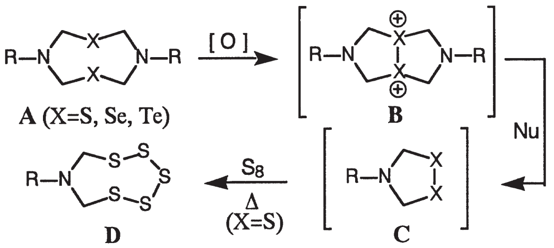
Novel Synthesis and Thermal Ring Fission of 7-Aryl-1,2,3,4,5,7-pentathiazocanes

Kazuaki Shimada, Takamasa Yoshida, Kenshiro Makino, Tatsuya Otsuka, Yuki Onuma, Shigenobu Aoyagi, Yuji Takikawa,*
and Chizuko Kabuto†
Department of Chemical Engineering, Faculty of Engineering, Iwate University, Morioka, Iwate 020-8551
†*Instrumental Analysis Center for Chemistry, Graduate School of Science, Tohoku University, Sendai, Miyagi 980-8578*

(Received October 11, 2001; CL-010997)

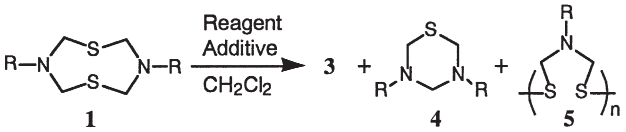
Treatment of 1,5,3,7-dithiadiazocanes **1** with bromine-elemental sulfur or disulfur dichloride (S_2Cl_2) afforded 1,2,3,4,5,7-pentathiazocanes **3**, and heating of **3** caused unusual thermal ring fission to give an inseparable mixture of polysulfide chains bearing a thioformamide moiety on each terminal.

Syntheses of macrocyclic polysulfides are of great interest in the light of their structures, reactivities, and synthetic applications. However, in spite of the potentiality concerning the practical uses for antibacterial drugs, natural flavors, or as industrial vulcanizing agents, only limited studies on medium-sized cyclic polysulfides have been achieved due to their difficulty for preparation and their lability toward various reagents.[1] During our studies on cyclic polychalcogenoacetals, we reported an oxidative ring contraction of 1,5,3,7-dichalcogenadiazocanes **A** (X = Se, Te) to give 1,2,4-dichalcogenazolanes **C** (X = Se, Te) *via* dications **B**,[2] and it was naturally expected that a similar oxidation of sulfur analogues **A** (X = S) would afford macrocyclic polysulfides *via* strained 1,2,4-dithiazolanes **C** (X = S).[3] Along with such assumption, we attempted oxidation of **A** (X = S), and in this paper we would like to describe a novel synthesis of 1,2,3,4,5,7-pentathiazocanes **3**. An unusual thermal ring fission of **D** is also reported in this paper.



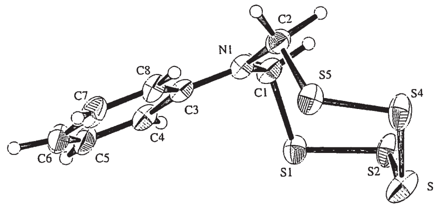
1,5,3,7-Dithiadiazocanes **1a**-**d** were prepared according to the reported methods.[2,4,5] Subsequently, treatment of a CH_2Cl_2 solution of **1** with Br_2 (1.1 mol amt.) at −78 °C afforded trace amounts of 1,3,5-thiadiazixanes **4**[6] and insoluble products **5** along with unexpected 1,2,3,4,5,7-pentathiazocanes **3** in low yields. Yields of **3** were dramatically improved by treating **1** with Br_2–S_8 or S_2Cl_2. However, the optimized amount of S_2Cl_2 for the reactions was 1.5 mol amt. for **1**, and the use of more than 2.0 molar amount of S_2Cl_2 mainly afforded **5**. In all cases, 1,2,4-dithiazolanes **2** were not found in the crude products.[2f,2g] Independent treatment of **1a** with $BF_3{\cdot}OEt_2$ (0.2 mol amt.) in CH_3CN also afforded the same ring contraction product **4a**(22%) along with 5-phenyl-1,3,5-dithiazixane (35%). These results indicated that **4** were given through acid-induced ring fission and recombination of **1**. All results of synthesis of **3** through oxidation of **1** are summarized in Table 1. Structural determination of **3a** was achieved by X-ray analysis, and the ORTEP drawing of **3a** is shown in Figure . The X-Ray data exhibited that **3a** possessed a crown-type polysulfide ring system,[5,7] and the conformational feature of **3a** showed a similarity to those of the reported eight-membered cyclic polysulfides, such as **1c**, S_8, S_8O, and heptathiaphosphocanes.

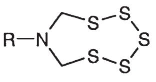
Table 1. Synthesis of 1,2,3,4,5,7-Pentathiazocanes **3**



Substrate		Reagent	Additive	Temp	Time	Yield
R	1	(mol amt.)	(mol amt.)	/°C	/min	**3** /%
C_6H_5	**1a**	Br_2 (1.1)	S_8 (0.38)	-78	60	54 (**3a**)[a]
C_6H_5	**1a**	S_2Cl_2 (1.5)	-	-78	60	72 (**3a**)
p-ClC_6H_4	**1b**	S_2Cl_2 (1.1)	-	-78	60	47 (**3b**)[b]
p-$CH_3OC_6H_4$	**1c**	S_2Cl_2 (1.5)	-	-78	90	30 (**3c**)[c]
p-$CH_3C_6H_4$	**1d**	Br_2 (1.1)	S_8 (0.38)	-78	10	30 (**3d**)[c]
p-$CH_3C_6H_4$	**1d**	S_2Cl_2 (1.0)	-	-78	5	18 (**3d**)[c]

[a]1,3,5-Thiadiazixane **4a** was obtained in 18% yield. [b]1,3,5-Thiadiazixane **4b** was obtained in 51% yield. [c]Insoluble polymeric byproduct **5** was mainly obtained.





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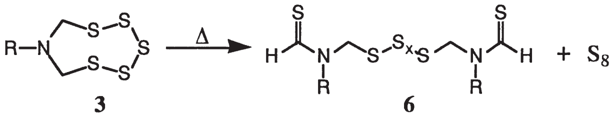
The ^1H NMR monitoring of the reaction of **1a** with S_2Cl_2 (1.5 mol amt.) in an NMR tube at −50 °C in CD_2Cl_2 showed two pairs of AB-type doublets ($\delta = 5.11$ and 5.16 ppm, and $\delta = 5.79$ and 5.82 ppm) and a sole sharp singlet ($\delta = 5.68$ ppm), and the former signals gradually disappeared along with the raising up of the temperature. In contrast, the latter remained unchanged even when the measuring temperature was raised up till 25 °C. The ^{13}C NMR monitoring also showed the similar results. The three methylene signals ($\delta = 63.9$, 71.5, and 68.5 ppm) were initially observed and only the last signal remained unchanged at a higher temperature. The significant downfield shifts of the methylene signals of the NMR spectra of the reaction mixture from those of starting **1a** suggested that the initially-formed species was a cyclic sulfonium ion and the thermally-stable secondary species was assumed to be a symmetrical dithia dication **B** (X = S). It was noteworthy that the signals of **3a** or **4a** were not observed at all throughout the NMR monitoring. These results suggested that **3** were given from **1** through a plausible route involving oxidative transannular S-S bond formation to form **B** (X = S) and the subsequent removal of the half part of **B** by the attack of some nucleophiles during the usual workup process. Especially, **3** should be formed mainly as the less-strained eight-membered cyclic polysulfides through thermal equilibration of the reaction mixture involving elemental sulfur.

Compounds **3** were unreactive toward aerobic exposure and oxidizing agents (*m*CPBA, aq. H_2O_2 solution, or CH_3CO_3H). In contrast, treatment of **3** with nucleophiles (propylamine, NaCN, or PPh_3) or reducing agents ($NaBH_4$ or $LiAlH_4$) gave a complex mixture, and treating a CH_2Cl_2 solution of **3** with HCl (gas, excess) or $BF_3 \cdot OEt_2$ (1.0 mol amt.) afforded insoluble solids. Treatment of **3a** with S_2Cl_2 (1.0 mol amt.) from $-78\,^\circ C$ to R.T. also gave polymeric product **5a** and elemental sulfur.

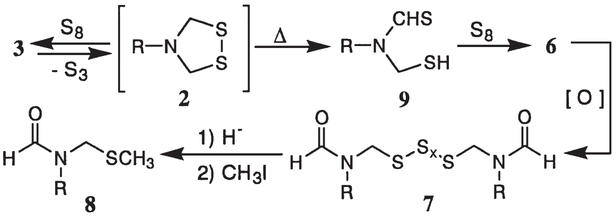
Heating of a benzene solution of **3** at refluxing temperature in the presence or absence of Et_3N (excess) gave the recovery of **3**. However, **3** was converted into inseparable mixtures of polysulfides **6** (x = 1, 2, and 3) by heating in toluene at refluxing temperature. The mass spectra of **6** revealed the parent ion peaks of each components, and the ^1H NMR spectra of **6** showed several signals of the thioformyl protons and the methylene protons at $\delta = 9.50$–9.60 and $\delta = 5.20$–5.50 ppm, respectively. The ^{13}C NMR spectra of **6** also exhibited the corresponding signals of the thioformyl carbons and the methylene carbons at $\delta = 189$–190 and $\delta = 58$–60 ppm, respectively. From the MS data and the elemental analysis data of **6**, the average values of x for **6** were approximately estimated to be 1.5 in all cases. Especially, trisulfide **6a** (x = 1, 8%) was obtained after chromatographic separation. In addition, the mixture of **6a** (x = 1.5 approximately) was converted into a mixture of bisformamides **7a** (x = 0 and 1, about 1 : 1) by aerobic exposure for 2 weeks, and the $LiAlH_4$ reduction of the mixture of **7a** in THF followed by treating CH_3I afforded **8a** in 61% yield. Results of the thermal reactions of **3** are given in Table 2.

Table 2. Thermal Reaction of 1,2,3,4,5,7-Pentathiazocanes **3**



Substrate		Solvent	Temp	Time	Yield /%	
R	3		/ °C	/ h	6	S_8
C_6H_5	**3a**	Benzene	Reflux	24	0 (**6a**)[a]	-
C_6H_5	**3a**	Toluene	Reflux	7	89 (**6a**)[b]	+
p-$CH_3OC_6H_4$	**3c**	Toluene	Reflux	7	93 (**6c**)[b]	+

[a]Compound **3a** was recovered in 98% yield. [b]Estimation of the yields was based on the average value of x to be 1.5 for **6a** and **6c**.



Scheme 1.

The ^1H NMR monitoring of the thermal reaction of **3a** in C_6D_6 at $108\,^\circ C$ in an NMR tube showed the signals assigned to thiol **9a** ($\delta = 3.28$ ppm (1H, t, $J = 8.9$ Hz) and $\delta = 4.71$ ppm (2H, d, $J = 8.9$ Hz) for N-CH_2-SH, and $\delta = 9.10$ ppm (1H, s) for N-CHS) among the signals of **6** and unidentified complex signals along with gradual decreasing of **3a**. This result indicated that thermal ring fission of **3** afforded thiols **9** and the reaction of **9** with elemental sulfur would give polysulfides **6**. It was suggested that **9** were given by thermal ring fission from **3** directly or, more probably, from **2** which might be generated through thermal sulfur extrusion of **3**. However, all attempts for isolation or trapping of **2** or thiol **9a** using phenylacetylene, DMAD, or CH_3I were not successful.

In conclusion, we found a synthesis and thermal ring fission of 1,2,3,4,5,7-pentathiazocanes **3**. Further mechanistic inspection for the formation of **3** from **1** are under way in our laboratory.

This work was partially supported by Grant-in-Aid for Scientific Research (No. 12650843) from the Ministry of Education, Science, Sports, and Culture.

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7 The X-ray crystallographic data of **3a** ($R = C_6H_5$): $C_8H_9NS_5$, $M_w = 279.47$, Colorless Prism, Monoclinic, $P2_1/c$(No. 14), $a = 13.533(3)$, $b = 4.7633(9)$, $c = 19.485(3)$ Å, $\beta = 110.15(1)\,^\circ$, $V = 1179.1(4)$ Å^3, $Z = 4$, $D_{calc} = 1.574$ g/cm^3, $\mu(CuK_\alpha) = 87.29\,cm^{-1}$, $R = 0.065$, $R_w = 0.067$.

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