# Synthesis and conformational studies of 9-methoxy- and 9-methyl-2,11-dithia[3.3]metacyclophanes

Tomoe Shimizu, Takayuki Maeda, Katsuhiro Hida and Takehiko Yamato\*

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

A series of 9-methoxy- and 9-methyl-2,11-dithia[3.3]metacyclophanes are obtained by the coupling reaction of the corresponding 1,3-bis(bromomethyl)benzenes and bis(sulfanylmethyl)benzenes in ethanol under the high dilution conditions. The conformational studies of 2,11-dithia[3.3]metacyclophanes as well as the ring current interactions derived from benzene ring are also described.

Keywords: cyclophanes, dithia[3.3]metacyclophanes, conformations, ring current effect, charge transfer complex

For many years, various research groups have been attracted by the structures of the [3.3]MCP ([3.3]MCP = [3.3]metacyclophane) skeleton.<sup>1-4</sup> When both internal substituents of a [3.3]phane such as **1** are H, the molecule may be mobile. Mitchell and his coworkers demonstrated that 9,18-dimethyl-2,11-dithia[3.3]MCP exists in *syn-* (*syn-*2**b**) and *anti-* (*anti-*2**b**) conformers, which do not interconvert below 200 °C.<sup>6–9</sup> As in the case of the [2.2]phanes,<sup>2–4</sup> the internal methyl protons of *anti-*2**b** are shielded at  $\delta$  1.30 ppm by 1.24 from those of *syn-*2**b** ( $\delta$  2.54 ppm), which is relatively normal for a toluene derivative.

Even one internal methyl substituent is sufficient to allow the isolation of a discrete *syn* or *anti* isomer; for example, in *anti*-**2a** the internal proton (H<sup>i</sup>) appears at  $\delta$  5.50 ppm and the internal methyl protons (Me<sup>i</sup>) at  $\delta$  2.18 ppm. The reduced shielding of Me<sup>i</sup> relative to *anti*-**2b** indicates that **2a** adopts a different geometry from that of *anti*-**2b**.

Vögtle *et al.*<sup>10</sup> have made extensive studies of *syn-anti* conversions in other dithia[3.3]MCPs, especially in relation to the size of the substituents. When electron-withdrawing groups such as halo, nitro, and cyano are present, the yields of the *syn* isomers increase substantially. Very bulky groups, such as *tert*-butyl, decrease the yields of *syn* isomers. Although the effect on the ratio of *syn* and *anti* conformers of dithia[3.3]MCPs was reported, it is still not clear what the effects are, not only properties of the internal substituents, but also having unsymmetrically substituted benzene rings arising from charge-transfer-type interactions between two benzene rings as well as steric effects of substituents at the 6 and 15-positions.

All of the previous compounds are internally unsubstituted or methyl-substituted dithia[3.3]MCPs and it is surprising that there are very few reports on the preparation of 9methoxy analogues. We report here the synthesis and stereochemical assignments of 9-methoxy- and 9-methyl-2,11-dithia[3.3]MCPs using the above method, as well as studies of their conformation by the ring current interactions derived from benzene ring.

## **Results and discussion**

2,6-Bis(sulfanylmethyl)anisoles **4** were prepared by treatment of the corresponding 2,6-bis(bromomethyl) 4-substituted anisoles **3** with thiourea and potassium hydroxide in ethanol.<sup>11–15</sup> 5-*tert*-Butyl-1,3-bis(bromomethyl)benzene **5** was prepared by bromination of 5-*tert*-butyl-1,3-dimethylbenzene with *N*-bromosuccinimide in the presence of 2,2'-azobis(2,4dimethylpentanenitrile) in a methylene dichloride solution according to our reported procedure.<sup>11,13</sup>

The cyclisations of 5-*tert*-butyl-1,3-bis(bromomethyl) benzene **5** and 2,6-bis(sulfanylmethyl)anisoles **4** were carried



Fig. 1 syn- and anti-Conformers of dithia[3.3]metacyclophane 2.

out under high-dilution conditions in 10% ethanolic KOH in the presence of a small amount of NaBH<sub>4</sub>,  $^{11-15}$  giving *syn*-9-methoxy-2,11-dithia[3.3]MCPs **6a–e** in 16–60% yields, respectively (Scheme 1).

The structures of 6 were established on the basis of the base peak molecular ions in their mass spectra, and they were assigned the syn-stereochemistry syn-6 on the basis of their <sup>1</sup>H NMR spectra by comparison with the known syn-cyclophane **2a**, since the 9-proton of *syn*-**6** appears at around  $\delta$  6.9 ppm (that for *syn*-2a is at  $\delta$  6.82 ppm),<sup>5,7,8</sup> *i.e.* relatively normal for a benzene, whereas if 6 existed as the anti conformers they might be expected to be shielded by the opposite ring to  $ca \delta$ 5 ppm. The same shift of the internal methoxy protons at around  $\delta$  3.66–3.68 ppm as that of an anisole was observed in syn-6. Further, the other aryl hydrogens can clearly be seen to be shielded at  $\delta$  6.87–6.90 ppm by the adjacent ring, a common consequence of a face-to-face benzene ring.<sup>7</sup> Also the tert-butyl protons of syn-6a-6d were observed at higher field,  $\delta$  1.08–1.19 ppm due to the strong shielding effect of the benzene ring except syn-6e ( $\delta$  1.25 ppm). These observations strongly suggest that compounds 6a-e all adopt synconformations. The chemical shifts ( $\delta$ ) of the internal methoxy protons, the aromatic internal protons at the 18-position and the tert-butyl protons of syn-9-methoxy-2,11-dithia[3.3]MCPs syn-6a–e are com piled in Table 1. All the bridged  $CH_2SCH_2$ protons of the above-prepared cyclophane 6b are observed as a pair of doublets at  $\delta$  3.42, 4.22 ppm (J = 14.3 Hz) and  $\delta$  3.70, 3.79 ppm (J = 14.5 Hz) in <sup>1</sup>H NMR spectra at room temperature. With increasing temperature in DMSO-d<sub>6</sub>,

<sup>\*</sup> Correspondent. E-mail: yamatot@cc.saga-u.ac.jp

Table 1	Chemical shifts ( $\delta$ ) of the internal methoxy protons, aromatic internal proton at 18 position and <i>tert</i> -butyl protons of <i>syl</i>
9-metho:	xy-2,11-dithia[3.3]MCPs syn-6a–e and anti-9-methyl-2,11-dithia[3.3]MCPs anti-8a–b <sup>a</sup>

Compound	Methoxy and methyl protons	Aromatic proton at 18-position	tert-Butyl protons	Assignment
6a	3.68	6.90	1.18	syn
6b	3.66	6.93	1.19	syn
6c	3.67	6.93	1.10	syn
6d	3.66	6.87	1.08, 1.14	syn
6e	3.67	6.90	1.25	syn
8a	2.17	5.65	1.31	anti
8b	2.00	5.00	1.24, 1.28	anti

<sup>a</sup>Determined in CDCl<sub>3</sub> by using SiMe<sub>4</sub> as a reference and expressed in ppm.



#### Scheme 1

the doublets do not coalescenc below  $150 \,^{\circ}$ C, respectively, and the energy barriers of flipping are both above 25 kcal mol<sup>-1.8,9,10</sup> Similar findings were obtained in dithia[3.3]MCPs **6a**, **6c**-**6e**. These observations strongly suggest that compounds **6** adopt rigid *syn*-conformation.

In contrast, the cyclisation of 1,3-bis(bromomethyl)-5-tertbutylbenzene **5** and 2,6-bis(sulfanylmethyl)toluenes **7a** and **7b** were carried out under high dilution conditions in 10% ethanolic KOH in the presence of a small amount of NaBH<sub>4</sub>, giving exclusively *anti*-9-methyl-2,11-dithia[3.3]MCPs *anti*-**8a** and *anti*-**8b** in 60 and 85% yields, respectively (Scheme 2). The assignments of structure for the *anti* and *syn* conformers were readily apparent from their <sup>1</sup>H NMR spectra (Table 1). The <sup>1</sup>H NMR spectra of conformer *anti*-**8a** and *anti*-**8b** show the internal aromatic proton at the 18-position at  $\delta$ 5.65 and 5.00 ppm, respectively. Thus, the internal aromatic proton of the *anti* conformers shows an upfield shift due to the ring current of the opposite aromatic ring.<sup>3,4</sup> However, the internal methyl protons appeared at  $\delta$  2.18 and 2.00 ppm different from those observed in 9,18-dimethyl-2,11dithia[3.3]MCP *anti*-**2b** ( $\delta$  1.33 ppm). No ring current effects of the opposing benzene was observed. These findings might be attributable to the different structure between *anti*-**8** and *anti*-**2b**. The internal aromatic proton at the 18-position of *anti*-**8** is observed at  $\delta$  5.00–5.65 ppm. The *tert*-butyl protons of *anti*-**8** was also observed at much lower field ( $\delta$  1.24–1.31 ppm) than that of *syn*-**6d** at  $\delta$  1.08 ppm. These observations strongly suggest compounds *anti*-**8a** and *anti*-**8b** adopt an *anti*-conformation. Dependent on the OMe and Me substitution, different yields (inversion of selectivity) of *anti*-and *syn*-conformers were formed. Thus 9-methoxy analogues are exclusively formed as *syn*-conformers, but other 9-methyl analogues are exclusively formed as *anti*-conformers.

These findings suggest that in the case of 9-methoxy analogue the through-space interaction between the nonbonding electron pairs of the oxygen atom of the methoxy





Fig. 2 Reaction intermediate for the cyclisation to form dithia[3.3]MCPs.

group and the opposite aromatic  $\pi$ -electrons of the *anti*conformer may disfavour the formation of the latter as shown in Fig. 2. In contrast, in the case of a 9-methyl analogue the aromatic  $\pi$ - $\pi$  interaction between the two opposite benzene rings and the steric crowding at the internal positions 9 and 18 may inhibit the formation of the *syn*-conformer in the [3.3]MCP system and that in turn the C–H– $\pi$  interaction<sup>16</sup> between the methyl and the opposite aromatic  $\pi$ -electrons may favour the formation of an *anti*-conformer during the cyclisation process. C–H– $\pi$  interactions involving aliphatic CH moieties are well documented<sup>16</sup> as being either conformation controlling intramolecular processes or involving crystalstructure controlling intermolecular forces, especially for inclusion complexes of calixarene derivatives.<sup>17–23</sup>

A solution of 15-*tert*-butyl-9-methoxy-2,11-dithia[3.3]MCP (*syn*-**6a**) and TCNE in CH<sub>2</sub>Cl<sub>2</sub> presents a reddish brown colour and the charge-transfer band at 521 nm (log  $\varepsilon = 1.307$ ) was observed in its UV spectrum. This absorption is due to the formation of 1:1 charge-transfer complex among the electron donor, *syn*-**6a** and the electron acceptor, TCNE. The position of absorption maximum and the shape of absorption curve remain unchanged when a 4–12-fold excess of TCNE was added. The charge transfer band positions of other 15-*tert*-butyl-9-methoxy-2,11-dithia[3.3]MCPs (*syn*-**6b**, *syn*-**6c** and *syn*-**6e**), 2,6-dimethylanisole **9** and 5-*tert*-butyl-1,3-dimethylbenzene **10** with TCNE complexes are summarised in Table 2.

TCNE complexes have often been used in studies on the relative  $\pi$ -base strength of various methyl-substituted benzenes.<sup>24</sup> The  $\pi$ -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-toface overlapping between aromatic nuclei. In contrast to the

**Table 2** Charge-transfer bands of  $\pi$ - $\pi$  salts of *syn*-**6a**, **b**, **c**, **e** and reference compounds **9**, **10** with TCNE in CH<sub>2</sub>Cl<sub>2</sub><sup>a</sup>

Compounds	R	λ <sub>CT</sub> (nm)	log ε
syn-6a	Н	521	1.307
syn-6b	Me	520	1.364
syn-6c	Et	522	1.414
syn-6e	Br	470	1.386
9	_	455	1.287
10	-	422	1.364

<sup>a</sup>The complexes were prepared in  $CH_2Cl_2$  using equimolar quantities of substrate and TCNE at 25 °C.



**Fig. 3** Possible structures of charge-transfer complex for *syn*-15-*tert*-butyl-9-methoxy-2,11-dithia[3.3]MCPs *syn*-6a–e with TCNE.

cyclophanes having symmetric donor-sites, unsymmetric cyclophanes containing non-equivalent donor-sites such as 4-acetyl- and 4-methoxy[2.2]paracyclophanes<sup>25</sup> can be expected to form two isomeric one-to-one complexes with TCNE, *i.e.*, pseudo-configurational isomers.<sup>26</sup> An important factor for determining which isomeric compex is more predominant or exclusive is the magnitude of ionisation potentials of the constituent donor moieties. Similarly, two possible pseudo-configurational isomers **A** and **B** are also expected for the one-to-one complex of *syn*-15-*tert*-butyl-9-methoxy-2,11-dithia[3.3]MCPs *syn*-**6** as shown in Fig. 3.

In studying the electron spectra of *syn-6*-TCNE complexes, it is advantageous also to examine the spectra of TCNE complex of 6,15-di-tert-butyl-9,18-dimethoxy-2,11-dithia-[3.3]MCP (11). In contrast to 15-tert-butyl-9-methoxy-2,11dithia[3.3]MCP (syn-6a), which exhibits a charge-transfer absorption band with TCNE at 521 nm (log  $\varepsilon = 1.307$ ), a mixture of TCNE and 11 exhibits no band in the visible region. However, the charge-transfer absorption band of the reference compound 2,6-dimethylanisole (9) with TCNE was observed at 455 nm (log  $\varepsilon = 1.287$ ).<sup>27</sup> Complexing with TCNE is considered to be difficult in the case of 11 owing to the cyclophane structure as well as the steric hindrance of the methoxy group at the 8-position, in spite of the increased  $\pi$ -basicity of the benzene ring due to the methoxy groups. Thus the observed charge-transfer bands of the *svn*-6-TCNE complexes should be attributed to the internally unsubstituted benzene-site one. Although the charge-transfer of the 5-tertbutyl-1,3-dimethylbenzene 10-TCNE complex exhibits an absorption peak at 422 nm, that of syn-6a is shifted to 521 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  $\pi$ -electron donor.

Similar redshifts were observed in the 15-*tert*-butyl-8-methoxy-6-substituted-2,11-dithia[3.3]MCPs *syn*-6b and *syn*-6c, each of which possesses an electron-donating group,



Fig. 4 Reference compounds 9, 10 and 11.

such as a methyl or ethyl group at the 6-position, respectively, due to the increased transannular  $\pi$ -electron donation from the non-complexed to the complexed benzene ring. In contrast, the charge-transfer band of *syn*-**6e**, having an electron-withdrawing bromine atom at the 6-position, would certainly be shifted less than that of *syn*-**6a**, so that the overall transannular effect of the uncomplexed ring would be electron withdrawing. These findings strongly support the attribution of the observed charge-transfer bands of the *syn*-8methoxy[3.3]MCP (*syn*-**6**)–TCNE complexes to the internally unsubstituted benzene-site complex.

### Conclusions

In conclusion, we have demonstrated for the first time a through-space interaction between the non-bonding electron pairs of the oxygen atom of the methoxy group and the opposite aromatic  $\pi$ -electrons which may disfavour formation of the anti-conformer during the coupling reaction of the corresponding 5-tert-butyl-2,6-bis(bromomethyl)benzene 5 and 4-tert-butyl-2,6-bis(sulfanylmethyl)anisole 4 to afford syn-9-methoxy-2,11-dithia[3.3]MCPs svn-6 exclusively. In contrast, the corresponding 9-methyl analogues anti-8 are exclusively formed as anti-conformers. Dependent on the OMe and Me substitution, different yields (inversion of selectivity) of syn- and anti-conformers were formed. The substituent effect at the 6-position does exist in the complexation of syn-8-methoxy-2,11-dithia[3.3]MCPs (syn-6) with TCNE and that a through-space electronic interaction of the opposite uncomplexed benzene ring must be considered. Further chemical properties and the charge-transfer complexes of the present novel unsymmetrically substituted syn-[3.3]MCP derivatives are currently under study in our laboratory.

### Experimental

All melting points are uncorrected. <sup>1</sup>H NMR spectra were recorded at 300 MHz on a Nippon Denshi JEOL FT-300 NMR spectrometer in deuteriochloroform with Me<sub>4</sub>Si as an internal reference. UV-vis spectra were recorded on a Perkin Elmer Lambda 19 UV/VIS/NIR 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 2,6-bis(halomethyl)-4-substituted anisoles 3a-e, 2,6-bis(sulfanylmethyl)-4-substituted anisoles 4a, 4b,  $4d^{28}$  and 5-*tert*-butyl-1,3-bis(bromomethyl)benzene 5 were previously described.<sup>11,13</sup> The TCNE was recrystallised twice from chlorobenzene and sublimed twice at 125 °C (4 mmHg).

2,6-Bis(sulfarylmethyl)-4-ethylanisole (4c). A solution of 3c (1.20 g, 5.1 mmol) and thiourea (854 mg, 11.22 mmol) in ethanol (18 mL) was refluxed for 8 h under an atmosphere of nitrogen. After the reaction mixture was cooled to room temperature and KOH (858 mg, 15.3 mmol) and NaBH<sub>4</sub> (38.6 mg, 1.02 mmol) was added. The solution was refluxed for 10 h, acidified with aqueous 10% HCl and extracted with CH<sub>2</sub>Cl<sub>2</sub> (100 mL × 2). The CH<sub>2</sub>Cl<sub>2</sub> extract was washed with water (100 mL) followed by saturated aqueous NaCl (100 mL), and dried (Na<sub>2</sub>SO<sub>4</sub>) and evaporated *in vacuo* to leave a colourless solid. Recrystallisation from hexane gave the 4c as a colourless liquid (592 mg, 51%), b.p.133–134 °C/3 torr; v<sub>max</sub>/cm<sup>-1</sup> (NaCl) 3040, 2924, 2540, 1428, 1216, 1122, 994 and 870;  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 1.22 (3H, t, J = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.90 (2H, t, J = 7.4 Hz, SH), 2.59 (2H, q, J = 7.5 Hz, CH<sub>2</sub>CH<sub>3</sub>), 3.75 (4H, t, J = 7.4 Hz, CH<sub>2</sub>SH), 3.87 (3H, s, OCH<sub>3</sub>) and 7.06 (2H, s, ArH); *ml* 228 (M<sup>+</sup>); HRMS (CI): *mlz* Calcd for C11H<sub>16</sub>OS<sub>2</sub> (M<sup>+</sup>) 228.06427. Found 228.06387 (Found: C, 57.74; H, 7.03. C<sub>11</sub>H<sub>16</sub>OS<sub>2</sub> (228.37) requires C, 57.86; H, 7.06%).

Compound 4e was prepared in the same manner as described for 4c in 20% yield.

2,6-Bis(sulfanylmethyl)-4-bromoanisole (4e): Colourless liquid, b.p.165–167 °C/10 torr;  $v_{max}$ /cm<sup>-1</sup> (NaCl) 3040, 2912, 2540, 1570, 1420, 1202, 984 and 848;  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 1.91 (2H, t, *J* = 7.7 Hz, *SH*), 3.72 (4H, d, *J* = 7.7 Hz, *CH*<sub>2</sub>SH), 3.87 (3H, s, OCH<sub>3</sub>) and 7.38 (2H, s, ArH); *m*/z 278, 280 (M<sup>+)</sup>; HRMS (CI): *m*/z Calcd for C<sub>9</sub>H<sub>11</sub>Br  $OS_2\ (M^+)\ 277.94348.$  Found 277.94333 (Found: C, 38.84; H, 3.85.  $C_9H_{11}BrOS_2\ (279.21)$  requires C, 38.72; H, 3.97%).

# *Cyclisation reaction of* **4** *and* **5** *to give dithia*[3.3]*metacyclophanes* **6**; *typical procedure*

A solution of 1,3-bis(bromomethyl)-5-tert-butylbenzene 5 (2.0 g, 4.5 mmol) and 2,6-bis(sulfanylmethyl)anisole 4a (811 mg, 4.5 mmol) in benzene (100 mL) was added dropwise from a Hershberg funnel with stirring under nitrogen to a solution of potassium hydroxide (700 mg, 12.4 mmol) and sodium borohydride (100 mg, 2.5 mmol) in ethanol (3.0 L). When addition was complete (6 h), the reaction mixture was concentrated in vacuo and the residue was extracted with CH<sub>2</sub>Cl<sub>2</sub> (500 mL). The CH<sub>2</sub>Cl<sub>2</sub> extract was washed with water and dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. The residue was chromatographed over silica gel (Walo, C-300; 100 g) with hexane-CH<sub>2</sub>Cl<sub>2</sub> 1:1 as eluent to give a colourless solid, which was recrystallised from hexane to yield the desired 15-tert-butyl-9-methoxy-2,11-dithia[3.3] metacyclophane (*syn*-**6a**) (773 mg, 48%) as prisms (from hexane), m.p. 103–105 °C;  $v_{max}$ (KBr)/cm<sup>-1</sup> 2900, 1590, 1430, 1166, 1008;  $\delta_{H}$ (CDCl<sub>3</sub>) 1.18 (9H, s, *tBu*), 3.46 (2H, d, J = 14.1 Hz, 1,12-*CH*<sub>2</sub>), 3.68 (3H, s, OMe), 3.69 (2H, d, J = 14.4 Hz, 3,10-CH<sub>2</sub>), 3.79 (2H, d, J = 14.4 Hz, 3,10- $CH_2$ ), 4.25 (2H, d, J = 14.1 Hz, 1,12- $CH_2$ ), 6.60 (1H, t, J = 7.8 Hz, 15-ArH), 6.90 (1H, s, 9-ArH), 6.91 (2H, d, J = 7.8 Hz, 14,16-ArH) and 6.92 (2H, s, 5,7-ArH); m/z 358 (M<sup>+</sup>); HRMS (CI): m/z Calc. for C21H26OS2 (M+) 358.1425; Found 358.1431 (Found: C, 70.47; H, 7.38. C<sub>21</sub>H<sub>26</sub>OS<sub>2</sub> (358.56) requires C, 70.34; H, 7.31%).

Compounds *syn-6b–syn-6e* were prepared in the same manner as described for *syn-6a*. The yields are compiled in Scheme 1.

15-tert-Butyl-9-methoxy-6-methyl-2,11-dithia[3.3]metacyclophane (syn-**6b**). Prisms (from hexane), m.p. 110–112 °C;  $v_{max}$ (KBr)/cm<sup>-1</sup> 2930, 1590, 1160 and 898;  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 1.19 (9H, s, *tBu*), 1.99 (3H, s, *Me*), 3.42 (2H, d, *J* = 14.3 Hz, 3,10-*CH*<sub>2</sub>), 3.66 (3H, s, O*Me*), 3.70 (2H, d, *J* = 14.5 Hz, 1,12-*CH*<sub>2</sub>), 3.79 (2H, d, *J* = 14.5 Hz, 1,12-*CH*<sub>2</sub>), 4.22 (2H, d, *J* = 14.3 Hz, 3,10-*CH*<sub>2</sub>), 6.70 (2H, s, 14,16-Ar*H*) and 6.93 (3H, s, 5,7,18-Ar*H*); *m*/z 372 (M<sup>+</sup>); HRMS (CI): *m*/z Calcd for C<sub>22</sub>H<sub>28</sub>OS<sub>2</sub> (M<sup>+</sup>) 372.1582. Found 372.1568 (Found: C, 70.74; H, 7.65. C<sub>22</sub>H<sub>28</sub>OS<sub>2</sub> (372.59) requires C, 70.92; H, 7.57%).

syn-15-tert-Butyl-6-ethyl-9-methoxy-2,11-dithia[3.3]metacyclophane (syn-**6c**): Prisms (from hexane), m.p. 70–72 °C;  $v_{max}$ (KBr)/cm<sup>-1</sup> 2904, 1592, 1432, 1208, 1116, 1002 and 870;  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 1.02 (3H, t, J = 7.7 Hz, CH<sub>2</sub>CH<sub>3</sub>), 1.17 (9H, s, *tBu*), 2.30 (2H, q, J = 7.7 Hz, CH<sub>2</sub>CH<sub>3</sub>), 3.45 (2H, d, J = 14.4 Hz, 3, 10-CH<sub>2</sub>), 3.67 (3H, s, OMe), 3.68 (2H, d, J = 14.7 Hz, 1,12-CH<sub>2</sub>), 3.79 (2H, d, J = 14.7 Hz, 1,12-CH<sub>2</sub>), 4.22 (2H, d, J = 14.4 Hz, 3, 10-CH<sub>2</sub>), 6.72 (2H, s, 14,16-ArH), 6.91 (2H, s, 5,7-ArH) and 6.93 (1H, s, 18-ArH); *m/z* 386 (M<sup>+</sup>); HRMS (Cl): *m/z* Calcd for C<sub>23</sub>H<sub>30</sub>OS<sub>2</sub> (386.62) requires C, 71.45; H, 7.82%).

*syn*-6,15-*Di*-*tert*-*butyl*-9-*methoxy*-2,11-*dithia*[3.3]*metacyclophane* (*syn*-6d): Prisms (from hexane), m.p. 115–117 °C;  $\delta_{\rm H}$ (CDCl<sub>3</sub>) 1.08 (9H, s, *t*Bu), 1.14 (9H, s, *tBu*), 3.46 (2H, d, *J* = 15.0 Hz, *CH*<sub>2</sub>), 3.60 (2H, d, *J* = 15.0 Hz, *CH*<sub>2</sub>), 3.66 (3H, s, OMe), 3.78 (2H, d, *J* = 15.0 Hz, *CH*<sub>2</sub>), 4.19 (2H, d, *J* = 15.0 Hz, *CH*<sub>2</sub>) and 6.84–6.90 (5H, m, Ar*H*); *m*/*z* 414 (M<sup>+</sup>) (Found: C, 72.19; H, 8.17. C<sub>25</sub>H<sub>34</sub>OS<sub>2</sub> (414.67) requires C, 72.41; H, 8.27%).

syn-6-Bromo-15-tert-butyl-9-methoxy-2,11-dithia[3.3]metacyclophane (syn-6e): Prisms (from hexane), m.p. 153–154 °C;  $v_{max}(KBr)/cm^{-1}$  2908, 1574, 1420, 1200, 1002 and 846;  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 1.25 (9H, s, *tBu*), 3.40 (2H, d, J = 14.3 Hz, 3,10-*CH*<sub>2</sub>), 3.67 (3H, s, OMe), 3.70 (2 H, d, J = 14.6 Hz, 1,12-*CH*<sub>2</sub>), 3.77 (2H, d, J = 14.6 Hz, 1,12-*CH*<sub>2</sub>), 3.77 (2H, d, J = 14.6 Hz, 1,12-*CH*<sub>2</sub>), 4.19 (2H, d, J = 14.3 Hz, 3,10-*CH*<sub>2</sub>), 6.90 (1H, s, 18-Ar*H*), 6.98 (2H, s, 14,16-ArH) and 7.02 (2H, s, 5,7-ArH); *m/z* 436, 438 (M<sup>+</sup>); HRMS (CI): *m/z* Calcd for C<sub>21</sub>H<sub>25</sub>BrOS<sub>2</sub> (M<sup>+)</sup> 436.05303. Found 436.05179 (Found: C, 57.49; H, 5.67. C<sub>21</sub>H<sub>25</sub>BrOS<sub>2</sub> (437.46) requires C, 57.66; H, 5.76%).

Similarly, compounds *anti*-**8a** and *anti*-**8b** were synthesised in the same manner as described in 60 and 85% yields, respectively.

anti-15-tert-Butyl-9-methyl-2,11-dithia[3.3]metacyclophane (anti-**8a**): 60% as prisms (from hexane); m.p. 83–84 °C;  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 1.31 (9H, s, *tBu*), 2.17 (3H, s, *Me*), 3.55 (2H, d, *J* = 15.0 Hz, *CH*<sub>2</sub>), 3.71 (2H, d, *J* = 15.0 Hz, *CH*<sub>2</sub>), 3.78 (2H, d, *J* = 13.8 Hz, *CH*<sub>2</sub>), 3.94 (2H, d, *J* = 13.8 Hz, *CH*<sub>2</sub>), 5.65 (1H, broad s, internal-*H*<sub>18</sub>), 6.78 (2H, t, *J* = 7.5 Hz, Ar*H*), 6.84 (2H, s, Ar*H*) and 6.97 (1H, t, *J* = 7.5 Hz, Ar*H*); m/z 342 (M<sup>+</sup>) (Found: C, 73.91; H, 7.53. C<sub>21</sub>H<sub>26</sub>S<sub>2</sub> (342.56) requires C, 73.63; H, 7.65%).

anti-6,15-Di-tert-butyl-9-methyl-2,11-dithia[3.3]metacyclophane (anti-**8b**): 85% as prisms (from hexane); m.p. 101–102°C;  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 1.24 (9H, s, *tBu*), 1.28 (9H, s, *tBu*), 2.00 (3H, s, *Me*), 3.54  $(2H, d, J = 15.0 \text{ Hz}, CH_2), 3.70 (2H, d, J = 15.0 \text{ Hz}, CH_2), 3.77 (2H, d, J = 15.0 \text{ Hz}, CH_2)), 3.77 (2H, d, J = 15.0 \text{ Hz}, CH_2)), 3.77 (2H, d, J = 15.0 \text{ Hz}, CH_2)), 3.77 (2H, d, J = 15.0 \text{ Hz}, CH_2)), 3.77 (2H, d, J = 15.0 \text{ Hz}, CH_2)), 3.77 (2H, d, J = 15.0 \text{ Hz}, CH_2)), 3.77 (2H, d, J = 15.0 \text{ Hz}, CH_2)), 3.77 (2H, d, J = 15.0 \text{ Hz}, CH_2)), 3.77 ($ d, J = 15.0 Hz,  $CH_2$ ), 3.93 (2H, d, J = 15.0 Hz,  $CH_2$ ), 5.00 (1H, broad s, internal-H<sub>18</sub>), 6.88 (2H, s, ArH) and 7.08 (2H, s, ArH); m/z 398 (M<sup>+</sup>) (Found: C, 75.19; H, 8.53. C<sub>25</sub>H<sub>34</sub>S<sub>2</sub> requires C, 75.32; H, 8.60%).

Received 22 April 2009; accepted 26 June 2009 Paper 09/0600 doi: 10.3184/030823409X12474221035244 Published online: 10 August 2009

#### References

- K. Meurer and F. Vögtle, *Top. Curr. Chem.*, 1985, **127**, 1. V. Boekelheide, *Top. Cur. Chem.*, 1983, **113**, 87. 1
- 2
- P.M. Keehn and S.M. Rosenfield (eds), Cyclophanes, Academic Press, 3 New York, 1983, vol. 1, chap. 6, p. 428.
- F. Vögtle, Cyclophane-chemistry, Wiley, Chichester, 1993.
- 5 R.H. Mitchell and V. Boekelheide, Tetrahedron Lett., 1970, 1197.
- R.H. Mitchell and V. Boekelheide, J. Chem. Soc., Chem. Commun., 1970, 6 1555
- 7 W. Anker, G.W. Bushnell and R.H. Mitchell, Can. J. Chem., 1979, 57, 3080.
- R.H. Mitchell, R.J. Carruther, L. Mazuch and T.W. Dingle, J. Am. Chem. Soc., 1982, 104, 2544.
- 9 R.H. Mitchell and V. Boekelheide, J. Am. Chem. Soc., 1974, 96, 1547.
  10 F. Vögtle and L. Schunder, Chem. Ber., 1969, 102, 2677.
- 11 M. Tashiro and T. Yamato, J. Org. Chem., 1981, 46, 1543.

- 12 M. Tashiro, K. Koya and T. Yamato, J. Am. Chem. Soc., 1982, 104, 3707.
- M. Tashiro and T. Yamato, J. Org. Chem., 1985, 50, 2939. 13
- T. Yamato, T. Arimura and M. Tashiro, J. Chem. Soc., Perkin Trans. 1, 14 1987.1.
- 15 M. Tashiro, A. Tsuge, T. Sawada, T. Makishima, S. Horie, T. Arimura, S. Mataka and T. Yamato, J. Org. Chem., 1990, 55, 2404.
- M. Nishio and M. Horita, Tetrahedron, 1989, 45, 7201. 16
- C.D. Andreetti, R. Ungaro and A. Pochini, J. Chem. Soc., Chem. Commun., 1979, 1005. 17
- 18 R. Ungaro, A. Pochini, C.D. Andreettiand O. Domiano, J. Chem. Soc., Perkin Trans. 2, 1985, 197.
- M.A. McKervey, E.M. Seward, G. Ferguson and B.L. Ruhl, J. Org. Chem., 1986, 51, 3581.
- 20 D.J. Cram, S. Karbach, H.-E. Kim, C.B. Knobler, E.F. Marverick, J.L. Ericson and R.C. Helgeson, J. Am. Chem. Soc., 1988, 110, 2229.
- 21 P. Soncini, S. Bonsignore, E. Dalcanale and F. Ugozzoli, J. Org. Chem., 1992, 57, 4608.
- J.L. Atwood, S.G. Bott, C. Jones and C.L. Raston, J. Chem. Soc., Chem. 22 Commun., 1992, 1349
- 23 K. Kobayashi, Y. Asakawa, Y. Kikuchi, H. Toi and Y. Aoyama, J. Am. Chem. Soc., 1993, 115, 2648.
- R.E. Merrifield and W.D. Phillips, J. Am. Chem. Soc., 1958, 80, 2778. 24
- 25 L.A. Singer and D.J. Cram, J. Am. Chem. Soc., 1963, 85, 1080.
- 26 T. Kaneda and S. Misumi, Bull. Chem. Soc. Jap., 1977, 50, 3310.
- T. Yamato, J. Matsumoto, N. Shinoda, S. Ide, M. Shigekuni and 27 M. Tashiro, J. Chem. Res. (S), 1994, 178.
- 28 T. Yamato, S. Kabu, K. Tokuhisa and M. Tashiro, J. Org. Chem., 1992, 57, 271.