



岐阜大学機関リポジトリ

Gifu University Institutional Repository

Title	4-Hydroxy-4-methyl-6-phenyl-2-p-toly-5,6-dihydro-4H-1,3-selenazine(本文(Fulltext))
Author(s)	KOKETSU, Mamoru; EBIHARA, Masahiro; ISHIHARA, Hideharu
Citation	[Acta Crystallographica Section E-Structure Reports Online] vol.[62] no.[Part4] p.[O1347]-[O1349]
Issue Date	2006-04
Rights	International Union of Crystallography
Version	出版社版 (publisher version) postprint
URL	http://hdl.handle.net/20.500.12099/28360

この資料の著作権は、各資料の著者・学協会・出版社等に帰属します。

4-Hydroxy-4-methyl-6-phenyl-2-*p*-tolyl-5,6-dihydro-4*H*-1,3-selenazineMamoru Koketsu,^{a*} Masahiro Ebihara^b and Hideharu Ishihara^b^aDivision of Instrumental Analysis, Life Science Research Center, Gifu University, Yanagido, Gifu, 501-1193, Japan, and ^bDepartment of Chemistry, Faculty of Engineering, Gifu University, Yanagido, Gifu, 501-1193, JapanCorrespondence e-mail:
koketsu@cc.gifu-u.ac.jp

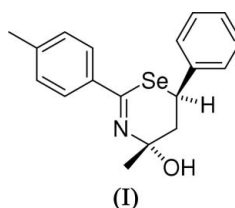
Key indicators

Single-crystal X-ray study
T = 190 K
Mean $\sigma(\text{C}-\text{C}) = 0.003 \text{ \AA}$
R factor = 0.030
wR factor = 0.068
Data-to-parameter ratio = 19.2For details of how these key indicators were automatically derived from the article, see <http://journals.iucr.org/e>.

In the title crystal structure, $\text{C}_{18}\text{H}_{19}\text{NOSe}$, there are two molecules in the asymmetric unit. Pairs of molecules are linked into a centrosymmetric dimer *via* intermolecular O—H···N hydrogen bonds [$\text{O}\cdots\text{N} = 2.872(2)$ and $2.893(2) \text{ \AA}$].

Comment

4-Hydroxy-5,6-dihydro-4*H*-1,3-selenazine derivatives have been reported to show antibacterial activity and antitumor effects (Cho *et al.*, 2000; Gutzkow *et al.*, 2003; Koketsu & Ishihara, 2003; Koketsu *et al.*, 1998; Koketsu, Ishihara *et al.*, 1999; Wu *et al.*, 1999). In order to study structure–biological activity relationships of selenazine derivatives, it is essential to determine the configuration of the selenazine ring. 4,6-Disubstituted 4-hydroxy-5,6-dihydro-4*H*-1,3-selenazines have been obtained by reaction of primary selenoamides with α,β -unsaturated ketones in the presence of $\text{BF}_3\cdot\text{Et}_2\text{O}$ (Koketsu, Senda *et al.*, 1999; Koketsu *et al.*, 2001, 2003). They were obtained as diastereomers resulting from the asymmetric centers at the 4- and 6-positions of the selenazine ring. From the structure determination of the title compound, (I), the diastereomer was confirmed to have a *trans* relationship between the OH group bonded to atom C2 (or C20) and the phenyl group bonded to atom C4 (or C22).



In the crystal structure of (I) there are two independent molecules in the asymmetric unit. The molecular structures are shown in Figs. 1 and 2. There are no significant geometric differences between the molecules, except the orientations of the phenyl rings (Table 1). The selenazine ring is essentially planar except for one C atom (C3 and C21), forming a sofa conformation. Each of the independent molecules forms a centrosymmetric hydrogen-bonded dimer (Fig. 3). Hydrogen-bond distances are similar in both independent dimers (Table 2).

Experimental

4-Phenyl-3-buten-2-one (0.15 g, 1.0 mmol) was added to a stirred solution of 4-methylselenobenzamide (0.20 g, 1.0 mmol) in dry chloroform (10 ml) under an argon atmosphere. Then $\text{BF}_3\cdot\text{Et}_2\text{O}$ (1 equivalent) was added to the mixture. The reaction mixture was

Received 24 February 2006
Accepted 3 March 2006

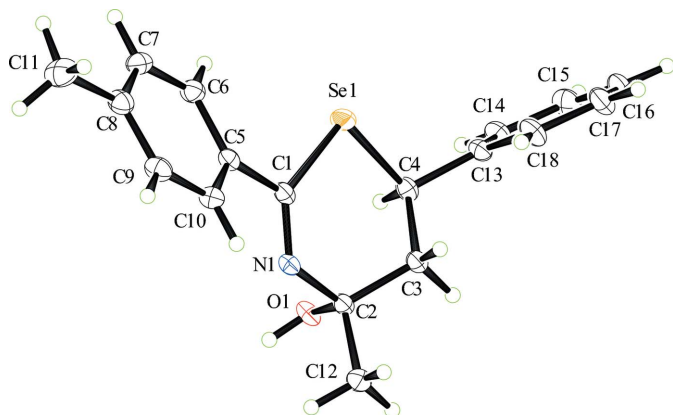


Figure 1
The molecular structure of the first of the two independent molecules in (I) which includes atom Se1. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

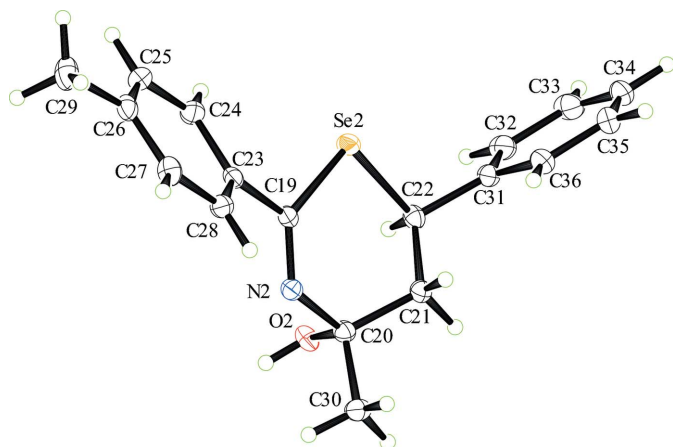


Figure 2
The molecular structure of the second independent molecule in (I) which includes atom Se2. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

stirred at 273 K for 3 h. The mixture was extracted with dichloromethane and washed with saturated sodium carbonate solution. The organic layer was dried over sodium sulfate and evaporated to dryness. The residue was purified by flash chromatography on silica gel with dichloromethane to give (I) in quantitative yield (0.35 g). Crystals were prepared by recrystallization of (I) from diethyl ether/hexane (4:6) (m.p. 378.3–379.3 K). ¹H NMR (400 MHz, CDCl₃): δ 1.49 (3H, s, CH₃), 1.96 (1H, t, J = 13.6 Hz), 2.19 (1H, dd, J = 4.4, 13.6 Hz), 2.36 (3H, s, CH₃), 3.13 (1H, br, OH), 4.69 (1H, dd, J = 4.4, 13.6 Hz, C6), 7.18 (2H, d, J = 7.8 Hz, Ar), 7.24–7.29 (1H, m, Ar), 7.33–7.38 (4H, m, Ar), 7.66 (2H, d, J = 7.8 Hz, Ar).

Crystal data

C₁₈H₁₉NOSe
M_r = 344.30
Monoclinic, P2₁/c
a = 18.0846 (10) Å
b = 16.9821 (10) Å
c = 10.8354 (10) Å
β = 103.190 (10)°
V = 3239.9 (4) Å³
Z = 8

D_x = 1.412 Mg m⁻³
Mo Kα radiation
Cell parameters from 13476 reflections
θ = 2.9–27.5°
μ = 2.32 mm⁻¹
T = 190 (2) K
Prism, colorless
0.32 × 0.20 × 0.10 mm

Data collection

Bruker-Nonius KappaCCD diffractometer
φ scans and ω scans with κ offsets
Absorption correction: multi-scan (SCALEPACK; Otwinowski & Minor, 1997)
T_{min} = 0.524, T_{max} = 0.801
26451 measured reflections

7417 independent reflections
6160 reflections with I > 2σ(I)
R_{int} = 0.034
θ_{max} = 27.5°
h = -23 → 23
k = -22 → 20
l = -14 → 14

Refinement

Refinement on F²
R[F² > 2σ(F²)] = 0.030
wR(F²) = 0.068
S = 1.03
7417 reflections
387 parameters
H-atom parameters constrained

w = 1/[σ²(F_o²) + (0.0236P)² + 1.8946P]
where P = (F_o² + 2F_c²)/3
(Δ/σ)_{max} = 0.003
Δρ_{max} = 0.53 e Å⁻³
Δρ_{min} = -0.54 e Å⁻³

Table 1

Selected geometric parameters (Å, °).

Se1—C1	1.9197 (18)	Se2—C19	1.9206 (18)
Se1—C4	1.968 (2)	Se2—C22	1.9731 (19)
C1—N1	1.266 (2)	C19—N2	1.267 (2)
C1—C5	1.485 (3)	C19—C23	1.486 (3)
N1—C2	1.478 (2)	N2—C20	1.483 (2)
C2—O1	1.418 (2)	C20—O2	1.417 (2)
C2—C12	1.521 (3)	C20—C30	1.520 (3)
C2—C3	1.525 (2)	C20—C21	1.528 (2)
C3—C4	1.522 (3)	C21—C22	1.521 (3)
C4—C13	1.509 (3)	C22—C31	1.514 (3)
C1—Se1—C4	98.50 (8)	C19—Se2—C22	99.28 (8)
N1—C1—C5	119.01 (16)	N2—C19—C23	120.36 (16)
N1—C1—Se1	127.61 (15)	N2—C19—Se2	127.74 (14)
C5—C1—Se1	113.36 (13)	C23—C19—Se2	111.87 (13)
C1—N1—C2	123.50 (15)	C19—N2—C20	122.60 (16)
O1—C2—N1	108.14 (15)	O2—C20—N2	107.84 (15)
O1—C2—C12	111.18 (16)	O2—C20—C30	111.12 (16)
N1—C2—C12	106.23 (15)	N2—C20—C30	106.71 (16)
O1—C2—C3	107.03 (15)	O2—C20—C21	106.79 (15)
N1—C2—C3	114.14 (15)	N2—C20—C21	114.48 (15)
C12—C2—C3	110.16 (16)	C30—C20—C21	109.94 (16)
C4—C3—C2	113.34 (16)	C22—C21—C20	114.04 (16)
C13—C4—C3	113.66 (16)	C31—C22—C21	115.87 (16)
C13—C4—Se1	109.10 (13)	C31—C22—Se2	106.47 (12)
C3—C4—Se1	108.48 (13)	C21—C22—Se2	108.80 (13)
N1—C1—C5—C10	31.1 (3)	N2—C19—C23—C28	39.3 (3)
Se1—C1—C5—C10	-147.47 (15)	Se2—C19—C23—C28	-139.10 (15)
N1—C1—C5—C6	-147.67 (19)	N2—C19—C23—C24	-140.36 (19)
Se1—C1—C5—C6	33.8 (2)	Se2—C19—C23—C24	41.2 (2)
C3—C4—C13—C18	-53.1 (3)	C21—C22—C31—C36	-48.0 (3)
Se1—C4—C13—C18	68.1 (2)	Se2—C22—C31—C36	73.1 (2)
C3—C4—C13—C14	124.3 (2)	C21—C22—C31—C32	134.69 (19)
Se1—C4—C13—C14	-114.51 (18)	Se2—C22—C31—C32	-104.19 (18)

Table 2

Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O1—H11···N1 ⁱ	0.84	2.04	2.872 (2)	173
O2—H30···N2 ⁱⁱ	0.84	2.06	2.893 (2)	175

Symmetry codes: (i) -x + 1, -y, -z + 1; (ii) -x, -y + 1, -z + 1.

All H atoms were placed in idealized positions and treated as riding atoms, with C–H = 0.95–0.99 Å and O–H = 0.84 Å, and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C}, \text{O})$ or $1.5U_{\text{eq}}(\text{methyl C})$.

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *SCALEPACK* and *DENZO* (Otwinowski & Minor, 1997); program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *ORTEPII* (Johnson, 1976); software used to prepare material for publication: *SHELXL97*.

This work was supported by a Grant-in-Aid for Science Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan (Nos. 15550030 and 17550099) to which we are grateful.

References

- Cho, S. I., Koketsu, M., Ishihara, H., Matsushita, M., Nairn, A. C., Fukazawa, H. & Uehara, Y. (2000). *Biochim. Biophys. Acta*, **1475**, 207–215.
- Gutzkow, K. B., Lähne, H. U., Naderi, S., Torgersen, K. M. Skålhegg, B., Koketsu, M., Uehara, Y. & Blomhoff, H. K. (2003). *Cell. Signal.* **15**, 871–881.
- Johnson, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
- Koketsu, M. & Ishihara, H. (2003). *Curr. Org. Chem.* **7**, 175–185.
- Koketsu, M., Ishihara, H. & Hatsu, M. (1998). *Res. Commun. Mol. Pathol. Pharmacol.* **101**, 179–186.
- Koketsu, M., Ishihara, H., Wu, W., Murakami, K. & Saiki, I. (1999). *Eur. J. Pharm. Sci.* **9**, 157–161.
- Koketsu, M., Senda, T., Yoshimura, K. & Ishihara, H. (1999). *J. Chem. Soc. Perkin Trans. 1*, pp. 453–456.
- Koketsu, M., Takenaka, Y., Hiramatsu, S. & Ishihara, H. (2001). *Heterocycles*, **55**, 1181–1188.

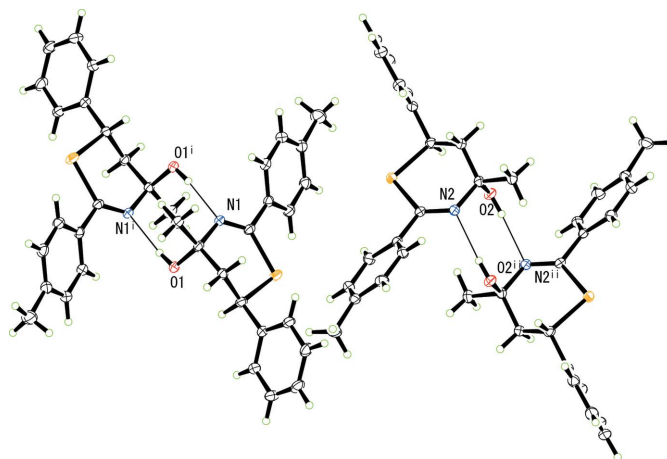


Figure 3

The hydrogen-bonded (thin lines) dimeric structure of (I). Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii. Symmetry codes are as given in Table 2.

- Koketsu, M., Takenaka, Y. & Ishihara, H. (2003). *Heteroatom Chem.* **14**, 106–110.
- Nonius (2000). *COLLECT*. Nonius BV, Delft, The Netherlands.
- Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter, Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
- Sheldrick, G. M. (1997). *SHELXS97* and *SHELXL97*. University of Göttingen, Germany.
- Wu, W., Murakami, K., Koketsu, M., Yamada, Y. & Saiki, I. (1999). *Anticancer Res.* **19**, 5375–5382.