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Topological Resonance Energies of Some Forms of the Flavylium Chromophoric System*

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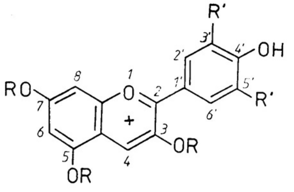
The topological resonance energy (TRE) model was used to study the aromatic stability of cationic AH^+ and anhydrobase from A of the flavylium chromophoric system. The calculated values of *TRE* are within the regular limits for the aromatic molecules, with the cationic forms being more aromatic than the anhydrobase forms. Higher stability of 4-CH_3 flavylium salts is expected relative to 4-H flavylium salts.

INTRODUCTION

The chemistry of flavylium compounds *1* has been undergoing a rapid development during the last few years[1-3] due to the increasing interest in the use of natural colours for food products. However, the largest number of isolated natural flavylium compounds (anthocyanins and anthocyanidins) that differ according to the character, number and position of substituents, as well as an even higher number of flavylium compounds that were obtained synthetically and can be synthesized, are reactive and unstable.[4]



R = H, sugar, acylated sugar; R' = H, OH, OCH_3

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The coloured, cationic form AH^+ of flavylium chromophoric system is transformed by acidity reduction through deprotonation into the coloured, anhydrobase form A. Hydration reactions that take place at cationic and/or anhydrobase form[2] cause a rapid discoloration of solution due to the formation of colourless pseudobase B and/or chalcone forms C. Early studies[5-7] indicated that the hydration reactions take place with anhydrobases. More recent studies,[8-10] however, assert that the hydration reactions take place only at the cationic form. These structural transformations are illustrated in Figure 1.

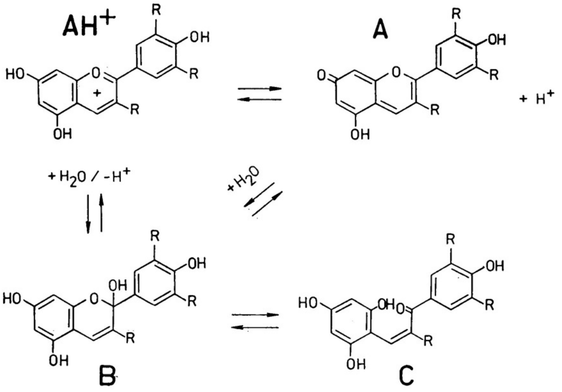

Figure 1. Structural transformations of flavylium compounds.

Substitution of hydrogen atom at the C-4 position by the methyl group results in a considerable increase in the stability of the flavylium chromo-phoric system.[11-14] As hydration reactions are carried out at a considerably reduced rate, the solutions of 4-substituted flavylium salts remain coloured within a large interval of pH-values.

In spite of the abundance of experimental data, theoretical predictions of the reactivity and stability of flavylium salts are very rare in literature, and are limited to HMO and PPP SCF MO calculations.[15-17] This paper presents calculations of the aromatic stability of the cationc from AH^+ and anhydrobase form A of a number of synthetic flavylium salts using a topological resonance energy, TRE, model.[18-20] All the studied structures are presented in Figure 2.

COMPUTATIONS

Topological resonance energy, by definition, *TRE* is the difference between the pi-electronic energy of the conjugated molecule and the pi-electronic energy of the reference (virtual) structure, which the studied molecule would possess with minimal delocalization of pi-electrons. Numerical values of *TRE* were calculated according to the following equation:

$$TRE = \sum_{i=1}^{N} g_i \, (x_i - x_i^{ac})$$

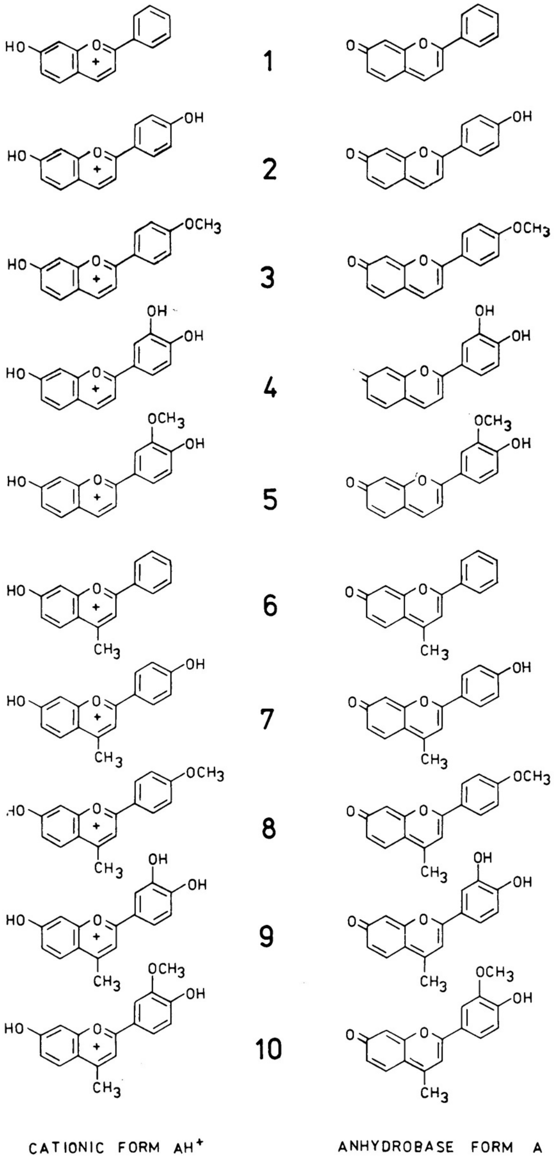

Figure 2. Shematic representation of studied molecules.

where x_i's are Hückel eigenvalues, while x_i^{ac}'s are those of the acyclic (reference) polynomial.[21] The g_i is the orbital occupancy number of molecular orbitals while N represents the number of pi-centres in a given molecule.

Parameters for heteroatoms are given in Table I.

TABLE I

Parameter values for the TRE calculations

Element of Group X	Coulomb Integral h_x	Resonance Integral $K_{c—x}$	Reference
Carbon C	0	1	22
Pyrylium oxygen O^+	2	0.9	17
Ether oxygen Ö	2	0.34	23
Ketone oxygen $O^{\cdot}$	0.22	0.99	24
Hydroxyl OH	1.2	0.8	25
Methoxyl OCH_3	1.65	0.9	26
Methyl CH_3			
Heteroatom model	2	0.7	22
Conjugation model	—2.3	3.1	27
Inductive model	—0.5	—	27

The value of topological resonance energy per electron, *TRE(PE)* is calculated according to equation:

$$TRE(PE) = TRE/N(pi)$$

where N(pi) is the total number of pi electrons in the molecule. According to the value of *TRE(PE)*, conjugated molecules can be roughly classified into three groups[19]: aromatic molecules $TRE(PE) > 0.01$, nonaromatic molecules $TRE(PE) = 0$ and antiaromatic molecules $TRE(PE) < —0.01$. The percentage of aromatic character of the studied molecule relative to benzene, *% B*, is calculated according to equation:

$$\%\,B = \frac{TRE(PE)}{TRE(PE)\ (\text{benzene})} * 100$$

The computation of *TRE* and the computer program are detailed elsewhere.[28]

The *TRE* approach has been found, in spite of some limitations, to be quite a reliable model for predicting aromaticity in various classes of conjugated systems.[29]

RESULTS AND DISCUSSION

Calculated topological resonance energies, topological resonance energies per electron, percentage of aromatic character relative to benzene and *TRE* HOMO-LUMO separations are presented in Table II.

TABLE II

Indices of the aromatic character of cationic AH^+ and anhydrobase A forms of the studied flavylium salts

Compound	Cationic form AH^+			Anhydrobase form A			*TRE* HOMO-LUMO[a]		
	TRE	*TRE(PE)*	*% B*	*TRE*	*TRE(PE)*	*% B*	AH^+	A	
1	0.4992	0.0277	61	0.3274	0.0181	40	0.372	0.013	30
2	0.4717	0.0235	52	0.3107	0.0155	34	0.337	0.022	31
3	0.4753	0.0237	52	0.3133	0.0156	34	0.353	0.020	32
4	0.4655	0.02111	47	0.3047	0.0138	30	0.303	0.042	31
5	0.4671	0.0212	47	0.3062	0.0139	31	0.321	0.040	31
6	0.5153	0.0286	63	0.3525	0.0195	43	0.412	0.048	33
7	0.4895	0.0244	54	0.3348	0.0167	37	0.370	0.048	33
8	0.4928	0.0246	54	0.3375	0.0168	37	0.387	0.047	33
9	0.4847	0.0220	48	0.3297	0.0149	33	0.337	0.062	33
10	0.4863	0.0221	49	0.3313	0.0150	33	0.354	0.059	33

[a] Reference to preparative work.

Numeric values of *TRE(PE)* of the studied AH^+ and A forms of flavylium chromophoric system demonstrate that both forms are aromatic molecules. *TRE* values of AH^+ form 0.4655—0.5153 (47—63%) of the aromatic character of benzene) are higher than *TRE* values of A form 0.3047—0.3525 (30—43% of the aromatic character of benzene). Based on these values, it can be predicted that nucleophilic addition of water will take place more readily on anhydrobase forms than with cationic forms, which is confirmed by experimental data.[5–7] In support of the above statement we give, in Figures 3 and 4, UV-VIS spectra of 7,4'-di-OH flavylium perchlorate. It can be easily seen that immediately after preparing a sample for measurement, the existence of anhydrobase which disappears with time is in agreement with our prediction. This is also in agreement with the calculated indices of superdelocalization for the nucleophilic attack $S_r(N)$ at positions C-2 and C-4 of the studied cationic and anhydrobase forms.[34] *TRE* HOMO-LUMO separation of 4-H flavylium compounds is lower in comparison with the 4-CH_3 flavylium compounds, which is in agreement with the batochromic shift of the maxima in absorption bands of the corresponding UV-VIS spectra.

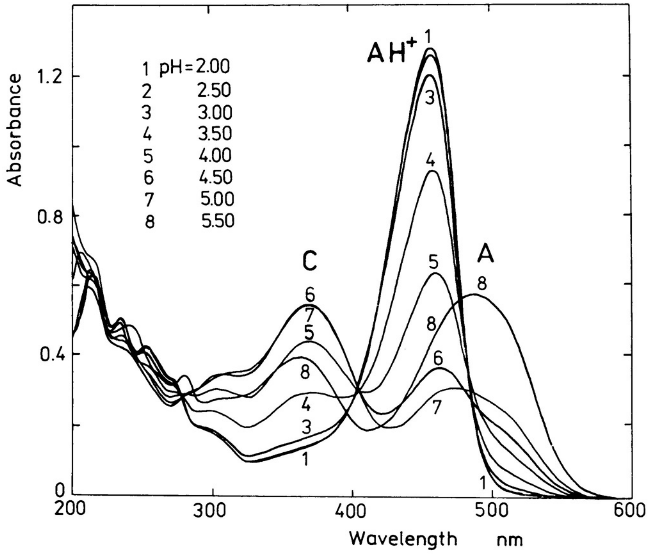

Figure 3. Absorption spectra of 7,4'-di-OH flavylium perchlorate at 293 K, concentration $3.05 \cdot 10^{-5}$ mol/dm^3, after 3 minutes.

The CH_3 group was studied according to the conjugation, heteroatom and inductive models.[27] The inductive model was demonstrated to be the most appropriate for the interpretation of experimentally obtained results (Table III).

The stabilizing effect of 4-CH_3 group (Table IV) is demonstrated by a higher stabilization of the more reactive, *i. e.* anhydrobase form (average Δ *TRE* = 0.0247), relative to the more stable, cationic form (Δ *TRE* = 0.0180). p*K* values of the total transformation: $AH^+ \rightarrow (A + B + C) + H^+$ and wavelengths of maximum absorption were taken from references.[33–37]

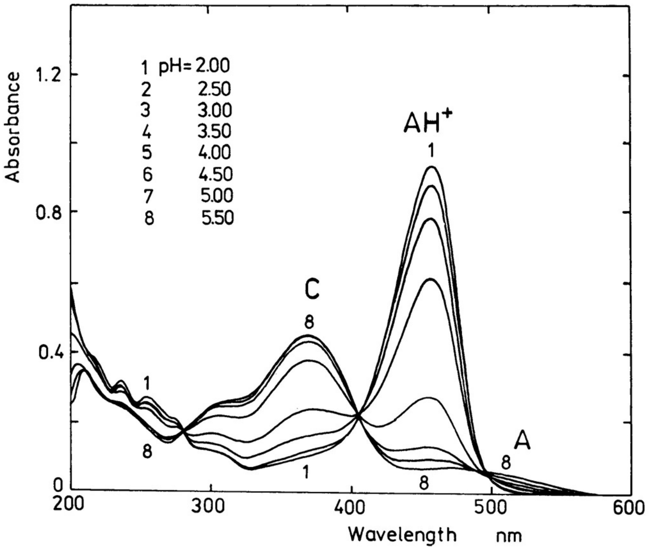

Figure 4. Absorption spectra of 7,4'-di-OH flavylium perchlorate at 293 K, concentration $2.25 \cdot 10^{-5}$ mol/dm^3, after standing for 2 hours.

TABLE III

Stabilizing effect of the CH_3 group — mean values

Model: 4-CH_3—4-H	Conjugation		Heteroatom		Inductive	
	AH^+	A	AH^+	A	AH^+	A
Δ *TRE*	0.0079	0.0132	0.0085	0.0131	0.0180	0.0247
Δ HOMO-LUMO	0.045	0.026	0.049	0.030	0.115	0.077

TABLE IV

Stabilizing effect of the CH_3 group (inductive model) at position C-4 of the flavylium chromophoric system

Flavylium chloride	Δ *TRE* 4-CH_3 — 4-H		Δ *TRE* HOMO-LUMO 4-CH_3 — 4-H			Δ λ_{max} nm
	AH^+	A	AH^+	A		AH^+
7-OH	0.0161	0.0251	0.040	0.035	1.72	15
7,4'-di-OH	0.0178	0.0241	0.033	0.026	1.54	14
7-OH-4'-OCH_3	0.0175	0.0242	0.034	0.027	1.66	12
7,3',4'-tri-OH	0.0192	0.0250	0.034	0.020	1.60	—
7,4'-di-OH-3'-OCH_3	0.0192	0.0251	0.033	0.019	1.58	15
Average:	0.0180	0.0247	0.035	0.025	1.62	14

The experimentally determined, indicated p*K* values show that the 4-CH_3 group increases the stability of the cationic form by the amount of 1.62 p*K* units relative to the 4-H group. This value can correlate with the values of Δ *TRE* = 0.0180 and Δ *TRE* HOMO-LUMO = 0.035.

In this paper the topological resonance energy model was applied, for the first time, to the flavylium chromophoric system and its different forms. The demonstrated agreement of *TRE*, *TRE(PE)* and % *B* values with the experimental findings confirm that the *TRE* method can be successfuly used with this class of heterocyclic conjugated molecules. The agreement of experimental findings with the predictions obtained using the *TRE* model for the influence of individual substituents (especially OH and OCH_3 groups) on the stability of flavylium chromophoric system is currently being studied.

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SAŽETAK

Topologijske rezonancijske energije nekih oblika flavilijevog kromofornog sustava

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Metoda topologijske rezonancijske energije *(TRE)* upotrijebljena je za proučavanje aromatičke stabilnosti kationskog AH^+ i anhidrobaznog A oblika flavilijeva kromofornog sustava. Izračunane vrijednosti *TRE* kreću se u granicama koje vrijede za aromatske molekule, pri čemu su kationski oblici aromatičniji od anhidrobaznih. Predviđa se veća stabilnost 4-CH_3 flavilijevih soli u odnosu na 4-H flavilijeve soli.