

HETEROCYCLES, Vol. 65, No. 8, 2005, pp. 1903 - 1915

Received, 28th April, 2005, Accepted, 5th July, 2005, Published online, 7th July, 2005

SYNTHESIS OF 2-SELENOXO-1,3-THIAZOLIDIN-4-ONES AND 2-SELENOXO-1,3-THIAZINAN-4-ONES FROM ISOSELENOCYANATES

Geoffroy L. Sommen,¹ Anthony Linden, and Heinz Heimgartner*

Institute of Organic Chemistry, University of Zürich, Winterthurerstrasse 190, CH-8057 Zürich, Switzerland; E-mail: heimgart@oci.unizh.ch

Abstract – 2-Selenoxo-1,3-thiazolidin-4-ones (selenorhodanines) (**7a-h**) and 2-selenoxo-1,3-thiazinanes (**8a-c**) can easily be synthesized in a one-pot procedure from aryl isoselenocyanates and α - and β -mercapto carboxylic acids, respectively.

INTRODUCTION

During the last 25 years, organoselenium chemistry underwent a spectacular mutation: from an exotic area of science, practised by a few specialists, it became a relatively well-mastered methodology widely used by organic chemists. The key to this success is that a fair number of selenium based reagents and reactions have been discovered, which allow specific transformations to be performed selectively and often under mild conditions. The interest in selenium-containing compounds has increased not only because of their remarkable reactivities and chemical properties²⁻⁸ but also because of their pharmaceutical applications.⁹⁻¹⁶ Organoselenium compounds are now an important class of biologically active products.^{17,18} Shamberger¹⁵ widely evidenced the importance of selenium in biology, in human health,¹⁹ in cancer chemoprevention,²⁰ in food,²¹⁻²³ and in plants.^{24,25}

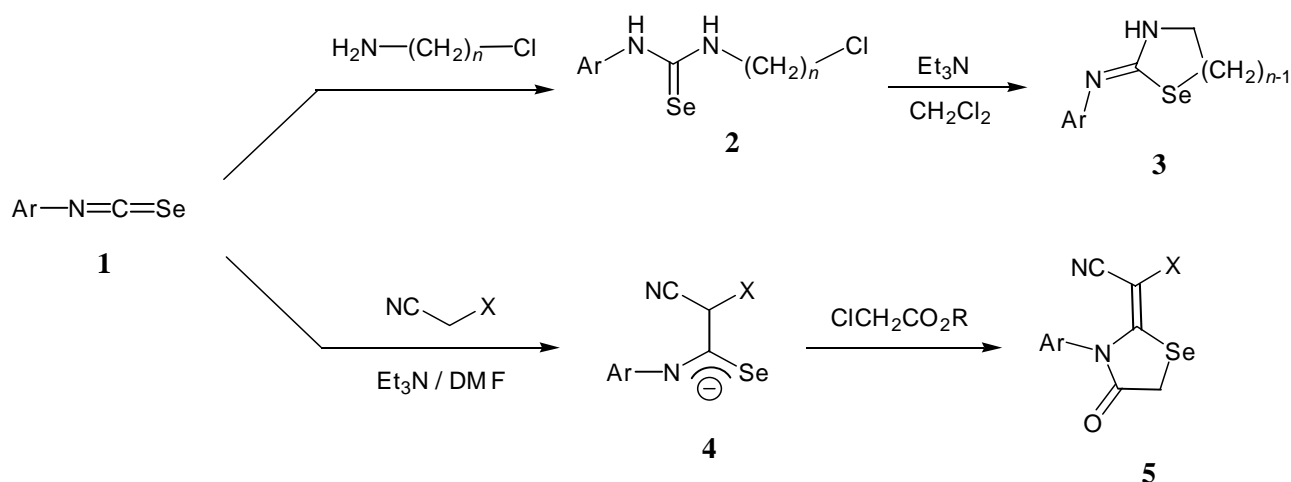
Many syntheses of selenium-containing heterocycles involve the use of toxic selenium reagents, which are often difficult to handle and to store. On the other hand, isoselenocyanates are very useful starting materials²⁶ since they are easy to prepare²⁷ and are relatively stable.

We have shown that they are the reagents of choice for the preparation of selenium-containing heterocycles such as 1,3-selenazole[5,4-*b*]pyridines,²⁸ selenet-2(2*H*)-imines,²⁹ 1,3-selenazoles,^{30,31} imidazole diselenides,³² 6*H*-[5,1,3]benzoselenadiazocines,³³ and 1,2,3-selenadiazoles.³⁴

Rhodanine derivatives (2-thioxo-1,3-thiazolidin-4-ones) have been extensively investigated. They exhibit various biological activities,³⁵ e.g., antidiabetic,³⁶ antibacterial, fungicidal, antiparasitic, and antituberculous.^{37,38} On the other hand, there were no reports on the synthesis of 2-selenorhodanine derivatives until the recent work of Tejchman and Korohoda.³⁹ As in several other reports, the C=Se bond was introduced by the use of highly toxic hydrogen selenide. The key step of this method is the substitution of a MeS group or a R(Me)N group by HSe in various derivatives of imidazolidine,^{40a} 1,3-thiazolidine,^{40b} 1,3-thiazoline,^{40c,41} and pyridine.⁴²

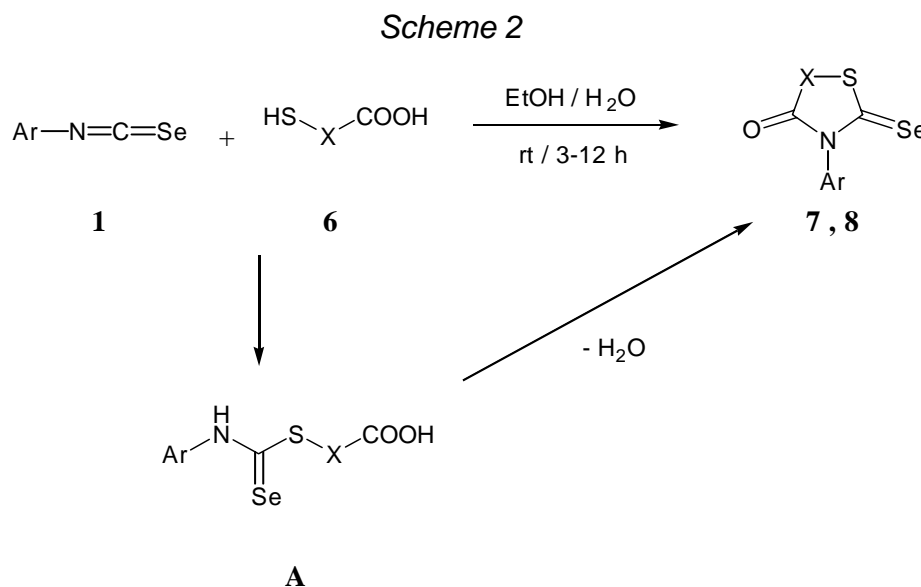
Recently, we have described the synthesis of 2-imino-1,3-selenazolidines (**3**, $n = 2$),⁴³ 2-imino-1,3-selenazinanes (**3**, $n = 3$),⁴³ and 1,3-selenazolidin-4-ones (**5**)⁴⁴ from isoselenocyanates by the nucleophilic attack of a primary amine and a carbon nucleophile, respectively (Scheme 1). To the best of our knowledge, only a few articles concerning the nucleophilic attack of a thiol on isothiocyanates have been published^{45–50} and even less involving isoselenocyanates.^{51,52} For this reason, we investigated the reactions of mercapto carboxylic acids with isoselenocyanates with the aim of preparing selenaheterocycles by a subsequent cyclization of the initially formed adducts.

Scheme 1



RESULTS AND DISCUSSION

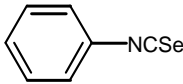
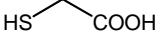
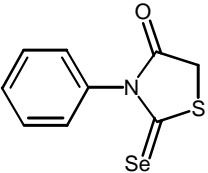
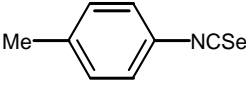
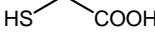
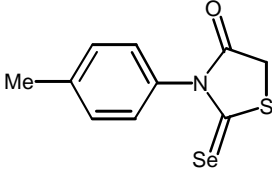
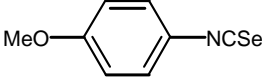
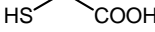
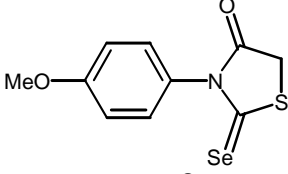
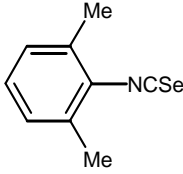
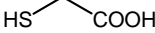
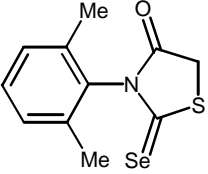
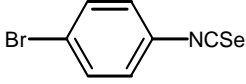
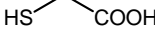
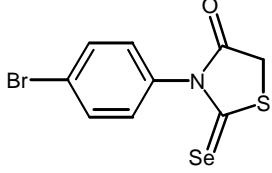
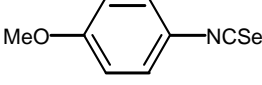
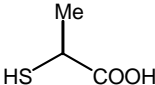
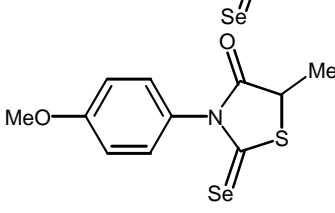
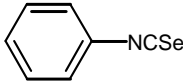
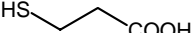
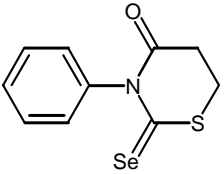
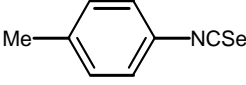
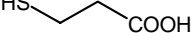
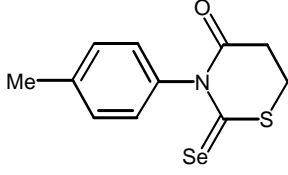
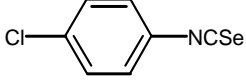
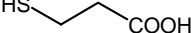
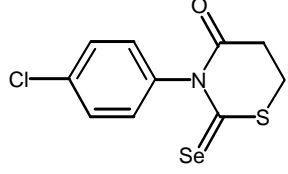
The reactions of aryl isoselenocyanates (**1a-e**) with equimolar amounts of 2-mercaptoacetic acid (**6a**) in a mixture of ethanol and water occurred already at room temperature. Typically, the reactions were completed after 3–4 h (TLC control). After aqueous workup and recrystallization of the precipitate from EtOH, 2-selenoxo-1,3-thiazolidin-4-ones (**7a-e**), *i.e.*, selenorhodanines, were obtained as orange crystals in good to excellent yields (*Scheme 2*, *Table 1*). In the NMR spectra (CDCl₃), the CH₂ group appears as a singlet at 3.85–4.26 ppm (¹H) and at 37.3–38.2 ppm (¹³C), respectively. The characteristic absorptions of C(4)=O and C(2)=Se are observed at 171.8–173.8 ppm and at 200.2–205.5 ppm. The CI-MS spectra (NH₃) show the [M+H]⁺ peak as the base peak, in addition to an intensive [M+NH₄]⁺ peak, and all products gave correct elemental analyses for C, H, N, and S.



Finally, the structure of **7a** was established unambiguously by X-Ray crystallography (*Figure 1*). The 1,3-thiazolidine ring is almost planar, and the attached atoms Se, O(4), and C(6) deviate only slightly from this plane. On the other hand, the benzene ring at N(3) is twisted out of this plane and is oriented almost orthogonal to the plane of the heterocycle with a dihedral angle between these planes of 71.7(1)°.

Analogously, the reaction of 4-methoxyphenyl isoselenocyanate (**1c**) with 2-mercaptoacetic acid (**6b**) gave 2-(4-methoxyphenyl)-5-methylselenorhodanine (**7f**) in 74% yield.

Table 1. Synthesis of Thiazolidinones (**7a-f**) and Thiazinanones (**8a-c**) from Isoselenocyanates

Isoselenocyanate (1)	Mercapto Acid (6)	Products	Yield (%) [Time,h]
			7a 96 [3]
			7b 91 [3]
			7c 93 [4]
			7d 56 [12]
			7e 89 [3]
			7f 74 [6]
			8a 82 [12]
			8b 63 [12]
			8c 60 [12]

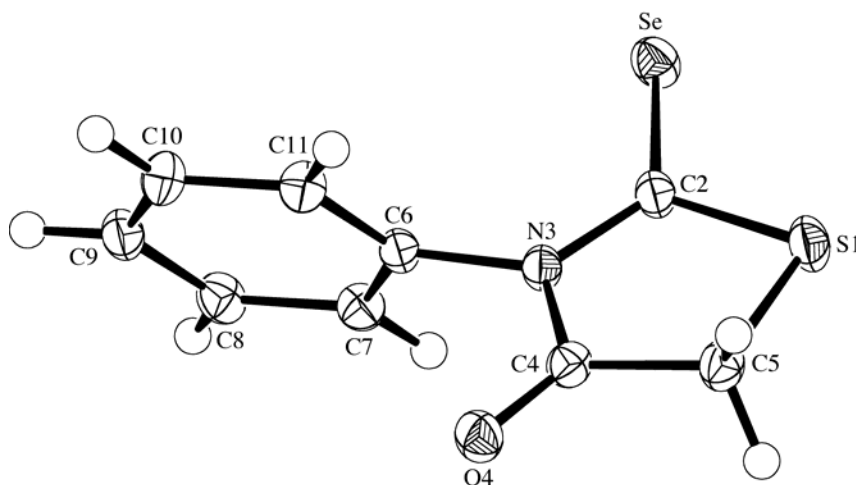


Figure 1. ORTEP plot⁵³ of the molecular structure of **7a** (arbitrary numbering of the atoms; 50% probability ellipsoids)

Furthermore, the corresponding reactions of **1a**, **b**, and **f** with 3-mercaptopropanoic acid (**6c**) afforded the 2-selenoxo-1,3-thiazinan-4-ones (**8a-c**), *i.e.*, the six-membered homologues of selenorhodanines (*Scheme 2, Table 1*). In the ¹H-NMR spectra of **8a-c**, the two CH₂ groups resonate at *ca.* 2.75 and 3.50 ppm, whereas their ¹³C-signals appear at *ca.* 33.5 and 45.0 ppm. The chemical shifts of C(4)=O and C(2)=Se (*ca.* 173 and 204 ppm, respectively) are almost unaffected by the ring size (*cf.* **7a-f**).

A reaction mechanism for the formation of **7** and **8** is proposed in *Scheme 2*. The nucleophilic mercapto group undergoes an addition to the isoselenocyanate (**1**) to give a (seleno)(thio)carbamate **A** as an intermediate. It is worth mentioning that no additional base is needed to catalyze the reaction. The subsequent cyclization of **A'** occurs almost instantaneously with loss of water to afford the selenorhodanines (**7**) in a one-pot-reaction. In the case of the sterically crowded isoselenocyanate (**1d**), a longer reaction time of 12 h is needed. Similarly, in the case of the reactions of **1a**, **b**, and **f** with 3-mercaptopropanoic acid (**6c**), the starting material had been consumed complete only after 12 h.

It is noteworthy that the ring closure of **A/A'** occurs exclusively *via* nucleophilic attack of the N-atom at the carboxylic group. None of the corresponding 2-imino-1,3-selenathiolanone or its homologue has been detected, in contrast to the previously described formation of 2-imino-1,3-

selenazolidines and 2-imino-1,3-selenazinanes (**3**),⁴³ 2-arylamino-selenazolo[5,4-*b*]pyrid-ines,²⁸ 1*H*-5-selena-1,3,6-triazaaceanthrylenes,⁵⁴ and 6*H*-[5,1,3]benzoselenadiazocines.³³ On the other hand, in the reaction of 2-aminobenzonitrile with phenyl isoselenocyanate, the intermediate selenourea derivatives undergo a cyclization by nucleophilic attack of the N-atom at the nitrile group, which leads to 4-phenylaminoquinazoline-2(1*H*)-selones.⁵⁵

In conclusion, the reaction of isoselenocyanates (**1**) with α - or β -mercaptocarboxylic acids is a novel, rapid and efficient synthesis of 2-selenoxo-1,3-thiazolidine-4-ones (**7**, selenorhodanines) and 2-selenoxo-1,3-thiazinan-4-ones (**8**).

EXPERIMENTAL

General remarks. TLC: silica gel 60 F₂₅₄ plates (0.25 mm, Merck). Column chromatography (CC): silica gel 60 (0.040–0.063 mesh, Merck). Melting points: Büchi B-540 apparatus, in a capillary, uncorrected. ¹H-NMR (300 MHz) and ¹³C-NMR (75 MHz) spectra: Bruker ARX-300 instrument, in CDCl₃; chemical shifts in ppm, coupling constants *J* in Hz. EI-MS and CI-MS: Finnigan SSQ-700 or MAT-90 instrument; EI mode: 70 eV; CI mode: NH₃ as carrier gas.

Starting materials. 2-Mercaptoacetic acid (**6a**), 2-mercaptopropanoic acid (**6b**), 3-mercaptopropanoic acid (**6c**), and formanilid are commercially available (Fluka). Isoselenocyanates (**1**) were prepared according to Barton's procedure, which starts from formamides.²⁷ *N*-(4-Chlorophenyl)-, *N*-(4-bromophenyl)-, *N*-(4-methoxyphenyl)-, *N*-(4-methylphenyl)-, and *N*-(2,6-dimethylphenyl)formamide were prepared from the respective commercial aniline and 95% formic acid by using a slightly modified procedure.⁵⁶ The solution was heated to reflux for 30 min and evaporated to dryness in vacuo. The residue was dissolved in Et₂O and washed with dilute acetic acid (5%), water, and aqueous NaHCO₃ (5%). The aqueous layer was extracted with Et₂O, the combined organic extracts were dried with MgSO₄ and evaporated under reduced pressure. The crude products were purified by recrystallization using a mixture of EtOH and water.

Synthesis of 2-Selenoxo-1,3-thiazolidin-4-ones (7a-f) and 2-Selenoxo-1,3-thiazinan-4-ones (8a-c). General Procedure. A round bottom flask equipped with a condenser and a magnetic stirrer was charged with an aryl isoselenocyanate (1.0 mmol) in 20 mL of a mixture of EtOH and water (2:1). The respective mercapto carboxylic acid was then added dropwise. The

mixture was stirred at rt for several hours (see table) before being poured onto 50 mL of cold water. After 2 h of stirring, the precipitate formed was filtered and purified, if necessary, by recrystallization from EtOH.

3-Phenyl-2-selenoxo-1,3-thiazolidin-4-one (7a). Orange plates, mp 217–219°C (EtOH). ¹H-NMR: 4.26 (s, CH₂); 7.40 (d, *J* = 8.2, 2 arom. H); 7.59–7.67 (*m*, 3 arom. H). ¹³C-NMR: 38.2 (CH₂); 128.6 (2 arom. CH); 129.1 (3 arom. CH); 136.5 (1 arom. C); 173.8 (CO); 205.5 (CSe). CI-MS: 275 (26, [M+NH₄]⁺), 258 (100, [M+H]⁺). Anal. Calcd for C₉H₇NOSSe: C, 42.19; H, 2.75; N, 5.47; S, 12.52. Found: C, 42.20; H, 2.75; N, 5.42; S, 12.40.

3-(4-Methylphenyl)-2-selenoxo-1,3-thiazolidin-4-one (7b). Orange crystals, mp 201–203°C (EtOH). ¹H-NMR: 2.42 (s, Me); 3.90 (s, CH₂); 7.10, 7.35 (*AA'BB'*, *J* = 8.2, 4 arom. H). ¹³C-NMR: 21.3 (Me); 37.4 (CH₂); 128.0 (2 arom. CH); 130.3 (2 arom. CH); 133.2, 140.0 (2 arom. C); 173.2 (CO); 203.3 (CSe). CI-MS: 289 (31, [M+NH₄]⁺), 272 (100, [M+H]⁺). Anal. Calcd for C₁₀H₉NOSSe: C, 44.45; H, 3.36; N, 5.18; S, 11.87. Found: C, 44.30; H, 3.21; N, 5.03; S, 11.78.

3-(4-Methoxyphenyl)-2-selenoxo-1,3-thiazolidin-4-one (7c). Orange crystals, mp 182–184°C (EtOH). ¹H-NMR: 3.85 (s, MeO); 3.89 (s, CH₂); 7.03, 7.14 (*AA'BB'*, *J* = 8.2, 4 arom. H). ¹³C-NMR: 37.3 (CH₂); 55.4 (MeO); 114.9 (2 arom. CH); 128.2 (1 arom. C); 129.4 (2 arom. CH); 160.3 (1 arom. C); 173.3 (CO); 203.6 (CSe). CI-MS: 305 (32, [M+NH₄]⁺), 288 (100, [M+H]⁺). Anal. Calcd for C₁₀H₉NO₂SSe: C, 41.96; H, 3.17; N, 4.89; S, 11.20. Found: C, 42.23; H, 3.33; N, 4.88; S, 11.12.

3-(2,6-Dimethylphenyl)-2-selenoxo-1,3-thiazolidin-4-one (7d). Orange crystals, mp 123–125°C (EtOH). ¹H-NMR: 2.10 (s, 2 Me); 3.95 (s, CH₂); 7.18–7.33 (*m*, 3 arom. H). ¹³C-NMR: 117.5 (2 Me); 37.3 (CH₂); 127.5 (1 arom. CH); 127.9 (2 arom. CH); 130.0, 136.1 (2 arom. C); 173.2 (CO); 200.2 (CSe). CI-MS: 303 (60, [M+NH₄]⁺), 286 (100, [M+H]⁺). Anal. Calcd for C₁₁H₁₁NOSSe: C, 46.48; H, 3.90; N, 4.93; S, 11.28. Found: C, 46.33; H, 4.12; N, 5.00; S, 11.32.

3-(4-Bromophenyl)-2-selenoxo-1,3-thiazolidin-4-one (7e). Orange crystals, mp 111–113°C (EtOH). ¹H-NMR: 3.92 (s, CH₂); 7.11, 7.67 (*AA'BB'*, *J* = 8.1, 4 arom. H). ¹³C-NMR: 37.4 (CH₂); 123.3 (1 arom. C); 130.0 (2 arom. CH); 132.9 (2 arom. CH); 138.5 (1 arom. C); 171.8 (CO);

203.8 (CSe). CI-MS: 353 (35, [M+NH₄]⁺), 336 (100, [M+H]⁺). Anal. Calcd for C₉H₆NOBrSSe: C, 32.26; H, 1.80; N, 4.18; S, 9.57. Found: C, 32.41; H, 2.02; N, 3.98; S, 10.00.

3-(4-Methoxyphenyl)-5-methyl-2-selenoxo-1,3-thiazolidin-4-one (7f). Orange crystals, mp 133–135°C (EtOH). ¹H-NMR: 1.78 (*d*, *J* = 7.3, Me); 3.81 (*s*, MeO); 4.11 (*q*, *J* = 7.2, CH); 6.88, 7.22 (*AA'BB'*, *J* = 8.2, 4 arom. H). ¹³C-NMR: 17.5 (Me); 46.7 (CH); 55.4 (MeO); 114.7 (2 arom. CH); 127.3 (2 arom. CH); 129.4, 159.1 (2 arom. C); 174.4 (CO); 204.2 (CSe). CI-MS: 319 (46, [M+NH₄]⁺), 302 (100, [M+H]⁺). Anal. Calcd for C₁₁H₁₁NO₂SSe: C, 44.00; H, 3.69; N, 4.67; S, 10.68. Found: C, 43.79; H, 3.82; N, 4.33; S, 11.00.

3-Phenyl-2-selenoxo-1,3-thiazinan-4-one (8a). Orange crystals, mp 152–154°C (EtOH). ¹H-NMR: 2.76, 3.55 (*2t*, *J* = 6.9, 2 CH₂); 7.36–7.58 (*m*, 5 arom. H). ¹³C-NMR: 33.3, 45.3 (2 CH₂); 125.0 (1 arom. CH); 126.2 (2 arom. CH); 128.8 (2 arom. CH); 139.6 (1 arom. C); 172.6 (CO); 204.2 (CSe). CI-MS: 288 (100, [M+NH₄]⁺), 272 (54, [M+H]⁺). Anal. Calcd for C₁₀H₉NOSSe: C, 44.45; H, 3.36; N, 5.18; S, 11.87. Found: C, 44.32; H, 3.12; N, 5.34; S, 12.01.

3-(4-Methylphenyl)-2-selenoxo-1,3-thiazinan-4-one (8b). Orange crystals, mp 164–166°C (EtOH). ¹H-NMR: 2.73, 3.53 (*2t*, *J* = 6.9, 2 CH₂); 7.12, 7.38 (*AA'BB'*, *J* = 8.1, 4 arom. H). ¹³C-NMR: 20.2 (Me); 33.6, 45.0 (2 CH₂); 128.9 (2 arom. CH); 130.8 (2 arom. CH); 134.4, 139.9 (2 arom. C); 174.0 (CO); 203.8 (CSe). CI-MS: 303 (100, [M+NH₄]⁺), 286 (67, [M+H]⁺). Anal. Calcd for C₁₁H₁₁NOSSe: C, 46.48; H, 3.90; N, 4.93; S, 11.28. Found: C, 46.45; H, 4.12; N, 5.13; S, 11.07.

3-(4-Chlorophenyl)-2-selenoxo-1,3-thiazinan-4-one (8c). Orange crystals, mp 163–165°C (EtOH). ¹H-NMR: 2.72 (*t*, *J* = 6.9, CH₂); 3.45 (*t*, *J* = 7.0, CH₂); 7.22, 7.38 (*d*, *J* = 8.1, 4 arom. H). ¹³C-NMR: 33.1, 45.0 (2 CH₂); 129.9 (2 arom. CH); 132.5 (2 arom. CH); 133.1, 138.3 (2 arom. C); 173.4 (CO); 204.0 (CSe). CI-MS: 323 (100, [M+NH₄]⁺), 306 (44, [M+H]⁺). Anal. Calcd for C₁₀H₈NOCISSe: C, 39.42; H, 2.65; N, 4.60; S, 10.53. Found: C, 39.22; H, 2.85; N, 4.34; S, 11.11.

X-Ray Crystal-Structure Determination of 7a (see Table 2 and Figure 1).⁵⁷ All measurements were performed on a *Nonius KappaCCD* area-detector diffractometer⁵⁸ using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream 700*

cooler. The data collection and refinement parameters are given in *Table 2*, and a view of the molecule is shown in *Figure 1*. Data reduction was performed with *HKL Denzo* and *Scalepack*.⁵⁹ The intensities were corrected for *Lorentz* and polarization effects, and an absorption correction based on the multi-scan method⁶⁰ was applied. The structure was solved by direct methods using *SIR92*,⁶¹ which revealed the positions of all non-H-atoms. All non-H-atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined using a riding model where each atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{\text{eq}}$ of its parent atom. The refinement of the structure was carried out on F^2 using full-matrix least-squares procedures, which minimized the function $\sum w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was applied. Neutral atom scattering factors for non-H-atoms were taken from ref.^{62a}, and the scattering factors for H-atoms were taken from ref.⁶³ Anomalous dispersion effects were included in F_c ;⁶⁴ the values for f' and f'' were those of ref.^{62b} The values of the mass attenuation coefficients are those of ref.^{62c} All calculations were performed using the *SHELXL97* program.⁶⁵

ACKNOWLEDGMENTS

We thank the analytical services of our institute for NMR and MS spectra and elemental analyses, and Mr. *B. Bürgi* for his assistance with the determination of the crystal structure. Financial support of this work by the *Dr. Helmut Legerlotz-Foundation* and *F. Hoffmann-La Roche AG*, Basel, is gratefully acknowledged.

REFERENCES AND NOTES

1. Postdoctoral stay at the University of Zürich, 2004–2005.
2. H. J. Reich, '*Organoselenium Chemistry*', *Top. Curr. Chem.*, Vol. 208, ed. by T. Wirth, Springer Verlag, Berlin, 2000.
3. T. Wirth, *Tetrahedron*, 1999, **55**, 1.
4. '*Organoselenium Chemistry, A Practical Approach*', ed. by T. G. Back, Oxford University Press, Oxford, 1999.
5. V. P. Litvinov and V. D. Dyachenko, *Russ. Chem. Rev.*, 1997, **66**, 923.
6. C. Paulmier, '*Selenium Reagents and Intermediates in Organic Synthesis*', Pergamon Press, Oxford, 1986.

Table 2. Crystallographic Data of Compound (7a)

Crystallized from	MeCN
Empirical formula	C ₉ H ₇ NOSse
Formula weight [g mol ⁻¹]	256.12
Crystal color, habit	orange, plate
Crystal dimensions [mm]	0.05 × 0.15 × 0.15
Temperature [K]	160(1)
Crystal system	monoclinic
Space group	<i>P</i> 2 ₁ / <i>c</i>
<i>Z</i>	4
Reflections for cell determination	19295
2θ range for cell determination [°]	4–60
Unit cell parameters	
<i>a</i> [Å]	12.9370(3)
<i>b</i> [Å]	5.6096(1)
<i>c</i> [Å]	12.7020(4)
β [°]	93.493(2)
<i>V</i> [Å ³]	920.09(4)
<i>D_x</i> [g cm ⁻³]	1.849
μ(MoK _α) [mm ⁻¹]	4.259
Scan type	φ and ω
2θ _(max) [°]	60
Transmission factors (min; max)	0.640; 0.816
Total reflections measured	27219
Symmetry independent reflections	2683
Reflections with <i>I</i> > 2σ(<i>I</i>)	2202
Reflections used in refinement	2683
Parameters refined	119
Final <i>R</i> (<i>F</i>) [<i>I</i> > 2σ(<i>I</i>) reflections]	0.0315
<i>wR</i> (<i>F</i> ²) (all data)*	0.0717
Goodness of fit	1.071
Secondary extinction coefficient	0.0033(8)
Final Δ _{max} /σ	0.001
Δρ (max; min) [e Å ⁻³]	0.69; -0.62

* $w = [\sigma^2(F_o^2) + (0.0312P)^2 + 0.4892P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$

7. M. Renson, '*The Chemistry of Organic Selenium and Tellurium Compounds*', Vol. 1, ed. by S. Patai and Z. Rappoport, J. Wiley & Sons, New York, 1986.
8. D. L. Klayman and W. H. H. Günther, '*Organic Selenium Compounds: Their Chemistry and Biology*', J. Wiley & Sons, New York, 1973.
9. H. E. Ganther, *Bioorg. Med. Chem.*, 2001, **9**, 1459.
10. Y. Ogasawara, G. Lacourciere, and T. C. Stadtman, *Proc. Natl. Acad. Sci. USA*, 2001, **98**, 9494.
11. Y. Xu and E. T. Kool, *J. Am. Chem. Soc.*, 2000, **122**, 9040.
12. S. Janzsu, G. Hoppert, J. Shodiere, and J.-C. Yerdon, *Jpn. Kokai Tokkyo Koho JP 11140067* 1999.
13. R. F. Burk, '*Selenium in Biology and Human Health*', Springer Verlag, New York, 1994.
14. '*Selenium in Biology and Medicine*', ed. by A. Wengel, Springer Verlag, Berlin, 1989.
15. R. J. Shamberger, '*Biochemistry of Selenium*', Plenum Press, New York, 1983.
16. R. A. Passwaters, '*Selenium as Food & Medicine*', Pivot Original Press, New Canaan, 1980.
17. G. Mugesh, W.-W. Du Mont, and H. Sies, *Chem. Rev.*, 2001, **101**, 2125.
18. S. W. May, *Exp. Opin. Invest. Drugs*, 2002, **11**, 1261.
19. D. L. Hatfield, '*Selenium. Its Molecular Biology and Role in Human Health*', Kluwer Academic Publishers, Boston, 2001.
20. K. El-Bayoumy and R. Sinha, *Mutation Research*, 2004, **551**, 181.
21. C. Ip, M. Birringer, E. Block, M. Kotrebai, J. F. Tyson, P. C. Uden, and D. J. Lisk, *J. Agric. Food Chem.*, 2000, **48**, 2062.
22. J. Lintschinger, N. Fuchs, J. Moser, D. Kuehnelt, and W. Goessler, *J. Agric. Food Chem.*, 2000, **48**, 5362.
23. V. Poggi, A. Arcioni, P. Filippini, and P. G. Pifferi, *J. Agric. Food Chem.*, 2000, **48**, 4749.
24. P. Ximenez-Embun, I. Alonso, Y. Madrid-Albarran, and C. Camara, *J. Agric. Food Chem.*, 2004, **52**, 832.
25. D. B. Vickerman, J. T. Trumble, G. N. George, I. J. Pickering, and H. Nichol, *Environ. Sci. Technol.*, 2004, **38**, 3581.
26. M. L. Petrov and N. I. Zmitrovich, *Russ. J. Gen. Chem.*, 1999, **69**, 245.
27. a) D. H. R. Barton, S. I. Parekh, M. Tajbakhsh, E. A. Theodorakis, and C.-L. Tse, *Tetrahedron*, 1994, **50**, 639; b) M. T. Bakhsh, Y. S. Behshtiha, and M. M. Heravi *J. Chem. Soc. Pakistan*, 1996, **18**, 159.
28. P. K. Atanassov, A. Linden, and H. Heimgartner, *Heterocycles*, 2003, **61**, 569.

29. P. K. Atanassov, A. Linden, and H. Heimgartner, *Heterocycles*, 2004, **62**, 521.
30. H. Maeda, N. Kambe, N. Sonoda, S.-I. Fujiwara, and T. Shin-ike, *Tetrahedron*, 1997, **53**, 13667.
31. Y. Zhou, A. Linden, and H. Heimgartner, *Helv. Chim. Acta*, 2000, **83**, 1576.
32. P. K. Atanassov, Y. Zhou, A. Linden, and H. Heimgartner, *Helv. Chim. Acta*, 2002, **85**, 1102.
33. P. K. Atanassov, A. Linden, and H. Heimgartner, *Helv. Chim. Acta*, 2004, **87**, 1452.
34. Y. Zhou and H. Heimgartner, *Helv. Chim. Acta*, 2000, **83**, 539.
35. D. Deidda, G. Lampis, C. Maullu, R. Pompei, F. Isaia, V. Lippolis, and G. Verani, *Pharm. Res.*, 1997, **36**, 193.
36. N. Ueda, Y. Nomura, Y. Muta, Y. Matsuzaki, M. Hayashibe, Y. Ino, S. Suzuki, and M. Kurumi, *Arzneim.-Forsch./Drug Res.*, 1998, **48**, 651.
37. F. C. Brown, *Chem. Rev.*, 1961, **61**, 463.
38. S. P. Singh, S. S. Parmar, K. Raman, and V.I. Stenberg, *Chem. Rev.*, 1981, **81**, 175.
39. a) W. Tejchman and M. J. Korohoda, *Polish J. Chem.*, 1996, **70**, 1124; b) W. Tejchman and M. J. Korohoda, *Polish J. Chem.*, 1999, **73**, 1315.
40. a) M. J. Korohoda, *Polish J. Chem.*, 1980, **54**, 683; b) M. J. Korohoda, *Polish J. Chem.*, 1981, **55**, 359; c) M. J. Korohoda, *Polish J. Chem.*, 1983, **57**, 875.
41. M. J. Korohoda and A. B. Bojarska, *Polish J. Chem.*, 1984, **58**, 447.
42. M. J. Korohoda, E. Slomska, and H. Szczurek, *Polish J. Chem.*, 1989, **63**, 165.
43. G. L. Sommen, A. Linden, and H. Heimgartner, *Eur. J. Org. Chem.*, 2005, in press.
44. G. L. Sommen, A. Linden, and H. Heimgartner, in preparation.
45. T. Bacchetti, *Gazz. Chim. Ital.*, 1956, **86**, 316.
46. K. Rühlmann, A. Grosalski, and U. Schräpler, *J. Prakt. Chem.*, 1960, **11**, 54.
47. H. Hartmann and R. Mayer, *Z. Chem.*, 1965, **4**, 152.
48. R. Andreash and A. Zipser, *Monatsh. Chem.*, 1903, **24**, 499.
49. J. L. Garraway, *J. Chem. Soc.*, 1961, 3733.
50. E. Cherbuliez, J. Marszalek, and J. Rabinowitz, *Helv. Chim. Acta*, 1964, **47**, 1666.
51. P. Kristián, G. Suchár, and D. Podhradsky, *Coll. Czech. Chem. Comm.*, 1975, **40**, 2838.
52. H. von Spies, K. Gewalt, and R. Mayer, *J. Prakt. Chem.*, 1972, **314**, 646.
53. C. K. Johnson, *ORTEP II*, Report ORNL-5138; Oak Ridge National Laboratory, Oak Ridge, Tennessee, 1976.
54. P. Atanassov, A. Linden, and H. Heimgartner, *Helv. Chim. Acta*, 2003, **86**, 3235.
55. P. Atanassov, A. Linden, and H. Heimgartner, *Helv. Chim. Acta*, 2004, **87**, 1873.

56. A .R. Katritzky, R. L. Parris, E. S. Ignatchenko, S. M. Allin, and M. Siskin, *J. Prakt. Chem.*, 1997, **339**, 59.
57. CCDC-269289 contains the supplementary crystallographic data for compound (**7a**). These data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)1223-336033; e-mail:deposit@ccdc.cam.ac.uk)).
58. R. Hooft, *KappaCCD Collect Software*, Nonius BV, Delft, The Netherlands, 1999.
59. Z. Otwinowski and W. Minor, in *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, ed. by C. W. Carter Jr. and R. M. Sweet, Academic Press, New York, 1997, p. 307.
60. R. H. Blessing, *Acta Crystallogr., Sect. A*, 1995, **51**, 33.
61. A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, and M. Camalli, *SIR92, J. Appl. Crystallogr.*, 1994, **27**, 435.
62. a) E. N. Maslen, A. G. Fox, and M. A. O'Keefe, in *International Tables for Crystallography*, ed. by A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 6.1.1.1, p. 477; b) D. C. Creagh and W. J. McAuley, *ibid.*, Table 4.2.6.8, p. 219; c) D. C. Creagh and J. H. Hubbell, *ibid.*, Table 4.2.4.3, p. 200.
63. R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.
64. J. A. Ibers and W. C. Hamilton, *Acta Crystallogr.*, 1964, **17**, 781.
65. G. M. Sheldrick, *SHELXL97*, Program for the Refinement of Crystal Structures, University of Göttingen, Germany, 1997.