Synthesis of Novel Tetraazapentalenes with Fused Cyclic Systems: Reaction of Tetraazapentalene Derivatives with 2-Bromoethyl and 3-Bromopropyl Isothiocyanates

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The novel 1-substituted 4,5,7,8-tetrahydro-3H-6,8-b-dithia(8a-SIV)-1,2a,5a-triaza-8a-azoniacyclo[a,cd]indene-2(1H)-thione bromides, the corresponding 8b-selena(8b-SeIV) derivatives, and 1-substituted 4,5,8,9-tetrahydro-3H,7H-6,9-b-dithia(9b-SeIV)-1,2a,5a-triaza-9a-azoniacyclopenta[k]thiophene-2(1H)-thione bromide and the corresponding 9b-selena(9b-SeIV) derivatives were synthesized by the reaction of tetraazapentalene derivatives 1a,b and 2a,b with 2-bromoethyl and 3-bromopropyl isothiocyanates, respectively, in good yields.

The hydropervulgar sulfur compounds with a 10 π-electron system, such as 1,6,6a-trithia(6a-SIV)pentalenes and 6a-thia(6a-SIV)-1,6-diazapentalenes, have attracted much attention because of the unusual electronic structure and chemical behavior.1−14 Recently, we have developed the 12 π-tetraazapentalene derivatives 1a,b and 2a,b with hydropervulgar sulfur and selenium by a one-pot synthetic method using lithium thiourea or selenoureide, phenacly chloride, and alkyl (or allyl) isothiocyanate as the starting materials.15,16 Furthermore, we have reported that the isothiocyanate moiety of the tetraazapentalenes 1a, b is replaced17,18 by various isocyanates and isothiocyanates, and that the tetraazapentalenes 1a,b and 2a,b arealkylated with alkyl iodides to give the S-monooalkylated tetraazapentalene derivatives in good yields.19 These results led us to explore the reactions of 1a,b and 2a,b with 2-bromoethyl and 3-bromoethyl isothiocyanates which are expected to form a fused cyclic system by intramolecular cyclization. In this paper, we describe the synthesis of the novel tetraazapentalene derivatives 3a−d and 4a−d containing a fused five- or six-membered ring, which is formed by intramolecular cyclization. A part of these results has already been reported in a preliminary paper.20 The reactions of 1a,b and 2a,b with two equivalents of α-Bromoalkyl isothiocyanates [Br-(CH3)2-C=S, n = 2 and 3], were prepared from the corresponding α-bromoalkylamine hydrobromides and thiophosgene according to the method described by Fris51 were examined at first. When the reactions were carried out in benzene at 80 °C, a white solid separated out within a few minutes, and the mixture was then refluxed for 2 hours. The resulting colorless precipitates filtered off, washed with benzene, and recrystallized from ethanol to give the tetraazapentalenes 3a−d and 4a−d with fused cyclic systems in high yields (Scheme 1).

The filtrate was concentrated in vacuo, and the residue was chromatographed on silica gel with dichloromethane to give only trace amounts of the recovered 1a,b and 2a,b. The structure of the products 3a−d and 4a−d was determined by IR, 1H-NMR, and 13C-NMR spectra, and elemental analysis (Table).

In the IR spectrum of 3a, no peak in the region of 2000−2200 cm−1 was observed. This fact indicates that the product 3a does not contain the isothiocyanate group. The 13C-NMR spectrum of 3a in methanol-d4 showed nine carbon signals, and FAB-MS spectrum of 3a showed m/z = 273 as a parent peak of the cationic part of 3a. In general, the compounds 3a−d were stable in the atmosphere. However, the products 4a−d with a hydropervulgar selenium atom were slightly unstable and changed gradually to red in the atmosphere. Although further reaction of 3a−d with 2-bromoethyl isothiocyanate was carried out, no formation of tetraazapentalenes with two fused rings was observed. Furthermore, the S-alkylated tetraazapentalenes with the -S-(CH3)2-C=S group were not obtained at all. When the reaction of the unsymmetrical tetraazapentalene 1c22 with two molar equivalents of 2-bromoethyl isothiocyanate in benzene was carried out under reflux for 15 h, the products 3a and 3c were obtained as a mixture in 44% and 15% yields, respectively (Scheme 2). The yields of 3a and 3c were determined from the integral ratio in the 1H-NMR spectrum of the mixture. Consequently, it was found that the allyl isothiocyanate moiety of 1c is replaced by 2-bromoethyl isothiocyanate in preference to the methyl isothiocyanate moiety.

Scheme 1

Scheme 2
Table. Tetraazapentalene Derivatives 3a-d and 4a-d Prepared

<table>
<thead>
<tr>
<th>Product</th>
<th>Yield* (%)</th>
<th>mp (°C) (solvent)</th>
<th>Molecular Formula*</th>
<th>IR (KBr) ν (cm⁻¹)</th>
<th>¹H-NMR (CDOD/TMS) δ, J (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3a</td>
<td>84</td>
<td>237-238 (dec) (EtOH)</td>
<td>C₄H₁₃BrN₃S₃ (353.3)</td>
<td>2930, 1610, 1560, 1490, 1340, 1270</td>
<td>2.52 (m, 2H), 3.54 (s, 3H), 3.96 (t, 2H, J = 8.1), 4.27 (t, 2H, J = 6.0), 4.38 (t, 2H, J = 6.0), 4.46 (t, 2H, J = 8.1)</td>
</tr>
<tr>
<td>3b</td>
<td>86</td>
<td>220-222 (dec) (EtOH)</td>
<td>C₁₀H₁₄BrN₃S₃ (367.4)</td>
<td>2930, 1620, 1560, 1490, 1380, 1320</td>
<td>2.25 (m, 2H), 2.58 (m, 2H), 3.40 (s, 3H), 3.41 (t, 2H, J = 6.0), 3.97 (t, 2H, J = 6.0), 4.47 (t, 2H, J = 6.0), 4.55 (t, 2H, J = 6.0)</td>
</tr>
<tr>
<td>3c</td>
<td>97</td>
<td>150-152 (dec) (EtOH)</td>
<td>C₁₂H₁₄BrN₃S₃ (379.4)</td>
<td>2910, 1610, 1560, 1480, 1380, 1340</td>
<td>2.59 (m, 2H), 3.86 (t, 2H, J = 8.0), 4.43 (t, 2H, J = 8.0), 4.54-4.64 (m, 6H), 5.43-5.49 (m, 2H), 5.94-6.02 (m, 1H)</td>
</tr>
<tr>
<td>3d</td>
<td>95</td>
<td>176-177 (dec) (EtOH)</td>
<td>C₁₂H₁₄BrN₃S₃ (393.4)</td>
<td>2930, 1620, 1570, 1490, 1315, 1260</td>
<td>2.23 (m, 2H), 2.58 (m, 2H), 3.47 (t, 2H, J = 6.0), 3.95 (t, 2H, J = 6.0), 4.47-4.59 (m, 6H), 5.37-5.40 (m, 2H), 5.92-6.00 (m, 1H)</td>
</tr>
<tr>
<td>4a</td>
<td>81</td>
<td>212-214 (dec) (EtOH)</td>
<td>C₁₄H₁₃BrN₃S₂Se (400.2)</td>
<td>2910, 1590, 1550, 1480, 1400, 1370</td>
<td>2.48 (m, 2H), 3.45 (s, 3H), 3.99 (t, 2H, J = 8.3), 4.25 (t, 2H, J = 5.8), 4.43 (t, 2H, J = 6.1), 4.46 (t, 2H, J = 8.2)</td>
</tr>
<tr>
<td>4b</td>
<td>75</td>
<td>221-222 (dec) (EtOH)</td>
<td>C₁₄H₁₃BrN₃S₂Se (414.2)</td>
<td>2930, 1600, 1550, 1480, 1400, 1370</td>
<td>2.20 (m, 2H), 2.46 (m, 2H), 3.41 (s, 3H), 3.47 (t, 2H, J = 5.8), 4.02 (t, 2H, J = 5.3), 4.23 (t, 2H, J = 5.9), 4.47 (t, 2H, J = 5.5)</td>
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<tr>
<td>4c</td>
<td>58</td>
<td>150-152 (dec) (EtOH)</td>
<td>C₁₄H₁₃BrN₃S₂Se (426.3)</td>
<td>2950, 1640, 1600, 1570, 1480, 1430</td>
<td>2.51 (m, 2H), 3.99 (t, 2H, J = 8.3), 4.28 (t, 2H, J = 8.2), 4.41-4.60 (m, 6H), 5.23-5.40 (m, 2H), 6.00-6.10 (m, 1H)</td>
</tr>
<tr>
<td>4d</td>
<td>85</td>
<td>178-180 (dec) (EtOH)</td>
<td>C₁₂H₁₃BrN₃S₂Se (440.3)</td>
<td>2920, 1590, 1560, 1490, 1470, 1420</td>
<td>2.19 (m, 2H), 2.47 (m, 2H), 3.47 (t, 2H, J = 5.8), 3.99 (t, 2H, J = 5.8), 4.22 (t, 2H, J = 5.8), 4.47 (t, 2H, J = 5.8), 4.57 (d, 2H, J = 1.2), 5.26-5.36 (m, 2H), 5.97-6.07 (m, 1H)</td>
</tr>
</tbody>
</table>

* Yields of the isolated products 3a-d and 4a-d were based on 1a, b and 2a, b.

** Satisfactory microanalyses obtained: C ± 0.29, H ± 0.29, N ± 0.27.

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Next, the reaction of 1a with 2-chloroethyl isothiocyanate in benzene was carried out under reflux for 2 hours. The resulting precipitate was filtered off, washed with benzene, and recrystallized from ethanol to give the tetraazapentalene 5 with a fused cyclic system in 15% yield. The filtrate was concentrated in vacuo, and the residue was chromatographed on a preparative TLC to give the mono- and bis-(2-chloroethyl)tetraazapentalenes (6 and 7) as byproducts in 20 and 9% yields, respectively (Scheme 3). The structure of the products 5, 6, and 7 was determined by IR and ¹H-NMR spectra, and elemental analysis. In this reaction, the yield of the tetraazapentalene 5 with a fused ring decreased remarkably.

Thus, the yields of the products with a fused ring were affected by the type of the halogen atom in the ortho-haloalkyl isothiocyanates used. In addition, we have found that the tetraazapentalene 6 is converted to 5 in 33% yield by heating it in benzene under reflux for 60 hours. The reaction is considered to proceed through the replacement of the methyl or allyl isothiocyanate moiety of 1a, b by 2-bromoethyl isothiocyanate, followed by intramolecular cyclization, as shown in Scheme 4.

As described above, we established the synthetic method for preparing the tetraazapentalene derivatives fused by a five- or six-membered ring.

Melting points were determined on a Yanagimoto MP-S3 melting point apparatus and are uncorrected. The ¹H- and ¹³C-NMR spectra were obtained using a JEOL JNM-GX270 spectrometer. The IR spectra were determined on a Hitachi 215 Grating infrared spectrophotometer. Mass spectrum was obtained using a JEOL...
JMS-AX505SW spectrometer with FAB ionization. Elemental analyses were recorded on a Yanagimoto MT-3 CHN recorder. Column chromatography was performed on Wakogel C-300.

**1-Methyl-4,5,7,8-tetrahydro-3H-6,8-b-dithia(8-b-SN)1,2,4,5,8-a-azoniadicyclo[α,ɛ7.5]indene-2(1H)-thione Bromide (3a): Typical Procedure**

To a solution of 1a (104 mg, 0.4 mmol) in benzene (20 mL) is added 2-bromoethyl isothiocyanate (133 mg, 0.8 mmol) with stirring at r.t. The mixture is refluxed for 2 h. The resulting precipitate is filtered off, washed with benzene, and recrystallized from EtOH to give a white solid of yield: 119 mg (84%).

$^{13}$C-NMR (CD$_2$OD): $\delta = 20.63, 34.80, 38.94, 48.34, 50.33, 58.90, 165.19, 165.49, 174.75.$

MS (FAB): m/z (%) = 273 (parent ion peak of the cationic part, 55).

The filtrate is concentrated in vacuo. The residue is chromatographed on a preparative TLC (silica gel, CH$_2$Cl$_2$) to give trace amounts of the recovered 1a.

**1-Methyl-4,5,7,8-tetrahydro-3H-6,8-b-dithia(8-b-SN)1,2,4,5,8-a-azoniadicyclo[α,ɛ7.5]indene-2(1H)-thione Chloride (5):** 2-Methyl-3-(2-chloroethyl)-6,7-dihydro-5H-2-a-thia(2-a-SN)-2,3,4,7-tetraaza-1H-cyclooctatetra[cd e]indene-1,4(2H,3H)-dithione (6) and 2,3-Bis(2-chloroethyl)-6,7-dihydro-5H-2-a-thia(2-a-SN)-2,3,4,7-tetraaza-1H-cyclooctatetra[cd e]indene-1,4(2H,3H)-dithione (7):

To a solution of 1a (104 mg, 0.4 mmol) in benzene (20 mL) is added 2-chloroethyl isothiocyanate (98 mg, 0.8 mmol) with stirring at r.t. The mixture is refluxed for 2 h. The resulting precipitate is filtered off, washed with benzene, and recrystallized from EtOH to give a white solid of 5 (19 mg). The filtrate is concentrated in vacuum. The residue is chromatographed on a silica gel column using CH$_2$Cl$_2$/CCl$_4$ (5:1) as an eluent to give 6 (2.5 mg) and 7 (13 mg) as white solids. Recrystallization from hexane/CHCl$_3$ gives pure samples.

5; yield: 19 mg (15%); mp 204–205°C (doc).

C$_6$H$_5$ClC$_5$N$_3$ calc. C 35.00 H 4.42 N 18.14 (308.9) found 34.85 4.12 18.00

IR (KBr): $\nu = 2930, 1610, 1550 \text{ cm}^{-1}$.

$^1$H-NMR (CD$_2$OD): $\delta = 2.47$ (m, 2 H, NCH$_2$CH$_2$N$_2$), 3.50 (s, 3 H, CH$_3$). $\delta$ (2 H, J = 8.1 Hz, SCH$_2$N$_2$), 4.22 (t, 2 H, J = 5.8 Hz, NCH$_2$CH$_2$N$_2$), 4.33 (t, 2 H, J = 5.8 Hz, NCH$_2$CH$_2$N$_2$), 4.42 (t, 2 H, J = 8.2 Hz, SCH$_2$N$_2$).

6; yield: 25 mg (20%); mp 175–176°C (doc).

C$_6$H$_5$ClC$_5$N$_3$ calc. C 35.00 H 4.42 N 18.14 (308.9) found 34.74 4.13 17.87

IR (KBr): $\nu = 2900, 1570, 1530 \text{ cm}^{-1}$.

$^1$H-NMR (CD$_2$OD): $\delta = 2.38$ (m, 2 H, NCH$_2$CH$_2$N$_2$), 3.26 (s, 3 H, CH$_3$). $\delta$ (t, 2 H, J = 6.0 Hz, NCH$_2$CH$_2$Cl), 4.03 (t, 2 H, J = 6.0 Hz, NCH$_2$CH$_2$Cl), 4.42–4.45 (m, 2 H, NCH$_2$CH$_2$Cl).

7; yield: 13 mg (9%); 123–125°C (doc).

C$_6$H$_5$ClC$_5$N$_3$S$_3$ calc. C 33.61 H 3.95 N 15.68 (357.4) found 33.31 3.93 15.40

IR (KBr): $\nu = 2910, 1580, 1530 \text{ cm}^{-1}$.

$^1$H-NMR (CD$_2$OD): $\delta = 2.40$ (m, 2 H, NCH$_2$CH$_2$N$_2$), 3.85 (t, 4 H, J = 5.5 Hz, 2 × NCH$_2$CH$_2$Cl), 4.06 (t, 4 H, J = 5.5 Hz, 2 × NCH$_2$CH$_2$Cl), 4.42 (t, 4 H, J = 6.0 Hz, NCH$_2$CH$_2$Cl).

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