

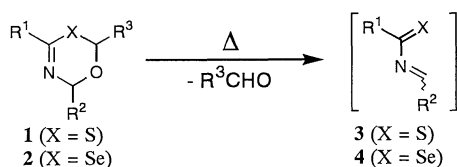
# Generation of 1,3-Selenaza-1,3-butadienes by Thermal Cycloreversion of 2,4,6-Trisubstituted 6H-1,3,5-Oxaselenazines

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1,3-Selenaza-1,3-butadienes were generated by thermal cycloreversion of 6H-1,3,5-oxaselenazines, and were trapped with dienophiles or nucleophiles to give the corresponding [4+2] cycloadducts or 1,4-adducts, respectively.

Recently, reactive heterodienes have been well-documented as new tools for the syntheses of various heterocycles. However, the heterodienes possessing a selenocarbonyl functionality<sup>1</sup> have been less studied in contrast to those of the sulfur analogues.<sup>2</sup> During our studies on the reactive species containing carbon-chalcogen double bonds for the use of novel building blocks of heterocycles, we have expected that 1,3-selenaza-1,3-butadienes **4**<sup>3</sup> would be easily generated by thermal cycloreversion of 6H-1,3,5-oxaselenazines **2** in a similar manner to those of the sulfur analogues **1**. In this paper, we wish to describe a generation of novel heterodienes **4** and the trapping of the species by using reactive dienophiles, alcohols, or thiols.



Scheme 1.

6H-1,3,5-Oxathiazine (**1a**) and 6H-1,3,5-oxaselenazines (**2a-c**) were prepared by treating thiobenzamide or selenoamides with 2,4,6-trimethyl-1,3,5-trioxane or pivalaldehyde and  $BF_3 \cdot OEt_2$  according to Sonoda's method.<sup>4</sup> Subsequently, a benzene or a toluene solution of **1a** or **2a-c** was treated with an acetylenic dienophile at refluxing temperature, and the crude reaction mixture was subjected to chromatographic separation to give 4H-1,3-thiazines (**5a**, **6a**) or 4H-1,3-selenazines (**7**, **8**).<sup>5</sup> Especially, the reaction of **1a**, **2a** or **2c** with methyl propiolate gave sole regioisomers bearing a methoxycarbonyl group at the C-5 position of the products,<sup>6</sup> as expected from the FMO theory. The similar treatment of **2a** with *p*-benzoquinone or diethyl azodicarboxylate (DEAD) also afforded **9a**(36%) or **10a**(45%), respectively. All results of the reactions are given in Table 1.

Furthermore, when **1a** or **2a-c** were heated in an alcoholic media, the corresponding 1,4-adducts of the heterodienes with the alcohols, **11-13**, were obtained in modest yields,<sup>5</sup> and the similar treatment of a benzene solution of **2** with thiols (10 mol amt.) also afforded **14** or **15**, as shown in Table 2. These results indicated the *in situ* generation of 1,3-thiaza-1,3-butadiene **3** and 1,3-selenaza-1,3-butadienes **4** through thermal cycloreversion of **1** or **2**. In contrast, treating a benzene solution of **2a** with propylamine (10 mol amt.) only afforded *N*-propylselenobenzamide in 56% yield.

However, all attempts for isolation or spectral detection of **4** were not successful. Heating of a benzene solution of **2a-c** in the absence of trapping agents gave **16**, **17**, **18**, and **19** in all cases,<sup>5</sup> and the heating of **2** in the presence of an excess amount of inactivated alkenes or alkynes also gave similar results. The

structure of **16a**, possessing an unexpected 6H-1,3,5-selenadiazine ring system, was finally determined by X-ray crystallographic analysis.<sup>8</sup> All results of the reactions are given in Table 3.

Table 1. Heating of **1a** or **2** in the presence of acetylenic dienophiles

Substrate				Dienophile	Solvent	Yield
R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	<b>1, 2</b>	R <sup>4</sup>		<b>5-8</b> / %
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>1a</b>	CO <sub>2</sub> CH <sub>3</sub>	Benzene	91( <b>5a</b> )
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>1a</b>	H	Benzene	42( <b>6a</b> ) <sup>a</sup>
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2a</b>	CO <sub>2</sub> CH <sub>3</sub>	Benzene	78( <b>7a</b> )
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2a</b>	H	Benzene	76( <b>8a</b> ) <sup>a</sup>
C <sub>6</sub> H <sub>5</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<b>2b</b>	CO <sub>2</sub> CH <sub>3</sub>	Benzene	53( <b>7b</b> ) <sup>b</sup>
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2c</b>	CO <sub>2</sub> CH <sub>3</sub>	Benzene	14( <b>7c</b> )
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2c</b>	H	Toluene	33( <b>8c</b> ) <sup>a</sup>

<sup>a</sup> Given as a single regioisomer. <sup>b</sup> Isolated as a trienolic form.

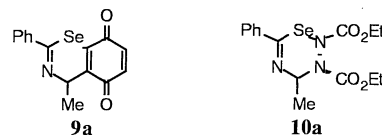


Table 2. Heating of **1** or **2** in the presence of nucleophilic reagents

Substrate				Nucleophile	Yield
R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	<b>1, 2</b>	/ Nu-H	<b>11-15</b> / %
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>1a</b>	<i>i</i> -C <sub>3</sub> H <sub>7</sub> OH <sup>a</sup>	95( <b>11a</b> )
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2a</b>	CH <sub>3</sub> OH <sup>a</sup>	62( <b>12a</b> )
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2a</b>	C <sub>2</sub> H <sub>5</sub> OH <sup>a</sup>	66( <b>13a</b> )
C <sub>6</sub> H <sub>5</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<b>2b</b>	C <sub>2</sub> H <sub>5</sub> OH <sup>a</sup>	53( <b>13b</b> )
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2c</b>	CH <sub>3</sub> OH <sup>a</sup>	92( <b>12c</b> )
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2c</b>	C <sub>2</sub> H <sub>5</sub> OH <sup>a</sup>	85( <b>13c</b> )
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2a</b>	C <sub>6</sub> H <sub>5</sub> SH <sup>b</sup>	85( <b>14a</b> )
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2a</b>	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> SH <sup>b</sup>	82( <b>15a</b> )

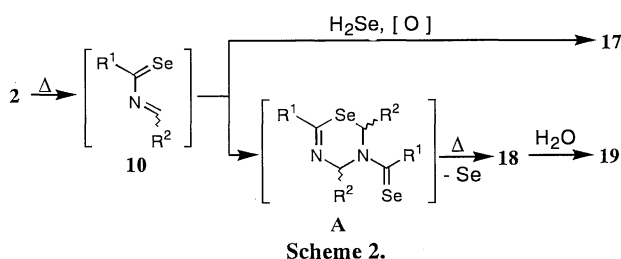
<sup>a</sup> Used as the solvent. <sup>b</sup> A benzene solution of **2** was treated with thiol (10 mol amt.).

**Table 3.** Thermal ring fission of 6*H*-1,3,5-oxaselenazines (**2a-c**) in the absence of trapping agents.

Reaction scheme showing the thermal ring fission of 6H-1,3,5-oxaselenazine **2** to products **16**, **17**, **18**, **19**, and **20**. The reaction is initiated by heat ( $\Delta$ ) and an aromatic group (Ar). Product **19** is further converted to **20** using mCPBA (1.1 mol amt.) in  $\text{CH}_2\text{Cl}_2$  at  $-78^\circ\text{C}$  for 5 min, yielding **20a** from **19a** in 67% yield.

Substrate			Additive	Solvent	Temp	Time	Yields / %				
R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	<b>2</b>	(mol amt.)		/°C	/h	<b>16</b>	<b>17</b>	<b>18</b> (major:minor) <sup>a,b</sup>	<b>19</b>
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2a</b>	-	CH <sub>2</sub> Cl <sub>2</sub>	reflux	6 <sup>c</sup>	0 ( <b>16a</b> )	0 ( <b>17a</b> )	0 ( <b>18a</b> , 2:1)	0 ( <b>19a</b> )
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2a</b>	-	benzene	reflux	5	23 ( <b>16a</b> )	29 ( <b>17a</b> )	37 ( <b>18a</b> , 2:1)	11 ( <b>19a</b> )
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2a</b>	phenylacetylene (10)	benzene	reflux	2.5	13 ( <b>16a</b> )	37 ( <b>17a</b> )	33 ( <b>18a</b> , 2:1)	trace ( <b>19a</b> )
C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2a</b>	<i>p</i> -tolunitrile (10)	benzene	reflux	3	trace ( <b>16a</b> )	8 ( <b>17a</b> )	79 ( <b>18a</b> , 2:1)	trace ( <b>19a</b> )
C <sub>6</sub> H <sub>5</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	<b>2b</b>	-	benzene	reflux	5	10 ( <b>16b</b> )	43 ( <b>17b</b> )	0 ( <b>18b</b> )	42 ( <b>19b</b> )
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	CH <sub>3</sub>	CH <sub>3</sub>	<b>2c</b>	-	benzene	reflux	5	28 ( <b>16c</b> )	24 ( <b>17c</b> )	30 ( <b>18c</b> , 2:1)	18 ( <b>19c</b> )

<sup>a</sup> Estimated by the integration of the <sup>1</sup>H NMR spectrum of **18**. <sup>b</sup> The relative stereochemistry of major and/or minor isomer of **18** were not clarified by NOE experiments. <sup>c</sup> Compound **2a** was recovered in quantitative yield.



The treatment of a CH<sub>2</sub>Cl<sub>2</sub> solution of **2a** with (Me<sub>3</sub>Si)<sub>2</sub>Se-BF<sub>3</sub>•OEt<sub>2</sub>-AlCl<sub>3</sub><sup>9</sup> even at 0 °C afforded **17a** in 29% yield along with a small amount of **16a**, **18a**, **19a**, and **2a**. This result suggested that **17** were afforded from **4** through 1,4-addition of H<sub>2</sub>Se followed by oxidation similar to the formation of 3*H*-1,2,4-dithiazoles from 1,3-thiaza-1,3-butadienes and H<sub>2</sub>S.<sup>2i,3a</sup> It was also supposed that **18** were afforded through Diels-Alder type or ionic dimerization of **4**<sup>2j</sup> and the subsequent selenium extrusion from the dimers **A** and **19** were also generated by hydrolytic ring cleavage of **18**. However, the mechanism of the formation of **16** remained unclear. When a benzene solution of **2a** was heated in the presence of *p*-tolunitrile or 2,3-dimethyl-1,3-butadiene, the product compositions were essentially similar in all cases to that of the heating of **2a** without any additives, and neither **16**<sup>2k-19</sup> bearing *p*-tolyl substituents nor the cycloaddition products originated from selenoacetaldehyde and the diene were found. These results showed that **16** were not formed through the mechanism involving retro [2+2+2] type ring fission of **2** and the subsequent recombination of nitriles with selenoaldehydes. However, attempts for the trapping of the intermediates of the reaction were not successful at all.

In conclusion, we have achieved a generation of 1,3-selenaza-1,3-butadienes **4** by thermal cycloreversion of 2,4,6-trisubstituted 6*H*-1,3,5-oxaselenazines **2**. Applications of the *in situ* generated heterodienes **4** to the syntheses of various selenium-containing heterocycles are in progress in our laboratory.

## References and Notes

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- 5 The physical properties of **1-19**, the X-ray crystallographic data of **16a**, and the ORTEP drawing of **16a** are available as the supplementary materials.
- 6 The small *J* values (0-1.4 Hz) due to the long-range coupling between the signals of the protons at the C-4 and C-6 positions were revealed in the <sup>1</sup>H NMR spectra of **4a** and **6a**.
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- 8 Crystal data for **16a**: C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>Se, M<sub>w</sub> = 313.26, Yellow prism, monoclinic, C2<sub>1</sub>/c (No.15), *a* = 30.816(4), *b* = 10.524(2), *c* = 8.684(2) Å, β = 93.97(2)°, *V* = 2809.3(9) Å<sup>3</sup>, *Z* = 8; *D*<sub>calcd</sub> = 1.48 g/cm<sup>3</sup>, μ(MoKα) = 26.31 cm<sup>-1</sup>, *R* = 0.059, *R*<sub>w</sub> = 0.055.
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