Preparation and spectroscopic study of 13-substituted 2,11-dithiahexahydro[3.3]paracyclophanes

Shaw-Tao Lin[a,*], Ya-Chen Yang[b], Shu-Farn Lin[a] and Lih-Jiun Hwang[a]

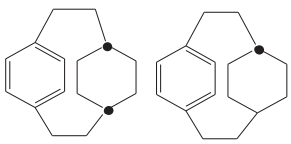
[a]*Department of Applied Chemistry, Providence University, Sha-Lu, Taichung Hsien, Taiwan, 433*

[b]*Department of Applied Life Science, Asia University, Wufeng, Taichung hsien, Taiwan 413*

A series of 13-substituted 2,11-dithiahexahydro[3.3]paracyclophanes each containing a substituent on the benzene ring were prepared for ^{1}H NMR and X-ray diffraction analyses. The benzene ring and the cyclohexane ring demonstrate shielding of the hydrogen(s) of the opposite ring. The benzene ring is distorted by the substituent on that ring.

Keywords: 13-substituted 2,11-dithiahexahydro[3.3]paracyclophanes

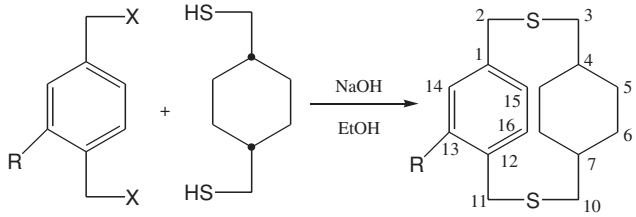
Cyclophanes have drawn the attention of many chemists due to the rigidity in their structure and the interaction between two rings. Recent reviews have discussed in some depth their preparation and properties.[1] The majority of hydrocarbon cyclophanes containing two arene rings have been reported. However, studies are limited of the unsubstituted dithia[3.3]CPs and [2.2]CPs ([CP = cyclophane]). In the past few years, we have successfully prepared another series of paracyclophanes (= [PCP]) bearing a benzene ring and a *cis*- or *trans*-cyclohexane ring bridged with two carbons, *i.e.* 3*e*,4,5,6*e*,7,8-hexahydro[2.2]paracyclophane (cHHPCP) (**1**)[2] and 3*a*,4,5,6*e*,7,8-hexahydro- [2.2]paracyclophane (tHHPCP) (**2**)[3]. Compound **1** was reduced using Li/NH_3 to form a diene,[3] which is different from the dienes obtained by the catalytic hydrogenation of [2.2]paracyclophane.[4] The methylene hydrogens of the cyclohexano group in the rigid structure of **2** appear at high field (δ–2.36) because of its placement over the π-cloud of the benzene ring. In our previous studies, we have also prepared the [2.2]*meta*-, *ortho*-, and *para*-cyclophanes containing the 1,4-cyclohexano group,[5] as well as [2.2]-*para*, *meta*- and *ortho*-cyclophanes containing 1,3-cyclohexano group.[6] In continuation of our interest in the spectroscopic study of cyclophanes, we wished to prepare a series of 2,11-dithiahexahydro[3.3]paracyclo phanes, which contain benzene rings bearing a substituent and cyclohexano units, via the coupling reactions of 1,4-bis(mercaptomethyl)cyclohexane and the corresponding 1,4-bis(halomethyl)benzenes. Due to the rigidity of PCP, the two rings face each other at a short distance. In the past, studies of their chemical behavior and the ^{1}H chemical shifts concluded that the π-electron cloud of benzene and the cyclohexano unit can interact with each other. Here, we have prepared 13-substituted 2,11-dithiahexahydro[3.3]paracyclophanes for the investigation of the interaction between monosubstituted benzene ring and cyclohexane ring by means of ^{1}H NMR spectra.



1 **2**

Results and discussion

13-Substituted 2,11-dithiahexahydro[3.3]paracyclophanes **9–12** were obtained by the coupling reactions of the corresponding 1,4-bis(halomethyl)benzenes **3–7** with *cis*-1,4-bis(mercaptomethyl)cyclohexane under high dilution conditions in 10 % ethanolic NaOH solution.[7] (Scheme 1)



3 R = H, X = Br
4 R = Cl, X= Br
5 R = Br, X= Br
6 R = OCH_3, X = Br
7 R = NO_2, X= Cl

8 R = H
9 R = Cl
10 R = Br
11 R = OCH_3
12 R = NO_2
13 R=NH_2
14 R=NMe_2

Scheme 1

In the previous studies, unsubstituted 2,11-dithiahexahydro-[3.3]paracyclophanes were obtained in good yield. However, the preparation of 13-substituted (-Cl, -Br, -OCH_3, and -NO_2) 2,11-dithiahexahydro[3.3]paracyclophanes gave relatively low yields. These results may be attributed to the combination of a steric and electronic effect of the substituents which could inhibit the formation of products during the cyclisation process. 2,11-Dithia-hexahydro[3.3]-13-aminoparacyclophane **13** was obtained by catalytic hydrogenation of its nitro-counterpart **12** in the presence of 10% Pd/C with N_2H_4 as a hydrogen source.[8] During the hydrogenation process, the activity of palladium was not effected by the presence of the sulfur of compound **12**. The dimethylamino derivative **14** was prepared from the reaction of compound **13** and HCHO with $NaBH_4$ as a reducing agent.[9]

Compounds **9–14** contain a monosubstituted benzene ring and a cyclohexano unit with two bridges containing sulfur atoms. The cyclohexane ring is known to be present as a chair form in the HHPCPs. Under those circumstances, two methylene groups will be forced toward the benzene ring. In this [3.3]PCP series, the distance between hydrogens of the cyclohexane and the benzene ring is expected to be small. The proximity factor of the benzene ring current will result in an up-field shift for some hydrogens of the cyclohexane ring. Some characteristic chemical shifts for the protons of the cyclohexane rings are summarised in Table 1. Due to the instability of free amino- and dimethylamino-bis(1,4-dihalomethyl)benzene, no chemical shift is available for comparison with the aryl protons. The chemical shifts of the methylene protons are divided into two classes, *i.e.*, one is at 0.37–0.45 ppm; and another group is at 0.02–0.06 ppm. Also, in comparison with substituted 1,4-bis(halomethyl)benzenes, the change in chemical shifts of aryl protons was position dependent. Thus while the aryl protons move to up-field by

* Correspondent.

Table 1 Some characteristic chemical shifts (ppm) in cyclophanes.

R	Cyclophane					
	Cyclohexane ring	Bridging				
	H	–CH_2–		Ar–H	Ar–H[a]	Δ[b]
H	0.45	3.58		6.96	7.40	–0.44
MeO	0.38	3.56	3.32	6.67	6.93	–0.26(*p*)[c]
		3.64	4.01	6.96	7.28	–0.32(*m*)
				6.84	6.90	–0.06(*o*)
Br	0.34	3.52	3.62	7.02	7.30	–0.28(*p*)
		3.57	4.00	7.11	7.41	–0.30(*m*)
				7.57	7.60	–0.03(*o*)
Cl	0.37	3.58	3.49	6.99	7.27	–0.28(*p*)
		3.63	4.03	7.11	7.41	–0.30(*m*)
				7.36	7.28	0.08(*o*)
NO_2	0.03	3.64	3.45	7.19	7.69	–0.50(*p*)
		3.74	4.62	7.28	7.41	–0.41(*m*)
				8.13	8.08	0.05(*o*)
NH^2	0.02	3.43–	3.59	6.46	—	
		3.67		6.80	—	
				6.74	—	
NMe_2	0.06	3.57	3.41	6.85	—	
		3.64	4.10	7.13	—	
				6.91	—	

[a]Substituted α,α'-dibromo-*p*-xylene; [b]$\delta_{(Ar\text{-}H)cyclophane} - \delta_{(Ar\text{-}H)dibromoxylene}$; [c]The positions are relative to the substituent at C_{13}.

0.26–0.45 ppm for *para*- and *meta*-protons (with respect to the substituent, *i.e.* hydrogen at C15 and C16) a rather constant shift is observed for the *ortho*-proton (hydrogen at C14) for substituted HHPCPs **9**–**14**. When the bromine atoms are replaced by sulfur atoms (*i.e.* dithiocyclophanes) on both halomethyl groups, the chemical shifts of the aryl protons are expected to be changed to the same extent. In the unsubstituted cyclophane **8**, four aryl protons move upfield 0.44 ppm compared with dibromoxylene indicating that the benzene ring is parallel with the cyclohexano unit leading to an equivalent environment for four aryl protons. In other words, the different degree in the up-shifts of protons on the C14, C15, C16 indicate that the benzene ring is not parallel with cyclohexano unit for compounds **9**–**14** for the steric reasons. The substituent on the benzene ring will keep away from the cyclohexano unit, *i.e.*, the unsubstituted side will be forced toward to the cyclohexane ring. In this circumstance, one of methine protons on the cyclohexano ring might be closer to the ring current of the benzene ring and result in the upfield shifts. The four protons on the methylene groups at the benzylic positions also show substantially different chemical shifts confirming the distortion of the benzene ring which results in different magnetic environments.

Our previous study on the X-ray crystallographic analysis of the 2,11-dithia-4,5,6,7,9-hexahydro[3.3]paracyclophane (**8**) demonstrates the high strain caused by a bent benzene ring.[11] In this work, the structures of compounds **12** and **13** have also been examined by X-ray single crystal analysis for comparison. The ORTEP drawings are shown in Fig. 1**.** Some of selected bond lengths and bond angles are listed in Table 2. From the Table we find that the lengths of the carbon–carbon bonds in the benzene ring of compounds **12**, **13** are distorted differently. While nitro derivative **12** gave longer bond lengths for C2–C3 (1.405Å), C4–C5 (1.388 Å) and C6–C7 (1.387 Å); amino counterpart (**13**) resulted in bond lengths on C2–C3 (1.402 Å), C3–C4 (1.384 Å), and C5–C6 (1.393 Å), demonstrating the localised, orientated benzene rings. The bond angles also show substantial difference on the $\angle_{C2\text{-}C3\text{-}C4}$ (122.87° *vs* 118.6°), $\angle_{C3\text{-}C4\text{-}C5}$ (120.2° *vs* 122.6°),

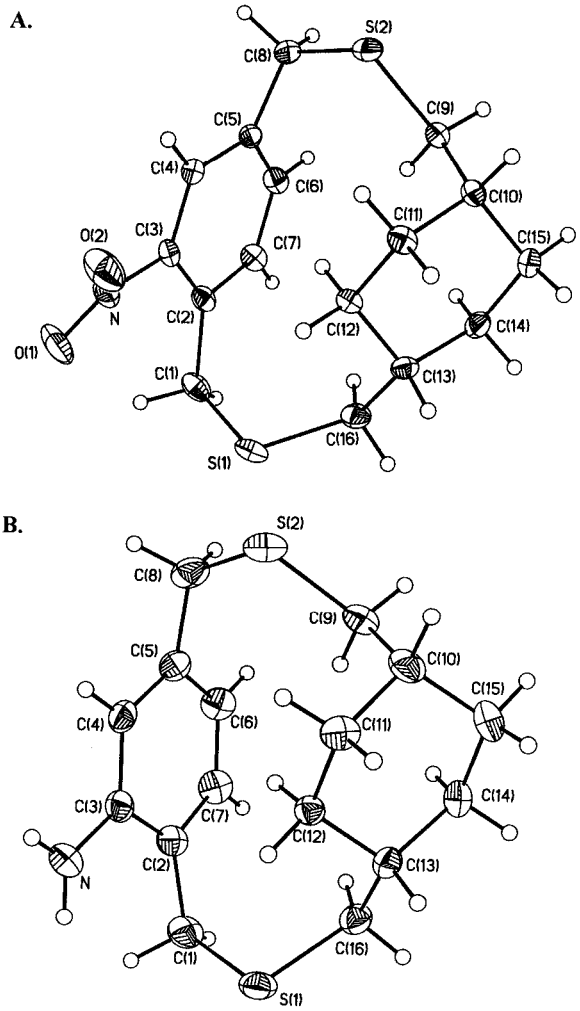


Fig. 1 Molecular structures of the compound A (12) and B (13). All hydrogen atoms are omitted for clarity.

and $\angle_{C7\text{-}C2\text{-}C3}$ (115.0° *vs* 118.0°) for compounds **12** and **13,** respectively. The distortion of the benzene ring of the cyclophanes **12** and **13** are affected by the electronic and steric factors of the substituents. The bent angles in the benzene ring moiety and the methylene of nitroPCP **12** and aminoPCP **13** are shown in Fig. 2. The benzene ring and two methylene groups at the *para* position of the ring are non-coplanar and the degrees of bending are denoted as α and β respectively. In general, the benzene ring bending angles α in compounds **12** and **13** are smaller than that in compound **8**. This might be rationalised by the longer bond lengths in the benzene ring of compounds **12**, and **13** leading to distortion and less strain of the benzene ring. On the other hand, the β angles of **12 (13)**, at 7.6° (3.5°) and 4.5° (4.0°), are the bending angles of methylene group from the plane of the benzene ring. The direction of this distortion in such the *p*-xylyl unit is bowed toward the concave face of the cyclohaxane ring. Compound **12** has a more asymmetric structure than those of compounds **8** and **13**. Larger β angles for compound **12** resulted from the shorter bond length of C1–S1 and C2–C3 in comparison with compound **13**. The strong electron-withdrawing nature of the nitro group at C3 draws the electron cloud from the sulfur atom to reduce the bond lengths of C1–S1 (1.816 Å (12) *vs* 1.835 Å (13)).

From the ^{1}H NMR chemical shift information, we find the larger variation of chemical shifts in the cyclophanes consisting of the benzene ring and cyclohexane ring compared with that of the cyclophanes consisting of two benzene rings.

Table 2 Selected bond distances/Å, angles/°, and torsion angles/° with e.s.d.s in parentheses

	NO_2(**12**)	NH_2 (**13**)
S1–C16	1.816(2)	1.815(3)
S1–C1	1.816(3)	1.835(3)
S2–C9	1.811(2)	1.815(3)
S2–C8	1.823(2)	1.829(3)
N–C3	1.472(3)	1.379(3)
C1–C2	1.496(3)	1.499(4)
C2–C7	1.382(3)	1.382(4)
C2–C3	1.405(3)	1.412(4)
C3–C4	1.374(3)	1.384(3)
C4–C5	1.388(3)	1.372(3)
C5–C6	1.371(3)	1.393(4)
C5–C8	1.503(3)	1.498(4)
C6–C7	1.387(3)	1.376(4)
C9–C10	1.524(3)	1.521(4)
C13–C16	1.531(3)	1.530(3)
C1–S1–C16	102.90(11)	103.00(13)
C9–S2–C8	103.93(11)	103.77(13)
C2–C1–S1	113.07(15)	114.26(17)
N–C3–C2	120.53(19)	121.3(2)
C2–C3–C1	122.3(2)	125.34(19)
C2–C3–C4	122.87(19)	118.6(2)
C4–C3–N	119.9(2)	116.40(18)
C3–C4–C5	120.2(2)	122.6(2)
C4–C5–C6	118.02(19)	118.5(2)
C4–C5–C8	121.6(2)	121.7(2)
C6–C5–C8	120.17(19)	119.5(2)
C5–C6–C7	121.0(2)	119.4(2)
C7–C2–C1	118.95(19)	119.4(3)
C2–C7–C6	122.4(2)	122.4(2)
C2–C3–C7	115.08(19)	118.0(2)
C5–C8–S2	112.85(15)	113.14(18)
C10–C9–S2	113.43(15)	113.4(2)
C13–C16–S1	117.98(15)	117.16(18)
O2–N–O1	122.8(2)	
O2–N–C12	118.0(2)	
O1–N–C12	119.2(2)	

The X-ray analysis of the nitro derivative demonstrated that the nitro group on the benzene ring is able to draw the electron cloud from the sulfur resulting in shorter bond lengths and a larger bending angle β.

Experimental

^{1}H NMR spectra were recorded at 250 MHz, and ^{13}C NMR at 62.86 MHz at ambient temperature on a Bruker AC-250 spectrometer. Chemical shifts (δ) for the samples in deuteriochloroform solution are reported in δ units relative to tetramethylsilane. EI mass spectra were obtained on a JEOL JMS DX-300 double-focusing mass spectrometer at an ionization potential of 70 eV. Samples were introduced via a direct insertion probe.

Typical Procedure for bromination of substituted xylenes:[11] Benzoyl peroxide (0.25 g) was added to a solution of substituted *p*-xylene (0.03 mol) and *N*-bromosuccinimide (11.3 g, 0.06 mol) in CCl_4 (200 ml). The mixture was refluxed for 1 h and then cooled to room temperature and filtered. The solvent was then removed at reduced pressure from the filtrate to obtain a crude solid. Crystallisation of the product from ethanol gave pure 1,4-bis(bromomethyl)-2-chlorobenzene **4**;[12] 1,4-bis(bromomethyl)-2-bromobenzene **5**;[12] 1,4-bis(bromomethyl)-2-methoxybenzene **6**.[11] Their m.p.s and ^{1}H NMR spectra were identical to authentic samples.

Nitration of 1,4-bis(chloromethyl)benzene. Nitric acid (60%, 10 ml) was added at 0 °C to a solution of 1,4-bis(chloromethyl)benzene (15.0 g, 0.085 mol) in concentrated aqueous H_2SO_4 (95%, 15 ml). The mixture was stirred at 60 °C for 2 h. The solution was cooled, poured into 500 ml ice-water and filtered to give a yellow solid, which was washed with water (3 × 200 ml). Crystallisation of the product from ethanol gave 1,4-bis(chloromethyl)-2- nitrobenzene (**7**) yellow needle (13.1 g, 70%): m.p. 39–40 °C.(Lit.[13] m.p. 39–40 °C).

Typical procedure for the coupling reaction.: A solution of α,α'-dihaloxylene **3** (1.24 g, 6.8 mmol) and 1,4-bis(mercaptomethyl) cyclohexane (1.21 g, 6.8 mmol) was added over a period of 70 h to a solution of NaOH (0.6 g, 1.5 mmol) in 95% ethanol (200 ml), using the high dilution technique. The solution was refluxed for an additional 2 h and then concentrated *in vacuo* to give a viscous residue. The residue was extracted with CH_2Cl_2 (3 × 20 ml). The extract was dried over $MgSO_4$, filtered, and evaporated to give a waxy residue. The residue was separated chromatographically on silica gel with CH_2Cl_2/*n*-hexane (2/3: v/v) as an eluent to yield compounds **8–12**, respectively.

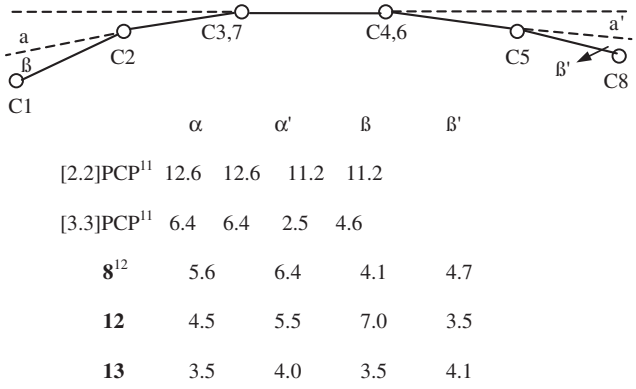


Fig. 2 Comparison of the bending angles of the benzene ring (α,α′) and the extending methylene groups (β,β′) in compounds [2.2]paracyclophane ([2.2]PCP), [3.3]paracyclophane ([3.3]PCP), **8, 12**, and **13**.

2,11-Dithia-4,5,6,7,8,9-hexahydro[3.3]paracyclophane (**8**): Yield 3.72 g (68% yield), colourless crystals, m.p. 142 °C (from hexane–CH_2Cl_2, lit.[14] 140–141.5 °C); ^{1}H NMR δ0.45 (br., 2H,), 0.95–1.65 (br., 8H), 2.33 (br., 4H), 3.58 (s, 4H), 6.96 (s, 4H).

13-Chloro-2,11-dithia-4,5,6,7,8,9-hexahydro[3.3]paracyclophane (**9**)**:** Yield 0.57 g (27%), colourless crystals, m.p. 110–111 °C; ^{1}H NMR δ0.37 (br, 1H), 0.80 (br, 1H), 1.04 (br, 3H), 1.29–1.42 (br, 5H), 2.18 (br, 2H), 2.39 (br, 2H), 3.49 (d, 1H, *J* = 12.5Hz), 3.58 (d, 1H, *J* = 7.5 Hz), 3.63 (d, 1H, *J* = 7.5 Hz), 4.03 (d, 1H, *J* = 12.5 Hz), 6.99 (d, 1H, *J* = 5 Hz, C_{15}–*H*), 7.11 (d, 1H, *J* = 5 Hz, C_{16}–*H*), 7.36 (s, 1H, C_{14}–*H*); ^{13}C NMR δ 23.6, 24.4, 24.6, 24.8, 27.7, 31.8, 32.2, 32.5, 34.9, 36.5, 128.0(C_{15}), 131.1(C_{16}), 131.4(C_{14}), 131.7(C_{12}), 134.9(C_{13}), 139.6(C_1); EIMS *m/z* (rel. int.) 314[(M+2)$^{+\cdot}$, 9], 312(M$^{+\cdot}$, 24), 138 (100), 103 (25), 77 (15). Anal. Calcd. for $C_{16}H_{21}S_2Cl$: C, 61.4 ; H, 6.8. Found: C, 61.5; H, 6.8 %.

13-Bromo-2,11-dithia-4,5,6,7,8,9-hexahydro[3.3]paracyclophane (**10**): Yield 0.36 g (15%), colourless crystals, m.p. 120–121 °C; ^{1}H NMR δ0.34 (br, 1H), 0.85(br, 1H), 1.04 (br, 2H), 1.22 (br, 5H), 2.14 (br, 2H), 2.54 (br, 2H), 3.52 (d, 1H, *J* = 7.5 Hz), 3.57 (d, 1H, *J* = 7.5 Hz), 3.62 (d, 1H, *J* = 12.5 Hz), 4.00 (d, 1H, *J* = 12.5 Hz), 7.02 (d, 1H, *J* = 7.5 Hz, C_{15}–*H*), 7.11 (d, 1H, *J* = 7.5Hz, C_{16}–*H*), 7.57 (s, 1H, C_{14}–*H*); ^{13}C NMR δ25.3, 25.8, 25.9, 27.9, 32.1, 32.4, 32.6, 36.7, 37.6, 126.1(C_{15}), 128.8(C_{16}), 131.2(C_{13}), 135.3(C_{14}), 136.7(C_{12}), 140.0(C_1); EIMS *m/z* (rel. int.) 358[(M+2)$^{+\cdot}$, 23]356 (M$^{+\cdot}$, 24), 182 (100), 141 (77), 103 (40), 77 (41); Anal. Calcd. for $C_{16}H_{21}BrS_2$: C, 53.8; H, 5.9. Found: C, 53.7; H, 6.1%.

13-Methoxy-2,11-dithia-4,5,6,7,8,9-hexahydro[3.3]paracyclophane (**11**)**:** Yield 0.22 g (26%), colourless crystals, m.p. 123–124 °C; ^{1}H NMR δ0.31 (br, 1H), 0.83–1.39 (br, 9H), 2.13 (br, 2H), 2.55 (br, 2H), 3.32 (d, 1H, *J* = 12.5 Hz), 3.56 (d, 1H, *J* = 12.5 Hz), 3.64 (d, 1H, *J* = 12.5 Hz), 3.85 (s, 3H), 4.01 (d, 1H, *J* = 12.5Hz), 6.67 (d, 1H, *J* = 7.5 Hz, C_{15}–*H*), 6.84 (1H, s, C_{14}–*H*); 6.96(d, 1H, *J* = 7.5 Hz, C_{16}–H); ^{13}C NMR δ23.9, 24.8, 28.6, 29.2, 32.3, 32.6, 32.9, 34.3, 37.0, 118.4(C_{14}), 120.1(C_{12}), 122.9(C_{15}), 131.5(C_{16}), 138.2(C_1), 159.1(C_{13}); EIMS *m/z* (rel. int.) 308 (M$^{+\cdot}$, 23), 134 (100), 104 (37), 77 (14); Anal. Calcd. for $C_{17}H_{24}S_2O$: C, 66.2; H, 7.8. Found: C, 66.1; H, 7.95%.

13-Nitro-2,11-dithia-4,5,6,7,8,9-hexahydro[3.3]paracyclophane (**12**): Yield 0.75 g (34%), yellow crystals, m.p. 133–135 °C (from *n*-hexane-CH_2Cl_2); ^{1}H NMR δ0.03 (1H, br), 0.91–1.39 (9H, br), 1.97 (2H, br), 2.65 (2H, br), 3.74 (1H, d, *J* = 13.3 Hz), 3.64 (1H, d, *J* = 13.3 Hz), 3.45 (1H, d, *J* = 13.5 Hz), 4.62 (1H, d, *J* = 13.5 Hz), 7.19 (1H, d, *J* = 7.8 Hz, C_{15}–*H*), 7.28 (1H, d, *J* = 7.5 Hz, C_{16}–*H*), 8.13 (1H, s, C_{14}–*H*); ^{13}C NMR δ24.2, 24.5, 28.5, 29.6, 31.8, 32.1, 32.6, 33.3, 35.5, 36.6, 128.5(C_{14}), 132.3(C_{12}), 133.5(C_{16}), 133.8(C_{15}), 140.1(C_1), 150.2(C_{13}); EIMS *m/z* (rel. int.) 323(M$^{+\cdot}$, 51), 181(34), 149 (77), 141 (63), 105 (75), 91 (100), 77 (88), 67 (82), 55 (57); Anal. Calcd. for $C_{16}H_{21}S_2NO_2$: C, 59.4; H, 6.5. Found: C, 59.3; H, 6.6%.

13-Amino-2,11-dithia-4,5,6,7,8,9-hexahydro[3.3]paracyclophane (**13**)[8]: N_2H_4 (20 ml) was added slowly to 13-nitro-2,11-dithia-4,5,6,7,8,9-hexahydro[3.3]paracyclophane (0.2 g, 6 mmol) and Pd/C (10 %, 0.1g) in ethanol (50 ml). The solution was heated at 80 °C for 2 h, and after the mixture was cooled down to room temperature, the mixture was filtered through a layer of Celite, and water was added to quench the reaction. The aqueous mixture was extracted with hexane (3 × 20ml). The extract was dried over $MgSO_4$, filtered, and the organic phase was evaporated to give a waxy residue. The residue was separated chromatographically on silica gel with CH_2Cl_2/*n*-hexane (3:1 v/v) as an eluent to yield **13;** yield 1.05 g (60%), yellow crystals, m.p. 108–110 °C (from *n*-hexane–CH_2Cl_2); ^{1}H NMR δ0.01 (1H, br), 0.96–1.36 (9H, br), 1.99 (d, 1H, *J* = 11.1 Hz), 2.09 (d, 1H, *J* = 11.1 Hz), 2.64 (1H, dd, *J* = 5.2, 13.4 Hz), 2.76(1H, dd, *J* = 5.2, 13.4 Hz), 3.43–3.59 (3H, m), 3.67 (d, 1H, *J* = 15Hz), 4.02 (2H, s), 6.47 (1H, dd, *J* = 1.3, 7.4 Hz, C_{15}–*H*), 6.74 (1H, d, *J* = 1.3, C_{14}–*H*), 6.79 (1H, d, *J* = 7.5 Hz, C_{16}–*H*); ^{13}C NMR δ23.1, 24.2, 28.8, 29.0, 32.0, 32.1, 32.2, 33.5, 34.2, 37.3, 119.4(C_{14}), 120.9(C_{15}), 122.1(C_{12}), 130.5(C_{16}), 139.5(C_1), 146.9(C_{13}); EIMS *m/z* (rel. int.) 293 ($M^{+\cdot}$, 39), 184 (17), 150 (26), 119 (100), 106 (42), 91 (56), 67(25), 67 (25), 55 (16); Anal. Calcd. for $C_{16}H_{23}NS_2$: C, 65.5; H, 7.9. Found: C, 65.2; H, 7.7%.

13-Dimethylamino-2,11-dithia-4,5,6,7,8,9-hexahydro[3.3]paracyclophane (**14**)[9]: To a solution of 13-amino-2,11-dithia-4,5,6,7,8,9-hexahydro[3.3]paracyclophane (0.29 g, 1.0 mmol), H_2SO_4 (3.0 M, 0.5 ml) and formaldehyde (40%, 5.3 ml, 7.0 mmol) in THF (7.0 ml) at 0°C, $NaBH_4$ (0.22 g, 6 mmol) was added in small portions for a period of 1 h. After the mixture was neutralised with $NaHCO_3$, it was extracted with ether (5.0 ml × 3). The extract was dried over $MgSO_4$, filtered, and evaporated to give a high viscous residue. The residue was separated chromatographically on silica gel with CH_2Cl_2/*n*-hexane (3:1 v/v) as an eluent to yield **14** as a light yellow highly viscous liquid. Yield 0.23 (72 %); ^{1}H NMR 0.06 (1H, br), 0.45–1.75(9H, br.), 2.38(4H, br.), 2.74(6H, s), 3.41(1H, d, *J* = 13.1 Hz), 3.57(1H, d, *J* = 12.9Hz), 3.64(1H, d, *J* = 12.9 Hz), 4.10(1H, d, *J* = 13.1 Hz), 6.85(1H, d, *J* = 7.5 Hz, C_{15}–*H*), 6.96(1H, s, C_{14}–*H*), 7.13(1H, d, *J* = 7.5 Hz, C_{16}–*H*); ^{13}C NMR 29.7, 31.6, 31.9, 34.5, 36.3, 36.5, 37.1, 37.5, 44.9, 45.4, 119.6(C_{14}), 120.5(C_{15}), 120.5(C_{12}), 130.9(C_{16}), 131.7(C_1), 137.9(C_{13}); EIMS *m/z* (rel. int.) 321(M^+, 34), 178(18), 147(100), 118(16), 91(12); Anal. Calcd. For $C_{18}H_{27}NS_2$: C, 67.2; H, 8.5. Found: C, 67.1; H, 8.6%.

Crystal data: Compound **12** $C_{16}H_{21}NO_2S_2$, orthorhombic space group P2(1)/n, *a*=9.7706(18) Å, *b*=12.592(2) Å, *c*=12.741(2) Å, β=90.145(4), *V*=1567.5(5) Å^3, Z=4, *D*c=1.371 Mg/m^3, μ= 0.343mm^{-1}, F(000) = 688, reflections collected = 8741, independent reflections 3115,θ range for data collection 2.27–26.14°, data/restrains/parameter 3115/0/190; goodness of fit on F2° 1.118; R1=0.0594,wR^2=0.1566; (all data); compound **13** $C_{16}H_{23}N_2S_2$, orthorhombic space group P2(1)/n, *a*=12.689(2) Å, *b*=9.1690(16) Å, *c*=13.753(2) Å, β= 105.935(3), *V*=1538.6(5) Å^3, Z=4, *D*c=1.267 Mg/m^3, μ =0.333 mm^{-1}, F(000)=632, reflections collected = 8404, independent reflections 3019,θ range for data collection 2.56–26.12°, data/restrains/parameter 3019/0/172; goodness of fit on F2° 1.142; R1=0.0668, wR^2=0.1806.

Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos 230956 for the compound **13** and 230957 for the compound **12**. They can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request.cif.

Financial support by the Nation Science Council of the Republic of China (NSC91-2113-M-126-001) and technical information supported by National Centre for High-performance Computing are gratefully acknowledged.

Received 2 July 2004; accepted 27 June 2005
Paper 04/2612

References

1 (a) F.N. Diederich, *Cyclophanes*, Royal Society of Chemistry, Cambridge, 1991; (b) F. Vogtle, *Cyclophane Chemistry: Synthesis, Structures and Reactions*, John Wiley & Sons, Chichester, 1993.
2 F.M. Yang and S.T. Lin *J. Org. Chem*., 1997, **62**, 2727.
3 S.T. Lin, F.M. Yang and L.H. Lin, *Tetrahedron,* 1997, **53**, 16123.
4 (a) D.J. Cram and N. Allinger, *J. Am. Chem. Soc.,* 1955, **77**, 6289; (b) S.T. Lin, D.L. Wharry, R.L. Yates, N. Garti, J. Pranata, S. Siegel and P. Skrabal, *J. Org. Chem.,* 1994, **59**, 7056.
5 S.T. Lin, F.M. Yang and W.F. Tien, *J. Chem. Res., (S)*, 1999, 608.
6 S.T. Lin, F.M. Yang, H.J. Yang and D.W. Liang, *J. Chem. Soc., Perkin Trans., 1*, 1999, 1725.
7 (a) A.C. Davis, *Chem. Ind*., 1977, 203; (b) T. Yamato, K. Noda, K. Tokuhisa and M. Tashiro, *J. Chem. Res., (S)*, 1994, 210.
8 S.T. Lin, F.M. Yang, H.J. Yang and K.F. Huang, *J. Chem. Res.,* (S), 1995, 372.
9 A.G. Giumanini, G. Chiavari and F.L. Scarponi, *Anal. Chem*., 1976, **48**, 484.
10 (a) L. Ernst, *Progress in Nuclear Magnetic Resonance Spectroscopy*, 2000, **37**, 47; (b) C.E. Johnson and F.A. Bovey, *J. Chem. Phys.*, 1958, **29**, 1012; Bovey's *Table of Predicted Values of Shielding Contributions from Ring Currents in Aromatic Hydrocarbons* is contained in Appendix B of J.W. Emsley, J. Feeney and L.H. Sutcliffe, *High Resolution Nuclear Magnetic Resonance Spectroscopy*, Pergamon Press, New York, 1964.
11 B. Kovac, M. Mohraz, E. Heilbronner and V. Boekelheide, *J. Am. Chem. Soc*., 1980, **104**, 4314; P.M. Keehn, in *Cyclophanes*, eds. P.M. Keehn and S.M. Rosenfeld, Academic Press, New York, 1983, p.68; P.J. Dyson, D.G. Humphrey, J.E. Mogrady, D.P. Mingos and D.J. Wilson, *J. Chem. Soc. Dalton Trans*., 1995, 4039.
12 P.N. Swepston, S.T. Lin, A. Hawkins, S. Humphrey, S. Siegel and A.W. Cordes, *J. Org. Chem.,* 1981, **46**, 3753.
13 M. Hibert and G. Solladie, *J. Org. Chem*., 1980, **45**, 4496.
14 J. Eldo, E. Arunkumor and A. Ajayaghosh, *Tetrahedron Lett*., 2000, **41**, 6241.
15 K.Y. Kay and Y.G. Baek, *Chem. Ber. Recl.,* 1997, 581.