July, 1988] *© 1988 The Chemical Society of Japan* NOTES *Bull. Chem. Soc. Jpn.*, *61*, *2675—2677 (1988)* 2675

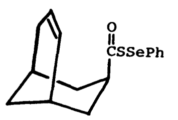
Radical Cyclization to Seleno-Substituted Thiahomoprotoadamantanone and Its Unexpected Conversion to the Vinyl Selenide

Takeshi Toru,* Toshiya Kanefusa, Eturô Maekawa, Yoshio Ueno,
Kazumoto Kondo,† and Shoji Eguchi*,†
Department of Applied Chemistry, Faculty of Engineering, Nagoya Institute of Technology,
Gokiso, Showa-ku, Nagoya 466
†Institute of Applied Organic Chemistry, Faculty of Engineering, Nagoya University,
Furo-cho, Chikusa-ku, Nagoya 464
(Received December 8, 1987)

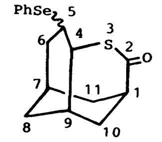
Synopsis. Heating *Se*-phenyl bicyclo[3.3.1]non-6-ene-3-(selenothioperoxy)carboxylate with AIBN gives 5-phenylseleno-3-thia-2-homoprotoadamantan-2-one which is unexpectedly converted to the vinyl selenide via the selenoxide by oxidation with hydrogen peroxide or *m*CPBA.

Se-Phenyl (selenothioperoxy)carboxylates are useful reagents for introducing both a thioester and a phenylseleno group into a molecule. Intermolecular addition of *Se*-phenyl(selenothioperoxy)benzoate to olefins gave addition products, i.e. *S*-phenylselenoalkyl thiobenzoate,[1] whereas *Se*-phenyl (selenothioperoxy)carboxylates bearing an unsaturated bond resulted in intramolecular selenothiolactonization to give phenylseleno-substituted thiolactones.[2] These reactions proceed via a free-radical pathway[1] involving the inter- or intramolecular attack of initially formed thiyl radical on the olefinic carbon and subsequent chain transfer of the carbon radical with the (selenothioperoxy)carboxylate. The construction of polycyclic molecules such as adamantane analogs could be of great interest because of their unique structures and reactivities.[3] We here disclose a new free-radical cyclization of *Se*-phenyl bicyclo[3.3.1]non-6-ene-3-(selenothioperoxy)carboxylate (**1**) into 5-phenylseleno-3-thia-2-homoprotoadamantan-2-one (5-phenylseleno-3-thiatricyclo[5.3.1.$0^{4,9}$]undecan-2-one) (**2**) and also an oxidative conversion of **2** to unexpected 5-phenylseleno-3-thia-2-homoprotoadmant-5-en-2-one (**5**).

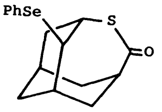
(Selenothioperoxy)carboxylate **1** was prepared[4] in 87% overall yield according to the following sequence: Bicyclo[3.3.1]non-6-ene-3-carboxylic acid[5] was converted to acid chloride, which was then transformed to thiocarboxylic acid. The thiocarboxylic acid was treated with *N*-(phenylseleno)phthalimide to give compound **1**. A 0.04 M (1 M=1 mol dm^{-3}) solution of (selenothioperoxy)carboxylate **1** in benzene was heated under reflux for 4 h in the presence of azobis(isobutyronitrile) (AIBN) (10 mol%). After removing the solvent the mixture was purified by chromatography to give 5-phenylseleno-3-thia-2-homoprotoadamantan-2-one (**2**) in 97% yield. There was no indication of the formation of any significant amount of 4-thiahomoadamantan-5-one derivative **3**. Compound **2** was shown to be homogeneous by an inspection of its ^{13}C NMR spectrum, although the configuration of the phenylseleno group in **2** is uncertain at present.[6] We have observed the formation of both trans and cis isomers in the selenothiolactonization[2] as well as in the addition reactions of *Se*-phenyl (selenothioperoxy)benzoate to cycloalkenes.[1] But in the present case there must exist a stronger steric requirement for a chain transfer of the intermediate carbon radical, leading to the exclusive formation of one isomer.



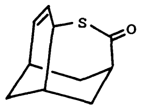
1



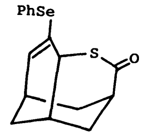
2



3



4



5

The present cyclization shows a notable reaction feature via a radical intermediate; i.e. the cyclization led to thiahomoprotoadamantanone **2**, but not to thiahomoadamantanone **3**. These results seem to be in accord with the predominant cyclization of 1-hexenyl radicals to five-membered rings.[7] Thus, the cyclization to thiahomoprotoadamantanone **2** can probably be ascribed to the stereoelectronically more favorable approach of the thiyl radical to the C-6 olefinic carbon than to the C-7 carbon, although a theoretical calculation is not presently available. In contrast, the ionic ring-closure of bicyclo[3.3.1]non-6-enes carrying internal nucleophiles at the 3-position generally results in an exclusive formation of homoadamantane ring systems, e.g., 4-thiahomoadmantane[8] from 3-mercaptomethylbicyclo[3.3.1]non-6-ene epoxide, 4-oxahomoadamantane[9] from 3-hydroxymethylbicyclo[3.3.1]non-6-ene, 2-bromo-4-oxatricyclo-[4.3.1.$1^{3,8}$]undecan-5-one[10] from the corresponding 3-carboxylic acid derivative.

Anticipating the formation of thiahomoprotoadamantenone **4**, we attempted on oxidation of the seleno group in **2** by hydrogen peroxide in the presence of pyridine in dichloromethane at ambient temperature, followed by heating the crude selenoxide under reflux in benzene for 1.5 h. This reaction, however, did not lead to the elimination of benzeneselenenic acid (PhSeOH), which would give thiahomoprotoadamantenone **4**. Instead, it gave unexpected selenothiahomoprotoadamantenone **5** bearing a vinyl selenide moiety in 82% yield. Oxidation of selenide **2** by *m*-

chloroperbenzoic acid (*m*CPBA) in dichloromethane at −40°C and subsequent heating under reflux with pyridine in benzene also gave vinyl selenide **5** in 70% yield. The spectral data showed an assigned structure that was concretely confirmed by the X-ray analysis (see Tables 1 and 2).

It is noteworthy that the oxidation of selenide **2** under conditions which usually induce the PhSeOH elimination to an olefin,11) did not result in the formation of olefin **4** but, instead, gave vinyl selenide **5**. Sterically compressed steroidal sulfoxides have been reported12) to give vinyl sulfoxides under the Pummerer reaction conditions involving the inevitable step of acylation of the corresponding sulfoxides. Another example is the oxidation of α-silyl selenides via the silyl rearrangement to the oxygen of the selenoxides, the reaction course of which is similar to that of the Pummerer reaction.13 The present conversion of selenide **2** to vinyl selenide **5** via the selenoxide was carried out under conditions different from those for the typical Pummerer reaction. The selenoxide could not undergo a smooth syn-elimination of PhSeOH, probably because of its highly strained arrangement. Instead, it afforded vinyl selenide **5** through a possible proton-abstraction from the α-carbon attached to the selenoxide. Unfortunately, there is presently insufficient evidence to permit an equivocal conclusion regarding the mechanism. Further experiments are now in progress that are designed to assess the steric factor in the above reaction as well as in the radical cyclization of bridged bicyclic compounds.

Experimental

***Se*-Phenyl Bicyclo[3.3.1]non-6-ene-3-(selenothioperoxy)-carboxylate (1).** To a suspension of sodium hydride (60% oil dispersion, 29 mg, 0.73 mmol), washed three times with pentane, in tetrahydrofuran (0.8 ml) was added at 0 °C a solution of bicyclo[3.3.1]non-6-ene-3-carboxylic acid (110 mg, 0.66 mmol) in tetrahydrofuran (0.5 ml). The reaction mixture was stirred for further 15 min after the evolution of hydrogen had ceased. The solvent was evaporated under reduced pressure and to the residual solid was added dry benzene (1.2 ml) and pyridine (0.1 ml). Then, oxalyl dichloride (0.17 ml, 1.97 mmol) was added to the ice-cooled mixture over a period of 6 min and the mixture was stirred for 20 min at that temperature, while white precipitate appeared. The mixture was filtered and solvent was removed by evaporation under reduced pressure to leave crude acid chloride. The acid chloride was taken up to tetrahydrofuran (2 ml) and the solution was added dropwise at 5 °C under vigorous stirring to a solution of sodium hydrogensulfide (70% purity, 265 mg, 3.31 mmol) in 80% aqueous ethanol (0.34 ml). The mixture was stirred for 5 min after the addition and, then, concentrated under reduced pressure. To the residue were added diethyl ether (15 ml) and water (5 ml). The aqueous layer was acidified with 1 M HCl (1 M=1 mol dm^{-3}). The organic layer was separated and the aqueous layer was extracted with diethyl ether (10 ml). The combined ethereal extracts were washed with brine several times, dried over anhydrous $MgSO_4$, and concentrated under reduced pressure to give crude thiocarboxylic acid as a colorless solid. It was dissolved in dichloromethane (2 ml) and the solution was added to a solution of *N*-(phenylseleno)phthalimide (240 mg, 0.79 mmol) in dichloromethane (0.5 ml) at −70 °C. The reaction was completed within a minute. Hexane (15 ml) was then added and the resultant precipitate was filtered off. Evaporation under reduced pressure gave a crude product, which was purified by flash column chromatography (silica gel 18 g, hexane/ethyl acetate 200:1 and then 99:1) to give (selenothioperoxy)carboxylate **1** (194 mg, 87%). ^{1}H NMR (CCl_4) δ=1.48—2.93 (m, 11H), 4.89—5.70 (m, 2H), 7.00—7.75 (m, 5H); IR (film) 1715 cm^{-1}; MS (70 eV) *m/z* (rel intensity) 338, 336 (M$^+$, ^{80}Se, 17, ^{78}Se, 9), 314, 312 ((PhSe)$_2$, ^{80}Se, 9, ^{78}Se, 5), 189, 187 (PhSeS$^+$, ^{80}Se, 10, ^{78}Se, 7), 181 (24), 157, 155 (PhSe$^+$, ^{80}Se, 69, ^{78}Se, 34), 149 (100), 121 (99). Found: C, 56.83; H, 5.52%. Calcd for $C_{16}H_{18}OSSe$: C, 56.97; H, 5.38%.

5-Phenylseleno-3-thiatricyclo[5.3.1.0^{4,9}]undecan-2-one (2). A mixture of (selenothioperoxy)carboxylate **1** (185 mg, 0.55 mmol) and azobis(isobutyronitrile) (9 mg, 0.055 mmol) in degassed benzene (13 ml) was heated for 7 h. After removing the solvent by evaporation under reduced pressure, the residue was purified by flash column chromatography (silica gel 5 g, hexane/ethyl acetate 95:5) to give thiahomoprotoadamantanone **2** (180 mg, 97%), mp 57—58 °C (from diethyl ether). ^{1}H NMR (500 MHz, $CDCl_3$) δ=1.57 (dddd, *J*=13.0, 5.6, 3.6, 1.6 Hz, C-8H), 1.96 (ddd, *J*=13.7, 6.3, 4.9 Hz, C-11H), 1.99 (m, C-11H′), 2.00 (ddd, *J*=13.6, 6.3, 4.9 Hz, C-10H), 2.07 (m, C-10H′), 2.12 (dddd, *J*=14.3, 3.9, 2.5, 1.9 Hz, C-6H), 2.14—2.22 (m, C-7H, C-8H), 2.43 (m, C-9H), 2.88 (ddd, *J*=14.3, 6.3, 3.8 Hz, C-6H′), 3.08 (tt, *J*=6.3, 2.5 Hz, C-1H), 3.17 (ddd, *J*=6.3, 2.5, 1.0 Hz, C-5H), 4.10 (dddd, *J*=1.9, 1.6, 1.0, 0.1 Hz, C-4H), 7.25—7.60 (m, phenyl H); ^{13}C NMR ($CDCl_3$) δ=26.4 (CH), 29.5 (CH_2), 29.8 (CH_2), 31.4 (CH_2), 32.4 (CH), 34.4 (CH_2), 40.9 (CH), 50.7 (CH), 52.7 (CH), 127.9 (CH), 129.5 (CH), 129.7 (C), 133.9 (CH), 209.7 (C=O); IR (KBr) 1653 cm^{-1}; MS (70 eV) *m/z* (rel intensity) 338, 336 (M$^+$, ^{80}Se, 3, ^{78}Se, 2), 306 (13), 278 (12), 261 (5), 181 (100), 157 (15), 155 (8), 149 (40). Found: C, 50.07; H, 5.58%. Calcd for $C_{16}H_{18}OSSe$: C, 56.97; H, 5.38%.

5-Phenylseleno-3-thiatricyclo[5.3.1.0^{4,9}]undec-5-en-2-one (5). Method A: To a solution of (selenothioperoxy)carboxylate **1** (54 mg, 0.16 mmol) and pyridine (54 μl, 0.66 mmol) in dichloromethane (7 ml) was added 35% hydrogen peroxide (150 μl, 0.87 mmol) under vigorous stirring at room temperature and the mixture was stirred until all the starting selenide was converted to the selenoxide, which could easily be confirmed by TLC (selenide; R_f=0.28, hexane/ethyl acetate 9:1, selenoxide; R_f=0.38, chloroform/methanol 95:5). After 1 h diethyl ether (30 ml) was added to the mixture and the resulting solution was washed succesively with water and brine. The organic solution was dried over anhydrous $MgSO_4$. The solvent was removed by evaporation under reduced pressure. Benzene (3 ml) was then added to the residue and the solution was refluxed for 1.5 h. The residue obtained after removing the solvent by evaporation under reduced pressure was purified by flash column chromatography to give vinyl selenide **5** (45 mg, 82%).

Method B: To a solution of (selenothioperoxy)carboxylate **1** (23 mg, 0.068 mmol) in dichloromethane (0.5 ml) was added *m*CPBA (80% purity, 16 mg, 0.74 mmol) at −40 °C. The mixture was stirred for 10 min at this temperature. After the cooling bath had been removed, pyridine (22 μl, 0.27 mmol) and benzene (1 ml) were added to the mixture. The reaction mixture was then heated under reflux for 6 h. The mixture was allowed to cool to room temperature and solvent was removed by evaporation under reduced pressure to give a residue which was purified as mentioned above to afford vinyl selenide **5** (16 mg, 70%). ^{1}H NMR (200 MHz,

Table 1. Bond Angles for **5**[a)]

Bond angle (ϕ/deg)			
C(2)-C(1)-C(10)	110.2(6)	C(6)-C(5)-Se(13)	120.3(4)
C(2)-C(1)-C(11)	115.1(6)	C(5)-C(6)-C(7)	120.3(6)
C(10)-C(1)-C(11)	112.1(6)	C(6)-C(7)-C(8)	106.3(6)
C(1)-C(2)-S(3)	117.6(5)	C(6)-C(7)-C(11)	114.1(6)
C(1)-C(2)-O(12)	124.0(6)	C(8)-C(7)-C(11)	111.3(6)
S(3)-C(2)-O(12)	118.3(5)	C(7)-C(8)-C(9)	109.1(6)
C(2)-S(3)-C(4)	100.2(3)	C(4)-C(9)-C(8)	110.7(5)
S(3)-C(4)-C(5)	105.2(4)	C(4)-C(9)-C(10)	112.1(5)
S(3)-C(4)-C(9)	114.8(4)	C(8)-C(9)-C(10)	107.2(6)
C(5)-C(4)-C(9)	113.9(5)	C(1)-C(10)-C(9)	109.0(6)
C(4)-C(5)-C(6)	121.6(5)	C(1)-C(11)-C(7)	116.3(6)
C(4)-C(5)-Se(13)	117.8(4)	C(5)-Se(13)-C(14)	98.6(3)

a) Labeling corresponds to that indicated in Figure. Estimated standard deviations in parentheses.

Table 2. Bond Lengths for **5**[a)]

Bond length (l/Å)			
C(1)-C(2)	1.494(10)	C(7)-C(8)	1.492(11)
C(1)-C(10)	1.523(10)	C(7)-C(11)	1.529(11)
C(1)-C(11)	1.543(10)	C(8)-C(9)	1.526(10)
C(2)-S(3)	1.788(7)	C(9)-C(10)	1.530(9)
C(2)-O(12)	1.213(8)	Se(13)-C(14)	1.914(6)
S(3)-C(4)	1.846(6)	C(14)-C(15)	1.394(9)
C(4)-C(5)	1.497(8)	C(14)-C(19)	1.382(10)
C(4)-C(9)	1.570(9)	C(15)-C(16)	1.391(13)
C(5)-C(6)	1.322(9)	C(16)-C(17)	1.368(15)
C(5)-Se(13)	1.922(6)	C(17)-C(18)	1.397(13)
C(6)-C(7)	1.496(9)	C(18)-C(19)	1.377(11)

a) Labeling corresponds to that indicated in figure. Estimated standard deviations in parentheses.

$CDCl_3$) δ=1.72—2.32 (m, 5H), 2.49 (m, 2H), 2.79 (m, 1H), 2.95 (m, 1H), 4.08 (d, J=9.9 Hz, 1H), 6.33 (d, J=8.0 Hz, 1H), 7.12—7.65 (m, 5H); ^{13}C NMR ($CDCl_3$) δ=26.9 (CH), 28.9 (CH_2), 31.1 (CH), 35.8 (CH_2), 36.0 (CH_2), 47.3 (CH), 50.2 (CH), 127.3 (CH), 129.3 (CH), 129.4 (C), 132.8 (CH), 138.1 (C), 141.3 (CH), 208.2 (C=O); IR ($CHCl_3$ solution) 1665 cm^{-1}; MS (70 eV) m/z (rel intensity) 336, 334 (M$^+$, ^{80}Se, 100, ^{78}Se, 49), 157 (61), 155 (33). Found: C, 57.25; H, 4.92%. Calcd for $C_{16}H_{16}OSSe$: C, 57.31; H, 4.81%.

Crystallographic Study of Vinyl Selenide 5. Crystal was obtained by slow crystallization from diethyl ether-hexane. D_m was measured by flotation. A Rigaku automated four-circles diffractometer AFC-5 was used with graphite monochromated Cu radiation (Cu K=1.5418 Å).

$C_{16}H_{16}OSSe$, M_r=335.32; monoclinic, $Pbca$, a=12.835(1) Å, b=18.190(2) Å, c=12.137(2) Å, α=90.03(1)°, β=89.99(1)°, γ=90.01(1)°, V=2837 Å^3, D_x=1.570 g cm^{-3}, D_m=1.574 g cm^{-3}; Z=8; Crystal size, 0.10×0.20×0.40 mm; 2687. Intensities were collected, $2\theta_{max}$=126°.

Structures were solved by the Monte-Carlo direct method with the aids of MULTAN78 program system using 2089 non-zero unique reflections, and refined by the full-matrix least-squares program with the analytical absorption correction. Non-hydrogen atoms were assigned anisotropic temperature factors. All the atoms were located by using a difference Fourier map and refined with the equivalent isotropic temperature factor to that for the bonded carbon atoms. R=0.0681, $S=[\sum w(|F_o|^2-|F_c|^2)^2/(m-n)]^{1/2}=1.4$, $w=1/\sigma^2(F^2)$, $\Delta\rho_{max}$=5.6 e Å^{-3}. Atomic scattering factors from International Tables for X-Ray Crystallography, Kynoch press, Birmingham, England (1974), Vol. 4. All calculations were made on a FACOM M-382 at the computer center of Nagoya University. Selected bond lengths and bond angles for **5** are shown in Tables 1 and 2.

The present work was partially supported by a Grant-in-Aid for Scientific Research No. 61470086 from the Ministry of Education, Science and Culture.

References

1) T. Toru, T. Seko, and E. Maekawa, *Tetrahedron Lett.*, **26**, 3263 (1985).

2) T. Toru, T. Kanefusa, and E, Maekawa, *Tetrahedron Lett.*, **27**, 1583 (1986).

3) R. C. Fort, Jr., "Adamantane: The Chemistry of Diamond Molecules," Marcel Dekker, New York (1976).

4) T. Toru, M. Nishigaki, T. Seko, T. Kanefusa, and E. Maekawa, *Synthesis*, **1985**, 879.

5) A. C. Udding, H. Wynberg, and J. Strating, *Tetrahedron Lett.*, **1968**, 5719; T. Sasaki, S. Eguchi, and T. Toru, *J. Am. Chem. Soc.*, **91**, 3390 (1969).

6) The ^{1}H NMR study in which each proton was assigned by the double resonance technique showed that the cyclohexane ring bearing a phenylseleno group might adopt a pseudo boat form since C-4 proton attached to the thio ester showed two long range couplings with C-6 and C-8 protons. Furthermore, from the model study the vicinal coupling constants between C-5 proton, attached to the phenylseleno group, and protons at C-4, C-6, and C-6′ position are more likely in accord with those anticipated from their dihedral angles in the structure having the anti configuration.

7) A. L. J. Beckwith, *Tetrahedron*, **37**, 3073 (1981); **41**, 3925 (1985); B. Giese, "Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds," Pergamon Press, Oxford (1986).

8) T. Sasaki, S. Eguchi, and H. Ban, *J. Org. Chem.*, **48**, 4073 (1983).

9) M. A. Mckervey, D. Faulkner, and H. Hamill, *Tetrahedron Lett.*, **1970**, 1971.

10) Takeshi Toru, Ph. D. Thesis, Nagoya University, Nagoya, Japan, 1971; W. H. Staas and L. A. Spurlock, *J. Org. Chem.*, **39**, 3822 (1974).

11) D. N. Jones, D. Mundy, and R. D. Whitehouse, *J. Chem. Soc., Chem. Commun.*, **1970**, 86; K. B. Sharpless, M. W. Young, and R. F. Lauer, *Tetrahedron Lett.*, **1973**, 1979; H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, **97**, 5434 (1975).

12) D. N. Jones, E. Helmy, and R. D. Whitehouse, *J. Chem. Soc., Perkin Trans. 1*, **1972**, 1329.

13) H. J. Reich and S. K. Shah, *J. Org. Chem.*, **42**, 1773 (1977).