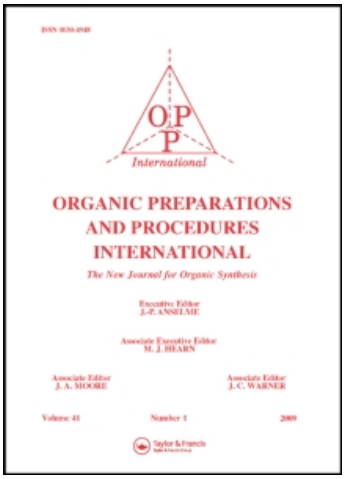

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OPPI BRIEFS

A NOVEL SYNTHESIS OF 2*H*-1,4-BENZOSELENAZINES FROM (*o*-NITROPHENYL)DISELENIDES AND *ω*-BROMOKETONES PROMOTED BY Sm/$TiCl_4$ SYSTEM

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(10/18/00)

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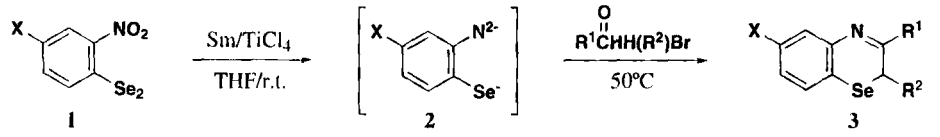
Organoselenium compounds have received considerable attention as useful reagents and intermediates in organic synthesis.[1] A number of methods have been introduced to prepare organoselenium derivatives.[2] However, relatively few studies on the synthesis of heterocycles containing selenium have been reported.[3] Low-valent titanium reagent has been widely used in organic synthesis.[4] It was reported that nitro group and sulfur-sulfur, selenium-selenium and tellurium-tellurium bonds could be reduced or cleaved by low-valent titanium reagent.[5] Recently we reported that low-valent titanium reagent derived from a Sm/$TiCl_4$ system could induce simultaneous reduction of nitro group and S-S bond in bis(*o*-nitrophenyl)disulfides to give heterocycles containing nitrogen and sulfur.[6] Compared with S-S bond, Se-Se bond is easier to reduce by the Sm/$TiCl_4$ system.[5] In order to extend the application of Sm/$TiCl_4$, we investigated if the Sm/$TiCl_4$ system could induce simultaneous reduction of nitro group and Se-Se bond in bis(*o*-nitrophenyl)diselenides.

When *bis*(*o*-nitrophenyl)diselenides **1** were treated with the Sm/$TiCl_4$ system in anhydrous THF at room temperature, the deep dark color of the solution gradually turned into brownish red within half an hour. This change in color indicated that the nitro group had been reduced and the Se-Se bond had been reductively cleaved simultaneously by Sm/$TiCl_4$ to the active intermediates **2**. Although a detailed mechanism of this reaction has not been clarified, we consider that the intermediates **2** are "living" double-anion species (nitride anions and selenide anions) generated *in situ*.[5] These new anion species reacted readily with *w*-bromoketones to afford the desired 2*H*-1,4-benzoselenazines **3** in moderate to high yields (*Table 1*).



1 2 3

Table 1. Synthesis of 2*H*-1,4-benzoselenazines induced by Sm/$TiCl_4$ system

Entry	X	R^1	R^2	Time (h)	Product	Yield (%)[a]
1	H	C_6H_5	H	2	**3a**	63
2	H	p-MeC_6H_4	H	2	**3b**	52
3	H	p-ClC_6H_4	H	4	**3c**	70
4	H	p-BrC_6H_4	H	4	**3d**	67
5	H	C_6H_5	Me	2	**3e**	54
6	H	CH_3	H	12	**3f**	35
7	Cl	C_6H_5	H	2	**3g**	62
8	Cl	p-ClC_6H_4	H	4	**3h**	65
9	Cl	p-$MeOC_6H_4$	H	4	**3i**	54

[a]Isolated yields based on bis(*o*-nitrophenyl)diselenides.

EXPERIMENTAL SECTION

Tetrahydrofuran (THF) was distilled from sodium-benzophenone immediately prior to use. All reactions were conducted under a nitrogen atmosphere. Melting points are uncorrected. Infrared spectra were recorded on an Shimadzu IR-408 spectrometer in KBr or as a film with absorption in cm^{-1}. ^1H NMR spectra were determined in a Bruker AC-80 spectrometer as $CDCl_3$ solutions. J values are in Hz. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Mass spectra were recorded on a HP 5989B MS spectrometer. Microanalysis was carried out on a Carlo Erba EA 1110 instrument.

General Procedure.- Under an inert atmosphere of nitrogen, $TiCl_4$ (0.33 mL, 3 mmol) was added dropwise using a syringe to a stirred suspension of powdered samarium (0.45 g, 3 mmol) in freshly distilled dry THF (20 mL) at room temperature. When the addition was complete, the mixture was refluxed for 2 h; a suspension of the low-valent titanium reagent was formed and cooled to room temperature. A solution of bis(*o*-nitrophenyl)diselenides **1** (0.5 mmol) in anhydrous THF (2 mL) was added dropwise to this solution and the deep dark color of the mixture gradually turned into brownish red within half an hour. Then a solution of ω-bromoketone (1.1 mmol) in THF (1 mL) was added to the mixture. After being stirred at 50° for the time indicated in **Table 1**, the reaction was quenched by the addition of a dilute HCl (0.1 mol/L, 2 mL) solution, and then extracted with ether (3 x 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 thin layer chromatography on silica gel using ethyl acetate and cyclohexane (1:7) as eluent to afford the product.

3-Phenyl-2*H*-1,4-benzoselenazine (**3a**), light yellow crystals, mp 61-63°. IR(KBr): 2930, 1475 (CH_2), 1650 (C=N) cm^{-1}. ^1H NMR: δ 7.42-6.87 (9H, m, ArH), 3.03 (2H, s, CH_2). MS (EI): *m/z* (%) 272 (Se^{80}-M^+, 16.2), 258 (Se^{80}-M–14, 100), 183 (85.4), 156 (52.0).

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

3-(4'-Methylphenyl)-2*H*-1,4-benzoselenazine (**3b**), light yellow crystals, mp 67-69°. IR (KBr): 2980, 2930, 1475, 1380 (CH_3, CH_2), 1660 (C=N) cm^{-1}. ^1H NMR: δ 8.00-6.80 (8H, m, ArH), 2.98 (2H, s, CH_2), 2.32 (3H, s, CH_3). MS (EI): *m/z* (%) 286 (Se^{80}-M^+, 7.8), 272 (Se^{80}-M–14, 70.3), 185 (60.4), 156 (35.4), 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

3-(4'-Chlorophenyl)-2*H*-1,4-benzoselenazine (**3c**), light yellow crystals, mp 71-73°. IR (KBr): 2930, 1475 (CH_2), 1630 (C=N) cm^{-1}, 740 (C-Cl). ^1H NMR: δ 7.78-6.93 (8H, m, ArH), 3.05 (2H, s, CH_2). MS (EI): *m/z* (%) 306 (Se^{80}-M^+, 15.7), 292 (Se^{80}-M–14, 100), 185 (53.6), 183 (56.2), 156 (21.7), 111 (30.3).

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

3-(4'-Bromophenyl)-2*H*-1,4-benzoselenazine (**3d**), light yellow crystals, mp 103-105°. IR (KBr): 2925, 2850, 1465 (CH_2), 1650 (C=N) cm^{-1}. ^1H NMR: δ 7.87-7.14 (8H, m, ArH), 3.02 (2H, s, CH_2). MS (EI): *m/z* (%) 351 (Se^{80}-M^+, 12.4), 337 (Se^{80}-M–14, 100), 185 (90.7), 183 (95.4), 156 (42.0).

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

2-Methyl-3-phenyl-2*H*-1,4-benzoselenazine (**3e**), yellow crystals, mp 75-77°. IR (KBr): 2980, 2840, 1380 (CH_3, CH_2), 1660 (C=N) cm^{-1}. ^1H NMR: δ 7.62-6.71 (9H, m, ArH), 3.63 (1H, q, J=5Hz, CH), 1.20 (3H, d, J=5Hz, CH_3). MS (EI): *m/z* (%) 286 (Se^{80}-M^+, 7.8), 258 (Se^{80}-M^+–28, 100), 183 (65.1), 156 (46.2).

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

3-Methyl-2*H*-1,4-benzoselenazine (**3f**), oil, IR (neat): 2980, 2930, 1475, 1380 (CH_3, CH_2), 1650 (C=N) cm^{-1}, 742 (C-Cl). ^1H NMR: δ 7.58-6.92 (3H, m, ArH), 2.97 (2H, s, CH_2), 2.13 (3H, s, CH_3). MS (EI): *m/z* (%) 210 (Se^{80}-M^+, 3.5), 196 (Se^{80}-M–14, 60.3), 183 (100), 156 (52.3).

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

6-Chloro-3-phenyl-2*H*-1,4-benzoselenazine (**3g**), yellow crystals, mp 77-79°. IR (KBr): 2930, 1475 (CH_2), 1660 (C=N) cm^{-1}, 740 (C-Cl). ^1H NMR: δ 7.51-6.85 (8H, m, ArH), 3.08 (2H, CH_2). MS (EI): *m/z* (%) 306 (Se^{80}-M^+, 15.7), 292 (Se^{80}-M–14, 100), 218 (75.3), 191 (37.6).

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

6-Chloro-3-(4'-chlorophenyl)-2*H*-1,4-benzoselenazine (**3h**), light yellow crystals, mp 130-132°, IR (KBr): 2940, 1465 (CH_2), 1645 (C=N) cm^{-1}, 740 (C-Cl). ^1H NMR: δ 7.63-6.83 (8H, m, ArH), 3.03 (2H, s, CH_2). MS (EI): *m/z* (%) 341 (Se^{80}-M^+, 13.3), 327 (Se^{80}-M–14, 100), 218 (80.7), 191 (52.0), 111 (33.4).

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

6-Chloro-3-(4'-methoxyphenyl)-2*H*-1,4-benzoselenazine (**3i**), light yellow crystals, mp 132-134°, IR (KBr): 2980, 2925, 1475, 1380 (CH_3, CH_2), 1650 (C=N) cm^{-1}, 1250 (C-O-C), 740 (C-Cl). ^1H

NMR: δ 7.85-6.70 (7H, m, ArH), 3.86 (3H, s, OCH_3), 2.95 (2H, s, CH_2). MS (EI): *m/z* (%) 336 (Se^{80}-M^+, 17.5), 322 (Se^{80}-M–14, 100), 218, 191 (42.0), 107 (33.7).

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

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