Stereoselective Syntheses of Alkyl *Z*-2-(2-amino-4-oxo-1,3-selenazol-5(4*H*)-ylidene)acetates in Solvent-Free Conditions, X-Ray Single Crystal Structure Analysis of Ethyl *Z*-2-(2-amino-4-oxo-1,3-selenazol-5(4*H*)-ylidene)acetate

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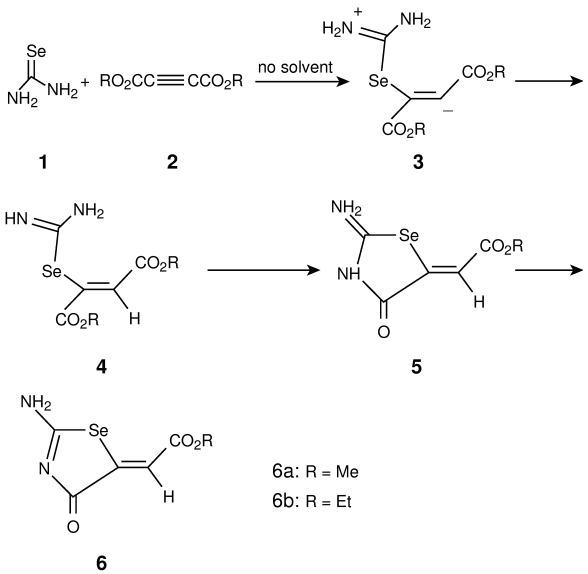
Selenourea reacts with dialkyl acetylenedicarboxylates under solvent-free conditions to form 1:1 adducts, which undergo a cyclization reaction to produce alkyl *Z*-2-(2-amino-4-oxo-1,3-selenazol-5(4*H*)-ylidene)acetates, in good yields. The stereochemistry of the ethyl *Z*-2-(2-amino-4-oxo-1,3-selenazol-5(4*H*)-ylidene)acetate was established by X-ray single crystal structure analysis. The reaction is completely stereoselective.

Key words: Selenourea, Acetylenic Ester, Michael Addition, Stereoselectivity, 1,3-Selenazol

Introduction

Though syntheses of sulfur-containing heterocyclic compounds have been extensively studied, syntheses of selenium analogues have not been appreciably investigated [1 – 4]. Recently, however, reports on synthesis of selenium-containing heterocyclic compounds have gradually increased not only because of the interesting reactivity of the products but also because of their potential pharmaceutical applications. For example, 1,3-selenazines show significant *anti*-bacterial activity against both Gram-negative and Gram-positive bacteria and potential *anti*-tumor effects against several kinds of human cancer cell lines. Selenazofurin demonstrates significant anti-tumor properties in animals and broad-spectrum antiviral activity in cell culture experiments [3 – 5]. Selenoureas and selenoamides have been used as the precursors in most of the syntheses of 1,3-selenazines and 1,3-selenazoles [3]. Dialkyl acetylenedicarboxylates (**2**) are reactive systems, which take part in many chemical reactions [6]. These results promoted us to examine the one-pot reaction of dialkyl acetylenedicarboxylates (**2**) with selenourea (**1**) in solvent-free systems (Scheme 1).



Scheme 1.

Discussion

Compounds **6a, b** may result from an initial Michael addition reaction of selenourea (**1**) to the acetylenic es-

Table 1. Crystal data and structure refinement for ethyl *Z*-2-(2-amino-4-oxo-1,3-selenazol-5(4*H*)-ylidene)acetate (**6b**).

Empirical formula	$C_7H_8N_2O_3Se$
Molecular weight	247.11
Temperature [K]	193(2)
Wavelength [Å]	0.71073
Crystal system	monoclinic
Space group	$P2_1/c$
a [Å]	12.190(2)
b [Å]	6.6430(10)
c [Å]	11.234(2)
β [°]	93.21(2)
V [Å^3]	908.3(3)
Z	4
$D_{calcd.}$ [g cm^{-3}]	1.807
μ [mm^{-1}]	4.110
$F(000)$	488
Crystal size [mm^3]	$0.68 \times 0.16 \times 0.03$
θ Range [°]	1.67 to 25.73
Index ranges	$-14 \le h \le 14$, $-8 \le k \le 7$, $-13 \le l \le 13$
Reflections collected	11282
Independent reflections (R_{int})	1709 (0.0370)
Reflections observed ($> 2\sigma$)	1443
Absorption correction	Numerical
Max. and min. transmissions	0.90 and 0.22
Data / restraints / parameters	1709 / 0 / 150
Goodness-of-fit on F^2	1.027
$R[I > 2\sigma(I)]$	$R1 = 0.0370$, $wR2 = 0.0596$
R (all data)	$R1 = 0.0269$, $wR2 = 0.0568$
Largest diff. peak and hole [e·Å^{-3}]	0.482 and -0.371

ter **2** and concomitant proton transfer in the 1:1 adducts **3**, followed by attack of the imine nitrogen atom on the carbonyl group of the esters to form intermediates **5** (Scheme 1). The proton shift in intermdiates **5** leads to formation of the alkyl *Z*-2-(2-amino-4-oxo-1,3-selenazol-5(4*H*)-ylidene)acetates **6a, b**, in good yields. TLC indicated that the reaction was complete under solvent-free conditions at room temperature after 25 min. The structures of **6a, b** were deduced from the IR, ^{1}H NMR and ^{13}C NMR spectra. The stereochemistry of **6b** was established by X-ray single crystal structure analysis. The reaction appears to be completely stereoselective. Other aspects of this process are under investigation.

The ORTEP diagram is shown in Fig. 1 and selected bond lengths and angles are given in Table 2. The crystal structure of this compound consists of monomeric units.

Table 2. Bond lengths [Å] and angles (°) for **6b**.

C1–C2	1.325(4)	C1–C6	1.504(4)
C1–Se1	1.881(3)	C2–C3	1.472(4)
C3–O3	1.206(4)	C3–O2	1.336(4)
C4–O2	1.462(3)	C4–C5	1.499(5)
C6–O4	1.226(4)	C6–N6	1.354(4)
C7–N5	1.301(4)	C7–N6	1.326(4)
C7–Se1	1.930(3)		
C2–C1–C6	122.9(3)	C2–C1–Se1	126.9(2)
C6–C1–Se1	110.12(19)	C1–C2–C3	121.5(3)
O3–C3–O2	124.9(3)	O3–C3–C2	123.9(3)
O2–C3–C2	111.1(3)	O2–C4–C5	106.6(3)
O4–C6–N6	123.8(2)	O4–C6–C1	120.5(2)
N6–C6–C1	115.7(2)	N5–C7–N6	123.0(2)
N5–C7–Se1	120.1(2)	N6–C7–Se1	116.88(19)
C7–N6–C6	113.6(2)	C3–O2–C4	115.5(2)
C1–Se1–C7	83.63(11)		

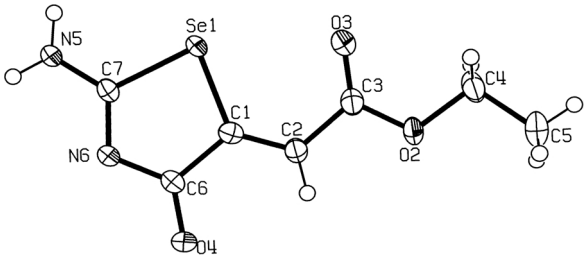


Fig. 1. ORTEP diagram of **6b**.

Experimental Section

Physical measurements

IR spectra were recorded as nujol mulls using Perkin-Elmer 597 and Nicolet 510P spectrophotometers. Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were measured with a BRUKER DRX-500 AVANCE spectrometer at 500 and 125 MHz, respectively.

*General procedure for the preparation of alkyl Z-2-(2-amino-4-oxo-1,3-selenazol-5(4H)-ylidene)acetates (***6a**, **b***)*

Selenourea **1** (0.123 g, 1 mmol) and the acetylene dicarboxylic ester **2** (1 mmol) were ground at room temperature for 25 min. The mixture was then washed with cold acetone (3 ml) and a white powder of **6** were collected by filtration.

*Methyl Z-2-(2-amino-4-oxo-1,3-selenazol-5(4H)-ylidene)acetate (***6a***):* White crystals, m. p. 233 °C, yield 58.2%. – IR (KBr): ν = 3217, 1689, 1666, 1496, 1365, 1288; 1180 cm^{-1}. – ^{1}H NMR ([D$_6$]-DMSO): δ = 3.77 (3H, s, CH_3), 6.95 (1H, s, =CH), 9.4 (1H, br. s, NH), 9.7 (1H, br. s, NH). – ^{13}C NMR ([D$_6$]-DMSO): δ = 52.65 (CH_3), 118.11 (=CH), 152.44 (=CSe), 167.07 (C-NH_2), 174.69 and 181.00 (2 C=O).

*Ethyl Z-2-(2-amino-4-oxo-1,3-selenazol-5(4H)-ylidene)-acetate (***6b***):* White crystals, m.p. 214.4 – 216.9 °C, yield 56.5%. – IR (KBr): ν = 3209; 3055; 2985; 2823; 2970; 1705; 1674; 1501; 1280; 1195 cm^{-1}. – ^{1}H NMR ([D$_6$]-DMSO): δ = 1.25 (3H, t, ^3J = 7.1 Hz, CH_3), 4.23 (2H, q, ^3J = 7.1 Hz, OCH_2), 6.92 (1H, s, =CH), 9.27 (1H, br. s, NH), 9.76 (1H,

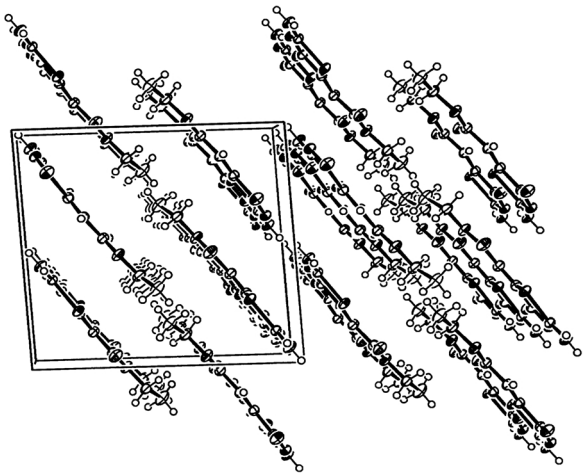


Fig. 2. Packing diagram of **6b**.

br. s, NH). – ^{13}C NMR ([D$_6$]-DMSO): $\delta = 13.99$ (CH_3), 61.49 (OCH2), 118.41 (=CH); 152.21 (=CSe), 166.49 (C-NH_2), 174.71 and 181.01 (2 C=O).

A white powder (0.01 g) of **6b** was dissolved in the boiling mixture of 5 ml ethanol and methanol $(2:1)$ and the resulting clear solution was left for 24 h. at room temperature. Colorless single crystals of **6b** were collected *via* filtration, washed with a cold mixture of ethanol/ water $(2:1)$ and dried at room temperature (m.p. 214.8 – 216.2 °C).

X-ray crystallography of **6b**

The intensity data of **6b** were collected using a STOE IPDS 2 diffratometer (Mo-K_*alpha* radiation) at 193 K. The structure was solved by direct methods using SIR97 [7] and refined by a full-matrix least-squares procedure (SHELXL-97) [8]. The molecular plots were prepared by using ORTEP-3 [9]. WinGX [10] was used as an interface during the structure solution procedure. The details of X-ray crystal structure analysis are summarized in Table 1. Selected bond lengths and angles are given in Table 2. The ORTEP diagrams and a perspective view of the packing in the unit cells are shown in Figs 1 and 2.

Supplementary material

Complete bond lengths and angles, co-ordinates and displacement parameters for **6b** have been deposited at Cambridge Crystallography Data Centre. Supplementary data are available from the CCDC, 12 Union Road , Cambridge CB2 1EZ, UK on request, quoting the deposition number 253133.

Acknowledgements

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