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Synthesis and Structural Studies of Some [14]Paracyclo-bis-(1,2)pyrazolium- and (1,3)imidazolium-phanes

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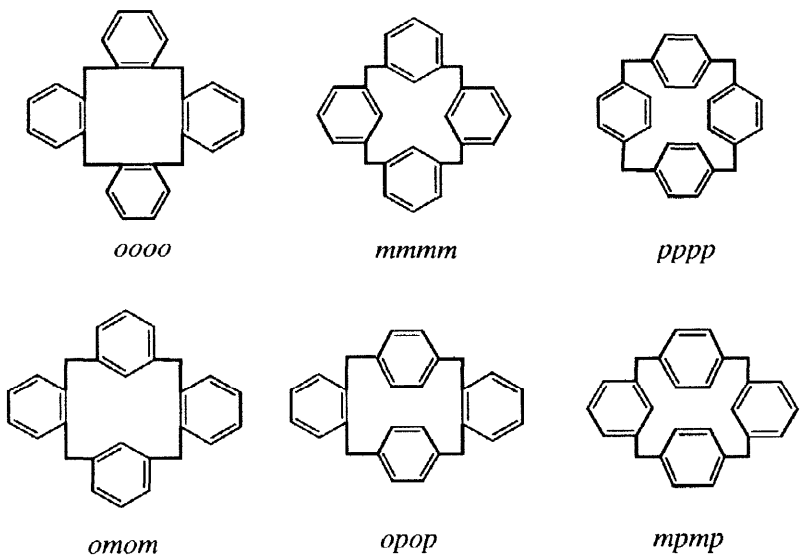
Abstract.- The crystal and molecular structure of [14]paracyclo-bis-(1,2)pyrazoliumphane dibromide (**1a**) has been determined. The compound exists in the solid state in the chair (**C**) conformation while both chair (**C**) and boat (**B**) conformations are present in solution in comparable amounts. The barrier to the **C** $\rightleftharpoons$ **B** interconversion has been determined by ^{1}H NMR spectroscopy ($\Delta G^{\ddagger} \approx 17$ kcal mol^{-1}). AM1 semiempirical calculations conveniently reproduce the difference in stability between the chair (**C**) and the boat (**B**) conformations.

INTRODUCTION

Considering only consecutive situations (no Ar-Ar bonds), macrocycles of the general formula $(C_6H_4CH_2)_4$ can present twenty-one isomers. In Scheme 1 we have represented six cases, the three most regular isomers and three cases pertinent to this work, as well as the simple notation (based on *ortho*, *meta*, *para* substitution) we have introduced [a list of all the isomers (from *oooo* to *omop*) can be obtained from the authors].



Scheme 1. Six isomers of general formula $(C_6H_4CH_2)_4$

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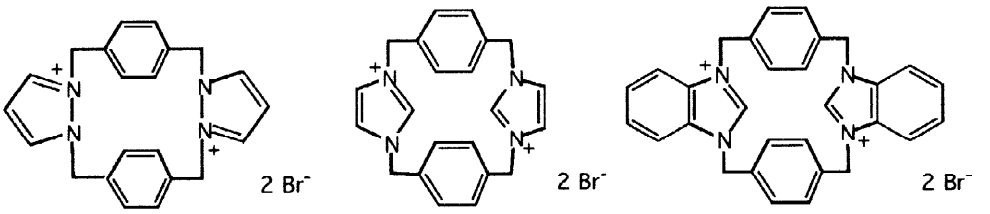
One of them (*mmmm*) corresponds to a very well known class of compounds with representatives like calixarenes and carcerands,[1-5] while another (*oooo*) is related to cyclotetraveratrylene.[6-9] Structure (*pppp*) corresponds to [1,1,1,1]paracyclophane, which is still unknown. The IUPAC names of these compounds are rather cumbersome, for instance, unsubstituted *oooo* and *mmmm* are 5,10,15,20-tetrahydro-tetrabenzo[*a,d,g,j*]cyclododecene and [19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11,13(27),15,17,19(26),21,23-dodecaene. For this reason we will use the short four-letter notation.

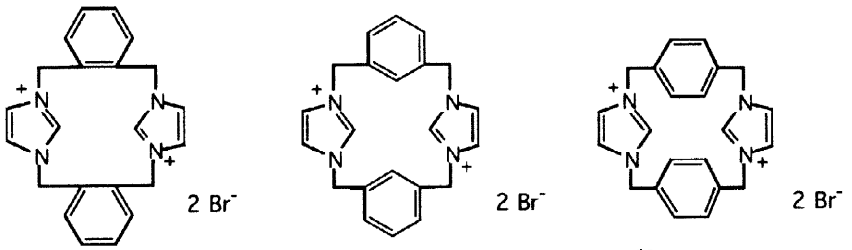
Using six-membered heterocycles, *e.g.* pyridines, *mmmm*-type structures, with either four pyridines or four pyridinium units, have recently been described.[10,11] When five-membered rings are used to replace benzene rings, only *ortho* (1,2) and *meta* (1,3) situations are possible; again the *mmmm* situation is very well known since it comprises porphyrinogens and derivatives.[12-14] Recently, Alcalde *et al.* have described [1$_4$](*ortho-meta*)heterophanes with an *omom* structure.[15]

In this paper we want to report the synthesis and structural study in solution and in the solid state of compound **1a**, a bis-pyrazolium salt, which is the first example of an *opop*-type. In a subsidiary way, we have also prepared compounds **1b** and **1c**, this latter one being related to larger-ring benzimidazolophanes.[16] We already described in 1996 the study of the fast atom bombardment mass spectra (MS-FAB$^+$) of the salts [1$_4$]paracyclo-bis-(1,2)pyrazoliumphane dibromide (**1a**), [1$_4$]paracyclo-bis-(1,3)imidazoliumphane dibromide (**1b**) and [1$_4$] paracyclo-bis-(1,3)benzimidazoliumphane dibromide (**1c**).[17]



1a **1b** **1c**

The work most related to our own results is the independent synthesis of three imidazolium cyclophanes by Zhou, Xie and Zhao in 1996.[18] These authors reported the compounds represented in Scheme 2 which they obtain from imidazolate anion and the three *bis*(bromomethyl)benzenes (*ortho*, *meta* and *para*) in good yields. The ^{1}H NMR chemical shifts (in D_2O at 90 MHz) they reported for **1b** do not coincide with ours.

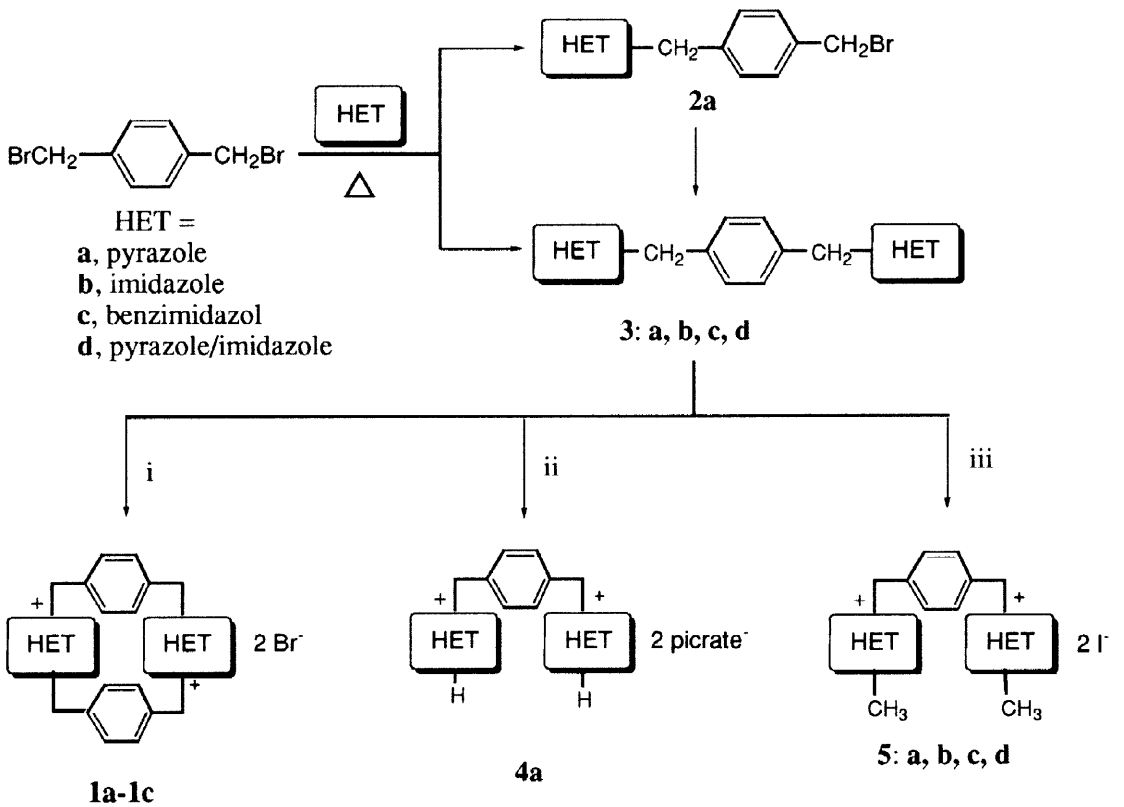


omom *mmmm* **1b** *mpmp*

Scheme 2. Three isomeric imidazolium cyclophanes

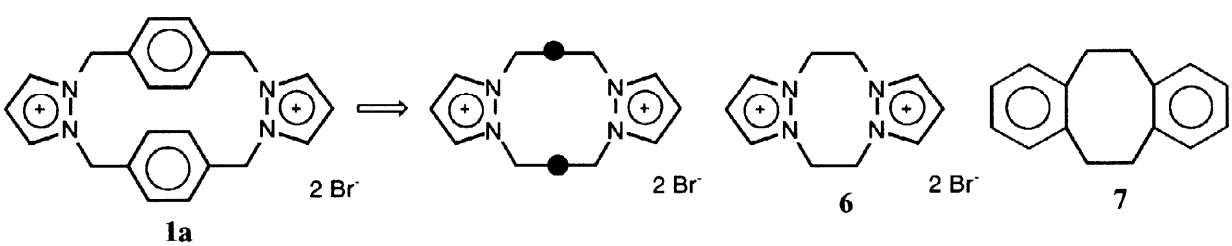
RESULTS AND DISCUSSION

Synthesis.- The three compounds (**1a**)-(**1c**) were prepared from α,α'-dibromo-*p*-xylene and the corresponding azolates as represented in Scheme 3. Depending on the reactants and the experimental conditions, cyclophanes **1**, *p*-bromomethylbenzylpyrazole **2a**, 1,4-bis(azol-1-ylmethyl)benzenes **3**, double picrate **4a** or double quaternary salts **5** were isolated.



Scheme 3. Reagents: i: α,α'-dibromo-*p*-xylene; ii: picric acid; iii: methyl iodide

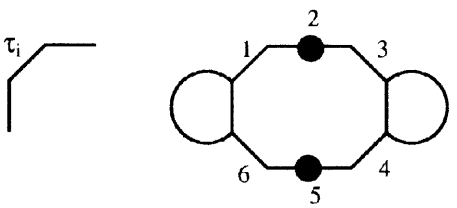
Conformational analysis of compound ***1a***. To describe the conformational surface of [1$_4$]paracyclobis-(1,2)pyrazoliumphane **1a** we have assumed that the *para*-substituted phenyl rings can be assimilated to linear spacers:



This shows the analogy of **1a** with **6** (5,6,12,13-tetrahydrobispyrazolo[1,2-*a*:1',2'-*e*][1,2,5,6] tetrazocinediium cation) and **7** (5,6,11,12-tetrahydrodibenzo[*a,e*]cyclooctene).[19-21] These systems present two conformations of minimum energy, a chair **C** (+-+-+-) and a boat **B** (+0-+0-) which interconvert by a pyrazolium flip (or a benzene flip in the case of **7**). The corresponding activation barriers are 13.5 kcal mol^{-1} for **6**[22] and 10.5

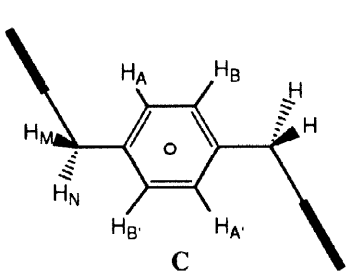
kcal mol^{-1} for **7**.[23,24] In all these systems, the chair **C** is a perfect chair but the boat **B** is a twisted boat (actually two chiral boats interconverting through the perfect boat with a very low energy barrier).[19-24] The six torsional angles which characterize compounds **6** and **7** are reported in Table 1.

Table 1. Conformation (torsion angles) of compound 1a and model compounds

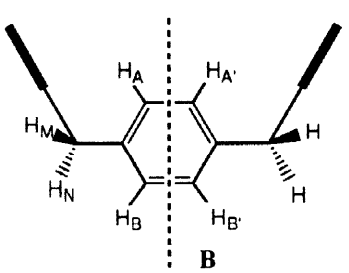


Compound	τ_1	τ_2	τ_3	τ_4	τ_5	τ_6
6 (chair, X-ray)[19]	72	-105	75	-75	105	-72
6 (chair, calc.)	74.5	-105	74.5	-74.5	105	-74.5
6 (boat, calc.)	72	0	-72	72	0	-72
7 (chair, X-ray)[20]	74	-109	73	-73	109	-74
7 (chair, calc.)	74.5	-109	74.5	-74.5	109	-74.5
7 (boat, calc.)	74	0	-74	74	0	-74
1a (chair A, X-ray)	78.3	-104.4	77.8	-78.3	104.4	-77.8
1a (chair B, X-ray)	82.1	-103.5	72.1	-82.1	103.5	-72.1
1a (chair, calc.)	75.3	-98.2	75.3	-75.3	98.2	-75.3
1a (boat, calc.)	75.0	0.0	-75.0	75.0	0.0	-75.0
1a ($TS^{\ddagger}$, calc.)	71.2	-65.1	56.1	-85.6	56.4	34.9

NMR Spectroscopy. a) Static Aspects. For [1$_4$]paracyclo-bis-(1,2)pyrazoliumphane dibromide **1a** two species are in equilibrium in solution (Tables 2 and 3). ^{1}H NMR spectra, both in D_2O and in DMSO-d_6, show that they are in a 56/46 ratio. To assign these species to the chair (54%) and the boat (46%) we have used symmetry considerations similar to those that differentiate *d,l* and *meso* isomers. The AA'BB' (neglecting benzylic couplings) systems of the four aromatic protons are different for the chair (an inversion center) and for the boat (a mirror plane):



C



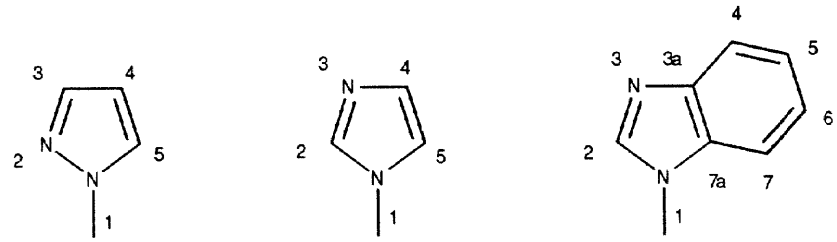
B

Table 2. ^{1}H NMR Chemical Shifts (δ in ppm) and Coupling Constants (J in Hz) of Compounds 1a-1c

Compound	Solvent	CH_2 CH_2'	H_2 H_2'	H_3 H_3'	H_4 H_4'	H_5 H_5'	H_6 H_6'	H_7 H_7'	Aryl protons
1a[a,b]	D_2O	5.49 (M)	—		6.88(t)	8.46(d)	—	—	6.19(d) (A), 6.85(d) (B)
54%		5.83 (N)		8.46(d)		^3J = 3.02			^3J = 8.0, ^4J = 2.25
C		$^2J_{gem}$ = 16.9		^3J = 3.02					^5J = 0.3
1a		5.49 (M)	—	8.43(d)	6.84(t)	8.43(d)			6.12(d) (A), 6.98(d) (B)
46%		5.84 (N)		^3J = 3.01		^3J = 3.01			^3J = 8.0, ^4J = 2.2
B		$^2J_{gem}$ = 16.9							^5J = 0.3
1a[a]	DMSO-d_6	5.80 (M)	—	8.91(d)	7.15(t)	8.91(d)	—	—	6.10(d) (A), 6.96(d) (B)
54%		6.03 (N)		^3J = 2.9		^3J=2.9			^3J = 8.0
C		$^2J_{gem}$ = 16.7							^4J = 1.9
1a		5.79 (M)	—	8.88(d)	7.11(t)	8.88(d)			6.06(d) (A), 7.09(d) (B)
46%		6.02 (N)		^3J = 2.9		^3J = 2.9			^4J = 1.5
B		$^2J_{gem}$ = 16.7							
1b	DMSO-d_6	5.33(s)	7.94(s)	—	7.96(s)	7.96(s)	—	—	7.36(s)
	D_2O	5.27(s)	7.39(s)	—	7.68(s)	7.68(s)	—	—	7.34(s)
1c	DMSO-d_6 80 °C	5.66(s)	7.91(s)	—	8.30-8.35 (m)	7.80-7.85 (m)	7.80-7.85 (m)	8.30-8.35 (m)	7.51(s)

[a] Assignments made on the basis of (^{1}H-^{1}H) Cosy 90 and Noesy experiments; [b] Data obtained by iterative analysis using the WIN-DAISY 3.0 program.

Table 3. ^{13}C NMR Chemical Shifts (δ in ppm) and Coupling Constants (J in Hz) of Compounds 1a-1c



Compound	Solvent	CH_2 CH_2'	C_2 C_2'	C_3 C_3'	C_{3a} C_{7a}	C_4 C_4'	C_5 C_5'	C_6	C_7	Aryl carbons C_{ipso}	 C-H
1a[a] **C**	D_2O	52.67 ^1J = 145.8	—	139.24 ^1J = 204.3 ^2J = 4.0 ^3J = 6.8	—	106.91 ^1J = 191.0 $^2J = {}^2J$ = 6.3	139.24 ^1J = 204.3 ^2J = 4.0 ^3J = 6.8	—	—	131.09	125.53 ^1J=162.0 128.16 ^1J=162.1
1a **B**		52.55 ^1J = 145.9 $^3J = {}^3J$ = 4.3		139.35 ^1J = 204.0 ^2J = 3.4 ^3J = 6.2		- 107.01 ^1J = 190.9 $^2J = {}^2J$ = 6.5	139.35 ^1J = 204.0 ^2J = 3.4 ^3J = 6.2			131.13	126.05 ^1J=163.9 128.18 ^1J=162.1
1b	D_2O+TFA	51.8 ^1J = 146.5	132.3	—	—	122.0 ^1J = 210.0	121.9	—	—	132.9	129.4 ^1J=162.9
	DMSO-d_6	52.4 ^1J = 146.0	134.9 ^1J = 215.0	—	—	122.9 ^1J = 208.0	122.9	—	—	136.1	129.8 ^1J = 163.5
1c	DMSO-d_6 80 °C	50.0 ^1J = 146.8	140.1 ^1J = 220.0	—	131.6	113.9 ^1J = 166.0	127.2 ^1J = 165.0	127.2	113.9	134.4	130.8 ^1J=162.0

[a] At 400 MHz.

In the chair J_{AB} is a $^3J_{ortho}$ coupling (8.0 Hz) while in the boat J_{AB} is a $^4J_{meta}$ coupling (2.2 Hz). The experimental spectra have been analyzed using an iterative program (Table 2). The geminal protons of the four equivalent CH_2 groups as well as the A and B aromatic protons have been identified through a small $^5J_{zig\text{-}zag}$ coupling, which results in a broadening of some signals. This coupling is observed only if the protons are in a coplanar disposition. An examination of the models (AM1 calculations) shows that H_N is synperiplanar while H_M is anticlinal with regard to the phenyl ring. Thus the $^5J_{zig\text{-}zag}$ coupling involves H_N and H_B in **C** and H_N and $H_{A'}$ in **B**, thus allowing the assignments reported in Table 2. The assignment is moreover consistent with shieldings by phenyl and pyrazolium aromatic rings.

b) Dynamic Aspects. The ^1H NMR spectrum of compound **1a** has been recorded in D_2O between 50 and 80 °C and in DMSO-d_6 between 50 and 110 °C with intervals of 5 °C. Several coalescences were observed at different temperatures [T_c (K)] which allow determination of the corresponding values of $\Delta G^{\ddagger}_{Tc}$ (Table 6). Although the use of several coalescences in the same compound is not a precise method to determine $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$,[25a] it has been used successfully in other cases.[26] A representation of $\Delta G^{\ddagger}_{Tc}$ *vs* T (K) for four (D_2O) or five signals (DMSO-d_6) shows a linear variation allowing an estimation of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$. In D_2O, $\Delta H^{\ddagger}$ = 11.7 kcal mol^{-1} and $\Delta S^{\ddagger}$ = -18 cal mol^{-1} K^{-1} and in DMSO-d_6, $\Delta H^{\ddagger}$ = 10.9 kcal mol^{-1} and $\Delta S^{\ddagger}$ = -21 cal mol^{-1} K^{-1} (these large values of $\Delta S^{\ddagger}$ are probably overestimated[27] and are given here more for the sign than for the absolute value). At 298 K, $\Delta G^{\ddagger}_{298}$ = 17.0 kcal mol^{-1} (D_2O) and 17.2 kcal mol^{-1} (DMSO-d_6). The barrier in compound **1a** is thus considerably higher than in the related compound **6** (13.5 kcal mol^{-1}).[22]

*Solid State Crystal Structure of **1a**.* In [14]paracyclo-bis-(1,2)pyrazoliumphane dibromide **1a** there are two independent half-molecules in the unit cell (labelled A and B, Figures 1 and 2). Both are in the **C** conformation with torsion angles reported in Table 1. Although the bond lengths and angles in both molecules are identical within the levels of accuracy of the refinement, there are small, but significant differences in torsion angles between the two molecules (examples are given in Table 4). The pyrazolium and phenyl rings are planar to within < 0.025 Å. Within each molecule, the phenyl rings are forced to be parallel by symmetry across a centre of inversion. There are no intermolecular stacking effects. The bromide anions are located outside the macrocyclic ring. The distances between the bromides and the protons of the pyrazolium rings are in the range of 2.717-2.972 Å which is shorter than the sum of the van der Waals radius of a H-atom radius and the ionic radius of a bromide anion (3.17 Å).

Table 4. Some relevant crystallographic features

Selected torsion angles (°)	A	B
N(1)-N(5)-C(6)-C(7)	74.77(2.28)	-80.06(2.21)
N(5)-C(6)-C(7)-C(8)	65.00(2.21)	-54.33(2.34)
Angle between planes of phenyl and pyrazolium rings	80.59(0.60)	81.27(0.70)
Br···H contact distances (Å)	2.717-2.932	2.780-2.972

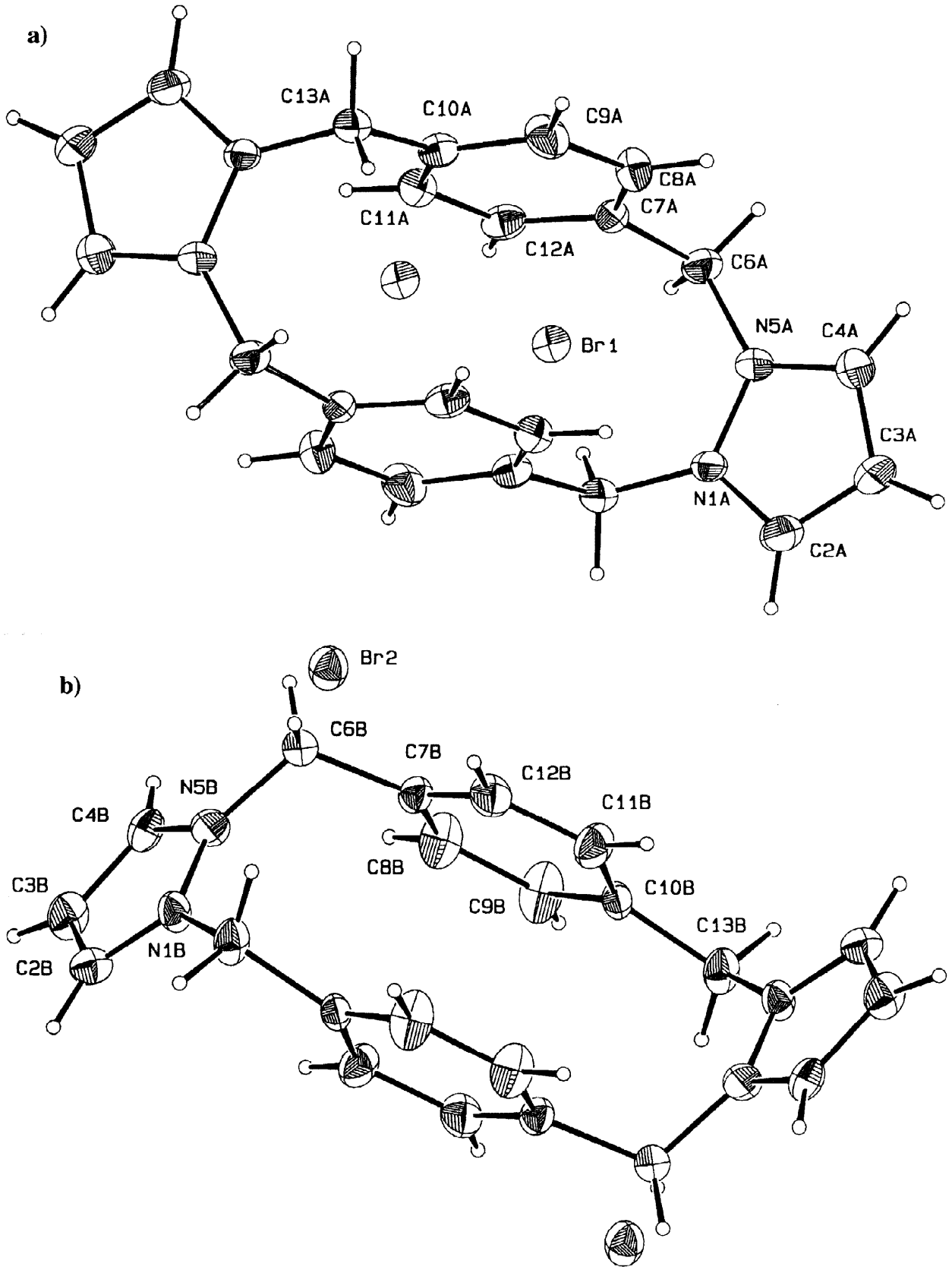


Figure 1. Compound **1a** showed in two differents views and the atomic numbering used: a) molecule A, b) molecule B.

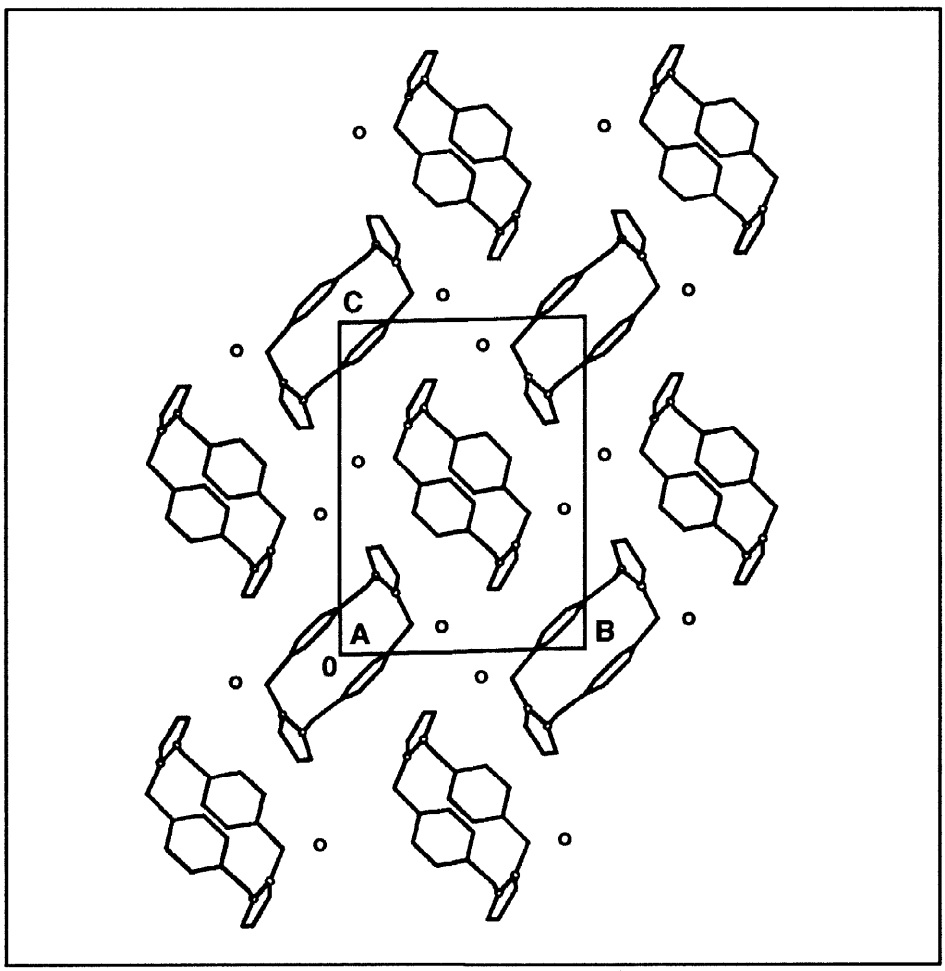


Figure 2. View of the packing present in compound **1a**. Molecule A is at (1/2 0 0) and molecule B at (1/2 1/2 1/2).

AM1 calculations of the chair (C) and the boat (B) conformations and the interconversion barrier. The calculations reported in Table 1 for compound **1a** show that the X-ray structures for molecules A and B correspond to the calculated chair conformation. The experimental geometries of the two independent molecules and the calculated geometry for the chair are very similar, not only in torsion angles (Table 1). The calculated energies of the boat **B** and the chair **C** are 577.51 and 577.35 kcal mol^{-1}, therefore, the conformation **C** is more stable than conformation **B** by 0.16 kcal mol^{-1}. The experimental result (54% **C**/46% **B** at 300 K), corresponds to 0.10 kcal mol^{-1}. The **C** $\rightleftharpoons$ **B** interconversion process is a "one-pyrazolium" flip accompanied by a twist of the "planar" pyrazolium ring, the transition state is 11.5 kcal mol^{-1} higher than the ground states (almost identical in energy), therefore, the calculated value of the barrier is lower than the experimentally determined one (17.0 kcal mol^{-1}).

CONCLUDING REMARKS

Comparing the central eight-membered ring of compounds **6** and **7** with the sixteen-membered ring of compound **1a**, both the difference in stability ΔG(**C**/**B**) and the inversion barrier $\Delta G^{\ddagger}$(**C** $\rightleftharpoons$ **B**) are modified.

	7 (bz)	**6** (pz^+)	**1a** (pz^+, ph)
ΔG(**C/B**)	-1.2 (12% **C**)	>1.8 (>95% **C**)	0.1 (54% **C**)
$\Delta G^{\ddagger}$(**C** $\rightleftharpoons$ **B**)	10.5	13.5	17.0

To compound **7** corresponds the lowest barrier and the greatest stability of the boat **B**. The replacement of the benzene rings by pyrazolium rings, realized in compound **6**, destabilizes considerably the boat **B** by electrostatic repulsion and increases the barrier by modification of the geometry (pentagonal instead of hexagonal lateral rings). In compound **1a**, increasing the distance between the pyrazolium rings compared with **6**, decreases the discrimination of the boat **B** relatively to the chair **C**; actually both pyrazolium rings are so far apart that **C** and **B** have almost the same energy. On the other hand, the barrier in **1a** increases considerably with regard to **6** due to the increased rigidity of the central ring as a consequence of the two *p*-phenyl spacers.

EXPERIMENTAL SECTION

General Methods.

Melting points were determined on a hot-stage microscope and are uncorrected. Analytical thin layer chromatography was performed on silica gel Merck 60F254 with a layer thickness of 0.2 mm. Column chromatography was carried out with silica gel Merck 60 (70-230 mesh, ASTM). Nuclear magnetic resonance (NMR) spectra were obtained on Bruker AC-200 and DRX-400 instruments. The ^1H and ^{13}C NMR chemical shifts (δ, ppm) are given relative to tetramethylsilane. In all cases, integrals correspond to the number of protons. ^1H NMR variable temperature experiments were performed with the Bruker AC-200 spectrometer under standard conditions. IR spectra (KBr) were recorded on a Philips PU 9714 between 1000 and 2000 cm^{-1}. Combustion analyses were performed with a Perkin-Elmer 2400 CHN instrument.

***p*-Bromomethylbenzylpyrazole 2a**. A mixture of pyrazole (0.68 g, 10 mmol) and α,α'-dibromo-*p*-xylene (3.0 g, 12 mmol) in 20 mL of xylene was stirred at 130 °C for 6 h. After evaporation of the xylene, the residue was chromatographed with dichloromethane as eluent to give **2a** as a white solid (40%), mp 56-57 °C. ^1H NMR ($CDCl_3$) δ 4.46 (s, CH_2Br), 5.32 (s, CH_2Pyrazole), 7.40 (d, H_3, ^3J = 1.5 Hz), 6.29 (q, H_4, ^3J = 1.5 and 2.1 Hz), 7.55 (d, H_5, ^3J = 2.1 Hz), 7.15-7.37 (m, Aryl protons); ^{13}C NMR ($CDCl_3$) δ 32.9 (^1J = 152.9 Hz), 55.3 (^1J = 139.6), 139.6 (C_3, ^1J = 185.3, ^3J = 8.4, ^2J = 5.8 Hz), 106.0 (C_4, ^1J = 176.7, ^2J = 8.7, ^2J = 10.3 Hz), 129.2 (C_5, ^1J = 185.5 Hz), 136.9, 137.4, 127.8 (^1J = 159.5 Hz), 129.4 (^1J = 160.0 Hz). IR (KBr) cm^{-1} 1510, 1435, 1420, 1400, 1350, 1270, 1210, 1090. Analysis Calcd. for $C_{11}H_{11}N_2Br$: C 52.61, H 4.41, N 11.16. Found C 52.84, H 4.50, N 10.98.

1,4-Bis(pyrazol-1-ylmethyl)benzene 3a. This compound was prepared by Hartshorn and Steel[28] [mp 103-104 °C (using phase transfer catalysis conditions)] and by Goodgame *et al.*[29] [mp 103-105 °C]. Our sample, a white solid, had mp 108 °C. ^1H NMR ($CDCl_3$) δ 5.30 (s, CH_2Pyrazole), 7.54 (d, H_3, ^3J =1.4 Hz), 6.27 (q, H_4, ^3J = 1.4 and 2.2 Hz), 7.37 (d, H_5, ^3J = 2.2 Hz), 7.17 (s, Aryl protons); ^{13}C NMR ($CDCl_3$) δ 55.4 (^1J = 139.4 Hz), 139.6 (C_3, ^1J = 185.3, ^3J = 8.4, ^2J = 5.9 Hz), 105.9 (C_4, ^1J = 176.6, ^2J = 8.7, ^2J = 10.4 Hz), 129.2 (C_5, ^1J = 187.8 Hz), 136.5, 127.9 (^1J = 160.1 Hz). IR (KBr) cm^{-1} 1505, 1435, 1420, 1395, 1355, 1285, 1230, 1165, 1090, 1050, 1020.

Dipicrate (4a), a yellow solid, had mp 176-179 °C. ^{1}H NMR (DMSO-d_6) δ 5.31 (s, CH_2Pyrazole), 7.85 (s, H_3), 6.29 (s, H_4), 7.52 (s, H_5), 7.15 (s, Aryl protons). Picryl protons: 8.59 (s) and 10.11-10.17 (bs); ^{13}C NMR (DMSO-d_6) δ 54.3 (^1J = 140.3 Hz), 138.7 (C_3, ^1J = 185.5, ^3J = 8.0, ^2J = 6.0 Hz), 105.8 (C_4, ^1J = 177.5, $^2J = {}^2J$ = 9.5 Hz), 130.8 (C_5, ^1J = 193.5 Hz), 136.9, 127.8 (^1J = 161.8 Hz). Picryl carbons: 125.0, 125.3 (^1J = 168.4, ^3J = 5.6 Hz), 141.8 and 160.4. IR (KBr) cm^{-1} 1600, 1570, 1530, 1425, 1360, 1340, 1315, 1270, 1160, 1090, 1080. Analysis Calcd. for $C_{26}H_{20}N_{10}O_{14}$: C 44.84, H 2.89, N 20.11. Found C 44.67, H 3.01, N 19.97.

1,4-Bis(imidazol-1-ylmethyl)benzene 3b. This compound was described by Dhal and Arnold[30] [mp 148-150 °C (sodium hydride, imidazole and α,α'-dibromo-*p*-xylene)]. White solid, ^{1}H NMR (DMSO-d_6) δ 5.14 (s, CH_2Imidazole), 7.72 (s, H_2), 7.14 (s, H_4), 6.87 (s, H_5), 7.22 (s, Aryl protons); ^{13}C NMR (DMSO-d_6) δ 49.3 (^1J = 139.8 Hz), 137.5 (C_2, ^1J = 211.2 Hz), 128.8 (C_4, ^1J = 187.8, ^3J = 10.6, ^2J = 10.6 Hz), 119.8 (C_5, ^1J = 200.6, ^2J = 15.5 Hz), 137.4, 128.0 (^1J = 159.9 Hz). IR (KBr) cm^{-1} 1505, 1450, 1435, 1420, 1395, 1355, 1285, 1230, 1170, 1090, 1050, 1020.

1,4-Bis(benzimidazol-1-ylmethyl)benzene 3c. A mixture of benzimidazole (1.18 g, 10 mmol), α,α'-dibromo-*p*-xylene (1.32 g, 5.0 mmol), NaOH (0.40 g, 10.0 mmol), and Na_2CO_3 (1.06 g, 10.0 mmol) in 20 mL of xylene was stirred at 130 °C for 6 h. The solvent was evaporated under vacuum and the residue chromatographed with dichloromethane to yield **3c** (50%) as a white solid, mp 124-126 °C. ^{1}H NMR (DMSO-d_6) δ 5.44 (s, CH_2Benzimidazole), 8.37 (s, H_2), 7.62-7.67 (m, H_4), 7.14-7.18 (m, H_5 and H_6), 7.44-7.48 (m, H_7), 7.26 (s, Aryl protons); ^{13}C NMR (DMSO-d_6) δ 47.2 (^1J = 140.9 Hz), 144.2 (C_2, ^1J = 207.4, ^3J = 3.9 Hz), 143.5 (C_{3a}), 119.5 (C_4, ^1J = 160.5, ^3J = 6.5, ^2J = 2.5 Hz), 121.6 (C_5, ^1J = 158.8, ^3J = 7.6 Hz), 122.4 (C_6, ^1J = 161.0, ^3J = 7.7 Hz), 110.7 (C_7, ^1J = 162.6, ^3J = 5.0), 133.6 (C_{7a}), 136.5, 127.7 (^1J = 160.4 Hz). IR (KBr) cm^{-1} 1610, 1550, 1490, 1450, 1410, 1370, 1295, 1255, 1240, 1180, 1130, 1005. Analysis Calcd. for $C_{22}H_{18}N_4$: C 78.08, H 5.36, N 16.56. Found C 78.23, H 5.12, N 16.54.

1-(Imidazol-1-ylmethyl)-4-(pyrazol-1-ylmethyl)benzene 3d. *p*-Bromomethylbenzylpyrazole **2a** (251 mg, 1.0 mmol) was heated, with magnetical stirring at 130 °C, with imidazole (136 mg, 2.0 mmol) in 20 mL of xylene during 6 h. The residue obtained after removal of the solvent was purified by column chromatography with dichloromethane. Compound **3d** (50%), white solid, had mp 86-88 °C. ^{1}H NMR ($CDCl_3$) δ 5.09 (s, CH_2Imidazole), 5.31 (s, CH_2Pyrazole), 7.54 (d, H_3Pyrazole, ^3J = 1.4 Hz), 6.28 (q, H_4Pyrazole, ^3J = 1.4 and 2.1 Hz), 7.39 (d, H_5Pyrazole, ^3J = 2.1 Hz), 7.54 (s, H_2Imidazole), 7.08 (s, H_4Imidazole), 6.87 (s, H_5Imidazole), 7.08-7.20 (m, Aryl protons); ^{13}C NMR ($CDCl_3$) δ 50.2 (CH_2Imidazole, ^1J = 139.6 Hz), 55.1 (CH_2Pyrazole, ^1J = 139.6, $^2J = {}^2J$ = 3.6 Hz), 139.5 (C_3Pyrazole, ^1J = 185.2, ^3J = 8.3, ^2J = 5.7 Hz), 105.9 (C_4Pyrazole, ^1J = 176.9, ^2J = 8.6, ^2J = 10.4 Hz), 129.2 (C_5Pyrazole, ^1J = 187.4 Hz), 137.3 (C_2Imidazole, ^1J = 210.0 Hz), 129.6 (C_4Imidazole, ^1J = 189.7, ^2J = 10.2 Hz), 119.2 (C_5Imidazole, ^1J = 188.8 Hz), 135.8, 136.7, 127.5 (^1J = 159.0, ^3J = 9.9, ^2J = 4.1 Hz), 127.9 (^1J = 159.7, ^3J = 9.9, ^2J = 4.2 Hz). IR (KBr) cm^{-1} 1500, 1445, 1425, 1390, 1345, 1270, 1230, 1210, 1145, 1110, 1105, 1090, 1080, 1060, 1030. Analysis Calcd. for $C_{14}H_{14}N_4$: C 70.57, H 5.92, N 23.51. Found C 70.67, H 5.84, N 23.39.

[1$_4$]Paracyclo-bis-(1,2)pyrazoliumphane dibromide 1a. To a solution of 238 mg (1.0 mmol) of 1,4-bis(pyrazol-1-ylmethyl)benzene **3a** in 20 mL of acetonitrile, 264 mg (1.0 mmol) of α,α'-dibromo-*p*-xylene were added. The reaction was heated at 60 °C for 6 h, then the solvent was removed and the residue dissolved in hot ethanol. This solution was treated with charcoal, and after filtration, **1a** precipitated as a colourless crystal, mp > 350 °C (80%). Cation weight: 342 Da.[17] IR (KBr) cm^{-1} 1510, 1435, 1405, 1360, 1270, 1220, 1210, 1140, 1095. Analysis Calcd. for $C_{22}H_{22}N_4Br_2 \cdot 1/2H_2O$: C 51.68, H 4.53, N 10.96. Found C 51.76, H 4.59, N 10.83.

[1$_4$]Paracyclo-bis-(1,3)imidazoliumphane dibromide 1b. Compound (**1b**), a colourless crystal, was prepared starting from 1,4-bis(imidazol-1-ylmethyl)benzene (**3b**) and proceeding similarly to the experimental procedure described above for **1a** (90%). Zhou *et al*[18] reported the cyclophane **1b** [mp > 350 °C] although their ^{1}H chemical shifts (in D_2O at 90 MHz) do not coincide with ours. Cation weight: 342 Da.[17] IR (KBr) cm^{-1} 1550, 1505, 1450, 1425, 1315, 1130, 1085.

[1$_4$]Paracyclo-bis-(1,3)benzimidazoliumphane dibromide 1c. In a similar manner to what has been described for (**1a**) and (**1b**), but using 1,4-bis(benzimidazol-1-ylmethyl)benzene (**3c**) as starting compound. The cyclophane **1c**, a colourless crystal, had mp > 320 °C (90%). Cation weight: 442 Da.[17] IR (KBr) cm^{-1} 1605, 1555, 1480, 1450, 1415, 1370, 1325, 1260, 1175, 1130, 1015. Analysis Calcd. for $C_{30}H_{26}N_4Br_2{\cdot}2H_2O$: C 56.44, H 4.74, N 8.78. Found C 56.30, H 4.69, N 8.88.

Quaternary salts (5a), (5b), (5c) and (5d). All derivatives were obtained by methylation of the corresponding neutral molecules (**3a**), (**3b**), (**3c**) and (**3d**), with an excess of methyl iodide in acetonitrile at room temperature during 24 h. The diiodides precipitated as colourless crystals and were collected by filtration from the reaction mixture.

– **α,α'-Bis-(2-methylpyrazolium)-*p*-xylene diiodide 5a**. mp 214-216 °C (70%). Analysis Calcd. for $C_{16}H_{20}N_4I_2$: C 36.80, H 3.86, N 10.73. Found C 36.46, H 3.80, N 10.48. ^{1}H NMR (D_2O) δ 4.02 (s, CH_3), 5.75 (s, CH_2Pyrazolium), 8.23 (d, H_3), 6.80 (t, H_4, ^3J = ^3J = 3.0 Hz), 8.22 (d, H_5,), 7.36 (s, Aryl protons); ^{13}C NMR (D_2O) δ 35.7 (^1J = 146.0 Hz), 51.4 (^1J = 145.7 Hz), 136.4 (C_3, ^1J = 203.8 Hz), 106.1 (C_4, ^1J = 190.3, ^2J = 6.7 Hz), 137.5 (C_5, ^1J = 203.3 Hz), 131.4, 127.4 (^1J = 162.2 Hz). IR (KBr) cm^{-1} 1525, 1460, 1435, 1385, 1330, 1300, 1240, 1100, 1090, 1075, 1010. Analysis Calcd. for $C_{16}H_{20}N_4I_2$: C 36.80, H 3.86, N 10.73. Found C 36.80, H 3.91, N 10.88.

– **α,α'-Bis-(3-methylimidazolium)-*p*-xylene diiodide 5b**. mp 260-262 °C (90%). Analysis Calcd. for $C_{16}H_{20}N_4I_2$ C 36.80, H 3.86, N 10.73. Found C 36.54, H 3.81, N 10.69. ^{1}H NMR (DMSO-d_6) δ 3.84 (s, CH_3), 5.41 (s, CH_2Imidazolium), 9.20 (s, H_2), 7.75 (s, H_4), 7.70 (s, H_5), 7.45 (s, Aryl protons); ^{13}C NMR (D_2O) δ 36.1 (^1J = 144.8 Hz), 52.6 (^1J = 146.4 Hz), 138.0 (C_2, ^1J = 222.8 Hz), 124.1 (C_4, ^1J = 202.8 Hz), 122.5 (C_5, ^1J = 207.2 Hz), 134.8, 129.6 (^1J = 161.0 Hz). IR (KBr) cm^{-1} 1500, 1425, 1405, 1360, 1335, 1315, 1245, 1235, 1150, 1110, 1095, 1085. Analysis Calcd. for $C_{16}H_{20}N_4I_2$: C 36.80, H 3.86, N 10.73. Found C 36.76, H 3.75, N 10.77.

– **α,α'-Bis-(3-methylbenzimidazolium)-*p*-xylene diiodide 5c**. mp 295 °C (dec) (78%). Analysis Calcd. for $C_{24}H_{24}N_4I_2$ C 46.32, H 3.89, N 9.00. Found C 46.20, H 4.07, N 8.61. ^{1}H NMR (DMSO-d_6) δ 4.11 (s, CH_3), 5.73 (s, CH_2Benzimidazolium), 9.90 (s, H_2), 7.90 (d, H_4, ^{3}J = 7.9 Hz), 7.52-7.65 (m, H_5 and H_6), 7.82 (d, H_7, ^{3}J = 8.0 Hz), 7.49 (s, Aryl protons); ^{13}C NMR (DMSO-d_6, 318 K) δ 33.3 (^1J = 143.9 Hz), 49.2 (^1J = 143.9 Hz), 142.8 (C_2, ^1J = 220.3 Hz), 131.9 (C_{3a}), 113.6 (C_4, ^1J = 170.5 Hz), 126.6 (C_5, ^1J = 166.0 Hz), 126.7 (C_6, ^1J = 166.2 Hz), 113.4 (C_7, ^1J = 170.3 Hz), 130.5 (C_{7a}), 134.3, 128.7 (^1J = 162.5 Hz). IR (KBr) cm^{-1} 1600, 1555, 1480, 1445, 1415, 1370, 1360, 1320, 1270, 1255, 1175, 1130, 1010. Analysis Calcd. for $C_{24}H_{24}N_4I_2$: C 46.32, H 3.89, N 9.00. Found C 46.22, H 4.03, N 8.98.

– **α-(3-Methylimidazolium),α'-(2-methylpyrazolium)-*p*-xylene diiodide 5d**. mp 169-170 °C (60%). ^{1}H NMR (D_2O) δ 3.79 (s, CH_3Imidazolium), 3.93 (s, CH_3Pyrazolium), 5.33 (s, CH_2Imidazolium), 5.66 (s, CH_2Pyrazolium), 6.72 (t, H_4Pyrazolium), 8.14 (bs, H_3 and H_5Pyrazolium), 8.68 (s, H_2Imidazolium), 7.36 (s, H_4 and H_5 Imidazolium), 7.18-7.49 (m, Aryl protons); ^{13}C NMR (DMSO-d_6) δ 36.0 (CH_3Pyrazolium, ^1J = 143.4 Hz), 37.2 (CH_3Imidazolium, ^1J = 144.8 Hz), 51.2 (CH_2Pyrazolium, ^1J = 144.1 Hz), 51.9

(CH_2Imidazolium, ^1J = 146.0 Hz), 138.8 (C_3Pyrazolium, ^1J = 198.3 Hz), 107.4 (C_4Pyrazolium, ^1J = 189.7, ^2J = ^2J = 6.9 Hz), 137.8 (C_5Pyrazolium, ^1J = 206.2 Hz), 136.6 (C_2Imidazolium, ^1J = 222.0 Hz), 124.0 (C_4Imidazolium, ^1J = 203.4 Hz), 122.2 (C_5Imidazolium, ^1J = 202.6 Hz), 133.0, 135.5, 128.4 (^1J = 161.2 Hz), 129.2 (^1J = 161.8 Hz). IR (KBr) cm^{-1} 1515, 1500, 1455, 1410, 1360, 1325, 1300, 1255, 1235, 1150, 1110, 1090, 1080. Analysis Calcd. for $C_{16}H_{20}N_4I_2$: C 36.80, H 3.86, N 10.73. Found C 36.94, H 3.52, N 10.61.

Crystal Structure of Compound (1a). Crystals suitable for X-ray diffraction were obtained by recrystallization from water. Intensity X-ray data were collected on a NONIUS KapaCCD diffractometer using 1kWatt Mo radiation with a graphite monochromator. The data were collected at 20 °C using a 1° rotation in ϕ and 40 sec exposure per image. A total of 200 exposures were collected at $\chi = 0°$ before the crystal was rotated to $\chi = 90°$ and a further 37 exposures collected at 1° rotation in ω per image. The data thus obtained were processed using DENZO-SMN.[31]

The structure was solved by direct methods using SHELXS86[32] and refined using full-matrix least squares on F^2 in SHELXL97.[33] All non hydrogen atoms were refined anisotropically and hydrogens were placed in geometrically calculated positions and linked to common isotropic temperature factors. Two regions of high electron density (*ca.* 1.3 Å from Br1 and Br2) were not accounted for by the model. There are two independent formula units in the cell. The asymmetric unit consists of the two independent half-heterocyclophanes, each situated on a centre of symmetry [at (1/2 0 0) and (1/2 1/2 1/2)]. Each heterocyclophane is in the chair conformation. The phenyl and pyrazole rings are planar, with maximum deviations from the least-square planes <0.03 Å. The heterocyclophanes pack in herringbone fashion. There are no short intermolecular contacts.

^{1}H NMR variable temperature experiments. The ^{1}H NMR variable temperature experiments were carried out on a 200 MHz spectrometer. The barriers at the coalescence temperatures were calculated using the formula $\Delta G^{\ddagger}_{Tc} = 4.57\ T_c\ [9.97 + \log (T_c/\Delta\nu)]$ which applies to systems, like **1a**, where the populations of the **C** and **B** sites are equal.[25b] The results are reported in Table 5.

Table 5. Temperature variable experiments (^{1}H NMR spectroscopy at 200 MHz)

	Signal	Δν (Hz)	T_c (K)	$\Delta G^{\ddagger}$ (kcal mol^{-1})
D_2O				
	H_3, H_5	5	323	17.4
	H_4	8	331	17.5
	H_A	15	343	17.8
	H_B	26	353	17.9
DMSO-d_6				
	H_3, H_5	6	338	18.1
	H_4	8	343	18.2
	H_A	8	343	18.2
	H_B	26	368	18.7
	CH_2	46	383	19.1

Computational calculations. The AM1 Hamiltonian[35] was used within its original formalism. In all cases, the PRECISE keyword was used and full geometry optimization was carried out (with the Fletcher-Powell algorithm).

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