Medium-sized cyclophanes. Part 58.[1] Synthesis and conformational studies of [2.*n*]metacyclophan-1-enes and [*n*.1]metacyclophanes

Takehiko Yamato,*[a] Koji Fujita[a] and Hirohisa Tsuzuki[b]

[a] *Department of Applied Chemistry, Faculty of Science and Engineering, Saga University, Honjo-machi 1, Saga-shi, Saga 840-8502, Japan. E-mail: yamatot@cc.saga-u.ac.jp; Fax: +81 0952 28 8591*

[b] *Tohwa Institute for Science, Tohwa University, 1-1-1 Chikushigaoka, Minami-ku, Fukuoka-shi, Fukuoka 815-8510, Japan*

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A series of *syn*- and *anti*-[2.*n*]metacyclophan-1-enes and [2.*n*]metacyclophane-1,2-diols are prepared in good yields by a McMurry cyclization of 1,*n*-bis(5-acetyl-2-methoxyphenyl)alkanes. Interestingly, in the same coupling reaction in the absence of pyridine the pinacol rearrangement of [2.*n*]metacyclophane-1,2-diols to afford [*n*.1]metacyclophanes is observed, attributable to the $TiCl_4$ or acids generated from the McMurry reagent occurring during the cyclization reaction. In fact, protic acid- or Lewis-acid induced pinacol rearrangements of [2.*n*]metacyclophane-1,2-diols afford [*n*.1]metacyclophanes in good yield. The [2.*n*]metacyclophan-1-ene-to-[*n*.1]metacyclophane ratio of the products is strongly governed by the number of the methylene bridges. The proportion of the rearrangement product increases with increasing length of the bridge. Conformational studies of [*n*.1]metacyclophanes as well as of [2.*n*]metacyclophan-1-enes in both solution and solid state are also described.

Introduction

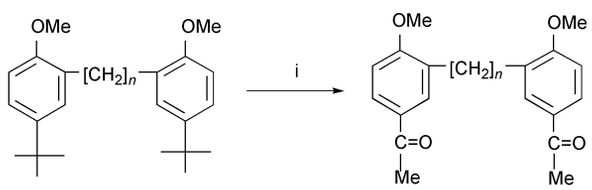
Although [*n*.1]MCPs (MCP = metacyclophane) have been prepared by various workers, the synthetic routes used in previous methods were too long for practical purposes. Vögtle[2] reported the first synthesis of both [4.1]- and [5.1]MCP[3] by use of the sulfone pyrolysis method. Later, Lin *et al.* succeeded in preparing the lower [3.1]homologue by a photochemical method.[4] However, it was quite difficult to obtain sufficient amounts for further studies by this route.

In cyclophane chemistry the reductive coupling of carbonyl compounds by low-valent titanium, the McMurry reaction,[5] has been used before by Mitchell *et al.*[6] to synthesize cyclophanes with glycol units as bridges, by Tanner and Wennerström,[7] and recently by Hopf[8] and Grützmacher *et al.*[9] for a cyclization of suitable dialdehydes to yield unsaturated cyclophanes. On the other hand, it is well known that acid-catalyzed pinacol rearrangement of 1,2-glycols affords the corresponding ketones;[10] *e.g.*, 2,3-diaryl-2,3-dihydroxybutanes afford 3,3-diarylbutan-2-ones or 1,2-diaryl-2-methylpropan-1-ones *via* aryl or methyl shift, respectively. Thus, there is substantial interest in the systematic investigation of the pinacol rearrangement of [*n*.2]cyclophanes with glycol units at the ethylene bridges to afford either [*n*.1]cyclophanes by ring contraction or [*n*.2]cyclophane ketones.

In this paper, we describe a new preparative route for a series of *anti*-[2.*n*]MCP-1-enes and [2.*n*]MCP-1,2-diols using the low-valent-titanium-induced McMurry reaction. The latter compounds were further converted to [*n*.1]MCPs by pinacol rearrangement. Conformational studies of [*n*.1]MCPs as well as of [2.*n*]MCP-1-enes in both solution and solid state are also described.

Results and discussion

1,*n*-Bis(5-*tert*-butyl-2-methoxyphenyl)alkanes **1** have been prepared according to our previous papers.[11] The $AlCl_3$–$MeNO_2$-catalyzed acetylation of compounds **1** with acetic anhydride or acetyl chloride at 20 °C led to an *ipso*-acylation reaction,[12] affording the desired 1,*n*-bis(5-acetyl-2-methoxyphenyl)alkanes **2** in good yield (Scheme 1).[13]



1a; *n* = 2
b; *n* = 3
c; *n* = 4
d; *n* = 5
e; *n* = 6

2a; *n* = 2 (58%)
b; *n* = 3 (72%)
c; *n* = 4 (74%)
d; *n* = 5 (80%)
e; *n* = 6 (64%)

Scheme 1 *Reagents and conditions:* i, MeCOCl, $AlCl_3$–$MeNO_2$, CH_2Cl_2 room temp. for 1 h.

1,2-Bis(5-acetyl-2-methoxyphenyl)ethane **2a**[13] was subjected to reductive coupling by the McMurry reaction following Grützmacher's procedure[9] (Scheme 2). Although none of the desired [2.2]MCP-1-ene **3a** was observed, the dimer **6a** was obtained in 11% yield.

Interestingly, when pyridine was used in the present cyclization reaction, [2.2]MCP-1,2-diol **4a** was obtained in 10% yield, but the formation of the desired [2.2]MCP-1-ene **3a** was again not observed. This finding seems to be due to the much more strained structure of **3a** than that of diol **4a** containing the larger ring during formation of the unsaturated C=C linkage. Thus, during the McMurry reaction the intramolecular cyclization to afford **3a** might be quite difficult. Interestingly, when the reductive coupling reaction of **2a** was carried out in the presence of pyridine at room temperature, the yield of [2.2]MCP-1,2-diol **4a** increased from 10% to 30% along with trace amount of dimer **6a**. Results of the McMurry reaction for substrates **2a**–**e** are presented in Table 1.

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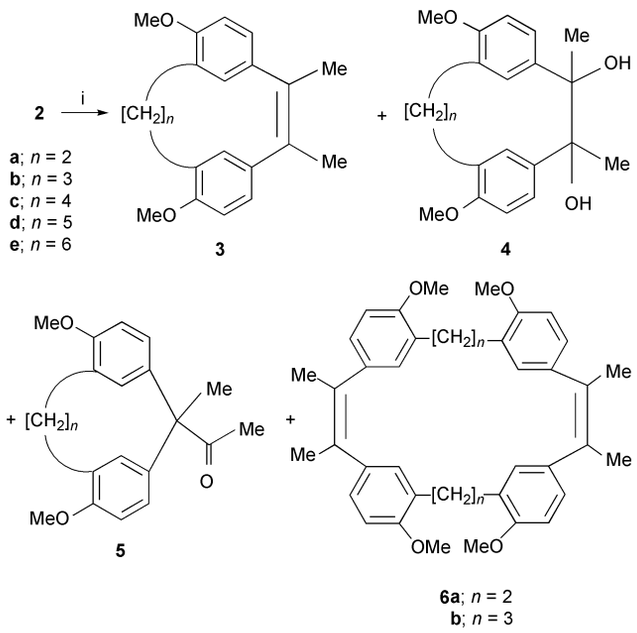
Table 1 McMurry reaction of 1,*n*-bis(5-acetyl-2-methoxyphenyl)alkanes **2**

Run	Substrate	Number of methylene units, *n*	Conditions[a]	Products (% yield)[b]		
1	**2a**	2	A[c]	**3a** (0)	**4a** (0)	**5a** (0)
2	**2a**	2	B	**3a** (0)	**4a** (10)	**5a** (0)
3	**2a**	2	B[d]	**3a** (0)	**4a** (30)	**5a** (0)
4	**2b**	3	A[c]	**3b** (70)	**4b** (0)	**5b** (0)
5	**2b**	3	B	**3b** (80)	**4b** (7)	**5b** (0)
6	**2c**	4	A	**3c** (69)	**4c** (13)	**5c** (0)
7	**2c**	4	B	**3c** (83)	**4c** (15)	**5c** (0)
8	**2d**	5	A	**3d** (45)	**4d** (0)	**5d** (34)
9	**2d**	5	B	**3d** (77)	**4d** (8)	**5d** (4)
10	**2e**	6	A	**3e** (19)	**4e** (0)	**5e** (60)

[a] Reaction conditions: A; The reaction was carried out in the absence of pyridine. B; The reaction was carried out in the presence of pyridine. [b] Isolated yields. [c] The dimers **6a** and **6b** were obtained in 11% and 2% yield, respectively. [d] The reaction was carried out at room temperature.

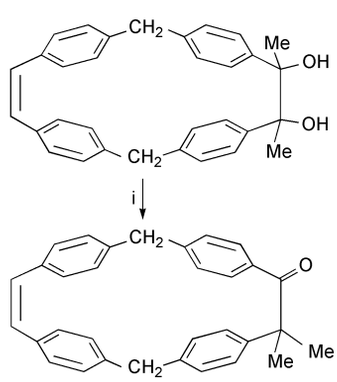


Scheme 2 (see Table 1). *Reagents and conditions:* i, $TiCl_4$–Zn–pyridine, THF, reflux for 60 h.

The structures of products, diol **4a** and dimer **6a** were determined on the basis of their elemental analyses and spectral data. Thus, Griffin *et al.* reported[14] the structure of 1,2-dimethyl[2.2]MCP and assigned the *exo*-*endo*-arrangement. We have assigned the ^{1}H NMR signals of **4a** in a similar fashion. In the ^{1}H NMR spectrum of **4a** in $CDCl_3$ upfield shifts and the different chemical shifts for internal aromatic protons at δ 4.36 and 4.83 due to the ring current of the opposite aromatic ring were observed.[15,16] These data strongly suggest that the structure of **4a** is the *anti*-conformer. Furthermore, the two methyl groups show different chemical shifts at δ 1.30 and 1.83 each as a singlet. The four external aromatic protons were also observed as different chemical shifts at δ 6.81, 6.88, 7.13 and 7.40; the latter proton is in a strongly deshielding region of the oxygen atom of the *endo*-OH on the ethylene bridge. In contrast, one of the two internal aromatic protons was observed at lower field (δ 4.83) attributable to being in a strongly deshielding region of the oxygen atom of the *exo*-OH on the ethylene bridge. These data strongly support the suggestion that the two OH groups are in an *endo*- and *exo*-arrangement and, therefore, *anti*-**4a** is found to be the *trans*-diol.

The mass spectral data for dimer **6a** (M^+ = 588) strongly support a cyclic dimeric structure. In the ^{1}H NMR spectrum of the tetramethoxy[2$_4$]MCP **6a**, protons of methyl groups, methoxy groups and ArCH_2CH_2Ar methylene protons each appear as a singlet at 27 °C. This behaviour indicates that the rate of conformational ring flipping of macrocycle **6a** is faster than the NMR time-scale above this temperature. However, in dimer **6a** even at −60 °C in $CDCl_3$–CS_2 (1 : 3) the singlet signal of the ArCH_2CH_2Ar ethylene protons remains unsplit. These observations indicate the flexible structure of **6a**, similar to that of [2$_4$]MCP in spite of the introduction of two additional double bonds of the ethylene bridge.[17]

Similar McMurry cyclization of 1,3-bis(5-acetyl-2-methoxyphenyl)propane **2b** carried out under the same reaction conditions afforded the desired [2.3]MCP-1-ene **3b** in 70% yield along with a trace amount of dimer **6b**. When pyridine was used in the present cyclization reaction, the yield of **3b** increased to 80%.The same results were obtained in the case of the longer diacetyldiphenylbutane **2c** except for the formation of [4.2]MCP-11,12-diol **4c**. Interestingly, the coupling reaction of 1,5-bis(5-acetyl-2-methoxyphenyl)pentane **2d** with low-valent titanium ($TiCl_4$/Zn) in the absence of pyridine led to the intramolecular cyclization affording 1,2-dimethyl[2.5]MCP-1-ene **3d** along with the [5.1]MCP **5d** in 34% yield. The formation of the corresponding 1,2-diol **4d** was not observed. This finding suggests that the pinacol rearrangement of 1,2-diol **4d** catalyzed by $TiCl_4$ or acids generated from the McMurry reagent occurred during the cyclization reaction. In fact, when the same reaction was carried out in the presence of an excess of pyridine, the corresponding 1,2-diol **4d** was obtained in 8% yield. In the case of 1,6-bis(5-acetyl-2-methoxyphenyl)hexane **2e** the preference for formation of the rearrangement product **5e** was observed. Thus, the [2.*n*]MCP-to-[*n*.1]MCP ratio of products is strongly governed by the number of methylene bridges. The portion of the rearrangement product increases with increasing length of the bridge. To the best of our knowledge the present rearrangements of [2.*n*]MCPs to the smaller-ring-size [*n*.1]MCPs by a ring contraction are the first such case in cyclophane chemistry. In fact Grützmacher *et al.* reported[18] a similar acid-catalyzed rearrangement of [2.1.2.1]paracyclophane-1,2-diol to afford the corresponding ketones by a pinacol rearrangement. No ring contraction was observed in spite of the much larger ring size than the present [2.*n*]MCP-1,2-diols (see Scheme 3).



Scheme 3 *Reagents and conditions:* i, H_2SO_4.

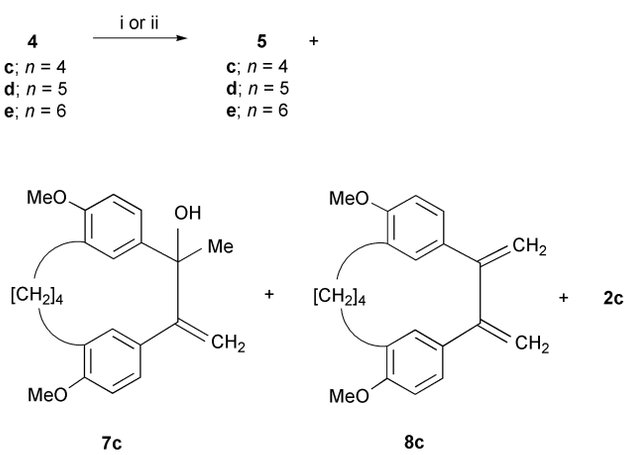
Table 2 Pinacol rearrangement of [2.*n*]MCP-1,2-diols **4c–e**

Run	Substrate	Number of methylene units, *n*	Conditions[a]	Products (% yield)[b]
1	**4c**	4	A	**5c** (45) **7c** (5), **8c** (7), **2c** (8)
2	**4c**	4	B	**5c** (33)[c]
3	**4d**	5	A	**5d** (65)
4	**4d**	5	B	**5d** (62)
5	**4e**	6	A	**5e** (95)
6	**4e**	6	B	**5e** (96)

[a] Reaction conditions: A; I_2–HOAc, 1,4-dioxane, reflux for 30 min. B; $BF_3{\cdot}Et_2O$, CH_2Cl_2, room temperature for 30 min. [b] Isolated yields. [c] Intractable mixture was also obtained.

As mentioned previously, synthesis of [*n*.1]MCPs have not been commonplace due to the lack of a general method such as that developed by Boekelheide for the [2.2]MCPs.[19] As mentioned previously, Vögtle[2] reported the first synthesis of both [4.1]- and [5.1]-MCP by use of the sulfone pyrolysis method. Later, Lin *et al.* succeeded in preparing the lower [3.1]homologue by a photochemical method.[4] However, the synthesis of [*n*.1]MCPs has not been established so far due to both the low-yield preparation and the unsuccessful attempts to prepare the lower [3.1]homologue except by photochemical synthesis. On the other hand, substituent effects on the pinacol rearrangement have been reported.[10,20] Thus, there is substantial interest in pinacol rearrangement of [*n*.2]cyclophanes with glycol units at the ethylene bridge to afford either [*n*.1]cyclophanes by ring contraction or [*n*.2]cyclophane ketones. From the above results, the present pinacol rearrangement could be used for the preparation of novel [*n*.1]MCPs.

An attempted pinacol rearrangement of [4.2]MCP-11,12-diol **4c** with I_2–HOAc[10b,21] in 1,4-dioxane under reflux for 3 h led to the desired [4.1]MCP **5c** in 45% yield along with the dehydration products **7c** and **8c** in 5 and 7% yield (Scheme 4,

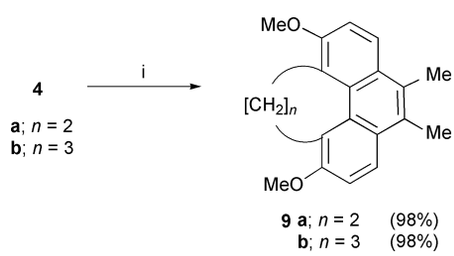


Scheme 4 (see Table 2). *Reagents and conditions:* i, I_2–HOAc, 1,4-dioxane, reflux for 30 min; $BF_3{\cdot}Et_2O$, CH_2Cl_2 room temperature for 30 min.

Table 2). Furthermore, the ring cleavage at the 1,2-diol moiety occurred to form 1,4-bis(5-acetyl-2-methoxyphenyl)butane **2c** in 8% yield under the conditions used. The same reaction carried out in the presence of $BF_3{\cdot}Et_2O$ afforded the rearrangement product **5c** in 33% yield along with a mixture of intractable products. In contrast, in the case of treatment of [5.2]MCP-12,13-diol **4d** and [6.2]MCP-13,14-diol **4e** with I_2–HOAc in 1,4-dioxane the desired pinacol rearrangement products [5.1]MCP **5d** and **5e** were the main products, obtained in 65, 95% yield, respectively. No formation of dehydration product or ring-cleavage product was observed. Similar results were also obtained in the presence of $BF_3{\cdot}Et_2O$ as a catalyst. The yields of the rearrangement products **5** increase with the number of the methylene bridges. This result might be attributed to the decrease of ring strain in [*n*.1]MCPs.

The structures of pinacol rearrangement products **5c–e** and dehydration products **7c**, **8c** were determined on the basis of their elemental analyses and spectral data. In particular, in the case of [4.1]- and [2.4]-systems, for example, the mass spectral data for **5c** (M^+ = 338) and **7c**, **8c** (M^+ = 338 and 320) strongly support a cyclic structure. The reaction pathway in which the rearrangement products **5** would be formed *via* the protic-acid-catalyzed rearrangement of the 1,2-diols **4** is the same as that of the rearrangement of 4-methoxyacetophenone pinacol.[10b]

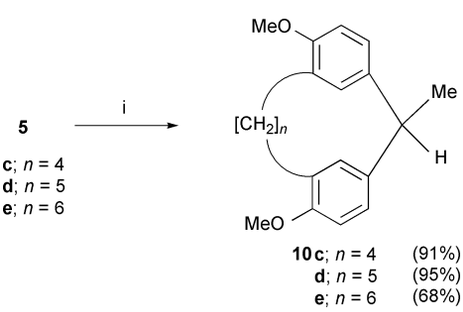
However, in the case of [2.2]MCP-1,2-diol **4a** and [3.2]MCP-10,11-diol **4b** with $BF_3{\cdot}Et_2O$ in dichloromethane the formation of the desired pinacol rearrangement products [2.1]MCP **5a** and [3.1]MCP **5b** was not observed under the reaction conditions used. Only the transannular cyclization products **9a** and **9b** were obtained, along with a large amount of a mixture of intractable products. When CF_3SO_3H was used in the present reaction, the transannular cyclization products **9a** and **9b** were obtained in almost quantitative yields (Scheme 5). These results



Scheme 5 *Reagents and conditions:* i, CF_3SO_3H, CH_2Cl_2, room temperature for 30 min.

are consistent with the results obtained from the *anti*-[2.2]- and -[2.3]MCP-1-enes, which undergo transannular cyclization reactions under the acidic conditions or photoirradiation attributable to the proximity of the intra-annular positions and the release of the considerable strain energy.[9a,9b,22]

Deacetylation of ketone **5c** with molten potassium hydroxide gave the bridge-methyl-substituted [*n*.1]MCP **10c** in 91% yield. Similar treatment of ketones **5d** and **5e** afforded the desired products **10d** and **10e** in 95 and 68% yield, respectively (Scheme 6).



Scheme 6 *Reagents and conditions:* i, KOH, 180 °C for 3 h.

Although the preparations of [*n*.1]MCPs were reported by various research groups,[2–4] we have accomplished the first successful, convenient preparation of a series of [*n*.1]MCPs by

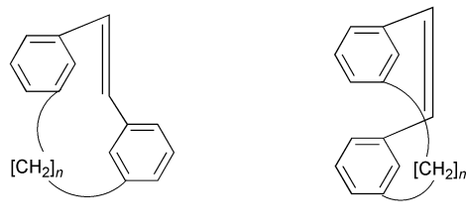


Fig. 1 Possible conformations of [2.*n*]MCP-1-enes.

pinacol rearrangement *via* ring contraction of [*n*.2]MCPs **4** having a 1,2-diol unit on the ethylene bridge.

[2.*n*]MCP-1-enes adopt either a 'stair-case' *anti* conformation or a *syn* conformation with overlaying aromatic rings (Fig. 1).[9b,15,23] Depending on the size of the bridges and on the presence of intra-annular substituents, the interconversion between the *syn* and *anti* conformers occurs by ring flipping.[24]

The conformation of 1,2-dimethyl[2.*n*]MCP-1-enes **3** was readily apparent from their ^{1}H NMR spectrum. Thus, the internal aromatic proton shows an upfield shift (δ 5.69–6.77) due to the ring current of the opposite benzene ring.[15,16] The ^{1}H NMR spectrum of 1,2-dimethyl[2.3]MCP-1-ene **3b** at 27 °C showed a broad singlet of the intra-annular proton H_i at δ 5.69, apart from those at δ 6.72 and 7.03 for the other two protons on the aromatic rings. The methyl protons at the bridged double bond and the methoxy protons were observed each as a singlet at δ = 2.19 and 3.83, respectively, and the protons of the trimethylene bridge generate a complicated signal pattern as expected for a rigid *anti*-[2.3]MCP-1-ene. The protons of the benzylic CH_2 group were observed as two multiplets centred at δ 1.95 and 2.92, which are further split by coupling with the protons of the central CH_2 group. This central CH_2 group was also observed as a multiplet centred at δ 1.69. This peak pattern ascribed to six chemically distinct protons of the propano bridge confirms the absence of an *anti-anti* interconversion which would exchange HA and HB of each CH_2 group. As the temperature of the solution of **3b** in $CDBr_3$ is increased, the individual peaks of the benzyl protons merge and eventually a single peak is observed above 70 °C. This observation indicates that the rate of conformational ring flipping of **3b** is faster than the NMR time-scale at this temperature. The energy barrier to the conformational ring flipping estimated from the coalescence temperature (T_c) is 15.6 kcal mol^{-1}. †

Similar findings were also observed in the ^{1}H NMR spectrum of 1,2-dimethyl[2.4]MCP-1-ene **3c** at 27 °C, but the protons of the butane bridge give rise to two multiplets centered at δ 1.57 and 2.47, respectively, providing a fast interconversion of the two *anti* conformations of **3c** by ring flipping. However, as the temperature of the solution in $CDCl_3$–CS_2 (1 : 3) is decreased, a single peak for the benzyl protons splits into a pair of doublets below −30 °C. The energy barrier to the conformational ring flipping estimated from the coalescence temperature (T_c) is 10.7 kcal mol^{-1}. This finding indicates a more flexible structure for **3c** than of **3b**, attributable to the larger cyclophane ring size. In spite of a decrease in temperature to −100 °C in $CDCl_3$–CS_2 (1 : 3), no change in the spectrum is observed for the [2.5]-system **3d**. The solution conformation of 1,2-dimethyl-[2.*n*]MCP-1-enes **3** is sensitive to the chain length of the bridge. The ring-inversion barriers determined by variable-temperature ^{1}H NMR decrease with increasing length of the bridges. Values for coalescence temperature and ring-flipping energy barriers are given in Table 3

Similarly, the conformation of [*n*.1]MCPs **5** and **10** was readily apparent from their ^{1}H NMR spectrum. For example, in the ^{1}H NMR spectrum of 11-acetyl-11-methyl-6,15-dimethoxy-[4.1]MCP **5c** in $CDCl_3$ upfield shifts and the different chemical shifts for internal aromatic protons at δ 6.33 and 6.56 due to the ring current of the opposite aromatic ring were observed.[15,16] These data strongly suggest that the structure of **5c** is the *anti*-conformer. Furthermore, the two methoxy groups show different chemical shifts at δ 3.80 and 3.81, each as a singlet. The four external aromatic protons were also observed as different chemical shifts at δ 6.66, 6.72, 6.91 and 7.21; the latter proton is in a strongly deshielding region of the oxygen atom of the acetyl group on the methylene bridge. Thus, **5c** adopts a 'stair-case' *anti* conformation as known for other [2.3]MCP-1-enes[9b,23e] and [3.2]MCPs[24] having the same 11-membered ring. The ^{1}H NMR spectrum of **5c** in $CDCl_3$ at room temperature exhibits a split pattern for the benzyl protons as two multiplets centred at δ 2.34 and 2.7. The central CH_2 group was also observed as two multiplets centred at δ 0.95 and 1.69. These findings suggest a rigid structure of [4.1]MCP **5c** at this temperature. However, as the temperature of the solution in $CDBr_3$ is increased, a pair of multiplets of the benzyl protons merged into a single peak above 90 °C. The energy barrier to conformational ring flipping estimated from the coalescence temperature (T_c) is 17.3 kcal mol^{-1}. The energy barrier for the [4.1]-system **10c** was also estimated to be the same [17.3 (T_c = 90 °C) kcal mol^{-1}]. This energy is much lower than that of the rigid [2.2]MCP (>27 kcal mol^{-1})[25,26] and is similar to that for the homologous [3.2]MCPs (15.8–19.1 kcal mol^{-1}).[27] This finding indicates a more rigid structure for [4.1]MCP **5c** and **10c** (*ca.* 6.6 kcal mol^{-1}) than that for [2.4]MCP-1-ene **3c** ($\Delta G_c^{\ddagger}$ = 10.7 kcal mol^{-1}) attributable to the one methylene decrease. It was also found that the solution conformation of [*n*.1]MCPs is sensitive to the chain length of the bridges. The ring-inversion barriers determined by variable-temperature ^{1}H NMR dramatically decrease with increasing length of the bridge by one unit.

Usually, parent [*n*.2]MCPs in which intra-annular substituents are absent preferably adopt an *anti*-conformation.[28,29] Similarly, in the case of the [4.1]MCP **5c** the *anti*-conformation was found to be favorable. The conformation of **5c** has also been confirmed by X-ray crystallographic analysis. Single colorless crystals of 6,14-dimethoxy-1,2-dimethyl[2.4]MCP-1-ene **3c** and of 11-acetyl-11-methyl-6,15-dimethoxy[4.1]MCP **5c** suitable for X-ray crystallography were both obtained by recrystallization from methanol–chloroform (1 : 1).

The perspective ORTEP drawings of **3c** and **5c** are illustrated in Figs. 2 and 3, with the atom-numbering system. Compound **3c** crystallized in centrosymmetric orthorhombic space group *Pbcn* (No. 60) and is located about a two-fold axis, since this molecule has crystallographic C_2 symmetry. Therefore, the asymmetric unit contains one half of a molecule (Z = 4). Compound **5c** crystallized in monoclinic space group $P2_1/c$ (No. 14) (Z = 4).

The X-ray crystallography clearly shows that both conformations of **3c** and **5c** adopt the *anti* form in which two aromatic rings are in a non-planar chain form. In **3c** the selected bond lengths of C1–C2 and C2–C3 in the tetramethylene chains and

Table 3 Coalescence temperature (T_c) and $\Delta G_c^{\ddagger}$ for conformational ring inversion of [2.*n*]MCP-1-enes **3**, and [*n*.1]MCPs **5** and **10**

Compd.	Number of methylene units, *n*	T_c/°C[a]	$\Delta G_c^{\ddagger}$ (kcal mol^{-1})[a]
3b	3	70	15.6
3c	4	−30	10.7
3d	5	<−100	
5c	4	90	17.3
5d	5	<−100	
10c	4	90	17.3
10d	5	<−100	

[a] T_c and $\Delta G_c^{\ddagger}$ were determined in $CDCl_3$–CS_2 (1 : 3) or $CDBr_3$, using $SiMe_4$ as a reference.

† 1 cal = 4.184 J.

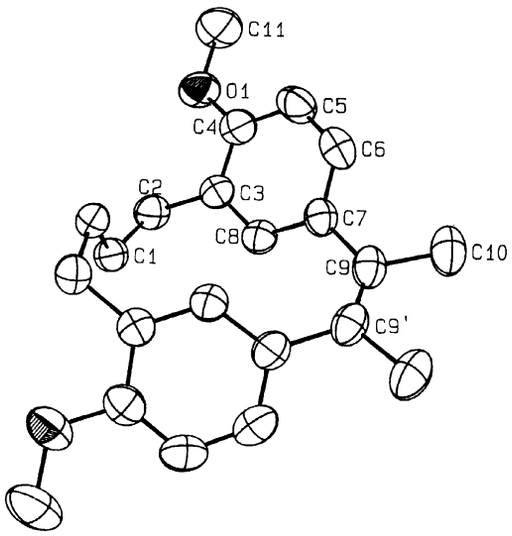


Fig. 2 X-Ray structure of 6,14-dimethoxy-1,2-dimethyl[2.4]MCP-1-ene **3c**. Thermal ellipsoids are drawn at the 50% probability level. For clarity all hydrogen atoms are omitted.

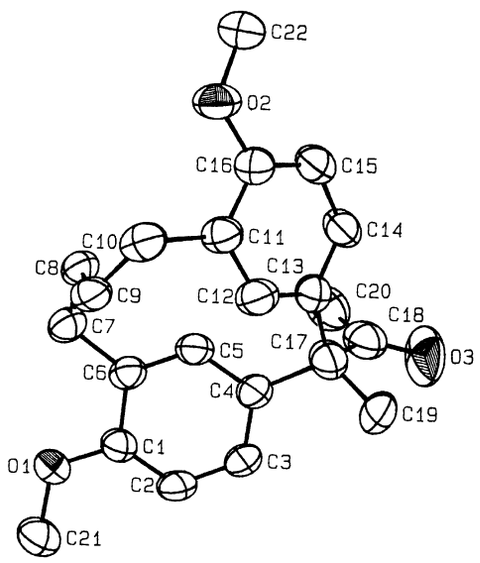


Fig. 3 X-Ray structure of 11-acetyl-6,15-dimethoxy-11-methyl[4.1]-MCP **5c**. Thermal ellipsoids are drawn at the 50% probability level. For clarity all hydrogen atoms are omitted.

C7–C9 and C9–C10 in the ethylenic chains have suitable values, 1.530(4), 1.507(4), 1.503(4), and 1.509(5) Å, respectively, and the length of the double bond is 1.359(4) Å. The bond angles defined by C8–C7–C9 and C7–C9–C9′ are 124.1(3) and 123.0(3)°, showing that **3c** displays a slightly distorted conformation. The two benzene rings of **3c** distort into a slight boat shape and slightly deviate from planarity; the dihedral angles of the plane defined by C3–C4–C6–C7 between the planes defined by C3–C8–C7 and C4–C5–C6 are 3.67(3)° and 1.58(3)°, respectively. The tetramethylene bridge chains do not display a fully extended *anti* conformation, probably to minimize the strain. Both methoxy groups on the benzene rings of **3c** point towards the out side, away from the tetramethylene bridge chain. This might contribute to avoiding steric crowding with hydrogens and carbons of the bridge chains.

Again, in **5c** both methoxy groups on the benzene rings, as in **3c**, point towards the outside, away from the tetramethylene bridge chain. In **5c** the two benzene rings also distort into a slight boat shape. The bond angle of the bridged methylene moiety, C13–C17–C4 is 106.6 (3)°, and the torsional twists of the two benzene rings (C1–C2–C3–C4–C5–C6 and C11–C12–C13–C14–C15–C16) relative to the C13–C17–C4 plane are 33.2 (3)° and 44.2 (3)°, respectively.

The UV spectra of the [*n*.1]MCPs **10c**,**d** showed different absorption curves to that of the model acyclic compound, 1,1-bis(4-methoxyphenyl)ethane **11**. A small bathochromic shift at 285 nm (log $\varepsilon_{max} = 3.55$) in comparison with that of **11** at 277 nm (log $\varepsilon_{max} = 3.62$) was observed for the [4.1]MCPs **10c**, which is ascribed to a transannular interaction between the two benzene rings and an increase in the strain of these systems.[15] The same phenomenon is also observed in [5.1]MCP **10d** but the bathochromic shift is smaller than that of [4.1]MCPs **10c**.

Tetracyanoethylene (TCNE) complexes have often been used in studies on the relative π-base strength of various methyl-substituted benzenes.[30] The π-basicity of the donor molecules increases with an increase in the number of substituted methyl groups and/or stacking benzene rings and an increase in the face-to-face overlapping between aromatic nuclei.[31] A solution of [4.1]MCP **10c** and TCNE in CH_2Cl_2 present a purple color and the charge-transfer band at 606 nm (log $\varepsilon = 1.138$) was observed in its UV spectrum. This absorption is due to the formation of 1 : 1 charge-transfer complex among the electron donor, [4.1]MCP, and the electron acceptor, TCNE. The position of the absorption maximum and the shape of the absorption curve remain unchanged when a 4–12-fold excess of TCNE was added. However, the charge-transfer absorption band of the reference compound, 2,4-dimethylanisole **12**, with TCNE was observed at 414 nm (log $\varepsilon = 2.073$). Such a red shift could be due to the through-space electronic interaction of the opposite uncomplexed benzene ring, which tends to work as a π-electron donor. In contrast to [4.1]MCP **10c**, which exhibits the charge-transfer absorption band with TCNE at 606 nm (log $\varepsilon = 1.138$), a mixture of TCNE and [5.1]MCP **10d** exhibits an absorption peak at 510 nm (log $\varepsilon = 1.716$), while that of [6.1]MCP **10e** is shifted to 501 nm (log $\varepsilon = 0.931$). Introduction of the one methylene inert to the tetramethylene bridge of **10c** causes a larger blue shift as indicated by the 96 nm shift for the CT-band of **10d** due to the decreased transannular π-electron donation from the non-complexed benzene ring to the complexed benzene ring.

In conclusion, a new synthesis of [2.*n*]MCP-1-enes and [2.*n*]MCP-1,2-diols by a McMurry cyclization has been developed. Protic acid- or Lewis acid-induced pinacol rearrangements of [2.*n*]MCP-1,2-diols can be applied to the synthesis of [*n*.1]MCPs. Further studies on the present novel ring contraction of [2.*n*]cyclophanes with glycol units at the ethylene bridge to afford [*n*.1]cyclophanes are now in progress.

Experimental

Mps (Yanagimoto MP-S1) and bps are uncorrected. NMR spectra were determined at 270 MHz with a Nippon Denshi JEOL FT-270 NMR spectrometer with $SiMe_4$ as an internal reference: *J*-values are given in Hz. IR spectra were measured for samples as KBr pellets or a liquid film on NaCl plates in a Nippon Denshi JIR-AQ2OM spectrophotometer. UV spectra were measured by a Shimadzu 240 spectrophotometer. Mass spectra were obtained on a Nippon Denshi JMS-01SA-2 spectrometer at 75 eV using a direct-inlet system through GLC.

Materials

The preparations of 1,*n*-bis(5-*tert*-butyl-2-methoxyphenyl)-alkanes **1**[11] and 1,*n*-bis(5-acetyl-2-methoxyphenyl)alkanes **2a**–**2c**[13] have been previously described. 1,1-Bis(4-methoxyphenyl)-ethane **11** was prepared according to the literature procedure.[10*b*]

Acetylation of 1,*n*-bis(5-*tert*-butyl-2-methoxyphenyl)alkanes 1 with acetyl chloride in the presence of $AlCl_3$–$MeNO_2$

Typical procedure. To a solution of 1,5-bis(5-*tert*-butyl-2-methoxyphenyl)pentane **1d** (3.96 g, 10 mmol) and acetyl chlor-

ide (2.1 cm^3, 30 mmol) in CH_2Cl_2 (80 cm^3) was added a solution of aluminium chloride (5.94 g, 44.5 mmol) in nitromethane (10 cm^3) at 0 °C. After the reaction mixture had been stirred at room temperature for 2 h, it was poured into ice–water (100 cm^3). The organic layer was extracted with CH_2Cl_2 (50 $cm^3 \times 2$). The extract was washed with water (50 $cm^3 \times 2$), dried (Na_2SO_4), and concentrated. The residue was chromatographed over silica gel (Wako C-300, 300 g) with $CHCl_3$ as eluent to give crude **2d** as a colorless solid. Recrystallization from hexane–benzene (1 : 1) gave *1,5-bis(5-acetyl-2-methoxyphenyl)pentane* **2d** (3.35 g, 80%) as prisms, mp 91–92 °C; ν_{max}(KBr)/cm^{-1} 1672 (C=O); δ_H($CDCl_3$) 1.40–1.46 (2 H, m), 1.60–1.66 (4 H, m), 2.56 (6 H, s), 2.63 (4 H, t, *J* 7.8), 3.89 (6 H, s), 6.86 (2 H, d, *J* 8.8), 7.77 (2 H, d, *J* 2.4) and 7.82 (2 H, dd, *J* 8.8 and 2.4); *m*/*z* 368 (M^+) (Found: C, 75.20; H, 7.75. $C_{23}H_{28}O_4$ requires C, 74.97; H, 7.66%).

Similarly, compound **2e** was prepared in 64% yield in the same manner as described above.

1,6-Bis(5-acetyl-2-methoxyphenyl)hexane ***2e***. This compound was obtained as prisms [from hexane–benzene (1 : 1)], mp 118–120 °C; ν_{max}(KBr)/cm^{-1} 1667 (C=O); δ_H($CDCl_3$) 1.35–1.42 (4 H, m), 1.51–1.64 (4 H, m), 2.55 (6 H, s), 2.62 (4 H, t, *J* 7.6), 3.88 (6 H, s), 6.87 (2 H, d, *J* 8.8), 7.77 (2 H, d, *J* 2.0) and 7.83 (2 H, dd, *J* 8.8 and 2.0); *m*/*z* 382 (M^+) (Found: C, 75.52; H, 7.90. $C_{24}H_{30}O_4$ requires C, 75.36; H, 7.91%).

General procedure for the McMurry coupling reaction of 2

Typical procedure. The McMurry reagent was prepared from $TiCl_4$ [23.8 g (13.8 cm^3), 125 mmol] and 18 g (275 mmol) of Zn powder in 500 cm^3 of dry THF, under nitrogen. A solution of 1,3-bis(5-acetyl-2-methoxyphenyl)propane **2b** (2.14 g, 6.3 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 an additional 8 h, cooled to room temperature, and hydrolyzed with 10% aq. K_2CO_3 (200 cm^3) at 0 °C. The reaction mixture was extracted with CH_2Cl_2 (200 $cm^3 \times 3$). 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 (1 : 1)benzene and $CHCl_3$ as eluents to give **3b** (1.55 g, 80%), **6b** (10 mg, 0.5%) and **4b** (151 mg, 7%) each as a colorless solid. Recrystallization of crude **3b** from methanol gave *6,13-dimethoxy-1,2-dimethyl[2.3]metacyclophan-1-ene* **3b** as prisms, mp 122–125 °C; ν_{max}(KBr)/cm^{-1} 2911, 2836, 1598, 1498, 1458, 1252, 1237, 1142, 1029 and 803; δ_H($CDCl_3$; 27 °C) 1.69 (2 H, br m), 1.95 (2 H, br m), 2.19 (6 H, s), 2.92 (2 H, br m), 3.83 (6 H, s), 5.69 (2 H, br s), 6.72 (2 H, br d) and 7.03 (2 H, br dd); δ_H($CDCl_3$–CS_2, 1 : 3; −40 °C) 1.59–1.77 (2 H, m), 1.90–2.05 (2 H, m), 2.20 (6 H, s), 2.86–2.98 (2 H, m), 3.85 (6 H, s), 5.68 (2 H, d, *J* 2.4), 6.73 (2 H, d, *J* 8.3) and 7.08 (2 H, dd, *J* 2.4 and 8.3); *m*/*z* 308 (M^+) (Found: C, 81.88; H, 7.74. $C_{21}H_{24}O_2$ requires C, 81.78; H, 7.84%).

6,13,23,30-Tetramethoxy-1,2,18,19-tetramethyl[2.3.2.3]metacyclophane-1,18-diene ***6b***. This compound was obtained as prisms [from hexane–benzene (1 : 1)], mp 234–236 °C; ν_{max}(KBr)/cm^{-1} 2949, 2832, 1606, 1500, 1463, 1244, 1033 and 890; δ_H($CDCl_3$) 1.34–1.47 (4 H, m), 2.14 (12 H, s), 2.22 (8 H, t, *J* 7.8), 3.72 (12 H, s), 6.63 (4 H, d, *J* 8.3), 6.65 (4 H, d, *J* 2.4) and 6.87 (4 H, dd, *J* 8.3 and 2.4); *m*/*z* 616 (M^+) (Found: C, 81.84; H, 7.85. $C_{42}H_{48}O_4$ requires C, 81.78; H, 7.84%).

10,11-Dihydroxy-5,15-dimethoxy-10,11-dimethyl[3.2]metacyclophane ***4b***. This compound was obtained as prisms [from hexane–benzene (2 : 1)], mp 216–218 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3400 (OH), 2941, 1606, 1505, 1250, 1108, 1032, 818; δ_H($CDCl_3$) 1.40 (3 H, s), 1.78 (3 H, s), 1.78–1.99 (2 H, m), 2.04–2.18 (2 H, m), 2.30 (1 H, s, replaced by D_2O), 2.91–3.06 (2 H, m), 3.02 (1 H, br s, replaced by D_2O), 3.86 (3 H, s), 3.87 (3 H, s), 4.96 (1 H, d, *J* 2.4), 5.49 (1 H, d, *J* 2.4), 6.74 (1 H, d, *J* 8.8), 6.79 (1 H, d, *J* 8.8), 7.15 (1 H, dd, *J* 8.8 and 2.4) and 7.36 (1 H, dd, *J* 8.8 and 2.4); *m*/*z* 342 (M^+) (Found: C, 74.64; H, 7.75. $C_{21}H_{26}O_4$ requires C, 74.63; H, 7.51%).

Similarly, compounds **6a**, **3c**–**3e**, **4a**, **4c**, **4d** and **5d**, **5e** were prepared in the same manner as described above. The yields are listed in Table 1.

1,2-Dihydroxy-6,12-dimethoxy-1,2-dimethyl[2.2]metacyclophane ***4a***. This compound was obtained as prisms [from hexane–benzene (1 : 2)], mp 202 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3505, 3381 (OH), 2960, 2923, 1598, 1502, 1252, 1136, 1081, 1023, 818, 618; δ_H($CDCl_3$) 1.30 (3 H, s), 1.54–1.72 (2 H, m), 1.83 (3 H, s), 2.08 (1 H, s, replaced by D_2O), 2.94 (1 H, s, replaced by D_2O), 3.47–3.58 (2 H, m), 3.88 (6 H, s), 4.36 (1 H, d, *J* 2.4), 4.83 (1 H, d, *J* 2.4), 6.81 (1 H, d, *J* 8.5), 6.88 (1 H, d, *J* 8.5), 7.13 (1 H, dd, *J* 8.5, 2.4) and 7.40 (1 H, dd, *J* 8.5 and 2.4); *m*/*z* 328 (M^+) (Found: C, 73.34; H, 7.29. $C_{20}H_{24}O_4$ requires C, 73.15; H, 7.37%).

6,12,22,28-Tetramethoxy-1,2,17,18-tetramethyl-[2.2.2.2]metacyclophane-1,17-diene ***6a***. This compound was obtained as prisms [from hexane–benzene (1 : 3)], mp 262–264 °C; ν_{max}(KBr)/cm^{-1} 2926, 2833, 1603, 1500, 1458, 1244, 1032 and 810; δ_H($CDCl_3$) 2.17 (12 H, s), 2.51 (8 H, s), 3.72 (12 H, s), 6.57 (4 H, d, *J* 8.8), 6.79 (4 H, dd, *J* 8.8 and 2.4) and 6.91 (4 H, d, *J* 2.4); *m*/*z* 588 (M^+) (Found: C, 81.35; H, 7.55. $C_{40}H_{44}O_4$ requires C, 81.60; H, 7.53%).

6,14-Dimethoxy-1,2-dimethyl[2.4]metacyclophan-1-ene ***3c***. This compound was obtained as prisms (from methanol), mp 122–124 °C; ν_{max}(KBr)/cm^{-1} 2955, 2929, 2867, 2834, 1598, 1497, 1457, 1286, 1238, 1137, 1100, 1026 and 811; δ_H($CDCl_3$; 27 °C) 1.57 (4 H, br s), 2.20 (6 H, s), 2.47 (4 H, br s), 3.77 (6 H, s), 6.62 (2 H, d, *J* 2.4), 6.79 (2 H, d, *J* 8.4) and 7.08 (2 H, dd, *J* 8.4 and 2.4); δ_H($CDCl_3$–CS_2, 1 : 3; −70 °C) 0.60–0.87 (2 H, m), 1.32–1.55 (2 H, m), 1.90–2.19 (2 H, m), 2.15 (6 H, s), 2.62–2.84 (2 H, m), 3.76 (6 H, s), 6.51 (2 H, d, *J* 2.4), 6.73 (2 H, d, *J* 8.8) and 7.03 (2 H, dd, *J* 8.8 and 2.4); *m*/*z* 322 (M^+) (Found: C, 82.17; H, 8.24. $C_{22}H_{26}O_2$ requires C, 81.95; H, 8.13%).

6,15-Dimethoxy-1,2-dimethyl[2.5]metacyclophan-1-ene ***3d***. This compound was obtained as prisms (from methanol), mp 105–107 °C; ν_{max}(KBr)/cm^{-1} 2926, 1859, 1604, 1504, 1461, 1256, 1238, 1129, 1103, 1033 and 807; δ_H($CDCl_3$) 0.73–0.78 (2 H, m), 1.37–1.47 (4 H, m), 2.06 (6 H, s), 2.45–2.49 (4 H, m), 3.65 (6 H, s), 6.67 (2 H, d, *J* 8.8), 6.76 (2 H, d, *J* 2.4) and 6.92 (2 H, dd, *J* 8.8 and 2.4); *m*/*z* 336 (M^+) (Found: C, 81.97; H, 8.46. $C_{23}H_{28}O_2$ requires C, 82.10; H, 8.39%).

6,16-Dimethoxy-1,2-dimethyl[2.6]metacyclophan-1-ene ***3e***. This compound was obtained as prisms (from methanol), mp 114–115 °C; ν_{max}(KBr)/cm^{-1} 2916, 2855, 1603, 1495, 1463, 1298, 1238, 1132, 1034 and 818; δ_H($CDCl_3$) 0.80–0.92 (4 H, m), 1.50–1.61 (4 H, m), 2.11 (6 H, s), 2.45–2.52 (4 H, m), 3.72 (6 H, s), 6.58 (2 H, d, *J* 8.8), 6.77 (2 H, d, *J* 2.4) and 6.80 (2 H, dd, *J* 8.8 and 2.4); *m*/*z* 350 (M^+) (Found: C, 82.38; H, 8.68. $C_{24}H_{30}O_2$ requires C, 82.24; H, 8.63%).

11,12-Dihydroxy-6,16-dimethoxy-11,12-dimethyl[4.2]metacyclophane ***4c***. This compound was obtained as prisms [from hexane–benzene (2 : 1)], mp 186–189 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3488 (OH); δ_H($CDCl_3$) 1.06–1.09 (2 H, m), 1.36 (6 H, s), 1.60–1.68 (2 H, m), 2.15–2.32 (2 H, m), 2.52 (2 H, s, replaced by D_2O), 2.81–2.99 (2 H, m), 3.83 (6 H, s), 6.04 (2 H, d, *J* 2.4), 6.85 (2 H, d, *J* 8.8) and 7.61 (2 H, dd, *J* 8.8 and 2.4); *m*/*z* 356 (M^+) (Found: C, 73.94; H, 7.86. $C_{22}H_{28}O_4$ requires C, 74.13; H, 7.92%).

12,13-Dihydroxy-6,17-dimethoxy-12,13-dimethyl[5.2]metacyclophane ***4d***. This compound was obtained as prisms [from hexane–benzene (2 : 1)], mp 154–156 °C; ν_{max}(KBr)/cm^{-1} 3495 (OH); δ_H($CDCl_3$) 1.11–1.16 (2 H, m), 1.34–1.43 (4 H, m), 1.54 (6 H, s), 2.06–2.10 (2 H, m), 2.40 (2 H, s, replaced by D_2O), 2.73–2.78 (2 H, m), 3.83 (6 H, s), 6.13 (2 H, d, *J* 8.8), 6.84 (2 H, d, *J* 2.4) and 7.57 (2 H, dd, *J* 8.8 and 2.4); *m*/*z* 370 (M^+) (Found: C, 74.54; H, 8.19. $C_{23}H_{30}O_4$ requires C, 74.56; H, 8.16%).

12-Acetyl-7,16-dimethoxy-12-methyl[5.1]metacyclophane ***5d***. This compound was obtained as prisms (from hexane), mp 161–164 °C; ν_{max}(KBr)/cm^{-1} 1708 (C=O); δ_H($CDCl_3$) 1.20–1.26 (2 H, m), 1.40–1.50 (4 H, m), 1.84 (3 H, s), 2.19 (3 H, s), 2.48–2.54 (4 H, m), 3.83 (6 H, s), 6.72 (2 H, d, *J* 2.4), 6.78 (2 H, d, *J* 8.8) and 7.10 (2 H, dd, *J* 8.8 and 2.4); *m*/*z* 352 (M^+) (Found: C, 78.07; H, 7.99. $C_{23}H_{28}O_3$ requires C, 78.38; H, 8.01%).

13-Acetyl-8,17-dimethoxy-13-methyl[6.1]metacyclophane ***5e***. This compound was obtained as pale yellow prisms (from hexane), mp 144–146 °C; ν_{max}(KBr)/cm^{-1} 1711 (C=O); δ_H($CDCl_3$) 1.12–1.18 (4 H, m), 1.63–1.75 (4 H, m), 1.74 (3 H, s), 2.11 (3 H, s), 2.54–2.62 (4 H, m), 3.83 (6 H, s), 6.80 (2 H, d, *J* 8.8), 6.90 (2 H, d, *J* 2.9) and 7.08 (2 H, dd, *J* 8.8 and 2.9); *m*/*z* 366 (M^+) (Found: C, 78.76; H, 8.25. $C_{24}H_{30}O_3$ requires C, 78.65; H, 8.25%).

Treatment of 4c with iodine–acetic acid in 1,4-dioxane

To a solution of 1,2-dihydroxy-6,14-dimethoxy-1,2-dimethyl-[2.4]metacyclophane **4c** (356 mg, 1 mmol) in a mixture of 1,4-dioxane (20 cm^3) and acetic acid (40 cm^3) was added powdered iodine (100 mg, 0.39 mmol) at room temperature. After the reaction mixture had been stirred under reflux for 30 min, it was poured into ice–water (100 cm^3). The organic layer was extracted with CH_2Cl_2 (50 cm^3 × 2). The extract was washed successively with 10% aq. sodium thiosulfate (20 cm^3 × 2) and water (50 cm^3 × 2), dried (Na_2SO_4), and concentrated. The residue was chromatographed over silica gel (Wako C-300, 300 g) with hexane–benzene (1 : 1), benzene, benzene–$CHCl_3$, and $CHCl_3$ as eluent and recrystallization from methanol or hexane–benzene (1 : 1) to give **8c** (29 mg, 7%), **5c** (156 mg, 45%), **7c** (20 mg, 5%), and **2c** (30 mg, 8%) as colorless prisms, respectively.

6,16-Dimethoxy-11,12-dimethylene[4.2]metacyclophane 8c. This compound was obtained as prisms (from methanol), mp 101–102 °C; ν_{max}(KBr)/cm^{-1} 2929, 1500, 1244, 1119, 1029 and 902; δ_H($CDCl_3$) 1.33–1.44 (4 H, m), 2.46–2.58 (4 H, m), 3.76 (6 H, s), 5.04 (2 H, d, *J* 2.2), 5.46 (2 H, d, *J* 2.2), 6.42 (2 H, d, *J* 2.0), 6.73 (2 H, d, *J* 8.3) and 6.99 (2 H, d, *J* 2.0 and 8.3); *m*/*z* 320 (M^+) (Found: C, 82.04; H, 7.75. $C_{22}H_{24}O_2$ requires C, 82.46; H, 7.55%).

11-Hydroxy-6,16-dimethoxy-11-methyl-12-methylene[4.2]-metacyclophane 7c. This compound was obtained as yellow oil; ν_{max}(NaCl)/cm^{-1} 3488 (OH); δ_H($CDCl_3$) 1.07–1.44 (4 H, br m), 1.67 (3 H, br s), 2.18–2.75 (4 H, br m), 2.68 (1 H, s, replaced by D_2O), 3.79 (3 H, s), 3.84 (3 H, s), 4.86 (1 H, d, *J* 1.7), 5.44 (1 H, d, *J* 1.7), 5.57 (1 H, br d), 6.60 (1 H, br d), 6.77 (1 H, d, *J* 8.3), 6.91 (1 H, d, *J* 8.3), 6.99 (1 H, dd, *J* 8.3 and 2.0) and 7.42 (1 H, br d); *m*/*z* 338 (M^+) (Found: C, 78.34; H, 7.67. $C_{22}H_{26}O_3$ requires C, 78.07; H, 7.74%).

11-Acetyl-6,15-dimethoxy-11-methyl[4.1]metacyclophane 5c. This compound was obtained as prisms [from hexane–benzene (1 : 1)], mp 126–128 °C; ν_{max}(KBr)/cm^{-1} 1704 (C=O); δ_H($CDCl_3$) 0.84–1.06 (2 H, m), 1.56–1.81 (2 H, m), 1.80 (3 H, s), 2.22 (3 H, s), 2.27–2.41 (2 H, m), 2.62–2.77 (2 H, m), 3.80 (3 H, s), 3.81 (3 H, s), 6.33 (1 H, br s), 6.56 (1 H, d, br s), 6.66 (1 H, d, *J* 8.3), 6.72 (1 H, d, *J* 8.3), 6.91 (1 H, dd, *J* 8.3 and 2.4) and 7.21 (1 H, dd, *J* 8.3 and 2.4); δ_C($CDCl_3$) 24.15, 24.22, 24.35, 27.81, 55.04, 61.33, 107.34, 107.39, 123.87, 124.59, 126.78, 127.75, 133.92, 136.88, 137.87, 140.35, 156.62, 156.90 and 208.98; *m*/*z* 338 (M^+) (Found: C, 78.28; H, 7.67. $C_{22}H_{26}O_3$ requires C, 78.07; H, 7.74%).

Similarly, compounds **5d** and **5e** were prepared in 65, 95% yields in the same manner as described above.

Treatment of 4c with BF_3–diethyl ether in dichloromethane

To a suspension of **4c** (35.6 mg, 0.1 mmol) in CH_2Cl_2 (3 cm^3) was added BF_3·Et_2O (8.4 mg, 0.059 mmol) and the mixture was stirred at room temperature for 30 min. The reaction mixture was quenched by water (5 cm^3), and extracted with CH_2Cl_2 (10 cm^3 × 2). The combined extracts were washed successively with 5% aq. $NaHCO_3$ (10 cm^3) and water (10 cm^3 × 2), dried with Na_2SO_4, and concentrated to leave a residue, which was chromatographed over silica gel (Wako C-300, 300 g) with benzene as eluent, and recrystallized from hexane–benzene (1 : 1) to give **5c** (11 mg, 33%) as colorless prisms.

Similarly, compounds **4d** and **4e** were treated with BF_3–diethyl ether as described above to give **5d** and **5e** in 62, 96% yield, respectively.

Treatment of 4b with trifluoromethanesulfonic acid in dichloromethane

To a suspension of **4b** (34 mg, 0.1 mmol) in CH_2Cl_2 (4 cm^3) was added trifluoromethanesulfonic acid (0.02 cm^3, 0.2 mmol) and the mixture was stirred at room temperature for 30 min. The cooled solution was quenched by water (5 cm^3), and extracted with CH_2Cl_2 (10 cm^3 × 2). The combined extracts were washed successively with 5% aq. $NaHCO_3$ (10 cm^3) and water (10 cm^3 × 2), dried with Na_2SO_4, and concentrated to leave a residue, which was chromatographed over silica gel (Wako C-300, 300 g) with benzene as eluent and recrystallized from hexane–benzene (1 : 1) to give **9b** (30 mg, 98%) as pale brown solid. Recrystallization from methanol to give *3,6-dimethoxy-9,10-dimethyl-4,5-propanophenanthrene* **9b** as colorless prisms, mp 161–163 °C; ν_{max}(KBr)/cm^{-1} 2927, 1588, 1498, 1264, 1218, 1131, 1032 and 798; δ_H($CDCl_3$) 2.45–2.56 (2 H, m), 2.59 (6 H, s), 2.81–2.84 (4 H, m), 3.97 (6 H, s), 7.27 (2 H, d, *J* 8.8), 7.88 (2 H, d, *J* 8.8); *m*/*z* 306 (M^+) [Calc. for $C_{21}H_{22}O_2$ (306.41): C, 82.32; H, 7.24. Found: C, 82.07; H, 7.20%].

Similarly, compound **2a** was treated with trifluoromethanesulfonic acid as described above for 1 min to give **9a** in 98% yield.

3,6-Dimethoxy-9,10-dimethyl-4,5-ethanophenanthrene ***9a***. This compound was obtained as pale brown prisms (from MeOH), mp 198–200 °C; δ_H($CDCl_3$) 2.54 (6 H, s), 3.14 (4 H, s), 3.88 (6 H, s), 7.16 (2 H, d, *J* 9.3), 7.77 (2 H, d, *J* 9.3); *m*/*z* 292 (M^+) [Calc. for $C_{20}H_{20}O_2$ (292.38): C, 82.16; H, 6.89. Found: C, 82.23; H, 6.73%].

Cleavage reaction of ketones 5 with KOH to give 10

Typical procedure. A mixture of **5c** (33 mg, 0.1 mmol) and potassium hydroxide (1.6 g, 40 mmol) was heated at 180 °C for 3 h. The cooled melt was dissolved in water (10 cm^3) and extracted with CH_2Cl_2 (20 cm^3 × 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 (1 : 1) as eluent to give **10c** (28 mg, 91%) as a colorless solid. Recrystallization of crude **10c** from methanol gave 6,15-dimethoxy-11-methyl[4.1]metacyclophane **10c** as prisms, mp 148–149 °C; ν_{max}(KBr)/cm^{-1} 2862, 1498, 1254, 1235, 1110, 1034 and 806; δ_H($CDCl_3$) 0.74–0.94 (2 H, m), 1.50–1.69 (2 H, m), 1.63 (3 H, d, *J* 7.2), 2.22–2.34 (2 H, m), 2.62–2.82 (2 H, m), 3.75 (3 H, s), 3.76 (3 H, s), 4.12 (1 H, q, *J* 7.2), 6.00 (1 H, br s), 6.21 (1 H, br s), 6.68 (1 H, d, *J* 8.3), 6.73 (1 H, d, *J* 8.3), 7.11 (1 H, dd, *J* 8.3 and 2.4), 7.17 (1 H, dd, *J* 8.3 and 2.4); *m*/*z* 296 (M^+) (Found: C, 81.22; H, 8.03. $C_{20}H_{24}O_2$ requires C, 81.04; H, 8.16%).

Similarly, compounds **10d** and **10e** were prepared in 95, 68% yield in the same manner as described above.

7,16-Dimethoxy-12-methyl[5.1]metacyclophane ***10d***. This compound was obtained as prisms (from MeOH), mp 105–106 °C; ν_{max}(KBr)/cm^{-1} 2930, 1498, 1239, 1124, 1034 and 810; δ_H($CDCl_3$) 0.94–1.13 (2 H, m), 1.35–1.48 (4 H, m), 1.65 (3 H, d, *J* 7.3), 2.42–2.54 (4 H, m), 3.79 (6 H, s), 4.09 (1 H, q, *J* 7.3), 6.56 (2 H, d, *J* 2.2), 6.73 (2 H, d, *J* 8.3) and 7.12 (2 H, dd, *J* 8.3 and

Table 4 Crystallographic data and data-collection details for 6,14-dimethoxy-1,2-dimethyl[2.4]MCP-1-ene **3c** and 11-acetyl-6,15-dimethoxy-11-methyl[4.1]MCP **5c**

	3c	**5c**
Formula	$C_{22}H_{26}O_2$	$C_{22}H_{26}O_3$
FW	322.45	338.45
Size/mm	0.35 × 0.35 × 0.10	0.30 × 0.25 × 0.20
Crystal system	Orthorhombic	Monoclinic
Space group	*Pbcn* (No. 60)	$P2_1/c$ (No. 14)
a/Å	8.6418 (6)	14.8271 (13)
b/Å	10.318 (1)	12.8995 (1)
c/Å	19.776 (1)	9.5892 (5)
β/°		95.9810 (57)
V/Å^3	1763.4 (2)	1824.1 (2)
Z	4	4
ρ_{calc}/g cm^{-3}	1.124	1.066
T/K	295	295
Radiation	Cu-K_α	Cu-K_α
λ/Å	1.541 84	1.541 84
μ/cm^{-1}	5.19	6.02
No. of reflections	2101	4061
Unique reflections	1813	3665
Observed reflections	1039	2489
R	0.059	0.083
R_w[a]	0.077	0.121
S	2.51	3.89

[a] $\omega = 4(F_o)^2/[(\sigma I_o)2 + 0.0016(F_o)^4]$.

2.2); *m*/*z* 310 (M^+) [Found: C, 81.31; H, 8.54. $C_{21}H_{26}O_2$ (310.44) requires C, 81.25; H, 8.44%].

8,17-Dimethoxy-13-methyl[6.1]metacyclophane ***10e***. This compound was obtained as prisms (from MeOH), mp 115–116 °C; ν_{max}(KBr)/cm^{-1} 2933, 1500, 1249, 1112, 1032 and 810; δ_H($CDCl_3$) 0.96–1.05 (4 H, m), 1.52–1.68 (4 H, m), 1.61 (3 H, d, *J* 6.8), 2.50–2.54 (4 H, m), 3.82 (6 H, s), 4.10 (1 H, q, *J* 6.8), 6.57 (2 H, d, *J* 2.4), 6.79 (2 H, d, *J* 8.3) and 7.19 (2 H, dd, *J* 8.3 and 2.4); *m*/*z* 324 (M^+) [Found: C, 81.53; H, 8.65. $C_{22}H_{28}O_2$ (324.47) requires C, 81.44; H, 8.7%].

Crystal data and refinement details for 6,14-dimethoxy-1,2-dimethyl[2.4]metacyclophan-1-ene 3c‡

The X-ray analysis was performed with the MolEN program package[32] and the structure was solved uneventfully by direct methods (SIR 88).[33] Refinement was by full-matrix least squares and the 110 parameters refined were atomic coordinates, temperature factors (anisotropic for carbon atoms), scale factor, and secondary extinction coefficient. No corrections were made for absorption. The 12 independent non-hydrogen atoms were refined anisotropically. The 13 independent hydrogen atoms were located at calculated positions thermally fixed at B_{iso} = 5.0 Å and were included in refinement, but restrained to ride on the atoms to which they are bonded.

Crystal data and refinement details for 11-acetyl-6,15-dimethoxy-11-methyl[4.1]metacyclophane 5c‡

The X-ray analysis was performed with the MolEN program package[32] and the structure was solved uneventfully by direct methods (SIR 88).[33] Refinement was by full-matrix least squares and the 227 parameters refined were atomic coordinates, temperature factors (anisotropic for carbon atoms), scale factor, and secondary extinction coefficient. No corrections were made for absorption. The 25 independent non-hydrogen atoms were refined anisotropically. The 26 independent hydrogen atoms were located at calculated positions thermally fixed at B_{iso} = 5.0 Å^2 and were included in the refinement, but restrained to ride on the atoms to which they are bonded.

‡ CCDC reference numbers 155635 and 155636. See http://www.rsc.org/suppdata/p1/b0/b010075g/ for crystallographic files in .cif or other electronic format.

Crystallographic data and data-collection details for **3c** and **5c** are given in Table 4.

The refined non-hydrogen atomic coordinates, temperature factors (anisotropic for carbon atoms), scale factor, and secondary estimation coefficient are available, on request, from the Cambridge Crystallographic Data Centre.

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