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

Kazuaki Shimada, Kei Aikawa, Takuji Fujita, Shigenobu Aoyagi, Yuji Takikawa,* and Chizuko Kabuto†
Department of Applied Chemistry and Molecular Science, Faculty of Engineering, Iwate University, Morioka, Iwate 020
†*Department of Chemistry, Faculty of Science, Tohoku University, Sendai, Miyagi 980-55*

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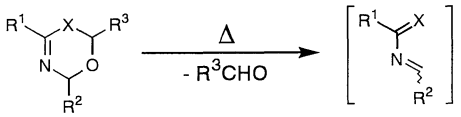
1,3-Selenaza-1,3-butadienes were generated by thermal cycloreversion of 6*H*-1,3,5-oxaselenazines, and were trapped with dienophiles or nucleophiles to give the corresponding [4+2] cycloadducts or 1,4-adducts, respectively.

Recently, reactive heterodienes have been well-documented as new tools for the syntheses of various heterocycles. However, the heterodienes possessing a selenocarbonyl functionality[1] have been less studied in contrast to those of the sulfur analogues.[2] 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**[3] would be easily generated by thermal cycloreversion of 6*H*-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.



1 (X = S)
2 (X = Se)

3 (X = S)
4 (X = Se)

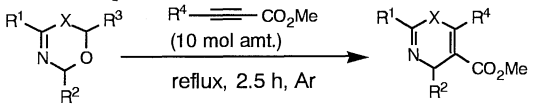
Scheme 1.

6*H*-1,3,5-Oxathiazine (**1a**) and 6*H*-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•OEt_2 according to Sonoda's method.[4] 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 4*H*-1,3-thiazines (**5a**, **6a**) or 4*H*-1,3-selenazines (**7**, **8**).[5] 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,[6] 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,[5] 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,[5] 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 6*H*-1,3,5-selenadiazine ring system, was finally determined by X-ray crystallographic analysis.[8] All results of the reactions are given in Table 3.

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

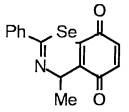


1 (X = S)
2 (X = Se)

5, **6** (X = S)
7, **8** (X = Se)

Substrate				Dienophile	Solvent	Yield
R^1	R^2	R^3	1, 2	R^4		**5-8** / %
C_6H_5	CH_3	CH_3	**1a**	CO_2CH_3	Benzene	91(**5a**)
C_6H_5	CH_3	CH_3	**1a**	H	Benzene	42(**6a**)[a]
C_6H_5	CH_3	CH_3	**2a**	CO_2CH_3	Benzene	78(**7a**)
C_6H_5	CH_3	CH_3	**2a**	H	Benzene	76(**8a**)[a]
C_6H_5	*t*-C_4H_9	*t*-C_4H_9	**2b**	CO_2CH_3	Benzene	53(**7b**)[b]
p-ClC_6H_4	CH_3	CH_3	**2c**	CO_2CH_3	Benzene	14(**7c**)
p-ClC_6H_4	CH_3	CH_3	**2c**	H	Toluene	33(**8c**)[a]

[a] Given as a single regioisomer. [b] Isolated as a trienolic form.



9a

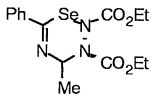


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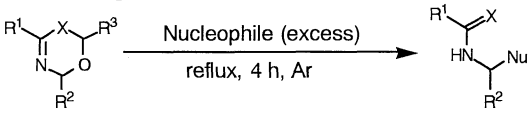
Table 2. Heating of **1** or **2** in the presence of nucleophilic reagents



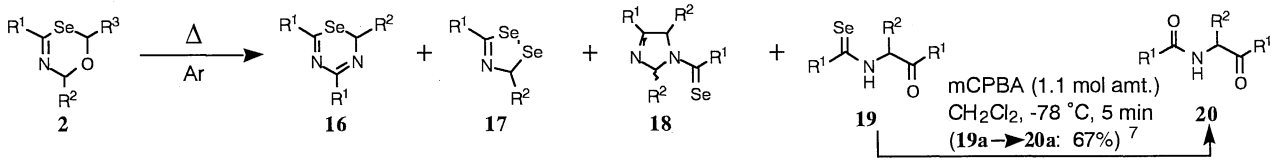
1 (X = S)
2 (X = Se)

11 (X = S)
12-15 (X = Se)

Substrate				Nucleophile	Yield
R^1	R^2	R^3	1, 2	/ Nu-H	**11-15** / %
C_6H_5	CH_3	CH_3	**1a**	*i*-C_3H_7OH[a]	95(**11a**)
C_6H_5	CH_3	CH_3	**2a**	CH_3OH[a]	62(**12a**)
C_6H_5	CH_3	CH_3	**2a**	C_2H_5OH[a]	66(**13a**)
C_6H_5	*t*-C_4H_9	*t*-C_4H_9	**2b**	C_2H_5OH[a]	53(**13b**)
p-ClC_6H_4	CH_3	CH_3	**2c**	CH_3OH[a]	92(**12c**)
p-ClC_6H_4	CH_3	CH_3	**2c**	C_2H_5OH[a]	85(**13c**)
C_6H_5	CH_3	CH_3	**2a**	C_6H_5SH[b]	85(**14a**)
C_6H_5	CH_3	CH_3	**2a**	$C_6H_5CH_2SH$[b]	82(**15a**)

[a] Used as the solvent. [b] A benzene solution of **2** was treated with thiol (10 mol amt.).

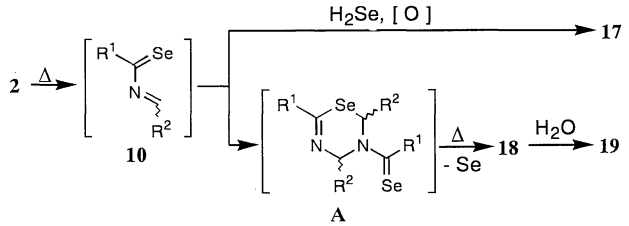
Table 3. Thermal ring fission of *6H*-1,3,5-oxaselenazines (**2a-c**) in the absence of trapping agents.



2 **16** **17** **18** **19** **20**

Substrate				Additive	Solvent	Temp	Time	Yields / %			
R^1	R^2	R^3	**2**	(mol amt.)		/°C	/h	**16**	**17**	**18** (major:minor)[a,b]	**19**
C_6H_5	CH_3	CH_3	**2a**	-	CH_2Cl_2	reflux	6 [c]	0 (**16a**)	0 (**17a**)	0 (**18a**, 2:1)	0 (**19a**)
C_6H_5	CH_3	CH_3	**2a**	-	benzene	reflux	5	23 (**16a**)	29 (**17a**)	37 (**18a**, 2:1)	11 (**19a**)
C_6H_5	CH_3	CH_3	**2a**	phenylacetylene (10)	benzene	reflux	2.5	13 (**16a**)	37 (**17a**)	33 (**18a**, 2:1)	trace (**19a**)
C_6H_5	CH_3	CH_3	**2a**	*p*-tolunitrile (10)	benzene	reflux	3	trace (**16a**)	8 (**17a**)	79 (**18a**, 2:1)	trace (**19a**)
C_6H_5	*t*-C_4H_9	*t*-C_4H_9	**2b**	-	benzene	reflux	5	10 (**16b**)	43 (**17b**)	0 (**18b**)	42 (**19b**)
p-ClC_6H_4	CH_3	CH_3	**2c**	-	benzene	reflux	5	28 (**16c**)	24 (**17c**)	30 (**18c**, 2:1)	18 (**19c**)

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



Scheme 2.

The treatment of a CH_2Cl_2 solution of **2a** with $(Me_3Si)_2Se$-BF_3•OEt_2-$AlCl_3$[9] 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_2Se followed by oxidation similar to the formation of *3H*-1,2,4-dithiazoles from 1,3-thiaza-1,3-butadienes and H_2S.[2i,3a] It was also supposed that **18** were afforded through Diels-Alder type or ionic dimerization of **4**[2j] 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**[2k]-**19** 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 *6H*-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

1 a) W. Ando, Y. Kumamoto, and N. Tokitoh, *Tetrahedron Lett.*, **27**, 5699 (1987); b) Guang Ming Li, M. Segi, and T. Nakajima, *Tetrahedron Lett.*, **33**, 3515 (1992); c) K. Okuma, K. Kojima, I. Kaneko, and H. Ohta, *Tetrahedron Lett.*, **33**, 1333 (1992).

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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 ^1H NMR spectra of **4a** and **6a**.

7 The structure of **19a** was also confirmed by the conversion into **20a**(63%) by treating with mCPBA. a) K. S. Kochhar, D. A. Cottrell, and H. W. Pinnick, *Tetrahedron Lett.*, **24**, 1323 (1983); b) K. Shimada, S. Akimoto, H. Itoh, H. Nakamura, and Y. Takikawa, *Chem. Lett.*, **1994**, 1743.

8 Crystal data for **16a**: $C_{16}H_{14}N_2Se$, M_W = 313.26, Yellow prism, monoclinic, $C2_1/c$(No.15), a = 30.816(4), b = 10.524(2), c = 8.684(2) Å, β = 93.97(2)°, V = 2809.3(9) Å^3, Z = 8, D_{calcd} = 1.48 g/cm^3, μ(MoKα) = 26.31 cm^{-1}, R = 0.059, R_W = 0.055.

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