Synthesis and structures of [2.*n*]metacyclophane-1,2-diones

Tatsunori Saisyo, Mikiko Shiino, Tomoe Shimizu, Arjun Paudel and Takehiko Yamato*

Department of Applied Chemistry, Faculty of Science and Engineering, Saga University, Honjo-machi 1, Saga 840-8502, Japan

McMurry cyclisation of 1,*n*-bis(5-formyl-2-methoxyphenyl)alkanes afforded dimethoxy[2.*n*]metacyclophan-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 Br_3) 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-ene[13] 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]

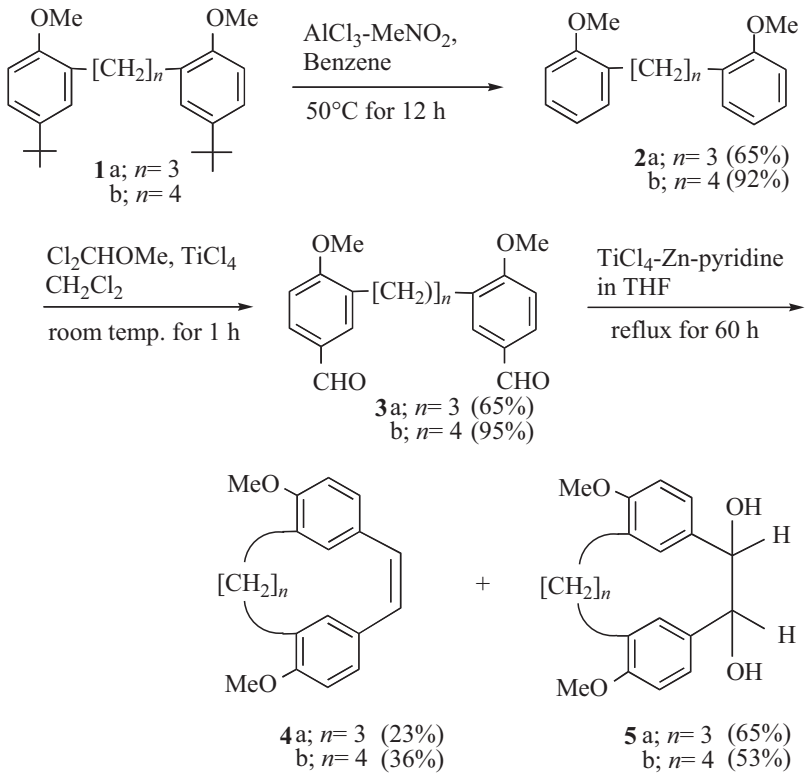
On the other hand, in cyclophane chemistry, the reductive coupling of carbonyl compounds by low-valent titanium, the McMurry reaction,[18–21] has been used before by Mitchell and Weerawarna[22] to synthesise cyclophanes with glycol units as bridges, by Tanner and Wennerström,[23] and recently by Hopf and Mlynek,[24] and Grützmacher and Neumann[25] 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 $AlCl_3$–$MeNO_2$-catalysed trans-*tert*-butylation of **1** in benzene at 50 °C for 12 h afforded 1,*n*-bis(2-methoxyphenyl)alkanes **2** in good yield. The $TiCl_4$ 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 $TiCl_4$–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 $TiCl_4$ or acids induced pinacol rearrangements.[32–34] Similarly, 6,14-dimethoxy[2.4]MCP-1-ene **4b** and 1,2-dihydroxy-6,14-dimethoxy[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 ^{1}H 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 ^{1}H 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 δ = 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

* Correspondent. E-mail: yamatot@cc.saga-u.ac.jp



Scheme 1

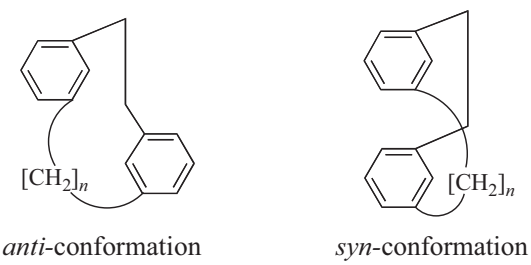


Fig. 1 Possible conformations of [2.*n*]metacyclophanes.

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**.

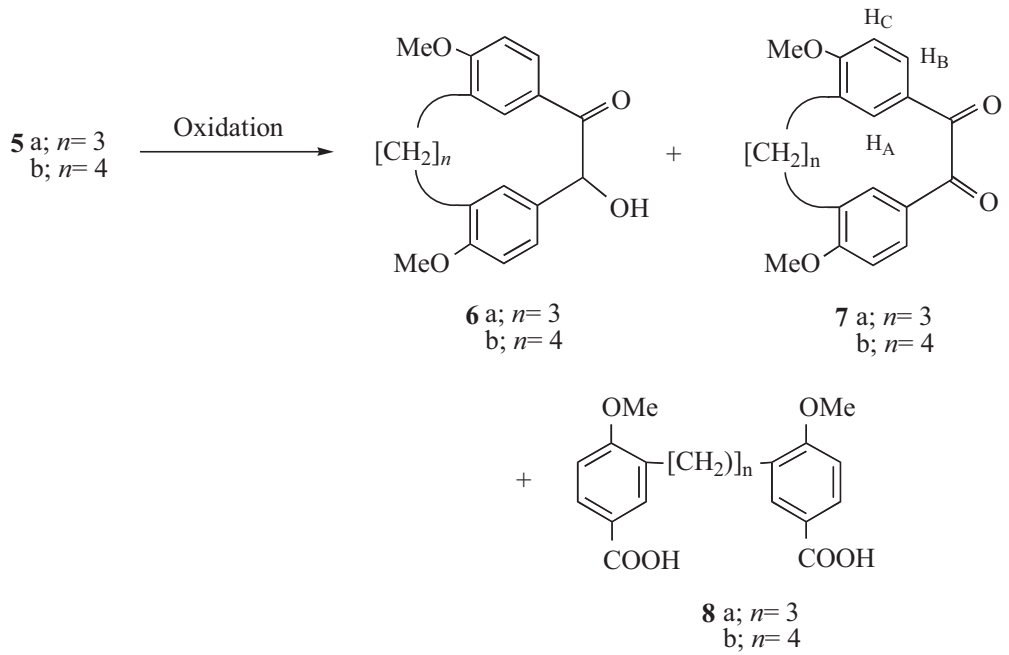
Although Mitchell and Weerawarna[22] reported the first preparation of [2.2]MCP-1,2-dione from oxidation of the corresponding [2.2]MCP-1,2-diol, the physical and chemical properties have not established so far. Thus, there is substantial interest in the oxidation of [2.n]MCPs **4** having a 1,2-diol 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 oxidation[39] of **5a** using DMSO and oxalyl chloride in CH_2Cl_2 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–Goldman[26] oxidation of **5a** with DMSO–Ac_2O at room temperature for 20 h succeeded in affording the desired [2.3]MCP diketone in

Table 1 Oxidation of [2.*n*]metacyclophan-1,2-diols **5**

Run	Substrate	Reagents	Time (h)	Products (% yield)[a]		
				6	**7**	**8**
1	**5a**	PCC	1	0	0	100
2	**5a**	DMSO-$(COCl)_2$[b]	1	30	0	20
3	**5a**	DMSO-Ac_2O	20	0	35[c]	0
4	**5b**	DMSO-Ac_2O	20	0	61	0

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



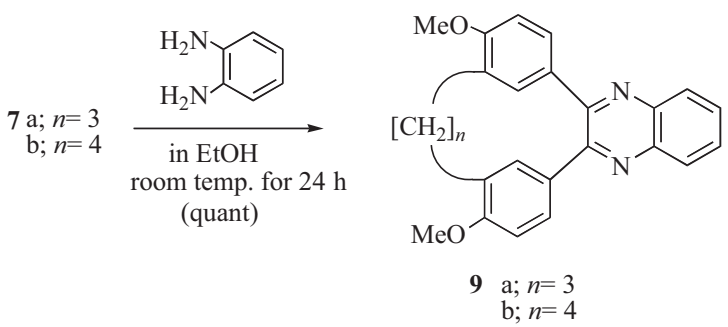
Scheme 2

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 ^{1}H NMR spectrum and the carbonyl frequency in the IR spectrum are tabulated along with the reference compound benzil **10** in Table 1.

In the ^{1}H 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



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, *n*	Aromatic protons			IR, υ ($_{C=O}$) [cm^{-1}]	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	

[a]Determined in $CDCl_3$ by using $SiMe_4$ 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

^{1}H 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 cm^3) was added a solution of anhydrous aluminum chloride (1.60 g, 12.0 mmol) in nitromethane (3.2 cm^3). 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 Na_2SO_4, 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; ν_{max}(KBr)/cm^{-1}: 3000, 2939, 2856, 1601, 1588, 1494, 1466, 1434, 1325, 1291, 1242, 1174, 1158, 1049, 1026, 927, 828, 756; δ_H ($CDCl_3$) 1.83–1.95 (2H, m, $ArCH_2CH_2CH_2Ar$), 2.67 (4H, t, J = 7.1 Hz, $ArCH_2CH_2CH_2Ar$), 3.77 (6 H, s, O*Me*), 6.79–6.88 (4H, m, Ar*H*), 7.12–7.17 (4H, m, Ar*H*); *m/z*: 256 (M^+) (Found: C, 79.45; H, 7.58. $C_{17}H_{20}O_2$ (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; ν_{max}(KBr)/cm^{-1}: 3000, 2939, 2856, 1601, 1588, 1494, 1466, 1434, 1325, 1291, 1242, 1174, 1158, 1049, 1026, 927, 828, 756; δ_H ($CDCl_3$) 1.61–1.67 (4H, m, $ArCH_2CH_2CH_2CH_2Ar$), 2.64 (4H, t, J = 7.1 Hz, $ArCH_2CH_2CH_2Ar$), 3.80 (6 H, s, Me), 6.81–6.89 (4H, m, Ar*H*), 7.11–7.18 (4H, m, Ar*H*); *m/z*: 270 (M^+) (Found: C, 80.23; H, 8.33. $C_{18}H_{22}O_2$ (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 cm^3, 12.6 mmol) in CH_2Cl_2 (10 cm^3) was added a solution of $TiCl_4$ (3.0 cm^3, 27.3 mmol) in CH_2Cl_2 (10 cm^3) 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 cm^3) and extracted with CH_2Cl_2 (2 × 20 cm^3). The combined extracts were washed with water, dried with Na_2SO_4 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; ν_{max} (KBr)/cm^{-1} 1679 (C=O); δ_H($CDCl_3$) 1.90–1.96 (m, 2 H, $ArCH_2CH_2CH_2Ar$), 2.71 (4H, t, J = 7.8 Hz, $ArCH_2CH_2CH_2Ar$), 3.91 (6 H, s, O*Me*), 6.91 (2H, d, J = 7.8 Hz, Ar*H*), 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. $C_{19}H_{20}O_4$ (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; ν_{max} (KBr)/cm^{-1} 1679 (C=O); δ_H($CDCl_3$) 1.61–1.18 (4H, m, $ArCH_2CH_2CH_2CH_2Ar$), 2.69 (4H, t, J = 8.7 Hz, $ArCH_2CH_2CH_2Ar$), 3.96 (6 H, s, O*Me*), 6.94 (2H, d, J = 8.3 Hz, Ar*H*), 7.67 (2H, d, J = 2.2 Hz, Ar*H*), 7.70 (2 H, dd, J = 2.0, 8.3 Hz, Ar*H*), 9.85 (2H, s, *CHO*); *m/z*: 326 (M^+) (Found C, 73.53; H, 6.89. $C_{20}H_{22}O_4$ (326.4) requires C, 73.59; H, 6.79%).

McMurry coupling reaction of **3**

The McMurry reagent was prepared from $TiCl_4$ [23.8 g (13.8 cm^3), 125 mmol] and Zn powder (18 g, 275 mmol) in dry THF (500 cm^3) under nitrogen. A solution of 1,3-bis(5-formyl-2-methoxyphenyl)propane **3a** (2.81 g, 9.0 mmol) and pyridine (22.8 cm^3, 200 mmol) in dry THF (250 cm^3) 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% K_2CO_3 (200 cm^3) at 0 °C. The reaction mixture was extracted with CH_2Cl_2 (3 × 200 cm^3). The combined extracts were washed with water, dried with Na_2SO_4 and concentrated. The residue was chromatographed over silica gel (Wako C-300, 300 g) with hexane–benzene (2:1) and $CHCl_3$–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; ν_{max} (KBr)/cm^{-1} 2936, 2898, 2833, 1601, 1496, 1438, 1288, 1248, 1187, 1127, 1032, 948, 815, 783; δ_H($CDCl_3$, 27 °C) 1.93–1.98 (2H, m, $ArCH_2CH_2CH_2Ar$), 2.35 (4H, broad s, $ArCH_2CH_2CH_2Ar$), 3.82 (6H, s, O*Me*), 5.95 (2H, d, J = 2.4 Hz, Ar*H*), 6.58 (2H, s, *CH*), 6.68 (2H, d, J = 8.2 Hz, Ar*H*), 6.93 (2H, dd, J = 2.4, 8.2 Hz, Ar*H*); δ_H($CDCl_3$/CS_2, 1 : 3, –40 °C) 0.82–0.92 (1H, m, $ArCH_2CH_2CH_2Ar$), 1.71–0.84 (1H, m, $ArCH_2CH_2CH_2Ar$), 1.93–2.03 (2H, m, $ArCH_2CH_2CH_2Ar$), 2.90–3.02 (2H, m, $ArCH_2CH_2CH_2Ar$), 3.82 (6H, s, O*Me*), 5.95 (2H, d, J = 2.4 Hz, Ar*H*), 6.58 (2H, s, *CH*), 6.68 (2H, d, J = 8.2 Hz, Ar*H*), 6.93 (2H, dd, J = 2.4, 8.2 Hz, Ar*H*); *m/z*: 280 (M^+) (Found C, 81.32; H, 7.31. $C_{19}H_{20}O_2$ (280.37) requires C, 81.40; H, 7.19%).

1-endo-2-endo-dihydroxy-6,13-dimethoxy[2.3]metacyclophane **5a**: Colourless prisms (from petroleum ether), m.p. 218–219 °C; ν_{max} (KBr)/cm^{-1} 3563, 3327 (OH), 2941, 1608, 1502, 1244, 1128, 1027, 825, 615; δ_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, O*Me*), 4.34 (2H, s, *CH*), 4.99 (2H, d, J = 2.4 Hz, Ar*H*), 6.80 (2H, d, J = 7.8 Hz, Ar*H*), 7.39 (2H, dd, J = 2.4, 7.8 Hz, Ar*H*); *m/z*: 314 (M^+) (Found C, 72.53; H, 7.06. $C_{19}H_{22}O_4$ (314.38) requires C, 72.59; H, 7.05%).

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; ν_{max} (KBr)/cm^{-1} 2954, 2912, 2835, 1500, 1263, 1245, 1116, 1029, 824; δ_H($CDCl_3$) 1.18–1.32 (2H, m, $ArCH_2CH_2CH_2CH_2Ar$), 1.52–1.68 (2H, m, $ArCH_2CH_2CH_2CH_2Ar$), 2.23–2.38 (2H, broad s, $ArCH_2CH_2CH_2CH_2Ar$), 2.75–2.93 (2H, broad s, $ArCH_2CH_2CH_2CH_2Ar$), 3.81 (6H, s, O*Me*), 6.39 (2H, s, *CH*), 6.77 (2H, d, J = 8.3 Hz, Ar*H*), 6.98 (2H, dd, J = 2.4, 8.2 Hz, Ar*H*), 7.55 (2H, d, J = 2.4, Ar*H*); *m/z*: 294 (M^+) (Found C, 81.69; H, 7.53. $C_{20}H_{22}O_2$ (294.39) requires C, 81.60; H, 7.53%).

1-endo-2-endo-Dihydroxy-6,14-dimethoxy[2.4]metacyclophane **5b**: Colourless needles (from CH_2Cl_2), m.p. 218–219 °C; ν_{max} (KBr)/cm^{-1} 3558 3386 (OH), 2931, 2863, 1250, 1182, 1111, 1079, 1056; δ_H($CDCl_3$) 0.75–1.68 (2H, broad s, $ArCH_2CH_2CH_2CH_2Ar$), 1.41–1.65 (2H, broad s, $ArCH_2CH_2CH_2CH_2Ar$), 2.09–2.38 (2H, broad s, $ArCH_2CH_2CH_2CH_2Ar$), 2.85 (2H, s, *OH*), 2.72–3.10 (2H, broad s,

ArC*H*$_2$CH$_2$CH$_2$C*H*$_2$Ar), 3.82 (6H, s, O*Me*), 4.34 (2H, s, *CH*), 5.78 (2H, broad s, Ar*H*), 6.90 (2 H, d, *J* = 8.3 Hz, Ar*H*), 7.56 (2H, broad d, Ar*H*); *m/z*: 314 (M^+) (Found C, 73.03; H, 7.23. $C_{20}H_{24}O_4$ (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 cm^3) 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 CH_2Cl_2 (3 × 10 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; ν_{max} (KBr)/cm^{-1}: 3410–2965 (OH), 1679 (C=O), 1605, 1502, 1447, 1306, 1251, 722, 632; δ_H ($CDCl_3$): 1.74–1.88 (2H, m, $CH_2CH_2CH_2$), 2.55–2.68 (4H, m, $CH_2CH_2CH_2$), 3.83 (6 H, s, OMe), 7.02 (2H, d, *J* = 8.7 Hz, Ar*H*), 7.71 (2H, d, *J* = 1.0 Hz, Ar*H*), 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. $C_{19}H_{20}O_6$ (344.37) requires C, 66.27; H, 5.85%).

Swern oxidation of **5a**: To a solution of oxalyl chloride (0.25 cm^3, 2.75 mmol) in CH_2Cl_2 (25.0 cm^3) was added DMSO (0.126 cm^3, 1.65 mmol) and then **5a** (110 mg, 0.35 mmol) in CH_2Cl_2 (1.0 cm^3) 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 cm^3) was added and the reaction mixture was extracted with CH_2Cl_2 (3 × 10 cm^3). The dichloromethane solution was washed with water, dried over Na_2SO_4, and evaporated *in vacuum* to a residue. ^{1}H 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 ($CDCl_3$): 1.67–1.85 (2H, m, $CH_2CH_2CH_2$), 2.00–2.14 (2H, m, $CH_2CH_2CH_2$), 2.85–3.00 (2H, m, $CH_2CH_2CH_2$), 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, Ar*H, H*$_{8,17}$), 6.65, 6.85 (2H, each d, *J* = 8.3 Hz, Ar*H, H*$_{5,14}$), 7.35, 7.65 (2H, each dd, *J* = 1.0, 8.3 Hz, Ar*H, H*$_{4,15}$).

Albright–Goldman oxidation of **5a**: To a solution of acetic anhydride (0.6 cm^3) and **5a** (110 mg, 0.35 mmol) was added DMSO (0.9 cm^3, 12.6 mmol) at room temperature. After the reaction mixture had been stirred at room temperature for 20 h, ethanol (0.5 cm^3) and triethylamine (2 cm^3, 14.2 mmol) was added and stirred for an additional 30 min. Then, water (5 cm^3) was added and the reaction mixture was extracted with CH_2Cl_2 (3 × 5 cm^3). The dichloromethane solution was washed with water, dried over Na_2SO_4, and evaporated *in vacuum* to a residue. ^{1}H 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–CH_2Cl_2, 5:1 to give a pale yellow solid. The solid was washed with hexane–CH_2Cl_2, 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); δ_H ($CDCl_3$): 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, ArH_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 cm^3) 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 ($CDCl_3$): 1.88 (2H, broad s, ArCH_2CH$_2$CH_2Ar), 2.0 (2H, broad s, ArCH$_2$CH_2CH$_2$Ar), 3.00 (2H, broad s, ArCH_2CH$_2$CH_2Ar), 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, Ar*H*) 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. $C_{25}H_{22}N_2O_2$ (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 cm^3) and **5b** (440 mg, 1.34 mmol) was added DMSO (3.78 cm^3, 53.2 mmol) at room temperature. After the reaction mixture had been stirred at room temperature for 20 h, ethanol (2 cm^3) and triethylamine (8.4 cm^3, 60 mmol) was added and stirred for an additional 30 min. Then, water (10 cm^3) was added and the reaction mixture was extracted with CH_2Cl_2 (3 × 10 cm^3). The dichloromethane solution was washed with water, dried over Na_2SO_4, and evaporated *in vacuum* to a residue. The residue was crystallised by adding a small amount of hexane–CH_2Cl_2, 5:1 to give a yellow solid. Recrystallisation from hexane–CH_2Cl_2, 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 ($CDCl_3$): 1.13 (2H, broad s, ArCH$_2$CH_2CH$_2$CH$_2$Ar), 1.66 (2H, broad s, ArCH$_2$CH_2CH$_2$CH$_2$Ar), 2.32 (2H, broad s, ArCH_2CH$_2$CH$_2$CH_2Ar), 2.92 (2H, broad s, ArCH_2CH$_2$CH$_2$CH_2Ar), 3.95 (6H, s, *OMe*), 7.01 (2H, d, *J* = 8.7 Hz, ArH_C), 7.51 (2H, d, *J* = 2.4 Hz, ArH_A), 8.18 (2H, dd, *J* = 2.4, 8.7 Hz, ArH_B); *m/z*: 324 (M^+). (Found C, 73.93; H, 6.17. $C_{20}H_{20}O_4$ (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 ($CDCl_3$): 1.18–1.21 (4H, m, ArCH$_2$CH_2CH$_2$CH$_2$CH$_2$Ar), 2.56 (4H, broad s, ArCH_2CH$_2$CH$_2$CH_2Ar), 3.80 (6H, s, *OMe*), 6.96 (2H, d, *J* = 8.2 Hz, Ar*H, H*$_{5,15}$), 6.97 (2H, d, *J* = 2.2, Ar*H, H*$_{8,18}$), 7.64 (2H, dd *J* = 3.4, 6.3 Hz, Ar*H*), 7.78 (2H, d, *J* = 2.2, 8.2 Hz, Ar*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. $C_{26}H_{24}O_2N_2$ (396.49) requires C, 78.76; H, 6.10; N, 7.07%).

Received 8 May 2008; accepted 25 June 2008
Paper 08/5269 *doi: 10.3184/030823408X338701*
Published online: 26 August 2008

References

1 T. Saisyo, M. Shiino, J. Hu and T. Yamato, *J. Chem. Res.*, 2007, 691.
2 R.W. Griffin, *J. Chem. Rev.*, 1963, **63**, 45.
3 D.J. Cram, *Acc. Chem. Res.*, 1971, **4**, 204.
4 C.J. Brown, *J. Chem. Soc.*, 1953, 3278.
5 S. Akabori, T. Sato and K. Hata, *J. Org. Chem*., 1968, **33**, 3277.
6 T. Sato, S. Akabori, M. Kainosho and K. Hata, *Bull. Chem. Soc. Jpn.*, 1966, **39**, 856.
7 T. Sato, S. Akabori, M. Kainosho and K. Hata, *Bull. Chem. Soc. Jpn.*, 1968, **41**, 218.
8 R.W. Griffin, Jr., R.W. Baughman and C.E. Ramey, *Tetrahedron Lett.*, 1968, 5419.
9 H.W. Gschwend, *J. Am. Chem. Soc.*, 1972, **94**, 8430.
10 W.S. Lindsey, P. Stokes, L.G. Humber and V. Boekelheide, *J. Am. Chem. Soc.*, 1961, **83**, 943.
11 B.H. Smith. *Bridged Aromatic Compounds*. Academic Press Inc., New York, N. Y., 1964.
12 R.E. Singler and D.J. Cram, *J. Am. Chem. Soc.*, 1972, **94**, 3512.
13 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1982, **46**, 1543.
14 M. Tashiro and T. Yamato, *J. Am. Chem. Soc.*, 1982, **104**, 3701.
15 T. Yamato, J. Matsumoto, S. Ide, K. Suehiro, K. Kobayashi and M. Tashiro, *Chem. Ber.*, 1993, **126**, 447.
16 T. Yamato, M. Sato, K. Noda, J. Matsumoto and M. Tashiro, *J. Chem. Res. (S)*, 1993, 394.
17 T. Yamato, K. Fujita, S. Ide and Y. Nagano, *J. Chem. Res. (S)*, 1997.
18 J.E. McMurry, M.P. Fleming, K.L. Kees and L.R. Krepski, *J. Org. Chem.*, 1978, **43**, 3255.
19 J.E. McMurry, *Acct. Chem. Res.*, 1983, **16**, 405.
20 J.E. McMurry, G.J. Haley, J.R. Matz, J.C. Clardy and G.V. Duyne, *J. Am. Chem. Soc.,* 1984, **106**, 5018.
21 J.E. McMurry, *Chem. Rev.*, 1989, **89**, 1513.
22 R.H. Mitchell and S.A. Weerawarna, *Tetrahedron Lett.*, 1986, **27**, 453.
23 D. Tanner and O. Wennerström, *Acta Chem. Scand., Ser. B.*, 1983, **37**, 693.
24 H. Hopf and C. Mlynek, *J. Org. Chem.*, 1990, **55**, 1361.
25 H.-F. Grützmacher and E. Neumann, *Chem. Ber.*, 1993, **126**, 1495.
26 J.D. Albright and L. Goldman, *J. Am. Chem. Soc.,* 1967, **89**, 2416.
27 M. Tashiro and T. Yamato, *Synthesis*, 1981, 435.
28 T. Yamato, J. Matsumoto, K. Tokuhisa, K. Tsuji, K. Suehiro and M. Tashiro, *J. Chem. Soc., Perkin Trans. 1*, 1992, 2675.
29 T. Yamato, A. Miyazawa and M. Tashiro, *J. Chem. Soc., Perkin Trans. 1*, 1993, 3127.
30 T. Yamato, J. Matsumoto, K. Tokuhisa, K. Suehiro and M. Tashiro, *Chem. Ber.*, 1992, **125**, 2443.
31 T. Yamato, Y. Saruwatari, L.K. Doamekpor, K. Hasegawa and M. Koike, *Chem. Ber.*, 1993, **126**, 2501.
32 T. Yamato, K. Fujita, K. Futatsuki and H. Tsuzuki, *Can. J. Chem.,* 2000, **78**, 1089.
33 T. Yamato, K. Fujita, T. Abe and H. Tsuzuki, *New J. Chem*., 2001, **25**, 728.
34 T. Yamato, S. Miyamoto, T. Hironaka and Y. Miura, *Org. Lett.,* 2005, **7**, 3.
35 *Cyclophanes* (Eds.: P.M. Keehn and S.M. Rosenfield), Academic Press: New York, vol. 1&2, 1983.
36 F. Vögtle, *Cyclophane chemistry*, Wiley: Chichester, 1993.
37 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1981, **46**, 1543.
38 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1985, **50**, 2939.
39 A.J. Mancuso, S.L. Huang and D. Swern, *J. Org. Chem.*, 1978, **43**, 2480.
40 R.E. Singer and D.J. Cram, *J. Am. Chem. Soc.*, 1971, **93**, 4443.
41 D.J. Cram, R.B. Hornby, E.A. Truesdale, H.J. Reich, M.H. Delton and J.M. Cram, *Tetrahedron*, 1977, **30**, 1757.