April, 1993] *Bull. Chem. Soc. Jpn.*, ***66***, *1229—1234(1993)* 1229

Stability and Resonance Energy of Annulated 1-Azaazulenes

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(Received October 20, 1992)

The stability and resonance energy of heterocycle-annulated 1-azaazulenes such as cyclohepta[4,5]pyrrolo[1,2-*a*]imidazole (**5a**) and 12-methoxy-5*H*-cyclohepta[4,5]pyrrolo[2,3-*b*][1,5]benzodiazepine (**7**) were elucidated by means of Aihara's TRE and Gimarc's TCS rule. These compounds are predicted to be aromatic with positive resonance energies and in conformity with the TCS rule.

Since one of the authors (T. N.) and his co-workers synthesized[1a)] 1-azaazulene (**1**: $R^1=R^2=H$) almost 40 years ago, the chemistry of 1-azaazulene has been attracting attention for its interesting physical and chemical properties. A number of 1-azaazulene derivatives (**1**—**4**) have been synthesized[2)] and Kon reported a molecular orbital treatment of azaazulenes.[3)] However, there is no consistent view with respect to the stability and reactivity of azaazulenes. In keeping with our synthetic and theoretical interests, we recently started a reinvestigation of the electronic structures and reactivities of various troponoids and azulenoid compounds. In a previous paper, we reported[4)] that the fundamental skeleton of tropones possessing a unique heptagonal structure could be predicted to be aromatic with positive resonance energies[5)] conforming to Gimarc's topological charge stabilization rule (TCS rule).[6)]

We also reported[7)] the stability and formation pathways of azulenequinones by oxygenation in terms of Aihara's topological resonance energy (TRE)[5)] as well as the TCS rule.[6)]

For the past several years, one of the authors (N. A.) and his co-workers have studied the cycloaddition of 1-azaazulene and its derivatives.[8)] They obtained a wide variety of products possessing interesting structures of novel heterocycle-annulated azaazulenes such as 2-phenyl-1,3a-diazacyclopent[*a*]azulene (2-phenylcyclohepta[4,5]pyrrolo[1,2-*a*]imidazole) (**5b**) and cyclohepta[*hi*]imidazo[2,1,5-*cd*]indolizine [§] (**6b**). They have synthesized 12-methoxy-5*H*-cyclohepta[4,5]pyrrolo[2,3-*b*][1,5]benzodiazepine (**7**),[8b)] a novel peripheral 20π system, and the novel heterocycles fused with furan and thiophene (**8a**, **b**) (Chart 1).[8c)]

In this paper we describe the origin of the stability and aromaticity of annulated 1-azaazulenes in terms of the TCS rule and TRE.

Methods of Calculation

Aihara's TRE[5)] has been one of the most important principles in the study of the aromaticity and magnetic properties of molecules. Gimarc's TCS rule[6)] indicates that nature prefers to place heteroatoms of great electronegativity in positions where the isostructural, iso-π-electronic hydrocarbon has large charge densities. Calculations of TRE and TCS were carried out by means of the HMO method. Streitwieser evaluated the heteroatom parameters for the amine nitrogen, the imine nitrogen, the ether oxygen, and the ketone oxygen.[9)] In this paper, we adopt these values with some other heteroatom parameters.[10,11)] The MNDO[12)] calculations were carried out by the MOPAC program a FACOM M-360 computer at the Josai University Information Sciences Research Center.

Results and Discussion

π-Electronic Structures and Reactivities of 1-Azaazulenes (2—4). Abe et al. reported[8d)] the condensation of 2-amino-(**2**: $R^1=R^2=H$),[1a,2d)] 2-hydroxy-(**3**: $R^1=R^2=H$), and 2-mercapto-1-azaazulene (**4**: $R^1=R^2=H$) with reactive acetylenes such as dimethyl acetylenedicarboxylate (DMAD). When the condensation of DMAD takes place at the N-1 position of amino-form **2**, compound **9** is produced. An attack by DMAD at the C-3 position of imino-form **2a** and the successive reaction with another molecule of DMAD furnishes **10** (Chart 2).

In the ^{1}H NMR spectrum of **2** in $CDCl_3$, an equilibrium (80% of **2**, 20% of **2a**) was observed.[8d)] Compound **3** behaved as **3a** and the reaction with DMAD gave sim-

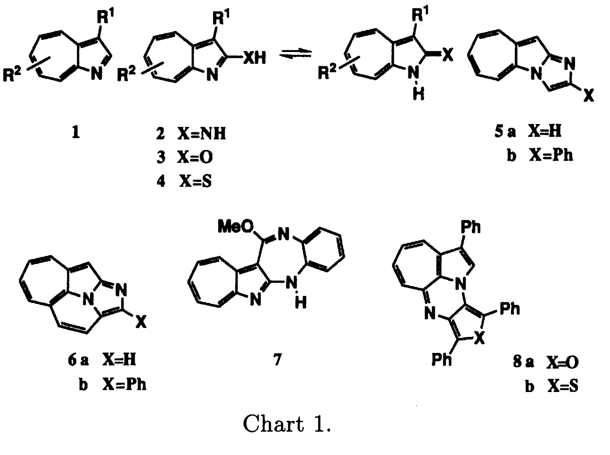


Chart 1.

[§] Cyclohepta[*hi*]imidazo[2,1,5-*cd*]indolizine was referred to as 2-azacyclohepta[*ef*]cycl[3.2.2]azine in the preceding paper.

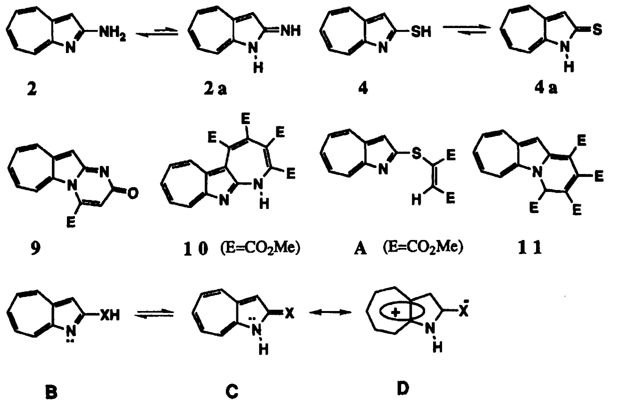


Chart 2.

ilar results as for 1-methyl-1-azaazulen-2-(1*H*)-one.[8d] Abe et al. also synthesized compound **11**[8d] and assumed that the reaction of **4a** with DMAD (considered to be a soft electrophile) would first occur on sulfur, which is the softest atom, giving rise to 1-azaazulene **A** as an intermediate. In the ^{1}H NMR spectrum of **4** in CDCl$_3$, the predominant existence of the thione form **4a** (over 95%) was observed.[8d] All these results have shown that DMAD first attacks the N-1 position of the 1-azaazulene form **B**, whereas DMAD first attacks the C-3 position or a soft atom of 1,2-dihydro-1-azaazulen-2-ylidene form **C**. In form the **B**, the N-1 atom is most electron-rich,[3] and a lone electron pair on the nitrogen would be more nucleophilic than the C-3 carbon. On the other hand, in form **C** the nucleophilicity of the lone electron pair on the N-1 atom would decrease owing to the contribution of the 10π-aromatic resonance system as form **D**. The calculated π-electron densities of **2**—**4** and **2a**—**4a** by means of the MNDO method[12] are listed in Fig. 1.

The experimentally-preferred site of attack by electrophiles is the atom with the largest π-HOMO coefficient or with the highest electron density. In the **B** form, the magnitudes of the π-HOMO coefficients of **2**—**4** are in the order of C-3>C-8a, while the π-electron densities are in the order of N-1>C-3. Therefore, the π-electron densities agree well with the experimental results. In the **C** form, the magnitudes of the π-HOMO coefficients of **2a**—**4a** are in the order of C-3>C-8a, while the π-electron densities are in the order of N-1>C-3.

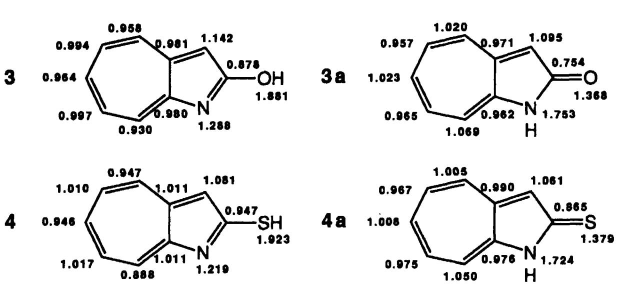


Fig. 1. π-Electron densities of **2**, **3**, and **4** by the MNDO method.

In order to clarify the stability and the π-electronic structures of **2**—**4**, the resonance energies have now been calculated by TRE.[5] The calculated resonance energies, resonance energies per π-electron, and heats of formation for **2**—**4** are given in Table 1. Compounds **2**—**4** are regarded as aromatics with positive resonance energies. Amino form **2** is more stable than imino form **2a** by comparison of their resonance energies and heats of formation. This result agrees well with its NMR spectrum. Form **3a** has a larger resonance energy and smaller heat of formation compared with **3**, indicating that **3a** is more stable than **3b**. However, **4** is more stable than thione form **4a** by comparison of their resonance energies and heats of formation. The calculated circuit resonance energies and circuit currents for **2**—**4** and **2a**—**4a** are given in Table 2. The π-electron ring systems in those compounds consist of three π-ring components, from r_1 to r_3, as shown in Table 2. The circuit resonance energies of r_1 and r_3 of **2**—**4** showed large positive values, while the values of r_2 were small. Therefore, **2**—**4** were stabilized as 10π-peripheral systems. In the **C** form, the circuit resonance energies of r_1 showed large positive values, while the values of r_2 and r_3 were small. Consequently, **2a**—**4a** were stabilized as the 6π-tropylium, but not as the 10π-peripheral system as form **D**.

Annulated 1-Azaazulenes and the TCS Rule. Abe et al.[8] synthesized **5**, **6**, dimethyl 1-phenyl-2a, 5-diazabenz[*cd*]azulene-3,4-dicarboxylate (**12**) and its analogue (**13**), tetramethyl 3-phenyl-9b-azaindeno[1,6,7-*bcd*]azulene-1,2,8,9-tetracarboxylate (**14**) and its analogue (**15**), and cyclohepta[4,5]pyrrolo[1,2-*a*]benzimidazole (**16**) from 2-amino-1-azaazulene (**2**)[1a,2d] and 1-azaazulene derivatives (Chart 3). The uniform reference frames (URF's)[6] for **2**—**4** (R^1=R^2=H), **5a**, the parent skeleton of **12**—**13**, **6a**, the parent skeleton of **14**—**15**, **16**, and **8** are shown in **17**—**22**, respectively. The URF's for **2**—**4** have a high charge density at position 1 and an *exo*-methylene carbon. The nitrogen atom is located at position 1 and the substituent is located at the

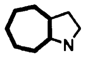
Table 1. RE, REPE, and Heats of Formation of **2**, **3**, and **4**

	RE	REPE	ΔH_f		RE	REPE	ΔH_f
2	0.2006	0.0167	71.4906	**2a**	0.1917	0.0160	77.1366
3	0.1905	0.0159	21.0384	**3a**	0.2029	0.0169	20.4720
4	0.1973	0.0164	71.1396	**4a**	0.1805	0.0150	78.2298

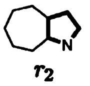
RE: Resonance energy (in β units). REPE: Resonance energy per π electron. ΔH_f: Heats of formation (in kcal mol^{-1}).

Table 2. Circuit Resonance Energies, Circuit Currents, and Bond Currents of **2**, **3**, and **4**

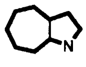
	Circuit resonance energies (in β units)			Circuit currents (in I_0 units)			Bond currents (in I_0 units)	
	r_1	r_2	r_3	r_1	r_2	r_3	r_1	r_2
2	0.0548	0.0193	0.0818	0.3446	0.0574	0.7586	1.1032	0.8160
3	0.0545	0.0161	0.0788	0.3431	0.0478	0.7310	1.0741	0.7788
4	0.0543	0.0198	0.0801	0.3417	0.0590	0.7425	1.0843	0.8016
2a	0.0887	0.0306	0.0401	0.5585	0.0912	0.3717	0.9302	0.4630
3a	0.1012	0.0337	0.0487	0.6369	0.1005	0.4511	1.0880	0.5516
4a	0.0882	0.0213	0.0398	0.5553	0.0635	0.3687	0.9240	0.4322



r_1

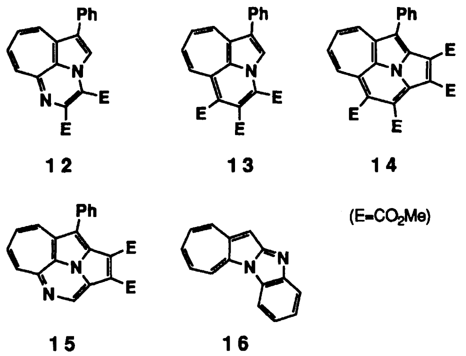


r_2



r_3

exo-methylene carbon of maximum charge in URF **17** (Chart 4). The URF's for forms **2a**—**4a** ($R^1=R^2=H$) are the same as those of **2**—**4**. The charge densities of URF's **18**—**22** reveal that the nitrogen atom occupies the site of the higher charge density in the corresponding URF's. According to the original TCS rule, it is not necessary to place heteroatoms at all of the sites of high charge density in the URF to stabilize molecules. However, it has become evident that annulated 1-azaazulenes conform to the TCS rule.



(E=CO₂Me)

Chart 3.

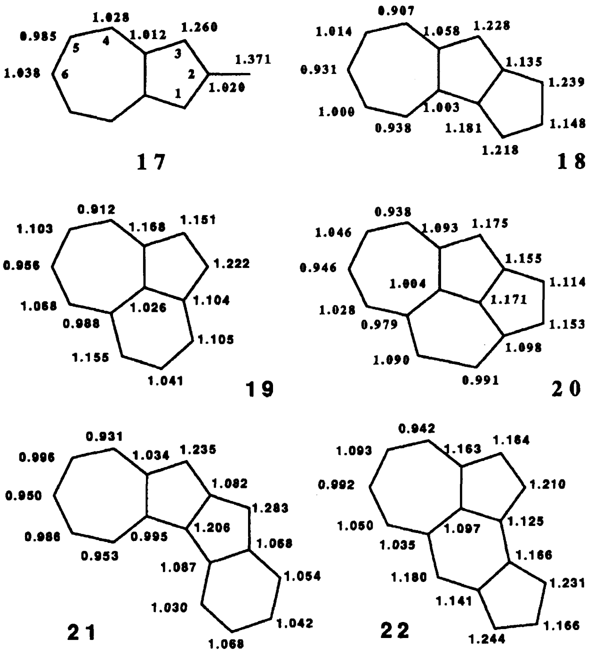


Chart 4.

TRE of Annulated 1-Azaazulenes. In order to clarify the origin of the aromaticity, we calculated the circuit resonance energies of compounds **1**, **5a**, **12**—**13**, **6a** and **14**—**15** by TRE.[5] Geometrically unidentical π-electron circuits and circuit resonance energies of these compounds are shown in Figs. 2, 3, and 4. The π-electron ring system in 1-azaazulene **1** consists of three π-ring components, from r_1 to r_3, as shown in Fig. 2. Among the calculated circuit resonance energies of **1**, the circuit resonance energy of r_3 showed the largest positive value. Consequently, 1-azaazulene **1** is stabilized as the 10π-peripheral system. The π-electron ring system in **5a** consists of six π-ring components r_1—r_6 as shown in Fig. 2. Among the calculated circuit resonance energies of compound **5a**, the circuit resonance energy of r_3 showed the largest positive value, while the value of r_5 was negative. The ^{1}H NMR spectrum of the seven-membered ring protons of **2** shows signals at $\delta=7.29$—8.12, whereas that of **5a** shows signals at $\delta=6.56$—7.90. The bond-currents of the seven-membered rings (r_1) of **2** and **5a** are 1.1031 I_0 and 1.017 I_0,

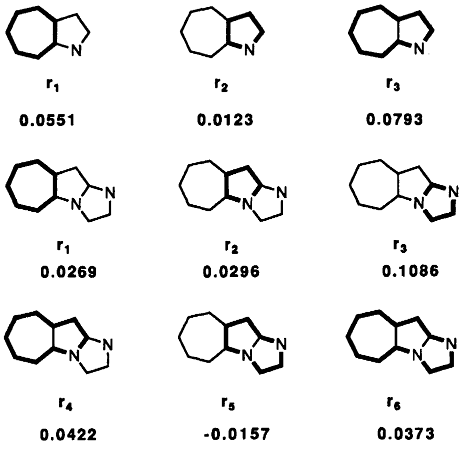
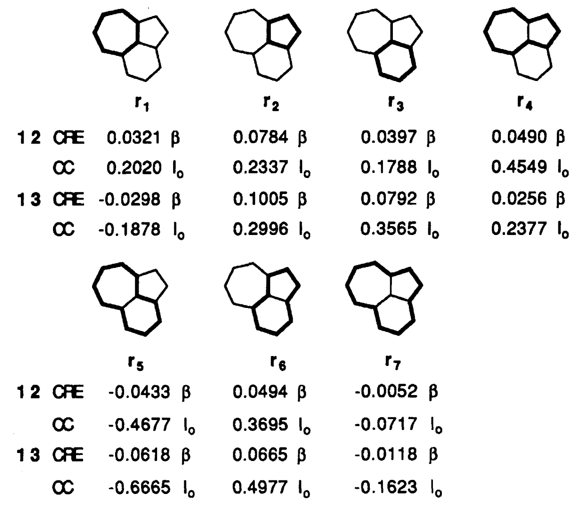


Fig. 2. Geometrically unidentical π-electron circuits and circuit resonance energies (in β units) for **1** and **5a**.

respectively. Therefore, the value of r_1 of **2** was larger than that of **5a** in agreement with their chemical shifts. Compounds **12** and **13** have 14π electrons. The π-electron ring system in **12** and **13** consists of seven π-ring components, from r_1 to r_7, as shown in Fig. 3. The circuit resonance energies of r_2, r_4, and r_6 of compound **12** showed large positive values, while the values of r_5 and r_7 were negative. Therefore, compound **12** is stabilized as an r_2–r_4–r_6 system. On the other hand, the circuit resonance energies of r_2, r_3, and r_6 of compound **13** showed large positive values, while the values of r_1, r_5, and r_7 were negative. Thus, compound **13** is stabilized as an r_2–r_3–r_6 system. Thus, the 10π-indolizine part contributed to the stability of **12** and **13** due to the relatively large values of r_6. Compounds **6a**, **14**, and **15** have 16π electrons. The π-electron ring system in **6a** consists of fourteen π-ring components, from r_1 to r_{14}, as shown in Fig. 4. The circuit resonance energies of r_2 and r_3 showed large positive values, while the values of r_6, r_7, r_{10}, r_{11}, r_{13}, and r_{14} were small or negative. Therefore, compound **6a** is stabilized as the resonance forms between **6a** and **E** (Chart 5). A similar tendency was also found for **14** and **15**. From the relatively large values of r_{12}, the π-electronic structure of the cyclazine part contributed to the stability of compounds **6a**, **14**, and **15**.

The URF's for the parent skeleton of compounds **7** and **23** are shown in **24** (Chart 6). The heteroatoms in these compounds are situated at the sites of large charge densities in the corresponding URF.

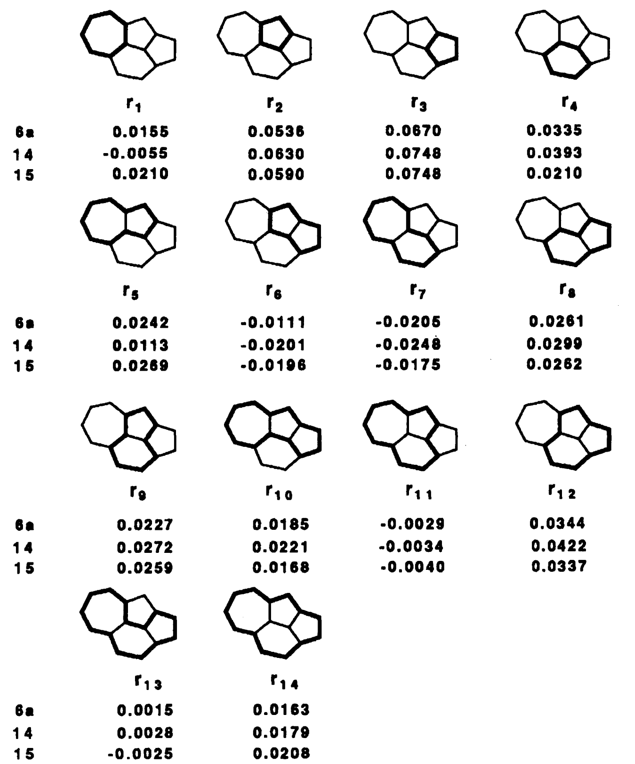
All the protons of **7** resonated at considerably higher fields than those of **23**, especially those of the seven-membered ring ($\Delta\delta > 0.5$ ppm) and the benzene ring ($\Delta\delta > 0.2$ ppm).[8b] Circuit resonance energies and circuit currents of compounds **23** and **7** were calculated by TRE.[6] Geometrically unidentical π-electron circuits of those compounds are shown in Figs. 5 and 6. The π-electron ring system in **7** and **23** consists of 10π-ring components, from r_1 to r_{10}, as shown in Figs. 5 and 6. The circuit resonance energies of r_1, r_4, and r_5 of compound **7** showed large positive values, while the values of r_2, r_6, r_9, r_3, r_7, r_8, and r_{10} were small or negative. Therefore, compound **7** was stabilized as the resonance between the 6π-tropylium-6π-benzenoid form and the 10π-azaazulene-6π-benzenoid form, but not as a 20π-peripheral system. A similar tendency was also found for **23**. The circuit currents of r_1, r_4, and r_5 of com-



		r_1	r_2	r_3	r_4
12	CRE	0.0321 β	0.0784 β	0.0397 β	0.0490 β
	CC	0.2020 I_0	0.2337 I_0	0.1788 I_0	0.4549 I_0
13	CRE	-0.0298 β	0.1005 β	0.0792 β	0.0256 β
	CC	-0.1878 I_0	0.2996 I_0	0.3565 I_0	0.2377 I_0

		r_5	r_6	r_7
12	CRE	-0.0433 β	0.0494 β	-0.0052 β
	CC	-0.4677 I_0	0.3695 I_0	-0.0717 I_0
13	CRE	-0.0618 β	0.0665 β	-0.0118 β
	CC	-0.6665 I_0	0.4977 I_0	-0.1623 I_0

Fig. 3. Geometrically unidentical π-electron circuits, circuit resonance energies (CRE, in β units), and circuit currents (CC, in I_0 units) of **12** and **13**.



	r_1	r_2	r_3	r_4
6a	0.0155	0.0536	0.0670	0.0335
14	-0.0055	0.0630	0.0748	0.0393
15	0.0210	0.0590	0.0748	0.0210

	r_5	r_6	r_7	r_8
6a	0.0242	-0.0111	-0.0205	0.0261
14	0.0113	-0.0201	-0.0248	0.0299
15	0.0269	-0.0196	-0.0175	0.0262

	r_9	r_{10}	r_{11}	r_{12}
6a	0.0227	0.0185	-0.0029	0.0344
14	0.0272	0.0221	-0.0034	0.0422
15	0.0259	0.0168	-0.0040	0.0337

	r_{13}	r_{14}
6a	0.0015	0.0163
14	0.0028	0.0179
15	-0.0025	0.0208

Fig. 4. Geometrically unidentical π-electron circuits and circuit resonance energies (in β units) for **6a**, **14a**, and **15a**.

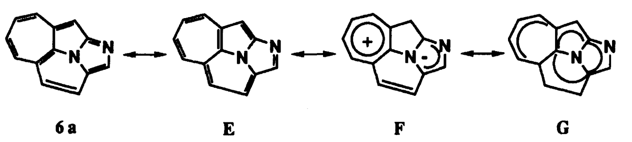
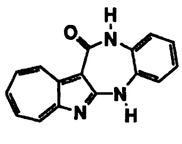
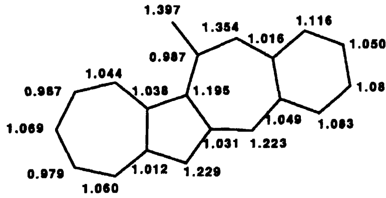


Chart 5.



23



24

Chart 6.

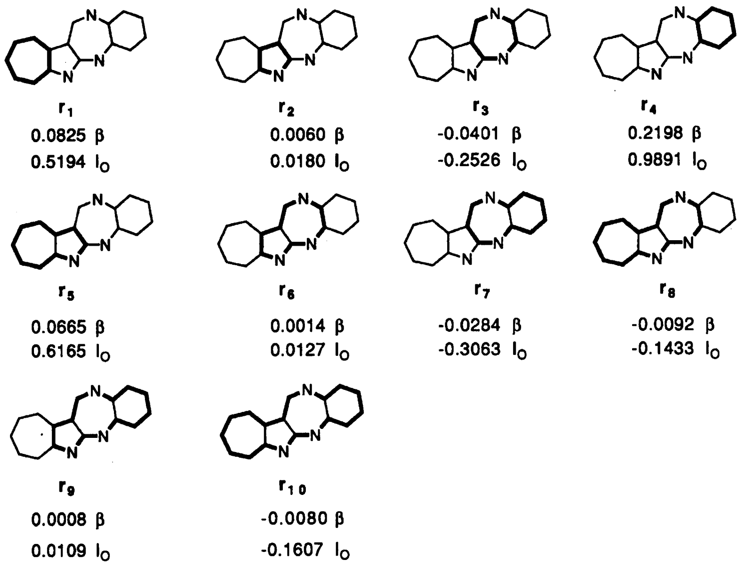


Fig. 5. Geometrically unidentical π-electron circuits, circuit resonance energies, and circuit currents for **7**.

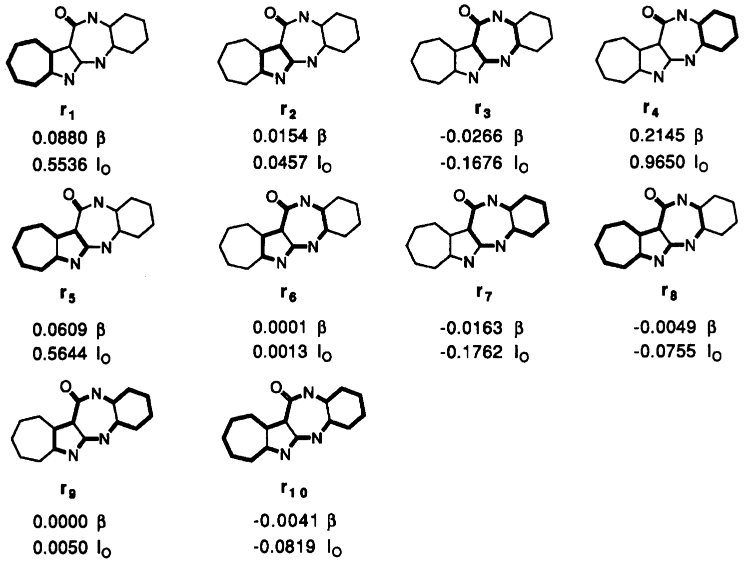


Fig. 6. Geometrically unidentical π-electron circuits, circuit resonance energies, and circuit currents for **23**.

pound **23** showed positive values, while the values of the other ring components were very small or negative. The plus and minus signs in Figs. 5 and 6 indicate diatropism and paratropism, respectively. Large diatropism was predicted to arise from r_1, r_4, and r_5, while large paratropism was predicted to arise from r_3 and r_7. As for compound **7**, the diatropism effect due to the 6π-tropylium structure (i.e., structure r_1: 0.5194 I_0), the 10π-azaazulene part (i.e., structure r_5: 0.6165 I_0), and the 6π-benzenoid part (i.e., structure r_4: 0.9891 I_0) was the main contributor to the magnetic effect, although a small contribution came from the diatropism effect of the five-membered part (i.e., structure r_2: 0.0180 I_0) and the paratropism effect due to the peripheral structure (i.e., structure r_{10}: -0.1607 I_0). The calculated bond-currents are listed in Table 3. The values of the bond-currents of the seven-membered ring (r_1) and benzene ring (r_4) or **7** were smaller than those of **23** in agreement with their chemical shifts.

Table 3. Bond Currents of **23** and **7**

	Bond currents (in benzene, I_0 units)			
	r_1	r_2	r_3	r_4
23	0.9606	0.4545	−0.4994	0.7074
7	0.8319	0.3541	−0.8392	0.5332

Concluding Remarks

As a measure of the characteristics of the 6π-tropylium structure (r_1) and the 10π-azaazulene structure (r_3), Table 2 and Figs. 2, 3, 4, 5, and 6 compare the circuit resonance energies contributed by the seven-membered ring and azaazulene part to the annulated 1-azaazulenes. In the cases of the annulated 1-azaazulenes having an indolizine moiety or a cyclazine moiety, the values of r_1 and r_3 are much smaller than that of 1-azaazulene **1**. In the cases of the 1-azaazulenes having an azepine moiety, the values of r_1 are larger than that of **1**, while the values of r_3 are slightly smaller that of **1**. These results suggest that the chemical properties of 1-azaazulene itself still remain in compounds **7** and **23**. As mentioned above, the annulated 1-azaazulenes are predicted to be aromatic with positive resonance energies and to conform to the TCS rule. Thus TRE and the TCS rule are very useful in order to clarify the origin of the aromaticity and stability of complex systems such as the annulated 1-azaazulenes.

We wish to thank Professor Hiroshi Yamamoto (Okayama Univ.) for his helpful advice.

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