# Reaction of Tetraazathiapentalene and Thiadiazolopyrimidine Derivatives with Heterocumulenes: Cycloaddition and Elimination Reactions *via* Hypervalent Sulfur Intermediates

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Tetraazathiapentalene derivative **1** reacts with heterocumulenes such as diphenylketene (**2**) and 2-pyridylisothiocyanate (**5**) to give heterocycles **3**, **6** and **7** with elimination of methylisothiocyanate. The reactions of thiadiazolopyrimidine derivatives **8a-b** with ethoxycarbonyl isothiocyanate (**9**) and carbon disulfide (**11**) gives heterocycles **10** and **12** *via* thermal decomposition of 1:1 cycloadducts **C** and **D** which have a hypervalent sulfur. The mechanistic and reactivity features of these reactions are described.

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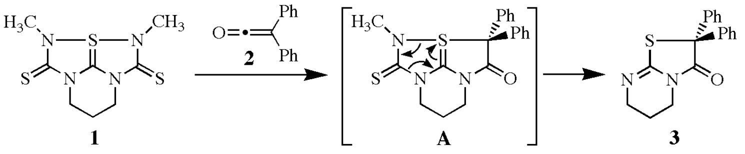
Ethylene trithiocarbonate [1], Hector's base (4-aryl-3-arylmino-5-imino-1,2,4-thiadiazolidines) [2], 4-alkyl-5-imino-3-methyl-$\Delta^2$-1,2,4-thiadiazolines [3], and 2-phenyl-1,3-oxathiols [4] are known to react with acetylenes to afford ring-opened products through a 1,3-dipolar cycloaddition [5]. These reactions have attracted much attention in connection with the chemistry of 6a-thiathiophtenes [6]. Previously, we have reported the synthesis and characterization of tetraazathiapentalene derivatives that are closely related to 6a-thiathiophtenes [7]. In our continuing study, we found that the reaction of **1** and thiadiazolopyrimidine derivatives **8a-b** with heterocumulenes afford unsymmetrical tetraazathiapentalene derivatives and ring-opened products *via* hypervalent sulfur intermediates. However, little is known about the stability and reactivity of tetraazathiapentalene derivatives containing hypervalent sulfur. In order to gain more information about their reactivities, we have studied the reactions of these compounds and related compounds with heterocumulenes. We now report the reactions of **1** with diphenylketene (**2**) and 2-pyridylisothiocyanate (**5**), and also the reactions of **8a-b** with ethoxycarbonyl isothiocyanate (**9**) and carbon disulfide (**11**).

Scheme 1



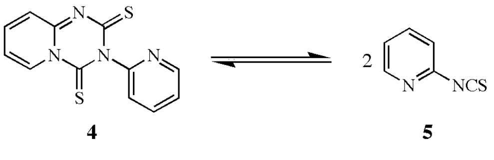
Reaction of **1** with **2**.

The reaction of **1** with 10 molar equivalents of **2** [8] in chloroform for 18 hours under reflux gave 6,7-dihydro-5,5-diphenyl-5*H*-thiazolo[2,3-*a*]pyrimidin-4(2*H*)-one (**3**) in a 75% yield (Scheme 1). The reaction of **3** with methyl isothiocyanate did not occur under the same reaction conditions. These results suggest that in the reaction of Scheme 1, the exchange reaction between **1** and **2** occurs first to give hypervalent sulfur compound **A** which has the $N\text{-}S^{IV}\text{-}C$ apical bond, and then thermolysis of **A** in boiling chloroform leads to **3** with release of methyl isothiocyanate. The structure of **3** was determined by its $^1$H NMR and mass spectra and elemental analysis. It should be pointed out here that the strength of the apical $N\text{-}S^{IV}\text{-}C$ bond in **A** differs from that of the apical $N\text{-}S^{IV}\text{-}N$ bond in **6**. In general, the apical $N\text{-}S^{IV}\text{-}C$ bond in pentalene derivatives is known to be very weak compared with the apical $N\text{-}S^{IV}\text{-}N$ bond, and the $N\text{-}S^{IV}$ bond in the $N\text{-}S^{IV}\text{-}C$ compounds is cleaved easily and selectively upon heating [3,9]. Consequently, intermediate **A** is converted to **3** by a quick fission of the $N\text{-}S^{IV}$ bond.

Reaction of **1** with **5**.

Compound **5** prepared from 2-aminopyridine and carbon disulfide usually exists as a brick-red crystalline dimer **4** under ambient conditions. This dimer slowly dissociates to a pale yellow monomer **5** on warming in organic solvents. Dissociation of **4** to **5** occurs at 55 °C in chloroform [10] and at 70 °C in DMSO [11] (Scheme 2).

Scheme 2



We carried out the reactions of **1** with **4** at 80 °C in DMSO. Therefore, **4** exists in fact, as **5** under these reaction conditions. The results are summarized in Scheme 3 and Table 1.

Scheme 3

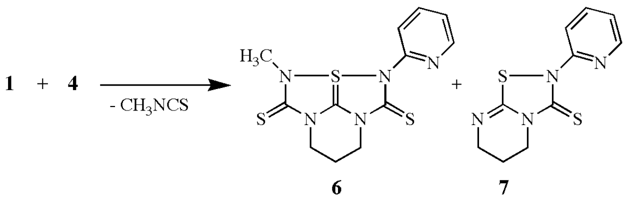


Table 1

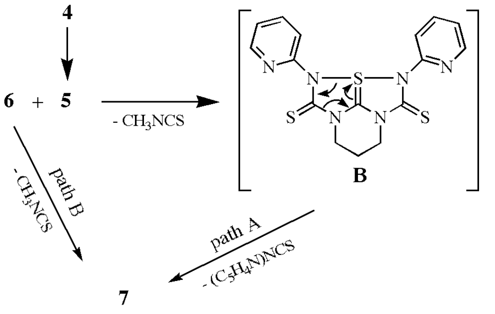
Reaction of **1** and **6** with **4**[a]

| Entry | Tetraazathia-pentalene | Molar ratio **1** or **6** : **4** | Time / h | Product Yield / %[b] **6** | **7** |
|---|---|---|---|---|---|
| 1 | **1** | 1 : 0.5 | 15 | 28 | 18 |
| 2 | **1** | 1 : 2.5 | 15 | 28 | 39 |
| 3 | **1** | 1 : 2.5 | 30 | 23 | 50 |
| 4 | **6** | 1 : 2.5 | 24 | trace | 75 |

[a] Reactions were carried out in DMSO at 80 °C; [b] Isolated yields

As shown in Table 1, the yields of **6** and **7** depended on the molar ratio of **1** to **4** and the reaction time. When the reaction of **1** with 0.5 molar equivalent of **4** in DMSO was carried out for 15 hours, mono-substituted tetraazathiapentalene derivative **6** and thiadiazolopyrimidine derivative **7** were obtained in 28 and 18% yields, respectively (entry 1). When the added amount of **4** was increased to 2.5 molar equivalents, the yield of **7** increased considerably (entry 2). Elongation of the reaction time merely led to the increase in the yield of **7** (entry 3). The reaction of **6** with 2.5 molar equivalents of **4** for 24 hours gave selectively **7** in a good yield along with a trace amount of **6**. When **6** was warmed at 80 °C in DMSO, a very small amount of **7** was obtained. The reaction of **7** with **4** under the same reaction conditions did not afford tetraazathiapentalene derivative **B**, resulting in the recovery of **7**. These results suggest that **B** is unstable compared with **6**; note that **6** can be isolated, but **B** cannot be isolated under the reaction conditions. Based on these results, we propose that **7** is formed *via* path A and path B as shown in Scheme 4, but path A appears to be the major pathway in the formation of **7**.

Scheme 4



Furthermore, we found that the reaction of **1** with ethoxycarbonylisothiocyanate (**9**) in refluxing chloroform for 5 hours results in a quantitatively recover of **1**.

### Reactions of Thiadiazolopyrimidine Derivatives **8a-b** with Ethoxycarbonyl Isothiocyanate and Carbon Disulfide.

The reactions of **8a-b**, which were prepared by thermolysis or oxidation of symmetrical tetraazathiapentalene derivatives [12], with ethoxycarbonyl isothiocyanate (**9**), which has an electron-wihdrawing group, gave 4-ethoxy-5-oxa-6-thia-1,3,8-triazabicyclo[5.4.0]undec-3,7-diene-2-thione (**10**) in moderate yields by a cycloaddition-elimination pathway *via* hypervalent sulfur intermediate **C** without production of tetraazathiapentalene derivatives such as **6**. The structure of **10** was characterized by its spectroscopic data and elemental analysis. A probable pathway for the formation of the product is given in Scheme 5, and the yields of the product are shown in Table 2.

The reaction of **8a-b** with a large excess of carbon disulfide (**11**) in chloroform at room temperature for 18 hours gave 5,6-dihydro-pyrimido[1,2-*d*][1,2,4]dithiazole-3(7*H*)-thione (**12**) in low yields as shown in Table 2. Compound **12** is considered to be produced *via* the hypervalent sulfur intermediate **D**, although **D** was unable to be isolated. The mode of this reaction was similar to that of the reaction of **8a-b** with ethoxycarbonyl isothioyanate (see Scheme 5). The structure of **12** was determined by comparison of melting point, IR, $^1$H NMR, and mass spectra with those of authentic specimen [13]. Detailed mechanism for the formation of **10** and **12** remains unexplored at present. But we now wish to propose a mechanism that involves a 1,3-dipo-

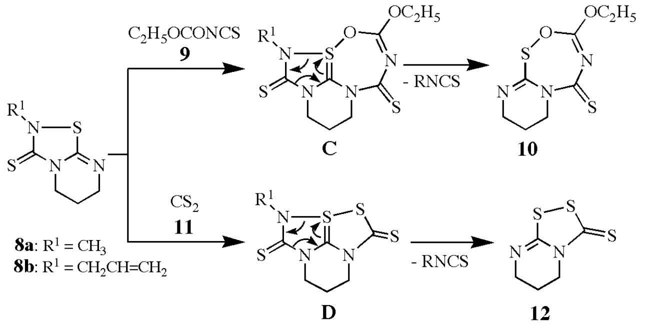
Table 2

Reaction of Thiadiazolopyrimidine Derivatives with Isothiocyanates[a] and Carbon Disulfide[b]

| Thiadiazolopyrimidine Derivative | Isothiocyanate | Product | Yield / %[c] |
|---|---|---|---|
| **8a** | $C_2H_5OCONCS$ | **10** | 77 |
| **8b** | $C_2H_5OCONCS$ | **10** | 67 |
| **8a** | $CS_2$ | **12** | 32 |
| **8b** | $CS_2$ | **12** | 25 |

[a] Reaction were carried out in refluxing chloroform for 3 hours; [b] Reactions were carried out at room temperature for 18 hours; [c] Isolated yields.

Scheme 5



lar cycloaddition of the S(1)-C(8a)=N moiety in **8a** and **8b** to the O=C-N=C=S and S=C=S parts through the tetravalent sulfur intermediates **C** and **D** (see Scheme 5).

## EXPERIMENTAL

All the solvents were purified by usual procedures. TLC was performed on a Merck Art 25 DC-plastikfolien Kieselgel 60 $F_{254}$. Column chromatography was performed on silica gel (Merck, 70-230 mesh). NMR spectra were obtained with a JEOL 270 NMR spectrometer. Chemical shits are expressed in ppm with TMS as an internal standard. Melting points were determined with a Yanako MP-500 and are uncorrected. Infrared spectra were recorded by a Jasco Herschel FT IR 230 or a PERKIN ERMER 1600. UV spectra were taken with a SHIMADZU UV-160A. MS spectra were determined on a JEOL-DX 303 HF. Elemental analyses were performed on a YANAGIMOTO CHN corder MT-3.

### Materials.

Tetraazathiapentalene derivative **1** [7c], diphenyl ketene (**2**) [8], 2-pyridyl isothiocyanate (**5**) [10-11], and thiadiazolopyrimidine derivatives **8a**-**b** [12] were prepared according to the procedures described in the literatures.

### 6,7-Dihydro-2,2-diphenyl-5*H*thiazolo[3,2-*a*]pyrimidin-3(2*H*)-one (**3**).

Compound **3** was obtained by the reaction of **1** with **2**. The reaction of **1** (73.4 mmg, 0.282 mmol) with 10 molar equivalents of **2** (2.82 mmol), which was generated *in situ* from diphenylacetyl chloride (651 mmg, 2.82 mmol) and triethylamine (342 mg, 3.38 mmol), was carried out in refluxing benzene (30 mL) for 18 hours under argon, and then the reaction mixture was evaporated. The residue was extracted with $CHCl_3$ and the extract was washed with water, dried ($Na_2SO_4$) and concentrated under reduced pressure. The residue was chromatographed on silica gel with $CH_2Cl_2$ to give **3** (62 mg, 75 %) as a colorless solid, mp 101-103 °C; ir (potasssium bromide): 1715, 1645, 1445, 1385, 1360, 1290, 1260, 960, 755, and 700 $cm^{-1}$; $^1H$ nmr (deuteriochloroform): δ 1.91 (m, 2H, $NCH_2C\mathit{H}_2CH_2N$), 3.61 (t, 2H, J = 5.5 Hz, $C{=}NC\mathit{H}_2$), 3.74 (t, 2H, J = 6.0 Hz, $NC\mathit{H}_2$), 7.25-7.46 (m, 10H, aromatic); ms: m/z 308 ($M^+$).

*Anal.* Calcd. For $C_{18}H_{16}N_2OS$: C, 70.10; H, 5.23; N, 9.08. Found: C, 70.01; H, 5.16; N, 9.14.

### Reaction of 1 with 5.

The dimer **4** of **5** was prepared according to the method described in the literature [10-11]. Typical procedure for the reaction was as follows: The reaction of **1** (80 mg, 0.307 mmol) with **4** (209 mg, 0.768 mmol) in DMSO (20 mL) was carried out at 80 °C for 30 hours, and then water was added to the reaction mixture. The mixture was extracted with $CH_2Cl_2$ (50 mL x 2). The extract was washed with water, dried ($Na_2SO_4$) and evaporated under reduced pressure. The residue was chromatographed on a preparative TLC ($CH_2Cl_2$:$CH_3COOEt$ = 4:1) to give **6** and **7**, respectively.

### 2-Methyl-3-(2-pyridyl)-6,7-dihydro-5*H*2a-thia(2a-$S^{IV}$)-2,3,4a,7a-tetraazacyclopent[*cd*]indene-1,4(2*H*,3*H*)-dithione (**6**).

This compound was isolated (23 mg, 23%) as colourless crystals, mp 155-157 °C(decomp); ir (potasssium bromide): 3400, 1560, 1470, 1430, 1300, 1240, 1180, 1140, 1100, 1060, 950, 780, and 740 $cm^{-1}$; $^1H$ nmr (deuteriochloroform): δ 2.41 (m, 2H, $NCH_2C\mathit{H}_2CH_2N$), 3.32 (s, 3H, $NC\mathit{H}_3$), 4.41 (t, 2H, J = 5.4 Hz, $NC\mathit{H}_2CH_2CH_2N$), 4.54 (t, 2H, J= 5.4 Hz, $NCH_2CH_2C\mathit{H}_2N$), 7.18 (t, 1H, J = 6.8 Hz, N=CHC*H*=CH), 7.78 (1H, J = 8.1 Hz, N=CH-CH=C*H*), 8.22 (d, 1H, J=8.1 Hz, N-CN=C*H*), 8.53 (d, 1H, J= 5.4 Hz, N=C*H*-CH=CH); ms: m/z 250 ($M^+$ - $CH_3NCS$).

*Anal.* Calcd. For $C_{18}H_{13}N_5S_3$: C, 44.55; H, 4.02; N, 21.65. Found: C, 44.34; H, 3.82; N, 21.78.

### 6,7-Dihydro-2-(2-pyridyl)-5*H*-1,2,4-thiadiazolo[4,5-*a*]pyrimidine-3(2*H*)-thione (**7**).

This compound was isolated (38.4 mg, 50 %) as colourless crystals, mp 147-148 °C; ir (potasssium bromide): 2950, 2850, 1630, 1520, 1470, 1460, 1370, 1340, 1150, and 780 $cm^{-1}$; $^1H$ nmr (deuteriochloroform): δ 1.97 (m, 2H, $NCH_2C\mathit{H}_2CH_2N$), 3.62 (t, 2H, J =5.4 Hz, $NC\mathit{H}_2CH_2CH_2N$), 4.15 (t, 2H, J = 5.4 Hz, $NCH_2CH_2C\mathit{H}_2N$), 7.03 (t, 1H, J= 6.8 Hz, N=CH-C*H*), 7.23 (d, 1H, J = 8.1 Hz, N-CN=C*H*), 7.71 (t, 1H, J=8.1 Hz, N=CH-C*H*=CH), 8.33 (d, 1H, J=5.4Hz, N=C*H*-CH=CH); ms: m/z 250 ($M^+$).

*Anal.* Calcd. For $C_{10}H_{10}N_4S_2$: C, 47.95; H, 3.80; N, 22.36. Found: C, 47.81; H, 3.81; N, 22.46.

### 4-Ethoxy-5-oxa-6-thia-1,3,8-triazabicyclo[5.4.0]undec-3,7-diene-2-thione (**10**).

This compound was isolated (yield from **8a**; 77% (57mg), yield from **8b**; 67% (49 mg)) as a white solid. A mixture of **8a** or **8b** (0.3 mmol) and **9** (0.45 mmol) in chloroform (30 ml) was refluxed for 3 hours. After the solvent was removed, the residue was chromatographed on a preparative TLC ($CH_2Cl_2$) to give **10**. Recrystallization from hexane-chloroform gave a pure sample as a colorless solid, mp 138-141 °C; ir (potasssium bromide): 2980, 2920, 2860, 1640, 1630, 1540, 1365, 1300, 1265, 1195, 1065, 960, and 795 $cm^{-1}$; $^1H$ nmr (deuteriochloroform): δ 1.36 (t, 3H, J=7.0 Hz, $OCH_2C\mathit{H}_3$), 1.93 (m, 2H, $NCH_2C\mathit{H}_2CH_2N$), 3.63 (t, 2H, J=6.0 Hz, $C{=}NC\mathit{H}_2$), 4.06 (t, 2H, J = 6.0 Hz, $NC\mathit{H}_2$), 4.28 (q, 2H, J= 7.0 Hz, $OC\mathit{H}_2CH_3$); $^{13}C$ nmr (deuteriochloroform): δ 14.36, 19.07, 47.31, 47.56, 63.04, 152.22, 163.75, and 171.78; ms: m/z 245 ($M^+$).

*Anal.* Calcd. For $C_{18}H_{11}N_3O_2S_2$: C, 39.17; H, 4.52; N, 17.13. Found: C, 39.33; H, 4.54; N, 17.18.

### 6,7-Dihydro-5*H*1,2,4-dithiazolo[4,5-*a*]pyrimidine-3(2*H*)-thione (**12**).

This compound was isolated (yield from **8a**; 32% (15 mg), yield from **8b**; 25% (12 mg)) as yellow crystals. Carbon disulfide (20.0 mmol) was added to a solution of **8a** or **8b** (0.25 mmol) in chloroform (30 mL), and the mixture was stirred at room temperature for 18 hours. After the solvent was evaporated, the residue was chromatographed on preparative TLC ($CH_2Cl_2$) to give **12** as yellow crystals; mp 155-157 °C (lit.[13] 154-156 °C); $^1H$ nmr (deuteriochloroform): δ 1.90 (m, 2H, $NCH_2C\mathit{H}_2CH_2N$), 3.55 (t, 2H, J=6.0 Hz, $C{=}NC\mathit{H}_2$), and 4.05 (t, 2H, J = 6.0 Hz, $NC\mathit{H}_2$).

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