

A Novel Conversion of 3,7-Disubstituted 2*H*,6*H*-Tetrahydro-1,5,3,7-diselenadiazocines to 4-Substituted 1,2,4-Diselenazolidines by Treating with Oxidizing Agents

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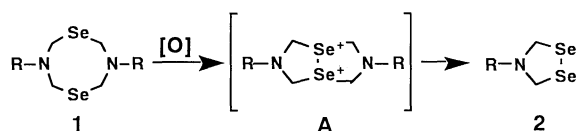
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Oxidation of 3,7-disubstituted 2*H*,6*H*-tetrahydro-1,5,3,7-diselenadiazocines afforded 4-substituted 1,2,4-diselenazolidines in modest yields. The intermediates of the reactions were supposed to be diselena dications possessing 1,5,3,7-diselenadiazabicyclo[3.3.0]octane skeleton generated transiently by the transannular interaction of two selenium atoms.

Current interest has been concentrated on the selenium atom-containing reactive species generated by the fragmentation of cyclic selenoacetals.¹ However, few studies on the oxidation of cyclic polyaminopolyselenoacetals have been achieved^{2,3} in spite of the expectation to give various selenium-containing heterocycles through the oxidative ring contraction. Especially, it was expected that oxidation of conformationally flexible eight-membered aminoselenoacetals would cause spontaneous transannular Se-Se interaction to give 1,5,3,7-diselenadiazabicyclo[3.3.0]octane-type diselena dications **A**, which would undergo further fragmentation to give novel cyclic diselenides by the attack of nucleophiles toward the methylene carbons of the dications **A**. In this paper, we would like to describe a novel ring contraction of 3,7-disubstituted 2*H*,6*H*-tetrahydro-1,5,3,7-diselenadiazocines **1** to 1,2,4-diselenazolidines **2** by treating with various oxidizing agents.



3,7-Dialkyl and 3,7-diaryl 2*H*,6*H*-tetrahydro-1,5,3,7-diselenadiazocines **1** were prepared by using modified Draguet's method,⁵ in which an ethanolic solution of a primary amine was treated with formalin and NaSeH.⁶ Physical properties including MS, IR, ¹H NMR, and ¹³C NMR spectra were fully consistent with the structure of **1**, and were also identical with the reported data.⁵ All results on the preparation of **1** are shown in Table 1. The structure of **1a** (R=C₆H₅) was finally defined by X-ray crystallographic analysis,⁷ and the ORTEP drawing of **1a** is shown in Figure 1. The crystal data of **1a** indicated that the eight-membered ring of **1a** possessed the crown-type conformation in which two selenium atoms were located close to each other.⁸ The atomic distance between the two selenium atoms (3.858 Å) is thought to be small enough to cause the facile transannular Se-Se interaction accompanied with the least motion of the atoms.

Table 1. Preparation of 3,7-Disubstituted 2*H*,6*H*-Tetrahydro-1,5,3,7-diselenadiazocines (**1**)

$\text{HCHO} \xrightarrow[2) \text{R-NH}_2]{1) \text{NaSeH / EtOH}} \text{R-N} \begin{array}{c} \text{Se} \\ \text{Se} \end{array} \text{N-R}$ 1				
R	Temp	Time /h	Product	Yield /% ^a
C ₆ H ₅	r.t.	2	1a	72
4-CH ₃ OC ₆ H ₄	r.t.	2	1b	89
CH ₃ ^b	r.t.	2	1c	64
c-C ₆ H ₁₁	r.t.	2	1d	92

^a Isolated yields based on the starting amines. ^b CH₃NH₂·HCl was used in place of CH₃NH₂.

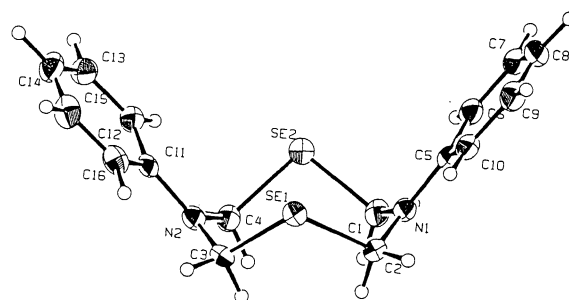


Fig.1 An ORTEP view of **1a**(R=Ph)

To a CH₂Cl₂ solution of **1a**(R=Ph) was added dropwise a CH₂Cl₂ solution of NBS(1.1 equiv.) at -78 °C and the reaction mixture was stirred for 3h under an Ar atmosphere. After quenching with an aqueous NaOH solution, the usual workup, and purification of the crude reaction product by column chromatography on silica-gel, 4-phenyl-1,2,4-diselenazolidine (**2a**) was obtained as stable reddish brown prisms in 83% yield along with succinimide derivative **3a**(85%).^{4,9} Other 2*H*,6*H*-tetrahydro-1,5,3,7-diselenadiazocines **1** were also converted to the corresponding 1,2,4-diselenazolidines **2** in good yields by treating with NBS in a similar method as shown above. Treatment of **1** with other oxidizing agents such as mCPBA and t-BuOOH, as well as the treatment of a CH₃CN solution of **1** with a catalytic amount of CuCl₂·2H₂O (0.1 equiv.) under an aerobic condition, were also effective for the conversion of **1** to **2**. The structures of **2** were confirmed by MS, IR, ¹H NMR, and ¹³C NMR spectra, and the elemental analysis data.⁴ The structural determination of **2** was finally achieved by X-ray crystallographic analysis of **2b** (R=4-CH₃OC₆H₄), and X-ray data revealed a 1,2,4-diselenazolidine

structure possessing a Se-Se bond (2.331 Å) and a quasi-axial 4-methoxyphenyl substituent on the nitrogen atom.⁷ The ORTEP view of **2b** is also shown in Figure 2. All results of the reactions are summarized in Table 2.

The mechanism of the formation of **2** remained unclear at this time. In line with Furukawa's extensive studies on cyclic dichalcogena dications,¹⁰⁻¹² it was assumed that diselenadication **A** possessing 1,5,3,7-diselenadiazabicyclo[3.3.0]octane skeleton were generated transiently in the first stage of the oxidation of **1**. In our cases, the 1,5,3,7-diselenadiazocine ring possesses the high flexibility and the most favored conformation of the rings has been estimated to be crown-type in which two selenium atoms occupied at the closed position.⁸ Thus, it was assumed that the transannular attack of the selenium atom to the initially-formed selenonium cation might cause easily to form **A**. However, all attempts for the direct detection of the intermediate of the reaction by monitoring with NMR were unsuccessful.¹³ In our case, the intermediates **A** possess the methylene groups adjacent to the cationic selenium atoms. Thus, it was assumed that the fragmentation of **A** might be initiated by the attack of

nucleophiles to the methylene carbons of **A** to give **2**.¹⁴ However, the stepwise ring contraction mechanism was not excluded out from these results.

In conclusion, 2*H*,6*H*-tetrahydro-1,5,3,7-diselenadiazocines **1** subjected to selective ring contraction by treating with various oxidizing agents gave 1,2,4-diselenazolidines **2**.

References and Notes

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- Supplementary materials containing the physical data of **1**, **2**, and **3a** are available.
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- Crystal Data for **1a**(R=C₆H₅): C₁₆H₁₈N₂Se₂, M_w=396.25, Colorless Prism, monoclinic, P2₁/c(No.14), a=13.876(1), b=5.334(1), c=21.200(2) Å, β=98.97(1)°, V=1550.0(3) Å³, Z=4, D_{calc}=1.69 g/cm³, μ(CuKα)=60.45 cm⁻¹, R=0.032, R_w=0.046. Crystal Data for **2b**(R=4-CH₃OC₆H₄): C₉H₁₁N₂OSe₂, M_w=307.11, Reddish Brown Prism, monoclinic, P2₁/c(No.14), a=5.787(5), b=9.993(3), c=17.828(7) Å, β=94.68(5)°, V=1027(1) Å³, Z=4, D_{calc}=1.985 g/cm³, μ(MoKα)=70.84 cm⁻¹, R=0.039, R_w=0.056. Supplementary materials including the X-ray crystallographic data of **1a** and **2b** are also available.
- The MM2 calculation indicated that the crown-type conformation of **1a** possessing C_{2v} symmetry was most favored as is corresponding with the results of X-ray crystallographic analysis shown in the text.
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- When a CDCl₃ solution of **1a** was treated with t-BuOOH(1.1 equiv.) in an NMR tube and the reaction mixture was subjected to NMR monitoring at 25 °C, no significant signals assigned to the intermediate **A** except for those assigned to **1a** and **2a** were revealed in the spectrum of the reaction mixture.
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Table 2. Conversion of 3,7-Disubstituted 2*H*,6*H*-Tetrahydro-1,5,3,7-diselenadiazocines (**1**) to 4-Substituted 3*H*-Dihydro-1,2,4-diselenazolidines (**2**)

Substrate R	Reagent (equiv.)	Temp /°C	Time /h	Yield of 2 ^a /%
C ₆ H ₅	NBS (1.1)	-78	3	83 (2a) ^b
C ₆ H ₅	mCPBA (1.1)	0	1	80 (2a)
C ₆ H ₅	t-BuOOH (1.1)	r.t.	25	68 (2a)
C ₆ H ₅	CuCl ₂ ·2H ₂ O (0.1) ^c	r.t.	94	46 (2a)
4-CH ₃ OC ₆ H ₄	NBS (1.1)	-78	2	89 (2b)
4-CH ₃ OC ₆ H ₄	CuCl ₂ ·2H ₂ O (0.1) ^d	r.t.	197	88 (2b)
CH ₃	NBS (1.1)	-78	2	76 (2c)
c-C ₆ H ₁₁	NBS (1.1)	-78	2	54 (2d)

^a Isolated yields. ^b Succinimide **3a**(R=Ph) was obtained in 85% yield along with **2a**. ^c The reaction was carried out in CH₃CN under an O₂ atmosphere. ^d Aerobic reaction condition.

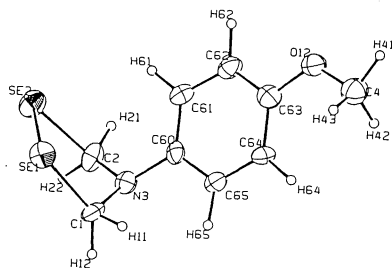


Fig.2 An ORTEP view of **2b**(R=4-CH₃OC₆H₄)