Research Article

Facile Synthesis of Pyrazole- and Benzotriazole-Containing Selenoethers

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Azole-containing selenoethers, 1,5-bis(3,5-dimethylpyrazol-1-yl)-3-selena pentane and 1,3-bis(1,2,3-benzotriazol-1-yl)-2-selena propane were prepared by the reaction of corresponding tosylate or chloride with sodium selenide generated in situ from elemental selenium and sodium formaldehydesulfoxylate (rongalite).

1. Introduction

Organoselenium compounds find applications due to their biological activity and useful synthetic properties (see [1, 2] and references cited therein). Selenoethers demonstrate potent ligating ability towards transition and main-group elements [3]. On the other hand, azole-containing thioethers are also known for their rich coordination chemistry [4]. Therefore, ligands carrying both azole- and selenoether moieties are especially interesting in view of their coordination chemistry. Nevertheless, only a few reports on compounds of this type have appeared in literature, demonstrating their use as building blocks for supramolecular architecture [5] and as ligands for catalysts [6–9]. Hodage et al. demonstrated potential glutathione peroxidase-like activity of some pyrazole-containing selenoethers [10]. Recently, Pop et al. prepared a series of late transition metal complexes of pyrazole-derived selenoethers [11].

Dialkyl selenides (selenoethers) are usually prepared from alkyl halides and Se²⁻ species, generated from various selenium compounds. Since selenide ions are very unstable towards oxygen, they are generated in situ using different reducing agents. Selenium in combination with aqueous NaOH [12], liquid ammonia and sodium [13], sodium in DMF [14], and sodium formaldehydesulfoxylate (rongalite) [15] were reported as sources of selenide ions. Other selenium compounds, such as selenium dioxide (reduced by trialkyl borohydrides) [16] or selenium tetrachloride [17], are less commonly used.

Herein we report improved methods for the preparation of pyrazole- and benzotriazole-containing selenoethers 1,5-bis(3,5-dimethylpyrazol-1-yl)-3-selena pentane (2) and 1,3-bis(1,2,3-benzotriazol-1-yl)-2-selena propane (4).

2. Results and Discussion

2.1. Synthesis of Selenoethers. In our preparation of azole-containing selenoethers we used elemental selenium and sodium formaldehydesulfoxylate (HOC₃H₂SO₂Na, rongalite) in aqueous NaOH [18]. The generated in situ sodium selenide was introduced into the reaction with 1-(2-tosyloxy ethyl)-3,5-dimethylpyrazole (1) or 1-chloromethyl benzotriazole (3) (Scheme 1). Due to low solubility of compound 3 in water acetonitrile was added to the reaction mixture in order to expedite the nucleophilic substitution. It should be noted that...
Selenium rings are within the usual range [21]. The lengths of Se–C bonds in diselenide are evident that compound 4 is indeed a selenoether and not a diselenide. The lengths of C–C and C–N bonds in pyrazole rings are within the usual range [21]. The lengths of Se–C bonds (1.95-1.96 Å) are also common for acyclic selenoethers [22].

2.2. X-Ray Crystal Structure Determination. In order to establish the structures of compounds 2 and 4 we have carried out single crystal X-ray structure determinations. Single crystals of compound 4 were obtained by crystallization from acetonitrile. Compound 2 has a relatively low melting point and crystallized rapidly from various solvents, preventing the formation of single crystals. However, with copper(II) nitrate compound 2 readily gave well-formed crystals of complex suitable for X-ray structure determination. The complex [Cu(2)(NO₃)₂] (5) was obtained in high yield (84%); therefore selenoether 2 and not some other impurity acted as a ligand and the structure of the complex can be used for the elucidation of compound 2 structure.

Complex 5 crystallizes in a monoclinic crystal system; crystallographic parameters and details of the diffraction experiment are given in Table 1. Molecular structure of the complex is shown in Figure 1, and selected bond lengths and angles are listed in Table 2. From the structure of complex 5 it is evident that compound 2 is indeed a selenoether and not a diselenide. The lengths of C–C and C–N bonds in pyrazole rings are within the usual range [21]. The lengths of Se–C bonds are slightly (by 0.01 Å) longer than in previously reported...
In summary, two selenoethers (pyrazole- and benzotriazole- containing, 2 and 4) were prepared using elemental selenium-rongalite system for in situ selenide ion generation. The structures, while C–Se–C angle is slightly sharper. The major type of intermolecular interactions, that is, probably responsible for low solubility and high melting point of compound 4, is Se–Se contacts (3.7936(3) Å, Figure 3), the length of which is in the range reported previously for selenoethers [24].

### 3. Conclusion

In summary, two selenoethers (pyrazole- and benzotriazole-containing, 2 and 4) were prepared using elemental selenium-rongalite system for in situ selenide ion generation. The proposed method uses inexpensive reagents, and provides higher yields compared to reported procedures.

### 4. Experimental

Elemental analyses were carried out on a Carlo Erba analyzer. Infrared (IR) spectra of solid samples as KBr pellets were

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**Table 1:** Crystallographic data, details of data collection, and structure refinement parameters for compounds 4 and 5.

| Example | 4 | 5 |
|---------|---|---|
| Chemical formula | C₁₄H₂₂N₆Se | C₁₄H₂₄CuN₆O₆Se |
| M (g mol⁻¹) | 343.26 | 512.88 |
| Temperature (K) | 100(2) | 100(2) |
| Wavelength (Å) | 0.71073 | 0.71073 |
| Crystal size (mm) | 0.14 × 0.11 × 0.11 | 0.14 × 0.11 × 0.11 |
| Crystal system | Monoclinic | Monoclinic |
| Space group | P 2₁/c | P 2₁/c |
| a (Å) | 11.2605(8) | 16.8873(9) |
| b (Å) | 9.1443(7) | 8.3578(5) |
| c (Å) | 13.6312(10) | 16.8873(9) |
| α (°) | 90 | 90 |
| β (°) | 102.2002(13) | 103.2610(10) |
| γ (°) | 90 | 90 |
| V (Å³) | 1371.90(18) | 1917.74(19) |
| Z | 4 | 4 |
| Dcal (g cm⁻³) | 1.662 | 1.776 |
| μ (mm⁻¹) | 2.740 | 3.082 |
| F(000) | 688 | 1036 |
| θ range for data collection (°) | 1.85 to 29.00 | 2.48 to 29.00 |
| Index ranges | −15 ≤ h ≤ 15, −23 ≤ h ≤ 23 | −12 ≤ k ≤ 12, −11 ≤ k ≤ 11 |
| −18 ≤ l ≤ 18, −19 ≤ l ≤ 19 | Reflections collected | 15771 | 22301 |
| Independent reflections | 3651 | 5086 |
| Completeness to 2θ (%) | [R(int) = 0.0446] | [R(int) = 0.0661] |
| Absorption correction | Semi-empirical from equivalents | Semi-empirical from equivalents |
| Max. and min. transmission | 0.753 and 0.700 | 0.913 and 0.694 |
| Data/restraints/parameters | 3651/0/190 | 5086/0/257 |
| Goodness-of-fit on F² | 1.002 | 1.018 |
| Final R₁, wR₂ [I > 2σ(I)] | R₁ = 0.0276 | R₁ = 0.0351 |
| wR₂ = 0.0575 | wR₂ = 0.0677 |
| R₁, wR₂ (all data) | R₁ = 0.0449 | R₁ = 0.0572 |
| wR₂ = 0.0643 | wR₂ = 0.0766 |
| Largest difference in peak and hole (e Å⁻³) | 0.434 and 0.343 | 0.590 and −0.604 |

**Table 2:** Selected bond distances (Å) and angles (°) for compounds 4 and 5.

For compounds 4:

| Bond/Angle | Value (Å) or ° |
|------------|---------------|
| Se(1)–C(1A) | 1.960(2) |
| N(1A)–C(1A) | 1.441(3) |
| C(1A)–Se(1)–C(1) | 95.88(9) |
| N(1A)–C(1A)–Se(1) | 112.83(14) |
| N(1A)–C(1A)–Se(1) | 111.81(13) |

For compounds 5:

| Bond/Angle | Value (Å) or ° |
|------------|---------------|
| Se(1)–C(7) | 1.955(3) |
| C(7)–Se(1)–C(14) | 99.87(12) |
| Se(1)–C(14) | 1.965(3) |
| Se(1)–C(14)–Cu(1) | 101.55(8) |
| Cu(1)–O(1) | 2.0504(19) |
| Cu(1)–N(2) | 1.971(2) |
| Cu(1)–Se(1) | 2.5110(4) |
| Cu(1)–N(2)–Se(1) | 87.11(6) |
| Cu(1)–O(1)–Se(1) | 88.00(8) |
| Cu(1)–N(2)–Se(1) | 175.68(9) |
| Cu(1)–N(2)–Se(1) | 88.00(8) |
| Cu(1)–O(1)–Se(1) | 87.11(6) |
| Cu(1)–O(1)–Se(1) | 95.72(6) |

**Figure 2:** Molecular structure of selenoether 4. Thermal ellipsoids for nonhydrogen atoms are drawn at 50% probability level. Hydrogen atoms are omitted for clarity.

**Figure 3:** Se–Se intermolecular contacts in the structure of 4. Some molecules in the unit cell are not shown for clarity.
recorded on a Nicolet 5700 (4000–400 cm\(^{-1}\)) spectrophotometer. NMR spectra were recorded on Bruker AV300 instrument operating at 300 MHz for \(^1\text{H}\) and 75 MHz for \(^{13}\text{C}\). EI MS measurements were carried out using TRACE DSQ (Thermo Electron Corporation, USA) instrument.

Single crystals of compounds 4 and 5 for crystal structure determination were mounted in inert oil and transferred to the cold gas stream of the diffractometer. The structure was determined at 153 K by conventional single crystal X-ray diffraction techniques using an automated four-circle Bruker-Nonius X8 Apex diffractometer equipped with a 2D CCD detector and graphite monochromated molybdenum source (\(\lambda = 0.71073\) Å). Intensity data were collected by \(\varphi\)-scanning of narrow frames (0.5°) to 2\(\theta\) = 54.96°. Absorption correction was applied empirically by the program SADABS [25]. The structure was solved by the direct method and refined using the full-matrix least-squares technique in the anisotropic approximation for nonhydrogen atoms with the program package SHELX-97 [26]. Hydrogen atoms were localized geometrically.

Tosylate 1 [27] and chloro-derivative 3 [28] were prepared according to known procedures; sodium formaldehydesulfoxylate dihydrate (rongalite) was purchased from Acros.

4.1. 1,5-Bis(3,5-dimethylpyrazol-1-yl)-3-selena Pentane (2). A suspension of selenium (0.395 g, 5 mmol), sodium formaldehydesulfoxylate dihydrate (3.08 g, 20 mmol), and NaOH (1.10 g, 27.5 mmol) in water (5 mL) was stirred at room temperature, until the initially formed red solution turned colorless and white precipitate of Na\(\text{Se}\) was formed (15–20 min). Tosylate 1 (2.94 g, 10 mmol) was then added in one portion, the mixture was brought to reflux and stirring was continued for 2 hours, deep-green crystals of the complex were formed, which were filtered, washed with acetone, and dried. The crystals were suitable for X-ray crystal structure determination. Yield 0.086 g (84%). IR (\(\nu, \text{ cm}^{-1}\)) 1556 (\(\nu_{\text{C-Se}}\)), 1026 (Pz breathing), 811 (\(\nu_{\text{C-Se}}\)). Anal. Calc’d for C\(_{14}\)H\(_2\)CuN\(_6\)O\(_6\)Se (512.87): C, 33.04; H, 4.50; N, 16.39. Found: C, 33.04; H, 4.50; N, 15.96.

4.2. 1,3-Bis(1,2,3-benzotriazol-1-yl)-2-selena Propane (4). Selenoether 4 was prepared similarly to compound 2 from 2.10 g (12.54 mmol) chloro-derivative 1 (0.50 g (6.27 mmol) of selenium, 2.31 g (15.0 mmol) of sodium formaldehydesulfoxylate dihydrate, and 1.38 g (34.5 mmol) of NaOH in 6 mL of water and 15 mL of acetonitrile. Yield 1.94 g (90%), colorless crystals, mp 182-183°C (DMF). IR (\(\nu, \text{ cm}^{-1}\)) 1612, 1496, 1453 (\(\nu_\text{br}\)), 754 (\(\nu_{\text{C-Se}}\)). \(^1\text{H}\) NMR (DMSO-d\(_6\)): 6.19 (s, 4H, CH\(_2\)), 7.44 (t, 2H, 5-H-Bta, \(J = 7.5\) Hz), 7.58 (t, 2H, 6-H-Bta, \(J = 7.5\) Hz), 7.97 (d, 2H, 4-H-Bta, \(J = 8\) Hz), 8.08 (d, 2H, 7-H-Bta, \(J = 8\) Hz). \(^{13}\text{C}\) NMR (DMSO-d\(_6\)): 42.5 (CH\(_3\)), 111.1 (7-C-Bta), 119.3 (6-C-Bta), 124.4 (5-C-Bta), 127.5 (6-C-Bta), 131.9 (8-C-Bta), 145.4 (9-C-Bta). Anal. Calc’d for C\(_{14}\)H\(_{12}\)N\(_6\)Se (343.25): C, 48.99; H, 3.52. Found: C, 49.30; H, 3.83.

4.3. 1,5-Bis(3,5-dimethylpyrazol-1-yl)-3-selena Pdinate-Dinitrato Copper (5). To a solution of selenoether 2 (0.065 g, 0.2 mmol) in acetone (0.2 mL), solution of Cu(NO\(_3\))\(_2\)·3H\(_2\)O (0.048 g, 0.2 mmol) in acetone (0.2 mL) was added. After standing for 2 hours, deep-green crystals of the complex were formed, which were filtered, washed with acetone, and dried. The crystals were suitable for X-ray crystal structure determination. Yield 0.086 g (84%). IR (\(\nu, \text{ cm}^{-1}\)) 1556 (\(\nu_{\text{C-Se}}\)), 1026 (Pz breathing), 811 (\(\nu_{\text{C-Se}}\)). Anal. Calc’d for C\(_{14}\)H\(_2\)CuN\(_6\)O\(_6\)Se (512.87): C, 32.79; H, 4.32; N, 16.39. Found: C, 33.04; H, 4.50; N, 15.96.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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