Reduction of the 1,2,5-Thiadiazole Ring of 3,6:12,15-Di-1,4-benzo[6.6](3,4)-1,2,5-thiadiazolo- and 3,5:11,13-Di-1,3-benzo-[6.6](3,4)-1,2,5-thiadiazolocyclophanes. Selective Preparation of *cis*- and *trans*-[2³]Cyclophane-1,2-diacetoamide

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The effect of the [2.2.2]cyclophane ring structure on the reduction of 1,2,5-thiadiazole ring incorporated in cyclophanes **1a-c** and **2a-c** was investigated. When reduced by sodium metal in ethanol followed by acetylation, para[2³]cyclophane **1** gave a mixture of the expected *cis*- and *trans*-diamides, **3** and **4**, in which **4** was the major product. On the other hand, reduction of **1** with lithium aluminum hydride proceeded in a *cis*-selective manner and gave **3** as a major product after a treatment of the reduced products with acetic anhydride. The reduction of metacyclophane **2**, which is less strained than **1**, proceeded exclusively in *cis*-fashion and a subsequent treatment of the reduction product with acetic anhydride gave only *cis*-diamide **6**.

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Chemical reactivity of functional groups which are incorporated in the cyclophane-ring structure is of interest because, reflecting their unique chemical environments and ring strain of cyclophane, they are expected to show unusual chmical behaviors. In order to prepare cyclophanes having functional group(s) in their bridge, we adapted heterocycles as synthons of functional group(s) and recently, prepared three [2³]cyclophanes having a 1,2-diketonic moiety by cleaving 1,2,5-thiadiazole ring in cyclophanes **1a-c** with Grignard reagents [1,2].

As 1,2,5-thiadiazole is known to give a *vic*-diamine on reduction [3-5], formation of [2³]cyclophane-1,2-diamine is expected. As a part of our study on cyclophanes bearing functional group(s) on the bridge, we investigated the reduction of 1,2,5-thiadiazolo[2³]cyclophanes **1a-c** and **2a-c**. The results are prsented in this paper.

Results and Discussion.

Cyclophanes **1a-c** and **2a-c** were reduced with sodium in ethanol or lithium aluminum hydride in tetrahydrofuran and the reduction products were treated with acetic anhydride. The results are summarized in Table 1 and Schemes 1 and 2.

It was previously reported that treatment of 3,4-diphenyl-1,2,5-thiadiazole with sodium in 95% ethanol gave 1,2-diphenylethylenediamine and the *meso*-diastereomer was isolated from the reaction mixture [2]. Cyclophane **1a**, which seems the most strained of [2³]cyclophanes used in this study, was similarly treated and the reduction product was acetylated with acetic anhydride, giving a 1:2.4-mixture of *cis*- and *trans*-diamides **3a** and **4a** in 86% yield. The reduction of less strained [2³]cyclophane **1b** proceeded in a *trans*-selective manner and afforded a 1:8-mixture of **3b** and **4b** on acetylation. Interestingly, flexible **2a** was not reduced under the above conditions and was recovered quantitatively.

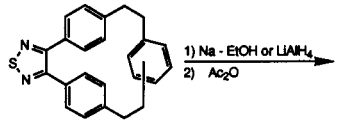
The stereochemistry of diamides **3** and **4** were determined by their ^{1}H nmr and thermal behaviors which will be mentioned later.

On the other hand, reduction of **1a-c** and **2a-c** with lithium aluminum hydride proceeded in a *cis*-selective manner.

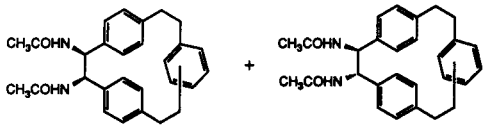
Reduction of **1a** with 6 equivalents of lithium aluminum hydride gave an unstable yellow solid. Its ir spectra showed peaks ascribable to an amino group at 3360 and 3300 cm^{-1} and the mass spectrum showed the expected parent peak of the expected diamine. When this solid was treated with acetic anhydride, the initial yellow color of the mixture immediately changed to wine-red. The color faded away with a precipitation of white solids and the usual work-up afforded a 20:1-mixture of *cis*-**3a** and *trans*-diamide **4a** in 43% yield. Interestingly, pyrazino[2,3-*a*:-

5,6-*a'*]bis[2³]cyclophane **5a** was obtained in 7% yield. Similarly, an unstable yellow solid obtained in the reduction of **1b** was treated with acetic anhydride, giving amides **3b** and **4b** in a 15:1-ratio in 47% total yield, together with a small amount of **5b** (2% yield). The reduction of **1c** and the treatment of the reduction product with acetic anhydride gave a 4:1-mixture of *cis*-diamide **3c** and *trans*-diamide **4c** in 51% yield from **1c**.

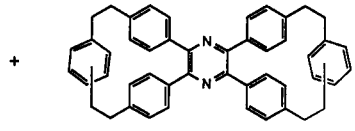
Scheme 1



1a - c



3a - c 4a - c

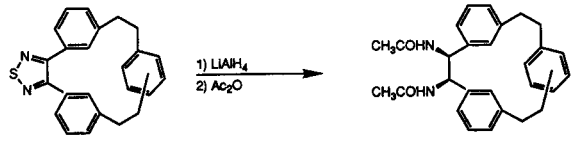


5a - b

a : para , b : meta , c : ortho

Only *cis*-diamides **6a-c** were obtained on treatment of the reduction product of *meta*-series [2³]cyclophanes **2a-c** with acetic anhydride.

Scheme 2



2a - c 6a - c

a : para , b : meta , c : ortho

Finally, reduction of 3,4-di(*m*-tolyl)-1,2,5-thiadiazole (**7**) was finally investigated (Scheme 3). Treatment of **7** with sodium metal in 95% ethanol followed by acetylation gave a 1:1-mixture of the corresponding *meso*- and *dl*-diamide, **8** and **9** in 85% yield. Compound **7** afforded only *meso*-diamide **9** in 37% yield on reduction with lithium aluminum hydride followed by acetylation.

In conclusion, reduction of the 1,2,5-thidiazole-ring of [2³]cyclophane **1** with sodium in ethanol proceeded selectively in *trans*-fashion, while *cis*-reduction was predominant in the reduction of **1** with lithium aluminum hydride. Reduction of **2** with lithium aluminum hydride proceeded exclusively in *cis*-manner.

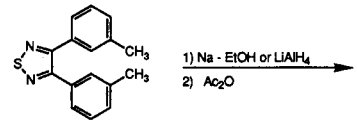
Table 1

Reduction of **1** and **2** Followed by Treatment of Acetic Anhydride

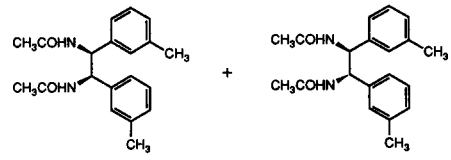
Substrate	Reducing reagent [a]	Product (Yield, %) [b]
1a	sodium/ethanol	**3a** (25) [c] **4a** (61) [c]
1b	sodium/ethanol	**3b** (10) [c] **4b** (79) [c]
1a	lithium aluminum hydride	**3a** (41) [c] **4a** (2) [c] **5a** (7)
1b	lithium aluminum hydride	**3b** (44) [c] **4b** (3), **5b** (2)
1c	lithium aluminum hydride	**3c** (42), **4c** (9)
2a	lithium aluminum hydride	**6a** (42)
2b	sodium/ethanol	**2a** (100)
2c	lithium aluminum hydride	**6b** (30)
2c	lithium aluminum hydride	**6c** (36)

[a] Molar ratio: sodium/substrate = 64; lithium aluminum hydride/substrate = 6. [b] Isolated yields are given unless otherwise stated. [c] Determined by ^{1}H-nmr.

Scheme 3



7

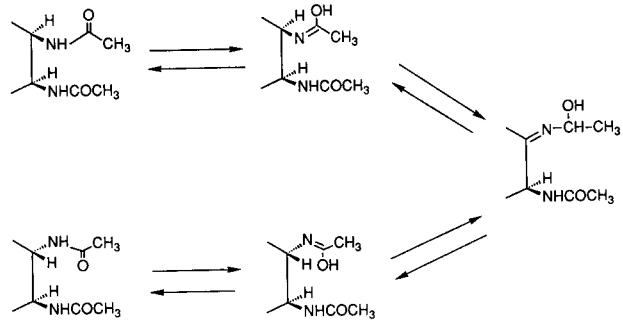


8 (meso -) 9 (dl -)

Thermal Isomerization of Amides **3** and **6**.

In order to establish the stereochemistry of diamides **3**, **4**, and **6**, their thermal isomerization was investigated. The results are given in Table 2 and Scheme 4.

Scheme 4



When heated at 450° under reduced pressure (0.5 mm Hg), *cis*-diamide **3a** afforded a 4:5-mixture of **3a** and isomerized *trans*-diamide **4a**. *Trans*-diamide **4a** did not iso-

Table 2

Thermolysis of *cis*-Amides **3** and **6a**

Substrate	Temperature (°C/mm Hg)	Product (Yield, %) [a]
3a	450/0.5	**3a** (40) [b] **4a** (49) [b]
3b	450/0.5	**3b** (45) [b] **4b** (8) [b] **10b** (15)
3c	450/0.5	**3c** (2), **4c** (45), **10c** (25)
6a	550/0.3	**6a** (50) [b] **11** (32) [b]

[a] Isolated yields are given unless otherwise stated. [b] Determined by ^{1}H-nmr.

merize under the above conditions and was recovered quantitatively. Similarly, **3b** gave isomerized **4b** in 8% yield with unchanged **3b** in 45% yield, and imidazoline **10a** was formed in 15% yield. Thermolysis of **3c** gave **4c** and **10b** in 45% and 25% yields, respectively, accompanied by a recovery of **3c** in 2% yield.

Amide **6a** of *meta*-cyclophane did not isomerize at 450° and was recovered quantitatively. When **6a** was heated at 550° under reduced pressure (0.3 mm Hg), *trans*-diamide **11** was formed as a 3:5-mixture with *cis*-diamide **6a**. In the ^{1}H-nmr spectra, aromatic protons of the 1,4-connected benzene ring of **6a** were observed as a broad singlet at 6.62 and 6.77 ppm, respectively, while those of **11** appeared as a singlet at 6.48 ppm, supporting the symmetric structure of *trans*-1,2-diamide of **11**.

These results clearly indicate the stereochemistry of **3** and **6** as *cis*, and, **4** and **11** as *trans*.

EXPERIMENTAL

All melting points are uncorrected. Mass spectra were obtained on a Nippon Denshi JMS-01SG-2 mass spectrometer at 75 eV using a direct inlet system. The ^{1}H-nmr spectra were recorded on a Nippon Denshi JEOL FT-100 NMR spectrometer using tetramethylsilane as an internal standard in deuteriochloroform unless otherwise stated. The ir spectra were measured on a Nippon-bunko A-102 spectrophotometer as potassium bromide pellets. Column chromatography was carried out on silica gel (Wako gel, C-300). Preparative thin-layer chromatography was accomplished on 2 mm precoated plates of silica gel (Merck Kieselgel $60F_{254}$S, 20 x 20 cm) with concentrating zone (4 x 20 cm).

Reduction of **1a** with Sodium in Ethanol.

Sodium (1.00 g) was added to a mixture of **1a** (250 mg) in 95% ethanol (10 ml) and refluxed for 4 hours. The solvent was evaporated *in vacuo* and to the residue, 10% hydrochloric acid (60 ml) was added. The mixture was made alkaline by an addition of 20% aqueous potassium hydroxide and extracted with methylene chloride (60 ml). The extract was dried over magnesium sulfate and evaporated *in vacuo*, giving a pale yellow solid (232 mg). It was dissolved in acetic acid (5 ml) and stirred at room temperature for 9 hours. Water (30 ml) was added and the entire mixture was stirred at room temperature for 2 hours. The precipitate was collected by filtration and dried, giving a 1:2.4-mixture of **3a** and **4a** (249 mg, 86%). Recrystallization of this mixture from chloroform gave pure **4a** (83 mg).

trans-1,2-Di(acetoamido)[2.2.2](1,4)(1,4)cyclophane (**4a**).

This compound was obtained as colorless needles (chloroform), mp >300°; ir: 3270, 1650 cm^{-1}; ^{1}H-nmr: (at 50°) δ 1.92 (s, 6H), 2.68-3.16 (m, 8H), 5.04-5.20 (m, 2H), 6.26 (br s, 2H), 6.64 (s, 4H), 6.70 (d, J = 8 Hz, 4H), 6.82 (d, J = 8 Hz, 4H); ms: m/e 426 (M+).

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.85; H, 7.23; N, 6.68.

Reduction of **1b** with Sodium in Ethanol.

Sodium (1.00 g) was added to a mixture of **1b** (250 mg) in 95% ethanol (10 ml) and the mixture was treated and worked up as described above, giving a 1:8-mixture of **3b** and **4b** (257 mg, 89%). Recrystallization of the mixture from chloroform afforded pure **4b** (121 mg).

trans-1,2-Di(acetoamido)[2.2.2](1,4)(1,3)(1,4)cyclophane (**4b**).

This compound was obtained as colorless needles (chloroform), mp >300°; ir: 3300, 1650 cm^{-1}; ^{1}H-nmr: (at 50°) δ 1.96 (s, 6H), 2.56-3.04 (m, 8H), 4.96-5.12 (m, 2H), 6.08 (br s, 2H), 6.40-6.60 (m, 6H), 6.72-7.20 (m, 7H); ms: m/e 426 (M$^+$).

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.95; H, 7.21; N, 6.88.

Reduction of **1a** with Lithium Aluminum Hydride.

After a mixture of **1a** (200 mg) and lithium aluminum hydride (124 mg) in dry tetrahydrofuran (20 ml) was stirred at room temperature under nitrogen for 2 hours, wet sodium fluoride (2.00 g) was added in small portions with external ice-cooling. Ether (50 ml) was added and the precipitate was filtered. The filtrate was dried over magnesium sulfate and solvent was evaporated *in vacuo*, giving a yellow solid (148 mg; ir: 3360, 3300 cm^{-1}; ms: m/e 342), which was treated with acetic anhydride (5 ml) at room temperature for 9 hours. The precipitated solid was filtered, washed with water (20 ml), and extracted with hot chloroform (50 ml). The extract was evaporated *in vacuo* to leave a residue which was chromatographed. Compound **5a** (12 mg, 7%) was eluted with chloroform and **3a** (70 mg, 31%) with methanol. The filtrate was poured into water (50 ml) and extracted with chloroform (50 ml). The extract was dried over magnesium sulfate and evaporated *in vacuo*, leaving a residue which, on chromatography with methanol as an eluent, afforded a mixture of **3a** and **4a**. On recrystallization of this mixture from a 1:1-mixture of benzene and ethyl acetate gave **3a** (19 mg, 8%). From the mother liquid, a 1:1-mixture (4 mg, 4%) of **3a** and **4a** was obtained.

cis-1,2-Di(acetoamido)[2.2.2](1,4)(1,4)cyclophane (**3a**).

This compound was obtained as colorless prisms (a mixture of benzene and ethyl acetate), mp 281-282° dec; ir: 3320, 1650 cm^{-1}; ^{1}H-nmr: δ 1.98, 2.01, and 2.10 (each single peak, 6H), 2.68-3.12 (m, 8H), 5.16-5.58 (m, 2H), 5.84-6.30 (m, 2H), 6.40-6.90 (m, 12H); ms: m/e 426 (M+).

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.90; H, 7.21; N, 6.72.

Pyrazino[2,3-*a*:5,6-*a'*]bis[2.2.2](1,4)(1,4)cyclophane (**5a**).

This compound was obtained as colorless prisms (benzene), mp >400°; ^{1}H-nmr: δ 2.76-3.32 (m, 16H), 6.81 (d, J = 8.5 Hz, 8H), 6.83 (s, 8H), 6.96 (d, J = 8.5 Hz, 8H); ms: m/e 644 (M+).

Anal. Calcd. for $C_{48}H_{40}N_2$: C, 89.40; H, 6.25; N, 4.34. Found; C, 89.34; H, 6.17; N, 4.56.

Reduction of **1b** with Lithium Aluminum Hydride.

Compound **1b** (200 mg) was treated with lithium aluminum

hydride (124 mg) in dry tetrahydrofuran (20 ml) and worked up as described above, giving pale yellow solid (129 mg, ir: 3400, 3320; ms: m/e 342), which was treated with acetic anhydride (5 ml) at room temperature for 9 hours. It was poured into water (50 ml) and extracted with methylene chloride (70 ml). The extract was dried over magnesium sulfate and evaporated *in vacuo*, leaving a residue which was chromatographed. Fraction eluted by chloroform was subjected to ptlc with benzene and recrystallized from a mixture of hexane and benzene, giving **5b** as colorless needles (3 mg, 2%). The fraction eluted by a 1:2-mixture of chloroform and acetonitrile was recrystallized from a mixture of chloroform and carbon tetrachloride, giving **3b** as colorless prisms (85 mg, 37%). From the mother liquid was obtained a 2:1-mixture (23 mg, 10%) of **3b** and **4b**.

cis-1,2-Di(acetoamido)[2.2.2](1,4)(1,3)(1,4)cyclophane (**3b**).

This compound had mp 235-237°; ir: 3330, 1650 cm^{-1}; ^{1}H-nmr: δ 1.96, 2.04, and 2.05 (each single peak, 6H), 2.84 (s, 8H), 5.12-5.50 (m, 2H), 6.08-7.32 (m, 14H); ms: m/e 426 (M+).

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.59; H, 6.96; N, 6.64.

Pyrazino[2,3-*a*:5,6-*a'*]bis[2.2.2](1,4)(1,3)(1,4)cyclophane (**5b**).

This compound had mp >300°; ^{1}H-nmr: δ 2.64-3.12 (m, 16H), 6.40 (br s, 2H), 6.78 (d, J = 8 Hz, 8H), 6.98 (d, J = 8 Hz, 8H), 7.04-7.36 (m, 6H); ms: m/e 645, 644 (M+).

Anal. Calcd. for ($C_{48}H_{40}N_2 \cdot \frac{2}{3} H_2O$): C, 87.77; H, 6.34; N, 4.26. Found: C, 87.77; H, 6.13; N, 4.20.

Reduction of **1c** with Lithium Aluminum Hydride.

After a mixture of **1c** (200 mg) and lithium aluminum hydride (124 mg) in dry tetrahydrofuran (20 ml) was treated and worked up as described above, giving yellow solids (170 mg; ir: 3380, 3300 cm^{-1}; ms: m/e 342), which was dissolved in acetic anhydride (5 ml) and the mixture was stirred at room temperature for 9 hours. Precipitates were filtered and recrystallized from a mixture of ethanol and chloroform to give **3c** as colorless needles (98 mg, 42%). The filtrate was poured into water (50 ml) and extracted with methylene chloride (50 ml). The extract was dried over magnesium sulfate and the solvent was evaporated *in vacuo*, leaving a residue, which, on preparative tlc with a 2:3-mixture of chloroform and acetonitrile, gave a white solid. Recrystallization from benzene gave **4c** (21 mg, 9%) as colorless needles.

cis-1,2-Di(acetoamido)[2.2.2](1,4)(1,2)(1,4)cyclophane (**3c**).

This compound had mp 298-300° dec; ir: 3340, 1650 cm^{-1}; ^{1}H-nmr: δ 1.98, 2.04, and 2.08 (each single peak, 6H), 2.54-3.17 (m, 8H), 5.08-5.48 (m, 2H), 5.92-6.24 (m, 2H), 6.28-6.78 (m, 8H), 7.06-7.52 (m, 4H); ms: m/e 426 (M+).

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.67; H, 7.02; N, 6.69.

trans-1,2-Di(acetoamido)[2.2.2](1,4)(1,2)(1,4)cyclophane (**4c**).

This compound had mp >400°; ir: 3320, 1650 cm^{-1}; ^{1}H-nmr: δ 1.96 and 2.02 (each single peak, 6H), 2.36-3.26 (m, 8H), 4.76-5.00 (m, 2H), 6.42 (s, 4H), 6.64 (d, J = 8 Hz, 2H), 6.82 (d, J = 8 Hz, 2H), 6.80-7.02 (m, 2H), 7.04-7.48 (m, 4H); ms: m/e 426 (M+).

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.40; H, 7.02; N, 6.28.

Reduction of **2**. Typical Procedure.

After a mixture of **2a** (100 mg) and lithium aluminum hydride (62 mg) in dry tetrahydrofuran (10 ml) was stirred at room temperature under nitrogen for 2 hours, ethyl acetate (6.5 ml) was added dropwise with ice-cooling and then, water (6.5 ml). The precipitate was filtered and washed with water (5 ml) and ether (10 ml). The filtrate and washings were combined and the organic layer was separated. It was dried over magnesium sulfate and the solvent was evaporated *in vacuo*, giving a yellow tar (89 mg; ir: 3390, 3320 cm^{-1}), which was dissolved in acetic anhydride (4.5 ml). The mixture was stirred at room temperature for 9 hours, poured into water (30 ml) and extracted with methylene chloride (30 ml). The extract was dried over magnesium sulfate and the solvent was evaporated *in vacuo*, leaving the residue, which, on preparative tlc with ethyl acetate, gave **6a** pale yellow solid (48 mg, 42%).

Compound **6b** and **6c** were similarly prepared.

cis-1,2-Di(acetoamido)[2.2.2](1,3)(1,4)(1,3)cyclophane (**6a**).

This compound was obtained as colorless prisms (carbon tetrachloride), mp 210°; ir: 3300, 1650 cm^{-1}; ^{1}H-nmr: δ 2.00 (s, 6H), 2.60-3.08 (m, 8H), 5.30 (d, J = 8 Hz, 2H), 6.02 (br s, 2H), 6.40 (br d, J = 8 Hz, 2H), 6.62 (br s, 2H), 6.77 (br s, 2H), 6.88-7.40 (m, 6H); ms: m/e 426 (M+).

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.44; H, 7.23; N, 6.35.

cis-1,2-Di(acetoamido)[2.2.2](1,3)(1,3)(1,3)cyclophane (**6b**).

This compound was obtained in 30% yield (35 mg) from **2b** (100 mg) as a complex with carbon tetrachloride used as solvent in recrystallization, colorless prisms, mp 110° dec; ir: 3300, 1650 cm^{-1}; ^{1}H-nmr: δ 2.00 (s, 6H), 2.60-3.04 (m, 8H), 5.08 (d, J = 7 Hz, 2H), 5.72 (br s, 2H), 6.29 (br d, J = 7 Hz, 2H), 6.64 (br s, 1H), 6.68-7.22 (m, 9H); ms: m/e 426 (M+).

Anal. Calcd. for $C_{28}H_{30}N_2O_2 \cdot 0.15CCl_4$: C, 75.20; H, 6.72; N, 6.23. Found: C, 75.61; H, 7.18; N, 6.15.

This complex was heated overnight at 110° under reduced pressure to give **6b**, colorless powder, mp 240-245°.

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.67; H, 7.11; N, 6.57.

cis-1,2-Di(acetoamido)[2.2.2](1,3)(1,2)(1,3)cyclophane (**6c**).

This compound was obtained in 36% yield (42 mg) from **2c** (100 mg) as colorless prisms (carbon tetrachloride), mp 110-113°; ir: 3300, 1650 cm^{-1}; ^{1}H-nmr: δ 2.00 (s, 6H), 2.84 (s, 8H), 5.26 (d, J = 8 Hz, 2H), 6.52 (br s, 2H), 6.75 (br d, J = 8 Hz, 2H), 6.96-7.40 (m, 10H); ms: m/e 426 (M+).

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.39; H, 7.30; N, 6.69.

Reduction of **7** with Sodium in 95% Ethanol.

Sodium (800 mg) was added in a mixture of **7** (250 mg) in 95% ethanol (8 ml) and the mixture was refluxed for 1 hour. The reaction mixture was worked up as described in the reduction of **1** with sodium in 95% ethanol, giving a 1:1-mixture (260 mg, 85%) of *meso*- and *dl*-diaccetoamides **8** and **9**. Separation of the two compounds was accomplished by dissolving the mixture in methylene chloride, in which **8** was less soluble than **9**.

meso-1,2-Diacetoamido-1,2-di(*m*-tolyl)ethane (**8**).

This compound was obtained in 21% yield (64 mg) as colorless needles (nitrobenzene), mp 300-302°; ir: 3310, 1650 cm^{-1}; ^{1}H-nmr (tetradeuteriomethanol): δ 1.68 (s, 6H), 2.32 (s, 6H), 5.20 (s, 2H), 6.96-7.20 (m, 10H); ms: m/e 324 (M+).

Anal. Calcd. for $C_{20}H_{24}N_2O_2$: C, 74.04; H, 7.46; N, 8.64. Found: C, 73.64; H, 7.53; N, 8.62.

dl-1,2-Diacetoamido-1,2-di(*m*-tolyl)ethane (**9**).

This compound was obtained in 23% yield (71 mg) as colorless needles (toluene), mp 240-240.5°; ir: 3310, 1650 cm^{-1}; ^{1}H-nmr (tetradeuteriomethanol): δ 1.96 (s, 6H), 2.21 (s, 6H), 5.12 (s, 2H), 6.96-7.20 (m, 10H); ^{1}H-nmr (dideuteriomethylene chloride): δ 1.96 (s, 6H), 2.22 (s, 6H), 5.20 (dd which became s with deuterium oxide-exchange, 2H), 6.90-7.20 (m, 10H); ms: m/e 324 (M+).

Anal. Calcd. for $C_{20}H_{24}N_2O_2$: C, 74.04; H, 7.46; N, 8.64. Found: C, 74.38; H, 7.56; N, 8.73.

Reduction of **7** with Lithium Aluminum Hydride.

After a mixture of **7** (200 mg) and lithium aluminum hydride (180 mg) in dry tetrahydrofuran (15 ml) was stirred at room temperature for 6 hours, ethyl acetate (4 ml) and, then water (1 ml) were added dropwise. Insoluble materials were removed by filtration over celite. The filtrate was dried over magnesium sulfate and, to it, acetic anhydride (4 ml) was added. After the whole mixture was stirred at room temperature for overnight, water (50 ml) was added and stirred for 1 hour. Precipitates collected by filtration and recrystallized from nitrobenzene, giving *meso*-diamide **8** (90 mg, 37%).

Thermal Isomerization of **3a**.

Compound **3a** (70 mg) was heated at 450° for 10 minutes at 0.5 mm Hg and extracted with hot chloroform. The extract was evaporated *in vacuo* and the residue was chromatographed on preparative tlc with a 1:2-mixture of chloroform and acetonitrile, giving a 4:5-mixture of **3a** and **4a** (62 mg, 89%).

Thermal Isomerization of **3b**.

Compound **3b** (100 mg) was similarly pyrolyzed and worked up as described above. First fraction was recrystallized from hexane, giving **10a** as colorless needles (14 mg, 15%). The second fraction gave a 6:1-mixture of **3b** and **4b** (53 mg, 53%).

8-Acetyl-9-methyl-7,11-dihydro-3,6:12,15-di-1,4-benzo[6,6](4,5)-imidazolometacyclophane (**10a**).

This compound had mp 138-139° dec; ir: 1690 cm^{-1}; ^{1}H-nmr: δ 1.90 (s, 3H), 2.62 (d, 3H, J = 2 Hz), 2.65-3.00 (m, 8H), 5.22 (d, 1H, J = 10 Hz), 5.48 (dq, 1H, J = 10 and 2 Hz), 6.13 (br s, 1H), 6.36-6.85 (m, 8H), 6.90-7.28 (m, 3H); ms: m/e 408 (M+).

Anal. Calcd. for $C_{28}H_{28}N_2O$: C, 82.32; H, 6.91; N, 6.86. Found: C, 82.16; H, 6.89; N, 6.70.

Thermal Isomerization of **3c**.

Compound **3c** (124 mg) was heated at 450° for 15 minutes at 0.5 mm Hg and extracted with a hot mixture of ethanol and chloroform. The extract was evaporated *in vacuo* and the residue was chromatographed. Fraction eluted by a 2:3-mixture of chloroform and acetonitrile was recrystallized from cyclohexane, giving **10b** as colorless prisms (30 mg, 25%). The fraction eluted with ethanol was triturated with hot chloroform (20 ml) and filtered, giving **3c** (3 mg, 2%). The filtrate was evaporated and the residue was recrystallized from a mixture of chloroform and benzene, giving **4c** (56 mg, 45%).

8-Acetyl-9-methyl-7,11-dihydro-3,6:12,15-di-1,4-benzo[6,6](4,5)-imidazoloorthocyclophane (**10b**).

This compound had mp 148-150° dec; ir: 1690 cm^{-1}; ^{1}H-nmr: δ 1.93 (s, 3H), 2.61 (d, J = 2 Hz, 3H), 2.64-3.08 (m, 8H), 5.22 (d, J = 11 Hz, 1H), 5.51 (dq, J = 11 and 2 Hz, 1H), 6.24-6.65 (m, 8H), 7.06-7.50 (m, 4H); ms: m/e 408 (M+).

Anal. Calcd. for $C_{28}H_{28}N_2O$: C, 82.32; H, 6.91; N, 6.86. Found: C, 82.19; H, 7.04; N, 6.56.

Thermal Isomerization of **6a**.

Compound **6a** (107 mg) was heated at 550° for 10 minutes at 0.3 mm Hg and extracted with methylene chloride. The extract was evaporated *in vacuo* and the residue was recrystallized from benzene, giving **11** as colorless needles (20 mg, 19%). From the mother liquid, a 4:1-mixture (66 mg, 63%) of **6a** and **11** was obtained.

trans-1,2-Di(acetoamido)[2.2.2](1,3)(1,4)(1,3)cyclophane (**11**).

This compound had mp >300°; ir: 3285, 1650 cm^{-1}; ^{1}H-nmr: δ 1.88 (s, 6H), 2.81 (m, 8H), 5.12-5.32 (m, 2H), 5.80-6.03 (m, 2H), 6.41 (br s, 2H), 6.48 (s, 4H), 6.96-7.20 (m, 6H); ms: m/e 426 (M+).

Anal. Calcd. for $C_{28}H_{30}N_2O_2$: C, 78.84; H, 7.09; N, 6.57. Found: C, 79.03; H, 7.07; N, 6.34.

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