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SYNTHESIS AND OPTICAL PROPERTIES OF AZULENO[1,2-*b*]BENZOTHIOPHENE AND SELENOPHENE

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Abstract – Benzothiophene- and benzoselenophene-fused azulene derivatives were synthesized by Cu-catalyzed tandem cyclization via the Ullmann-type S/Se-arylation and Csp²-H chalcogenation of 2-(2'-bromophenyl)azulene. The maximum absorption of tetracyclic products was red-shifted from that of 2-phenylazulene, which does not contain a bridged chalcogen atom. Single-crystal X-ray analysis of azuleno[1,2-*b*]benzoselenophene revealed that the benzo[*b*]selenophene and azulene rings are almost coplanar.

Azulene-fused heterocycles are building blocks for natural products and organic materials; hence, their synthesis, reactivity, and physical properties have garnered much attention.¹ For example, an unsubstituted azulene-fused tricyclic heterole containing sulfur, azuleno[1,2-*b*]thiophene **I**, was first synthesized by Fujimori *et al.*, and its molecular structure, spectroscopic features, and optical properties were investigated in the 1980s.² Furthermore, derivatization using the chemical reactivity of **I** was attempted, and the physical properties of the obtained compounds were evaluated.³ However, to the best of our knowledge, unsubstituted tetracyclic azulene-fused benzoheteroles **II** containing group 16 elements,

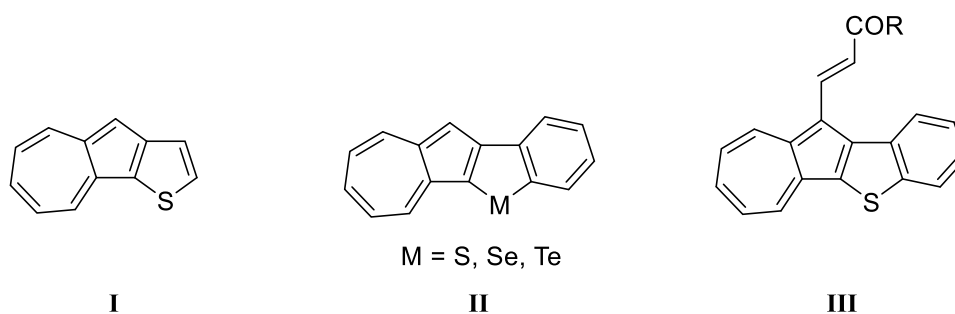


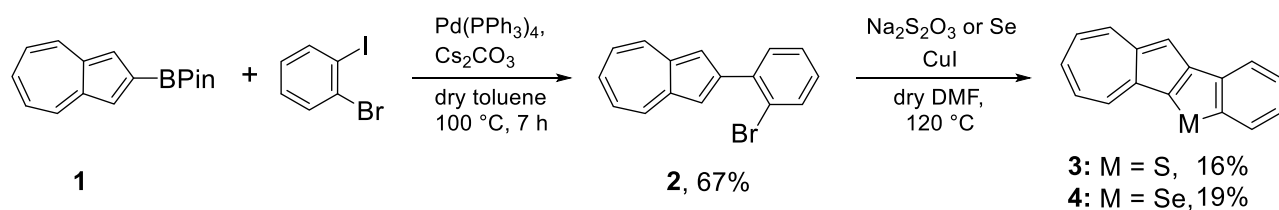
Figure 1. Azulene-fused heteroles having group 16 elements

azuleno[1,2-*b*]benzothiophene, selenophene, and tellurophene, have not been synthesized, and there are only two known reports on the synthesis of sulfur-containing azuleno[1,2-*b*]benzothiophenyl enones **III**.⁴ The synthesis method for obtaining **III** is not suitable for the parent azuleno benzoheterole **II** because the tropylium ion-mediated furan-ring-opening reactions afford 11-substituted azuleno[1,2-*b*]benzothiophene derivatives.

Noteworthy chemical modifications of azulene include transition-metal catalyzed regioselective C–H activation and coupling at the electron-rich 1-position.⁵ However, these reactions are limited to C–C bond formations, and C–chalcogen bond formation has not been reported. Cu-Catalyzed tandem reaction *via* a one-step Ullmann-type S/Se-arylation and Csp²–H thiolation/selenation are efficient methods for the synthesis of tetracyclic heterocycles such as benzothienoimidazopyridines, benzoselenoimidazopyridines, benzothienoindoles, and benzoselenoindoles.⁶ We reported the reaction of 2-(2'-haloaryl)imidazo[1,2-*a*]pyridines with Se using a CuI catalyst for the synthesis of benzo[*b*]selenophene-fused imidazo[1,2-*a*]pyridines, which proceeded smoothly.⁷ As part of our continuing studies, we herein attempted the synthesis of a novel parent azuleno[1,2-*b*]benzothiophene and azuleno[1,2-*b*]benzoselenophene *via* Cu-catalyzed double C–S/Se bond formation from 2-(2'-bromophenyl)azulene and evaluated the optical properties of the obtained products.

The synthetic sequence leading to tetracyclic azuleno[1,2-*b*]benzoheteroles is depicted in Scheme 1. Azulene-2-boronic acid pinacol ester **1** was prepared⁸ according to the published procedure⁸ and coupled with 2-bromoiodobenzene to obtain 2-(2'-bromophenyl)azulene **2** in 67% yield.⁹ Zhou *et al.* reported the Cu-catalyzed tandem reaction of alkyl bromide and imidazo[1,2-*a*]pyridine with Na₂S₂O₃ as the sulfur source in the presence of 10 mol% CuI in DMF at 120 °C under aerobic conditions for the synthesis of 3-alkylthio-2-phenylimidazo[1,2-*a*]pyridines.¹⁰ This procedure was applied to synthesize azuleno[1,2-*b*]benzothiophene **3** *via* double C–S bond formation from **2** in 16% yield.¹¹ The reaction of **2** with Se powder also gave azuleno[1,2-*b*]benzoselenophene **4** in 19% yield.¹¹ Unfortunately, when using Te powder, the corresponding azuleno[1,2-*b*]benzotellurophene was not obtained.

The molecular structures of **3** and **4** were confirmed by spectral analyses. In the NMR spectra, all the



Scheme 1. Synthesis of azulene-fused benzoheteroles containing sulfur (**3**) and selenium (**4**)

proton and carbon signals were in the aromatic region (7.1–8.5 ppm for ^1H NMR and 108–115 ppm for ^{13}C NMR), and the signal for H(11) showed **3**: 7.79 ppm and **4**: 7.80 ppm as a singlet in the ^1H NMR spectrum. Recrystallization was repeated for compounds **3** and **4**, and a single crystal suitable for X-ray analysis was obtained only from **4**. The molecular structures determined by single-crystal X-ray diffraction (SCXRD) analysis of **4** are illustrated in Figure 2.¹² The results revealed that the azulene-fused benzoselenophene rings are virtually coplanar (mean deviation 0.021 Å) to each other. The ten bond lengths in azulene moiety reveal that fusion of benzothiophene onto the azulene skeleton does indeed induce bond alternation: the average difference in length of adjacent peripheral bonds is 0.055 Å [1.381(7) Å for the short bonds, 1.436(7) Å for the long ones (See Supporting Information)]. This is in contrast to the azulene itself which has nearly equal bond lengths (1.387–1.404 Å) around its 10π -electron periphery.¹³ The crystal packing is classified into a herringbone-type (Figure 2b), with the interfacial distance between adjacent molecules being 2.705 Å and the distances between the nearest neighbor atoms (Se...C11) on adjacent molecules being 3.588 Å. The stacked columns show alternately changing tilt angles of approximately $\pm 52.92^\circ$. Adjacent columns are connected through CH- π interactions¹⁴ with a CH-centroid distance of 3.489–3.580 Å (Figure 2c).

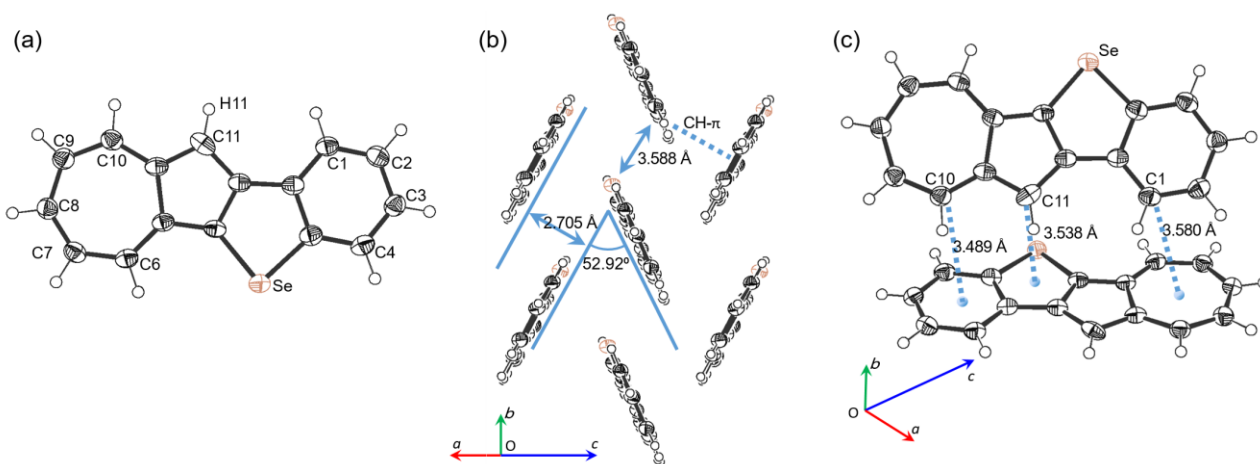


Figure 2. (a) ORTEP drawing of compound **4**. (b) Packing structure viewed along the molecular long axis, (c) CH- π interactions between adjacent molecules.

The photophysical properties of **3** and **4** were evaluated, and the corresponding data are shown in Figure 3 and Table 1. These compounds showed a well-resolved absorption profile with structured vibrational peaks, indicative of their rigid scaffolds. They exhibited strong absorptions from 290 to 330 nm and three moderate absorptions at 399, 381 and 364 nm for **3**, and at 399, 382 and 364 for **4**. Additionally, weak absorptions ($\epsilon = 450\text{--}500 \text{ M}^{-1}\text{cm}^{-1}$) were observed at 691 (for **3**) and 686 (for **4**) nm, corresponding to their $S_0 \rightarrow S_1$ transition. In contrast, 2-phenylazulene **5**, which does not contain a bridged chalcogen atom, showed the absorption maximum at 389 and 629 nm.¹⁵ These results revealed that the introduction of a chalcogen atom to 2-phenylazulene results in the formation of a bridge that fixes the molecular structure in a coplanar axis to form a heterole-fused system.

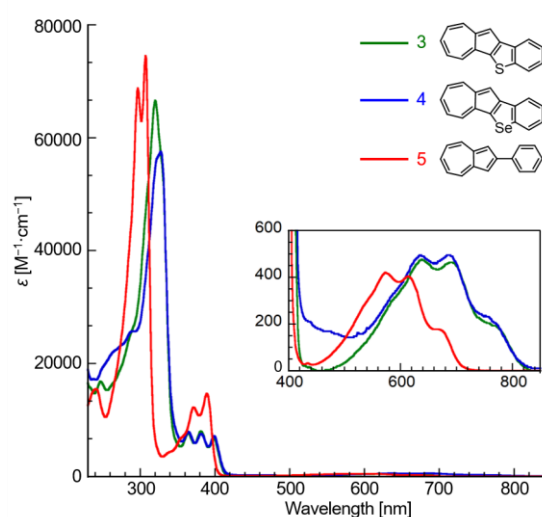


Figure 3. UV/Vis spectra of **3–5** in CHCl_3 with the magnified low-energy absorptions in the inset

Table 1. Absorption data of azulene derivatives^a

Compd.	λ (ϵ) [nm]				
3	320 (66600)	364 (6648)	381 (7800)	399 (7700)	691 (460)
4	328 (54600)	364 (6600)	382 (7500)	399 (7900)	686 (500)
5	307 (74500)	372 (12200)	389 (14700)	629 (340)	

^a Measured in CHCl_3 .

Further investigations for extending heteroacene chemistry to the development of functional materials, including those applicable to electronic devices and for elucidating the chemical/physical properties of these compounds by synthetic, theoretical, and spectroscopic studies are in progress.

ACKNOWLEDGEMENTS

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SUPPORTING INFORMATION

Supplementary (crystal data and NMR spectra) data associated with this article can be found, in the online version, at URL: <https://www.heterocycles.jp/newlibrary/downloads/PDFsi/27252/105/1>.

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9. 2-Bromoidobenzene (125 μ L, 1 mmol), tetrakis(triphenylphosphine)palladium (115 mg, 0.1 mmol), and cesium carbonate (1.62 g, 5 mmol) were added to a solution of azulene-2-boronic acid pinacol ester (**1**) (325 mg, 1.3 mmol) in dry toluene (5 mL) under argon atmosphere. The mixture was heated at 100 °C and stirred. After 7 h the reaction mixture was cooled and diluted with AcOEt and water. The phases were separated and the aqueous layer was extracted with AcOEt. The combined organic layer was washed with water, dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography using *n*-hexane/CH₂Cl₂ (10:1) as eluent to give **2** as blue amorphous (190 mg, 67%); ¹H NMR (400 MHz, CDCl₃) δ : 8.35 (d, *J* = 9.3 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 1H), 7.65 (s, 2H), 7.63-7.55 (m, 2H), 7.40 (td, *J* = 7.8, 1.0 Hz, 1H), 7.23-7.17 (m, 3H); ¹³C NMR (100 MHz, CDCl₃) δ : 149.5, 139.9, 138.5, 137.1,

- 136.8, 133.6, 132.4, 128.7, 127.4, 123.5, 122.7, 118.2; MS (EI): m/z (%) = 282 (83, M⁺), 202 (100), 101 (41), 176 (14); HRMS: m/z [M]⁺ calcd for C₁₆H₁₁Br: 282.0044. Found: 282.0047.
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11. 2-(2'-Bromophenyl)azulene (**2**) (566 mg, 2.0 mmol), chalcogen source (2.5 mmol), and copper(I) iodide (76 mg, 0.4 mmol) were dissolved in DMF (2 mL). The mixture was heated at 120 °C and stirred. After completion of the reaction, the reaction mixture was cooled and diluted with CH₂Cl₂ and sat. NH₄Cl aq.. The phases were separated, and the aqueous layer was extracted with CH₂Cl₂. The combined organic layers were washed with water, dried with MgSO₄, and concentrated under reduced pressure. The residue was purified by column chromatography using *n*-hexane/CH₂Cl₂ (10:1) as eluent. **3**: green plate (73 mg, 16%); mp: 236-238 °C (from *n*-hexane/CH₂Cl₂); ¹H NMR (400 MHz CDCl₃) δ: 8.43 (d, *J* = 3.6 Hz, 1H), 8.40 (d, *J* = 4.0 Hz, 1H), 8.24-8.22 (m, 1H), 7.97-7.93 (m, 1H), 7.79 (s, 1H), 7.62 (t, *J* = 8.4 Hz, 1H), 7.50-7.48 (m, 2H), 7.21 (t, *J* = 5.5 Hz, 1H), 7.16 (t, *J* = 3.8 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ: 149.3, 145.8, 142.8, 137.1, 136.9, 133.0, 132.1, 131.6, 128.1, 126.9, 124.4, 124.0, 123.7, 122.33, 122.30, 108.1; MS (EI): m/z (%) = 234 (100, M⁺), 104 (15), 122 (15), 189 (12); HRMS: m/z [M]⁺ calcd for C₁₆H₁₀S: 234.0503. Found: 234.0501.
- 4**: green plate (106 mg, 19%); mp: 220-220.5 °C (from *n*-hexane/CH₂Cl₂); ¹H NMR (400 MHz CDCl₃) δ: 8.38 (d, *J* = 4.0 Hz, 1H), 8.33 (d, *J* = 3.6 Hz, 1H), 8.22 (d, *J* = 3.0 Hz, 1H), 7.96 (d, *J* = 3.1 Hz, 1H), 7.80 (s, 1H), 7.61 (t, *J* = 8.0 Hz, 1H), 7.49 (t, *J* = 6.0 Hz, 1H), 7.41 (t, *J* = 6.0 Hz, 1H), 7.23-7.22 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ: 151.1, 145.0, 143.0, 136.9, 134.6, 134.3, 134.0, 127.18, 127.15, 125.9, 125.1, 124.9, 122.6, 122.5, 109.5; ⁷⁷Se NMR (76 MHz, CDCl₃) δ: 397.7; MS (EI): m/z (%) = 282 (100, M⁺), 202 (39), 141 (17), 176 (13); HRMS: m/z [M]⁺ calcd for C₁₆H₁₀Se: 281.9948. Found: 281.9945.
12. X-Ray crystallographic data of azuleno[1,2-*b*]selenophene **4** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 2075026.
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