Ring-Opening Reaction in Acidic Conditions of Tetraazapentalene Derivatives Containing a Hypervalent Sulfur

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The 10-S-3 type tetraazapentalene derivatives in acidic conditions were converted to the ring-opeining products, 1,3-disubstituted perhydropyrimidin-2-ones, in high yields with the release of a hypervalent sulfur.

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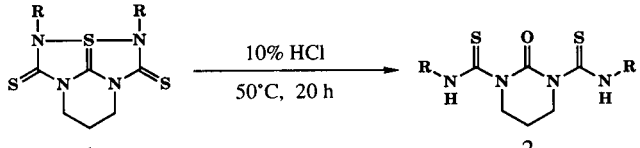
The chemistry of 1,6,6a-trithia(6a-S^{IV}) pentalenes and their analogs has attracted much attention because of their unusual electronic structure and chemical behavior [1a,b]. Recently we have synthesized successfully the 10-S-3 type tetraazapentalene derivatives, 2,3-disubstituted 6,7-dihydro-5*H*-2a-thia(2a-S^{IV})-2,3,4a,7a-tetraazacyclopent[*cd*]indene-1,4(2*H*,3*H*)-dithiones (**1**), and reported unique reactions which depended on the nature of the hypervalent sulfur [2a-h]. In order to get further information about the reactivity of **1**, we examined to investigate the reaction of **1** in acidic conditions. A few examples of the reactions of 1,6-dioxa-6a-thia- and 1,6,6a-trithiapentalenes in an acidic medium have been reported previously: 2,5-dimethyl-1,6-dioxa-6a-thia(6a-S^{IV})pentalene [3] was converted into 3-acetonyl-5-methyl-1,2-oxathiolium cation in trifluoroacetic acid containing 5% (v/v) perchloric acid, and 2-methyl-5-phenyl-1,6,6a-trithia(6a-S^{IV})pentalene [4] into (5-phenyl-1,2-dithiol-3-ylidene)acetone by heating in 96% sulfuric acid. In these reactions, the hypervalent sulfur was not removed from the molecule. We now report our recent findings that 10-S-3 type tetraazapentalene derivatives **1a-c** and **3a-c** undergo ring-opening reaction in 10% hydrochloric acid to give 1,3-disubstituted perhydropyrimidin-2-ones **2a-c** and **4a-c** with the release of the hypervalent sulfur.

A typical procedure for the ring-opening reaction of **1** in acidic conditions is as follows: The compound **1a** was stirred in 10% hydrochloric acid at 50° for 20 hours. After cooling to room temperature, the reaction mixture was poured into water. The solution was extracted several times with chloroform. The chloroform layer was then washed with water, dried over anhydrous sodium sulfate, and condensed under reduced pressure. The residue was chromatographed on a preparative TLC to give 1,3-bis(methylthiocarbamoyl)perhydropyrimidin-2-one (**2a**) in 71% yield.

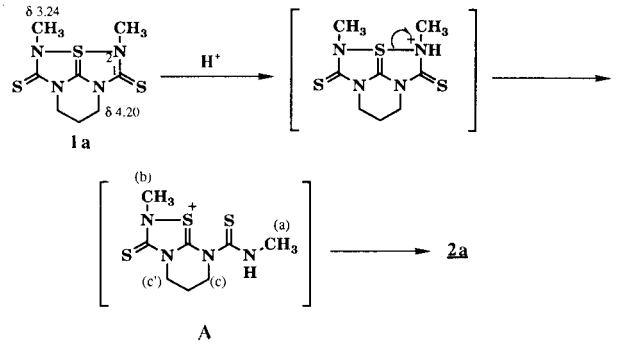


1 2

a: R = CH_3
b: R = CH_2=$CHCH_2$
c: R = CH_3CH_2

The results of the reactions of **1a-c** in 10% hydrochloric acid are summarized in Table 1. The reactions proceeded smoothly to give the corresponding ring-opening products **2a-c** with the release of the hypervalent sulfur in good yields. Although the reactions were carried out in 10% aqueous sodium hydroxide at 60°, the products **2a-c** were scarcely obtained. In order to obtain a detailed knowledge on the behavior of **1** in acidic conditions, we measured in ^{1}H nmr spectrum of **1a** in deuteriochloroform solution containing five equivalents of trifluoroacetic acid. Consequently, the signals at δ 2.52 (m, 2H), 3.20 (d, 3H, J = 4.3 Hz), 3.50 (s, 3H), 4.41 (t, 2H, J = 5.8 Hz), 4.48 (t, 2H, J = 5.8 Hz), and 9.13 (br, 1H) were observed. In contrast with the ^{1}H nmr spectrum of **1a** in deuteriochloroform [5], two signals due to the methyl groups appeared at 3.20 and 3.50 ppm. The signal at 3.20 ppm (a) is doublet and the chemical shift is almost similar to that of the methyl group of **1a** at 3.24 ppm. On the other hand, the signal at 3.50 ppm (b) is singlet and is shifted downfield remarkably from the signal of the methyl group of **1a**. Furthermore, two close triplets (c, 4.40 and c', 4.48 ppm) assigned to methylene protons adjacent to the nitrogen atoms were observed. These spectral results indicate that the azathiolium cation derivative **A** is formed by ring opening.

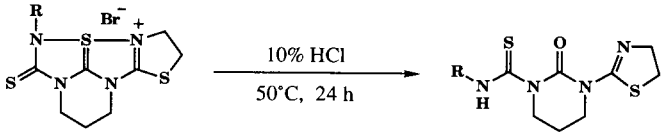
On the basis of the formation of **A**, the reaction is considered to proceed through the addition of proton on the nitrogen atom at the 2-position of **1**, followed by the cleavage of the S^{IV}-N^+H bond. In a preparative-scale experiment, we confirmed that **1a** in 10% aqueous trifluoroacetic acid (20 ml) at 50° for 1 day was converted to **2a** in 70% yield. Accordingly, the presence of water is considered to result in the hydrolytic cleavage of the C-S



bond of **A** to give the carbonyl group in hydrochloric acid.

We next investigated the reaction of the tetraazapentalene derivatives **3a-c** [6], which have the $C=S^{IV}$ and $C=N^+$ moieties in a molecule, in 10% hydrochloric acid at 50° for 24 hours. Usual workup and purification gave the ring-opening products **4a-c** in high yields (Table 1). The hydrolysis of the $C=N^+$ moiety did not occur at all. The reaction is considered to proceed by the process which is similar to the case of **1a-c**.

The yields and melting points of the products, **2a-c** and **4a-c**, are summarized in Table 1. The structure of all products was determined by the ir, ^1H nmr, ^{13}C nmr, and mass spectra, and elemental analyses.



a: R = CH_3
b: R = CH_2=$CHCH_2$
c: R = CH_3CH_2

Further studies on the reactivity of the tetraazapentalene derivatives **1** and **3** are currently under way.

Table 1

The Ring-Opening Reactions of the Tetraazapentalene Derivatives, **1a-c** and **3a-c**, under Acidic Conditions [a]

Tetraazapentalene	Time (hour)	Product	MP (°)	Yield (%) [b]
1a	20	**2a**	134-135	71
1b	20	**2b**	79.5-80.5	70
1c	20	**2c**	100-101	89
3a	24	**4a**	137-138	81
3b	24	**4b**	131-132	60
3c	24	**4c**	161.5-162.5	88

[a] The reactions were carried out in 10% hydrochloric acid at 50°. [b] Isolated yields were based on **1a-c** and **3a-c**.

EXPERIMENTAL

Melting points were determined on a Yanagimoto MP-S3 melting point apparatus and were uncorrected. The ^1H and ^{13}C nmr spectra were obtained using a JEOL JNM-GX270 spectrometer. Chemical shifts are reported in ppm from TMS as an internal standard and given δ units. The ir spectra were determined on a Hitachi 215 Grating infrared spectrometer. The mass spectra were obtained with a Shimadzu LKB-9000 spectrometer equipped with a solid injector; the ionizing voltage was 70 eV. Elemental analyses were recorded on a Yanagimoto MT-3 CHN recorder. Purification of products was conducted by preparative TLC on silica gel (Merck Kieselgel 60 GF_{254}).

Typical Procedure for the Ring-Opening Reaction of Tetraazapentalenes **1** in Acidic Conditions.

The compound **1a** (52 mg, 0.2 mmole) was stirred in 10% hydrochloric acid (20 ml) at 50° for 20 hours. After cooling to room temperature, the reaction mixture was poured into water. The solution was extracted several times with chloroform. The chloroform layer was then washed with water, dried over anhydrous sodium sulfate, and condensed under reduced pressure. The residue was chromatographed on a preparative tlc (silica gel, dichloromethane:tetrachloromethane = 2:1, v/v, as an eluent) to give 35 mg (71% yield) of **2a**. Recrystallization from hexane gave an analytically pure compound.

1,3-Bis(methylthiocarbamoyl)perhydropyrimidin-2-one (**2a**).

This compound was obtained by the ring-opening reaction of **1a** in 10% hydrochloric acid in 71% yield as a colorless solid, mp 134-135°; ir (potassium bromide): 3240, 2920, 1635, 1550, 1465, 1430, 1390, 1375, 1300, 1275, 1195, 1150, 1030, 950, 885, 845, 745, 700 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.09 (m, 2H, $NCH_2CH_2CH_2N$), 3.20 (d, 6H, J = 4.9 Hz, 2 x CH_3NH), 4.35 (t, 4H, J = 6.1 Hz, $NCH_2CH_2CH_2N$), 10.67 (br, 2H, 2 x NH); ^{13}C nmr (deuteriochloroform): δ 22.69, 33.71, 49.11, 157.49, 184.65; ms: m/z 246 (M^+).

Anal. Calcd. for $C_8H_{14}N_4OS_2$: C, 39.00; H, 5.73; N, 22.74%. Found: C, 38.92; H, 5.84; N, 23.01%.

1,3-Bis(allylthiocarbamoyl)perhydropyrimidin-2-one (**2b**).

This compound was obtained by the ring-opening reaction of **1b** in 10% hydrochloric acid in 70% yield as a colorless solid, mp 79.5-80.5°; ir (potassium bromide): 3240, 1635, 1530, 1465, 1405, 1380, 1315, 1280, 1190, 1160, 1140, 1090, 1055, 985, 945, 885, 850, 735 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.09 (m, 2H, $NCH_2CH_2CH_2N$), 4.33 (m, 8H, $NCH_2CH_2CH_2N$ and 2 x $CH_2=CHCH_2NH$), 5.28 (m, 4H, 2 x $CH_2=CHCH_2NH$), 5.97 (m, 2H, 2 x $CH_2=CHCH_2NH$), 10.71 (br, 2H, 2 x NH); ^{13}C nmr (deuteriochloroform): δ 22.75, 49.09, 49.60, 117.82, 132.12, 157.46, 183.64; ms: m/z 298 (M^+).

Anal. Calcd. for $C_{12}H_{18}N_4OS_2$: C, 48.30; H, 6.08; N, 18.77%. Found: C, 48.52; H, 6.13; N, 18.86%.

1,3-Bis(ethylthiocarbamoyl)perhydropyrimidin-2-one (**2c**).

This compound was obtained by the ring-opening reaction of **1c** in 10% hydrochloric acid in 89% yield as a colorless solid, mp 100-101°; ir (potassium bromide): 3230, 2960, 2925, 2850, 1635, 1535, 1470, 1410, 1385, 1355, 1320, 1280, 1245, 1065, 1025, 965, 910, 885, 830, 805, 750, 725, 660 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.31 (t, 6H, J = 7.3 Hz, 2 x CH_3CH_2NH), 2.07 (m, 2H, $NCH_2CH_2CH_2N$), 3.70 (d of q, 4H, J = 4.9 and 7.3 Hz, 2 x CH_3CH_2NH), 4.33 (t, 4H, J = 6.1 Hz, $NCH_2CH_2CH_2N$), 10.58 (br, 2H, 2 x NH); ^{13}C nmr (deuteriochloroform): δ 13.31, 22.73, 42.10, 48.83, 157.44, 183.30; ms: m/z 274 (M^+).

Anal. Calcd. for $C_{10}H_{18}N_4OS_2$: C, 43.77; H, 6.61; N, 20.42%. Found: C, 43.70; H, 6.72; N, 20.35%.

Typical Procedure for the Ring-Opening Reaction of Tetraazapentalenes **3** in Acidic Conditons.

The compound **3a** (71 mg, 0.2 mmole) was stirred in 10% hydrochloric acid (20 ml) at 50° for 24 hours. After cooling to room temperature, the reaction mixture was neutralized by aqueous potassium carbonate. The solution was extracted several times with chloroform. The chloroform layer was then washed with water, dried over anhydrous sodium sulfate, and condensed under reduced pressure. The residue was chromatographed on a preparative tlc (silica gel, dichloromethane as an eluent) to give 42 mg (81% yield) of **4a**. Recrystallization from hexane gave an analytically pure compound.

1-Methylthiocarbamoyl-3-(2-thiazolinyl)perhydropyrimidin-2-one (**4a**).

This compound was obtained by the ring-opening reaction of **3a** in 10% hydrochloric acid in 81% yield as a colorless solid, mp 137-138°; ir (potassium bromide): 3225, 2925, 1650, 1600, 1540, 1470, 1410, 1300, 1170, 1075, 1055, 1030, 750 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.09 (m, 2H, $NCH_2CH_2CH_2N$), 3.18 (d, 3H, J = 4.4 Hz, CH_3NH), 3.24 (t, 2H, J = 8.3 Hz, SCH_2CH_2N), 3.94 (t, 2H, J = 6.2 Hz, $NCH_2CH_2CH_2N$), 4.04 (t, 2H, J = 8.3 Hz, SCH_2CH_2N), 4.46 (t, 2H, J = 6.2 Hz, $NCH_2CH_2CH_2N$), 11.03 (br, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 22.02, 33.63, 34.15, 47.60, 47.66, 57.85, 155.26, 159.77, 184.45; ms: m/z 258 (M^+).

Anal. Calcd. for $C_9H_{14}N_4OS_2$: C, 41.84; H, 5.46; N, 21.68%. Found: C, 41.66; H, 5.54; N, 21.66%.

1-Allylthiocarbamoyl-3-(2-thiazolinyl)perhydropyrimidin-2-one (**4b**).

This compound was obtained by the ring-opening reaction of **3b** in 10% hydrochloric acid in 60% yield as a colorless solid, mp 131-132°; ir (potassium bromide): 3225, 1660, 1600, 1530, 1480, 1420, 1320, 1250, 1180, 1100, 1050, 1000, 950, 750 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.08 (m, 2H, $NCH_2CH_2CH_2N$), 3.24 (t, 2H, J = 8.3 Hz, SCH_2CH_2N), 3.94 (t, 2H, J = 6.2 Hz, $NCH_2CH_2CH_2N$), 4.04 (t, 2H, J = 8.3 Hz, SCH_2CH_2N), 4.32 (m, 2H, $CH_2=CHCH_2NH$), 4.46 (t, 2H, J = 6.1 Hz, $NCH_2CH_2CH_2N$), 5.26 (m, 2H, $CH_2=CHCH_2NH$), 5.95 (m, 1H, $CH_2=CHCH_2NH$), 11.14 (br, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 22.03, 34.15, 47.62, 49.50, 57.87, 77.27, 117.58, 132.28, 155.24, 159.83 and 183.52; ms: m/z 284 (M^+).

Anal. Calcd. for $C_{11}H_{16}N_4OS_2$: C, 46.46; H, 5.67; N, 19.70%. Found: C, 46.18; H, 5.69; N, 19.58%.

1-Ethylthiocarbamoyl-3-(2-thiazolinyl)perhydropyrimidin-2-one (**4c**).

This compound was obtained by the ring-opening reaction of **3c** in 10% hydrochloric acid in 88% yield as a colorless solid, mp 161.5-162.5°; ir (potassium bromide): 3210, 2925, 1655, 1595, 1530, 1470, 1410, 1380, 1320, 1290, 1250, 1205, 1170, 1070, 1000, 970, 740 cm^{-1}; ^{1} nmr (deuteriochloroform): δ 1.29 (t, 3H, J = 7.3 Hz, CH_3CH_2NH), 2.09 (m, 2H, $NCH_2CH_2CH_2N$), 3.24 (t, 2H, J = 8.2 Hz, SCH_2CH_2N), 3.69 (d of q, 2H, J = 5.2 and 7.2 Hz, CH_3CH_2NH), 3.93 (t, 2H, J = 6.4 Hz, $NCH_2CH_2CH_2N$), 4.04 (t, 2H, J = 8.2 Hz, SCH_2CH_2N), 4.45 (t, 2H, J = 6.0 Hz, $NCH_2CH_2CH_2N$), 11.00 (br, 1H, NH); ^{13}C nmr (deuteriochloroform): δ 13.25, 22.03, 34.15, 42.04, 47.35, 47.66, 57.87, 155.26, 159.81, 183.10; ms: m/z 272 (M^+).

Anal. Calcd. for $C_{10}H_{16}N_4OS_2$: C, 44.09; H, 5.92; N, 20.57%. Found: C, 44.02; H, 6.05; N, 20.86%.

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