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Conference Paper

On the Topological Resonance Energy of Coumarin and Its Derivates*

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Topological resonance energies of coumarin and the following derivatives: 3-hydroxycoumarin, 4-hydroxycoumarin, 3,4-dihydroxycoumarin, 4,6-dihydroxycoumarin, 4,5,7-trihydroxycoumarin, 3-carboxy-4-hydroxycoumarin, 3-bromo-4-hydroxycoumarin, and 6-bromo-4-hydroxycoumarin, are reported. Theoretical predictions that these all coumarins should exhibit aromatic properties are sustained by the ample experimental evidence. In addition, coumarin and isocoumarin are predicted to be much more stable than the corresponding quinonoid isomer.

In the present note*** the topological resonance energy, TRE , model^{1,2} is applied to coumarin and some of its derivatives (see Figure 1).

Coumarin is a molecule with a long history in organic chemistry³⁻⁵ which has many interesting chemical, pharmaceutical, and biological properties⁶⁻¹¹. Its aromatic stability has been discussed by a number of researchers¹²⁻¹⁴. We studied the aromatic stability of coumarin and its derivatives by means of the topological resonance energy approach which has been shown previously to be a quite reliable method for predicting aromaticity in various conjugated molecules^{1,2,15,16}, their ions, radicals, and ion-radicals^{17,18}, homoaromatic structures^{18,19}, and even aromaticity in the electronically excited states of conjugated systems^{18,20}.

The following TRE formula is used for the numerical work^{1,2,21,22}

$$TRE = \sum_{j=1}^N g_j (x_j - x_j^{ac}) \quad (1)$$

where x_j and x_j^{ac} represent the Hückel spectrum of a given structure and the spectrum of the corresponding acyclic polynomial^{1,2}, respectively, while g_j ($j = 1, 2, \dots, N$) are the orbital occupancy numbers. The heteroatomic parameters are taken from the work by Hess and Schaad²³⁻²⁵.

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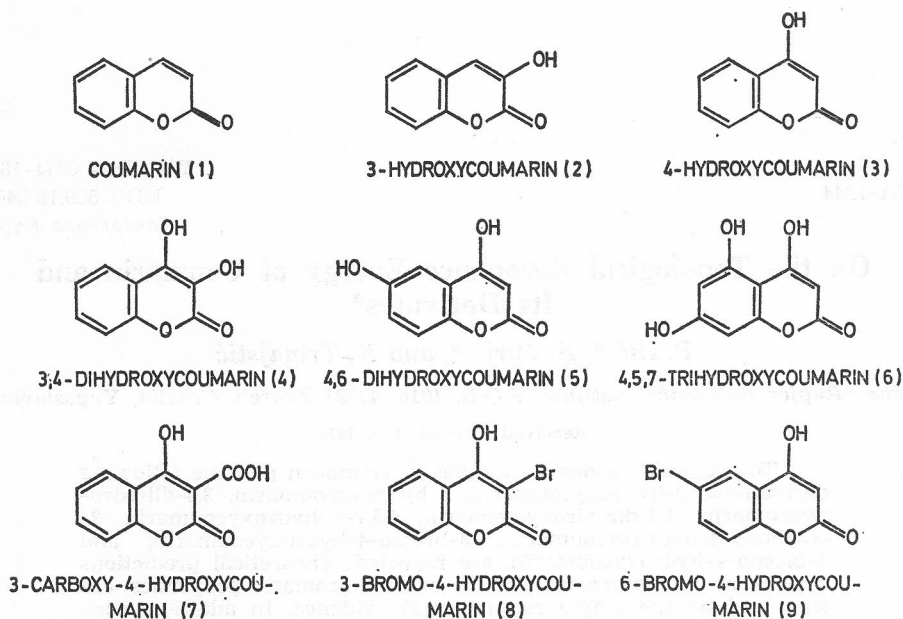


Figure 1. Coumarin and Some of Its Derivatives

In order to compare the aromatic stability of coumarin and related compounds the normalized form of TRE , TRE per electron, TRE (PE), is used²⁶,

$$TRE \text{ (PE)} = \frac{TRE}{N} \quad (2)$$

where N is the total number of π electrons in the systems. Numerical values of TRE and TRE (PE) are reported in the Table.

TABLE
Topological Resonance Energies of Coumarin and Its Derivatives

| COMPOUND ^a | TRE | TRE (PE) | Reference to the preparative work |
|-----------------------|-------|------------|-----------------------------------|
| 1 | 0.243 | 0.020 | b |
| 2 | 0.266 | 0.019 | c |
| 3 | 0.274 | 0.020 | d |
| 4 | 0.277 | 0.017 | - |
| 5 | 0.325 | 0.020 | e |
| 6 | 0.471 | 0.020 | e |
| 7 | 0.328 | 0.021 | f |
| 8 | 0.279 | 0.017 | g |
| 9 | 0.227 | 0.014 | h |

^a Compounds are listed in Figure 1.

^b W. H. Perkin, *J. Chem. Soc.* (1868) 53.

^c J. Lynch, *J. Chem. Soc.* (1912) 1758.

^d R. Auschutz, *Chem. Ber.* 36 (1903) 465.

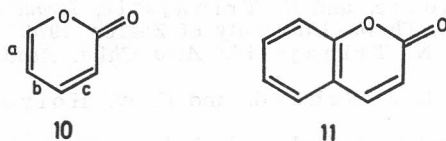
^e A. Sonn, *Chem. Ber.* 50 (1917) 1292.

^f S. Checchi, *Gazz. Chim. Ital.* 90 (1960) 440.

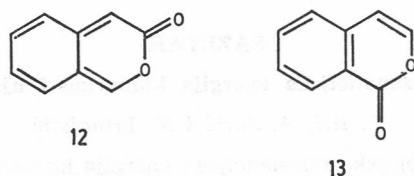
^g C. Huebner and K. P. Link, *J. Amer. Chem. Soc.* 66 (1944) 656.

^h M. Deželić and M. Trković, *J. Med. Chem.* 7 (1964) 284.

Both TRE and $TRE(PE)$ indices indicate coumarin and those derivatives studied to be aromatic compounds and comparable in their stabilities. (Accepted threshold values are as follows: aromatic compounds, $TRE(PE) > 0.01$; non-aromatic compounds, $TRE(PE) \approx 0.0$; and anti-aromatic compounds, $TRE(PE) < -0.01$, respectively.) Abundant experimental evidence supports this results. However, $TRE(PE)$ index reveals that the aromatic stability in coumarin is only 44% of the benzene ring stability. (TRE and $TRE(PE)$ values of benzene being 0.273 and 0.046 respectively)² The meaning of this result is that annelation of benzene to non-aromatic α -pyrone (10) ($TRE = 0.018$; $TRE(PE) = 0.002$) results in the distortion of the perfect conjugation within the six-membered ring.



α -pyrone has three position free for annelation. Annelation at position a produces coumarin (11). Annelation at b and c should produce two positional isomers of coumarin, compounds 12 and 13.



Compound 13 should be stable and comparable in its stability to coumarin ($TRE = 0.23$; $TRE(PE) = 0.019$). This is experimentally established²⁷. However, compound 12 should be less stable than either coumarin or isocoumarin because this kind of annelation, aromatic bond of one ring to an essentially single bond of the other ring, destroys aromaticity to a great extent within the benzene ring and produces the destabilization of the molecule as a whole. Therefore, we anticipate difficulties in the preparation of 12, the only quinonoid structure among the three positional isomers of coumarin, in accordance with its low stability ($TRE = 0.107$; $TRE(PE) = 0.009$). Thus, it is not surprising that molecule 12 is not reported as yet.

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SAŽETAK

Topologijska resonancijska energija kumarina i njegovih derivata

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Izračunana je topologijska resonancijska energija kumarina i slijedećih derivata: 3-hidroksikumarina, 4-hidroksikumarina, 3,4-hidroksikumarina, 4,6-dihidroksikumarina, 3-karboksi-4-hidroksikumarina, 3-bromo-4-hidroksikumarina, i 6-bromo-4-hidroksikumarina. Teorijsko predviđanje da su to sve aromatski spojevi poduprto je obilnim eksperimentalnim rezultatima. Od tri pozicijska izomera kumarina kinoidna struktura ima najnižu vrijednost topologijske resonancijske energije i još nije pripravljena.

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