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Theoretical studies of azapentalenes. Part 5: Bimanes

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ABSTRACT

The properties of 21 molecules related to azapentalenes and their conjugated acids have been calculated: energies, dipole moments, natural bond orders, bond lengths, bond critical points, HOMA, and NICS. The ring-opening processes of dioxopyrazolo[1,2-*a*] pyrazolium and pyrazolo[1,2-*a*][1,2,4]triazol-4-ium into ketenes and isocyanates have been studied. The calculations were carried out at the B3LYP/6-311++G(d,p) level.

1. Introduction

There are three kinds of azapentalenes, all of them formally derived from the pentalene dianion **I** (Scheme 1). They can be classified according to the number of nitrogen atoms on the ring fusion (positions 3a, 6a): none **II** and **III**, one **IV** and **V**, and two **VI**.

We have devoted several papers to the theoretical study of these compounds: Part 1. 'Heteropentalenes aromaticity: a theoretical study' (**II** and **III**);[1] Part 2. 'Molecular Complexes of pentazolo[1,2-*a*]pentazole, N_8 (**VI**);[2] Part 3. 'Application of Free-Wilson matrices to the analysis of the tautomerism and aromaticity of azapentalenes: a DFT study' (**IV** and **V**);[3] and Part 4. 'Theoretical study of the properties of 3a,6a-diazapentalene' (**VI**).[4] In these papers there is an abundant bibliography on azapentalenes.

In this last paper, we will devote our attention to compounds **VII**, **VIII**, **IX**, and **X**. Compounds **VII** and **VIII** (1,5-diazabicyclo[3.3.0]octadienediones) are known as bimanes and were first prepared by Kosower who did most of their chemistry and the study of their properties.[5] In recent years there has been a regain of interest in bimanes due to the strong fluorescent properties of the *syn* derivatives **VII**.[5] These derivatives are labeling agents and have been successfully used as fluorescent probes for protein structural analysis.[6] However important these compounds appear to be, almost no theoretical studies have been reported. Goldberg et al. have compared the experimental electron density map of *syn*- and *anti*-bimane with the calculated ones at the 4-31G level.[7]

The 1,3-isomer **IX** (anhydro-1-hydroxy-3-oxopyrazolo[1,2-*a*]pyrazolium hydroxyde or 1-oxo-1*H*-4λ^5-pyrazolo[1,2-*a*]pyrazol-4-ylium-3-olate) and its 2-aza derivative **X** (anhydro-1-hydroxy-3-oxopyrazolo[1,2-*a*][1,2,4]triazolium hydroxide or 2,3-dihydro-1,3-dioxo-1*H*-pyrazolo[1,2-*a*][1,2,4]triazol-4-ium inner salt) are much less known compounds. The ring system of **IX** was prepared for the first time in 1980 simultaneously by Potts et al.[8] and by Friedrichsen,[9] and further developed by Zvilichovsky and Mordechai in 1982[10] and by Friedrichsen et al. in 1993.[11] *C*-Substituted derivatives of **X** were described by Friedrichsen et al. in 1983 and 1988.[12,13] Compound **IX** belongs to cross-conjugated mesomeric betaines according to Ollis et al.[14]

2. Results and discussion

We decided to study not only the oxo- but some imino-derivatives as well. The compounds studied in this work are represented in Scheme 2 (*syn*-bimanes), Scheme 3 (*anti*-bimanes), Scheme 4 (1,3-diones), Scheme 5 (oxopyrazolo[1,2-*a*]pyrazolium), and Scheme 6 (pyrazolo[1,2-*a*][1,2,4]triazol-4-ium) and the corresponding energies in Table 1 [absolute (hartree) and relative (kJ mol^{-1}) energies neutral forms], Table 2 [absolute (hartree) and relative (kJ mol^{-1}) energies and proton affinities (kJ mol^{-1}) of protonated forms], Table 3 [absolute (hartree) and relative (kJ mol^{-1}) energies of oxopyrazolo[1,2-*a*]pyrazolium isomers] and Table 4 [absolute (hartree) and relative (kJ mol^{-1}) energies of pyrazolo[1,2-*a*][1,2,4]triazol-4-ium isomers].

2.1. Neutral molecules

In Scheme 7 we have reported the differences in energy related to the configuration of the imino groups (horizontal equilibria, Table 1) and to isomerism (vertical).

The stability of isomers is: *anti*-bimanes>1,3-derivatives>*syn*-bimanes (O and NH derivatives). Concerning the *E/Z* configuration of imines the order is **e**>**i** and **ee**>**ei**>**ii**, with the exception of **2i** and **3ei**, certainly due to intramolecular N–H···O/N–H···N hydrogen bonds.

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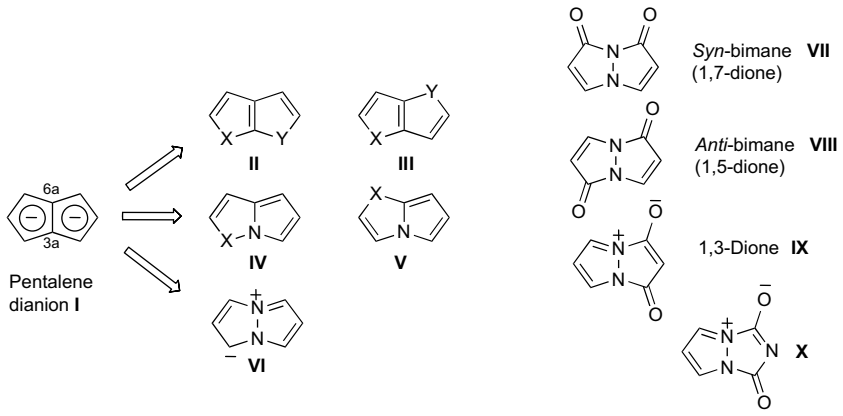
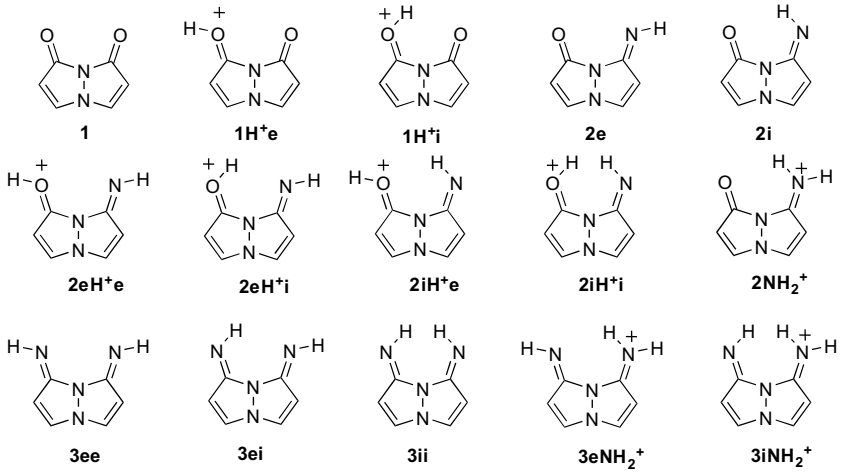


Scheme 1. Azapentalenes, X and Y=O, S, NR (the peripheral positions can be CR or N).

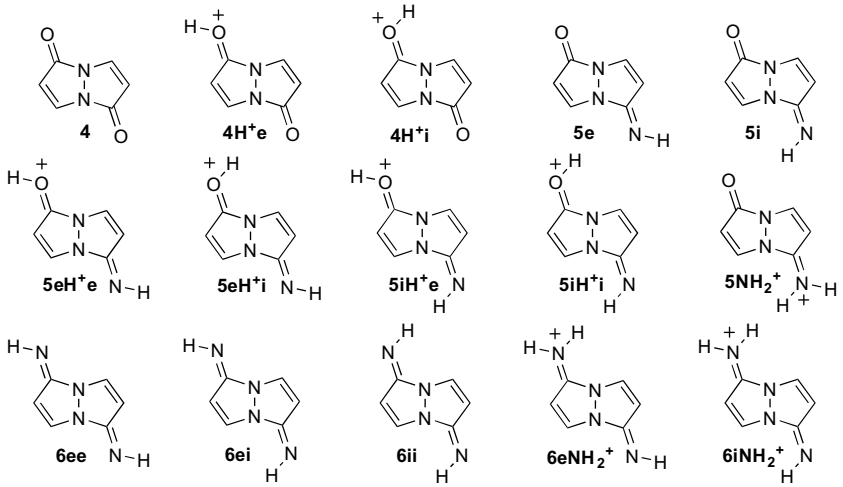


Scheme 2. *syn*-Bimane, its imino derivatives and their cations.

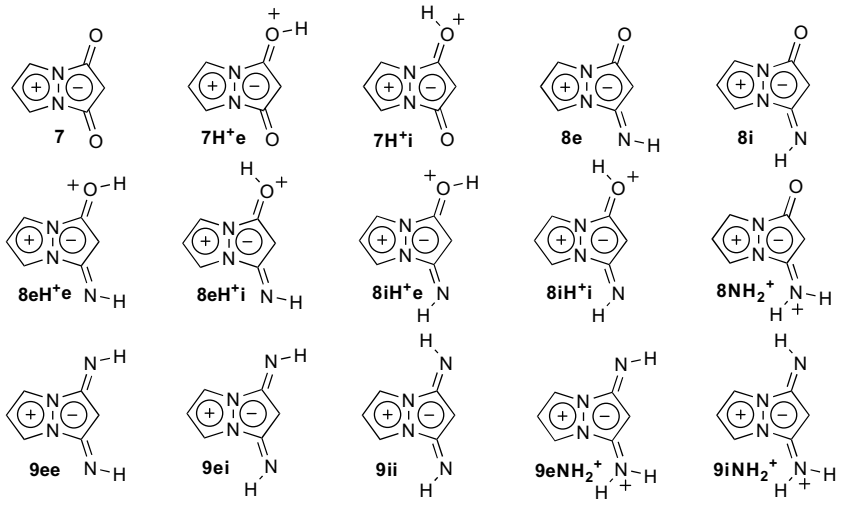
For compound **7** the neologism 'paraionic' (from the Greek meaning 'alongside') was coined by Zvilichovsky et al.[8,10] The term 'paraionic' is derived from the observation that both the anion and the cation coexist parallel to one another with the absence of conjugation between them (nothing related to aromatic *para*-positions). The structural implications behind this term have been questioned by Friedrichsen et al. (both for **7** and **14**).[12]

We have calculated the bond orders (NBO) of compounds **7** and **14** together with some model compounds (**18**–**22**), including 3a,6a-diazapentalene (**22**) from our previous paper (Table 5).[4] An aromatic bond order should be close to 1.5.

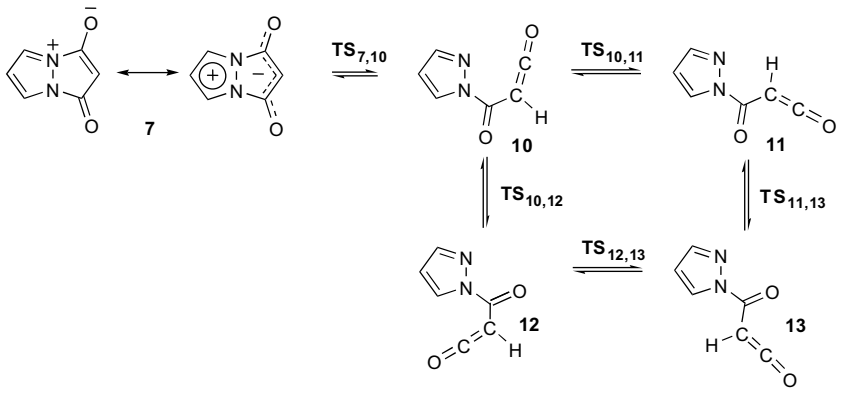
If these systems were 'paraionic', the bond orders of the left and right rings should be independent, i.e., the left part of **7** should resemble the left part of **18** and the right part of **7**, the right part of **19**



Scheme 3. *anti*-Bimane and its conjugated acids.



Scheme 4. 1,3-Dione, its imino derivatives and their cations.



Scheme 5. Ring-opening reactions of dioxopyrazolo[1,2-*a*]pyrazolium.

(analogously for **14**, **20**, and **21**). This is approximately true but there are some small differences in the right side ring (more pronounced for **7**/**19** than for **14**/**21**) in what concerns 3a-4 (6-6a) and 3a-6a. The main differences with **22** are found in 3-3a (6a-1) and 3a-6a.

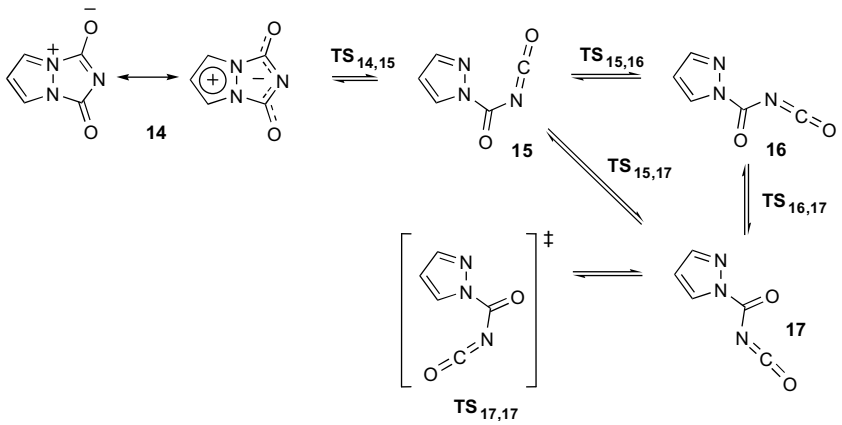
2.2. Protonated molecules

2.2.1. Differences in energy between cations

In the *O*,*O*-series the most stable cation is **7H**$^+$**e** (Scheme 8), which is expected since the neutral molecule bears a partial negative charge on the oxygen atoms but the following more stable cation is **1H**$^+$**i** that lies only 4.4 kJ mol^{-1} higher in energy. This cation and **2NH$_2^+$** and **3eNH$_2^+$** have in common an intramolecular hydrogen bond (IMHB) that stabilizes their structures. The AIM analysis of these three cations (AIM2000) illustrates the presence of the IMHB (Fig. 1).

2.2.2. Proton affinities

In almost all cases, the most stable neutral molecule lead to the most stable cation (Table 2): **1**→**1H**$^+$**i** (−910.8 kJ mol^{-1}); **2i**→



Scheme 6. Ring-opening reactions of pyrazolo[1,2-*a*][1,2,4]triazol-4-ium.

Table 1
Absolute (hartree), relative (kJ mol^{-1}) energies and dipole moments (D) of neutral forms

Compound	Symmetry	E_{total}	Dipole	E_{rel}
1	C_s	−491.084510	8.04	—
2e	C_1	−471.188841	7.54	18.1
2i	C_1	−471.195723	6.58	*0.0*
3ee	C_s	−451.291275	6.53	24.6
3ei	C_1	−451.300636	6.28	*0.0*
3ii	C_1	−451.295623	5.11	13.2
4	C_2	−491.092815	0.01	—
5e	C_1	−471.198126	2.56	*0.0*
5i	C_1	−471.194589	2.01	9.3
6ee	C_2	−451.302087	0.50	*0.0*
6ei	C_1	−451.298363	2.76	9.8
6ii	C_2	−451.295278	0.24	17.9
7	C_{2v}	−491.092355	5.47	—
8e	C_s	−471.196825	4.02	*0.0*
8i	C_s	−471.188382	6.60	22.2
9ee	C_{2v}	−451.297684	2.52	*0.0*
9ei	C_s	−451.289163	5.29	22.4
9ii	C_{2v}	−451.279622	8.03	47.4

2NH$_2^+$ (−1012.7 kJ mol^{-1}); **3ei→3iNH$_2^+$** (−910.8 kJ mol^{-1}); **4→4H$^+$e** (−887.3 kJ mol^{-1}); **5e→5NH$_2^+$** (−984.7 kJ mol^{-1}); **6ee→6eNH$_2^+$** (−1019.1 kJ mol^{-1}); **7→7H$^+$e** (−894.6 kJ mol^{-1}); **8e→8NH$_2^+$** (−987.2 kJ mol^{-1}). The only exception is **9ee** that vertically leads to **9eNH$_2^+$** (−1025.9 kJ mol^{-1}) and adiabatically the most stable cation is **9iNH$_2^+$** (−1007.1 kJ mol^{-1}) [remember that these two cations are related through an *E*/*Z* isomerization of the imino group].

2.3. Aromaticity studies

We will restrict the analysis of the aromaticity indexes to the oxygen derivatives **1**, **4**, and **7** and their cations (Tables 5 and 6) as models of their corresponding families. The aromaticity indexes for the rest of the compounds can be found in the Supplementary data.

The geometries of the *E*/*Z* isomers corresponding to C=O–H (**e** or **i**) are similar and not relevant to discuss the effects of protonation on the geometries and beyond on the aromaticity, thus only the **e** isomers will be considered.

Considering the double/single bond alternance as a criteria of aromaticity, in the case of **1** and **4**, protonation increases the aromaticity of the ring where protonation occurs while slightly decreases that of the other ring. In the case of **7**, the bond lengths of the neutral molecule correspond to a resonance form with two short C=O distances as represented in Scheme 9; its protonation produces an electronic localization in both rings (for instance the N–N distance increases). The non-protonated C=O bonds shortened by protonation on the other oxygen atom and the difference between **1H$^+$e** and **1H$^+$i** corresponds to the IMHB.

The HOMA index is close to 1 as the ring approaches perfect aromaticity.[1] Compounds **1** and **4** are not aromatic but one ring (the left one) becomes aromatic after protonation occurs (Table 7). The behavior of **7** is completely different: the left ring is aromatic while the right one is not (Scheme 9). After protonation (**7H$^+$e**), some increase in aromaticity occurs in the protonated ring, better described as a larger delocalization while the aromaticity of the left ring slightly decreases.

Since the rings are folded, there are two NICS per ring, one above (the convex part) and another below (the concave part, see Fig. 2). The values of Table 7 correspond to the second ones. In all aromatic azapentalenes, NICS are about −10 ppm,[4] according to this criterion only **7** and its cations are aromatic. Here again, compounds **1** and **4** are similar while compound **7** is very different. Bimanes are weakly aromatic, both rings being identical. Protonation results in a transfer of aromaticity from one ring (the neutral) to another (the protonated). The cross-conjugated mesomeric betaine **7** shows NICS value relatively insensitive to protonation: the left ring shows a decrease in aromaticity (more marked for **7H$^+$e** than for **7H$^+$i**),

Table 2
Absolute (hartree), relative (kJ mol^{-1}) energies, proton affinities (kJ mol^{-1}) and dipole moments (D) of protonated forms

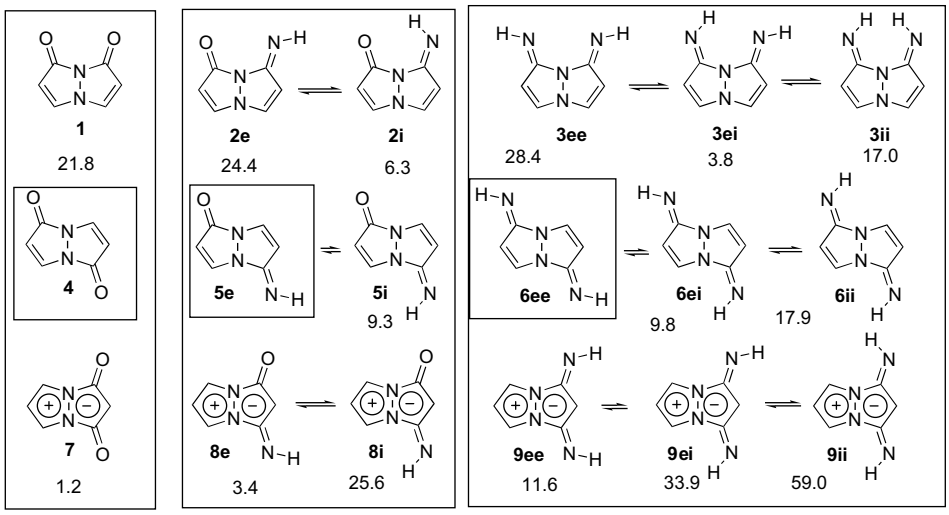
Compound	Symmetry	E_{total}	Dipole	E_{rel} series	PA	Ref. base
1H$^+$e	C_s	−491.429350	5.95	5.4	−905.4	**1**
1H$^+$i	C_1	−491.431413	4.48	*0.0*	−910.8	**1**
2eH$^+$e	C_s	−471.547676	3.63	88.7	−942.1	**2e**
2eH$^+$i	C_1	−471.554516	3.56	70.7	−960.1	**2e**
2iH$^+$e	C_s	−471.545756	4.79	93.7	−919.0	**2i**
2iH$^+$i	C_1	−471.535954	2.52	119.4	−893.3	**2i**
2NH$_2^+$	C_1	−471.581448	4.48	*0.0*	−1012.7	**2i**
3eNH$_2^+$	C_s	−451.701089	1.80	*0.0*	−1051.4	**3ei**
3iNH$_2^+$	C_1	−451.684464	3.97	43.6	−1007.7	**3ei**
4H$^+$e	C_s	−491.430777	5.07	*0.0*	−887.3	**4**
4H$^+$i	C_s	−491.423590	4.28	18.9	−868.4	**4**
5eH$^+$e	C_s	−471.549915	2.30	61.1	−923.6	**5e**
5eH$^+$i	C_s	−471.542749	3.07	79.9	−904.8	**5e**
5iH$^+$e	C_s	−471.544027	4.18	76.5	−917.4	**5i**
5iH$^+$i	C_s	−471.537441	2.11	93.8	−900.2	**5i**
5NH$_2^+$	C_s	−471.573175	7.02	*0.0*	−984.7	**5e**
6eNH$_2^+$	C_s	−451.690248	4.58	*0.0*	−1019.1	**6ee**
6iNH$_2^+$	C_s	−451.684956	5.24	13.9	−1015.0	**6ei**
7H$^+$e	C_s	−491.433086	3.91	*0.0*	−894.6	**7**
7H$^+$i	C_1	−491.422990	5.70	26.5	−868.1	**7**
8eH$^+$e	C_s	−471.550970	2.11	57.4	−929.8	**8e**
8eH$^+$i	C_1	−471.542235	2.71	80.3	−906.9	**8e**
8iH$^+$e	C_s	−471.544682	2.43	73.9	−935.5	**8i**
8iH$^+$i	C_s	−471.544680	2.43	73.9	−935.5	**8i**
8NH$_2^+$	C_s	−471.572826	6.40	*0.0*	−987.2	**8e**
9eNH$_2^+$	C_1	−451.688429	4.02	*0.0*	−1025.9	**9ee**
9iNH$_2^+$	C_1	−451.681269	4.33	18.8	−1029.4	**9ei**

Table 3
Absolute (hartree), relative (kJ mol^{-1}) energies and dipole moments (D) of dioxopyrazolo[1,2-*a*]pyrazolium isomers

Compound	Symmetry	ImFreqs	E_{total}	Dipole	E_{rel}
7	C_{2v}	0	−491.092355	5.47	5.8
10	C_s	0	−491.094565	1.87	*0.0*
11	C_s	0	−491.092658	2.45	5.0
12	C_1	0	−491.076375	4.02	47.8
13	C_1	0	−491.078759	5.25	41.5
TS$_{7,10}$	C_s	1	−491.090346		11.1
TS$_{10,11}$	C_1	1	−491.072106		59.0
TS$_{10,12}$	C_1	1	−491.071747		59.9
TS$_{11,13}$	C_1	1	−491.070611		62.9
TS$_{12,13}$	C_1	1	−491.066973		72.4

Table 4
Absolute (hartree), relative (kJ mol^{-1}) energies and dipole moments (D) of pyrazolo[1,2-*a*][1,2,4]triazol-4-ium isomers

Compound	Symmetry	ImFreqs	E_{total}	Dipole	E_{rel}
14	C_{2v}	0	−507.152497	7.48	42.1
15	C_s	0	−507.168533	3.45	*0.0*
16	C_s	0	−507.166505	2.85	5.3
17	C_s	0	−507.163304	4.10	13.7
TS$_{14,15}$	C_s	1	−507.152473	—	42.2
TS$_{15,16}$	C_1	1	−507.162845	—	14.9
TS$_{15,17}$	C_1	1	−507.144523	—	63.0
TS$_{16,17}$	C_1	1	−507.146201	—	58.6
TS$_{17,17}$	C_s	1	−507.153236		40.2



Scheme 7. Differences in energy in kJ mol^{-1}, the minima correspond to **4**, **5e**, and **6ee**.

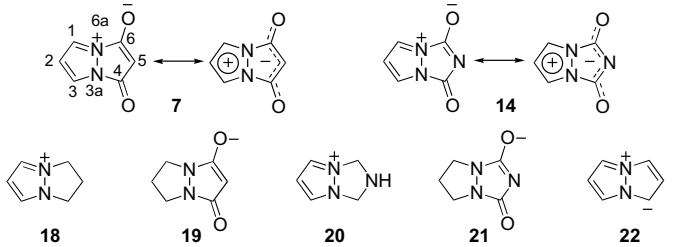
a conclusion consistent with those deduced from geometries and HOMA. At least in what concerns protonation effects, the rings are not 'paraionic' since the protonation on the right ring affects the left one.

2.4. Ring-opening reactions

In Schemes 5 and 6 we have represented the ring opening reactions of cross-conjugated mesomeric betaines compounds **7** and **14**, respectively. In the case of dioxopyrazolo[1,2-*a*]pyrazolium **7** (Table 3) the compound should isomerize into the ketene **10** that lies 5.8 kJ mol^{-1} below because the barrier is very low (11.1 kJ mol^{-1}). This has been considered but not observed in solution,[9] may be due to the fact that the dipole moment of **7** (5.47 D) is much higher than that of **10** (1.87 D). The lone pair/lone pair repulsion between pyrazole N2 and the C=O group explains why **12** and **13** are much less stable.

The case of the triazole derivative **14** is very different. The ring opening to an isocyanate has been studied by Friedrichsen et al. who carried out MNDO calculations on the parent systems **14** and **15**. Both isomers have been observed and can be interconverted by sublimation, melting or dissolution.[13] The isocyanate **15** is 42.1 kJ mol^{-1} more stable than the betaine **14** and although the barrier is higher than in the preceding case (42.2 instead of 11.1 kJ mol^{-1}) it should not be an obstacle for easy isomerization. Note also that the less stable ketene **12** corresponds in this series to a transition state, that of rotation of **17** about the N–CO bond. The ring/chain isomerism between **14** and **15** has been reported in a review.[15]

Table 5
NBO results (bond orders)



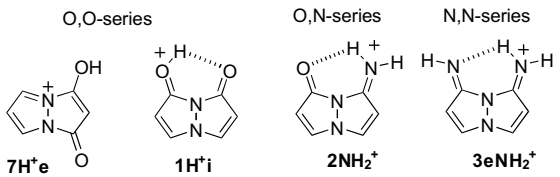
Compound	1-2	2-3	3-3a	3a-4	4-5	5-6	6-6a	6a-1	3a-6a
7	1.44	1.44	1.32	0.73	1.32	1.31	0.73	1.32	1.16
18	1.45	1.45	1.29	—	—	—	—	1.29	1.12
19	—	—	—	0.97	1.30	1.30	0.97	—	0.99
14	1.45	1.45	1.25	0.90	1.37	1.37	0.90	1.25	1.10
20	1.45	1.45	1.29	—	—	—	—	1.29	1.12
21	—	—	—	0.96	1.28	1.28	0.96	—	0.99
22	1.45	1.45	1.13	1.13	1.45	1.45	1.13	1.13	1.09

3. Computational details

The geometry of the systems has been fully optimized with the hybrid HF/DFT B3LYP[16,17] computational method and the 6-311++G(d,p) basis set[18] within the Gaussian 03 package.[19] Frequency calculations have been carried out at the same computational level to confirm that all relevant structures correspond to energetic minima or real transition states.

The electron density topology has been evaluated within the AIM methodology[20] with the AIM2000 program.[21] A Natural Bond Orbital analysis,[22] using the NBO 5.0 program,[23] has been used to study electronic parameters.

Two separate indexes of aromaticity have been investigated, employing both geometric (Harmonic Oscillator Model of Aromaticity, HOMA) and magnetic criteria (Nuclear Independent Chemical Shift, NICS). The geometry-based HOMA index[24] can be evaluated from the aromatic bond lengths by means of the equation: $\mathrm{HOMA}=1-[(\alpha/n)\Sigma(R_{opt}-R_i)^2]$, where R_{opt} and R_i correspond to optimal bond lengths and bond lengths in the real-system, respectively. The variable α is an empirical factor chosen to provide a HOMA value of zero for the Kekulé structure of benzene (archetypal aromatic system) and a value of one for the hypothetical system with all bond lengths equal to the optimal value R_{opt}. Finally,



Scheme 8. Most stable conjugated acids.

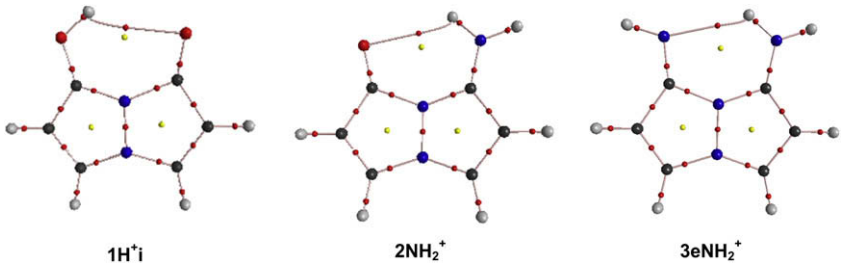
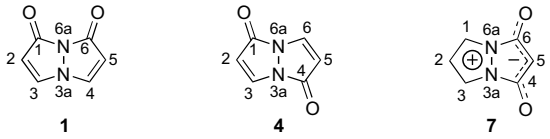
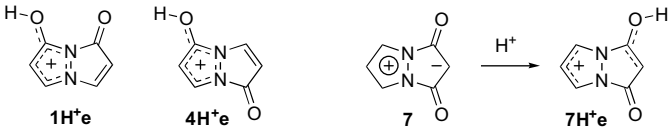


Figure 1. The bond critical points are shown in red and the ring critical points in yellow.

Table 6
Bond lengths (Å)



Compound	1-2	2-3	3-3a	3a-4	4-5	5-6	6-6a	6a-1	3a-6a	1-O	4-O	6-O
1	1.473	1.352	1.380	1.380	1.352	1.473	1.441	1.441	1.379	1.204	—	1.204
1H$^+$e	1.411	1.384	1.352	1.409	1.341	1.475	1.507	1.358	1.358	1.306(H$^+$)	—	1.182
1H+i	1.411	1.382	1.360	1.408	1.346	1.471	1.475	1.359	1.358	1.301(H$^+$)	—	1.192
4	1.469	1.355	1.379	1.435	1.469	1.355	1.379	1.435	1.374	1.208	1.208	—
4H$^+$e	1.412	1.384	1.352	1.488	1.480	1.340	1.416	1.354	1.357	1.311(H$^+$)	1.185	—
4H$^+$i	1.410	1.379	1.356	1.476	1.382	1.338	1.420	1.360	1.362	1.309(H$^+$)	1.186	—
7	1.399	1.399	1.338	1.560	1.405	1.405	1.560	1.338	1.332	—	1.201	1.201
7H$^+$e	1.393	1.399	1.342	1.529	1.457	1.352	1.423	1.351	1.347	—	1.181	1.311(H$^+$)
7H$^+$i	1.391	1.399	1.340	1.537	1.452	1.349	1.438	1.354	1.348	—	1.181	1.312(H$^+$)



Scheme 9. Effect of the protonation on the geometries.

n is the number of bonds considered in the system. The values used here for R_{opt} are 1.388, 1.334, and 1.309 Å and for α 257.7, 93.52, and 130.33 for the C–C, C–N, and N–N bonds, respectively. The second aromaticity index, the NICS, is defined as the negative absolute magnetic shielding computed in the center of the aromatic ring.[25]

Table 7
Aromaticity indexes. The angle (°) between the left and right rings, if different from 180° means that the molecule is not planar

Compound	Protonated ring	Angle (°)	HOMA		NICS(0)		NICS(1)	
		Left-right	Left	Right	Left	Right	Left	Right
1	—	161.2	0.18	0.18	−4.80	−4.80	−3.59	−3.59
1H$^+$e	Left	178.3	0.89	−0.23	−8.93	−0.81	−5.72	−0.75
1H$^+$i	Left	170.7	0.88	0.02	−8.33	−0.94	−5.44	−1.12
4	—	162.2	0.27	0.27	−3.68	−3.68	−3.07	−3.07
4H$^+$e	Left	179.0	0.90	−0.19	−8.45	−0.02	−5.60	−0.42
4H$^+$i	Left	179.7	0.88	−0.17	−8.15	−0.20	−5.44	−0.51
7	—	180.0	0.97	−0.95	−11.85	−1.21	−9.46	−0.33
7H$^+$e	Right	178.7	0.95	−0.21	−9.99	−0.58	−7.91	+0.13
7H$^+$i	Right	175.4	0.94	−0.30	−10.13	−0.28	−8.06	+0.32

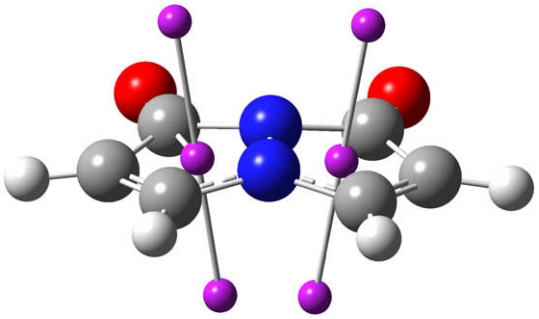


Figure 2. Location of NICS(1) above and below compound **1**.

Also presented here is the NICS(1) index calculated at 1 Å above the ring center.[26] Rings with highly negative NICS values are said to be aromatic whereas those with positive values are described as antiaromatic.

4. Conclusions

The main conclusions of the present work on azapentalenes are:

(i) IMHBs are determinant to stabilize the structure of protonated molecules;
(ii) protonation increases the aromaticity of bimanes;
(iii) the term 'paraionic' has been validated;
(iv) ring opening reactions of cross-conjugated mesomeric betaines are different for anhydro-1-hydroxy-3-oxopyrazolo[1,2-

a]pyrazolium hydroxyde (**7**) and its 2-aza derivative anhydro-1-hydroxy-3-oxopyrazolo[1,2-*a*][1,2,4]triazolium hydroxide (**14**).

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Supplementary data

Optimized geometry of the structures and aromatic indexes of all the systems considered in the present article. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.05.018.

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