

# A comparative study of the aromaticity of pyrrole, furan, thiophene, and their aza-derivatives

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**Abstract** The relative aromaticity of pyrrole, furan, thiophene, and their aza-derivatives has been examined using TRE (topological resonance energy), MRE (magnetic resonance energy), ring current (RC), and ring current diamagnetic susceptibility ( $\chi_G$ ) methods. The results obtained were compared with results obtained by others who used the energetic method ASE (aromatic stabilization energy), the geometric method HOMA (harmonic oscillator model of aromaticity), and the magnetic method NICS(1) (nucleus-independent chemical shift). The impact of nitrogen atoms on the aromaticity of the aza-derivatives of pyrrole, furan, and thiophene is discussed. An excellent correlation was found between the energetic (TRE, MRE) and magnetic (RC and  $\chi_G$ ) criteria of aromaticity for all compounds. It was expected that inclusion of a heteroatom would decrease the aromaticity relative to the cyclopentadienyl anion. Our results show that the type of the first heteroatom, which donates two electrons to the system, as well as the number of nitrogen atoms and their positions in the molecule have a strong effect on aromaticity. In general, aromaticity is enhanced when the nitrogen atom is adjacent to the first heteroatom. The magnitude of aromaticity is related closely with the uniformity of distribution of  $\pi$ -electrons in the molecule.

**Keywords** Aromaticity · Azoles · Diatropicity · Resonance energy · NICS(1)

## Introduction

Aromaticity is one of the most important concepts in organic chemistry [1]. Since aromaticity is not observable and not a directly measurable quantity, many indices of aromaticity have been introduced and discussed. The most widely used quantitative measures of the degree of aromaticity are energetic properties (resonance energies) [2, 3], structural properties (nearly equal bond lengths in the ring) [4, 5], and magnetic properties (such as ring current and magnetic susceptibilities) [6–11]. However, not all indices of aromaticity give consistent results among themselves and sometimes different aromaticity values derived from different indices lead to different aromaticity orders or different predictions [12–17]. Thus, aromaticity remains a challenge to theoretical and experimental chemists [18].

Among the magnetic criteria, the most commonly used method is the nucleus-independent chemical shift (NICS) method, which is defined as a negative value of magnetic shielding in a given point of the molecule [19]. It has been shown that a negative NICS value of a ring indicates the presence of an induced diatropic ring current, which is interpreted as aromaticity, whereas a positive value denotes a paratropic ring current and is interpreted as antiaromaticity [20]. The negative NICS value of the shielding computed at a ring center is denoted as NICS(0); the negative NICS value of the absolute shielding measured  $1\text{ \AA}^\circ$  above the center of the ring is denoted NICS(1); and the NICS value, computed as the zz component of the NICS tensor at  $1\text{ \AA}^\circ$  above the molecular plane, is denoted as NICS(1)zz [21–23].

The HOMA (harmonic oscillator model of aromaticity) value is a geometric indicator of aromaticity defined using the degree of bond-length alternation [4, 5].

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Aromaticity of monoheterocyclic compounds is a very popular topic in physical organic chemistry. Recently, Ramsden et al. [24, 25] studied the aromaticity of azoles using a set of aromaticity indices, including ASE (aromatic stabilization energy), [26–28], HOMA [4, 5] and NICS(1) [19] criteria. They claimed that all stationary structures obtained for azoles are aromatic and concluded that, within the entire set of the aza-derivatives of pyrrole, furan, and thiophene, the 2,5-diaza species have the highest aromaticity; the 3,4-diaza species have the lowest aromaticity; and that the difference in aromaticity is related to bond length equalization or to the uniformity of  $\pi$ -electron distribution in the molecule [24].

In this study, using the graph-theoretical approach, the TRE (topological resonance energy) [2, 3], MRE (magnetic resonance energy) [29], ring current (RC) [30] and ring current diamagnetic susceptibility ( $\chi_G$ ) [30] methods were used to determine the degree of aromaticity of pyrrole, furan, and thiophene as well as their position isomers caused by the replacement of CH fragment(s) by one or more nitrogen atoms. The correlation between the energetic and magnetic criteria of aromaticity is reported and examination is made of whether the set of four aromaticity indices (TRE, MRE, RC and  $\chi_G$ ) for quantifying aromaticity used herein give results consistent with ASE, HOMA and NICS(1) values. Based on the results of our calculations, the general trend of aromaticity and the dominant influencing factors relating to aromaticity are also discussed. It is important to emphasize that TRE and MRE belong to the energetic indices of aromaticity, whereas RC and  $\chi_G$  are magnetic indices.

## Methods of calculation

TRE is defined as the difference between the  $\pi$ -electron energy of a conjugated molecule and its hypothetical acyclic reference structure [2, 3]. We used TRE as a standard measure of aromaticity. TRE is given in units of  $|\beta|$ , where  $\beta$  is the standard resonance integral in Hückel theory.

$\pi$ -Electron currents induced in polycyclic species were calculated using a graph-theoretical variant [31–33] of Hückel-London theory. The characteristic and matching polynomials for a  $\pi$  system  $G$  are herein denoted by  $P_G(X)$  and  $R_G(X)$  respectively, and the roots of the equations  $P_G(X)=0$  and  $R_G(X)=0$  represent energies of the  $\pi$ -molecular orbitals in  $G$  and in the polyene reference, respectively. The quantity of ring current  $A_i$  induced in a polycyclic  $\pi$ -system is defined as follows [30, 33]:

$$A_i = 4 \prod_{m>n}^{r_i} k_{mn} \sum_j^{\text{occ}} \frac{P_{G-r_i}(X_j)}{P'_G(X_j)} \quad (1)$$

where  $r_i$  is a set of conjugated atoms that constitute the  $i$ th circuit  $c_i$ ;  $k_{mn}$  is the Hückel parameter for the resonance

integral between the  $\pi$ -bond formed by atoms  $m$  and  $n$ ;  $m$  and  $n$  run over all  $\pi$ -bonds that belong to  $r_i$ ;  $G-r_i$  is the subsystem of  $G$  obtained by deleting  $r_i$  from  $G$ ;  $P_G(X)$  and  $P_{G-r_i}(X)$  are the characteristic polynomials for  $G$  and  $G-r_i$ , respectively;  $X_j$  is the  $j$ th largest root of the equation  $P_G(X)=0$ ; a prime added to  $P_G(X)$  indicates the first derivative with respect to  $X$ ;  $j$  runs over all occupied  $\pi$  molecular orbitals. If some occupied molecular orbitals have the same energies, this formula must be replaced by another [34, 35].

Ring-current magnetic susceptibility is defined as the second derivative of total  $\pi$ -electron energy with respect to the intensity of the magnetic field and at the limit of a zero magnetic field. The contribution of the monocyclic  $\pi$ -system to ring-current diamagnetic susceptibility,  $\chi_G$ , is formally expressed as [36]:

$$\chi_G = 4.5 x_o A_i \left( \frac{S_i}{S_o} \right)^2 \quad (2)$$

where  $x_o$  is the benzene value and  $S_i$  and  $S_o$  are the areas of the five-membered ring and the benzene ring, respectively.

Circuit resonance energy (CRE) represents an energy gain or loss due to cyclic conjugation along a given circuit [30]. The  $A_i$  values or CREs of the five-membered ring represent the aromatic stabilization energy for an entire  $\pi$ -system. This is termed magnetic resonance energy (MRE), which means a TRE-like quantity derived from the magnetic response of a chosen molecule:

$$\text{MRE} = \sum_i^G A_i = \sum_i^G \text{CRE}_i \quad (3)$$

A  $\pi$ -electron current induced in each circuit may be called a circuit current (CC). Every circuit is supposed to sustain a  $\pi$ -electron current in the external magnetic field, the intensity of which is given by [30]:

$$I_i = 4.5 I_o A_i \frac{S}{S_o} \quad (4)$$

where  $I_o$  is the intensity of a  $\pi$ -electron current induced in the benzene ring.  $S_i$  and  $S_o$  are the areas of the five-membered ring and of the benzene ring, respectively. In general, ring current (RC) can be obtained by superposing all the CCs [30]. Positive and negative  $A$  values represent diatropic and paratropic currents, respectively. For simplicity, we have assumed that all the five-membered rings have the same ring area.

For the series of indices used herein, the higher the TRE, MRE, RC and  $\chi_G$  values, the more aromatic the rings are. Higher positive values in the ASE and HOMA indices, and higher absolute values in the NICS(1) index all reflect greater aromaticity. Van-Catledge's set of Hückel parameters for heteroatoms [37] has been used here.

## Results and discussion

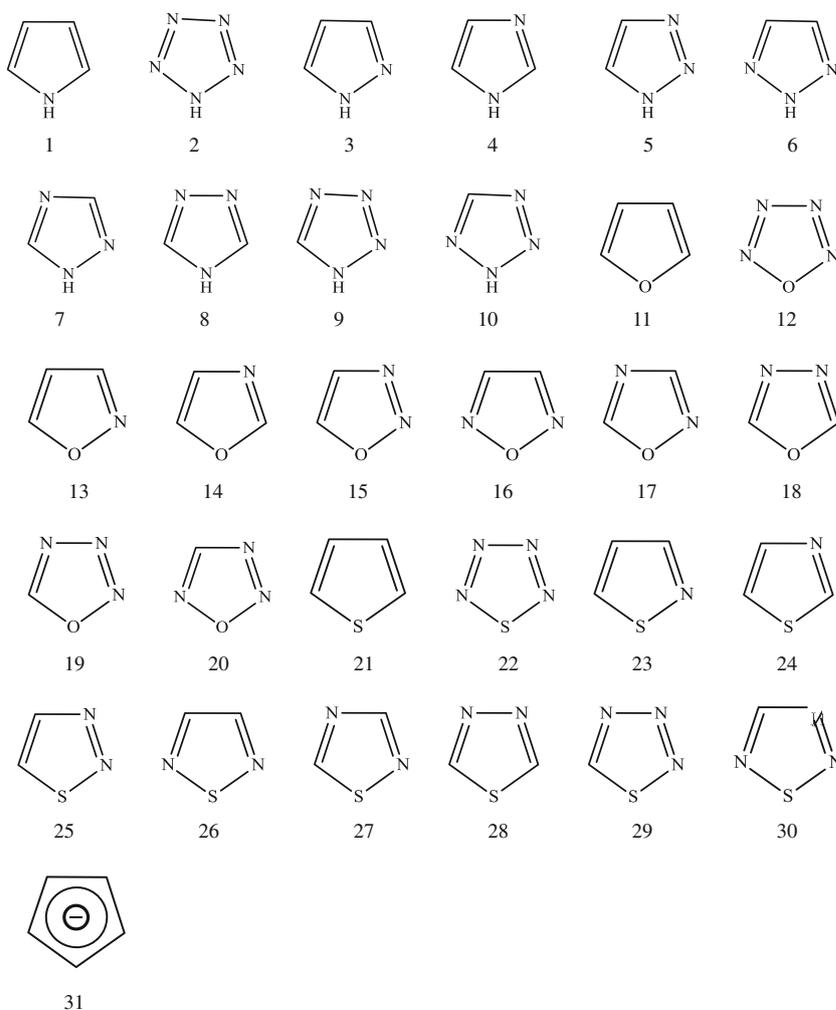
### TRE and MRE

The compounds studied are shown in Fig. 1. The TREs, MREs, RC intensities, and  $\chi_G$  values calculated for all compounds are presented in Table 1. All the compounds are isoelectronic with a cyclopentadienyl anion. In Table 1 we also present data from the ASE, HOMA, and NICS(1) literature regarding pyrrole, furan, thiophene and their aza-derivatives [24], as well as the cyclopentadienyl anion [38] for comparison with the values that we have calculated. Results of the mutual correlations of various aromaticity indices are summarized in Table 2. There are two types of atoms in the azoles: carbon and nitrogen. Of the nitrogen atoms there are two kinds: pyrrole-like ( $-\text{NH}-$ ) nitrogen, and pyridine-like ( $-\text{N}=\text{N}$ ) nitrogen, one or more of which are contained in the molecule. The former atom donates two electrons to the system; and the second type donates one electron to the system. All the compounds (**1–31**) exhibit 6  $\pi$ -electrons, fulfilling Hückel's ( $4n+2$ )  $\pi$ -electron rule for

aromaticity. As can be seen from Table 1, all the compounds (**1–31**) are predicted to be aromatic with positive TREs and positive MREs. An excellent correlation is found between TRE and MRE with a correlation coefficient of 0.9995. This indicates that not only TRE, but also MRE can be used as a reliable indicator of aromaticity.

According to the TRE and MRE results, we can predict that a cyclopentadienyl anion (**31**) has the largest aromaticity of any of the compounds (**1–30**). In other words, neither pyrrole, furan, thiophene, nor their aza derivatives will be stabilized by replacing the CH unit of their cyclopentadienyl anion (**31**) with one or more nitrogen atoms. Among the compounds into which only a single heteroatom has been substituted, the order of aromaticity determined was: **31** > **1** > **21** > **11**. The ASE results, indicated in Table 1, show the same order of aromaticity as we obtained, in agreement with the commonly accepted ordering of relative aromaticity [39], such as that of the multicenter index (MCI) [40]. However, comparing the magnitudes of HOMA and NICS(1) listed in Table 1 results in the following sequence of aromaticity: **21** > **1** > **31** > **11**. This order is somewhat different from the aromaticity order obtained above.

**Fig. 1** Structures of pyrrole, furan, thiophene and their aza-derivatives, as well as of the cyclopentadienyl anion (**31**)



**Table 1** Aromaticity indices for pyrrole, furan, thiophene and their aza-derivatives, as well as for the cyclopentadienyl anion (31)

Compounds	ASE	HOMA	NICS(1)	TRE   $\beta$	Mean	MRE   $\beta$	RC <sup>a</sup>	$\chi_G^b$
1	20.57	0.876	-10.60	0.2462		0.2094	0.6240	0.4132
2	–	0.950	-16.59	0.3058		0.2543	0.7577	0.5018
3	23.70	0.926	-11.93	0.2664		0.2241	0.6679	0.4423
4	18.78	0.908	-10.83	0.2431		0.2077	0.6189	0.4098
5	24.37	0.931	-13.51	0.2614	0.2687	0.2206	0.6573	0.4353
6	26.66	0.960	-13.61	0.2914		0.2417	0.7203	0.4770
7	21.33	0.940	-11.84	0.2585		0.2195	0.6541	0.4331
8	14.96	0.823	-11.52	0.2466		0.2110	0.6287	0.4163
9	18.26	0.897	-14.12	0.2738		0.2312	0.6888	0.4562
10	26.49	0.960	-14.64	0.2940	—	0.2447	0.7293	0.4830
11	14.77	0.298	-9.36	0.1360		0.1238	0.3689	0.2443
12	–	0.500	-15.34	0.2092		0.1833	0.5462	0.3689
13	17.29	0.527	-10.58	0.1608		0.1441	0.4295	0.2844
14	12.37	0.332	-9.45	0.1360		0.1240	0.3694	0.2446
15	17.20	0.443	-11.99	0.1697	0.1670	0.1513	0.4510	0.2986
16	20.19	0.677	-12.52	0.1945		0.1707	0.5088	0.3369
17	14.23	0.553	-10.40	0.1566		0.1412	0.4208	0.2787
18	7.78	0.243	-10.00	0.1392		0.1269	0.3780	0.2503
19	9.65	0.413	-12.29	0.1689		0.1514	0.4512	0.2988
20	18.71	0.586	-13.84	0.1993	—	0.1749	0.5212	0.3452
21	18.57	0.891	-10.79	0.1965		0.1710	0.5094	0.3373
22	–	–	-17.48	0.2624		0.2207	0.6577	0.4355
23	20.18	–	-11.66	0.2182		0.1872	0.5577	0.3693
24	17.43	0.905	-11.37	0.1961		0.1710	0.5095	0.3374
25	20.48	–	-13.72	0.2281	0.2217	0.1947	0.5803	0.3843
26	22.67	–	-12.96	0.2461		0.2072	0.6175	0.4089
27	18.28	–	-11.96	0.2129		0.1840	0.5483	0.3631
28	13.69	0.849	-12.34	0.2006		0.1749	0.5212	0.3451
29	14.72	–	-14.65	0.2283		0.1958	0.5836	0.3865
30	21.62	–	-14.96	0.2506	—	0.2113	0.6296	0.4169
31	22.05 <sup>c</sup>	0.736 <sup>c</sup>	-10.25 <sup>c</sup>	0.3168		0.2589	0.7715	0.5109

<sup>a</sup>All units are benzene units<sup>b</sup>All units are benzene units<sup>c</sup>NICS(1) at point 1.0 Å<sup>o</sup> above the ring centers, calculated at the B3LYP/6-311++G\* level [38]

Analyzing the trend of aromaticity, as indicated in Table 1, we find that the types and number of atoms adjacent to the –NH-type atom are the most important factors in determining the degree of aromaticity of these molecules. If two of the –N= type nitrogen atoms are adjacent to the –NH- type atom, they will

cause the structures to be of relatively high aromaticity. If only one –N= type nitrogen atom is adjacent to the –NH- type atom, it will cause the structure to be of relatively moderate aromaticity. If it is adjacent to carbon, the structure will be of relatively low aromaticity. Namely, the symmetrical substituting of

**Table 2** Correlation matrix estimated for all aromaticity indices used

	ASE	HOMA	NICS(1)	TRE	MRE	RC	$\chi_G$
ASE	1.0000						
HOMA	0.7456	1.0000					
NICS(1)	0.4652	0.4210	1.0000				
TRE	0.7837	0.8178	0.5422	1.0000			
MRE	0.7794	0.8231	0.5515	0.9995	1.0000		
RC	0.7795	0.8231	0.5517	0.9995	0.9999	1.0000	
$\chi_G$	0.7795	0.8200	0.5565	0.9992	0.9999	0.9999	1.0000

the two  $\text{-N=}$  type nitrogen atoms with respect to the  $\text{-NH-}$  type atom will result in higher TRE and MRE aromaticity values. The order predicted using TRE and MRE results is:

2, 5-diaza species > 2-aza species > others

These generalizations are fully consistent with the ASE and HOMA results [25]. Our observation gives support for the earlier supposition that, as the electronegativity differential between the heteroatom and its neighboring atoms is increased, the aromaticity is decreased [1]. According to the TRE and MRE values of the 2,5-diaza species, the predicted aromaticity is:  $2 > 10 > 6$ . This indicates that the number of nitrogen atoms linked to the  $\text{-NH-}$  type atom is the dominant factor governing aromaticity. Among the 2-aza species, the order of aromaticity is:  $9 > 3 > 5 > 7$ . The aromaticity of aza-azoles that do not contain a nitrogen atom either in position 2 or in position 5 is predicted to be:  $8 > 1 > 4$ . This result is in agreement with the MCI reported by Giambiagi et al. [40] in 2000. However, these findings stand in opposition to previous papers [24, 25, 41], which predicted that 3,4-diaza species would decrease in aromaticity. Our results indicate that substituting only one nitrogen atom in position 3 has a small destabilizing effect, whereas substituting the nitrogen atoms in both positions 3 and 4 has a small stabilizing effect on the  $\pi$ -system of pyrrole. Similar behavior was also found for all aza-derivatives of furan and thiophene. However, the above orders of aromaticity for each compound are not predicted by the ASE, HOMA, and NICS (1) indices, and using them will produce incorrect orders of aromaticity.

The mean values of TRE for the pyrrole and the aza-pyrrole group, for the furan and oxazole group, as well as for the thiophene and the thiazole group are presented in Table 1. Based on our results, as indicated in Table 1, the predicted order of aromaticity is:

$31 > (1-10)_{\text{mean}} > (21-30)_{\text{mean}} > (11-20)_{\text{mean}}$

It was found that, among compounds containing the same number of nitrogen atoms in the same positions, aromaticity indices decrease in the following order: nitrogen to sulfur to oxygen. This order is dictated by the type of the first heteroatom. An example would be  $5 > 25 > 15$ . This is the case for all compounds. In the ASE results, as indicated in Table 1, we also find the same trend of aromaticity. Moreover, based on the TRE and MRE values of **4** and **12**, we can conclude that the least aromatic azoles exhibit greater aromaticity than the most aromatic of the oxazoles. That is to say, each of the azoles possesses greater aromaticity than any of the oxazoles. This indicates that all of molecules in the furan and oxazole group are less delocalized than any of the molecules in the pyrrole and the aza-pyrrole group. From the above results, we can conclude that aromatic stability of the ring is determined

mainly by the type of the first heteroatom, which donates two electrons to the system. In general, the effect upon aromaticity of substitutions of nitrogen atoms in other positions is small. Our conclusions are consistent with the study by Cordell et al. [42], who claimed that the electronegativity of the heteroatom has a major effect in determining the aromaticity of five-membered heteroaromatic compounds.

### Magnetic descriptors of aromaticity

If a magnetic field is directed perpendicularly to the plane of the aromatic system, a ring current is induced in the delocalized  $\pi$  electrons of the aromatic ring. Numerous attempts have been made to quantify aromaticity with respect to the observed RC [6–11]. The most commonly used methods are RC intensity,  $\chi_G$ , and NICS(1). In this section, we compare our RC intensity and  $\chi_G$  values quantitatively with the other magnetic index, the NICS(1).

### Ring current

The RC intensity is calculated by Eq. (4), in which all susceptibility values are given in units of the RC intensity for benzene. In general, diamagnetic (counterclockwise) ring current is associated with aromaticity, whereas a paratropic (clockwise) ring current indicates antiaromaticity. The calculated RC values of compounds **1–31** are given in Table 1. The positive and negative RC values therein represent diatropicity and paratropicity, respectively. As shown in Table 1, all compounds **1–31** exhibit positive values; thus we can predict that all compounds **1–31** are diatropic. As shown in Table 2, the correlation between the TRE and the RC intensity is excellent, with  $R=0.9995$ . RC intensity gives the same order of aromaticity as that obtained when using the energetic criteria. The excellent correlation suggests that RC is also a reliable method for estimating the degree of aromaticity of monocyclic  $\pi$ -systems.

### Ring current diamagnetic susceptibility

The  $\chi_G$  value is calculated by Eq. (2). The  $\chi_G$  values of compounds **1–31** are given in Table 1, in which all susceptibility values are given in units of the ring-current susceptibility for benzene ( $\chi_o$ ). Positive and negative  $\chi_G$  values indicate diamagnetism and paramagnetism, respectively. For all compounds (**1–31**), the values we obtained using  $\chi_G$  were all positive values. With  $\chi_G$  as the criterion, it is expected that all compounds (**1–31**) will prove to be diatropic and aromatic. That is to say, the diatropicity of a monocyclic  $\pi$ -system is in accordance with aromaticity. For all compounds (**1–31**), the magnitudes of  $\chi_G$  values obtained by Eq. (2) are consistent with the corresponding larger TRE, MRE and RC values in the same molecule. This

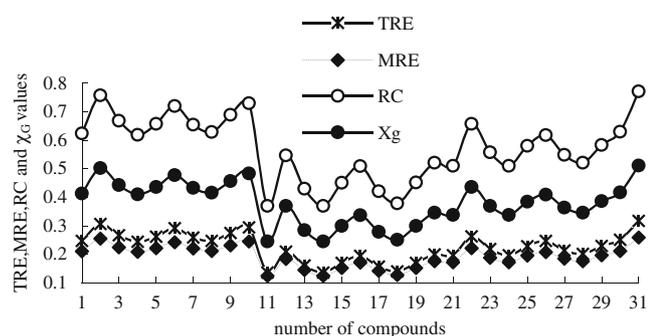
result convinced us that the ability of a molecule to produce a diamagnetic ring current is a useful and valid criterion of the aromaticity of a monocyclic  $\pi$ -system. It should be noted that  $\chi_G$  is defined by Eq. 2, and is a product of the  $A_i$  value and the circuit area squared. Based on this Eq. 2, large circuits in polycyclic  $\pi$ -systems contribute significantly to the  $\chi_G$ . For this reason  $\chi_G$  is not a reliable index for polycyclic  $\pi$ -systems. Based on the NICS(1) criterion, the more negative the NICS value is, the more aromatic the rings are. From Tables 1 and 2 we can see that even though the NICS (1) model provides a qualitative explanation for all the compounds (1–31), it fails to give quantitative predictions of the relative aromaticity. Its predictions are neither in line with the TRE and MRE results nor with RC and  $\chi_G$  results. Thus, we can conclude that both the magnitude of RC and  $\chi_G$  is a more valid measure of aromaticity for monocyclic  $\pi$ -systems than NICS(1) criteria.

#### Interrelations between TRE, MRE, RC, and $\chi_G$

The changes in the TRE, MRE, RC, and  $\chi_G$  values are shown in Fig. 2. The four curves follow each other closely. It has been shown that there are satisfying correlations between TRE, MRE, RC and  $\chi_G$  when applied to a series of monocyclic  $\pi$ -systems. The correlation coefficients of these four indices are all  $\geq 0.9995$ . The relative intensities of RC and  $\chi_G$  are proportional to aromaticity. This clearly shows that for the monocyclic  $\pi$ -systems studied, the energetic criterion of aromaticity are related closely to the magnetic ones, and all of them can serve as indices of aromaticity.

As seen above, the graph-theoretical approach can be regarded as a reliable method of determining aromaticity, one which shows direct correspondence between the energetic and magnetic criteria of aromaticity when analyzing monocyclic  $\pi$ -systems. Explanation must be given as to why the aromaticity of the cyclopentadienyl anion is larger than those for the corresponding heterocycles (1–30) and

why the differences in aromaticity between each molecule arise. It is well known that the  $6\pi$ -electrons in benzene are distributed uniformly over the six carbon atoms, and perfect delocalization causes it to have the highest aromaticity among organic compounds. In the cyclopentadienyl anion, all atoms in the ring are of the same electronegativity. Thus, the  $6\pi$ -electrons are distributed uniformly over the five carbon atoms. However, for pyrrole (1), furan (11), and thiophene (21) molecules, heteroatoms are more electronegative than carbon atoms. This results in a substantial electronic charge transfer from the carbon atoms to the neighboring heteroatom. The electrons are localized at the heteroatom, which decreases the local aromatic character of this five-membered ring. Thus, these heterocycles are destabilized by the presence of a heteroatom. That is to say, in order to enhance delocalization, it is necessary to decrease the inherent electronegativity differential between the adjacent atoms [43, 44]. In general, the  $\pi$ -electrons in an  $-\text{NH}-$  group are less likely to be delocalized in the conjugated  $\pi$ -system than those in an  $-\text{N}=\text{}$  group [12]. In the 2,5-diaza species of pyrrole, the electron extraction ability of an  $-\text{NH}-$  group is decreased by the formation of an  $=\text{N}-\text{NH}-\text{N}=\text{}$  unit, as it causes relatively high uniformity of distribution of  $\pi$ -electrons in the molecule. In the 2-aza species the electron extraction ability of the  $-\text{NH}-$  group exhibits a small decrease when an  $-\text{NH}-\text{N}=\text{}$  unit is formed, as it produces moderate uniformity of distribution of  $\pi$ -electrons in the molecule. That is to say, the system becomes more aromatic when the nitrogen atoms are linked to the  $-\text{NH}-$  group. The replacement of CH by an  $-\text{N}=\text{}$  group in position 3 disturbs the uniformity of the  $\pi$ -electrons of neighboring carbon atoms. Thus, this molecule is destabilized by the presence of a nitrogen atom. However, in the 3,4-diaza systems, the electron extraction ability of the nitrogen atoms in the  $=\text{N}-\text{N}=\text{}$  units cancel each other out, which tends to result in more uniform distribution of  $\pi$ -electrons compared to a system into which only one nitrogen atom is substituted. It seems that the highly electronegative nitrogen prefers electronegative nitrogen as a neighbor, rather than electropositive carbon as a neighbor. By increasing the number of nitrogen atoms, the electron extraction ability of the nitrogen atoms cancel each other out, which facilitates redistribution of  $\pi$ -electron density around the entire ring. With maximum nitrogen atom substitution, the  $\pi$ -electrons are again uniform and become more delocalized throughout the ring, resulting in increased aromaticity of the ring as indicated by the TRE and MRE values. The correlations in Fig. 2 support this view. The influence of nitrogen on the aromaticity of pyrroles and its aza-derivatives is essentially the same as on the aza-derivatives of furan and of thiophene. From the above results we can conclude that the uniformity of distribution of  $\pi$ -electrons in the molecule is an important factor in the determination of aromaticity.



**Fig. 2** Comparison of the topological resonance energy (TRE), magnetic resonance energy (MRE), ring current (RC) and ring current diamagnetic susceptibility ( $\chi_G$ ) results for compounds 1–31

## Conclusions

As has been mentioned above, NICS (1) leads to confusing results. It does not correlate with the set of aromaticity indices used in this study. On the other hand, the results provided by the ASE index are consistent with our energetic and magnetic criterion results to a certain extent. However, the ASE index results always vary significantly and depend strongly on the equations used, on the reference molecules adopted, on the computational levels, and on basis sets [41]. Moreover, without the necessary reference compounds, ASE values are not available for tetraaza derivatives. The HOMA values are not available for molecules with S–N bonds due to a lack of parameters. By studying the aromaticity of aza-derivatives of pyrrole, furan and thiophene, it has been demonstrated that graph-theoretical methods of analysis are not only able to verify the exact nature of aromaticity among different molecules, but also can distinguish the correct order of aromaticity among sets of aromatic molecules. Moreover, this method has advantages in that it can be applied to the present set of whole molecules, it is easy to compute, and straightforward to interpret. All results presented in this paper are based on HMO theory. As is well known, in HMO theory, only  $\pi$ -electrons are taken into account. In HMO theory, energies are determined solely by the topology of the molecule and are independent of structural parameters such as bond lengths and bond angles, with strain energy not being taken into consideration. This is due to the fact that aromaticity is a direct result of the  $\pi$ -electron delocalization between atoms in a cyclic molecule. Thus, we can conclude that the graph-theoretical approach provides the best indices to clarify the origin of the aromaticity of heterocyclic compounds such as pyrrole, furan, thiophene, and their aza-derivatives.

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