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QSPR Study of Polarographic Half-wave Reduction Potentials of Benzenoid Hydrocarbons*

Sonja Nikolić,[a] Ante Miličević,[b] and Nenad Trinajstić[a,]**

[a]*The Ruđer Bošković Institute, P.O.B. 180, HR-10002 Zagreb, Croatia*

[b]*The Institute for Medical Research and Occupational Health, P.O.B. 291, HR-10002 Zagreb, Croatia*

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Correlation between the polarographic half-wave reduction potentials and the set of molecular descriptors of lower benzenoid hydrocarbons was made by the CROMRsel modeling procedure. The following descriptors were used in the modeling procedure: electron affinities, Hückel π-electron energies, π-electron energies of the lowest unoccupied molecular orbitals, the number of Kekulé structures and the vertex-connectivity index. All models with one, two or three descriptors were considered. It was found that the π-electron energies of the lowest unoccupied molecular orbitals *E*(LUMO) were participating in all the best models. A single-descriptor model based on *E*(LUMO) was selected for testing. The statistical parameters obtained for the test set are comparable to those of the training set. The obtained results suggest that energies of the lowest unoccupied molecular orbitals are indeed very suitable descriptors for predicting the polarographic half-wave reduction potentials of benzenoid hydrocarbons.

Keywords
• benzenoid hydrocarbons
• lowest unoccupied molecular orbitals
• molecular descriptors
• polarographic half-wave reduction potentials
• QSPR

INTRODUCTION

Early in his career, Marko Branica was interested in polarography.[1–3] One of us (NT) did research for his degree thesis in polarography of bismuth in a solution of sodium acetate and acetic acid in order to determine the dependence of bismuth acetato complexes on the concentration of sodium acetate.[4] When NT joined the Ruđer Bošković Institute, he gave a talk on the polarography of organic compounds and afterwards had a number of discussions with Branica about polarography of different materials. One of the topics often discussed was the dependence of the polarographic half-wave potentials of conjugated compounds on their π-electronic and structural characteristics.

Here, we report a QSPR analysis of the polarographic half-wave reduction potentials, $E_{1/2}^{red}$, of 36 benzenoid hydrocarbons. This set of benzenoid hydrocarbons was split into a training set consisting of 23 benzenoid hydrocarbons and a test set consisting of 13 benzenoid hydrocarbons. The polarographic half-wave potentials were already used in QSPR by Richard and Kier,[5] but only as descriptors. The experimental values of $-E_{1/2}^{red}$ (in V) are taken from Bergman.[6] They are listed for the training set in Table I. Their graphs[7] are given in Figure 1.

* Dedicated to the memory of Marko Branica (1931–2004), an excellent marine scientist, electrochemist, stimulating teacher and good friend.

** Author to whom correspondence should be addressed. (E-mail: trina@irb.hr)

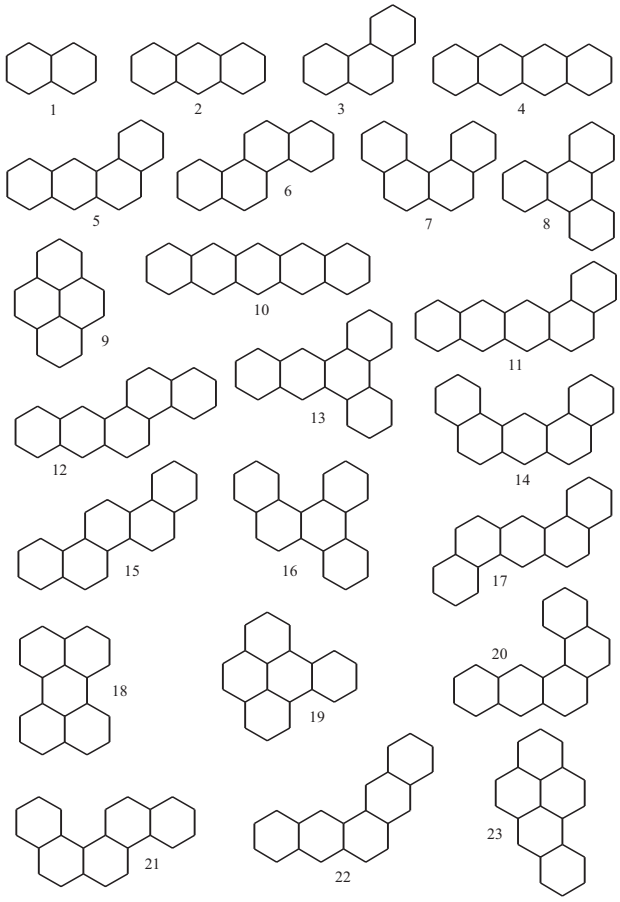

Figure 1. Graphs of benzenoid hydrocarbons in the training set.

TABLE I. Experimental values of the half-wave reduction potentials ($-E_{1/2}^{red}$), computed electron affinities (A), π-electron energies of the lowest unoccupied molecular orbitals (E(LUMO)), vertex-connectivity indices ($^1\chi$), total π-electron energies (E_π) and the number of Kekulé structures (K) of 23 benzenoids represented in Figure 1

Benzenoid	$-E_{1/2}^{red}$ / V	A / eV	$-E$(LUMO)	$^1\chi$	E_π	K
1	1.98	0.074	0.6180	4.9663	13.6832	2
2	1.46	0.653	0.4142	6.9327	19.3137	3
3	1.94	0.273	0.6052	6.9495	19.4483	5
4	1.14	1.060	0.2950	8.8990	24.9308	5
5	1.53	0.640	0.4523	8.9158	25.1012	7
6	1.81	0.516	0.5201	8.9327	25.1922	8
7	1.75	0.384	0.5676	8.9327	25.1875	8
8	1.97	0.251	0.6840	8.9495	25.2745	9
9	1.61	0.664	0.4450	7.9327	22.5055	6
10	0.86	1.341	0.2197	10.8650	30.5401	6
11	1.19	1.003	0.3271	10.8813	30.7256	9
12	1.44	0.800	0.4048	10.8982	30.8390	11
13	1.54	0.568	0.4991	10.9160	30.9418	13
14	1.57	0.583	0.4918	10.8990	30.8795	12
15	1.79	0.591	0.5019	10.9151	30.9432	13
16	1.65	0.600	0.5319	10.9320	30.9990	14
17	1.55	0.654	0.4735	10.8990	30.8805	12
18	1.25	0.956	0.3473	9.9327	28.2453	9
19	1.67	0.610	0.4970	9.9327	28.3361	11
20	1.40	0.757	0.4186	10.8982	30.8338	11
21	1.73	0.500	0.5498	10.9160	30.9386	13
22	1.53	0.707	0.4372	10.8820	30.7627	10
23	1.36	0.930	0.3711	9.9158	30.2220	9

MODELING PROCEDURE

The QSPR analysis was carried out by means of the CROMRsel modeling procedure described in several of our reports.[8–15] CROMRsel is a multivariate procedure that has been designed to select the best possible model among the set of models obtained for a given number of descriptors, the criterion being the standard error of estimate. The quality of models is expressed by fitted (descriptive) statistical parameters: the correlation coefficient (R_{fit}), the standard error of estimate (S_{fit}) and Fisher's test (F). The models are also cross(internally)-validated by a leave-one-out procedure. Statistical parameters for the cross-validated models are symbolized by R_{cv} and S_{cv}, where subscript cv denotes cross-validation.

The set of molecular descriptors for the training set of 23 benzenoid hydrocarbons that we used in the structure-polarographic half-wave reduction potential correlations consists of the electron affinities A (in eV), the Hückel total π-electron energies E_π (in β), E(LUMO) values (in β), the number of Kekule structures K and the vertex-connectivity index $^1\chi$. All these descriptors are also given in Table I. The electron affinities are taken from Dewar *et al.*[16] These authors computed electron affinities for a set of 76 aromatic compounds, consisting of 61 benzenoids and 15 nonbenzenoids, using the half-electron variant of the SCF MO theory.[17] Apparently, the computed electron affinities agree closely with the available experimental values.[18] The total π-electron energies E_π, E(LUMO) values and the K numbers are taken from Dias.[19] Correlations between $-E_{1/2}^{red}$, A and E(LUMO) were described by several authors in the past, *e.g.*[20,21] The vertex-connectivity indices of benzenoids are calculated using the following expression:[22]

$$^1\chi = e_{22}/2 + e_{23}/\sqrt{6} + e_{33}/3 \qquad (1)$$

where e_{22}, e_{23} and e_{33} are, respectively, the numbers of edges between vertices of degree 2, of degree 2 and 3, and of degree 3 in a given benzenoid.

We considered all models with one, two or three descriptors. Below we give the best models in each case. In the case of the single-descriptor models, there is no sur-

prise – the best structure-polarographic half-wave reduction potential models are based on E(LUMO) and on A:

$$-E_{1/2}^{red} = 0.412\ (\pm 0.066) + 2.459\ (\pm 0.138)\ E(\text{LUMO}) \quad (2)$$

$$N = 23 \quad R_{fit} = 0.968 \quad R_{cv} = 0.960 \quad S_{fit} = 0.071 \quad S_{cv} = 0.080 \quad F = 316$$

$$-E_{1/2}^{red} = 2.176\ (\pm 0.040) - 0.949\ (\pm 0.056)\ A \quad (3)$$

$$N = 23 \quad R_{fit} = 0.965 \quad R_{cv} = 0.957 \quad S_{fit} = 0.074 \quad S_{cv} = 0.082 \quad F = 285$$

It should also be noted that the statistical characteristics of the correlation between A and E(LUMO) are similar to the ones above:

$$A = 1.818\ (\pm 0.067) - 2.500\ (\pm 0.140)\ E(\text{LUMO}) \quad (4)$$

$$N = 23 \quad R_{fit} = 0.969 \quad R_{cv} = 0.957 \quad S_{fit} = 0.072 \quad S_{cv} = 0.083 \quad F = 318$$

The best two-descriptor model is based on A and E(LUMO):

$$-E_{1/2}^{red} = 1.199\ (\pm 0.365) - 0.433\ (\pm 0.198)\ A + 1.375\ (\pm 0.512)\ E(\text{LUMO}) \quad (5)$$

$$N = 23 \quad R_{fit} = 0.975 \quad R_{cv} = 0.967 \quad S_{fit} = 0.065 \quad S_{cv} = 0.074 \quad F = 189$$

The second two-descriptor model is based on E(LUMO) and the vertex-connectivity index and is only slightly inferior to model (5):

$$-E_{1/2}^{red} = 0.603\ (\pm 0.130) + 2.377\ (\pm 0.144)\ E(\text{LUMO}) + 0.015\ (\pm 0.009)\ {}^{1}\chi \quad (6)$$

$$N = 23 \quad R_{fit} = 0.972 \quad R_{cv} = 0.963 \quad S_{fit} = 0.068 \quad S_{cv} = 0.078 \quad F = 173$$

The best three-descriptor model is based on E(LUMO), ${}^{1}\chi$ and K:

$$-E_{1/2}^{red} = 1.083\ (\pm 0.305) + 1.978\ (\pm 0.266)\ E(\text{LUMO}) - 0.072\ (\pm 0.034)\ {}^{1}\chi + 0.027\ (\pm 0.016)\ K \quad (7)$$

$$N = 23 \quad R_{fit} = 0.976 \quad R_{cv} = 0.965 \quad S_{fit} = 0.065 \quad S_{cv} = 0.079 \quad F = 127$$

This model is not better than the models with one or two descriptors. Therefore, the pragmatic choice of the models for structure-polarographic half-wave reduction potential correlations for benzenoids are one-parameter models (2) and (3). However, E(LUMO) participates in all the best models, thus revealing the important role of the lowest empty molecular orbital in the mechanism of the reduction of benzenoid hydrocarbons by a reversible one-electron transfer to the radical ion, as has been pointed out by earlier authors. Hence, the model of our choice is model (2). The scatter plot of $(-E_{1/2}^{red})_{exp}$ *vs.* $(-E_{1/2}^{red})_{calc}$ for the training set of benzenoids is given in Figure 2.

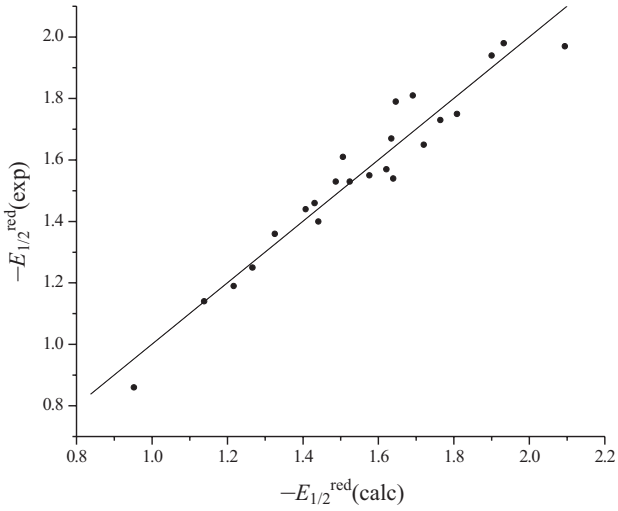

Figure 2. Scatter plot of $(-E_{1/2}^{red})_{exp}$ *vs.* $(-E_{1/2}^{red})_{calc}$ for the training set.

We used model (2) to predict the polarographic half-wave reduction potentials for the test set. Their graphs are given in Figure 3.

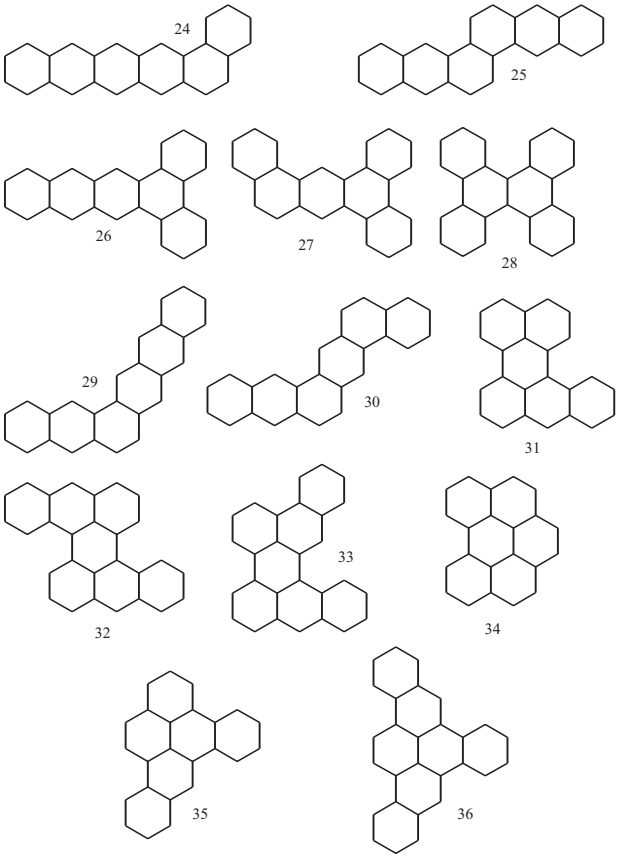

Figure 3. Graphs of benzenoid hydrocarbons in the test set.

TABLE II. Experimental and predicted values of the polarographic half-wave reduction potentials of 13 benzenoids represented in Figure 2

Benzenoid	$(-E_{1/2}^{red})_{exp}$	$-E$(LUMO)	$(-E_{1/2}^{red})_{pred}$
24	0.95	0.2436	1.01
25	1.33	0.3482	1.27
26	1.21	0.3557	1.29
27	1.57	0.5224	1.70
28	1.59	0.5115	1.67
29	1.22	0.3357	1.24
30	1.50	0.4287	1.47
31	0.97	0.2648	1.06
32	0.88	0.2135	0.94
33	1.00	0.2673	1.07
34	1.49	0.4392	1.49
35	1.45	0.4216	1.45
36	1.36	0.3711	1.32

The experimental and predicted polarographic half-wave reduction potentials of the test set are given in Table II. The statistical parameters for the test set are R_{test} = 0.974 and S = 0.071. The scatter plot of $(-E_{1/2}^{red})_{exp}$ *vs.* $(-E_{1/2}^{red})_{pred}$ for the test set is given in Figure 4.

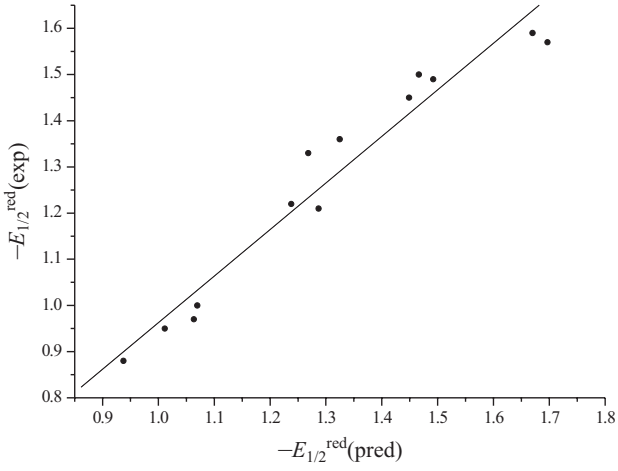

Figure 4. Scatter plot of $(-E_{1/2}^{red})_{exp}$ *vs.* $(-E_{1/2}^{red})_{pred}$ for the test set.

CONCLUSION

Since the statistical parameters obtained for the test set are comparable to those of the training set, the obtained results suggest, in agreement with a number of previously reported differently motivated analyses, that E(LUMO) are indeed very suitable descriptors for predicting the polarographic half-wave reduction potentials of benzenoid hydrocarbons.

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SAŽETAK

QSPR analiza polarografskih poluvalnih redukcijskih potencijala benzenoidnih ugljikovodika

Sonja Nikolić, Ante Miličević i Nenad Trinajstić

Razmatrana je korelacija između polarografskih poluvalnih redukcijskih potencijala i skupa molekularnih deskriptora benzenoidnih ugljikovodika pomoću CROMRsel postupka. Skup molekularnih deskriptora sastojao se od elektronskih afiniteta, Hückelovih π-elektronskih energija, π-elektronskih energija najnižih praznih molekularnih orbitala, broja Kekuléovih struktura i indeksa povezanosti. Generirani su svi modeli s jednim, dva i tri deskriptora na skupu za učenje koji se sastojao od 23 benzenoidna ugljikovodika. Utvrđeno je da vrijednosti najnižih praznih molekularnih orbitala sudjeluju u svim najboljim modelima. Odabrani je model (model (2) u tekstu) zatim testiran na novome skupu od 13 benzenoidnih ugljikovodika. Statistički parametri testa su u granicama koje su dobivene pri generiranju modela na ishodnome skupu molekula. Oni pokazuju da su najniže nevezne molekularne orbitale doista vrlo prikladni deskriptori za predviđanje polarografskih poluvalnih redukcijskih potencijala benzenoidnih ugjikovodika.