.03 (2H, s). *m/z* (%): 272 ($^{80}Se - M^+$, 16), 258 (100), 183 (85), 156 (52). Anal. Calcd. for $C_{14}H_{11}NSe$: C, 61.79; H, 4.07; N, 5.15. Found: C, 61.93; H, 3.87; N, 5.07%.

4b, 3-(4′-Methylphenyl)-2H-1,4-benzoselenazine: light yellow crystal, mp 67–69°C. ν_{max}: 2980, 2930, 1660, 1475, 1380 cm^{-1}. δ_H: 8.00–6.80 (8H, m), 2.98 (2H, s), 2.32 (3H, s). *m/z* (%): 286 ($^{80}Se - M^+$, 8), 272 (70), 185 (60), 156 (35), 91 (100). Anal. Calcd. for $C_{15}H_{13}NSe$: C, 62.96; H, 4.58; N, 4.89. Found: C, 62.81; H, 4.47; N, 5.04%.

4c, 3-(4′-Chlorophenyl)-2H-1,4-benzoselenazine: light yellow crystal, mp 71–73°C. ν_{max}: 2930, 1630, 1475 cm^{-1}. δ_H: 7.78–6.93 (8H, m), 3.05 (2H, s). *m/z* (%): 306 ($^{80}Se - M^+$, 16), 292 (100), 185 (53), 183 (56), 156 (21), 111 (30). Anal. Calcd. for $C_{14}H_{10}ClNSe$: C, 54.85; H, 3.29; N, 4.57. Found: C, 55.02; H, 3.36; N, 4.39%.

4d, 3-(4′-Bromophenyl)-2H-1,4-benzoselenazine: pale crystal, mp 103–105°C. ν_{max}: 2925, 2850, 1650, 1465 cm^{-1}. δ_H: 7.87–7.14 (8H, m), 3.02 (2H, s). *m/z* (%): 351 ($^{80}Se - M^+$, 12), 337 (100), 185 (90), 183 (95), 156 (42). Anal. Calcd. for $C_{14}H_{10}BrNSe$: C, 47.90; H, 2.87; N, 3.99. Found: C, 48.12; H, 2.78; N, 3.83%.

4e, 2-Methyl-3-phenyl-2H-1,4-benzoselenazine: yellow crystal, mp 75–77°C. ν_{max}: 2980, 2840, 1660, 1380 cm^{-1}. δ_H: 7.62–6.71 (9H, m), 3.63 (1H, q, J = 5 Hz), 1.20 (3H, d, J = 5 Hz). m/z (%): 286 (^{80}Se – M$^+$, 8), 258 (100), 183 (65), 156 (46). Anal. Calcd. for $C_{15}H_{13}NSe$: C, 62.96; H, 4.58; N, 4.89. Found: C, 63.11; H, 4.42; N, 4.84%.

4f, 3-Methyl-2H-1,4-benzoselenazine: oil. ν_{max}: 2980, 2930, 1650, 1475, 1380 cm^{-1}. δ_H: 7.58–6.92 (3H, m), 2.97 (2H, s), 2.13 (3H, s). m/z (%): 210 (^{80}Se – M$^+$, 4), 196 (60), 183 (100), 156 (52). Anal. Calcd. for C_9H_9NSe: C, 51.46; H, 4.32; N, 6.67. Found: C, 51.27; H, 4.45; N, 6.83%.

4g, 6-Chloro-3-phenyl-2H-1,4-benzoselenazine: yellow crystal, mp 77–79°C. ν_{max}: 2930, 1660, 1475 cm^{-1}. δ_H: 7.51–6.85 (8H, m), 3.08 (2H, s). m/z (%): 306 (^{80}Se – M$^+$, 16), 292 (100), 218 (75), 191 (37). Anal. Calcd. for $C_{14}H_{10}ClNSe$: C, 54.85; H, 3.29; N, 4.57. Found: C, 54.72; H, 3.42; N, 4.35%.

4h, 6-Chloro-3-(4′-chlorophenyl)-2H-1,4-benzoselenazine: light yellow crystal, mp 130–132°C. ν_{max}: 2940, 1645, 1465 cm^{-1}. δ_H 7.63–6.83 (7H, m), 3.03 (2H, s). m/z (%): 341 (^{80}Se – M$^+$, 13), 327 (100), 218 (81), 191 (52), 111 (33). Anal. Calcd. for $C_{14}H_9Cl_2NSe$: C, 49.31; H, 2.66; N, 4.11. Found: C, 49.45; H, 2.83; N, 3.96%.

4i, 6-Chloro-3-(4′-methoxyphenyl)-2H-1,4-benzoselenazine: light yellow crystal, mp 132–134°C, ν_{max}: 2980, 2925, 1475, 1380, 1650, 1250 cm^{-1}. δ_H: 7.85–6.70 (7H, m), 3.86 (3H, s), 2.95 (2H, s). m/z (%): 336 (^{80}Se – M$^+$, 18), 322 (100), 218 (34), 191 (42), 107 (33). Anal. Calcd. for $C_{15}H_{12}ClNOSe$: C, 53.52; H, 3.57; N, 4.16. Found: C, 53.73; H, 3.61; N, 3.99%.

5a, 2H-1,4-Benzoselenazin-3(4H)-one: light yellow crystal, mp 181–183°C (lit. [7] 185°C). 3330, 2830, 1650, 1475 cm^{-1}. δ_H: 10.1 (1H, br s), 7.40–6.90 (4H, m), 3.30 (2H, s).

5b, 2-Methyl-2H-1,4-benzoselenazin-3(4H)-one: light yellow crystal, mp 125–126°C. ν_{max}: 3332, 2980, 2830, 1655, 1375 cm^{-1}. δ_H: 9.72 (1H, br s), 7.47–6.97 (4H, m), 3.63 (1H, q, J = 7.2 Hz), 1.58 (3H, d, J = 7.2 Hz). m/z (%): 227 (^{80}Se – M$^+$, 67), 184 (17), 146 (27), 120 (100), 91 (24). Anal. Calcd. for C_9H_9NOSe: C, 47.82; H, 4.01; N, 6.20. Found: C, 47.68; H, 4.12; N, 6.06%.

5c, 2-Isopropyl-2H-1,4-benzoselenazin-3(4H)-one: light yellow crystal, mp 123–125°C. ν_{max}: 3335, 2980, 2830, 1655, 1375 cm^{-1}. δ_H: 9.82 (1H, br s), 7.46–6.95 (4H, m), 3.20 (1H, d, J = 8.0 Hz), 2.15–1.81 (1H, m), 1.07 (6H, d, J = 6.5 Hz). m/z (%): 255 (^{80}Se – M$^+$, 100), 213 (48), 211 (24), 184 (25), 132 (87), 83 (87). Anal. Calcd. for $C_{11}H_{13}NOSe$: C, 51.99; H, 5.16; N, 5.51. Found: C, 52.12; H, 5.03; N, 5.65%.

5d, 2-Phenyl-2H-1,4-benzoselenazin-3(4H)-one: light yellow crystal, mp 177–178°C. ν_{max}: 3335, 2840, 1665, 1475 cm^{-1}. δ_H: 10.32 (1H, br s), 7.49–6.90 (9H, m), 3.83 (1H, s). m/z (%): 289 (^{80}Se – M$^+$, 50), 212 (100), 184 (73), 132 (57). Anal. Calcd. for $C_{14}H_{11}NOSe$: C, 58.36; H, 3.85; N, 4.86. Found: C, 58.28; H, 3.97; N, 4.64%.

5e, 6-Chloro-2H-1,4-benzoselenazin-3(4H)-one: light yellow crystal, mp 184–186°C. ν_{max}: 3335, 2830, 1656, 1470 cm^{-1}. δ_H: 10.4 (1H, br s), 7.70–6.95 (3H, m), 3.36 (2H, s). m/z (%): 247 (^{80}Se – M$^+$, 100), 219 (54), 156 (33), 154 (30), 71 (49). Anal. Calcd. for $C_8H_6ClNOSe$: C, 38.98; H, 2.45; N, 5.68. Found: C, 38.76; H, 2.51; N, 5.54%.

5f, 6-Chloro-2-methyl-2H-1,4-benzoselenazin-3(4H)-one: light yellow crystal, mp 178–180°C. ν_{max}: 3335, 2960, 2830, 1660, 1380 cm^{-1}. δ_H: 10.23 (1H, br s), 7.60–6.85 (3H, m), 3.56 (1H, q, J = 7.2 Hz), 1.53 (3H, d, J = 7.2 Hz). m/z (%): 261 (^{80}Se – M$^+$, 82), 180 (24), 156 (33), 154 (100), 55 (27). Anal. Calcd. for $C_9H_8ClNOSe$: C, 41.49; H, 3.10; N, 5.38. Found: C, 41.56; H, 3.21; N, 5.14%.

5g, 6-Chloro-2-isopropyl-2H-1,4-benzoselenazin-3(4H)-one: light yellow crystal, mp 137–139°C. ν_{max}: 3330, 2980, 2830, 1650, 1375 cm^{-1}. δ_H: 10.02 (1H, br s), 7.56–6.98 (3H, m), 3.23 (1H, d, J = 8.0 Hz), 2.17–1.83 (1H, m), 1.12 (6H, d, J = 6.5 Hz). m/z (%): 289 (^{80}Se – M$^+$, 100), 246 (48), 244 (24), 218 (25), 209 (23), 166 (57). Anal. Calcd. for $C_{11}H_{12}ClNOSe$: C, 45.78; H, 4.19; N, 4.85. Found: C, 45.72; H, 4.03; N, 4.69%.

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