Synthesis, structure (NMR and mass spectrometry) and conformational analysis of heterocyclic analogues of dibenzo[*a*,*e*]cycloocta-1,5-diene: 5,6,12,13-tetrahydrobispyrazolo[1,2-*a*:1′,2′-*e*][1,2,5,6]tetraazocinediium dihalides

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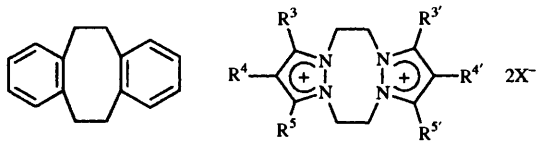
Several 5,6,12,13-tetrahydrobispyrazolo[1,2-*a*:1′,2′-*e*][1,2,5,6]tetraazocinediium dihalides 4a–d and 8 are prepared from pyrazole, 3,5-dimethylpyrazole, 4-(1-adamantyl)pyrazole and campho[2,3-*c*]pyrazole by stepwise alkylation with 1,2-dibromoethane or 1,2-dichloroethane. Their structural characterization has been achieved by NMR and mass spectrometry. Dynamic NMR spectroscopy allowed the measurement of the barrier for the chair–chair interconversion in the case of the parent compound 4a and the 1,3,8,10-tetramethyl derivative 4b. These barriers as well as the preferred chair conformation are rationalized through semi-empirical and molecular mechanics calculations with regard to dibenzo[*a*,*e*]cycloocta-1,5-diene. The study of doubly charged bispyrazolium salts allows demonstration of their reduction by addition of a hydride ion [$C^{++} + H^- \longrightarrow (C + H)^+$] during FABMS experiments.

Following our studies on the conformational analyses, in the solid state and in solution, of compounds derived from dibenzo[*a*,*e*]cycloocta-1,5-diene **I**,[1] in which the cyclooctadiene ring has been modified by introducing heteroatoms in the central ring, several 5,6,12,13-tetrahydrobispyrazolo[1,2-*a*:1′,2′-*e*][1,2,5,6]tetraazocinediium dihalides of general formulae **II** have been prepared from the corresponding pyrazoles by alkylation with 1,2-dibromoethane.[2]

Their structural characterization was made by means of elemental analyses, FABMS in the positive mode[3] and ^1H and ^{13}C NMR spectroscopy. We have shown by an X-ray diffraction study[2] that the parent compound, 5,6,12,13-tetrahydrobispyrazolo[1,2-*a*:1′,2′-*e*][1,2,5,6]tetraazocinediium dibromide **4a** in the solid state presents the tetraazocine central ring in a chair conformation. Moreover, MNDO and AM1 calculations indicate that the chair conformation is the most stable for this type of derivative.

We present here our results in solution by means of ^1H NMR variable temperature spectra at 300 MHz, which allowed the observation at 298 K of the A_4 system of the ethylene bridge protons as a broad signal that split into an AA′BB′ multiplet at low temperatures. The rotational barriers were estimated to be of about 13.5 kcal mol^{-1} † at T_c 288 K for **4a** in [$^2H_6$]ethylene glycol–D_2O (2:1) and 12.8 kcal mol^{-1} at T_c 276 K for **4b** in [$^2H_7$]DMF–CD_3OD (10:1).

Because of the potential utility of derivatives of dibenzo[*a*,*e*]cycloocta-1,5-diene as hosts, chiral complexes of this type have been synthesized. Tetrahydro(camphopyrazolo)-(pyrazolo)tetraazocinediium dibromide **8**, prepared from the corresponding (+)-camphopyrazoles **7** and **7′** turned out to be a salt soluble in common organic solvents. By the same procedure, tetrahydro(pulegopyrazolo)(pyrazolo)tetraazocinediium dibromide **14** and the bis(pulegopyrazolo) derivatives **15** have been prepared and characterized by mass spectrometry.‡



I **II**

Scheme 1

Results and discussion

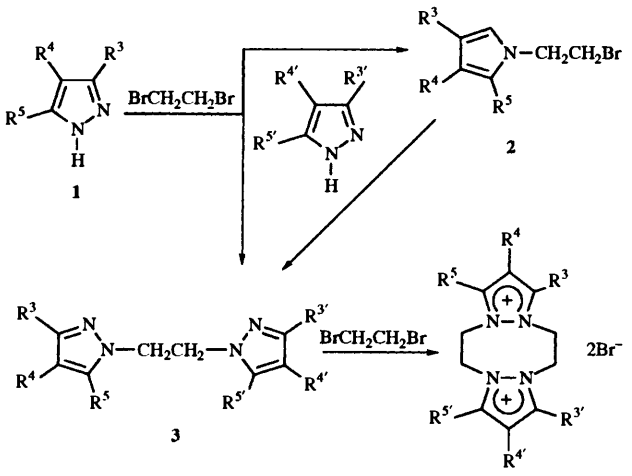
Chemistry and NMR characterization

From pyrazole **1a**, 3,5-dimethylpyrazole **1b**, 4-(1-adamantyl)pyrazole **1c**[4] and 1,2-dibromoethane, the 1-bromoethylpyrazoles **2a–c** were obtained. The subsequent treatment of **2** with another mole of pyrazole under phase transfer catalysis conditions yielded compounds **3a–d**.[5] Finally the quaternary salts **4a–d** were formed by treating the bis(pyrazol-1-yl)ethane derivatives **3** with an excess of 1,2-dibromoethane.[2]

The ^1H NMR data are reported in Table 1. The proton signals of the ethylene group range from a system AA′XX′ in compound **2** to an AA′BB′ in compound **3** and appear as broad A_4 singlets shifted to lower field in compounds **4**. The ^1H chemical shifts of the pyrazolium ring in the quaternary salts **4**

† 1 kcal = 4.184 kJ.

‡ Although using the IUPAC recommendations compounds **5** and **10** should be named (4*S*,7*R*)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-2*H*-indazole and (4*R*)-7-isopropylidene-4-methyl-4,5,6,7-tetrahydro-1*H*(2*H*)-indazole, respectively, the trivial names campho-pyrazole and pulegopyrazole have been used throughout this paper.



a $R^3, R^4, R^5 = H; R^{3'}, R^{4'}, R^{5'} = H$

b $R^3, R^5, R^{3'}, R^{5'} = Me; R^4, R^{4'} = H$

c $R^3, R^5, R^{3'}, R^{5'} = H; R^4, R^{4'} = Ad$

d $R^3, R^4, R^5, R^{4'} = H; R^{3'}, R^{5'} = Me$

Scheme 2

appear at higher fields than those of the neutral pyrazoles and the values of the coupling constants increase.

The ^{13}C NMR spectra are reported in Table 2. All signals are in agreement with the proposed structures. The quaternization effect on the NMR chemical shifts on going from the 1,2-bispyrazolylethanes **3a–d** to the tetrahydrobispyrazolo[1,2-*a*:1′,2′-*e*][1,2,5,6]tetraazocinediium dibromides **4a–d** is expressed in square brackets in Table 2. As expected the chemical shifts in the salts **4** appear at lower field than those of the neutral molecules **3**,[6] the average values for $\Delta\delta = \delta(\mathbf{4}) - \delta(\mathbf{3})$ are 0.8 (C-3), 3.5 (C-4) and 9.8 ppm (C-5). A similar effect has been observed on the solid-state ^{13}C CP-MAS data of derivatives **4a** and **4d**.

From commercial (+)-camphor it is easy to prepare campho[2,3-*c*]pyrazole **5** [(4*S*,7*R*)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*(2*H*)-indazole],[7] which is the starting material used to prepare the tetrahydrotetraazocinediium dibromide **8** (Scheme 3).

Alkylation of the camphopyrazole **5** with 1,2-dichloroethane in the presence of a phase transfer catalyst yielded two isomers, 1-(camphopyrazol-2-yl)-2-chloroethane **6** and 1-(camphopyrazol-1-yl)-2-chloroethane **6′** in a 50:50 ratio.

These two isomers have been separated by chromatography on silica gel for ^1H and ^{13}C NMR characterization. In both derivatives the signals of the AA′XX′ ethylene protons appear as triplets, between δ 3.7 and 4.4 (Table 3). The most significant differences between **6** and **6′** come from the C-3 and C-7a chemical shifts (Table 4). For the 2-substituted isomer, **6** δ(C-3) = 122.4 and δ(C-7a) = 167.7, and for the 1-chloroethyl derivative **6′**, δ(C-3) = 132.5 and δ(C-7a) = 154.8.

Substitution of the chlorine atom by a pyrazole group in both compounds **6** and **6′** gave 1-(camphopyrazolyl)-2-(pyrazolyl)ethanes **7** and **7′**, in which the same characteristic NMR features were observed. Tetrahydro(camphopyrazolo)(pyrazolo)tetraazocinediium dibromide **8** was obtained in 20% yield by treating the ethanes **7** and **7′** with 1,2-dibromoethane in excess without solvent. Quaternization ^{13}C chemical shift effects are mainly observed on C-3, C-3a and C-7a (Table 4) as in compounds **4** (Table 2).

Using the same procedures, we tried the synthesis of tetrahydrobis(camphopyrazolo)tetraazocinediium dibromide in which two campho[2,3-*c*]pyrazolo rings were present, but although we were able to obtain mixtures of isomers **9** and **9′** in low yield (MS:M^+ = 378 Dalton, corresponding to the molecular formula $C_{24}H_{34}N_4$), all our attempts to separate them failed and we did not further pursue this line.

In the series of (4*R*)-7-isopropylidene-4-methyl-4,5,6,7-tetrahydroindazole, or pulegopyrazole, **10**,[8] 1-chloro-2-(pulegopyrazol-2-yl)ethane **11** has been prepared by the same procedure used for the above mentioned derivatives (Scheme 3). In this case and most probably due to steric effects, the ^1H and ^{13}C NMR spectra confirm the formation of a single isomer (Tables 5 and 6).[9]

Substitution of the chlorine atom by pyrazole or pulegopyrazole, using phase transfer catalysis, yielded 1-(pulegopyrazol-2-yl)-2-(pyrazol-1-yl)ethane **12** and 1,2-bis(pulegopyrazol-2-yl)ethane **13**.

Preparation of the dibromide salts **14** and **15** was achieved by similar procedures to those used to make the salt of the campho derivative **8**, but due to the low yields and their difficult purification they were only characterized by FABMS.

Dynamic NMR spectroscopy

The ^1H NMR spectrum (300 MHz) of 5,6,12,13-tetrahydrobispyrazolo[1,2-*a*:1′,2′-*e*][1,2,5,6]tetraazocinediium dibromide **4a** in [$^2H_6$]ethylene glycol–D_2O (2:1) and that of 1,3,8,10-tetramethyl-5,6,12,13-tetrahydrobispyrazolo[1,2-*a*:1′,2′-*e*][1,2,5,6]tetraazocinediium dibromide **4b** in [$^2H_7$]DMF–CD_3OD (10:1) have been recorded for temperatures between +55 and −85 °C. At high (**4a**, 308 K) and room temperature (**4b**, 298 K) both molecules appear symmetrical due to rapid equilibration between all possible conformations on going from the chair (**C**) to the boat (**B**) and passing through different transition states.[1] Only a broad signal corresponding to an A_4 system is observed for the ethylene bridge protons CH_2–CH_2. However at lower temperatures, 253 K for **4a** and 218 K for **4b**, the chair conformation is frozen and AA′BB′ multiplets appear (see Fig. 1, note that the AA′BB′ system resembles an AB quartet because of the particular magnitudes of the coupling constants). For compound **4a** at 253 K the following values were found: 8.313 (3-H, 5-H, d, ^3J 2.7 Hz), 6.767 (4-H, t, ^3J 2.7 Hz), AA′BB′ system: 5.307 and 4.746, and for compound **4b** at 218 K the values are: 6.634 (H_4), 2.556 (3-Me, 5-Me), AA′BB′ system: 5.379 and 4.845.

The barriers for the chair–chair interconversion were calculated assuming the spectra correspond to AB systems; this is the usual approximation for degenerate AA′BB′ systems.[10] The values of the parameters used in the calculations are: **4a** $\nu_0\delta = \nu_A - \nu_B = 160.64$ Hz, $J_{AB} = 14.85$ Hz; **4b** $\nu_0\delta = 160.133$ Hz, $J_{AB} = 15.60$ Hz. Thus, using the Eyring equation,[10] $k_c = \pi/\sqrt{2}[\nu_0\delta^2 + 6\ J_{AB}{}^2]^{1/2}$ and $\Delta G^\ddagger = 4.575\ 10^{-3}\ T_c[10.319 + \log(T_c/k_c)]$; **4a** $T_c = 288$ K, $k_c = 366$ s^{-1}, $\Delta G^\ddagger = 13.5$ kcal mol^{-1} and **4b** $T_c = 276$ K, $k_c = 366$ s^{-1}, $\Delta G^\ddagger = 12.8$ kcal mol^{-1}.

An iterative analysis using the PANIC program[11] was performed on the spectrum of **4b** at 208 K. The analysis of the AA′BB′ system affords the following values: $\nu_A = 1613.82$ Hz, $\nu_B = 1453.59$ Hz, $J_{AB} = J_{A'B'} = J_{gem} = -17.15$ Hz, $J_{AB'} = J_{A'B} = 1.36$ Hz, $J_{AA'} = 9.88$ Hz, $J_{BB'} = 5.39$ Hz. The simulated spectrum is also reported on Fig. 1 (rms error = 0.14 Hz). To determine if the large value of J_{gem} is due to the pyrazolium cation or to the eight-membered ring, we prepared 2-benzylcampho[2,3-*c*]pyrazole **7bis** and measured J_{gem} of the benzyl protons (diastereotopic): 15.4 Hz in $CDCl_3$, C_6D_6 and $(CD_3)_2CO$, 15.7 Hz in C_6D_6–CF_3CO_2H and 15.8 Hz in CF_3CO_2H. Thus, both on neutral pyrazoles and on pyrazolium cations, J_{gem} is smaller than in compound **4b**.

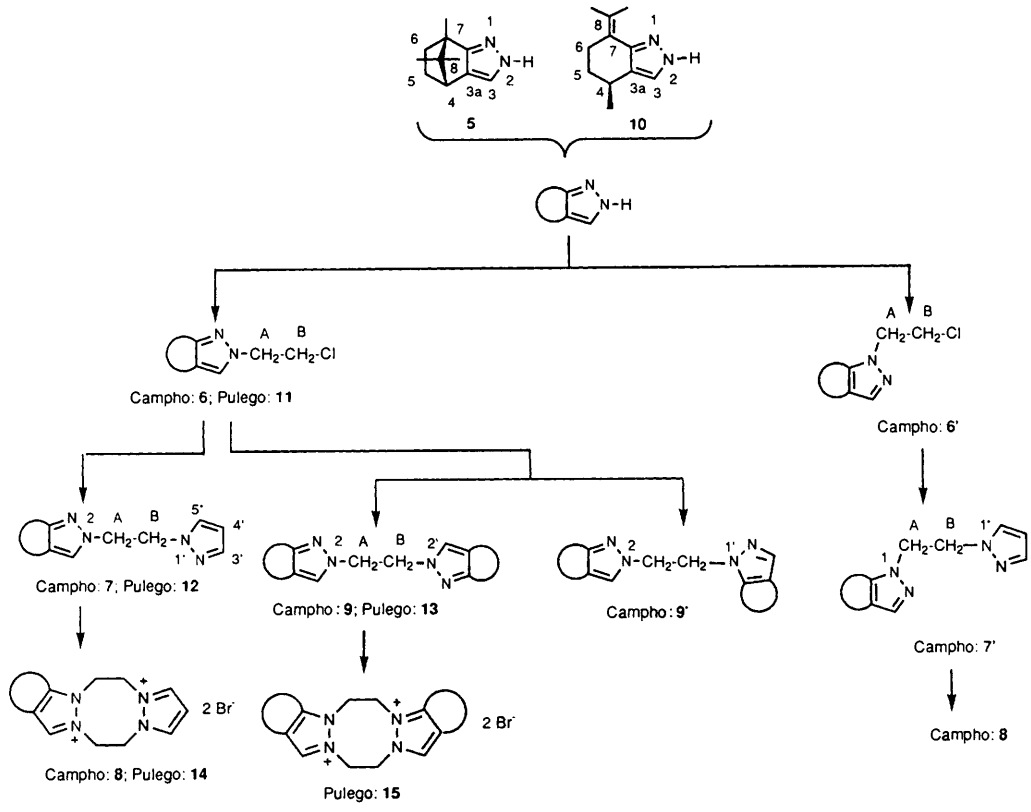
Using the $\Delta G^\ddagger$ value of 12.8 kcal mol^{-1}, a chair–chair interconversion model and the chemical shifts and coupling constants resulting from the spectral analysis, we obtained a perfect fit of the experimental and calculated spectra for 18 temperatures between −55 and +55 °C. This is an experimental proof of the correcteness of the $\Delta G^\ddagger$ values determined above using the AB approximation.

Table 1 ^{1}H NMR chemical shifts (δ) and coupling constants (J/Hz) of pyrazole derivatives **2–4**

Compound	Solvent	3-H	4-H	5-H	3′-H	4′-H	5′-H	CH_2–CH_2	3-Me 3′-Me	5-Me 5′-Me	Ad
2c	$CDCl_3$	7.42 (d) ^4J 0.7	—	7.21 (d)	—	—	—	3.69 (t) 4.43 (t) ^3J 6.6	—	—	1.74 (6 H, m, Hδ) 1.83 (6 H, m, Hβ) 2.01 (3 H, m, Hγ)
3a	$CDCl_3$	7.52 (d) ^3J 1.8	6.10 (dd)	6.91 (d) ^3J 2.4	7.52 (d)	6.10 (dd)	6.91 (d)	4.54 (s)	—	—	—
3b	$CDCl_3$	—	5.66 (s)	—	—	5.66 (s)	—	4.30 (s)	1.62 (s)	2.20 (s)	
3c	[$^2H_6$]DMSO	7.40 (s)	—	6.91 (s)	7.40 (s)	—	6.91 (s)	4.40 (s)	—	—	1.60–1.70 (12 H, m, Hβ, Hδ) 1.90–2.0 (3 H, m, Hγ)
3d	$CDCl_3$	7.50 (d) 3J 1.8	6.11 (dd)	7.25 (d) ^3J 2.3	—	5.64 (s)	—	4.30 4.53 AA′BB′	1.64 (s)	2.19 (s)	—
4a	D_2O	8.32 (d) 3J 2.8	6.76 (t)	8.32 (d)	8.32 (d) ^3J 2.8	6.76 (t)	8.32 (d)	5.23 (br s)	—	—	—
4b	D_2O	—	6.48 (s)	—	—	6.48 (s)	—	4.95 (br s)	2.42 (s)	2.42 (s)	—
4c	[$^2H_6$]DMSO +CF_3CO_2H	8.50 (s)	—	8.50 (s)	8.50 (s)	—	8.50 (s)	5.20 (br s)	—	—	1.70 (6 H, m, Hδ) 1.81 (6 H, m, Hβ) 2.01 (3 H, m, Hγ)
4d	D_2O	8.31 (d) ^3J 3.1	6.78 (t)	8.31 (d)	—	6.48 (s)	—	5.12 (m) 4.99 (m)	2.42 (s)	2.42 (s)	—

Table 2 ^{13}C NMR chemical shifts (δ) and coupling constants (J/Hz) of pyrazole derivatives **2–4**

Compound	Solvent	C-3	C-4	C-5	C-3′	C-4′	C-5′	C-A	C-B	3-Me 3′-Me	5-Me 5′-Me	Ad
2c	$CDCl_3$	137.0 ^1J 182.0 ^3J 7.9	133.6	125.6 ^1J 185.0	—	—	—	53.2 ^1J 141.8	30.2 ^1J 153.4	—	—	Cα = 31.1 Cβ = 44.0; ^1J 128.7 Cγ = 28.5; ^1J 133.5 Cδ = 36.6; ^1J 126.5
3a	$CDCl_3$	139.9 ^1J 184.8 ^2J 5.9 ^3J 8.3	105.3 ^1J 176.7 ^2J 8.7 ^2J 10.4	130.1 ^1J 186.9 ^2J 8.3 ^3J 4.4	139.9	105.3	130.1	51.6 ^1J 141.9	51.6	—	—	—
3b	$CDCl_3$	148.1 ^2J 6.1	104.8 ^1J 172.3 ^3J 3.8	140.4 ^2J 6.6	148.1	104.8	140.4	48.7 ^1J 141.0	48.7	13.4 ^1J 126.9	9.5 ^1J 128.8	—
3c	$[^2H_6]$DMSO	135.8 ^1J 182.1	132.6	126.0 ^1J 187.5	135.8	132.6	126.0	51.3 ^1J 141.5	51.3	—	—	Cα = 30.7 Cβ = 43.7; ^1J 128.2 Cγ = 28.1; ^1J 134.9 Cδ = 36.3; ^1J 126.3
3d	$CDCl_3$	139.9 ^1J 182.5 ^2J 7.0	105.4. ^1J 176.9 ^2J 9.6	130.1 ^1J 191.9	148.4	104.5 ^1J 176.0	140.4	51.9 ^1J 142.0	48.2 ^1J 140.9	13.3 ^1J 126.9	9.8 ^1J 128.0	—
4a	D_2O	141.7 [+1.8] ^1J 202.6 $^2J = {}^3J$ = 6.4	109.6[+4.3] ^1J 191.7 ^2J 6.6	141.7[+11.6]	141.7	109.6	141.7	50.7[−0.9] ^1J 148.9	50.7	—	—	—
	CP-MAS	142.4 137.8	106.6	142.4 137.8	142.4 137.8	106.6	142.4 137.8	51.0	51.0	—	—	—
4b	D_2O	147.8[−0.3]	108.1[+3.3] ^1J 187.6	147.8[+7.4]	147.8	108.1	147.8	44.2[−4.5] ^1J 147.2	44.2	10.7 ^1J 131.7	10.7	—
4c	$[^2H_6]$DMSO + CF_3CO_2H	138.4[+2.6]	136.5[+3.9]	138.4[+12.4]	138.4	136.5	138.4	50.4[−0.9]	50.4	—	—	Cα = 33.1 Cβ = 44.0 Cγ = 29.6 Cδ = 37.2
4d	D_2O	139.8[−0.1] ^1J 202.8	108.3[+2.9] ^1J 187.0	139.8[+9.7]	148.3[−0.1]	107.7[+3.2] ^1J 184.1	148.3[+7.9]	48.7[−3.2]	44.7[−3.5] ^1J 144.6	10.7 ^1J 133.7	10.7	—
	CP-MAS	139.7	108.3	139.7	148.9	108.3	148.9	52.3	48.3	15.0	15.0	—



Scheme 3

Table 3 ^{1}H NMR chemical shifts[a] (δ) and coupling constants (J/Hz) of camphor derivatives in $CDCl_3$

Compound	3-H	4-H	7-Me	8-Me (*anti*)	8-Me (*syn*)	3'-H	4'-H	5'-H	CH_2–CH_2
5	7.05 (s)	2.76 (d) ^3J 3.8	1.29 (s)	0.94 (s)	0.63 (s)	—	—	—	—
6	6.94 (s)	2.70 (d) ^3J 3.9	1.25 (s)	0.91 (s)	0.62 (s)	—	—	—	3.77 (t, 2 H), 4.31 (t, 1 H), 4.25 (t, 1 H) ^3J 6.0
6'	7.11 (s)	2.71 (d) ^3J 3.9	1.31 (s)	0.85 (s)	0.70 (s)	—	—	—	3.84 (t, 2 H), 4.31 (t, 1 H), 4.25 (t, 1 H) ^3J 6.0
7	6.37 (s)	2.62 (d) ^3J 3.5	1.08 (s)	0.77 (s)	0.52 (s)	7.48 (d) ^3J 2.1	6.04 (t)	6.85 (d) ^3J 2.3	4.61 (m, 2 H), 4.42 (m, 2 H)
7'	7.13 (s)	2.60 (d) ^3J 3.7	1.26 (s)	0.89 (s)	0.60 (s)	7.46 (d) ^3J 1.6	6.04 (t)	6.96 (d) ^3J 2.3	4.61 (m, 2 H), 4.42 (m, 2 H)
8[b]	8.24 (s)	3.01 (d) ^3J 3.3	1.42 (s)	0.96 (s)	0.69 (s)	8.67 (br) ^3J 2.9	6.95 (t)	8.67 (br)	5.48 (br s, 2 H), 5.37 (br s, 2 H), 5.25 (br s, 2 H), 5.17 (br s, 2 H)

[a] 5-H and 6-H appear as complex multiplets in the range of δ 1.2–2.05 for compounds **5**, **6** and **6'** and δ 0.45–2.20 for **7**, **7'** and **8** derivatives. [b] In [$^2H_6$]DMSO.

Table 4 ^{13}C NMR chemical shifts (δ) of camphor derivatives in $CDCl_3$

Compound	C-3	C-3a	C-4	C-5	C-6	C-7	C-7a	C-8	7-Me	8-Me (*anti*)	8-Me (*syn*)	C-3'	C-4'	C-5'	C-A	C-B
5	120.5	126.2	47.4	27.8	33.9	61.2	146.0	50.2	10.1	19.8	18.6	—	—	—	—	—
6	122.4	127.0	47.7	28.2	34.2	60.7	167.7	50.7	11.2	20.9	19.6	—	—	—	53.4	43.9
6'	132.5	128.8	47.9	28.2	34.2	63.5	154.8	51.8	12.0	20.7	20.1	—	—	—	53.0	43.8
7	122.4	126.3	50.2	27.8	33.8	60.4	167.3	51.2	10.7	20.3	19.1	140.0	105.0	130.1	53.3	47.1
7'	132.0	129.0	49.7	27.7	33.1	62.7	154.6	51.9	10.9	20.3	19.4	139.9	105.2	130.2	52.2	47.3
8[a]	141.9	131.4	48.6	27.7	33.4	64.9	164.6	50.9	10.9	20.9	19.2	142.1	109.7	133.0	56.3	48.9
															51.6	50.0

[a] In CD_3OD.

MNDO and AM1 semiempirical calculations

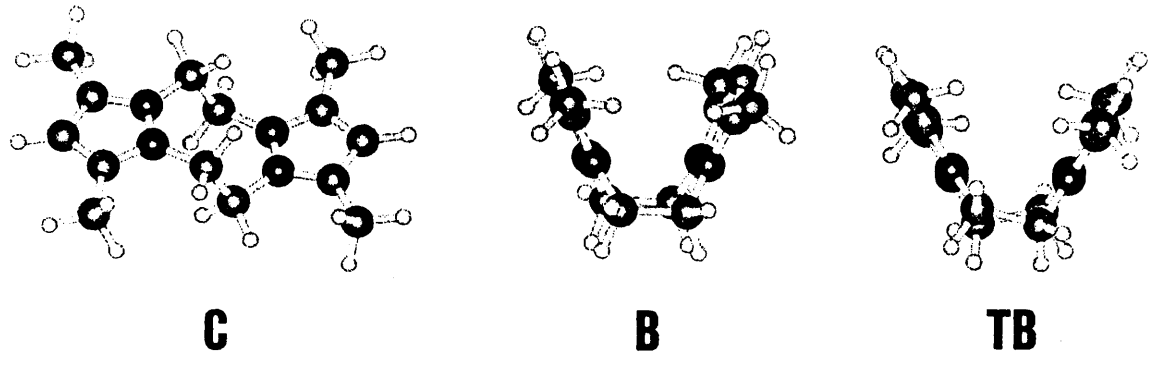
Prior to discussing our calculations, the work of St-Jacques,[12,13] Ollis[14] and Allinger[15] on dibenzo[*a*,*e*]cycloocta-1,5-diene **I** has to be summarized. This compound exists as a mixture of two conformations: the chair **C** (C_{2h}) and the boat **B** (C_{2v}) the latter being slightly more stable (0.2–0.6 kcal mol^{-1}). The boat is not a perfect boat, but a mixture of two enantiomeric twist boats, **TB**, interconverting through the perfect boat **B** (this barrier is too low to be determined by NMR and does not exchange the *inside* and *outside* protons). Two barriers have been measured: the **C**–**TB** of 10.0 kcal mol^{-1} and the **TB**–**TB*** of 7.8 kcal mol^{-1}. These barriers correspond to

Table 5 ^{1}H NMR chemical shifts (δ) and coupling constants (J/Hz) of pulegone derivatives in $CDCl_3$

Compound	3-H	4-H, 5-H and 6-H	4-Me	8-Me	8-Me	3'-H	4'-H	5'-H	CH_2–CH_2
10	7.24 (s)	1.20 (m, 1 H), 1.80 (m, 1 H) 1.08 (d) 2.08 (m, 1 H), 2.55 (m, 2 H) ^3J 6.7	1.72 (s)	1.99(s)	—	—	—	—	
11	7.17 (s)	1.40 (m, 1 H), 1.95 (m, 1 H) 1.24 (d) 2.10 (m, 1 H), 2.75 (m, 2 H) ^3J 6.8	1.89 (s)	2.31(s)	—	—	—	4.40 (t, 1 H), 4.41 (t, 1 H), 3.93 (t, 2 H) ^3J 6.2	
12	6.64 (s)	1.25 (m, 1 H), 1.90 (m, 1 H) 1.05 (d) 2.15 (m, 1 H), 2.65 (m, 2 H) ^3J 6.7	1.82 (s)	2.28(s)	7.51 (d) ^3J 1.4	6.10 (dd)	6.95 (d) ^3J 1.9	4.54 (m, 2 H), 4.44 (m, 2 H)	
13	6.76 (s)	1.25 (m, 2 H), 1.90 (m, 2 H) 1.09 (d) 2.20 (m, 2 H), 2.64 (m, 4 H) ^3J 6.7	1.84 (s)	2.30(s)	—	—	—	4.47 (s, 4 H)	

Table 6 ^{13}C NMR chemical shifts (δ) of pulegone derivatives in $CDCl_3$

Compound	C-3	C-3a C-7a	C-4 C-6	C-5	C-7	C-8	4-Me	8-Me 8-Me	C-3'	C-4'	C-5'	C-A	C-B
10	132.0	121.7 123.6	28.1 28.0	33.6	127.1	141.0	21.7	22.5 23.2	—	—	—	—	—
11	128.4	122.0 124.5	28.2 28.0	33.4	126.3	149.6	21.6	22.2 23.3	—	—	—	53.8	43.2
12	127.9	121.9 124.2	27.9 27.6	33.1	126.2	149.6	21.3	21.7 23.1	140.2	105.3	130.4	51.9	51.9
13	127.6	121.9 124.1	27.9 27.6	29.3	126.1	149.3	21.3	21.7 23.0	—	—	—	51.9	51.9



dynamic processes exchanging the inside and outside protons of the CH_2CH_2 bridges. All these results were reproduced by Allinger's MM calculations: **TB** 1.3 kcal mol^{-1} more stable than **C**, **C–TB** barrier 11.4 kcal mol^{-1} through the folded boat **FB** and **TB–TB*** barrier 7.0 kcal mol^{-1} through the twist $\mathbf{T}^{\ddagger}$ transition state (the **TB–TB** through **B** transformation has a calculated activation energy of 1.9 kcal mol^{-1}).

We decided to carry out semi-empirical calculations[16,17] on compounds **4a** and **4b**. The results are reported in Table 7.

In the case of bispyrazolotetraazocinediium salts, the chair **C** appears to be more stable than the twist boat **TB** (although the difference is small in AM1) in contrast to compound **1**, a difference which may be assigned to the repulsion between charged pyrazolium cations. The two transition states have AM1 energies very close to those measured in compound **1**. The experimental value, 13.2 ± 0.3 kcal mol^{-1} should correspond to the **C–C*** interconversion (AM1 calculated value 10.8 ± 0.5 kcal mol^{-1}) and to the fact that only form **C** is observed (the boat, necessary for the interconversion of the two chairs should be present in less than 5%).

We have calculated the values of the vicinal coupling constants by means of the Karplus equation[18] for cases **C**, **B** and for the average of **TB** and **TB*** using the optimized geometries the program provided (very similar to the semi-empirical geometries): chair **C**, $J_{AB'} = J_{A'B} = 1.1$ Hz ($\varphi = 100°$), $J_{AB'} = 10.2$ Hz ($\varphi = -15°$) and $J_{BB'} = 9.0$ Hz ($\varphi = -145°$); boat **B**, $J_{AB'} = J_{A'B} = 3.0$ Hz ($\varphi = 117°$), $J_{AA'} = 10.5$ Hz ($\varphi = 0°$) and $J_{BB'} = 10.5$ Hz ($\varphi = 0°$); **TB–TB***, $J_{AB'} = J_{A'B} = 4.8$ Hz, $J_{AA'} = 8.2$ Hz and $J_{BB'} = 8.2$ Hz. Although the experimental $J_{BB'}$ (5.4 Hz) is too small with regard to the calculations, the only form consistent with the measured values is the chair **C**. Using the H–C–C–H dihedral angles obtained by crystallography for compound **4a** (which exists as a chair)[2] another set of coupling constants is obtained: $J_{AB'} = J_{A'B} = 1.2$ Hz ($\varphi = 101.5°$), $J_{AA'} = 8.8$ Hz ($\varphi = 21.2°$) and $J_{BB'} = 6.0$ Hz ($\varphi = 135.8°$) which are closer to the experimental values (1.4, 9.9 and 5.4 Hz).

Mass spectrometry

The phenomenon of reduction often observed in FABMS (FAB = fast-atom bombardment) is due to the presence of electrons in the matrix. It results in several reactions: (i) hydrogen fixation:[19] $[M + H]^+ \longrightarrow [M + nH]^+$; (ii) substitution reactions [(*a*) substitution of an aromatic chlorine atom by a hydrogen atom,[20] and (*b*) other substitution reactions X–Y $\longrightarrow$ X–H (X = N,O, . . ., Y = N,O)[21]]; (iii) reduction of a doubly charged cation like $C^{++} \longrightarrow C^{+}$.[3,22]

We present here a new reduction reaction, resulting from the addition of a hydride anion, which was observed during the study of FAB mass spectra of doubly charged cations **4a**, **4b**, **4c**, **4d** and **8**. This phenomenon cannot be observed in simply charged cations since their reduction ($C^+ + H^- \longrightarrow CH$) leads to neutral species, which are not detected by mass spectrometry.

The existence of a reduction phenomenon in FABMS can be established by three different methods. (i) When there is a reduction, two products are present in the matrix, the starting material M_X and the reduced compound M_H. This implies that the collision activated dissociation (CAD) spectrum of the $[M_XH]^+$ ion must not contain the $[M_HH]^+$ ion;[23] (ii) the relative abundances of the $[M_XH]^+$ and $[M_HH]^+$ ions change

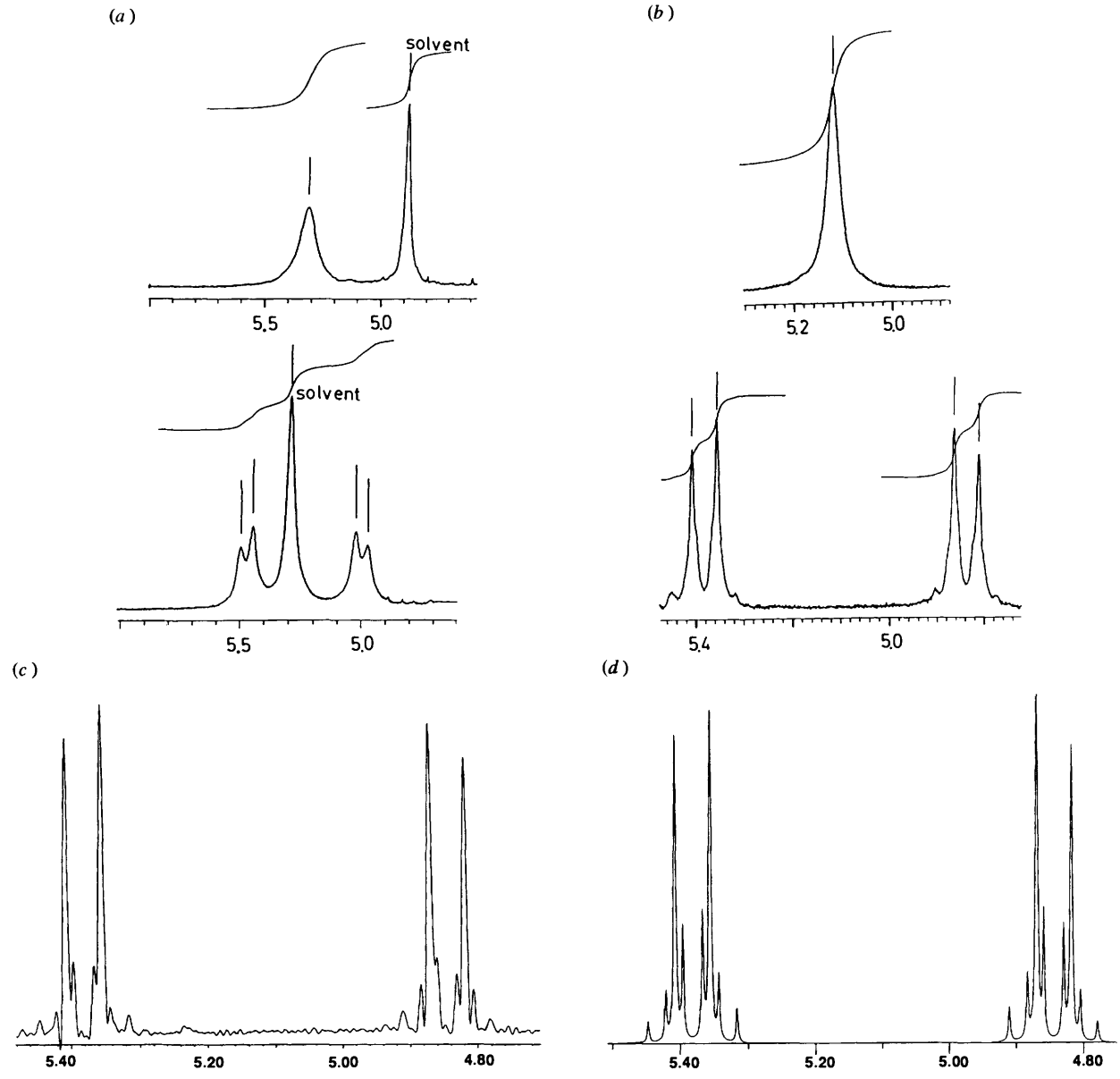


Fig. 1 ^{1}H NMR spectra of (*a*) compound **4a** at 308 and 253 K; (*b*) compound **4b** at 298 and 218 K; (*c*) experimental and (*d*) simulated spectrum of compound **4b** at 208 K

Table 7 Results of the semi-empirical calculations (all values in kcal mol^{-1})

Conformation	ΔH(MNDO)	$\delta\Delta H$(MNDO)	ΔH(AM1)	$\delta\Delta H$(AM1)
Compound **4a**				
Twist boat (**TB**)	513.0	2.9	550.4	0.8
Boat (**B**)	513.7	3.6	552.0	2.4
Chair (**C**)	510.1	0.0	549.6	0.0
Twist (**T**‡)	548.4	38.4	559.8	10.2
Folded boat (**FB**)	518.2	8.1	557.1	7.5
Compound **4b**				
Twist boat (**TB**)	470.8	2.8	503.6	0.7
Boat (**B**)	471.5	3.5	505.3	2.5
Chair (**C**)	468.0	0.0	502.8	0.0
Twist (**T**‡)	495.4	27.4	514.1	11.3
Folded boat (**FB**)	480.9	12.9	510.1	7.3

with time since they are two distinct compounds;[24] (iii) the importance of the reduction depends on the matrix used, the reduction being important with glycerol (G) but not with 3-nitrobenzyl alcohol (NBA).[25]

In the present work, we have used this last criterion since the studied reaction of reduction (fixation of a hydrogen atom) leads to an entity which differs in only 1 Dalton§ with regard to the starting compound. Thus, the first two criteria could lead to

§ 1 Dalton ≡ 1 u.

Table 8 FABMS results obtained with some tetrahydrobispyrazolotetraazocinediium dibromides[a]

Compound and matrix	C^{++}	CBr^+	$[C - H]^+$	$[C/2]^{++}$	$[C + H]^+$
4a	190	269	189	95	191
G[b]	—	(40)	(100)	(46)	(33)
NBA[c]	—	(33)	(100)	(60)	(11)
4b	246	325	245	123	247
G	—	(14)	(100)	(32)	(87)
NBA	—	(38)	(100)	(51)	(8)
4c	458	537	457	229	459
G	—	(37)	(100)	(37)	(56)
NBA	—	(30)	(100)	(34)	(14)
4d	218	297	217	109	219
G	—	(31)	(100)	(16)	(34)
NBA	—	(26)	(100)	(47)	(10)
8	298	377	297	149	299
G	—	(52)	(100)	—	(25)
NBA	—	(46)	(100)	—	(7)

[a] Figures in parentheses indicate abundances of ions in each matrix. [b] G = Glycerol. [c] NBA = 3-nitrobenzyl alcohol.

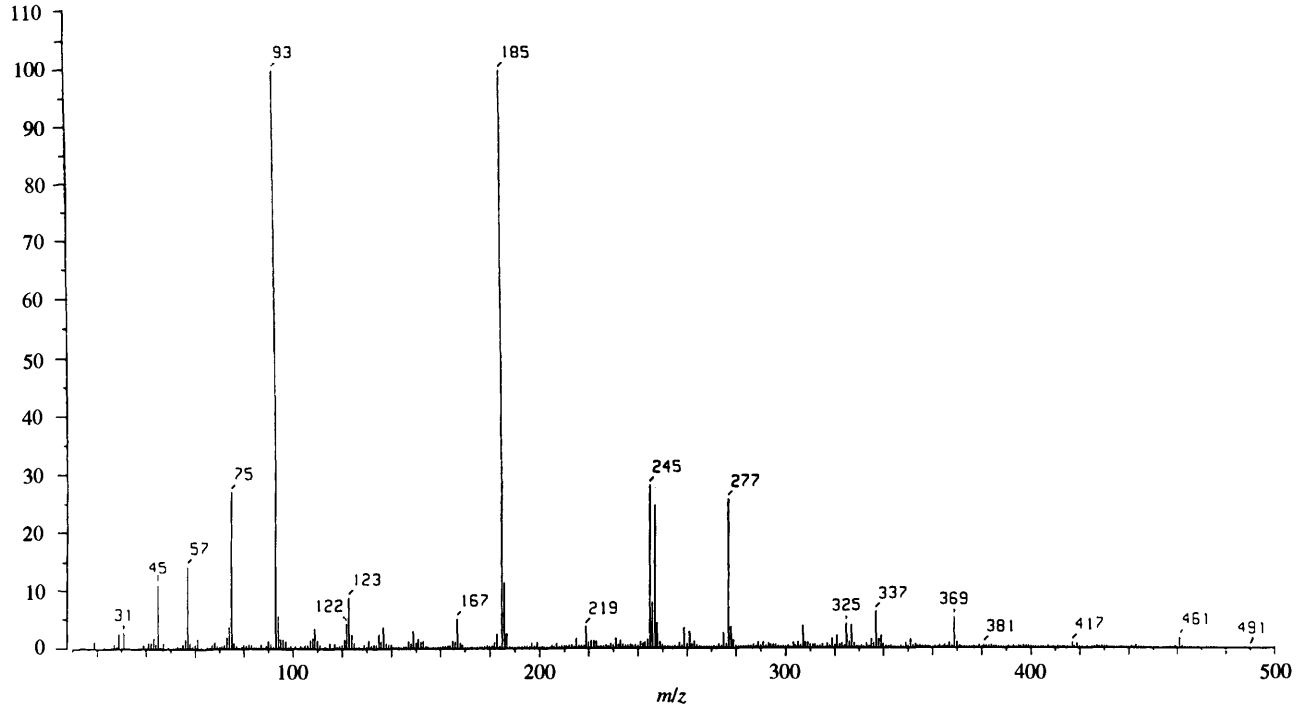


Fig. 2 FAB mass spectrum of compound **4b** (matrix: glycerol)

dubious results due to the natural isotopic distribution of the different elements, especially carbon.

Kelley has explained the inhibitory role played by the NBA matrix on the reduction process.[26] This matrix, due to its oxidative properties, acts as a scavenger of electrons forming again the starting compound from the radical-ion (electron transfer to the matrix pathway). On the other hand, using the G matrix which is clearly less oxidizing than NBA, the radical persists and the substitution can take place (dissociative capture pathway).

For each one of compounds **4a–d** and **8** we have recorded the FAB mass spectra in both matrices, glycerol and NBA. The observed ions with their abundances are reported in Table 8.

In the FABMS of the five compounds studied, the $[C + H]^+$ ion is always more abundant when the matrix is glycerol than when the matrix is NBA. This shows that we are observing a reduction process (Table 8 and Figs. 2 and 3). The process observed is related to the chemical reduction of pyrazolium ions by $AlLiH_4$ to afford Δ^3-pyrazolines.[27]

The FABMS reduction implies the previous formation of a hydride ion by the electrons present in the matrix (H^+, $H^\bullet$, ... + $e^- \longrightarrow H^-$); these electrons being less abundant when the matrix is NBA since this matrix is an electron scavenger. This explains why in NBA the reduction process is less important.

In all the FABMS spectra of these doubly charged cations (Table 8) three ions already described are present:[3,22,28] (i) a simple-charged ion obtained by loss of a proton, $[C–H]^+$ (process **b**, Scheme 4); (ii) the adduct-ion, CBr^+; (iii) the double-charged ion C^{++} which appears at m/z = C/2. For compounds **4a**, **4b** and **4d**, this double-charged ion is more abundant when the matrix is NBA since with the glycerol matrix the reduction predominates. The reason this C^{++} ion is absent in the FAB-MS of compounds **4c** and **8** is under study.

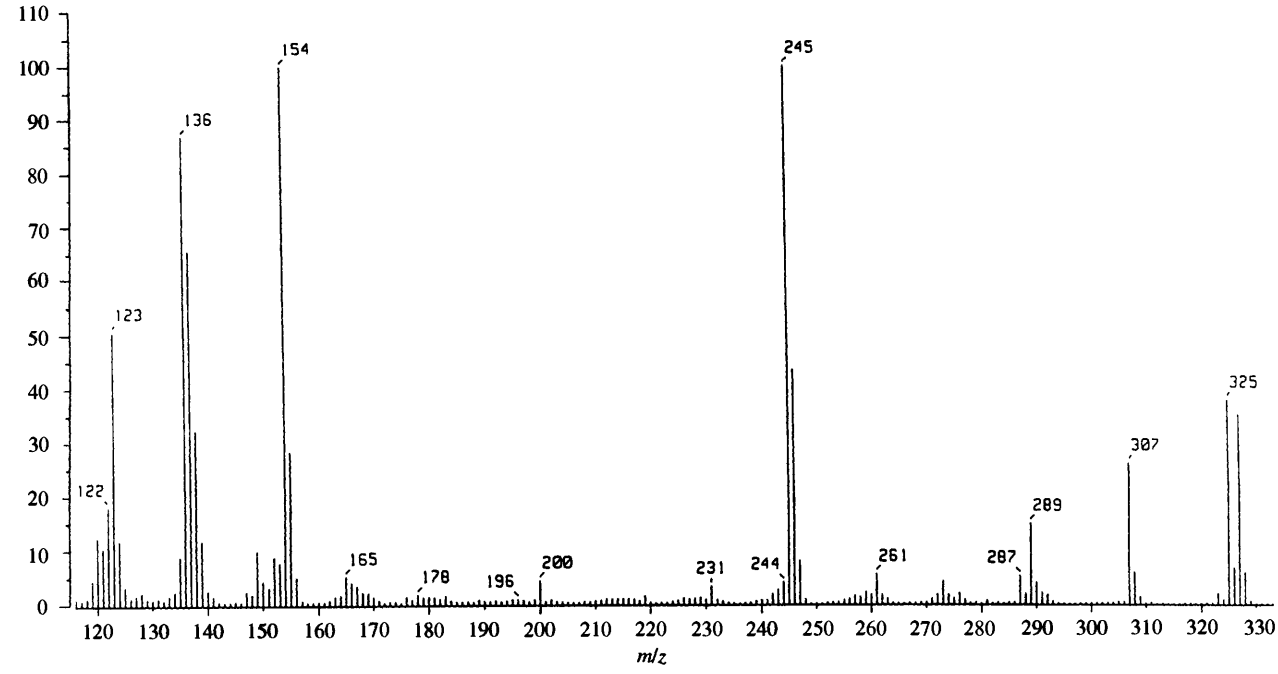
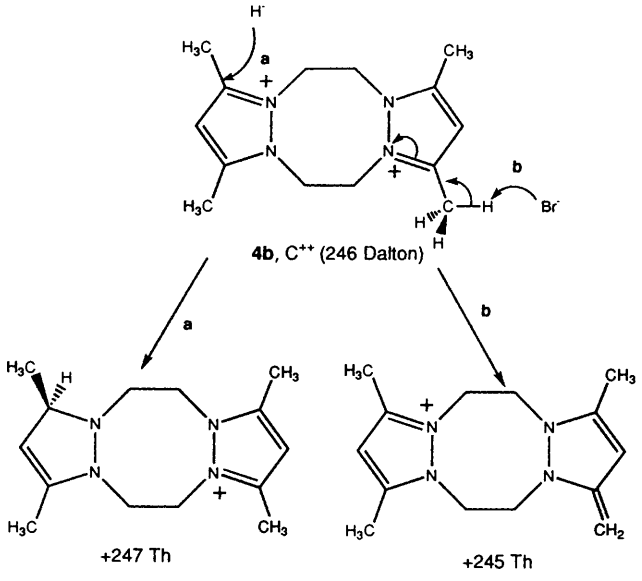


Fig. 3 FABMS of compound **4b** (matrix: 3-nitrobenzyl alcohol)



Scheme 4

Conclusions

In compound **I** the conformation present in the solid state is the chair **C**,[1] while in solution the twist-boat **TB** is more stable.[12,13] In the case of bispyrazolotetraazocinediium salts **4a** and **4b** the same conformation **C** is present in the solid state[2] and in solution. This is the main difference between the two series of compounds which otherwise behave rather similarly in NMR. In FABMS experiments this family of compounds is easily characterized by their reduction to monocharged ions.

Experimental

Melting points were determined with a hot-stage microscope and are uncorrected. Column chromatography was performed on silica gel Merck 60 (70–230 mesh) using the appropriate eluent in each case. ^{1}H and ^{13}C NMR spectra were obtained using Bruker AC-200 and Varian Gemini 200 instruments. The chemical shifts are accurate to 0.01 and 0.1 ppm for ^{1}H and ^{13}C NMR spectra, respectively. Coupling constants (J) are accurate to 0.2 Hz for ^{1}H NMR and 0.5 Hz for ^{13}C NMR spectra. ^{1}H NMR variable temperature experiments were achieved with a Varian Unity working at 299.95 MHz. The temperature of the probe was calibrated by the methanol and ethylene glycol standard method (± 0.5 K) and a delay of 600 s was used before registering the NMR spectra at each temperature. ^{1}H and ^{13}C NMR chemical shifts at low temperature are given from the apparatus internal standard references: [$^2H_6$]ethylene glycol and [$^2H_7$]DMF.

The FABMS were recorded on an SX102 type spectrometer (JEOL Ltd., Tokyo, Japan). Xenon was used in the FAB experiments. The energy of the neutral atom beam was 10 keV (emission current: 10 mA). Calibration was accomplished using Ultramark 1621 (Heraeus, Karlsruhe, Germany) as a reference. Samples were placed in the target by dissolving them directly in the minimum amount of the matrix. Matrices were obtained from commercial suppliers. Mass measurements at low resolution (EI) were obtained on a Finnigan TSQ-70 spectrometer operating at 75 eV.

The starting pyrazoles (**1a**, **1b**) and 1,2-dibromoethane are commercial products. The 4-(1-adamantyl)pyrazole **1c**,[4] campho[2,3-*c*]pyrazole or (4*S*,7*R*)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1*H*(2*H*)-indazole **5**,[7] and (4*R*)-7-isopropylidene-4-methyl-4,5,6,7-tetrahydro-2*H*-indazole or pulegopyrazole **10**,[8] were prepared according to literature. The preparation of 1-bromo-2-pyrazolylethanes **2a**,[29] **2b**[30] and bispyrazolylethanes (**3a**, **3b**)[5] has already been described.

The physical characteristics and the experimental conditions for the remaining new products **2**, **3** and **4** are shown in Table 9. The 5,6,12,13-tetrahydrobispyrazolo[1,2-*a*:1′,2′-*e*][1,2,5,6]-tetraazocinediium dibromides **4b–d** and **8** did not give correct microanalytical results.

General procedures

Method A

A mixture of pyrazole **1** (10 mmol), 10 cm^3 of 40% aq. NaOH, tetrabutylammonium bromide (TBAB, 1 mmol) and 10 cm^3 of 1,2-dibromoethane in 25 cm^3 of toluene was heated to reflux for 48 h. After cooling, the phases were separated, the aqueous

Table 9 Experimental conditions and physical characteristics

Compound	Procedure[a] isolation,[b] (Yield, %)	Formula	Molecular weight [M$^{\cdot+}$](%)	Microanalytical data (%) calc. C, H, N (found C, H, N)	Mp/°C
2c	A a, (80)	$C_{15}H_{21}N_2Br$	309.25 [308.1] (54.1) [309.95] (61.3)	C: 58.26, H: 6.84, N: 9.06	68–69
3c	B a, (75)	$C_{28}H_{38}N_4$	430.64 [430.3](12.4)	C: 78.10, H: 8.89, N: 13.01	54
3d	B a, (70)	$C_{10}H_{14}N_4$	190.25 [190.1] (8.4)	C: 63.14, H: 7.42, N: 29.44 (C: 63.03, H: 7.09, N: 29.15)	101
4b	C b, (25)	$C_{14}H_{22}N_4Br_2$	406.16	—	> 320 (dec)
4c	C b, (19)	$C_{30}H_{42}N_4Br_2$	618.49	—	> 320 (dec)
4d	C b, (20)	$C_{12}H_{18}N_4Br_2$	378.10	—	> 320 (dec)

[a] See Experimental section. [b] a = column chromatography on silica gel with dichloromethane–ethanol (98:2), b = crystallization from water.

phase was extracted with 3 × 40 cm^3 of dichloromethane and the extracts combined with the organic phase. The solvents were evaporated under vacuum and the crude product was purified.

Method B

Similar to method A but using 1-bromo-2-pyrazolylethane **2** instead of 1,2-dibromoethane.

Method C

A mixture of 1,2-bispyrazolylethane **3** (5 mmol) and of 1,2-dibromoethane in excess (5 cm^3) was heated under reflux. After 12 h a dark precipitate was formed which was filtered, washed with ethanol and purified by crystallization in water previously treated with charcoal.

1-Camphopyrazolyl-2-chloroethanes 6 and 6′

Camphopyrazole **5** (1.5 g, 8.5 mmol) in 40% aq. NaOH was heated to 80 °C for 30 min. Then TBAB (50 mg, 0.15 mmol) and 1,2-dichloroethane (60 cm^3) were added and the reaction mixture heated to 80 °C for 24 h. The organic layer was then separated and the aqueous solution was extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4 and evaporated. The residue was chromatographed on silica gel eluting with dichloromethane to give a 1:1 mixture of 1-(camphopyrazol-2-yl)-2-chloroethane **6** and 1-(camphopyrazol-1-yl)-2-chloroethane **6′** (89%) (Found: C, 65.4; H, 8.0; N, 11.7. $C_{13}H_{19}N_2Cl$ requires C, 65.40; H, 8.02; N, 11.73%); EI-MS (mixture of both isomers) *m/z* (relative intensity) 238 and 240 (M$^{\cdot+}$, $C_{13}H_{19}N_2Cl$, 29 and 14%).

1-Camphopyrazolyl-2-pyrazolylethanes 7 and 7′

Pyrazole **1a** (426 mg, 6.3 mmol) was dissolved in a solution of 40% aq. NaOH and heated to 70 °C for 30 min. Then 1-(camphopyrazolyl)-2-chloroethane **6** or **6′** (1.5 g, 6.3 mmol) in toluene (20 cm^3) and TBAB (150 mg, 0.5 mmol) were added to the solution. This reaction mixture was heated at 70 °C for 72 h. After extraction of the aqueous layer with dichloromethane the combined organic layers were dried over Na_2SO_4 and evaporated. Chromatography of the residue (silica gel, eluting with 1 to 50% ethanol in diethyl ether) yielded a 1:1 mixture of 1-(camphopyrazol-2-yl)-2-(pyrazol-1-yl)ethane **7** and 1-(camphopyrazol-1-yl)-2-(pyrazol-1-yl)ethane **7′** (58%) (Found: C, 70.9; H, 8.1; N, 20.5. $C_{16}H_{22}N_4$ requires: C, 71.08; H, 8.20; N, 20.72%); EI-MS (mixture of both isomers) *m/z* (relative intensity) 270 (M$^{\cdot+}$, $C_{16}H_{22}N_4$, 1%).

2-Benzylcampho[2,3-*c*]pyrazole (7bis)

Camphopyrazole (0.5 g, 2.8 mmol) in a solution of 40% aq. NaOH (10 cm^3) was heated at reflux for 15 min. Then TBAB (17 mg, 0.05 mmol) and benzyl chloride (20 cm^3) were added. The reaction mixture was stirred and kept refluxing for 20 h. After the usual treatment, the residue was chromatographed on silica gel eluting first with hexane–dichloromethane (1:9) to eliminate the excess of benzyl chloride, then with dichloromethane to yield compound **7bis** (56%). The compound was identified as the 2-benzyl isomer by its ^{13}C NMR spectrum: δ_C(C-3) 122.2 (see compounds **6** and **7** in Table 4).

Tetrahydro(camphopyrazolo)(pyrazolo)tetraazocinediium dibromide 8

1-(camphopyrazolyl)-2-pyrazolylethane (993 mg, 3.7 mmol) was dissolved in 1,2-dibromoethane (5 cm^3). This solution was heated at 120 °C for 3 days. The 1,2-dibromoethane was then evaporated and the residue was triturated with water. After evaporation of the filtrated aqueous solution the residue was washed with chloroform and dried to give compound **8** as a white solid (19%).

1-Chloro-2-(pulegopyrazol-2-yl)ethane 11

Pulegopyrazole **10** (7 g, 40 mmol) was treated at 100 °C with 40% aq. NaOH (50 cm^3). Then TBAB (2.58 g) and 1,2-dichloroethane (200 cm^3) were added. The reaction mixture was heated to 50–80 °C for 17 h. The organic layer was then separated and the aqueous solution extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4 and evaporated. The oily residue was chromatographed on silica gel eluting with dichloromethane. Evaporation of the first fraction gave compound **11** (6.3 g, 66%) (Found: C, 65.1; H, 7.9; N, 11.4. $C_{13}H_{19}N_2Cl$ requires: C, 65.40; H, 8.02; N, 11.73%); EI-MS *m/z* (relative intensity) 238 and 240 (M$^{\cdot+}$, $C_{13}H_{19}N_2Cl$, 100 and 44%).

1,2-Bis(pulegopyrazol-2-yl)ethane 13

Pulegopyrazole **10** (3.66 g, 21 mmol) was stirred with 40% aq. NaOH (50 cm^3) at 100 °C. Then TBAB (1.35 g) and 1-chloro-2-(pulegopyrazol-2-yl)ethane **11** (5 g, 21 mmol) were added. The reaction mixture was heated to 80 °C for 7 days. The organic layer was then separated, and the aqueous solution extracted with dichloromethane. The combined organic layers were dried over sodium sulfate and evaporated. The oily residue was chromatographed on silica gel eluting with dichloromethane to give compound **13** (2.99 g, 38%); EI-MS *m/z* (relative intensity) 378 (M$^{\cdot+}$, $C_{24}H_{34}N_4$, 39%).

1-(Pulegopyrazol-2-yl)-2-(pyrazol-1-yl)ethane 12

The procedure is similar to the one described previously for the preparation of 1,2-bis(pulegopyrazol-2-yl)ethane **13**. Pyrazole was treated with aq. NaOH and then with 1-chloro-2-(pulegopyrazol-2-yl)ethane. After purification by chromatography 1-(pulegopyrazol-2-yl)-2-(pyrazol-1-yl)ethane **12** (43%)

was obtained (Found: C, 70.9; H, 7.95; N, 20.5. $C_{16}H_{22}N_4$ requires: C, 71.08; H, 8.20; N, 20.72%); EI-MS *m/z* (relative intensity) 270 ($M^{\bullet+}$, $C_{16}H_{22}N_4$, 25%).

Tetrahydro(pulegopyrazolo)(pyrazolo)tetraazocinediium dibromide 14

1-(Pulegopyrazol-1-yl)-2-(pyrazol-1-yl)ethane **12** (450 mg, 1.7 mmol) was heated in 1,2-dibromoethane (6 cm^3) for five days. The reaction mixture was then filtered. The 1,2-dibromoethane solution was treated with charcoal then evaporated. The oily residue and 20 cm^3 H_2O were sonicated for 1 h. After filtration the aqueous solution was evaporated to yield the dibromide **14** (10 mg, 1.3%); MS (FAB^+) *m/z* (relative intensity) 377 ($[M - H - Br]^+$, $C_{18}H_{25}BrN_4$, 100%), 297 ($[M - H - 2Br]^+$, $C_{18}H_{22}N_4$, 25%).

Tetrahydrobis(pulegopyrazolo)tetraazocinediium dibromide 15

1,2-Bis(pulegopyrazol-2-yl)ethane **13** (330 mg, 0.9 mmol) was heated in 1,2-dibromoethane (5 cm^3) for three days. After evaporation of 1,2-dibromoethane, crystallization of the crude residue in dichloromethane–light petroleum (2:1) yielded the dibromide **15** (17 mg, 5%); EI-MS *m/z* (relative intensity) 485 ($[M - H - Br]^+$, $C_{26}H_{38}BrN_4$, 36%).

Acknowledgements

This work has been financially supported by DGICYT of Spain, project number PB93-0197-C02-01.

References

1 P. Domiano, P. Cozzini, R. M. Claramunt, J.-L. Lavandera, D. Sanz and J. Elguero, *J. Chem. Soc., Perkin Trans 2*, 1992, 1609.
2 C. Foces-Foces, F. H. Cano, P. Cabildo, R. M. Claramunt and J. Elguero, *Acta Crystallogr., Sect. C*, 1991, **47**, 2583.
3 J.-L. Aubagnac, R. M. Claramunt, J.-L. Lavandera and J. Elguero, *Bull. Soc. Chim. Belg.*, 1991, **100**, 459.
4 P. Cabildo, R. M. Claramunt, I. Forfar, C. Foces-Foces, A. L. Llamas-Saiz and J. Elguero, *Heterocycles*, 1994, **37**, 1623.
5 (*a*) J. Torres, J.-L. Lavandera, P. Cabildo, R. M. Claramunt and J. Elguero, *J. Heterocycl. Chem.*, 1988, **25**, 771; (*b*) C. Acerete, M. L. Bañón, P. Cabildo, R. M. Claramunt, J. Elguero and J.-L. Lavandera, *Rev. Roum. Chim.*, 1991, **36**, 629.
6 J. Torres, J.-L. Lavandera, P. Cabildo, R. M. Claramunt and J. Elguero, *Bull. Soc. Chim. Belg.*, 1992, **101**, 29.
7 (*a*) M. C. López, N. Jagerovic and P. Ballesteros, *Tetrahedron: Asymmetry*, 1994, **5** 1887; (*b*) H. Brunner, U. P. Singh, T. Boeck, S. Altmann, T. Scheck and B. Wrackmeyer, *J. Organomet. Chem.*, 1993, **443**, C16; A. L. Llamas-Saiz, C. Foces-Foces, I. Sobrados, J. Elguero and W. Meutermans, *Acta Crystallogr., Sect. C*, 1993, **49**, 724.
8 J. Elguero and B. Shimizu, *An. Quim.* 1988, **84**, 198.
9 (*a*) H. Gunther, *La Spectroscopie de RMN*, Masson, Paris, 1994; (*b*) J. B. Stothers, *Carbon-13 NMR Spectroscopy*, Academic Press, New York, 1972; (*c*) M. Begtrup, G. Boyer, P. Cabildo, C. Cativiela, R. M. Claramunt, J. Elguero, J. I. Garcia, C. Toiron and P. Vedsø, *Magn. Reson. Chem.*, 1993, **31**, 107.
10 (*a*) M. Oki, *Applications of Dynamic NMR Spectroscopy to Organic Chemistry*, VCH, Deerfield Beach, FL., 1985; (*b*) J. Sandström, *Dynamic NMR Spectroscopy*, Academic Press, London, 1982.
11 PANIC 86, Bruker Program Library, Germany.
12 D. Montecalvo, M. St-Jacques and R. Wasylishen, *J. Am. Chem. Soc.*, 1973, **95**, 2023.
13 F. Sauriol-Lord and M. St-Jacques, *Can. J. Chem.*, 1975, **53**, 3768.
14 R. Crossley, A. P. Downing, M. Nógrádi, A. B. de Oliveira, W. D. Ollis and I. O. Sutherland, *J. Chem. Soc., Perkin Trans. 1*, 1973, 205.
15 N. L. Allinger and J. T. Sprague, *Tetrahedron*, 1975, **31**, 21.
16 M. J. S. Dewar and W. Thiel, *J. Am. Chem. Soc.*, 1977, **99**, 4899; 4907.
17 M. J. S. Dewar, E. B. Zoebisch, E. F. Healy and J. J. P. Stewart, *J. Am. Chem. Soc.*, 1985, **108**, 8075.
18 C. A. G. Haasnoot, F. A. A. M. Leeuw and C. Altona, *Tetrahedron*, 1980, **36**, 2783.
19 R. L. Cerny and M. L. Gross, *Anal. Chem.*, 1985, **57**, 1160.
20 S. K. Sethi, C. C. Nelson and J. A. McCloskey, *Anal. Chem.*, 1984, **56**, 1975.
21 (*a*) J.-L. Aubagnac, R. M. Claramunt and D. Sanz, *Org. Mass Spectrom.*, 1990, **25**, 293; (*b*) J.-L. Aubagnac, S. Doulut, M. Rodríguez and J. Martínez, *Org. Mass Spectrom*, 1992, **27**, 645; (*c*) J.-L. Aubagnac, E. Bernardi and R. Lazaro, *Org. Mass Spectrom.*, 1993, **28**, 57; (*d*) J.-L. Aubagnac, I. Gilles, R. Astier, G. Gosselin, J.-L. Imbach and M. C. Bergogne, *Rapid Commun. Mass Spectrom.*, 1993, **7**, 41; (*e*) J.-L. Aubagnac, I. Gilles, P. Dumy, R. Escale and P. Vidal, *Bull. Soc. Chim. Fr.*, 1993, **130**, 467; (*f*) J.-L. Aubagnac, I. Gilles, R. Astier, C. Perigaud, P. Labataille and J.-L. Imbach, *Rapid Commun. Mass Spectrom.*, 1993, **7**, 704.
22 T. M. Ryan, R. J. Day and R. G. Cooks, *Anal. Chem.*, 1984, **52**, 2054.
23 (*a*) M. Yoneda, K. Tsujimoto, M. Ohashi, M. Shiratsuchi and Y. Ohkawa, *Org. Mass Spectrom.*, 1990, **25**, 146; (*b*) M. Yoneda, K. Tsujimoto, M. Ohashi, M. Shiratsuchi, Y. Ohkawa and K. Isa, *Chem. Pharm. Bull. Jpn.*, 1990, **38**, 3389.
24 B. Danieli, F. M. Rubino and A. Cremonesi, *Org. Mass Spectrom.*, 1989, **24**, 225.
25 A. N. R. Nedderman and D. H. Williams, *Biol. Mass Spectrom.*, 1989, **20**, 289.
26 S. M. Musser and J. A. Kelley, *Org. Mass Spectrom.*, 1993, **28**, 672.
27 (*a*) D. N. Heller, J. Yergey and R. J. Cotter, *Anal. Chem.*, 1983, **55**, 1310; (*b*) J. Claereboudt, W. Baeten, H. Geise and M. Claeys, *Org. Mass Spectrom.*, 1993, **28**, 71.
28 J. Elguero, R. Jacquier and D. Tizané, *Bull. Soc. Chim. Fr.*, 1970, 1121.
29 A. J. Canty and R. Th. Honeyman, *J. Organomet. Chem.*, 1990, **387**, 247.
30 H. Ochi, T. Misyasaka and K. Arakawa, *Yakugaku Zasshi*, 1978, **98**, 165 (*Chem. Abstr.* 1978, **89**, 24213k).

Paper 5/04500B
Received 10*th July* 1995
Accepted 9*th October* 1995