Synthesis of 8-methyl[2.2]metacyclophanes and their charge-transfer complexes with tetracyanoethylene

Tomoe Shimizu, Katsuhiro Hita, Shofiur Rahman and Takehiko Yamato*

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

The regioselective 1:1 charge-transfer band of 13-substituted 8-methyl[2.2]metacyclophanes with tetracyanoethylene in CH_2Cl_2, attributable to the 8-methyl substituted benzene-site complex, are observed in the field of 556–605 nm, which is strongly affected by π-electron density of the opposite aromatic ring.

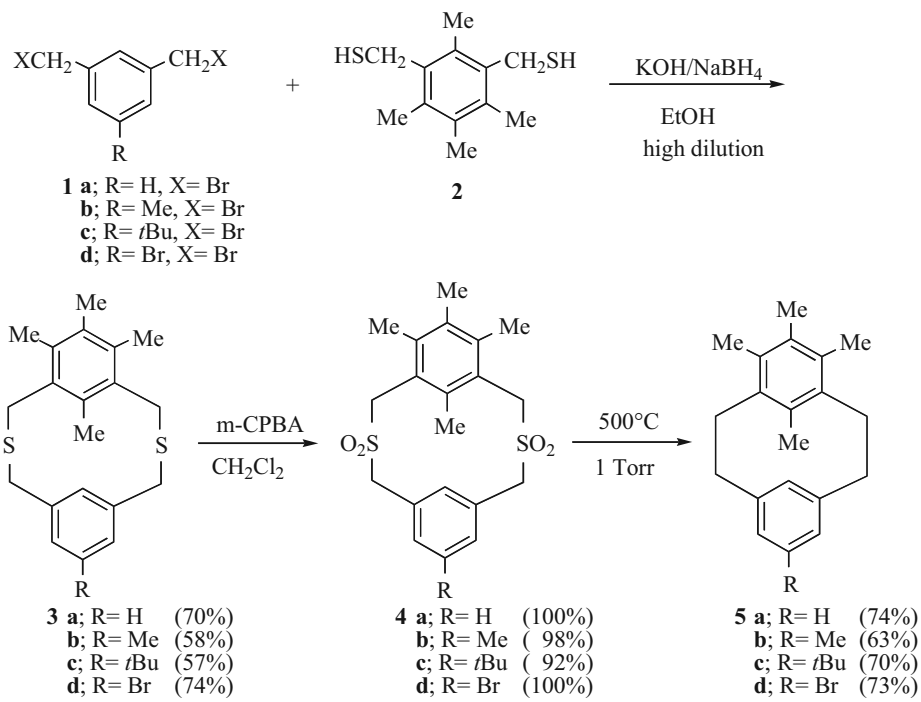
Keywords: cyclophanes, through-space electronic interaction, charge-transfer complex, substituent effect

[2.2]Metacyclophanes ([2.2]MCP) are distinguished by abnormal physical and chemical properties. Several qualitative explanations have been given for the origin of the abnormality: π-electron repulsion between the benzene rings,[1–7] hyperconjugation with the bridging C–C bonds,[8] nonplanarity of the benzene rings,[9] and transannular π–π interaction between the benzene rings.[10] Boschi and Schmidt[10] suggested from the ionisation energies and transannular π–π resonance integrals of [2.2]MCP that transannular π–π interaction may take place between C-8 and C-16. Later on, Sato and Takemura[11] comfirmed the transannular π–π interaction of [2.2]MCPs by comparison of the charge-transfer bands of cyclophane molecule with those of the corresponding acyclic models. [2.2]MCP showed only a moderate increase reflecting decreased overlap between the two aryl groups, compared with the large enhancement in the π-basicity in the lower membered paracyclophanes. However, only the charge transfer bands of 8,16-unsubstituted [2.2]MCP and its alkyl derivatives were investigated.

We have reported[12,13] the iodine-induced transannular cyclisation of 8-methoxy[2.2]MCPs to give 4,5,9,10-tetrahydropyrenes with remarkable ease and with high selectivity. The cycloisomerisation was found to be strongly affected by the substituents at C-13 and proceeded involvement of the iodine molecule, possibly via π complexation. These reactions are quite different from those of 8,16-unsubstituted [2.2]MCPs, which give 1,2,3,3a,4,5-hexahydropyrene[14,15] and might be attributed to the presense of the methoxy group at a position 8, which would increase the difference of the π-electron densities among the two benzene rings. Thus there is substantial interest in investigating the effects of substituents at positions 8 and 13 on the charge transfer complexes with tetracyanoethylene (TCNE). We report here on the synthesis and charge transfer complexation of a series of 8-methyl[2.2]MCPs with tetracyanoethylene.

Results and discussion

The preparative route of 13-substituted 8-methyl[2.2]MCPs **5a–d** is shown in Scheme 1. 1,3-Bis(bromomethyl)benzenes **1a–d** were prepared by bromination of the corresponding methylbenzenes with *N*-bromosuccinimide (NBS) in the presence of 2,2'-azobis(2,4-dimethylpentanenitrile) in a methylene dichloride solution. 1,3-Bis(sulfanylmethyl)-2,4,5,6-tetramethylbenzene **2** was prepared by chloromethylation of 1,3,4,5-tetramethylbenzene with chloromethyl methyl ether in the presence of $ZnCl_2$ followed



Scheme 1

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

by the treatment with thiourea as following to the reported procedure.[16] The cyclisation of bis(bromomethyl)benzenes **1a**–**d** and bis(sulfanylmethyl)benzene **2** was carried out under highly diluted conditions in 10% ethanolic KOH in the presence of a small amount of $NaBH_4$,[17–21] giving the desired 2,11-dithia[3.3]MCPs **3a**–**d** in good yield.

The assignment of structures for **3a**–**d** was readily apparent from its ^{1}H NMR spectrum. Thus the internal proton, methyl protons should show an upfield shift due to the ring current of the opposite aromatic ring.[1,2] For example, the ^{1}H NMR spectra of the dithia[3.3]MCP **3a** prepared in the present paper showed the internal proton and methyl protons at δ 5.58 and 1.82 ppm. The bridged CH_2SCH_2 bridge showed a pair of doublets at δ 3.27, 3.59 ppm (J = 16.0 Hz) and δ 3.80, 4.04 ppm (J = 12.0 Hz) at room temperature. With increasing temperature in DMSO-d_6, the doublets do not coalesce below 150 °C, respectively, and the energy barriers of flipping are both above 25 kcal mol^{-1}. These observations strongly suggest that compound **3a** adopts rigid *anti*-conformation. The similar findings were observed in **3b**–**d**. These data strongly support the rigid *anti*-[3.3]MCP structures **3b**–**d**.

Oxidation of **3a**–**d** with *m*-chloroperbenzoic acid in chloroform afforded the corresponding bis-sulfone **4a**–**d** in almost quantitative yield. Pyrolysis of **4a**–**d** under reduced pressure (1 torr) at 500 °C was carried out according to the reported method[17–21] to afford the corresponding desired 13-substituted 8-methyl[2.2]MCPs **5a**–**d** in good yields, respectively. Compound **5e** was obtained in 85% yield by the reaction of **5d** with MeONa in the presence of CuI in DMF–MeOH. Compound **5f** was obtained in 95% yield by the reaction of **5d** with CuCN in *N*-methylpyrrolidone.

The structures of **5a–f** were established on the basis of the base peak molecular ions in their mass spectra, and they were assigned the *anti*-stereochemistry on the basis of their ^{1}H NMR, since the 16-proton of **5a–f** appears at around δ 3.42–3.90 ppm, attributable to be shielded by the opposite ring. The similar upper field shifts of the internal methyl protons at 5-position were observed at around δ 0.48–1.09 ppm. These observations strongly suggest that compounds **5a–f** all adopt *anti*-conformations. The chemical shifts (δ) of the internal methyl protons and the aromatic internal protons at the 16-position of *anti*-8-methyl[2.2]MCPs **5a–f** are compiled in Table 1. The ring current effect of the opposite aromatic ring on the internal protons and methyl protons at the 8-position can be judged by the values of the chemical shift differences (Δδ).

In the ^{1}H NMR spectra of **5a**–**f**, the signals of the internal aromatic protons at 16 position and the methyl protons at 8-position are shifted to higher magnetic field by 3.10–3.58 ppm ($\delta_{2\text{-Ar}H}$ 7.00 ppm for 1,3-dimethyl-5-*tert*-butylbenzene) and 1.19–1.80 ppm ($\delta_{5\text{-Me}}$ 2.28 ppm for 1,2,3,5-tetramethylbenzene), respectively.[22] We have evaluated the substutuents effect of the 13-substituents by the chemical shift differences $\Delta\delta_{16\text{-H}}$ and $\Delta\delta_{8\text{-Me}}$ in comparison of the internal aromatic protons at 16 position and the methyl protons at 8-position of **5b**–**f** with those of **5a**. The introduction of the electron-donating group such as methyl, *tert*-butyl and methoxy group, caused the increase of the ring-current shielding of the internal aromatic protons at 16-position by $\Delta\delta_{8\text{-Me}}$ + 0.23–0.41 ppm attributable to the increased π-electrons density of the opposing benzene ring by the through-space electronic interaction. Interestingly, in the case of 13-cyano-8-methyl[2.2]MCP **5f** the large reduction of shielding of 8-methyl protons by $\Delta\delta_{8\text{-Me}}$ –0.60 ppm, whereas the large increase of shielding of the internal aromatic protons at 16-position by $\Delta\delta_{16\text{-H}}$ + 0.48 ppm. This can be interpreted as a reduction of the ring-current shielding caused by the opposite benzene ring by the introduction of the electron-withdrawing group such as cyano group. The through-space interaction between the 8-methyl group and the opposite benzene π-electrons arising from the C–H–π interaction may not shorten the distance between the 8-methyl group and the opposite benzene ring, whereas the 16–H–π interaction could make the distance between the 16-H proton and the opposite benzene ring shorter in the case of the cyano derivative **5f**. The different structures might be possible in the 8-methyl[2.2]MCPs **5** depending on the substituents at 13 position.

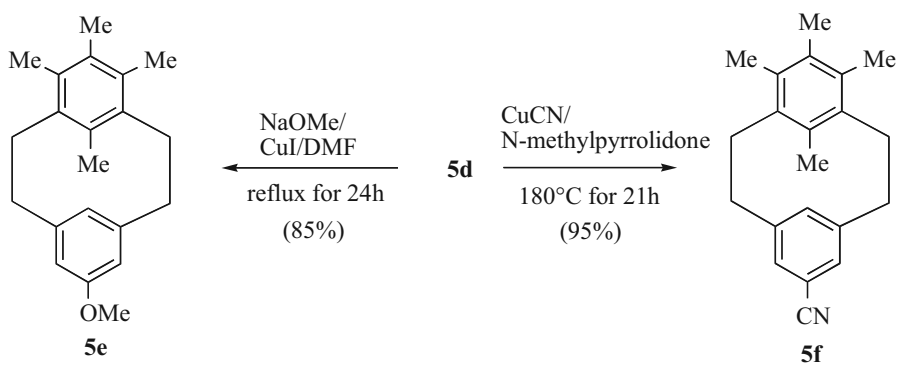
Charge-transfer (CT) complexes of cyclophanes with tetracyanoethylene (TCNE) have been studied in order to evaluate the π-basicity of the cyclophane rings and to demonstrate transannular interactions in such systems.[23,24] To this effect, the complexes of para- and metacyclophanes have been extensively studied. Thus, Cram and Bauer[25] established the order of the π base strength for [m.n]paracyclophanes and compared them to those of open chain arenes. Additionally, Singer and Cram[26] investigated transannular substituent effects in [2.2] and [3.3]paracyclophane–TCNE complexes.

Furthermore, Misumi *et al.*[27] reported that the absorption maxima of CT complexes of multilayered paracyclophanes with a TCNE shift to longer wavelengths with increasing

Table 1 Chemical shifts of the internal proton and methyl protons of 8-methyl[2.2]MCPs **5**[a]

Substrate	R	δ Internal H ($\Delta\delta_{16\text{-H}}$)[b]	δ Internal Me ($\Delta\delta_{8\text{-Me}}$)[b]
5a	R= H	3.90 (–)	0.49 (–)
5b	R=Me	3.62 (+0.28)	0.51 (–0.02)
5c	R= *t*Bu	3.67 (+0.23)	0.48 (+0.01)
5d	R= Br	3.68 (+0.22)	0.59 (–0.10)
5e	R= OMe	3.49 (+0.41)	0.63 (–0.14)
5f	R= CN	3.42 (+0.48)	1.09 (–0.60)

[a]Determined in $CDCl_3$ using $SiMe_4$ as a reference. [b]$\Delta\delta_{16\text{–H}} = \delta_{16\text{–H}} - \delta_{16\text{–HR}}$, $\Delta\delta_{8\text{–Me}} = \delta_{8\text{–Me}} - \delta_{8\text{–MeR}}$; – denotes the down field shift and + denotes the upfield shift due to ring current.



Scheme 2

Table 2 Charge-transfer bands of π–π salts of 8-methyl [2.2]MCPs **5** and tetracyanoethylene in CH_2Cl_2[a]

Substrate		λ_{max} (nm)	*log* ε
5a	R=H	584	2.297
5b	R=Me	592	1.996
5c	R=*t*Bu	596	1.881
5d	R=Br	571	1.797
5e	R=OMe	605	2.136
5f	R=CN	556	1.723

[a]The complexes were prepared in dichloromethane using equimolar quantities of substrate and TCNE at 25 °C.

number of layers. In the field of MCPs, Hayashi and Sato[28] showed that [2.2]MCP **6** affords a 1 : 1 complex with TCNE, which is stabilised due to a π–π interaction. Likewise, the work of Langer and Lehner[29] showed the formation of only 1 : 1 complexes with substituted and unsubstituted [2.2]MCPs.

A solution of 8-methyl[2.2]MCP (**5a**) and TCNE in CH_2Cl_2 present a reddish brown colour and the charge-transfer band at 584 nm (log ε 2.297) was observed in its UV spectrum. This absorption is due to the formation of 1 : 1 charge-transfer complex among the electron donor, [2.2]MCP and the electron acceptor, TCNE. No spectral changes occurred when a 4–12-fold excess of TCNE was added. The charge transfer band positions of other 8-methyl[2.2]MCPs **5a**–**f**–TCNE complexes are summarised in Table 2.

The stoichiometry of the 8-methyl[2.2]MCPs **5a**–**f** complexes with TCNE in dichloromethane was also determined by using the continuous variation method.

Typical Job plots[31] for 13-methoxy derivative **5e** is shown in Fig. 1. The absorbances for charge-transfer band reach maximum at 0.5 mole fraction when the 13-methoxy derivative **5e** and TCNE were changed systematically, indicating the formation of 1:1 complex. Also the 8-methyl[2.2]MCPs **5a**–**d** and **5f** form exclusively 1:1 charge transfer complexes with TCNE in dichloromethane, as can be similarly deduced from Job plots. TCNE complexes have often been used in studies on the relative π-base strength of various methyl-substituted benzenes.[23] 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. In contrast to the cyclophanes having symmmetric donor-sites, unsymmetric cyclophanes containing non-equivalent donor-sites such as 4-acetyl- and 4-methoxy[2.2]paracyclophanes[26] can be expected

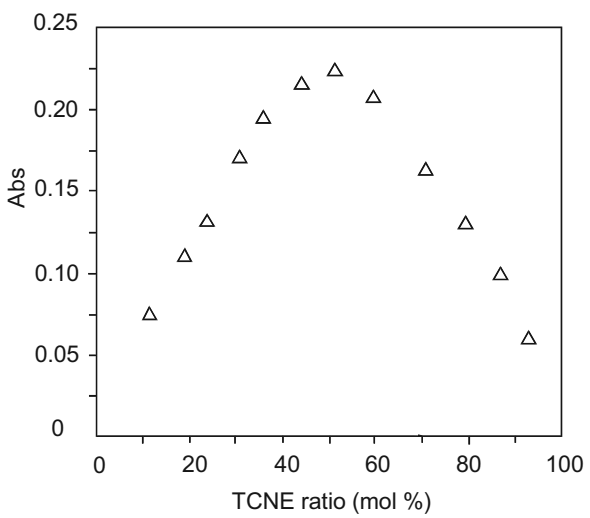


Fig. 1 Job plots of charge-transfer complexes of 13-methoxy-4,5,6,8-tetramethyl[2.2]MCP **5e** with TCNE in dichloromethane (1×10^{-2} M).

to form two isomeric one-to-one complexes with TCNE, *i.e.*, pseudo-configurational isomers.[31] An important factor for determining which isomeric compex is more predominant. Similarly, two possible pseudo-configurational isomers **A** and **B** are also expected for the one-to-one complex of 8-methyl[2.2]MCPs **5** as shown in Fig 2.

In studying the electronic spectra of **5**-TCNE complexes, it is advantageous to examine those of TCNE complexes of [2.2]MCP **6**. In contrast to [2.2]MCP **6**, which exhibits the charge-transfer absorption band with TCNE at 486 nm (log ε = 2.415),[16] a mixture of TCNE and 8-methyl[2.2]MCP **5a** exhibits CT-band at 584 nm (log ε 2.297).

Thus, introduction of the electron-donating group to [2.2]MCP **6** such as methyl groups at 4,5,6 and 8-positions causes a larger red shift (98 nm) for CT-band of **5a**. Complexing with TCNE is considered to be attributable to the increased π-basicity of the benzene ring by the methyl groups introduced. Thus the observed CT-bands of **5**-TCNE complexes should be due to the 8-methyl substituted benzene-site complex (**A**), but not to the unsubstituted benzene-site one (**B**).

Although the charge-transfer of [2.2]MCP **5a**-TCNE complex exhibits an absorption peak at 584 nm (log ε = 2.297), that of **5b** is shifted to 592 nm. Such a red shift could be due to the benzene ring at the other side of the molecule which tends to work as a π-electron donor. Introduction of the electron-donating group to [2.2]MCP **5a** such as methyl group at 13-position causes a larger red shift (8 nm) for CT-band of **5a**. Similar red shifts are observed for the CT-band of 13-*tert*-butyl- (**5c)** and 13-methoxy[2.2]MCP (**5e**) as indicated by the 12 and 21 nm shifts, respectively. Interestingly, the bulky group such as *tert*-butyl group at 13 position in **5c** did not inhibit the formation of the charge transfer complex. In contrast, introduction of electron-withdrawing groups such as bromine or cyano at 13-position causes a larger blue shift by 13 and 28 nm the CT-band for CT-band of 13-bromo-(**5d)** and 13-cyano respectively. These finding also strongly supports the observed CT-bands of 8-methyl[2.2]MCPs **5**-TCNE complexes should be attributed to the 8-methyl substituted benzene-site complex.

Conclusions

We have developed synthesis of a series of 8-methyl[2.2]MCPs **5** by the cyclisation of 1,3-bis(bromomethyl)benzenes **1** and 1,3-bis(sulfanylmethyl)-2,4,5,6-tetramethylbenzene **2** carried out under highly diluted conditions in 10% ethanolic KOH to afford 2,11-dithia[3.3]MPCPs **3**, follwed by oxidation and pyrolysis at 500 °C under reduced pressure. The present study indicates that the substituents effect at 8-position does exist in the complexation of 8-methyl[2.2]MCPs **5** with TCNE and through space electronic interaction of the opposite uncomplexed benzene ring must be considered. The further studies on the iodine-induced transannular cyclisation of **5** are now in progress.

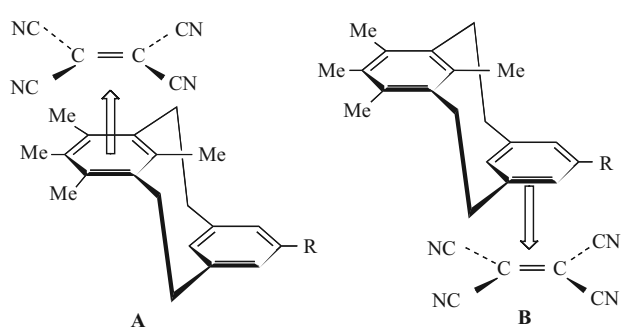


Fig. 2 Two possible charge transfer complexes of 8-methyl[2.2] MCPs **5** with TCNE.

Experimental

All melting points are uncorrected. ^{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. The visible and UV spectra were obtained by means of a Shimadzu spectrophotometer. The TCNE was recrystallised twice from chlorobenzene and sublimed twice at 125 °C (4 mmHg).

Materials

1,3-Bis(bromomethyl)benzenes **1a**–**d** were prepared by bromination of the corresponding methylbenzenes with *N*-bromosuccinimide (NBS) in the presence of 2,2'-azobis(2,4-dimethylpentanenitrile) in a methylene dichloride solution as following to the reported procedure.[17,19]

Preparation of 2,6-bis(chloromethyl)-1,3,4,5-tetramethylbenzene: Zinc chloride (40 g, 0.29 mol) at room temperature was added to a solution of 1,2,3,5-tetramethylbenzene (67.1 g, 0.5 mol) and chloromethyl methyl ether (150 mL). After the reaction mixture was stirred for 10 min, it was poured into ice-water (300 mL) and extracted with CH_2Cl_2 (200 mL × 3). The CH_2Cl_2 extract was washed with saturated aqueous NaCl (100 mL × 2), water (200 mL) and dried (Na_2SO_4) and evaporated *in vacuo* to leave a colourless solid. Recrystallisation from hexane gave the title compound as a colourless prism (88.0 g, 76.1%), m.p. 110–111 °C (lit.[15] 114 °C).

Preparation of 2,6-bis(sulfanylmethyl)-1,3,4,5-tetramethylbenzene (**2**): A solution of 2,6-bis(chloromethyl)-1,3,4,5-tetramethylbenzene (9.25 g, 0.40 mmol) and thiourea (6.7 g, 88 mmol) in DMSO (50 mL) was stirred at room temperature under atmosphere of nitrogen for 14 h. After the reaction mixture was poured into a solution of NaOH (20 g) in water (200 mL), the solution was stirred for 1 h, acidified with aqueous 10% HCl and extracted with CH_2Cl_2 (100 mL × 2). The CH_2Cl_2 extract was washed with water (100 mL) and saturated aqueous NaCl (100 mL), and dried (Na_2SO_4) and evaporated *in vacuo* to leave a colourless solid. Recrystallisation from hexane gave **2** as a colourless prism (6.5 g, 71.8%), m.p. 81–82 °C; ν_{max}/cm^{-1} (KBr) 3040, 2960, 2900, 2550, 1430, 1370, 1225, 1010, 790 and 675; δ_H ($CDCl_3$) 1.56 (2H, t, *J* = 6.6 Hz, *SH*), 2.28 (12H, s, *Me*) and 3.80 (4H, d, *J* = 6.6 Hz, CH_2); *m/z* 226 (M^+) (Found: C, 63.61; H, 8.13. $C_{12}H_{18}S_2$ (226.4) requires C, 63.66; H, 8.01%).

Preparation of 9-methyl-2,11-dithia[3.3]metacyclophanes (**3**); *typical procedure*

A solution of α,α'-dibromo-*m*-xylene (**1a**) (5.27 g, 20 mmol) and **2** (4.52 g, 20 mmol) in benzene (100 mL) was added dropwise over a period of 12 h from a Hershberg funnel with stirring under nitrogen to a solution of potassium hydroxide (4.0 g, 71 mmol) and sodium borohydride (1 g) in ethanol (4 l). After the addition, the reaction mixture was concentrated and the residue was extracted with CH_2Cl_2 (200 mL × 2). The CH_2Cl_2 extract was concentrated and the residue was chromatographed on silica gel (Wako C-300, 400 g) (hexane-benzene, 1:1 v/v, as eluent) to give a colourless solid. Recrystallisation from hexane/benzene 1:1 (v/v) gave 5,6,7,9-*tetramethyl*-2,11-*dithia*[3.3]*metacyclophane* (**3a**) as colourless prisms (4.59 g, 70%), m.p. 152–154 °C; ν_{max}/cm^{-1} (KBr) 3010, 2900, 1580, 1440, 1400, 1375, 1215, 1160, 1080, 910, 780, 760 and 700; δ_H ($CDCl_3$) 1.82 (3H, s, *Me*), 2.14 (3H, s, *Me*), 2.30 (6H, s, *Me*), 3.27 (2H, d, *J* = 16.0 Hz, CH_2), 3.59 (2H, d, *J* = 16.0 Hz, CH_2), 3.80 (2H, d, *J* = 12.0 Hz, CH_2), 4.04 (2H, d, *J* = 12.0 Hz, CH_2), 5.58 (1H, broad s, Ar*H*) and 6.84–7.01 (3H, broad s, Ar*H*); *m/z* 328 (M^+) (Found: C, 73.05; H, 7.28. $C_{20}H_{24}S_2$ (328.53) requires C, 73.12; H, 7.36%).

Cyclisation reaction of **1b–d** and **2** was carried out using the same procedure as described above to afford **3b**, **3c** and **3d** in 58, 57 and 74% yields, respectively.

5,6,7,9,15-Pentamethyl-2,11-dithia[3.3]metacyclophane (**3b**): Colourless prisms, m.p. 175–176 °C (from methanol); ν_{max}/cm^{-1} (KBr) 3010, 2900, 1590, 1440, 1400, 1370, 1220, 910, 860, 835, 720 and 700; δ_H ($CDCl_3$) 1.83 (3H, s, *Me*), 2.16 (3H, s, *Me*), 2.21 (3H, s, *Me*), 2.31 (6H, s, *Me*), 3.25 (2H, d, *J* = 16.0 Hz, CH_2), 3.56 (2H, d, *J* = 16.0 Hz, CH_2), 3.80 (2H, d, *J* = 14.0 Hz, CH_2), 4.02 (2H, d, *J* = 14.0 Hz, CH_2), 5.39 (1H, broad s, ArH) and 6.76 (2H, broad s, Ar*H*); *m/z* 342 (M^+) (Found: C, 73.86; H, 7.63. $C_{21}H_{26}S_2$ (342.56) requires C, 73.63; H, 7.65%).

15-tert-Butyl-5,6,7,9-tetramethyl-2,11-dithia[3.3]metacyclophane (**3c**): Colourless prisms, m.p. 158–160 °C (from hexane); ν_{max}/cm^{-1} (KBr) 3020, 2950, 2900, 1590, 1430, 1400, 1355, 1220, 910, 875, 720 and 700; δ_H ($CDCl_3$) 1.26 (9H, s, *tBu*), 1.80 (3H, s, *Me*), 2.15 (3H, s, *Me*), 2.32 (6H, s, *Me*), 3.30 (2H, d, *J* = 16.0 Hz, CH_2), 3.62 (2H, d, *J* = 16.0 Hz, CH_2), 3.82 (2H, d, *J* = 12.0 Hz, CH_2), 4.00 (2H, d, *J* = 12.0 Hz, CH_2), 5.55 (1H, broad s, Ar*H*) and 6.99 (2H, *J* = 1.5 Hz, Ar*H*); *m/z* 384 (M^+) (Found: C, 75.09; H, 8.28. $C_{24}H_{32}S_2$ (384.64) requires C, 74.94; H, 8.39%).

15-Bromo-5,6,7,9-tetramethyl-2,11-dithia[3.3]metacyclophane (**3d**): Colourless prisms, m.p. 154–155 °C [(from hexane-benzene 2 : 1 (v/v)); ν_{max}/cm^{-1} (KBr) 3020, 2950, 2900, 1590, 1560, 1420, 1400, 1370, 1245, 1240, 1215, 920, 860, 850, 810, 715 and 680; δ_H ($CDCl_3$) 2.06 (3H, s, *Me*), 2.11 (3H, s, *Me*), 2.25 (6H, s, *Me*), 3.33 (2H, d, *J* = 16.0 Hz, CH_2), 3.58 (2H, d, *J* = 16.0 Hz, CH_2), 3.82 (2H, d, *J* = 14.0 Hz, CH_2), 4.06 (2H, d, *J* = 14.0 Hz, CH_2), 5.94 (1H, broad s, Ar*H*) and 7.02 (2H, *J* = 2.0 Hz, Ar*H*); *m/z* 406 and 408 (M^+) (Found: C, 59.54; H, 5.67. $C_{20}H_{23}BrS_2$ (407.43) requires C, 58.96; H, 5.69%).

Preparation of 9-methyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (**4**); *typical procedure*

To a solution of **3a** (2.72 g, 8.3 mmol) in $CHCl_3$ (150 mL) was added *m*-chloroperbenzoic acid (3.96 g, 19.5 mmol, 85% purity) at 0 °C while stirring with a magnetic stirrer. After the solution was stirred for 24 h at room temperature, the solvent was evaporated *in vacuo* to leave the residue which was washed with 10% $NaHCO_3$ (100 mL), water (50 mL) and ethanol to afford 5,6,7,9-tetramethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (**4a**) as colourless prisms (3.26 g, 100%), m.p. >300 °C; ν_{max}/cm^{-1} (KBr) 3020, 2930, 1490, 1450, 1420, 1390, 1310, 1140, 1100, 920, 860, 810, 710 and 700; δ_H ($CDCl_3$) 1.49 (3H, s, *Me*), 2.40 (3H, s, *Me*), 2.57 (6H, s, *Me*), 3.99 (4H, s, CH_2), 4.50 (2H, d, *J* = 16.0 Hz, CH_2), 4.72 (2H, d, *J* = 16.0 Hz, CH_2), 5.00 (1H, broad s, Ar*H*) and 7.16–7.53 (3H, m, Ar*H*); *m/z* 264 (M^+–2SO_2) (Found: C, 60.99; H, 6.08. $C_{20}H_{24}O_4S_2$ (392.53) requires C, 61.19; H, 6.16%).

Oxidation of **3b–d** with *m*-CPBA was carried out using the same procedure as described above to afford **4b**, **4c** and **4d** in 98, 92 and 100% yields, respectively.

5,6,7,9,15-Pentamethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (**4b**): Colourless prisms, m.p. >300 °C; ν_{max}/cm^{-1} (KBr) 3000, 2910, 1600, 1455, 1385, 1295, 1245, 1140, 1100, 920, 860 and 710; δ_H ($CDCl_3$) 1.52 (3H, s, *Me*), 2.33 (3H, s, *Me*), 2.40 (3H, s, *Me*), 2.57 (6H, s, *Me*), 3.96 (4H, s, CH_2), 4.50 (2H, d, *J* = 16.0 Hz, CH_2), 4.72 (2H, d, *J* = 16.0 Hz, CH_2), 4.80 (1H, broad s, Ar*H*) and 7.27 (2H, broad s, Ar*H*); *m/z* 278 (M^+–2SO_2) (Found: C, 62.01; H, 6.24. $C_{21}H_{26}O_4S_2$ (406.56) requires C, 62.04; H, 6.45%).

15-tert-Butyl-5,6,7,9-tetramethyl-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (**4c**): Colourless prisms, m.p. >300 °C; ν_{max}/cm^{-1} (KBr) 3040, 2950, 1600, 1450, 1390, 1300, 1240, 1140, 1100, 910, 890, 800, 730 and 710; δ_H ($CDCl_3$) 1.31 (9H, s, *tBu*), 1.45 (3H, s, *Me*), 2.40 (3H, s, *Me*), 2.56 (6H, s, *Me*), 4.00 (4H, s, CH_2), 4.48 (2H, d, *J* = 16.0 Hz, CH_2), 4.48 (1H, broad s, Ar*H*), 4.71 (2H, d, *J* = 16.0 Hz, CH_2) and 7.51 (2H, *J* = 2.0 Hz, Ar*H*); *m/z* 320 (M^+–2SO_2) (Found: C, 64.00; H, 7.10. $C_{24}H_{32}O_4S_2$ (448.64) requires C, 64.25; H, 7.19%).

5,6,7,9-Tetramethyl-15-bromo-2,11-dithia[3.3]metacyclophane-2,2,11,11-tetraoxide (**4d**): Colourless prisms, m.p. >300 °C; ν_{max}/cm^{-1} (KBr) 3010, 2970, 2930, 1565, 1440, 1390, 1300, 1275, 1260, 1145, 1105, 880 and 705; δ_H ($CDCl_3$) 1.62 (3H, s, *Me*), 2.39 (3H, s, *Me*), 2.56 (6H, s, *Me*), 3.95 (4H, s, CH_2), 4.54 (2H, d, *J* = 16.0 Hz, CH_2), 4.75 (2 H, d, *J* = 16.0 Hz, CH_2), 5.00 (1H, broad s, Ar*H*) and 7.60 (2H, *J* 2.0 Hz, Ar*H*); *m/z* 342 and 344 (M^+–2SO_2) (Found: C, 50.50; H, 4.92. $C_{20}H_{23}BrO_4S_2$ (471.43) requires C, 50.96; H, 4.92%).

Pyrolysis of disulfone 4 to give 5-methyly[2.2]metacyclophanes (**5**); *typical procedure*

Pyrolysis of disulfones **4a** was carried out in an apparatus consisting of a horizontal tube (15 mm in diameter) passing through two adjacent tube furnace, each of which 20 cm long. The first furnace provided a temperature that would induce sublimation of the sulfone; the second was used at a higher temperature (500 °C) that would assure pyrolysis. A vacuum pump was connected at the exit from the second furnace. Disulfone **4a** (1 g, 2.55 mmol) was pyrolysed at 500 °C under reduced pressure (1 Torr) in the above apparatus as follows. The sample of disulfone was placed in the first furnace and small glass beads were packed into the second furnace. The product which sublimed was collected and chromatographed on silica gel (Wako C-300, 100 g) (hexane as eluent) to give a colourless solid. Recrystallisation from methanol gave 4,5,6,8-tetramethyl[2.2]metacyclophane (**3a**) as colourless prisms (498 mg, 74%), m.p. 129–130 °C;

ν_{max}/cm^{-1} (KBr) 3040, 2950, 2910, 1470, 1420, 1360, 1180, 1160, 1020, 940, 780 and 720; δ_H ($CDCl_3$) 0.49 (3H, s, *Me*), 1.96–2.54 (4H, m, CH_2), 2.26 (3H, s, *Me*), 2.31 (6H, s, *Me*), 2.80–3.34 (4H, m, CH_2), 3.80 (1H, s, Ar*H*) and 6.98–7.13 (3H, m, Ar*H*); *m/z* 264 (M^+) (Found: C, 90.95; H, 9.27. $C_{20}H_{24}$ (264.41) requires C, 90.85; H, 9.15%).

Pyrolysis of **4b–d** was carried out using the same procedure as described above to afford **5b**, **5c** and **5d** in 63, 70 and 73% yields, respectively.

4,5,6,8,13-Pentamethyl[2.2]metacyclophane (**5b**): Colourless prisms (from hexane), m.p. 169–170 °C; ν_{max}/cm^{-1} (KBr) 3000, 2900, 1580, 1470, 1435, 1410, 1365, 1325, 1180, 1135, 870, 840 and 720; δ_H ($CDCl_3$) 0.51 (3H, s, *Me*), 1.94–2.53 (4H, m, CH_2), 2.23 (6H, s, *Me*), 2.28 (6H, s, *Me*), 2.74–2.91 (2H, m, CH_2), 3.12–3.31 (2H, m, CH_2), 3.62 (1H, broad s, Ar*H*) and 6.85 (2H, broad s, Ar*H*); *m/z* 278 (M^+) (Found: C, 90.56; H, 9.70. $C_{21}H_{26}$ (278.44) requires C, 90.59; H, 9.41%).

13-tert-Butyl-4,5,6,8-tetramethyl[2.2]metacyclophane (**5c**): Colourless prisms (from methanol), m.p. 176–177 °C; ν_{max}/cm^{-1} (KBr) 3040, 2950, 1580, 1470, 1440, 1430, 1355, 1275, 1180, 880, 850 and 720; δ_H ($CDCl_3$) 0.48 (3H, s, *Me*), 1.28 (9H, s, *tBu*), 1.97–2.36 (4H, s, CH_2), 2.26 (3H, s, *Me*), 2.32 (6H, s, *Me*), 2.80–3.33 (4H, s, CH_2), 3.67 (1H, broad s, Ar*H*) and 7.08 (2H, *J* = 2.0 Hz, Ar*H*); *m/z* 320 (M^+) (Found: C, 89.97; H, 10.09. $C_{24}H_{32}$ (320.52) requires C, 89.94; H, 10.06%).

13-Bromo-4,5,6,8-tetramethyl[2.2]metacyclophane (**5d**): Colourless prisms [(from hexane–benzene 1 : 1 (v/v)), m.p. 220–221 °C; ν_{max}/cm^{-1} (KBr) 3010, 2970, 1460, 1440, 1410, 1370, 1325, 1180, 1160, 1020, 930, 880 and 745; δ_H ($CDCl_3$) 0.59 (3H, s, *Me*), 1.92–2.54 (4H, m, CH_2), 2.24 (3H, s, *Me*), 2.28 (6H, s, *Me*), 2.75–2.92 (2H, m, CH_2), 3.14–3.34 (2H, m, CH_2), 3.68 (1H, broad s, Ar*H*) and 7.19 (2H, d, *J* = 2.0 Hz, Ar*H*); *m/z* 342 and 344 (M^+) (Found: C, 69.92; H, 6.79. $C_{20}H_{23}Br$ (343.31) requires C, 69.97; H, 6.75%).

13-Methoxy-4,5,6,8-tetramethyl[2.2]metacyclophane (**5e**): Sodium (2.18 g, 95 mmol) and then a mixture of CuI (0.7 g) and **5d** (1.7 g, 5.64 mmol) in DMF (22 mL) was added to methanol (72 mL). After the reaction mixture was refluxed for 24 h, it was poured into a large amount of ice-water and extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with water, dried (Na_2SO_4) and the solvent was evaporated under reduced pressure. The residue was chromatographed on SiO_2 by using hexane as eluent. Recrystallisation from hexane gave **5e** as colourless prisms (1.41 g, 84%), m.p. 143–144 °C; ν_{max}/cm^{-1} (KBr) 2918, 1587, 1458, 1431, 1333, 1278, 1137, 1026, 846 and 838; δ_H ($CDCl_3$) 0.63 (3H, s, *Me*), 2.10–2.20 (2H, m, CH_2), 2.27 (3H, s, *Me*), 2.33 (6H, s, *Me*), 2.42–2.54 (2H, m, CH_2), 2.80–2.92 (2H, m, CH_2), 3.20–3.32 (2H, m, CH_2), 3.49 (1H, broad s, Ar*H*), 3.78 (3H, s, O*Me*) and 6.67 (2H, d, *J* = 1.2 Hz, Ar*H*); *m/z* 294 (M^+) (Found: C, 85.56; H, 8.79. $C_{21}H_{26}O$ (294.44) requires C, 85.67; H, 8.90%).

13-Cyano-4,5,6,8-tetramethyl[2.2]metacyclophane (**5f**): After a mixture of **5d** (686 mg, 2.0 mmol) and cuprous cyanide (4.0 g) in *N*-methylpyrrolidone (30 mL) was heated at 180–185 °C for 21 h, it was then poured into a mixture of water and concentrated aqueous ammonia [400 mL, 1 : 1 (v/v)]. After the resulting mixture had been stirred under cooling for 3 h, it was extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with water, dried (Na_2SO_4) and the solvent was evaporated under reduced pressure. The residue was chromatographed on SiO_2 by using CH_2Cl_2 as eluent. Recrystallisation from hexane–benzene 1 : 1 (v/v) gave **5f** as colourless prisms (550 mg, 95%), m.p. 229–230 °C; ν_{max}/cm^{-1} (KBr) 3050, 2950, 2920, 2220, 1580, 1430, 1365, 1270, 1180, 1160, 1040, 895, 875, 860 and 720; δ_H ($CDCl_3$) 1.09 (3H, s, *Me*), 1.47–2.08 (4H, m, CH_2), 1.77 (3H, s, *Me*), 1.81 (6H, s, *Me*), 2.35–2.96 (4H, m, CH_2), 3.42 (1H, broad s, Ar*H*) and 6.89 (2H, d, *J* = 2.0 Hz, Ar*H*); *m/z* 289 (M^+) (Found: C, 87.01; H, 8.11; N, 4.74. $C_{21}H_{23}N$ (289.42) requires C, 87.15; H, 8.01; N, 4.84%).

Received 20 January 2009; accepted 6 March 2009
Paper 09/0401 doi: 10.3184/030823409X447718
Published online: 22 May 2009

References

1 P.M. Keehn and S.M. Rosenfield (eds), *Cyclophanes*, Academic Press, New York, Vol. 1&2, 1983.
2 F. Vögtle, *Cyclophane chemistry*, Wiley, Chichester, 1993.
3 L.L. Ingraham, *J. Chem. Phys.*, 1957, **27**, 1228.
4 N.L. Allinger, M.A. Da Rooge and R.B. Hermann, *J. Am. Chem. Soc.*, 1961, **83**, 1974.
5 T. Sato, T. Takemura and M. Kainosho, *J. Chem. Soc., Chem. Commun.*, 1974, 97.
6 T. Sato, H. Matsui and R. Komaki, *J. Chem. Soc.*, *Perkin Trans. 1,* 1976, 2053.
7 T. Takemura and T. Sato, *Can. J. Chem.*, 1976, **54**, 3412.
8 R. Gleiter, *Tetrahedron Lett.*, 1969, 4453.
9 D.J. Cram, N.L. Allinger and H. Steinberg, *J. Am. Chem. Soc.*, 1954, **76**, 6132.
10 R. Boschi and W. Schmidt, *Angew. Chem., Int. Ed. Engl.*, 1973, **12**, 402.
11 T. Sato and T. Takemura, *J. Chem. Soc.*, *Perkin Trans. 2,* 1976, 1195.
12 M. Tashiro, T. Yamato, K. Kobayashi and T. Arimura, *J. Org. Chem.*, 1987, **52**, 3196.
13 T. Yamato, J. Matsumoto, N. Shinoda, S. Ide, M. Shigekuni and M. Tashiro, *J. Chem. Res. (S)*, 1994, 178.
14 T. Sato and K. Nishiyama, *J. Chem. Soc., Chem. Commun.*, 1973, 220.
15 T. Sato and K. Nishiyama, *J. Org. Chem.*, 1972, **37**, 3254.
16 T. Sato and T. Takemura, *J. Chem. Soc., Perkin 2*, 1976, 1195.
17 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1981, **46**, 1543.
18 M. Tashiro, K. Koya and T. Yamato, *J. Am. Chem. Soc.*, 1982, **104**, 3707.
19 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1985, **50**, 2939.
20 T. Yamato, T. Arimura and M. Tashiro, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1.
21 M. Tashiro, A. Tsuge, T. Sawada, T. Makishima, S. Horie, T. Arimura, S. Mataka and T. Yamato, *J. Org. Chem.*, 1990, **55**, 2404.
22 A. Paudel, T. Shimizu, J. Hu and T. Yamato, *J. Chem. Res.*, 2008, 731.
23 R.E. Merrifield and W.D. Phillips, *J. Am. Chem. Soc.*, 1958, **80**, 2778.
24 H.A. Staab, G. Voit, J. Weisener and M. Futscher, *Chem. Ber.,* 1992, **125**, 2303.
25 D.J. Cram and R.H. Bauer, *J. Am. Chem. Soc.,* 1959, **81**, 5971.
26 L.A. Singer and D.J. Cram, *J. Am. Chem. Soc.*, 1963, **85**, 1080.
27 T. Otsubo, S. Mizogami, I. Otsubo, Z. Tozuka, A. Sakagami, Y. Sakata and S. Misumi, *Bull. Chem. Soc. Jpn.,* 1973, **46**, 3519.
28 S. Hayashi and T. Sato, *Nippon Kagaku Zasshi*, 1970, **91**, 950.
29 E. Langer and H. Lehner, *Tetrahedron*, 1973, **29**, 375.
30 P. Job, *Ann. Chem.,* 1928, **9**, 113.
31 T. Kaneda and S. Misumi, *Bull. Chem. Soc. Jap.*, 1977, **50**, 3310.