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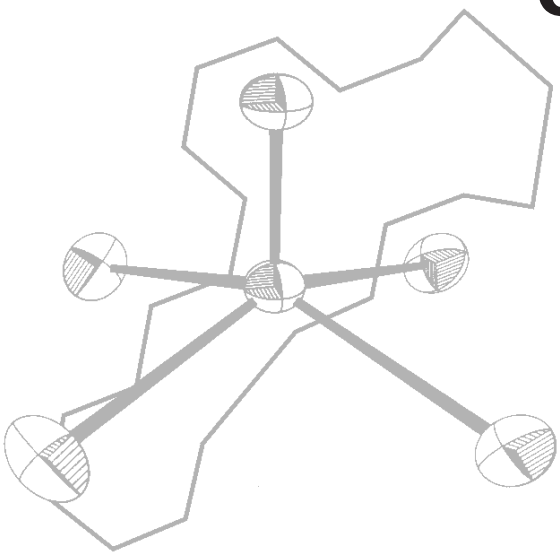

Volume 52, 1999

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Aust. J. Chem., 1999, **52**, 823–825

Rapid Communication. Imidazolium-Linked Cyclophanes

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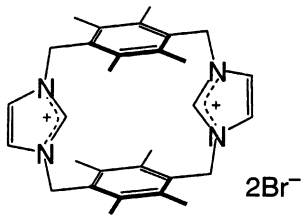
Cyclophanes have been of interest for many years and a huge variety of cyclophanes are known. A recent book by Vögtle[1] reviewed cyclophane chemistry in depth and included discussion of work with cyclophanes in fields as diverse as aromaticity, host–guest chemistry, molecular recognition, and self-replicating systems, to name just a few.

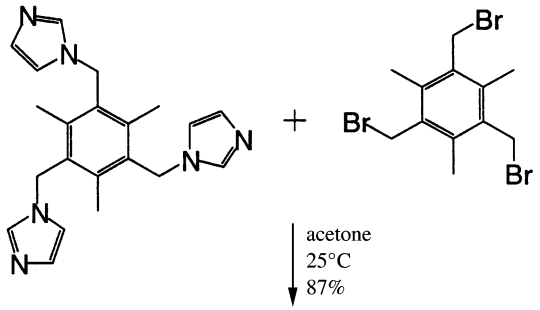
In the syntheses of many cyclophanes, competition between inter- and intra-molecular cyclization reactions results in low yields, and high-dilution conditions are often required. Recently some metacyclophanes, in which two benzene rings were linked by imidazolium units, were reported.[2] Synthetic details were not provided, but the metacyclophanes, which have structures reminiscent of calixarenes, were reported to interact with certain anions in solution and in the solid state.

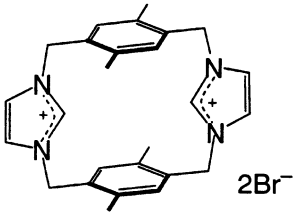
In this communication we report some of our own work on imidazolium-linked cyclophanes: the synthesis and structural characterization of the imidazolium-linked (1,3,5)-cyclophane (1) and related paracyclophanes (2)–(4). Cyclophanes (1)–(4) are easily synthesized in high yield by the reaction of (bromomethyl)benzenes with appropriate (imidazol-1-ylmethyl)benzenes. For example, without recourse to use of high-dilution conditions,[3] the triply bridged cyclophane (1) was obtained in an astonishingly high yield of 87% (after recrystallization) by treatment of 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene with 1 equiv. of 1,3,5-tris(imidazol-1-ylmethyl)-2,4,6-trimethylbenzene in acetone (Scheme 1). Paracyclophanes (2) and (3) were synthesized by analogous routes and obtained in yields of 77 and 67% respectively.

The imidazolium-linked cyclophanes, as their bromide salts, are insoluble in acetone, sparingly soluble in dimethyl sulfoxide, and freely soluble in water. In (D_6)dimethyl sulfoxide, the cyclophanes show beautifully simple n.m.r. spectra. For example, the ^{1}H n.m.r. spectrum of (1) ($(CD_3)_2SO$ solution) contains just four singlets due to the four sets of protons present (6×CH_3, 6×CH_2, 6×imidazolium

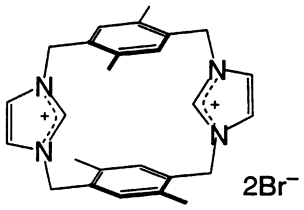


(2)

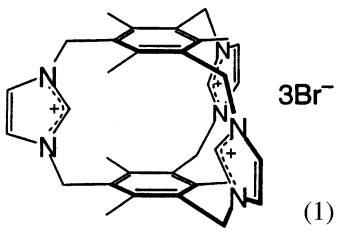




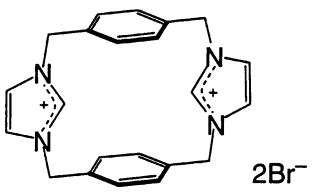
(3a)



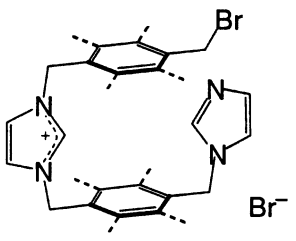
(3b)



(1)



(4)



(5)

Scheme 1

Manuscript received 27 August 1999

10.1071/CH99104 0004-9425/99/090823

H 4/H 5, 3×imidazolium H 2). The ^{1}H n.m.r. signal due to the imidazolium H 2 protons occurs at unusually high field (δ 5.60), indicating that these protons are directed towards the cyclophane cavity and the region shielded by the magnetically anisotropic benzene rings. For comparison, the ^{1}H n.m.r. signal due to H 2 in 1,3-dibenzylimidazolium chloride occurs at δ 10.79 ($CDCl_3$ solution).[4]

In the family of paracyclophanes exemplified by (2)–(4), compound (2) was consistently obtained in the highest yield and (3) was also obtained in good yield, but attempts to synthesize (4) without the use of high dilution afforded only insoluble, presumably polymeric products. The methyl groups present in the precursors of (2) and (3) would restrict the conformational freedom of the intermediate (5), and in

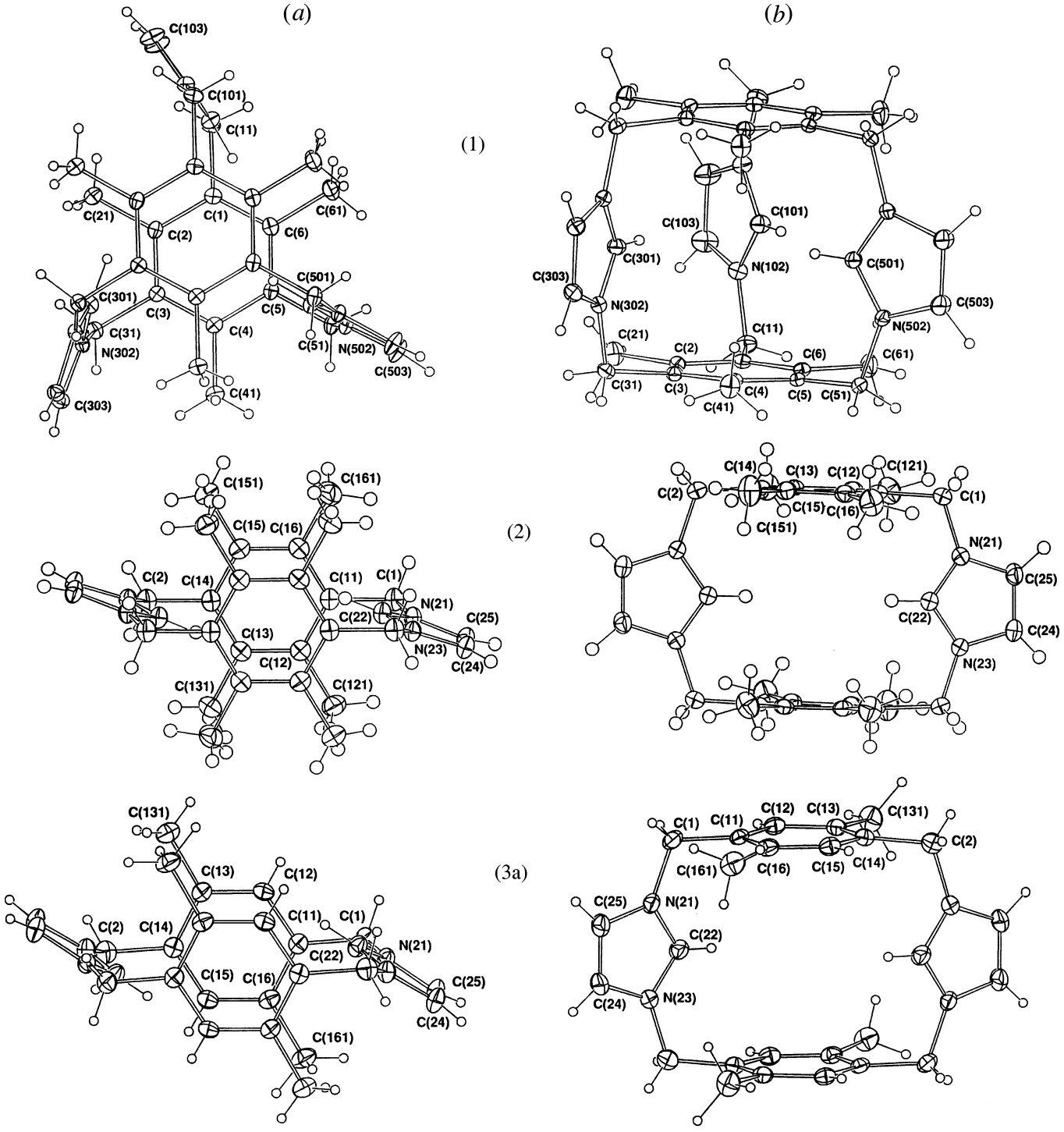


Fig. 1. Projections of the cations of (1)–(3a): (*a*) down; (*b*) normal to (both slightly oblique to) their putative principal axes. For (1) and (3a) 20%, and for (2) 50%, thermal ellipsoids are shown for the non-hydrogen atoms. Crystallographic symmetries are *m*, $\bar{1}$, $\bar{1}$ respectively.

doing so may favour cyclization of (5) over polymerization.[3,5] Similar arguments have been used to explain the ease of synthesis of certain macrocycles from precursors bearing bulky substituents.[3,5,6] In the reaction of 1,4-bis(bromomethyl)-2,5-dimethylbenzene with 1,4-bis(imidazol-1-ylmethyl)-2,5-dimethylbenzene, two cyclophane products are possible, the pseudo-geminal isomer (3a) and the pseudo-*ortho* isomer (3b), and both isomers are formed (ratio 1.7 : 1 respectively). The pseudo-geminal isomer (3a) was the less soluble isomer and was isolated by selective crystallization from methanol. In principle, (3a) and (3b) can be interconverted by rotation of one of the benzene rings about its C 1–C 4 axis, but such rotation does not occur even at temperatures up to 80°C; a pure sample of (3a) was unchanged after being heated in $(CD_3)_2SO$ at 80°C for 30 min.

(1), (2) and (3a) crystallized as hydrates from aqueous solutions and were characterized by single-crystal X-ray structural studies (Fig. 1). In each of the three structures, the cation is disposed about a crystallographic symmetry element—a mirror plane or an inversion centre—so that only one-half of the formula unit is crystallographically independent in each case. The benzene rings are parallel and separated by 5.15, 4.84 and 5.15 Å in (1), (2) and (3a) respectively. The imidazolium rings are oriented with their C 2–H bonds pointing into the cavities between the benzene rings, but oblique to the centres of the cavities. In no case is any species trapped in the cavity; the water molecules form hydrogen-bonded arrays with the bromide ions. The C–C bond lengths and bond angles are generally all close to their usual values, consistent with little or no strain within the cyclophane systems; this absence of strain may be a significant factor contributing to the high yielding syntheses of these cyclophanes.

Experimental

Nuclear magnetic resonance spectra were recorded with a Bruker ARX-500 spectrometer (500.1 MHz for ^{1}H, 125.8 MHz for ^{13}C) at ambient temperature and were referenced with respect to internal sodium 3-(trimethylsilyl)propane-1-sulfonate (δ 0.00). Microanalyses were performed by the Microanalytical Laboratory of the Australian National University, Canberra.

Synthesis of Cyclophanes

Cyclophane (1). A solution of 1,3,5-tris(imidazol-1-ylmethyl)-2,4,6-trimethylbenzene (1.00 g, 2.77 mmol, synthesized by reaction of 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene with imidazole in dimethylformamide) in acetone (75 ml) was added dropwise with stirring to a solution of 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene[7] (1.10 g, 2.77 mmol) in acetone (75 ml). The resulting solution was allowed to stand for 1 week, during which time a white solid slowly precipitated. This solid was collected by filtration and recrystallized from water/acetone, to give (1) as a white powder (1.90 g, 87%), m.p. >300°C (Found: C, 52.0; H, 5.0; N, 11.1. $C_{33}H_{39}Br_3N_6$ requires C, 52.2; H, 5.2; N, 11.1%). ^{1}H n.m.r. δ (D_2O) 2.21, s, CH_3; 5.61, s, CH_2; 5.79, br t, *J* 1.8 Hz, H 2; 7.97, d, *J* 1.8 Hz, H 4/H 5. ^{13}C n.m.r. δ (D_2O) 17.7, CH_3; 51.0, CH_2; 127.8, C 4/C 5; 131.9, C 2; 132.8, C; 144.5, C.

Cyclophanes (2) and (3) were synthesized in the same way as (1); satisfactory elemental analyses and n.m.r. data were obtained. *Cyclophane (4)* was synthesized by a similar procedure, but in less concentrated solution (50 mg of 1,4-bis(bromomethyl)benzene and 45 mg of 1,4-bis(imidazol-1-ylmethyl)benzene in 200 ml of acetone).

Crystallography

Crystals for X-ray diffraction studies were grown by vapour diffusion of dimethylformamide into aqueous solutions of (1), (2) and (3).

Cyclophane (1). $(C_{33}H_{39}N_6)Br_3{\cdot}2H_2O$, M_r 795.5. Monoclinic, $P2_1/m$ (No. 11), *a* 9.861(5), *b* 17.30(1), *c* 10.603(5) Å, β 114.34(4)°, *V* 1648 Å^3. $D_c(Z = 2)$ 1.60$_2$ g cm^{-3}; *F*(000) 808. μ_{Mo} 37 cm^{-1}; specimen: 0.26 by 0.65 by 0.10 mm; $T_{min,max}$ (Gaussian correction) 0.59, 0.71. $2\theta_{max}$ 60°. Temperature *c.* 295 K. 2933 (= N_o) 'observed' ($I > 3\sigma(I)$) out of *N* 4935 unique single counter diffractometer reflections refined by full matrix least squares (anisotropic thermal parameter refinement C,N,O,Br; ($x, y, z, U_{iso})_H$ refined) to conventional *R* on |*F*| 0.040, R_w (statistical weights) 0.048.

Cyclophane (2). $(C_{30}H_{38}N_4)Br_2{\cdot}6H_2O$, M_r 722.6. Monoclinic, *C* 2/*c* (No. 15), *a* 25.829(4), *b* 9.151(1), *c* 18.509(3) Å, β 127.379(2)°, *V* 3476 Å^3. $D_c(Z = 4)$ 1.38$_2$ g cm^{-3}; *F*(000) 1504. μ_{Mo} 23.8 cm^{-1}; specimen: 0.40 by 0.35 by 0.25 mm; '*T*'$_{min,max}$ 0.69, 0.80 ('empirical' correction ('SADABS')). $2\theta_{max}$ 58°. Temperature *c*. 153 K. N_o 3452 ($F > 4\sigma(F)$), *N* 4367merged (R_{int} = 0.017) from 19329 total Bruker AXS CCD reflections, refined by full matrix least squares to *R* 0.025, R_w 0.033 (($x, y, z, U_{iso})_H$ refined for cation, constrained for H_2O).

Cyclophane (3a). $(C_{26}H_{30}N_4)Br_2{\cdot}4H_2O$, M_r 630.4. Monoclinic, $P2_1/c$ (No. 14), *a* 9.976(3), *b* 11.799(5), *c* 13.319(3) Å, β 110.92(2)°, *V* 1464 Å^3. $D_c(Z = 2)$ 1.43$_0$ g cm^{-3}; *F*(000) 648. μ_{Mo} 28 cm^{-1}; specimen: 0.36 by 0.58 by 0.60 mm; $T_{min,max}$ 0.27, 0.41 (Gaussian correction). $2\theta_{max}$ 60°. Temperature *c*. 295 K. Data collection and refinement as for (1), *N* 4251, N_o 1793; *R* 0.040, R_w 0.051.

All structures. Monochromatic Mo Kα radiation, λ 0.7107$_3$ Å. Crystallographic data for (1)–(3a) have been deposited. Copies are available (coordinates, thermal parameters, non-hydrogen geometries, structure factors) from the Australian Journal of Chemistry, P.O. Box 1139, Collingwood, Vic. 3066, until 31 December 2004.

Acknowledgment

We thank the Australian Research Council for financial support.

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