SHORT PAPER

J. Chem. Research (S), 2003, 66-68

Preparation and structures of dithia(1,3)pyreno[3.3.*n*]-metacyclophanes†

Kan Tanaka[a]*, Hiroyuki Tsuchiya[a], Yoshiki Kakinaga[a], Toru Hironaka[a] and Takehiko Yamato[b]*

[a]*Department of Industrial Chemistry, Faculty of Engineering, Tohwa University, 1-1-1 Chikushigaoka, Minami-ku, Fukuoka-shi, Fukuoka 815-8510, Japan*
[b]*Department of Applied Chemistry, Faculty of Science and Engineering, Saga University, Honjo-machi 1, Saga-shi, Saga 840-8502, Japan*

Conformational studies are discussed of [3.3.2]metacyclophane **3b**, which adopts a flexible *anti*-saddle conformation, in comparison with the corresponding [3.3.1]metacyclophane **3a,** adopting a crown structure.

Keywords: metacyclophanes, pyrenophanes, conformation, ring current effect

Although many cyclophanes having a pyrene skeleton and related compounds have been prepared,[1-3] there have been few investigations of their chemical nature in spite of a large number of reports on their spectroscopic properties. Such investigation has been limited, because the preparation of pyrene having the substituents at 1- and 3-positions is not easy. We reported the $AlCl_3$-catalysed acetylation of 2,7-di-*t*-butylpyrene with acetyl chloride using the *t*-butyl group as a positional protective group to afford only the 4,9-di-acetylated product, 4,9-diacetyl-2,7-di-*t*-butylpyrene[4] and this strategy is also suitable for the preparation of 1,3-di-substituted pyrenes, which afforded convenient starting materials for the preparation of 1,3-bridged benzenopyrenophanes, 8-substituted [2]metacyclo[2](1,3) pyrenophanes.[5] Mitchell and Boekelheide have reported that 9,18-dimethyl-2,11-dithia[3.3]MCP (MCP = metacyclophane) exists in *syn*- and *anti*-conformers, which do not interconvert below 200°C.[6] Vögtle *et al.*[7] have made extensive studies of *syn-anti* conversions in other dithia[3.3]MCPs, especially in relation to the size of the substituents. Although studies on the *syn* and *anti* conformers of small ring compound, dithia[3.3]MCPs have been reported, the conformational analysis of medium and large ring compounds is not straightforward because these are highly flexible and have many conformers. Freezing conformational equilibrium, which is the common method of analysis, is often not effective in highly flexible molecules. Fukazawa *et al.*[8] developed a useful and very reliable method for the conformational analysis of flexible molecules using a combination of molecular mechanics calculations and chemical shift simulation of certain protons without the use of the freezing technique.

Although there exist two possible conformational isomers in dithia[3.3]MCPs: *syn* and *anti* conformation, three different conformational isomers; *i.e. syn*-crown, *syn*-saddle and *anti*-saddle conformers, being possible of which *syn*-saddle conformer is newly counted, due to the methylene bridges in dithia[3.3.*n*]MCPs. Thus, in contrast to two possible conformations in dithia[3.3]MCPs,[6] the conformational isomerism in the present system is slightly more complicated. Furthermore, the conformations regarding dithia[3.3.*n*]MCPs having a pyrene skeleton are not known so far. Thus, there is substantial interest in investigating the effects of the number of methylene bridges on the conformations of the dithia[3.3.*n*]MCPs **3**.

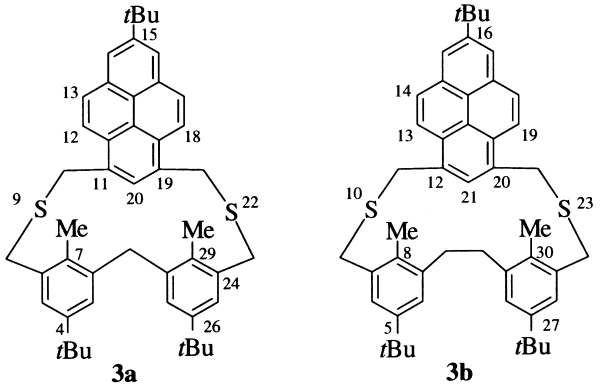


Fig. 1 Numbering scheme for dithia(1,3)pyreno[3.3.*n*]metacyclophane **3**.

We describe here the synthesis of macrocyclic pyrenophanes such as the title MCPs using the above method, as well as a study of their conformation and spectral characterisation.

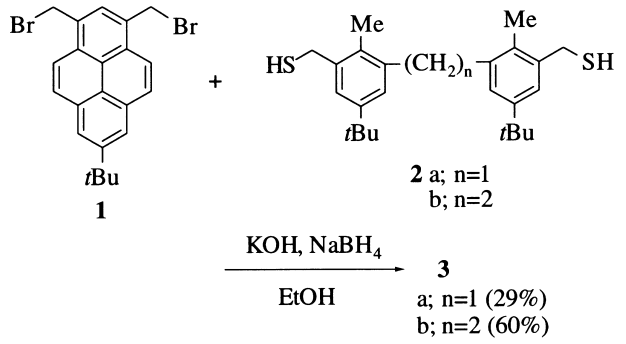
Results and discussion

1,3-Bis(bromomethyl)-7-*t*-butylpyrene (**1**) was prepared according to our reported procedure[5] from pyrene using *t*-butyl group as a positional protecting group on the aromatic ring. 1,*n*-Bis(mercaptomethyl)diphenylalkanes **2** are prepared according to the reported procedure[9] starting from the corresponding diphenylalkanes, which are chloromethylated with chloromethy methyl ether in the presence of $TiCl_4$ in CH_2Cl_2, followed by treatment with thiourea and potassium hydroxide in ethanol to afford the desired **2a** and **2b**.

Cyclisation of **1** with **2** under high-dilution conditions with 10% ethanolic potassium hydroxide in the presence of a small amount of sodium borohydride[10] gave the dithia(1,3)-pyreno[3.3.*n*]MCPs **3a** and **3b** in 29% and 60% yields, respectively, as shown in Scheme 1.

Relatively little is known about the conformation of mobile medium sized MCPs having more than three benzene rings. Tashiro *et al.*[11] have reported dithia[3.3.2]MCPs having three internal methyl groups are mobile. Vögtle *et al.*[12] prepared tetraphenyl[2.2.2.2]MCP with internal phenyl groups and studied the restricted rotation of the phenyl substituent by dynamic ^{1}H -NMR spectral investigation. Protons of the internal phenyl of the above cyclophane appeared at lower field. Also, two conformers, the stepped and folded forms, were postulated for [2.1.1]MCPs,[13] which favored the stepped one on the basis of the shielded aryl protons at δ 6.27 and

* To receive any correspondence. E-mail: yamatot@cc.saga-u.ac.jp
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*



Scheme 1

6.49 ppm. Although there are two possible conformational isomers for the above MCP, three different conformational isomers: *syn*-crown, *syn*-saddle and *anti*-saddle conformers are possible for **3** (Figure 2) due to the methylene and ethylene bridge. All the bridge protons of the above-prepared cyclophanes **3** are observed as a singlet in ^{1}H NMR spectra at 25°C. The conformations of **3a** and **3b** have been evaluated by dynamic ^{1}H NMR spectroscopy. However, the protons of the Ar*CH*$_2$*SCH*$_2$Ar methylene group and Ar*CH*$_2$Ar of dithia[3.3.1]MCP **3a** appear each as a singlet even below –60°C ($CDCl_3/CS_2$ 1/3), and the rate of conformational ring flipping of **3a** is faster than the NMR time scale above this temperature. Similar findings were obtained in dithia[3.3.2]MCP **3b**. These results indicate that the dithia-[3.3.*n*]MCPs are much more flexible than the dithia[3.3]MCPs.

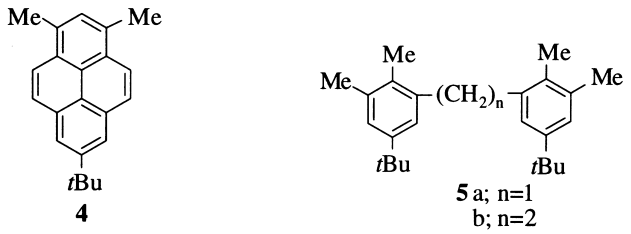


Table 1 Chemical shift (δ ppm) of an internal pyrene proton and methyl protons of dithia[3.3.*n*]metacyclophanes **3**[a]

Compound	Internal pyrene proton		Protons of internal methyl protons	
	δ_H	$\Delta\delta_H$[b]	δ_{Me}	$\Delta\delta_{Me}$[b]
3a	6.57	-1.06	2.04	-0.26
3b	6.90	-0.73	1.80	-0.41
4	7.63			
5a			2.30	
5b			2.21	

[a]Determined in $CDCl_3$ using $SiMe_4$ as a reference. [b]Upfield shift due to ring current. $\Delta\delta_H = \delta_H$cyclophane – $\delta_H$reference, $\Delta\delta_{Me} = \delta_{Me}$cyclophane – δ_{Me}reference.

The chemical shifts of only the internal pyrene protons and the internal methyl protons of **3** as well as the chemical shift differences ($\Delta\delta = \delta_{cyclophane} - \delta_{reference}$) with the proton ($H_2$) of 7-*t*-butyl-1,3-dimethylpyrene **4** and the methyl protons at position 2 and 2′ of 5,5′-di-*t*-butyl-2,2′,3,3′-tetramethyldiphenylalkanes **5** are summarised in Table 1. The ring current effect of the opposite aromatic ring on the internal protons can be judged by the values of the chemical shift differences (Δδ).[14,15] As shown in Table 1, the internal pyrene proton (H_{20} for **3a** and H_{21} for **3b**) on the pyrene ring is clearly shifted upfield ($\Delta\delta_H$ –1.06 for **3a** and –0.73 for **3b**) by the ring current in two opposite benzene rings. Also, the internal methyl protons of **3a** and **3b** show upfield shifts ($\Delta\delta_{Me}$ –0.26 for **3a** and –0.41 for **3b**) due to the ring current based on the pyrene ring of **3**. The value of $\Delta\delta_{Me}$ of cyclophane having ethylene bridge **3b** ($\Delta\delta_{Me}$ –0.41) is larger than those of cyclophanes having methylene bridge **3a** ($\Delta\delta_{Me}$ –0.26). This fact suggests that the internal methyl protons on the benzene rings of **3b** is also shielded by the another opposite benzene ring. Interstingly, the up-field shift of the internal pyrene proton of dithia[3.3.1]MCP **3a** ($\Delta\delta_H$ –1.06) is larger than that of dithia[3.3.2]MCP **3b** ($\Delta\delta_H$ –0.73). The internal pyrene proton in dithia[3.3.1]MCP **3a** can clearly be seen to be shielded by the adjacent ring, a common consequence of a face-to-face overlapping with the opposing benzene rings. This observation indicates that the preferential conformation of dithia[3.3.1]MCP **3a** might adopt *syn*-crown-conformation. In contrast, in the case of dithia[3.3.2]MCP **3b**, a singlet for the internal methyl groups is observed at an upper field shift δ = 1.80 ($\Delta\delta_{Me}$ –0.41) than that of dithia[3.3.1]MCP **3a** ($\Delta\delta_{Me}$ –0.26) due to the ring current of the opposing aromatic ring preferentially adopting *anti*-saddle conformation. Thus, depending on the number of methylene bridges of dithia[3.3.*n*]MCPs different preferential conformations might be proposed.

The heats of formation (H_f) of **3a** and **3b** by PM3 calculation are also shown in Fig. 2. In the case of the cyclophane having methylene bridge **3a**, the *anti*-saddle-**3a** conformer has higher energy, H_f = 33.461 kcal/mol, than *syn*-crown-**3a** conformer, H_f = 30.515 kcal/mol. On the other hand, in the case of the cyclophane having ethylene bridge **3b**, the *syn*-saddle conformer is less stable as compared to the *anti*-saddle conformer. The higher energy level in *syn*-conformer could be attributable to the fact that the 1,2-diarylethane moiety in the *syn*-saddle conformer and *syn*-crown conformer is eclipsed, whereas that of the *anti*-saddle conformer is staggered. These findings are consistent with their ^{1}H NMR data that **3b** adopt *anti*-saddle conformation. Accordingly, the internal methyl protons of **3a** might be slightly affected by the ring current of the pyrene ring than that of the opposite benzene ring having methyl group because of **3a** not favoured the *anti*-saddle conformer.

Conclusions

The preparation of dithia(1,3)pyreno[3.3.*n*]MCPs **3** by the coupling reaction of the corresponding 1,3-bis(bromomethyl)pyrene **1** with 1,*n*-bis(mercaptomethyl)diphenylalkanes **2** in ethanol under high-dilution conditions using a *t*-butyl group as a positional protecting group on pyrene ring appears to be a useful route to such compounds. An interesting result was obtained concerning conformations of dithia(1,3)pyreno[3.3.*n*]MCPs depending on the number of methylene bridges. Thus, the preferential conformation of dithia(1,3)pyreno[3.3.1]MCP **3a** might adopt *syn*-crown-conformation. In contrast, in the case of dithia(1,3)pyreno[3.3.2]MCP **3b** the *anti*-saddle conformation is more favourable than the *syn*-saddle conformation. Further studies on the chemical properties and the computational investigation for the conformers of dithia(1,3)pyreno[3.3.*n*]MCPs **3** are now in progress.

Experimental

^{1}H NMR spectra were recorded at 270 MHz on a Nippon Denshi JEOL FT-270 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-01SA-2 spectrometer at 75 eV using a direct-inlet system. Elemental analyses were performed by Yanaco MT-5. All computational calculations were done using Oxford Molecular CAChe (V 4.0) and Wavefunction MacSpartan

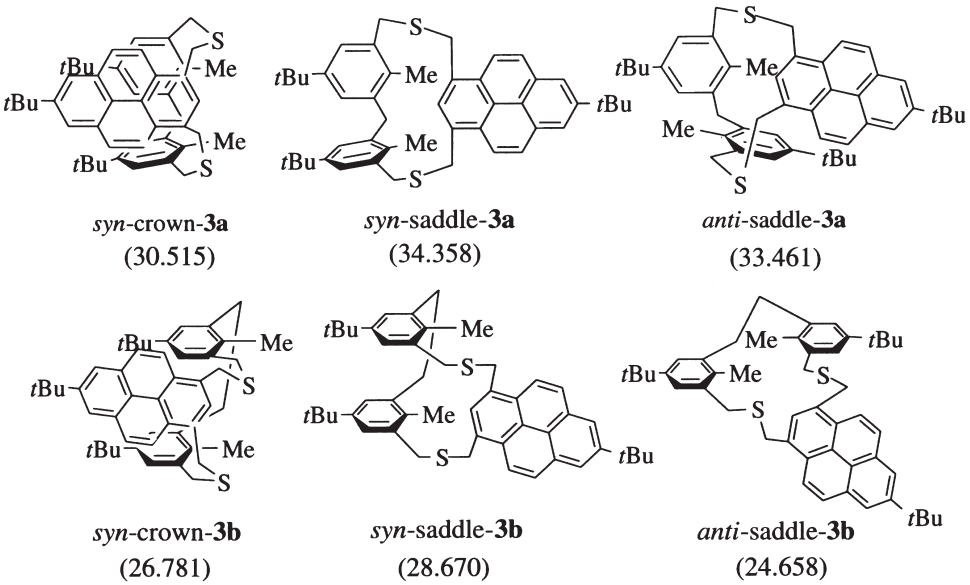


Fig. 2 Heats of formation (H_f/ kcal/mol) of comformers of dithia(1,3)pyreno[3.3.*n*]MCPs **3a** and **3b**.

Plus (V 1.2.2) as a calculation program on SGI INDY and Apple Macintosh G4.

Materials: Preparation of 1,3-bis(bromomethyl)-7-*t*-butylpyrene (**1**) has been previously described.[4] The preparation of 1,1-bis[5-*t*-butyl-3-(mercaptomethyl)-2-methylphenyl]methane (**2a**) and 1,2-bis[5-*t*-butyl-3-(mercaptomethyl)-2-methylphenyl]ethane (**2b**) was carried out as previously reported.[10,11]

Preparation of 5,16,27-tri-t-butyl-8,30-dimethyl-10,23-dithia (1,3)pyreno[3.3.2]metacyclophane **3b**: A solution of 1,2-bis[5-*t*-butyl-3-(mercaptomethyl)-2-methylphenyl]ethane (**2b**) (1.20 g, 2.9 mmol) and 1,3-bis(bromomethyl)-7-*t*-butylpyrene (**1**)[4] (1.29 g, 2.9 mmol) in benzene (100 cm^3) was added dropwise from Hershberg funnel with stirring to a solution of of KOH (0.48 g, 8.6 mmol) and $NaBH_4$ (0.22 g, 5.8 mmol) in EtOH (700 cm^3). When the addition was completed (addition time 3 h), solvent was evaporated and residue was extracted with $CHCl_3$. The extract was washed with water, dried over $MgSO_4$, and evaporated *in vacuo*. The residue was chromatographed over silica gel using a 40:1 mixture of hexane and ether as eluent to give a solid, which was recrystallised from hexane to afford the title compound **3b** (1.22 g, 60%) as pale yellow prisms, m.p. 104–105°C; ν_{max}(KBr)/cm^{-1} 2948, 1596, 1460, 1360, 1222, 1022; δ_H($CDCl_3$) 1.29 (18 H, s), 1.57 (9 H, s), 1.80 (6 H, s), 3.11 (4 H, s), 3.63 (4 H, s), 4.16 (4 H, s), 6.99 (1 H, s), 7.08 (2 H, s), 7.39 (2 H, s), 8.08 (2 H, d, *J* 9.2), 8.20 (2 H, s), 8.27 (2H, d, *J* 9.2); MS *m/z* 696 (M^+). HRMS (CI): *m/z* Calc. for $C_{48}H_{56}S_2$ (M^+) 696.3823; Found 696.3823.

4,15,26-Tri-*t*-butyl-7, 29-dimethyl-9,22-dithia(1,3)pyreno[3.3.1] metacyclophane (**3a**) was prepared in the same manner as pale yellow prisms in 29% yield. **3a** was obtained as pale yellow prisms (hexane), m.p. 165–168°C; ν_{max}(KBr)/ cm^{-1} 2928, 1594, 1440, 1200, 874; δ_H($CDCl_3$) 1.39 (18 H, s), 1.56 (9 H, s), 2.04 (6 H, s), 3.81 (8 H, s), 4.28 (2 H, s), 6.57 (1 H, s), 7.25 (2 H, s), 7.46 (2 H, s), 8.03 (2 H, d, *J* 9.3), 8.16 (2 H, s), 8.22 (2 H, d, *J* 9.3); MS *m/z* 682 (M^+). HRMS (CI): *m/z* Calc. for $C_{47}H_{54}S_2$ (M^+) 682.3667; Found 682.3665.

Received 15 October 2002; accepted 22 January 2003
Paper 02/1608

References

1 T. Umemoto, S. Satani, Y. Sakata and S. Misumi, *Tetrahedron Lett.*, 1975, 3159.
2 T. Kawashima, T. Otsubo, Y. Sakata and S. Misumi, *Chem. Lett.*, 1978, 5115.
3 R. H. Mitchell and R. Mahadevan, *Tetrahedron Lett.*, 1981, **22**, 5131.
4 T. Yamato, A. Miyazawa and M. Tashiro, *Chem. Ber.*, 1993, **126**, 2505.
5 T. Yamato, A. Miyazawa and M Tashiro, *J. Chem. Soc., Perkin Trans. 1*, 1993, 3127.
6 R. H. Mitchell and V. Boekelheide, *Tetrahedron Lett.*, 1970, 1197.
7 F. Vögtle and L. Schunder, *Chem. Ber.*, 1969, **102**, 2677.
8 Y. Fukazawa, T. Hayashibara, Y. Yang and S. Usui, *Tetrahedron Lett.*, 1995, **36**, 3349.
9 M. Tashiro and T. Yamato, *Synthesis*, 1981, 435.
10 M. Tashiro and T. Yamato, *J. Org. Chem.*, 1981, **46**, 1543.
11 M. Tashiro, T. Watanabe, A. Tsuge, T. Sawada and S. Mataka, *J. Org. Chem.*, 1989, **54**, 2632.
12 R. Bockmann and F. Vögtle, *Chem. Ber.*, 1981, **114**. 1048.
13 (a) T. Sato, M. Wakabayashi, K. Hata and M. Kainosho, *Tetrahedron*, 1971, **27**, 2737; (b) T. Yamato, N. Sakaue, T. Furusawa, M. Tashiro, G.K.S. Prakash and G.A. Olah, *J. Chem. Research (S)*, **1991**, 242. *(M)*, **1991**, 2414.
14 (a) F. Vögtle and P. Neumann, *Angew. Chem.*, 1972, **84**, 75; *Angew. Chem. Int. Ed. Engl.*, 1972, **11**, 73; (b) F. Vögtle and P. Neumann, *Synthesis*, 1973, 85; (c) F. Vögtle and G. Höhner, *Top. Curr. Chem.*, **74**, 1 (1978); (d) P. M. Keehn and S. M. Rosenfield, *Cyclophanes*, Academic Press, New York, 1983, vol. 1; (e) F. Vögtle, *Cyclophane Chemistry*, John Wiley & Sons New York Ltd., 1993.
15 (a) M. Tashiro and T. Yamato, *J. Org. Chem.*, 1981, **46**, 4556; (b) M. Tashiro and T. Yamato, *J. Org. Chem.*, 1983, **48**, 1461.