Synthesis and structures of [2.*n*]metacyclophane-1,2-diones Tatsunori Saisyo, Mikiko Shiino, Tomoe Shimizu, Arjun Paudel and Takehiko Yamato*

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McMurry cyclisation of 1,*n*-bis(5-formyl-2-methoxyphenyl)alkanes afforded dimethoxy[2.*n*]metacyclophane-1-enes and dimethoxy[2.*n*]metacyclophane-1,2-diols, in which latter one was converted to dimethoxy[2.*n*]metacyclophane-1,2-diones by Albright–Goldman oxidation.

Keywords: cyclophanes, McMurry reaction, [2.n]metacyclophane-1,2-diol, conformation, oxidation, 1,2-diketones

For many years various research groups have been attracted by the chemistry and spectral properties of the [2.2]MCP ([2.2]MCP = [2.2]metacyclophane) skeleton.¹⁻³ Its conformation, which was elucidated by X-ray measurements,⁴ is frozen into a chair-like non-planar form. Many attempts have been made directly to introduce functional groups into the methylene groups of [2.2]MCPs, but these have failed because of the deviation of the benzyl carbon atom from the plane of the benzene ring.^{5–11}

Singler and Cram^{12} have reported that bromination of [2.2]paracyclophan-1-ene with bromine affords the corresponding *cis*-adduct. Recently, we have reported that di-*tert*-butyldimethyl[2.*n*]MCP-1-enes were treated with an equimolar amount of benzyltrimethylammonium tribromide (BTMA Br₃) in methylene dichloride to afford the *cis*-adducts to the bridged double bond.^{13–16} This result indicates the first success in the introduction of two bromo groups into the methylene groups of dimethyl[*n*.2]MCPs. We have extended the novel reaction mentioned above and reported on the acetolysis of bromine adducts with silver acetate in acetic acid and the conversion to dimethyl[2.*n*]MCP-1,2-diones *via* hydrolysis followed by Swern oxidation of the dihydroxy derivatives.¹⁷

However, we have not yet succeeded in preparing [2.2]MCP-1,2-dione due to the novel transannular reaction arising from the electronic interaction between two benzene rings, the proximity of the 8,16-positions and the release of the considerable strain energy to form the more stable annulene π -electron system, 10b,10c-dihydropyrene. Thus, the reaction of 5,13-di-*tert*-butyl-8,16-dimethyl[2.2]MCP-1-ene¹³ with bromine affords 4,5,9,10-tetrabromo-2,7-di-*tert*-butyl-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrene in good yield, but not the adduct to the bridged double bond, which can be converted to the corresponding [2.2]MCP-1,2-dione.¹⁴

On the other hand, in cyclophane chemistry, the reductive coupling of carbonyl compounds by low-valent titanium, the McMurry reaction,^{18–21} has been used before by Mitchell and Weerawarna²² to synthesise cyclophanes with glycol units as bridges, by Tanner and Wennerström,²³ and recently by Hopf and Mlynek,²⁴ and Grützmacher and Neumann²⁵ for a cyclisation of suitable dialdehydes to yield unsaturated cyclophanes. Thus, there is substantial interest in the developing a more convenient preparation of [2.*n*]MCP-1-enes or 1,2-diols than the conventional sulfur method.^{13–16} We report here on the use of the McMurry coupling reaction to prepare a series of [2.*n*]MCP-1,2-diols and their conversion to 1,2-diones by Albright–Goldman oxidation.²⁶

Results and discussion

Preparation of dimethoxy[2.*n*]MCP-1-enes **4** and [2.*n*]MCP-1,2-diols **5** was carried out by following our recent reported procedure by using the *tert*-butyl group as a positional protective group on the aromatic ring (Scheme 1).^{27–29}

Thus, the AlCl₃-MeNO₂-catalysed trans-tert-butylation of 1 in benzene at 50°C for 12 h afforded 1,n-bis(2methoxyphenyl)alkanes 2 in good yield. The TiCl₄ formylation of compounds 2 with dichloromethyl methyl ether at 20 °C gave the desired 1,n-bis(5-formyl-2-methoxyphenyl)alkanes 3 in good yield. 1,3-Bis(5-formyl-2-methoxylphenyl)propane (3a) was subjected to reductive coupling by the McMurry reaction following the improved Grützmacher's procedure.²⁵ Thus, the reductive coupling reaction of **3a** carried out using TiCl₄–Zn in the presence of pyridine in refluxing THF under the high dilution conditions afforded the disired compound 6,13-dimethoxy[2.3]MCP-1-ene (4a) in 23% along with 1,2-dihydroxy-6,13-dimethoxy[2.3]MCP (5a) in 65% yield. Surprisingly, when the present cyclisation reaction was carried out in the absence of pyridine, the yield of 4a increased to 69%. This result was quite different from that of the similar McMurry cyclisation of 1,3-bis(5-acetyl-2-methoxyphenyl)propane, which afforded the corresponding [3.1]MCP by the TiCl₄ or acids induced pinacol rearrangements.32-34 Similarly, 6,14dimethoxy[2.4]MCP-1-ene 4b and 1,2-dihydroxy-6,14dimethoxy[2.4]MCP 5b were prepared by the McMurry reaction in 36 and 53% yields, respectively. Interestingly, the increased and preferential formation of [2.4]MCP-1-ene syn-4b in 36% yield was observed in the similar McMurry cyclisation of bis(formyl)diphenylbutane 3b. With increasing the length of the one methylene bridge the higher yield of [2.n]MCP-1-ene was obtained. This finding seems to support the notion that the strain of the [2.4]MCP-1-ene compared to the higher [2.3]MCP-1-ene decreases as the length of the one methylene bridge increases.

The structures of 4 and 5 were elucidated based on their elemental analyses and spectral data. Especially, the mass spectral data for 4a and 5a (M^+ = 280 for 4a and 314 for 5a) strongly supports the cyclic structure. [2.n]MCPs can adopt either a "stair-case" anti conformation or a syn conformation with overlaying aromatic rings (Fig. 1).^{35,36} Depending on the size of the bridges and on the presence of intraannular substituents, the interconversion between the syn and anti conformers occur by ring flipping.35,36 The conformation of 4 was readily apparent from its ¹H NMR spectrum. Thus, the internal aromatic proton shows an upfield shift (δ 5.95 ppm) due to the ring current of the opposite benzene ring.^{37,38} The ¹H NMR spectrum of the [2.3]MCP-1-ene 4a prepared in the present paper shows that its structure corresponds exclusively to the anti-conformer. In addition, the protons of the trimethylene bridge give rise to two multiplets centred at $\delta = 2.35$ and 1.95 ppm, respectively, providing a fast interconversion of the two anti conformations of 4a by ring flipping. However, as the temperature of the solution in $CDCl_3/CS_2$ (1:3) is decreased, a single peak of the benzyl protons splits into two multiplets at δ 1.98 and 2.95 ppm below 10 °C. The energy barrier to the conformational ring flipping estimated from the coalescence temperature (T_c) is 12.8 kcal mol⁻¹. We have assigned the structure of **5a** in a similar fashion. Thus, the structure of the anti-confomer is also readily assigned from the chemical shift of the internal

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Scheme 1



Fig. 1 Possible conformations of [2.*n*]metacyclophanes.

aromatic protons as a doublet at δ 5.95 ppm (J = 2.4 Hz). The other two aromatic protons was observed at δ 6.80 and 7.39 ppm; the latter protons are in a strongly deshielding region of oxygen atom of *endo*-OH on ethylene bridge. These observations are strongly supported that the two OH groups are *endo*, *endo*-arrangement and therefore, **5a** is found to be *trans*-diol.

In contrast, in the case of **4b**, the above up-field shift of the internal aromatic proton was not observed and shifted to lower field at δ 7.55 ppm due to the deshielding effect from the bridged double bond. This observation strongly suggests **5b** adopts syn-conformation different from that in **5a**.

Although Mitchell and Weerawarna²² reported the first preparation of [2.2]MCP-1,2-dione from oxidation of the corresponding [2.2]MCP-1,2-diol, the physical and chemical properties have not established so far. Thus, there is substantial interest in the oxidation of [2.n]MCPs 4 having a 1,2-diol to afford [2.n]MCP-1,2-diones. An attempted oxidation of the trans-diol 5a to the 1,2-dione 7a with PCC (pyridinium chlorochromate) carried out in a methylene dichloride solution under the same reaction conditions as described above failed. Only the cleavage reaction product, the dicarboxylic acid 8a, was obtained in quantitative yield. This finding seems to support the strained nature of the diketone 7a. Swern oxidation³⁹ of **5a** using DMSO and oxalyl chloride in CH₂Cl₂ at -60 °C only afforded [2.2]MCP monoketone 6a in only 30% yield along with the ring cleavage reaction product 8a and the starting compound 5a in 20 and 50% yields, respectively (Scheme 2, Table 1). Prolonged reaction time to 24 h at room temperature under the same reaction conditions resulted only a mixture of the [2.3]MCP monoketone 6a and the dicarboxylic acid 8a in almost same ratio.

This finding seems to support the strained nature of the diketone **7a** compared to the monoketones **6a**, in spite of these having the same ring size. Fortunately, the Albright–Goldman²⁶ oxidation of **5a** with DMSO–Ac₂O at room temperature for 20 h succeeded in affording the desired [2.3]MCP diketone in

Table 1	Oxidation of	2 nlmetacy	clophan-1	2-diols 5
Tuble I	Oxidution of			

Run	Substrate	Reagents	Time (h)	Products (% yield) ^a		
				6	7	8
1	5a	PCC	1	0	0	100
2	5a	DMSO-(COCI)2 ^b	1	30	0	20
3	5a	DMSO-Ac ₂ O	20	0	35°	0
4	5b	DMSO-Ac ₂ O	20	0	61	0

^alsolated yields are shown in parenthesis. ^bThe starting compound **5a** was recovered in 50% yield. ^cIsolated by the reaction of *o*-phenylenediamine to afford [2.3]metacyclophane **9a** having a quinoxaline skeleton.



Scheme 2

35% yield along with the starting compound **5a**. However, this diketone **7a** was found to be quite labile under treatment by silica gel column chromatrography and on refluxing in toluene to afford dicarboxylic acid **8a** in quantitative yield. Thus, a trapping reaction of diketone **7a** with *o*-phenylenediamine was attempted, in which the crude diketone **7a** was treated with *o*-phenylenediamine in ethanol at room temperature for 24 h to afford in almost quantitative yield the desired [2.3]MCP **9a** having a quinoxaline skeleton (Scheme 3).

In contrast, in the case of [2.4]MCP, similar Albright– Goldman oxidation of the *trans*-diol **5b** also succeeded in affording the desired diketone **7b** in 61% yield, as stable yellow prisms. This finding seems to support the notion that the strain of the [2.3]diketone **7a** compared to [2.4]MCP diketone **7b** increases as the length of the one methylene bridge decreases.

The structures of the diketones 7a-b, were assigned on the basis of elemental analyses and spectral data. The internal methoxy protons and aromatic protons in the ¹H NMR spectrum and the carbonyl frequency in the IR spectrum are tabulated along with the reference compound benzil **10** in Table 1.

In the ¹H NMR spectrum of **7a**, the internal proton (H_A) shows an upfield shift (δ 6.12 ppm as a doublet, J = 1.0 Hz) due to the ring current of the opposite benzene ring. Thus, its structure corresponds exclusively to the *anti*-conformer. The two aromatic protons (H_B and H_C) were observed at δ 7.84 (a doublet, J = 8.3 Hz) and 6.92 ppm (double doublets, J = 1.0, 8.3 Hz); the former protons are in a strongly deshielding region of oxigen atom of the bridged carbonyl





9 a; *n*= 3 b; *n*= 4

Scheme 3

 Table 2
 Spectral data of [2.n]MCP-1,2-diones (7a-b) and reference compound (10)^a

Compound	Number of methylene Units, <i>n</i>		Aromatic protons			Conformation
		H _A	H _B	H _c		
7a	3	6.12	7.84	6.92	1685	anti
7b	4	7.51	8.18	7.01	1667	syn
10	_	-	-	-	1662	

^aDetermined in CDCl₃ by using SiMe₄ as a reference and expressed in ppm.

group. In contrast, in the case of **7b**, the aromatic proton (H_A) was observed at δ 7.51 (a doublet, J = 2.4 Hz). This observation strongly suggests that **7b** adopts *syn*-conformation. This finding indicates the different conformation is possible in the [2.4]MCP-1,2-dione **7b** as the length of the one methylene bridge increases from the [2.3]MCP-1,2-dione **7a**. We also observed one of the aromatic protons (H_B) to be deshielded by the carbonyl group on the ethylene bridge resulting in a downfield shift (δ 8.18 ppm).

The higher frequency of C=O stretching vibration in the IR spectrum for [2.4]MCP-1,2-dione **7a** (1685 cm⁻¹) in comparison with that for the reference compound benzil **10** (1662 cm⁻¹) presumably reflects the deviation of the carbonyl group from the plane of the benzene ring rather than conjugation between the carbonyl group and the benzene ring. This finding is similar to those for the strained [2.2]paracyclophan-1-ones^{12,40,41} for which absorptions are toward wavelengths characteristic of unconjugated ketones due to the expanded O–C–C bond angles. Similar higher frequency was observed in the higher [2.4]MCP-1,2-dione **7b** (1667 cm⁻¹), but by increasing one methylene bridge, the C=O stretching vibration becomes to appear at the normal positions in [2.4]MCP-1,2-dione **7b**.

Conclusion

In conclusion, we have developed a convenient preparation of a series of *syn*- and *anti*-[2.n]MCP-1-enes **4** and [2.n]MCP-1,2-diols **5** by a McMurry cyclisation of 1,*n*-bis(5-formyl-2-methoxyphenyl)alkanes **3**. Also, [2.n]MCP-1,2-diols **5** were converted to the 1,2-diones 7 by Albright–Goldman oxidation. Further studies on the chemical properties of the diketones 7 are now in progress.

Experimental

¹H NMR spectra were recorded at 300 MHz on a Nippon Denshi JEOL FT-300 NMR spectrometer in deuteriochloroform with Me_4Si as an internal reference. IR spectra were measured as KBr pellets on a Nippon Denshi JIR-AQ2OM spectrometer. Mass spectra were obtained on a Nippon Denshi JMS-HX110A Ultrahigh Performance Mass Spectrometer at 75 eV using a direct-inlet system. Elemental analyses were performed by Yanaco MT-5.

Materials

Preparations of 1,*n*-bis(5-*tert*-butyl-2-methoxyphenyl)alkanes **1** was previously described.^{30,31}

Trans-tert-butylation of 1a to give

2a: To a solution of **1a** (2.21 g, 6.0 mmol) in benzene (16 cm³) was added a solution of anhydrous aluminum chloride (1.60 g, 12.0 mmol) in nitromethane (3.2 cm³). After the reaction mixture was stirred for 12 h at 50 °C, the reaction was quenched by the addition of 10% hydrochloric acid, and the solution was washed with water, dried over Na₂SO₄, and concentrated. The residue was chromatographed over silica gel (Wako C-300, 300 g) with hexane–benzene (1:1) as eluent to give crude **2a** as a colourless solid. Recrystallisation from petroleum ether gave 1,3-bis(2-methoxyphenyl)propane (**2a**) (1.0 g, 65%) as a colourless prisms, m.p. 63–65 °C; v_{max} (KBr)/cm⁻¹: 3000, 2939, 2856, 1601, 1588, 1494, 1466, 1434, 1325, 1291, 1242, 1174, 1158, 1049, 1026, 927, 828, 756; $\delta_{\rm H}$ (CDCl₃) 1.83–1.95 (2H, m, ArCH₂CH₂CH₂Ar), 2.67 (4H, t, *J* = 7.1 Hz, ArCH₂CH₂CH₂Ar), 3.77 (6 H, s, OMe), 6.79–6.88 (4H, m, ArH), 7.12–7.17 (4H, m, ArH); *m*/*z*: 256 (M⁺) (Found: C, 79.45; H, 7.58. C₁₇H₂₀O₂ (256.34) requires C, 79.65; H, 7.86%).

2b: Prepared as described for **2a** in 92% yield. 1,4-Bis(2-methoxyphenyl)butane (**2b**) was obtained as colourless prisms (petroleum ether); m.p. 74–76°C; v_{max} (KBr)/cm⁻¹: 3000, 2939, 2856, 1601, 1588, 1494, 1466, 1434, 1325, 1291, 1242, 1174, 1158, 1049, 1026, 927, 828, 756; $\delta_{\rm H}$ (CDCl₃) 1.61–1.67 (4H, m, ArCH₂CH₂CH₂CH₂CH₂Ar), 2.64 (4H, t, *J* = 7.1 Hz, ArCH₂CH₂CH₂Ar), 3.80 (6 H, s, Me), 6.81– 6.89 (4H, m, ArH), 7.11–7.18 (4H, m, ArH); *m*/z: 270 (M⁺) (Found: C, 80.23; H, 8.33. C₁₈H₂₂Q₂ (270.37) requires C, 79.96; H, 8.20%).

3a: To a solution of **2a** (1.15 g, 4.5 mmol) and Cl_2CHOCH_3 (1.14 cm³, 12.6 mmol) in CH_2Cl_2 (10 cm³) was added a solution of

TiCl₄ (3.0 cm³, 27.3 mmol) in CH₂Cl₂ (10 cm³) at 0 °C. After the reaction mixture was stirred at room temp. for 1 h, it was poured into a large amount of ice/water (50 cm³) and extracted with CH₂Cl₂ (2 × 20 cm³). The combined extracts were washed with water, dried with Na₂SO₄ and concentrated. The residue was chromatographed over silica gel (Wako C–300, 200 g) with benzene as eluent to give **3a** (914 mg, 65%) as a colourless solid. Recrystallisation from hexane gave 1,3-bis(5-formyl-2-methoxyphenyl)propane **3a** as colourless prisms, m.p. 82–84 °C; v_{max} (KBr)/cm⁻¹ 1679 (C=O); $\delta_{\rm H}$ (CDCl₃) 1.90–1.96 (m, 2 H, ArCH₂CH₂CH₂Ar), 2.71 (4H, t, J = 7.8 Hz, Ar*CH*₂CH₂CH₂Ar), 3.91 (6 H, s, OMe), 6.91 (2H, d, J = 7.8 Hz, Ar*CH*, 7.70 (2H, d, J = 2.0 Hz, Ar*H*), 7.72 (2H, dd, J = 2.0, 7.8 Hz), 9.86 (2H, s, *CHO*); *m*/z: 312 (M⁺) (Found C, 72.85; H, 6.55. C₁₉H₂₀O₄ (312.37) requires C, 73.06; H, 6.45%).

3b: Prepared as described for **3a** in 95% yield. 1,4-Bis(5-formyl-2-methoxyphenyl)butane (**3b**) was obtained as colourless prisms (petroleum ether); m.p. 95–97°C; v_{max} (KBr)/cm⁻¹ 1679 (C=O); $\delta_{\rm H}$ (CDCl₃) 1.61–1.18 (4H, m, ArCH₂CH₂CH₂CH₂CH₂Ar), 2.69 (4H, t, J = 8.7 Hz, ArCH₂CH₂CH₂Ar), 3.96 (6 H, s, OMe), 6.94 (2H, d, J = 2.0, 8.3 Hz, ArH), 7.67 (2H, d, J = 2.2 Hz, ArH), 7.70 (2 H, dd, J = 2.0, 8.3 Hz, ArH), 9.85 (2H, s, CHO); m/2: 326 (M⁺) (Found C, 73.53; H, 6.89. C₂₀H₂₂O₄ (326.4) requires C, 73.59; H, 6.79%).

McMurry coupling reaction of 3

The McMurry reagent was prepared from TiCl₄ [23.8 g (13.8 cm³), 125 mmol] and Zn powder (18 g, 275 mmol) in dry THF (500 cm³) under nitrogen. A solution of 1,3-bis(5-formyl-2-methoxyphenyl)propane **3a** (2.81 g, 9.0 mmol) and pyridine (22.8 cm³, 200 mmol) in dry THF (250 cm³) was added within 60 h to the black mixture of the McMurry reagent by using a high-dilution technique with continuous refluxing and stirring. The reaction mixture was refluxed for additional 8 h, cooled to room temperature, and treated with aqueous 10% K₂CO₃ (200 cm³) at 0°C. The reaction mixture was extracted with CH₂Cl₂ (3 × 200 cm³). The combined extracts were washed with water, dried with Na₂SO₄ and concentrated. The residue was chromatographed over silica gel (Wako C-300, 300 g) with hexane–benzene (2:1) and CHCl₃–EtOAc (1:1) as eluents to give **4a** (590 mg, 23%) and **5a** (1.84 g, 65%) as a colourless solid, respectively.

6,13-Dimethoxy[2.3]metacyclophan-1-ene **4a**: Colourless prisms (from methanol), m.p. 133–135 °C; v_{max} (KBr)/cm⁻¹ 2936, 2898, 2833, 1601, 1496, 1438, 1288, 1248, 1187, 1127, 1032, 948, 815, 783; $\delta_{\rm H}({\rm CDCl}_3, 27\,^{\circ}{\rm C})$ 1.93–1.98 (2H, m, ArCH₂CH₂CH₂Ar), 2.35 (4H, broad s, ArCH₂CH₂CH₂Ar), 3.82 (6H, s, OMe), 5.95 (2H, d, J = 2.4 Hz, ArH), 6.58 (2H, s, CH), 6.68 (2H, d, J = 8.2 Hz, ArH), 6.93 (2H, dd, J = 2.4, 8.2 Hz, ArH); $\delta_{\rm H}({\rm CDCl}_3/{\rm CS}_2, 1:3, -40\,^{\circ}{\rm C})$ 0.82–0.92 (1H, m, ArCH₂CH₂CH₂Ar), 1.71–0.84 (1H, m, ArCH₂CH₂CH₂Ar), 1.93–2.03 (2H, m, ArCH₂CH₂CH₂Ar), 2.90–3.02 (2H, m, ArCH₂CH₂CH₂Ar), 3.82 (6H, s, OMe), 5.95 (2H, d, J = 2.4 Hz, ArH), 6.58 (2H, s, CH), 6.68 (2H, d, J = 8.2 Hz, ArH), 6.58 (2H, s, CH), 6.68 (2H, d, J = 8.2 Hz, ArH), 6.58 (2H, s, CH), 6.93 (2H, m, ArCH₂CH₂CH₂Ar), 2.90–3.02 (2H, m, ArCH₂CH₂CH₂Ar), 3.82 (6H, s, OMe), 5.95 (2H, d, J = 2.4 Hz, ArH), 6.58 (2H, s, CH), 6.68 (2H, d, J = 8.2 Hz, ArH), 6.93 (2H, dd, J = 2.4, 8.2 Hz, ArH); 7.31. C₁₉H₂₀O₂ (280.37) requires C, 81.40; H, 7.19%).

 $\begin{array}{l} 1\text{-endo-2-endo-dihydroxy-6, 13-dimethoxy} [2.3] \text{metacyclophane} \\ \textbf{5a:} Colourless prisms (from petroleum ether), m.p. 218–219 °C; v_{max} \\ (KBr)/cm^{-1} 3563, 3327 (OH), 2941, 1608, 1502, 1244, 1128, 1027, \\ 825, 615; \delta_{H}(CDCl_3) 1.80–1.95 (2H, broad s, ArCH_2CH_2CH_2Ar), \\ 1.98–2.12 (2H, m, ArCH_2CH_2CH_2Ar), 2.75 (2H, s, OH), 2.94–3.05 \\ (2H, m, ArCH_2CH_2CH_2Ar), 3.82 (6H, s, OMe), 4.34 (2H, s, CH), \\ 4.99 (2H, d, J = 2.4 Hz, ArH), 6.80 (2H, d, J = 7.8 Hz, ArH), 7.39 \\ (2H, dd, J = 2.4, 7.8 Hz, ArH); m/z: 314 (M⁺) (Found C, 72.53; H, 7.06. C₁₉H₂₂O₄ (314.38) requires C, 72.59; H, 7.05%). \\ \end{array}$

Similarly, compounds **4b** and **5b** were prepared in the same manner as described above in 36 and 53% yields, respectively.

6,14-Dimethoxy[2.4]metacyclophan-1-ene **4b**: Colourless prisms (from methanol), m.p. 117–119 °C; v_{max} (KBr)/cm⁻¹ 2954, 2912, 2835, 1500, 1263, 1245, 1116, 1029, 824; δ_{H} (CDCl₃) 1.18–1.32 (2H, m, ArCH₂CH₂CH₂CH₂Ar), 1.52–1.68 (2H, m, ArCH₂CH₂CH₂CH₂Ar), 2.23–2.38 (2H, broad s, ArCH₂CH₂CH₂CH₂Ar), 2.75–2.93 (2H, broad s, ArCH₂CH₂CH₂CH₂Ar), 3.81 (6H, s, OMe), 6.39 (2H, s, CH), 6.77 (2H, d, J = 8.3 Hz, ArH), 6.98 (2H, dd, J = 2.4, 8.2 Hz, ArH), 7.55 (2H, d, J = 2.4, ArH); m/z: 294 (M⁺) (Found C, 81.69; H, 7.53. C₂₀H₂₂O₂ (294.39) requires C, 81.60; H, 7.53%).

1-endo-2-endo-Dihydroxy-6,14-dimethoxy[2.4]*metacyclophane* **5b**: Colourless needles (from CH₂Cl₂), m.p. 218–219 °C; v_{max} (KBr)/ cm⁻¹ 3558 3386 (OH), 2931, 2863, 1250, 1182, 1111, 1079, 1056; δ_H(CDCl₃) 0.75–1.68 (2H, broad s, ArCH₂CH₂CH₂CH₂Ar), 1.41– 1.65 (2H, broad s, ArCH₂CH₂CH₂Ar), 2.09–2.38 (2H, broad s, ArCH₂CH₂CH₂CH₂Ar), 2.85 (2H, s, OH), 2.72–3.10 (2H, broad s, ArCH2CH2CH2CH2Ar), 3.82 (6H, s, OMe), 4.34 (2H, s, CH), 5.78 (2H, broad s, ArH), 6.90 (2 H, d, J = 8.3 Hz, ArH), 7.56 (2H, broad d, ArH); m/z: 314 (M⁺) (Found C, 73.03; H, 7.23. C₂₀H₂₄O₄ (328.41) requires C, 73.15; H, 7.37%).

Oxidation of 5a with PCC: To a solution of 5a (100 mg, 0.32 mmol) and acetone (5 cm³) was added PCC (157 mg, 0.73 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 24 h. The reaction mixture was filtered and the filtrate extracted with CH2Cl2 $(3 \times 10 \text{ cm}^3)$. The extract was dried over anhydrous sodium sulfate and concentrated. The residue was subjected to silica-gel (Wako, C-300; 100 g) column chromatography using as eluent benzene to give dicarboxylic acid (8a) (105 mg, 95%) as a colourless solid. Recrystallisation from benzene afforded 8a as colourless prisms, m.p. 241–242 °C; v_{max} (KBr)/cm⁻¹: 3410–2965 (OH), 1679 (C=O), 1605, 1502, 1447, 1306, 1251, 722, 632; δ_H (CDCl₃): 1.74–1.88 (2H, m, CH₂CH₂CH₂), 2.55–2.68 (4H, m, CH₂CH₂CH₂), 3.83 (6 H, s, OMe), 7.02 (2H, d, J = 8.7 Hz, ArH), 7.71 (2H, d, J = 1.0 Hz, ArH), 7.82 (2H, dd, J = 8.7, 1.0 Hz), 12.50 (2 H, s, OH); m/z: 344 (M⁺) (Found C, 66.39; H, 5.897. C₁₉H₂₀O₆ (344.37) requires C, 66.27; H, 5.85%).

Swern oxidation of 5a: To a solution of of oxalyl chloride (0.25 cm³, 2.75 mmol) in CH₂Cl₂ (25.0 cm³) was added DMSO (0.126 cm³, 1.65 mmol) and then 5a (110 mg, 0.35 mmol) in CH₂Cl₂ (1.0 cm³) at -30 °C under nitrogen. After the reaction mixture had been stirred at -30 °C for 1 h, triethylamine (380 mg, 3.75 mmol) was added. The temperature of the reaction mixture was maintained at -30 °C for 30 min. under nitrogen, then allowed to warm to room temp. and stirred for an additional 1 h. Then, water (10 cm³) was added and the reaction mixture was extracted with CH_2Cl_2 (3 × 10 cm³). The dichloromethane solution was washed with water, dried over Na2SO4, and evaporated in vacuum to a residue. ¹H NMR spectrum of this oil was in accord with its being a mixture of three components, 5a, 6a, and 8a in the ratio of 50:30:20.

6a: δ_H (CDCl₃): 1.67–1.85 (2H, m, CH₂CH₂CH₂), 2.00–2.14 (2H, m, CH₂CH₂CH₂), 2.85-3.00 (2H, m, CH₂CH₂CH₂), 3.75 (3H, s, OMe), 3.88 (3H, s, OMe), 3.89 (1H, s, OH), 4.66 (1H, s, CH), 5.05, 5.55 (2H, each d, J = 1.0 Hz, ArH, $H_{8,17}$), 6.65, 6.85 (2H, each d, J = 8.3 Hz, ArH, $H_{5,14}$), 7.35, 7.65 (2H, each dd, J = 1.0, 8.3 Hz, ArH, $H_{4,15}$).

Albright-Goldman oxidation of 5a: To a solution of acetic anhydride (0.6 cm³) and **5a** (110 mg, 0.35 mmol) was added DMSO (0.9 cm³, 12.6 mmol) at room temperature. After the reaction mixture had been stirred at room temperature for 20 h, ethanol (0.5 cm³) and triethylamine (2 cm³, 14.2 mmol) was added and stirred for an additional 30 min. Then, water (5 cm³) was added and the reaction mixture was extracted with CH_2Cl_2 (3 × 5 cm³). The dichloromethane solution was washed with water, dried over Na2SO4, and evaporated in vacuum to a residue. ¹H NMR spectrum of this oil was in accord with its being a mixture of three components, 5a and 7a in the ratio of 35:65, which was crystallised by adding a small amount of hexane-CH₂Cl₂, 5:1 to give a pale yellow solid. The solid was washed with hexane-CH2Cl2, 10:1 to afford crude 6,13-dimethoxy[2.3]metacyclophane-1,2-dione 7a in 38 mg (35%) as pale yellow solid; ν_{max} (KBr)/cm^-1: 1685 (C=O); $\delta_{\rm H}$ (CDC_3) : 1.80 (2H, broad s, *CH*₂), 2.0–2.4 (4H, m, *CH*₂), 3.97 (6H, s, *OMe*), 6.12 (2H, d, *J* = 1.0 Hz, ArH_A), 6.92 (2H, d, *J* = 8.3 Hz, ArH_C), 7.84 (2H, dd, J = 1.0, 8.3 Hz, Ar H_B); m/z: 310 (M⁺).

However, attempted isolation of 7a pure failed. Thus, diketone 7a was found to be quite labile under treatment by silica gel column chromatrography and on refluxing in toluene to afford dicarboxylic acid 8a in quantitative yield as colourless solid.

Trapping reaction of 7a with o-phenylenediamine: To a solution of crude 7a (10.6 mg, 0.034 mmol) in ethanol (10 cm³) was added o-phenylenediamine (3.7 mg, 0.034 mmol) at room temperature. After the reaction mixture had been stirred at room temperature for 24 h, the solvent was evaporated in vacuum to leave a residue. The residue was washed successively with 10% aqueous hydrochloric acid, water, and ethanol to afford 9a (13 mg, 100%) as a brown solid, m.p. >300 °C; δ_H (CDCl₃): 1.88 (2H, broad s, Ar*CH*₂CH₂CH₂Ar), 2.0 (2H, broad s, ArCH2CH2CH2Ar), 3.00 (2H, broad s, ArCH2CH2CH2Ar), 3.90 (6H, s, *OMe*), 5.95 (2H, d, J = 1.0 Hz, Ar*H*, $H_{8,17}$), 6.82 (2H, d, J = 8.3 Hz, Ar*H*, $H_{5,14}$), 7.53 (2H, dd, J = 1.0, 8.3 Hz, Ar*H*, $H_{4,15}$), 7.65 (2H, dd, J = 3.4, 6.3 Hz, ArH) and 8.06 (2H, dd, J = 3.4, 6.3 Hz, Ar*H*); m/z: 382 (M⁺) (Found C, 78.25; H, 5.93; N, 7.38. C₂₅H₂₂N₂O₂ (382.47) requires C, 78.51; H, 5.8; N, 7.32%).

Albright-Goldman oxidation of 5b: To a solution of acetic anhydride (2.5 cm³) and **5b** (440 mg, 1.34 mmol) was added DMSO (3.78 cm³, 53.2 mmol) at room temperature. After the reaction mixture had been stirred at room temperature for 20 h, ethanol (2 cm³) and triethylamine (8.4 cm³, 60 mmol) was added and stirred for an additional 30 min. Then, water (10 cm³) was added and the reaction mixture was extracted with CH_2Cl_2 (3 × 10 cm³). The dichloromethane solution was washed with water, dried over Na₂SO₄, and evaporated in vacuum to a residue. The residue was crystallised by adding a small amount of hexane-CH₂Cl₂, 5:1 to give a yellow solid. Recrystallisation from hexane-CH2Cl2, 10:1 afforded 6,14-dimethoxy[2.4]metacyclophane-1,2-dione 7b (265 mg, 61%) as yellow prisms, m.p. 182 °C; ν_{max} (KBr)/cm⁻¹: 1667 (C=O); δ_{H} (CDCl₃): 1.13 (2H, broad s, ArCH₂CH₂CH₂CH₂Ar), 1.66 (2H, broad s, ArCH₂CH₂CH₂CH₂Ar), 2.32 (2H, broad s, ArCH₂CH₂CH₂CH₂Ar), 2.92 (2H, broad s, ArCH2CH2CH2CH2CH2Ar), 3.95 (6H, s, OMe), 7.01 $(2H, d, J = 8.7 \text{ Hz}, \text{Ar}H_{\text{C}}), 7.51 (2H, d, J = 2.4 \text{ Hz}, \text{Ar}H_{\text{A}}), 8.18 (2H, d, J = 2.4 \text{ Hz}, \text{Ar}H_{\text{A}}), 8.18 (2H, d, J = 2.4 \text{ Hz}, \text{Ar}H_{\text{A}})$ dd, J = 2.4, 8.7 Hz, Ar H_B); m/z: 324 (M⁺). (Found C, 73.93; H, 6.17. C₂₀H₂₀O₄ (324.37) requires C, 74.06; H, 6.21%).

Similarly, compound 9b was prepared in 100% yield.

Compound **9b** was obtained as yellow prisms (hexane), m.p. 262–263 °C; ν_{max} (KBr)/cm⁻¹: 1602, 1500, 1342, 1292, 1118, 761; δ_H (CDCl₃): 1.18–1.21 (4H, m, ArCH₂CH₂CH₂CH₂Ar), 2.56 (4H, broad s, ArCH₂CH₂CH₂CH₂Ar), 3.80 (6H, s, OMe), 6.96 (2H, d, J = 8.2 Hz, ArH, $H_{5,15}^{2}$), 6.97 (2H, d, J = 2.2, ArH, $H_{8,18}$), 7.64 (2H, dd J = 3.4, 6.3 Hz, År*H*), 7.78 (2H, d, J = 2.2, 8.2 Hz, År*H*, $H_{4,16}$), 8.09 (2H, dd, J = 3.4, 6.3 Hz, Ar*H*); *m*/*z*: 396 (M⁺) (Found C, 78.50; H, 6.14; N, 7.13. C₂₆H₂₄O₂N₂ (396.49) requires C, 78.76; H, 6.10; N, 7.07%).

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