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The azido-tetrazole tautomerism in azoles and its relationships with aromaticity and NMR properties

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Dedicated to Professor Minh Tho Nguyen for his prominent contribution to the problem of azido-tetrazole tautomerism

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ABSTRACT

The properties of 41 neutral molecules (azoles) together with 13 transition states as well as of 16 anions (azolates) with seven transition states belonging to the series of azido/azoles, have been calculated at the B3LYP/6-31G(d) and at the G3B3 levels. Energies, NICS, and bond critical points are used to discuss the ring-chain tautomerism of these compounds in relation with the magnetic aromaticity of the azoles (imidazoles, benzimidazoles, pyrazoles, indazoles, 1,2,4-triazoles, 1,2,3-triazoles and tetrazoles). The removal of the N–H proton has a considerable effect on the azido/tetrazole equilibrium and corresponds to a large stabilization (73 kJ mol^{-1} in average) of the tetrazoles. Cioslowski's exothermicity is related to the energy barriers (TSs). A study of the *E*/*Z* isomerism of the azides, determination of NICS(1) values and AIM analysis were also carried out.

1. Introduction

Ring-chain isomerism or tautomerism is an important aspect of organic chemistry.[1] The most studied case is the azidoazomethine/tetrazole[2] valence isomerism of tetrazoles (Scheme 1a).[3] The imino C=N bond can be part of a heterocyclic ring, either a six-membered ring (azines, Scheme 1b) or a five-membered ring (azoles, Scheme 1c). We have already studied the case of azidoazines.[4] In this second paper we will report our theoretical results concerning azoles. If the ring closure took place on a C=N bond, the resulting azapentalene will be 'classic' but if ring closure takes place on a single C–N bond, the resulting azapentalene will be mesoionic. Mesoionic compounds are the part of mesomeric betaines that concern five-membered rings. Baker et al.,[5] Ollis and Ramsden,[6] and Ramsden,[7] defined mesoionic systems as five-membered rings that cannot be represented by normal covalent structures. The designation mesoionic, first given by Baker et al. in 1949,[5] was refined by Ollis and Ramsden[6] as follows: 'A compound may appropriately be called mesoionic if it is a five-membered heterocycle, which cannot be satisfactorily represented by any one covalent or ionic structure and possesses a sextet of electrons in association with the five atoms comprising the ring.' In 1978, Potts[8] suggested, 'the term mesoionic should be restricted to five-membered heterocycles that cannot be satisfactorily represented by normal covalent structures but are better represented as a hybrid of all possible charged forms'.

We have devoted a large number of publications to case (c) including the related case of thiazoles and their derivatives (case d),[9] but only a few theoretical papers: one fundamental concerning case (a)[10] and another concerning a topological analysis of all azoles based on HMO calculations, case (c).[11] Literature results on these compounds are scarce, the most important ones being an experimental study of some azidoazoles,[12] and a high-level study of case (d) (solvent effects, substituent effects and thermo-chemistry).[13] Besides, the X-ray molecular structure of 5-azido-1*H*-tetrazole (**14AZ**, Scheme 6) has been determined.[14]

2. Results and discussion

The compounds we have studied are gathered in Schemes 2–6 (neutral molecules) and 7–11 (anions). In all cases, **A** is the azide, **T** is the tetrazole and the conformation of the azido substituent is defined using the *E*/*Z* convention based on the CIP priority rules.[15]

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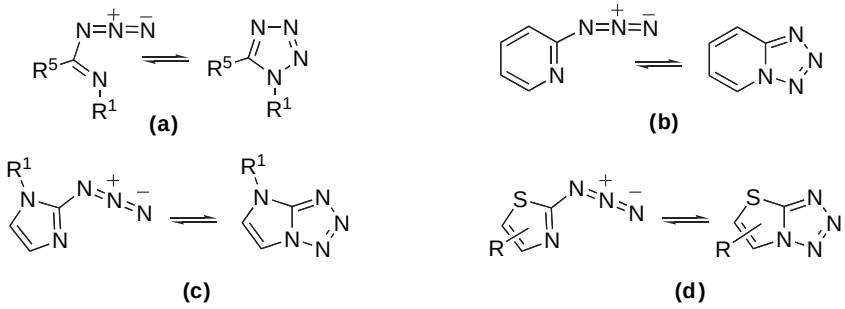
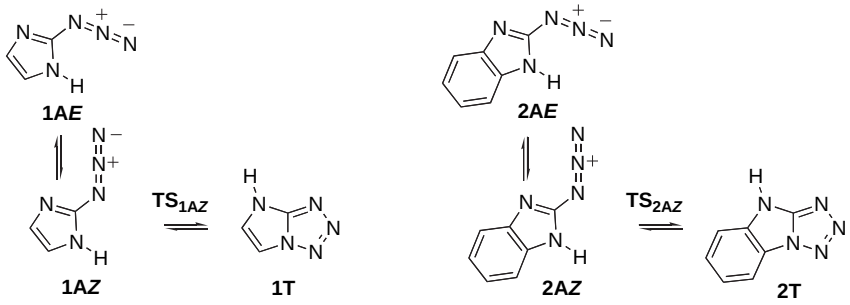
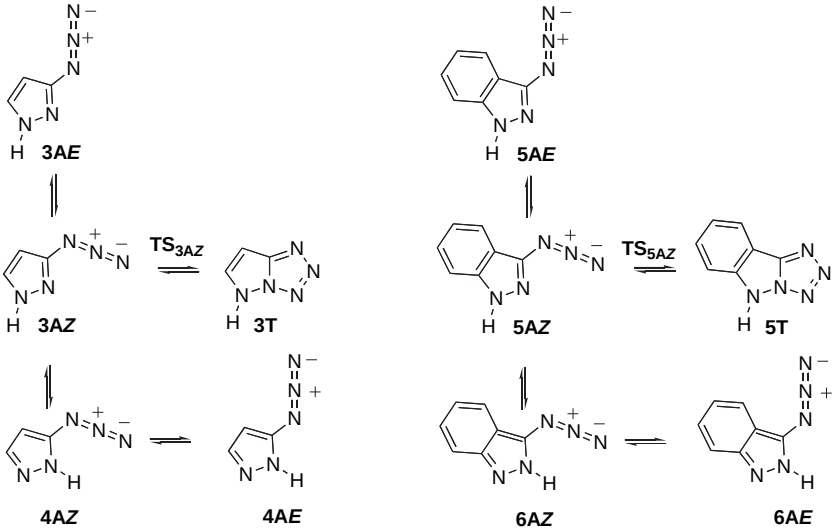


Scheme 1. Valence isomerism in the tetrazoles (a) and in the azine (b) and azole series (c). The case of thiazoles (d) is related to that of azoles. Always the open-chain compound (azide) is the reactant and the ring compound (tetrazole) is the product.



Scheme 2. Imidazole and benzimidazole series.



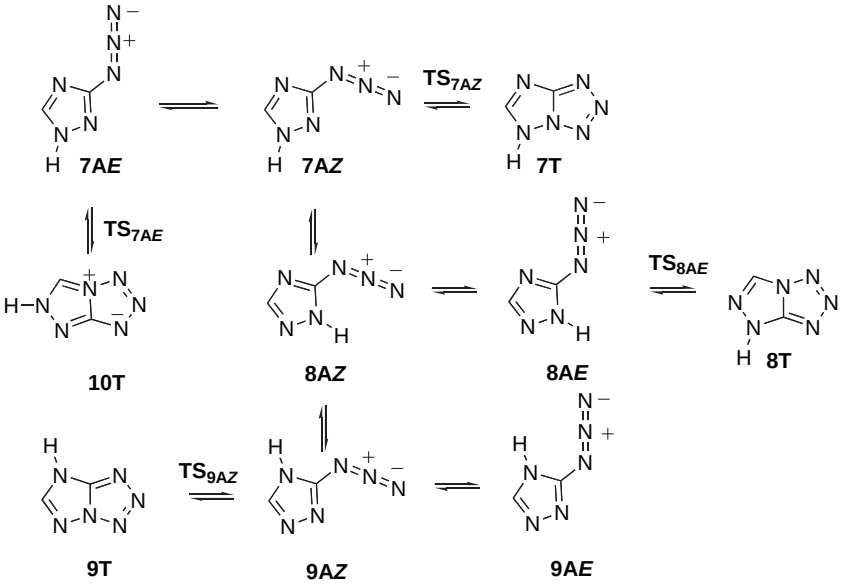
Scheme 3. Pyrazole and indazole series.

We have calculated the energies associated with the molecules of Schemes 2–11 including the transition states at two different levels (see Computational details): B3LYP/6-31G(d) and G3B3. The relative free energies at 298 K ($\Delta\Delta G$ in kJ mol^{-1}) are reported in Tables 1 and 2 (neutral molecules and anions, respectively) while the absolute values (in hartrees) can be found in the Supplementary data.

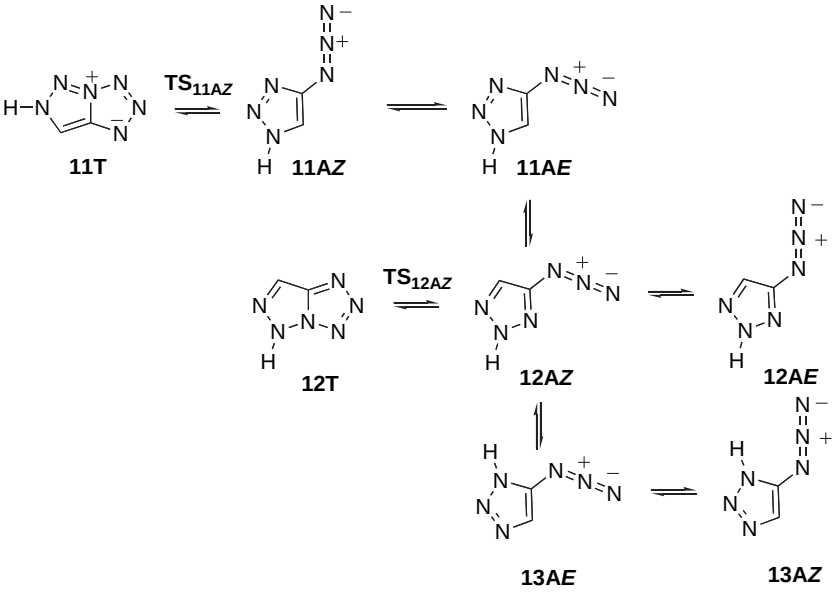
2.1. The minima

2.1.1. E/Z Isomerism. To analyze the results of Tables 1 in what the *E*/*Z* isomerism is concerned, we have applied a statistical approach on a presence/absence matrix (1 when the property is present, 0 when absent).[4,17] There are four situations (the *E*/*Z* nomenclature cannot be used because it depends on the nature of X and Y): lone-pair/N–H (**LP1**/**NH1**); lone-pair/C–H (**LP2**/**CH1**); C–H/N–H (**CH2**/**NH2**), and lone-pair/lone-pair (**LP3**/**LP4**). Besides, the case of C–H in indazoles should be distinguished from that in pyrazoles and the effect of going from neutral molecules to anions must be considered.

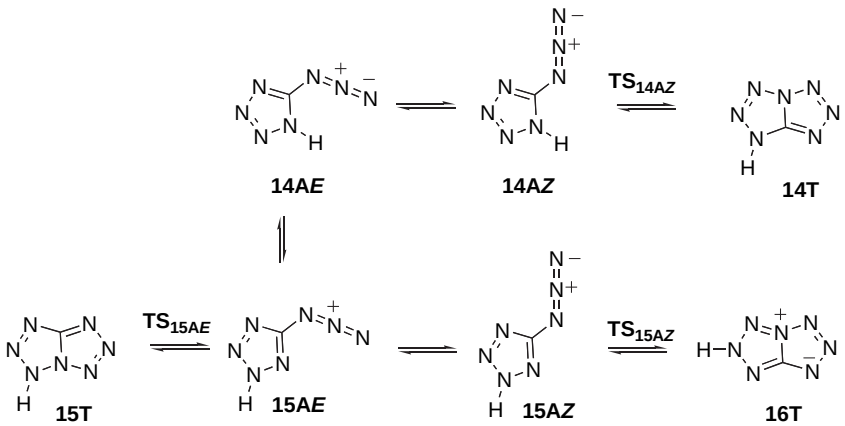
The results (18 values, R^2=0.995) are: **LP1** is preferred to **NH1** by (19.8±0.5) kJ mol^{-1}; **LP2** is preferred to **CH1** by (8.7±0.5) kJ mol^{-1}; **CH2** is preferred to **NH2** by (7.7±0.6) kJ mol^{-1}; and **LP3** is preferred to **LP4** by (2.5±0.7) kJ mol^{-1} when X=NH. Furthermore, indazole



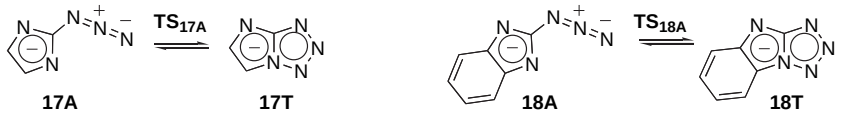
Scheme 4. 1,2,4-Triazole series.



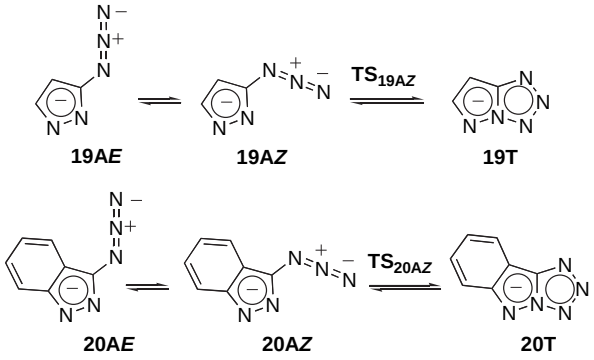
Scheme 5. 1,2,3-Triazole series.



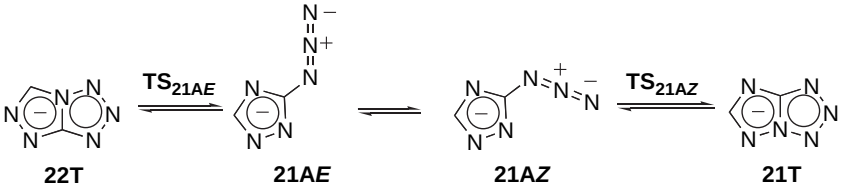
Scheme 6. Tetrazole series.



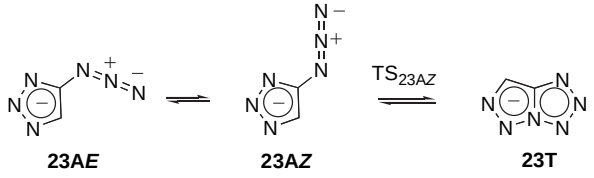
Scheme 7. Imidazolate and benzimidazolate series.



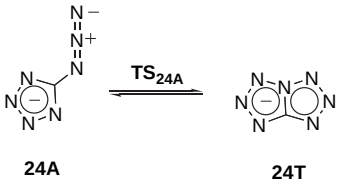
Scheme 8. Pyrazolate and indazolate series.



Scheme 9. 1,2,4-Triazolate series.



Scheme 10. 1,2,3-Triazolate series.[16]



Scheme 11. Tetrazolate series.

produces a small effect of (1.1±0.7) kJ mol^{-1} when compared to pyrazole and the formation of the anion reduces all the differences by (3.1±0.8) kJ mol^{-1} in average.

The origin of these conformational preferences is LP/LP repulsions (in red) that destabilize structures **NH1**, **CH1**, **LP3**, and **LP4**, attractive LP/H interactions that stabilize **LP1**, **LP2**, **CH2**, and **NH2** conformations. Since the N–H in **LP1** is more acidic than the C–H in **LP2**, the difference is larger for the **LP1**/**NH1** equilibrium than for the **LP2**/**CH1** one. The same argument applies to the **CH2**/**NH2** equilibrium. The LP (in red) appears to be more important in **LP4** than in **LP3**.

We have represented in Figure 1 the MEP (Molecular Electrostatic Potential) of hydrazoic acid: the lone pair at positions 1 and 3 are clearly represented.

A search in the CSD[18] affords five structures related to the present work (Scheme 13, the REFCODES are given): when there is a possibility of *E*/*Z* isomerism, the structure in the solid state always coincides with the energy minimum of Scheme 12.

We have determined in dioxane at 25 °C the dipole moments of azidoimidazole (3.70 D) and azidobenzimidazole (3.55 D) (Scheme 2), azidopyrazole (3.73 D) and azidoindazole (3.58 D) (Scheme 3), azido-1,2,4-triazole (4.18) (Scheme 4) and azido-1,2,3-triazole (2.35) (Scheme 5).[9d] If we compare the experimental values with the dipole moments (μ in D) of the azides of minimum energy, it appears that **8A*E*** (μ=1.88 D) cannot account for the experimental 4.18 D value but **7A*E*** (μ=4.34 D) can and it is only 2.2 kJ mol^{-1} higher in free energy. Therefore, Figure 2 uses this last tautomer. Although the correlation is acceptable neither the intercept nor the slope are.

To explain why in azidoindazole it is possible to measure some spin–spin coupling constants with the N–H proton in DMSO (a very rare example), we assume that the azido group 'protects' the N2 nitrogen suppressing the annular tautomerism: the compound behaves as an indole.[9g] The most stable structure, **5A*Z*** (Scheme 3) correspond to this hypothesis.

2.1.2. Azides tautomerism. The problem of the annular tautomerism of azoloazides is complex due to the concomitant *E*/*Z* isomerism. If one compares the tautomers for the same isomer, either *E* or *Z*, the most stable tautomers are **3A*E***, **3A*Z*** (1*H*-pyrazole-3-azide) **5A*E***, **5A*Z*** (1*H*-indazole), **8A*E*** (1*H*-1,2,4-triazole-5-azide), [but **7A*E*** (1*H*-1,2,4-triazole-3-azide), and **7A*Z*** (1*H*-1,2,4-triazole-3-azide) are only 2.2 and 4.5 kJ mol^{-1} less stable, respectively], **12A*Z*** (1*H*-3-azido-1,2,5-triazole) and **15A*Z*** (1*H*-3-azido-tetrazole), but **14A*Z*** (1*H*-5-azido-tetrazole) is only 5.3 kJ mol^{-1} less stable, in agreement with MP2/aug-cc-pVDZ calculations.[14]

Remember, from the precedent discussion, that **3A*Z***, **7A*Z***, and **14A*Z*** were found in the solid state (Scheme 13). Solution NMR studies proved that in the case of pyrazole and indazole, the most stable tautomers are **3** and **5**,[9b,g] thus **3A*Z*** and **5A*Z*** comply with this conclusion. Concerning 1,2,4-triazoloazides, although **8AE** is the most stable tautomer, the dipole moments points to **7A*E*** and/or **7AZ**.[9d] In the case of 1,2,3-triazole, tautomer **12A*Z*** agrees with the experimental dipole moment study.[9d] It is not safe to conclude about the **14A*Z***/**15A*Z*** (or **15A*E***) tautomerism in solution, since both kinds of tautomers are present in 1*H*-tetrazoles.[1]

2.1.3. Azapentalenes tautomerism. Since in the neutral molecules, there is always an azide **A**, that is, more stable than all tetrazoles **T**, there is no experimental data on these azapentalenes tautomerism.[1b] In the case of 1,2,4-triazoles (two tautomers and two isomers) the stability order is **9T** (**0.0**)>**8T**(3.8)>**7T** (46.0)>**10T** (47.0 kJ mol^{-1}); in the case of 1,2,3-triazoles, the order is **11T** (**0.0**)>

Table 1
Dipole moments (D) and relative free energies ($\Delta\Delta G$, kJ mol^{-1}) of the compounds of Schemes 2–6 (all minima and TS have C_s symmetry)[a] calculated at the B3LYP/6-31G (d) and G3B3 levels

No.	Compound number	Dipole B3LYP/ 6-31G(d)	$\Delta\Delta G$ B3LYP/ 6-31G(d)	$\Delta\Delta G$ G3B3
1	1*H*-2-Azidoimidazole (**1AZ**)	3.75	**0.0**	**0.0**
2	1*H*-2-Azidoimidazole (**1AE**)	3.83	18.5	19.2
3	4*H*-Imidazo[1,2-*e*]tetrazole (**1T**)	7.14	41.7	40.4
4	(**TS$_{1AZ}$**)	4.52	99.8	103.1
5	1*H*-2-Azidobenzimidazole (**2AZ**)	3.09	**0.0**	**0.0**
6	1*H*-2-Azidobenzimidazole (**2AE**)	3.36	19.1	20.1
7	Tetrazolo[1,5-*a*]benzimidazole (**2T**)	6.84	33.7	33.7
8	(**TS$_{2AZ}$**)	3.77	95.2	99.3
9	1*H*-3-Azidopyrazole (**3AZ**)	4.02	**0.0**	**0.0**
10	1*H*-3-Azidopyrazole (**3AE**)	4.13	6.6	7.2
11	5*H*-Pyrazolo[1,5-*e*]tetrazole (**3T**)	7.02	80.2	79.9
12	(**TS$_{3AZ}$**)	5.77	120.9	125.0
13	1*H*-5-Azidopyrazole (**4AZ**)	0.53	16.3	19.3
14	1*H*-5-Azidopyrazole (**4AE**)	0.71	7.7	10.9
15	1*H*-3-Azidoindazole (**5AZ**)	3.43	**0.0**	**0.0**
16	1*H*-3-Azidoindazole (**5AE**)	3.82	10.2	10.3
17	5H-Tetrazolo[1,5-*b*]indazole (**5T**)	6.94	57.4	55.2
18	(**TS$_{5AZ}$**)	4.87	118.4	120.5
19	2*H*-5-Azidoindazole (**6AZ**)	0.64	39.4	40.7
20	2*H*-5-Azidoindazole (**6AE**)	0.64	31.9	33.0
21	1*H*-3-Azido-1,2,4-triazole (**7AZ**)	4.32	5.4	4.5
22	1*H*-3-Azido-1,2,4-triazole (**7AE**)	4.34	2.9	2.2
23	5*H*-[1,2,4]Triazolo[1,5-*d*]tetrazole (**7T**)	7.29	112.4	112.8
24	(**TS$_{7AZ}$**)	6.37	147.7	151.4
25	5*H*-[1,2,4]Triazolo[4,3-*d*]tetrazol-7-ium-3-ide (**10T**)	7.99	112.0	113.8
26	(**TS$_{7AE}$**)	6.74	141.9	148.1
27	1*H*-5-Azido-1,2,4-triazole (**8AZ**)	2.20	18.5	19.2
28	1*H*-5-Azido-1,2,4-triazole (**8AE**)	1.88	**0.0**	**0.0**
29	4*H*-[1,2,4]Triazolo[4,3-*e*]tetrazole (**8T**)	4.51	70.2	70.6
30	(**TS$_{8AE}$**)	2.14	113.6	118.4
31	1*H*-2-Azido-1,3,4-triazole (**9AZ**)	4.98	28.9	27.1
32	1*H*-2-Azido-1,3,4-triazole (**9AE**)	5.26	48.6	47.3
33	7*H*-[1,2,4]Triazolo[1,5-*e*]tetrazole (**9T**)	7.23	69.5	66.8
34	(**TS$_{9AZ}$**)	4.84	130.6	132.2
35	1*H*-4-Azido-1,2,3-triazole (**11AZ**)	4.72	15.5	14.7
36	1*H*-4-Azido-1,2,3-triazole (**11AE**)	4.73	26.4	25.5
37	5*H*-[1,2,3]Triazolo[1,5-*d*]tetrazol-7-ium-3-ide (**11T**)	7.65	98.7	96.4
38	(**TS$_{11AZ}$**)	5.92	142.4	145.8
39	1*H*-3-Azido-1,2,5-triazole (**12AZ**)	1.44	**0.0**	**0.0**
40	1*H*-3-Azido-1,2,5-triazole (**12AE**)	1.60	6.8	7.6
41	5*H*-[1,2,3]Triazolo[1,5-*e*]tetrazole (**12T**)	4.37	103.5	102.7
42	(**TS$_{12AZ}$**)	3.46	142.3	146.1
43	1*H*-5-Azido-1,2,3-triazole (**13AZ**)	3.01	34.1	34.8
44	1*H*-5-Azido-1,2,3-triazole (**13AE**)	3.12	25.5	26.8
45	1*H*-5-Azidotetrazole (**14AZ**)	4.35	7.1	5.3
46	1*H*-5-Azidotetrazole (**14AE**)	4.81	26.8	25.6
47	3*H*-Tetrazolo[1,5-*e*]tetrazole (**14T**)	4.68	83.7	81.8
48	(**TS$_{14AZ}$**)	3.04	126.4	128.9
49	2*H*-5-Azidotetrazole (**15AZ**)	2.54	**0.0**	**0.0**
50	2*H*-5-Azidotetrazole (**15AE**)	2.99	3.0	2.7
51	1*H*-Tetrazolo[1,5-*d*]tetrazole (**15T**)	4.80	141.5	143.1
52	(**TS$_{15AE}$**)	4.74	168.3	172.6
53	2*H*-Tetrazolium[1,5-*d*]tetrazol-7-ium-3-ide (**16T**)	6.03	112.2	111.5
54	(**TS$_{15AZ}$**)	4.62	146.6	151.1

[a] In **3T**, **5T**, **7T**, **12T**, and **15T** minima, the proton of the N–H is slightly out of plane (C_1).

Table 2
Relative free energies ($\Delta\Delta G$, kJ mol^{-1}) of the compounds of Schemes 7–10 (all minima and TS have C_s symmetry) calculated at the B3LYP/6-31G(d) and G3B3 levels

No.	Compound number	$\Delta\Delta G$ B3LYP/ 6-31G(d)	$\Delta\Delta G$ G3B3
55	2-Azidoimidazolate (**17A**)	3.6	2.4
56	Imidazo[1,2-*e*]tetrazolate (**17T**)	**0.0**	**0.0**
57	(**TS$_{17A}$**)	93.6	94.9
58	2-Azidobenzimidazolate (**18A**)	**0.0**	**0.0**
59	Tetrazolo[1,5-*a*]benzimidazolate (**18T**)	2.4	4.7
60	(**TS$_{18A}$**)	89.2	93.4
61	3-Azidopyrazolate (**19AZ**)	35.4	31.4
62	3-Azidopyrazolate (**19AE**)	43.6	36.1
63	Pyrazolo[1,5-*e*]tetrazolate (**19T**)	**0.0**	**0.0**
64	(**TS$_{19AZ}$**)	116.0	111.6
65	3-Azidoindazolate (**20AZ**)	31.4	36.6
66	3-Azidoindazolate (**20AE**)	37.5	43.8
67	Tetrazolo[1,5-*b*]indazole (**20T**)	**0.0**	**0.0**
68	(**TS$_{20AZ}$**)	109.4	117.9
69	3-Azido-1,2,4-triazolate (**21AZ**)	11.9	10.8
70	3-Azido-1,2,4-triazolate (**21AE**)	11.6	10.2
71	[1,2,4]Triazolo[1,5-*e*]tetrazolate (**21T**)	**0.0**	**0.0**
72	(**TS$_{21AZ}$**)	102.6	103.9
73	[1,2,4]Triazolo[4,3-*e*]tetrazolate (**22T**)	37.5	39.7
74	(**TS$_{21AE}$**)	112.2	115.1
75	4-Azido-1,2,3-triazolate (**23AZ**)	3.5	2.2
76	4-Azido-1,2,3-triazolate (**23AE**)	10.1	8.2
77	[1,2,3]Triazolo[1,5-*e*]tetrazolate (**23T**)	**0.0**	**0.0**
78	(**TS$_{23AZ}$**)	92.6	93.8
79	5-Azido-tetrazole (**24A**)	**0.0**	**0.0**
80	Tetrazolo[1,5-*e*]tetrazolate (**24T**)	21.0	23.9
81	(**TS$_{24A}$**)	102.6	106.6

The G3B3 and the B3LYP/6-31G(d) values are linearly related so only the G3B3 values will be discussed in detail. The equation is B3LYP/6-31G(d)=(0.981±0.004) G3B3, n=81, R^2=0.999.

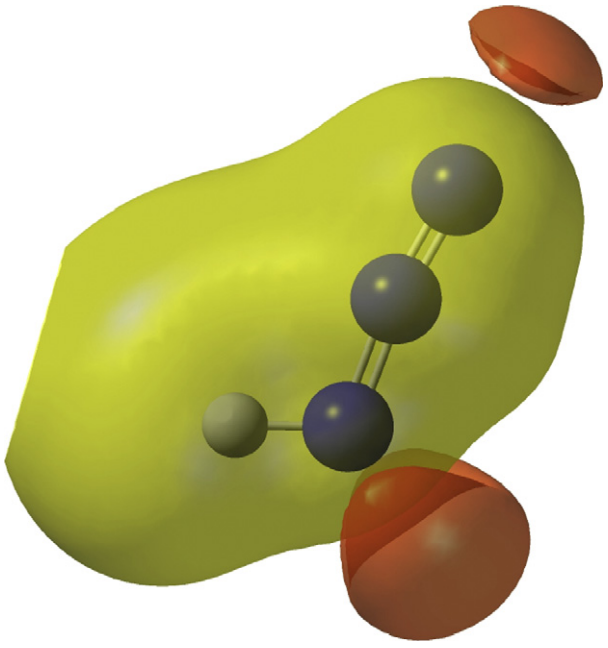
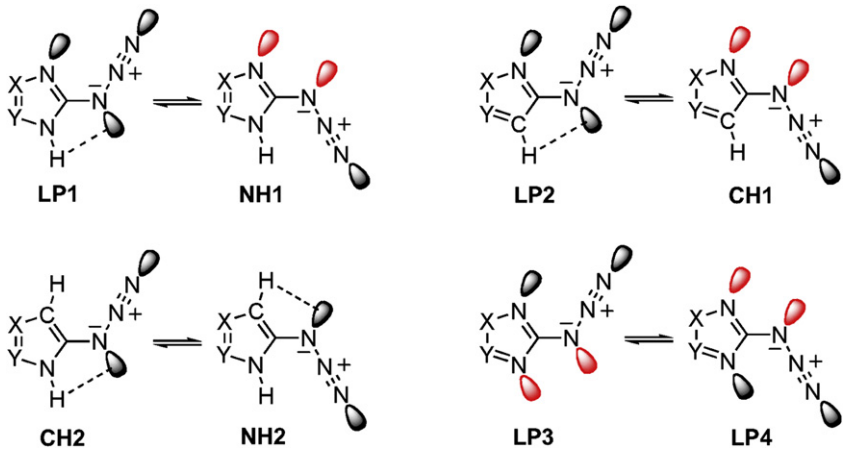


Figure 1. MEP of hydrazoic acid at ±0.03 au. isosurfaces.

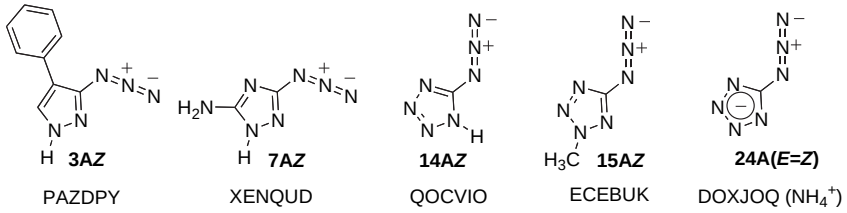
12T (6.3 kJ mol^{-1}), and in the case of tetrazoles the order is **14T** (**0.0**)>**16T** (29.7)>**15T** (61.3 kJ mol^{-1}). It appears that the mesoionic tautomers are in one case, **11T**, the most stable and in other, **16T**, the intermediate in stability.

2.1.4. The azido/tetrazole equilibrium. If we compare the most stable azide to the most stable tetrazole in each family (adiabatic), that is assuming that all the azides are in equilibrium (tautomeric as well as isomeric) and all the azapentalenes are also in equilibrium (tautomeric). In the corresponding anions, only the *E*/*Z* isomerism remains.

The fact that on going from neutral molecules to anions the tetrazoles are stabilized (in average by 72.6 kJ mol^{-1}) was



Scheme 12. Conformational preferences (left side isomer being the most stable).



Scheme 13. Conformations in the solid state.

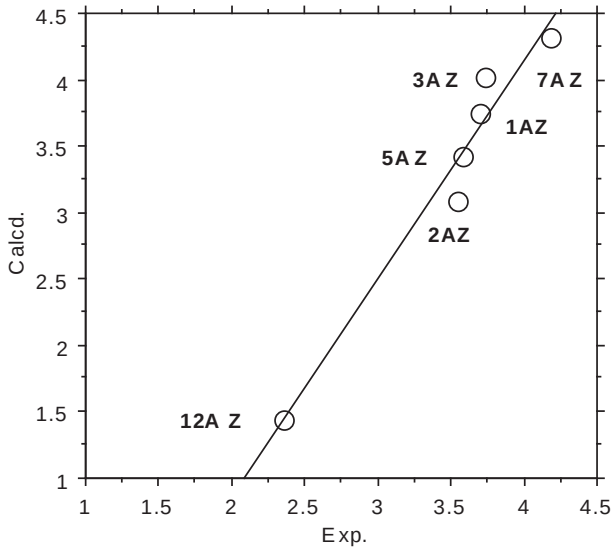


Figure 2. Plot of calculated versus experimental dipole moments (in D). The trendline corresponds to μ(Calcd)=−(2.4±0.6)+(1.64±0.17) μ(Exp.), R^2=0.96.

established for pyrazole,[9a,b] indazole,[9o] and 1,2,4-triazole.[9l] We have also established that the anions of azido-1,2,4-triazole **21A** cyclize into tetrazole **21T** and not into **22T**, in agreement with the present calculations.[9l]

The differences reported in Table 3 are difficult to rationalize, the order being quite different for neutral molecules (Benzimidazole<Imidazole<Indazole<1,2,4-Triazole<Pyrazole <Tetrazole<1,2,3-Trizole) and for anions (Indazole<Pyrazole <1,2,4-Triazole<Imidazole<1,2,3-Triazole<Benzimidazole <Tetrazole). These differences are not related to the aromaticity, at least as defined by NICS (see latter on). In Figure 3, we have

Table 3
Relative free energies ($\Delta\Delta G$, kJ mol^{-1}) calculated at G3B3 level and adiabatic differences

Heterocycle	Neutral		Anion		Difference
Imidazole	**0.0** (**1AZ**)	40.4 (**1T**)	2.4 (**17A**)	**0.0** (**17T**)	42.8
Benzimidazole	**0.0** (**2AZ**)	33.7 (**2T**)	**0.0** (**18A**)	4.7 (**18T**)	29.0
Pyrazole	**0.0** (**3AZ**)	79.9 (**3T**)	31.4 (**19AZ**)	**0.0** (**19T**)	111.3
Indazole	**0.0** (**5AZ**)	55.2 (**5T**)	36.6 (**20AZ**)	**0.0** (**20T**)	91.8
1,2,4-Triazole	**0.0** (**8AE**)	66.8 (**9T**)	10.2 (**21AZ**)	**0.0** (**21T**)	77.0
1,2,3-Triazole	**0.0** (**12AZ**)	96.4 (**11T**)	2.2 (**23AZ**)	**0.0** (**23T**)	98.6
Tetrazole	**0.0** (**15AZ**)	81.8 (**14T**)	**0.0** (**24A**)	23.9 (**24T**)	57.9

reported two plots: one using the acidity of the parent azole[19] and the other the number of lone-pair/lone-pair repulsion (two adjacent LPs).[20] It was expected that the more acidic the azole (low value of pK_a) the more stable the anion, i.e., the largest the difference (as the diagonal line). Some tendency is observed, but imidazole and benzimidazole are clear outsiders. When the neutral molecule is transformed into an anion (N–H to N$^-$) a new LP is created. If there are nearby LPs, then the number of LP/LP interactions will increase and the difference between neutral and anions should increase. Here again, some trend is observed, tetrazole being an outsider. It is possible to use a model including both effects:

$$\begin{aligned}\text{Diff}\left(\text{kJ mol}^{-1}\right) &= (16.7\pm6.7)\,\text{Diff LPs} \\ &\quad + (3.4\pm1.3)\,\text{Acid p}K\text{a},\ n \\ &= 7,\ R^2 = 0.92\ (\text{no intercept}),\end{aligned} \tag{1}$$

2.2. Transition states

We will discuss now the vertical energies, that is, those connecting an azide to the corresponding tetrazole. In average (Fig. 4), the ring structure decreases very much in energy to the point to be more stable than the azide and this drag down the TS.

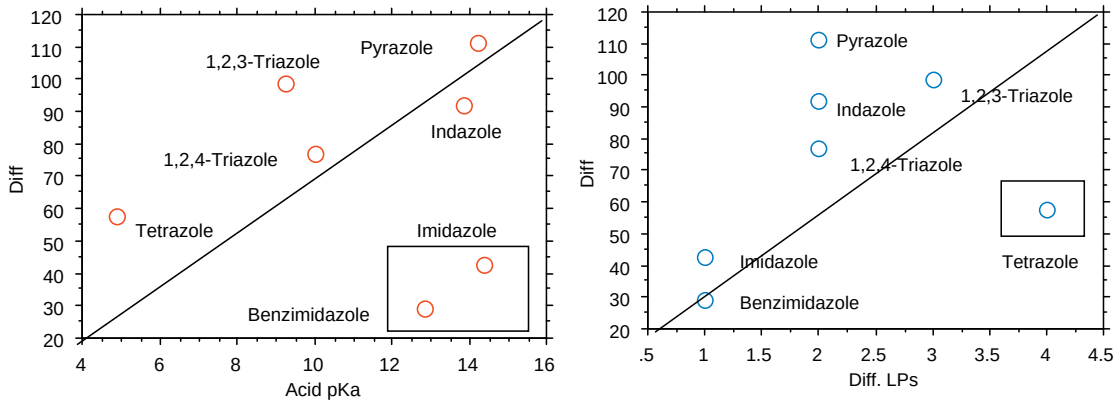


Figure 3. Representation of the differences shown in Table 3 (in kJ mol^{-1}) against the azoles acidity and against the differences in adjacent lone pairs.

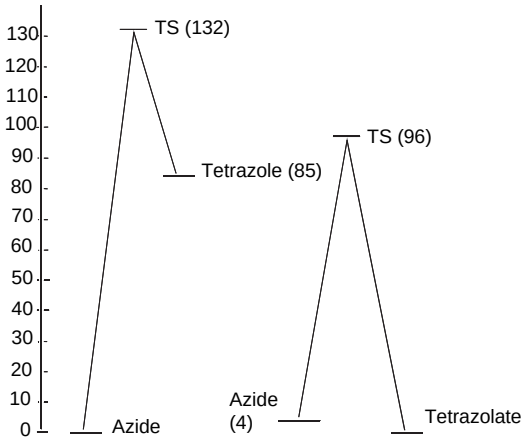


Figure 4. Average energy profiles for neutral (left) and anions (right). Values are given in kJ mol^{-1}.

It is not possible to determine the activation energy for the azido/tetrazole process in the case of neutral molecules because they exist as azides, but generating the anion (EtONa/EtOH) it is possible to follow the ring closure either by IR or by NMR. The first order kinetics of **17A** to **17T** and of **18A** to **18T** have barriers of 100.5 (IR and NMR) and 93.2 kJ mol^{-1} (IR), respectively.[9n] These values are close to the calculated ones (Fig. 5) for the transformation of azides into tetrazolates, 80.2 and 74.1 kJ mol^{-1} (Table 2), taking into account solvent effects (the ratio calculated/experimental is 1.25).

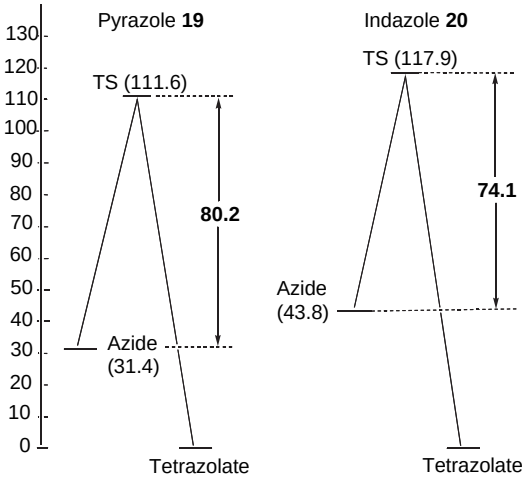


Figure 5. Energy profiles for pyrazole (left) and indazole anions (right). Values in kJ mol^{-1}.

2.3. Cioslowski analysis

Another possibility is to analyze the results using two parameters (β and γ) proposed by Cioslowski[21] in order to quantify the Hammond postulate concerning the geometry of the transition states (the postulate states that the structure of a transition state resembles that of the species nearest to it in free energy). Eq. 2 defines the exothermicity γ as:

$$\gamma = (E_T - E_A)/(2E_{TS} - E_A - E_T) \quad (2)$$

where E_T, E_A, and E_{TS} are the energies of the tetrazole, the azide and the TS, respectively. Eq. 3 defines β or geometrical proximity of the reactants to the transition state:

$$\beta = [d(A,TS) - d(T,TS)]/d(A,T) \quad (3)$$

$$d_{X-Y} = \left[\sum_{(i=1-4)} (R_{Xi} - R_{Yi})^2\right]^{0.5} \quad (4)$$

those d values have been evaluated using the similarity index given in Eq. 4. The two parameters defined in Eqs. (2 and 3) are dimensionless and vary between -1 and $+1$. Exothermic reactions are characterized by negative values of γ, while endothermic reactions show positive values of γ. β values will be close to 1 when the geometries of tetrazole and TS are very similar because then d (*T*,TS) approaches zero. Conversely, β will be close to -1 when the geometries of the azide and TS are alike.

Figure 6 shows the relationship between the two parameters β and γ for the 21 complexes (neutral and anions). As the reaction becomes more endothermic (positive values of γ) the β parameter indicate that TS and tetrazole are more alike. On the other hand, when the reaction is exothermic, negative values of γ appear, and the β parameter indicates that the TS geometry is more similar to azide. These observations are in agreement with the Hammond–Leffler postulate.[22]

We can go further than Figure 6 and ask ourselves if there is a relationship between γ and the energy barriers, TS. Since in the definition of γ it is indifferent who is E_T and who E_A, the TSs should correspond both to (E_T–E_A) and to (E_A–E_T), Figure 7.

The curve corresponds to Eq. 5:

$$TS\left(kJ\,mol^{-1}\right) = (104.3\pm1.8) + (136.5\pm9.0)\gamma^2,\ n = 42,\ R^2 = 0.85 \quad (5)$$

2.4. The NIC(1) values

NICS(1) values [NICS(0) values will not be reported] calculated at the B3LYP/6-31G(d) level are reported in Table 4.

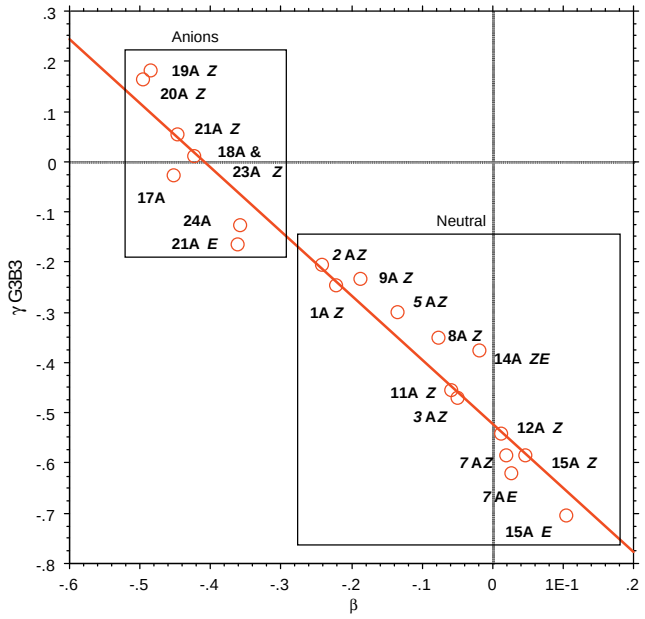


Figure 6. Cioslowski's diagram. The trendline corresponds to $\gamma=-(0.52\pm0.2)-(1.28\pm0.07)\,\beta$, $n=20$, $R^2=0.95$.

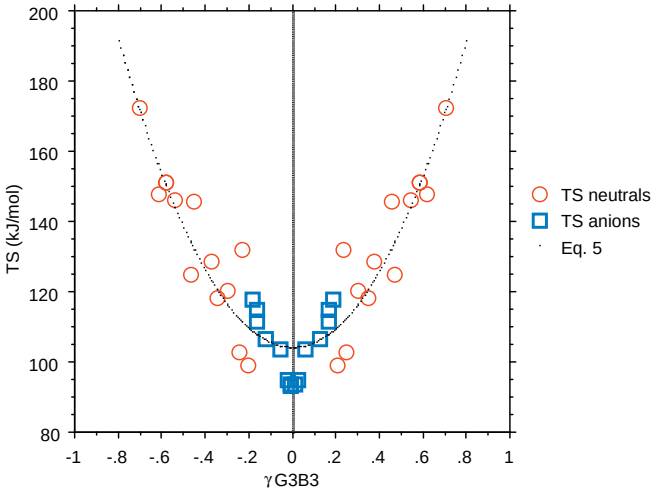


Figure 7. Representation of the energy barriers versus γ.

Table 4 deserves several comments:

(i) The NICS(1) average, maximum and minimum values are: azole ring in azides (11.77, 14.49, 9.60), azole ring in tetrazoles (10.02, 12.65, 6.32), azole ring in TSs (10.87, 13.94, 8.54), tetrazole ring in tetrazoles (13.08, 14.07, 12.50), tetrazole ring in TSs (7.31, 9.56, 4.86) and for the three mesoionic compounds, the azole (12.30, 12.85, 11.64) and the tetrazole one (13.72, 14.00, 13.30). We have represented the average values in Scheme 14.

(ii) There is no relationships between $\Delta\Delta G$ G3B3 (Table 2) or difference in $\Delta\Delta G$ G3B3 (Table 3) and NICS(1) (Table 4) in general or separating into families.

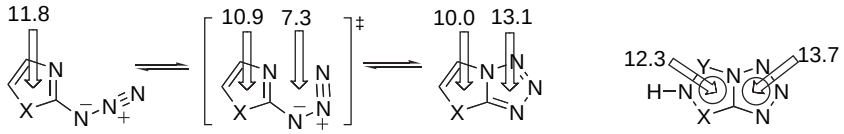
(iii) The NICS(1) values are related to some properties that appear in point (i); the best equations are:

Table 4
NICS(1) values in parts per million for the minima and the TS (only for heterocycles)

No.	Mol.	Azole (AT)	Tetrazole	No.	Mol.	Azole (A/T)	Tetrazole
1	(**1AZ**)	10.11	—	55	(**17A**)	11.31	—
2	(**1AE**)	10.16	—	56	(**17T**)	11.33	12.97
3	(**1T**)	8.82	13.13	57	(**TS$_{17A}$**)	11.44	6.46
4	(**TS$_{1AZ}$**)	9.62	7.44				
5	(**2AZ**)	9.61	—	58	(**18A**)	12.27	—
6	(**2AE**)	9.60	—	59	(**18T**)	10.90	12.65
7	(**2T**)	7.27	12.50	60	(**TS$_{18A}$**)	11.64	5.96
8	(**TS$_{2AZ}$**)	8.54	6.96				
9	(**3AZ**)	11.03	—	61	(**19AZ**)	11.88	—
10	(**3AE**)	11.16	—	62	(**19AE**)	11.92	—
11	(**3T**)	8.38	13.49	63	(**19T**)	11.61	13.08
12	(**TS$_{3AZ}$**)	10.44	9.22	64	(**TS$_{19AZ}$**)	11.78	6.03
13	(**4AZ**)	10.89	—				
14	(**4AE**)	11.02	—				
15	(**5AZ**)	11.33	—	65	(**20AZ**)	14.39	—
16	(**5AE**)	11.51	—	66	(**20AE**)	14.49	—
17	(**5T**)	6.32	13.12	67	(**20T**)	11.84	14.07
18	(**TS$_{5AZ}$**)	9.06	9.56	68	(**TS$_{20AZ}$**)	13.94	6.11
19	(**6AZ**)	12.92	—				
20	(**6AE**)	13.14	—				
21	(**7AZ**)	10.89	—	69	(**21AZ**)	11.77	—
22	(**7AE**)	10.82	—	70	(**21AE**)	11.68	—
23	(**7T**)	8.62	13.46	71	(**21T**)	11.01	12.98
24	(**TS$_{7AZ}$**)	9.98	9.01	72	(**TS$_{21AZ}$**)	10.29	6.69
25	(**10T**)	11.64	13.30	73	(**22T**)	11.70	12.92
26	(**TS$_{7AE}$**)	11.15	8.26	74	(**TS$_{21AE}$**)	11.44	5.80
27	(**8AZ**)	10.76	—				
28	(**8AE**)	10.64	—				
29	(**8T**)	9.20	12.57				
30	(**TS$_{8AE}$**)	9.12	6.79				
31	(**9AZ**)	10.22	—				
32	(**9AE**)	10.24	—				
33	(**9T**)	8.64	13.08				
34	(**TS$_{9AZ}$**)	9.43	7.06				
35	(**11AZ**)	12.38	—	75	(**23AZ**)	13.02	—
36	(**11AE**)	12.53	—	76	(**23AE**)	13.12	—
37	(**11T**)	12.40	14.00	77	(**23T**)	12.58	12.87
38	(TS$_{11AZ}$)	12.58	8.62	78	(TS$_{23AZ}$)	11.52	5.18
39	(**12AZ**)	12.34	—				
40	(**12AE**)	12.47	—				
41	(**12T**)	9.01	13.61				
42	(TS$_{12AZ}$)	10.76	9.06				
43	(**13AZ**)	11.89	—				
44	(**13AE**)	12.04	—				
45	(**14AZ**)	11.94	—	79	(**24A**)	13.55	—
46	(**14AE**)	12.02	—	80	(**24T**)	12.65	12.65
47	(**14T**)	10.20	12.74	81	(TS$_{24A}$)	11.47	4.86
48	(TS$_{14AZ}$)	10.05	6.73				
49	(**15AZ**)	12.88	—				
50	(**15AE**)	12.91	—				
51	(**15T**)	10.20	13.61				
52	(TS$_{15AE}$)	11.14	9.12				
53	(**16T**)	12.85	13.87				
54	(TS$_{15AZ}$)	12.78	8.60				

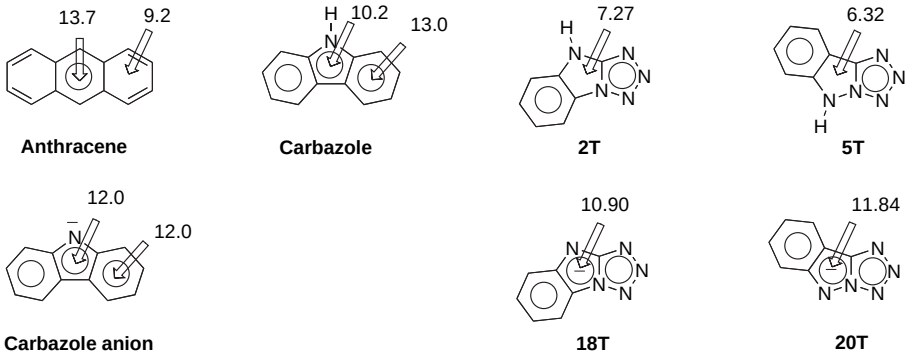
$$\begin{aligned}\mathrm{NICS(1)}_{\mathrm{Azolering}}(\mathrm{ppm}) = {} & (11.5\pm0.2)-(1.7\pm0.2)\mathrm{neutral}\\ & +(1.6\pm0.2)\mathrm{azide}+(2.5\pm0.4)\mathrm{mesoionic}\\ & -(2.9\pm0.7)\mathrm{tetrazoles}\,\mathbf{2T}\,\mathrm{and}\,\mathbf{5T}, n\\ & =81, R^2=0.63, \end{aligned} \quad (6)$$

$$\begin{aligned}\mathrm{NICS(1)}_{\mathrm{Tetrazole\ ring}}(\mathrm{ppm}) = {} & (12.4\pm0.3)+(1.2\pm0.3)\mathrm{neutral}\\ & -(5.9\pm0.3)\mathrm{TS},\ n\\ & =42, R^2=0.93, \end{aligned} \quad (7)$$



Scheme 14. Average NICS(1) values (in ppm).

The data matrix contains 1 and 0 for the properties (neutral 1, anion 0; azide 1, tetrazole 0; mesoionic 1, TS 1). The −5.9 ppm value of Eq. 7 reflects the partial tetrazole ring character of the TS (see Scheme 14). Bicyclic tetrazoles **2T** and **5T** (Schemes 2 and 3) have NICS(1) values in average 2.9 ppm lower than other tetrazoles, a typical situation of azapentalene-type compounds, where the central ring is less aromatic than the lateral ones (Scheme 15), phenomenon that disappears in anions **18T** and **20T** and that is the opposite of the anthracene situation,[23] but similar to that of carbazole and its conjugated base[24] [the NICS(1) of carbazole are 9.4 and 13.2 ppm].[25]



Scheme 15. NICS(1) values (in ppm) of compounds **2T**, **5T**, **18T**, **20T** and model compounds [those of carbazoles are NICS(0)].

2.5. AIM analysis

We have selected the TSs involving the imidazole ring, **1** and **17**, to show the results of the AIM topological analysis (see Computational details). Figure 8, shows clearly the tetrazole/imidazole aspect of TS_{1AZ} and TS_{17A}. This is independent of which the open form (azide) or the cyclic one (tetrazole) is the most stable. Besides, neutral compounds and anions are very similar.

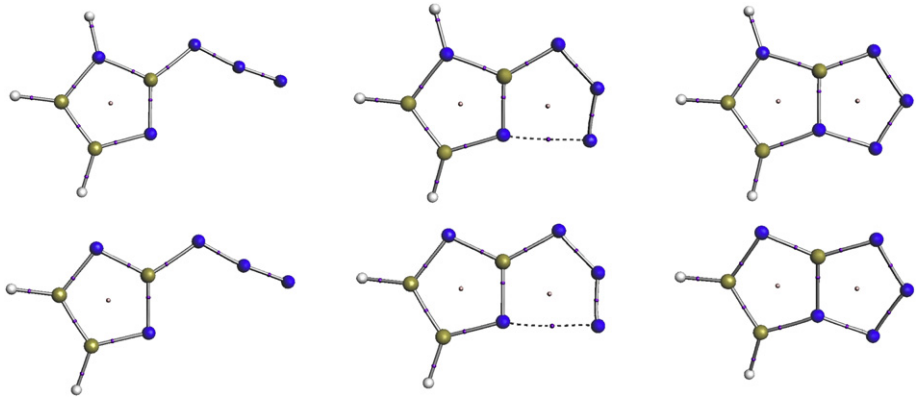


Figure 8. Molecular graph of the minima and TS structures of the neutral and anionic derivatives of the imidazole based on the calculated electron density. From top-left to bottom-rigth: **1AZ**, TS_{1AZ}, **1T**, **17A**, TS_{17A} and **17T**. Molecular graphs calculated at the B3LYP/6-31G(d) level. Bond critical points (bcp) and ring critical points (rcp) are shown as well as the bond paths.

The topological analysis of the electron density shows the presence of a bond critical point, bcp, for the elongated N–N bond, that is, forming (or breaking) in the TS structure (Fig. 8). Considering all the N–N contact together, a total of 199 bcp are found that span between 1.33 and 2.23 Å in the interatomic distances. The representation of the electron density and its Laplacian at the bcp versus the interatomic distances are shown in Figure 9. A good exponential relationship is obtained between the interatomic distance and the electron density as have been shown for other pair of atoms.[26,27]

The values of the Laplacian are negative for those N–N bonds that traditionally are considered as covalent while the N···N bond that are starting to be formed in the TS structures shows positive values. In addition it is worth mentioning that the values of the N1–N2 bonds show slightly different values to the rest of the N–N contacts, which can be associated to a different environment of this bond with respect to others studied here.[28]

3. Conclusions

This comprehensive analysis of the azido/tetrazole ring-chain tautomerism of azidoazoles has the double virtue of explaining most of the abundant experimental results and predicting all the non-studied cases. Again, we observe that NICS values are not useful for discussing energetic results, like we reported in our precedent work.[4] On the other hand, Cioslowski's analysis (exothermicity) offers an interesting way to approach the problem of the barriers separating azides and tetrazoles.

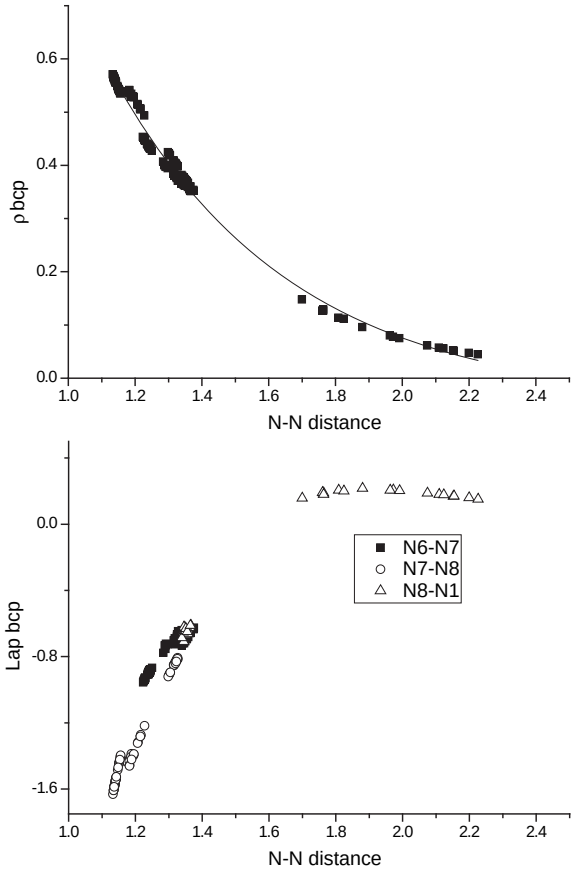


Figure 9. Plot of ρ (au) and Laplacian of ρ at the bcp versus the N···N distance (Å).

4. Computational details

The optimization of the geometries of the structures was carried out at the B3LYP/6-31G(d),[29–32] within the Gaussian-03 package.[33] Frequency calculations at both levels were carried out to confirm that the obtained structures correspond to energy minima or to TSs (number of imaginary frequencies 0 for the minima and 1 for the TSs).[34] G3B3 calculations were carried out for all cases.[35] NICS(1) values[36,37] were calculated within the GIAO approximation on the B3LYP/6-31G(d) optimized geometries at the same computational level. The electron density of the molecules has been analyzed within the atoms in molecules (AIM) methodology[38] with the AIMPAC and MORPHY98 programs.[39–41] The electron density molecular graphs have been represented with the MORPHY3 program.[42]

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tet.2010.04.119. These data include MOL files and InChiKeys of the most important compounds described in this article.

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