

# Preparation of [2<sup>3</sup>]Cyclophane-1,2-diones by the Reaction of 3,6;12,15-Di-1,4-benzo[6.6](3,4)-1,2,5-thiadiazolocyclophanes with Grignard Reagents

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3,6;12,15-Di-1,4-benzo[6.6](3,4)-1,2,5-thiadiazolocyclophanes **1a-c** were prepared starting from 3,4-di-*p*-tolyl-1,2,5-thiadiazole **3** and converted into [2<sup>3</sup>]cyclophane-1,2-diones **2a-c** by the reaction with Grignard reagents.

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Since heterocycles are well recognized as a synthon of functional group(s), the conversion of a heterocyclic ring in a cyclophane into the corresponding functional group(s) may provide a useful method for a cyclophane bearing functional group(s) in its bridge. The representative of the reported examples [1] is a furan nuclei which gives a 1,4-dicarbonyl moiety in the bridge.

In the present paper, we report the preparation of cyclophanes **1a-c** containing 1,2,5-thiadiazole ring and the reaction with Grignard reagents [2], giving [2<sup>3</sup>]cyclophane-1,2-diones **2a-c** which are the first cyclophanes with 1,2-dicarbonyl moiety in their bridge.

## Results and Discussion.

Cyclophanes **1a-c** were prepared according to Scheme 1.

Bromination of 3,4-di-*p*-tolyl-1,2,5-thiadiazole **3** [3] with *N*-bromosuccinimide was carried out and the results are summarized in Table 1. The desired 3,4-di(*p*-bromomethylphenyl)-1,2,5-thiadiazole **4** was obtained in 70% yield, accompanied by mono-**10** and tribromide **11**, when V-65 [4] was used as an initiator in refluxing methylenechloride. Compound **4** was converted into the corresponding dithiol **5** in 96% yield.

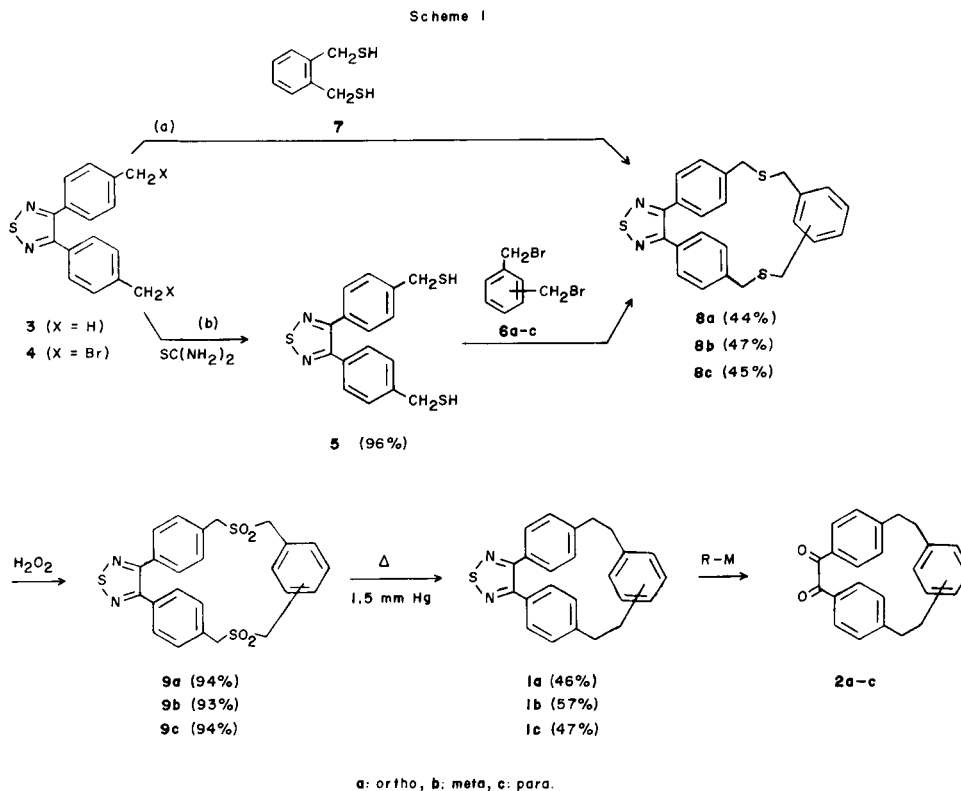
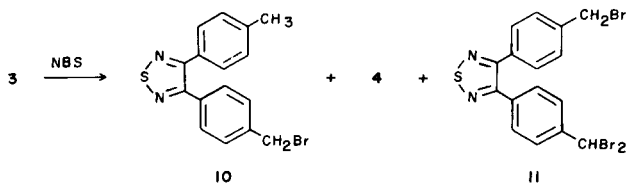


Table 1  
Bromination of **3**.

NBS/3 [a]	Initiator	Solvent	Time (hours)	Products, Isolated yield (%) [b]		
				<b>10</b>	<b>4</b>	<b>11</b>
2.2	BPO[c]	carbontetrachloride	2.5	+	29	11
2.2	AIBN [c]	carbontetrachloride	2.0	+	29	9
2.1	V-65 [4] [d]	methylenechloride	30	6	70	+

[a] Molar ratio. [b] Plus sign means less than 1%. [c] Molar ratio of initiator/NBS = 0.05. [d] Molar ratio of initiator/NBS = 0.01.



Dithiacyclophane **8a** was prepared by two ways; a) by the reaction of **4** with  $\alpha,\omega$ -dimercapto-*o*-xylene **7** and b) by the one of **5** with  $\alpha,\omega$ -dibromo-*o*-xylene **6a**. Both reactions gave the expected **8a** in 48 and 44% yields, respectively. Because of its unpleasant odour of dithiol **7**, **8b** and **8c** were prepared *via* route (b) in 47 and 45% yields, respectively.

Pyrolysis of **9a-c** under reduced pressure afforded the desired 3,6;12,15-di-1,4-benzo[6.6](3,4)-1,2,5-thiadiazolocyclophanes **1a-c** in the yields shown in Scheme 1.

Reaction of **1a-c** with Grignard reagents was investigated and the results are summarized in Table 2. Though the reaction of phenylmagnesium bromide with **1a** afforded the expected **2a** in only 6% yield, **2b** and **2c** were obtained in 52 and 54% yields, respectively, in the reaction with **1b** and **1c**. Methylmagnesium iodide gave a poor yield and butyl lithium gave only tarry materials. As a partial decomposition of **2a-c** was observed during recrystallization from hexane, forming resinous materials, purification of **2a-c** was carried out with de-oxygenated hexane to give pale yellow crystals.

Table 2  
Preparation of **2** [a]

1	R-M	Time (hours)	Yield (%) of <b>2</b>
<b>a</b>	PhMgBr	12	6
<b>b</b>	PhMgBr	4.5	52
<b>b</b>	PhMgBr	12	13
<b>b</b>	BuLi[b]	3.5	—
<b>c</b>	PhMgBr	12	54
<b>c</b>	CH <sub>3</sub> MgI	6	13

[a] Reactions were carried out at room temperature unless otherwise stated. [b] At  $-70 \sim 10^\circ$ .

Finally, although [2<sup>3</sup>](1,4)cyclophane is reported to form an abnormally tight 1:1-complex with silver triflate [5,6] at room temperature to dissolve silver triflate in chloroform, silver triflate did not dissolve into chloroform solution of [2<sup>3</sup>](1,4)cyclophane-1,2-dione **2c**. This means that the  $\pi$ -electron density of benzene rings of **2c** is lowered by two carbonyl groups and **2c** is unable to form complex with silver triflate under the above conditions.

## EXPERIMENTAL

All melting points are uncorrected. The ir spectra were measured on a Nippon Bunko A-102 spectrophotometer as potassium bromide pellets. The <sup>1</sup>H-nmr spectra were determined in deuteriochloroform unless otherwise stated at 100 MHz on a Nippon Denshi JEOL FT-100 using TMS as an internal standard. Mass spectra were obtained on a Nippon Denshi JMS-01SG-2 mass spectrometer at 75 eV using a direct inlet system. Column chromatography was carried out on silica gel (Wako gel C-300).

### Bromination of **3**.

After a mixture of **3** (15.0 g), *N*-bromosuccinimide (21.1 g) and V-65 [4] (0.30 g) in dry methylene chloride (300 ml) was heated at reflux for 30 hours, it was evaporated *in vacuo* to leave the residue which was extracted with hot carbon tetrachloride (200 ml). The extract was condensed and chromatographed using a 7:3-mixture of hexane and benzene. At first, monobromide **10**, then tribromide **11** and finally dibromide **4** (16.7 g) was eluted.

### 3,4-Di(*p*-bromomethylphenyl)-1,2,5-thiadiazole (**4**).

This compound was obtained as colorless prisms (cyclohexane), mp 121-122 $^\circ$ ; ms: *m/e* 424 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  4.46 (s, 4H), 7.32 (d, 4H, J = 8 Hz), 7.45 (d, 4H, J = 8 Hz).

Anal. Calcd. for C<sub>16</sub>H<sub>12</sub>Br<sub>2</sub>N<sub>2</sub>S: C, 45.31; H, 2.85; N, 6.60. Found: C, 45.54; H, 2.88; N, 6.78.

### 3-(*p*-Bromomethylphenyl)-4-(*p*-methylphenyl)-1,2,5-thiadiazole (**10**).

This compound was obtained as colorless needles (hexane), mp 99.5-100.5 $^\circ$ ; ms: *m/e* 345 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  2.37 (s, 3H), 4.47 (s, 2H), 7.14 (d, 2H, J = 8 Hz), 7.34 (d, 2H, J = 8 Hz), 7.37 (d, 2H, J = 8 Hz), 7.48 (d, 2H, J = 8 Hz).

Anal. Calcd. for C<sub>16</sub>H<sub>13</sub>BrN<sub>2</sub>S: C, 55.66; H, 3.80; N, 8.11. Found: C, 55.49; H, 3.82; N, 7.94.

### 3-(*p*-Bromomethylphenyl)-4-(*p*-dibromomethylphenyl)-1,2,5-thiadiazole (**11**).

This compound was obtained as colorless needles (hexane), mp 92.5-93.5 $^\circ$ ; ms: *m/e* 503 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  4.47 (s, 2H), 6.60 (s, 1H), 7.34 (d, 2H, J = 8 Hz), 7.45 (d, 2H, J = 8 Hz), 7.46 (d, 2H, J = 9 Hz), 7.55 (d, 2H, J = 9 Hz).

*Anal.* Calcd. for C<sub>16</sub>H<sub>11</sub>Br<sub>3</sub>N<sub>2</sub>S: C, 38.20; H, 2.20; N, 5.57. Found: C, 38.66; H, 2.41; N, 5.86.

#### Preparation of 5.

After a mixture of **4** (10.0 g) and thiourea (4.20 g) in dimethyl sulfoxide (100 ml) was stirred at room temperature under nitrogen atmosphere for 24 hours, it was poured into ice-cold 3% aqueous sodium hydroxide (400 ml) and the mixture was stirred at room temperature for 1.5 hours. It was made acidic with 10% hydrochloric acid, extracted with methylene chloride (300 ml), washed with water, dried over sodium sulfate and evaporated *in vacuo* to give pure **5** (7.5 g).

#### 3,4-Di(*p*-mercaptomethylphenyl)-1,2,5-thiadiazole (5).

This compound was obtained as colorless crystalline powder, mp 100-105° dec; ms: *m/e* 330 (M<sup>+</sup>).

*Anal.* Calcd. for C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>S<sub>2</sub>: C, 58.15; H, 4.27; N, 8.48. Found: C, 58.39; H, 4.44; N, 8.37.

#### Preparation of 8a-c. Typical Procedure.

A solution of **5** (5.00 g) in benzene (100 ml) and a solution of  $\alpha,\omega$ -dibromo-*o*-xylene (4.00 g) in benzene (100 ml) was added dropwise at the same rate each from a Hershberg funnel to a vigorously stirred refluxing mixture of 85% aqueous potassium hydroxide (2.70 g) and sodium borohydride (0.59 g) in degassed ethanol (4 l) for 30 hours. After the addition was completed the mixture was heated at reflux for additional 2 hours. Solvent was evaporated and the resultant residue was extracted methylene chloride (500 ml), washed with water, dried over sodium sulfate, condensed and chromatographed with benzene, affording **8a** (2.88 g).

#### 2,18-Dithia-4,7;13,16-di-1,4-benzo[7.7](3,4)-1,2,5-thiadiazolooorthocyclophane (8a).

This compound was obtained as colorless prisms (benzene), mp 194-195°; ms: *m/e* 432 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  3.32 (s, 4H), 3.64 (s, 4H), 7.07 (s, 8H), 7.16-7.34 (m, 2H), 7.48-7.66 (m, 2H).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>S<sub>2</sub>: C, 66.63; H, 4.66; N, 6.48. Found: C, 66.41; H, 4.75; N, 6.45.

#### 2,18-Dithia-4,7;13,16-di-1,4-benzo[7.7](3,4)-1,2,5-thiadiazolomethacyclophane (8b).

This compound was obtained as colorless needles (benzene), mp 249-250°; ms: *m/e* 432 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  3.32 (s, 4H), 3.62 (s, 4H), 7.24 (broad s, 12 H).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>S<sub>2</sub>: C, 66.63; H, 4.66; N, 6.48. Found: C, 66.82; H, 4.67; N, 6.50.

#### 2,18-Dithia-4,7;13,16-di-1,4-benzo[7.7](3,4)-1,2,5-thiadiazoloparacyclophane (8c).

This compound was obtained as colorless needles (ethyl acetate), mp 165-166°; ms: *m/e* 432 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  3.71 (s, 4H), 3.81 (s, 4H), 6.92 (d, 4H, J = 8 Hz), 7.08 (s, 4H), 7.12 (d, 4H, J = 8 Hz).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>S<sub>2</sub>: C, 66.63; H, 4.66; N, 6.48. Found: C, 66.62; H, 4.73; N, 6.45.

#### Oxydation of 8. Typical Procedure.

After a mixture of **8a** (1.70 g) and 30% hydrogen peroxide (5.20 ml) in glacial acetic acid (120 ml) was heated at 50-60° for 4 hours, precipitated solid was filtered and washed with ethanol and hexane, giving **9a** (1.83 g).

#### 2,18-Dithia-4,7;13,16-di-1,4-benzo[7.7](3,4)-1,2,5-thiadiazolooorthocyclophane-2,2,18,18-tetraoxide (9a).

This compound was obtained as colorless prisms, mp  $\delta$  400°; ms: *m/e* 368 (M<sup>+</sup> - 2SO<sub>2</sub>); <sup>1</sup>H-nmr (hexadeuteriodimethylsulfoxide): 4.28 (broad s, 4H), 4.68 (broad s, 4H), 7.24 (d, 4H, J = 8.5 Hz), 7.36 (d, 4H, J = 8.5 Hz), 7.40 (s, 4H).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>: C, 58.05; H, 4.06; N, 5.64. Found: C, 57.95; H, 4.34; N, 5.37.

#### 2,18-Dithia-4,7;13,16-di-1,4-benzo[7.7](3,4)-1,2,5-thiadiazolometacyclophane-2,2,18,18-tetraoxide (9b).

This compound was obtained as colorless prisms, mp 311-314° dec; ms: *m/e* 496 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  3.86 (s, 4H), 4.16 (s, 4H), 7.36 (broad s, 8H), 7.48-7.64 (m, 4H).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>: C, 58.05; H, 4.06; N, 5.64. Found: C, 57.79; H, 3.86; N, 5.30.

#### 2,18-Dithia-4,7;13,16-di-1,4-benzo[7.7](3,4)-1,2,5-thiadiazoloparacyclophane-2,2,18,18-tetraoxide (9c).

This compound was obtained as colorless prisms, mp 374-376° dec; ms: *m/e* 368 (M<sup>+</sup> - 2SO<sub>2</sub>); <sup>1</sup>H-nmr (hexadeuteriodimethylsulfoxide):  $\delta$  4.56 (s, 4H), 4.72 (s, 4H), 6.64 (s, 4H), 7.34 (s, 8H).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>O<sub>4</sub>S<sub>2</sub>: C, 58.05; H, 4.06; N, 5.64. Found: C, 57.76; H, 4.13; N, 5.40.

#### Pyrolysis of 9.

Pyrolysis of **9** was carried out under reduced pressure (1.5 mm Hg) in an apparatus described previously [7]. The sublimed product was collected and chromatographed with benzene, giving **1**. Compounds **9a** (1.00 g), **9b** (2.00 g), and **9c** (2.00 g) were pyrolyzed at 620°, 620°, and 520°, respectively, to yield **1a** (0.34 g), **1b** (0.84 g), and **1c** (0.70 g), respectively.

#### 3,6;12,15-Di-1,4-benzo[6.6](3,4)-1,2,5-thiadiazolooorthocyclophane (1a).

This compound was obtained as colorless prisms (ethanol), mp 175-177°; ms: *m/e* 368 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  2.65-3.14 (m, 8H), 6.63 (d, 4H, J = 9 Hz), 6.72 (d, 4H, J = 9 Hz), 7.12-7.28 (m, 2H), 7.36-7.52 (m, 2H).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>S: C, 78.23; H, 5.47; N, 7.60. Found: C, 78.41; H, 5.50; N, 7.68.

#### 3,6;12,15-Di-1,4-benzo[6.6](3,4)-1,2,5-thiadiazolometacyclophane (1b).

This compound was obtained as colorless prisms (hexane), mp 139-140°; ms: *m/e* 368 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  2.74-3.10 (m, 8H), 6.78 (s, 8H), 7.02-7.34 (m, 4H).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>S: C, 78.23; H, 5.47; N, 7.60. Found: C, 78.27; H, 5.50; N, 7.60.

#### 3,6;12,15-Di-1,4-benzo[6.6](3,4)-1,2,5-thiadiazoloparacyclophane (1c).

This compound was obtained as colorless prisms (hexane), mp 114-116°; ms: *m/e* 368 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  2.90-3.14 (m, 8H), 6.76 (s, 4H), 6.84 (s, 8H).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>N<sub>2</sub>S: C, 78.23; H, 5.47; N, 7.60. Found: C, 78.25; H, 5.52; N, 7.55.

#### Reaction of 1 with Phenylmagnesium Bromide. Typical Procedure.

To a stirred ether solution (5 ml) of phenylmagnesium bromide (prepared from 600 mg of bromobenzene and 93 mg of magnesium turnings) was added an ether solution (10 ml) of **1c** (200 mg) at room temperature under nitrogen stream and the mixture was stirred for 12 hours at this temperature. It was poured into ice-cold 5% hydrochloric acid (100 ml). Solid materials were collected by filtration and extracted with hot benzene (20 ml). The extract was combined with the organic layer of the filtrate, condensed and chromatographed using a 3:1-mixture of hexane and ethyl acetate to give **2c** (0.099 g).

#### [2<sup>3</sup>](1,4)(1,2)(1,4)Cyclophane-1,2-dione (2a).

This compound was obtained as pale yellow prisms (ethyl acetate), mp 230-231°; ir:  $\nu$  CO 1700 cm<sup>-1</sup>; ms: *m/e* 340 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  2.60-3.16 (m, 8H), 6.73 (d, 4H, J = 8 Hz), 6.93 (d, 4H, J = 8 Hz), 7.12-7.50 (m, 4H).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>O<sub>2</sub>: C, 84.68; H, 5.92. Found: C, 84.42; H, 6.10.

#### [2<sup>3</sup>](1,4)(1,3)(1,4)Cyclophane-1,2-dione (2b).

This compound was obtained as pale yellow needles (hexane), mp 145.5-147°; ir:  $\nu$  CO 1690 cm<sup>-1</sup>; ms: *m/e* 340 (M<sup>+</sup>); <sup>1</sup>H-nmr:  $\delta$  2.64-3.15 (m, 8H), 6.85 (d, 4H, J = 8.5 Hz), 7.13 (d, 4H, J = 8.5 Hz), 6.92-7.21 (m, 4H).

*Anal.* Calcd. for C<sub>24</sub>H<sub>20</sub>O<sub>2</sub>: C, 84.68; H, 5.92. Found: C, 84.49; H, 5.95.

[2<sup>3</sup>](1,4)Cyclophane-1,2-dione (**2c**).

This compound was obtained as pale yellow prisms (cyclohexane), mp 170-171°C; ir:  $\nu$  CO 1670, 1690  $\text{cm}^{-1}$ ; ms: m/e 340 ( $M^+$ );  $^1\text{H-nmr}$ :  $\delta$  2.82-3.15 (m, 8H), 6.68 (s, 4H), 6.89 (d, 4H,  $J = 8$  Hz), 7.13 (d, 4H,  $J = 8$  Hz).

Anal. Calcd. for  $\text{C}_{24}\text{H}_{20}\text{O}_2$ : C, 84.68; H, 5.92. Found: C, 84.85; H, 5.99.

## REFERENCE AND NOTES

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