511

Egypt. J. Chem. **Vol. 64,** No. 10 pp. 5433 – 5436 (2021)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Prediction of Thermal Isomerization Temperatures of Substituted Benzocyclobutenes to o- Quinodimethanes Using Hardness, Polarizability and energies of σ, σ* and π* orbitals.

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Abstract

The prediction of Thermal Isomerization temperatures (IT) of benzocyclobutenes is useful for their applications in synthesis and polymerization. In this study, ITs were predicted by equations formulated from the hardness, of the products transition states or the difference between the hardness of product and transition state. Also, It's predicted from the orbital energies of the σ, σ*, π and π* orbitals of the benzocyclobutenes.

*Keyword***:** benzocyclobutenes, hardness, polarizability, isomerization temperatures, regression.

Introduction

Benzocyclobutenes (BCBs) undergo ring opening isomerization when heated to generate highly reactive intermediate o-quinodimethanes (o-QDMs) 1 (scheme I).
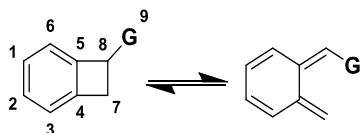
G = H,CH₂,OCH₃,OH,NH₂,Cl,CN,NO₂,CONH₂,Br

Scheme I

This isomerization is a useful source of very reactive functionalized dienes usually used in the synthesis of natural products polymerization or polymer cross-linking [1-5]. The temperature of isomerization (IT) is so important for these applications. However, substitution on C8 or (and), C7 with electron-releasing or electron-withdrawing groups has no systematic effects on IT. The literature contains two methods developed for the prediction of IT. The first was the correlation between IT and 13C chemical shifts NMR of benzocyclobutenes [6]. The second was the correlation of IT with the semi-empirical calculated enthalpy of activation [1]. In the present work, we present a correlation method for the prediction of IT of benzocyclobutenes

from computed quantum parameters. We found good conformity with the previous experimentally found values of the literature [1, 6-8].

With the development of the density functional theory (DFT) and the increase in the velocity of computers in the last decades, it becomes easy to estimate the chemical global reactivity parameters[9] such as hardness (η) , polarizability (α) [10, 11] electronegativity, electrophilicity, nucleophilicity, Fukui function[12].

By using Koopman's approximation [13], where the energy gap is

$= (\epsilon LUMO - \epsilon HOMO)$ ....(1)

we can estimate the hardness as follow:

$\eta = 1/2 (\epsilon LUMO - \epsilon HOMO)$................... (2)

Where εHOMO and εLUMO are energies of higher occupied and lower unoccupied molecular orbitals of the molecule respectively.

The polarizability is one-third of the diagonalized tensor [10, 12]:

$$\alpha = \frac{1}{3}(\alpha_{xx} + \alpha_{yy} + \alpha_{zz}) \quad \text{......} 3$$

Where αxx, αyy and αzz are the diagonalized components of the polarizability tensor.

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Computational Methods and Statistical Details

All the computations were done using Orca 4 0 0. Geometry optimizations of the title compounds were performed to determine molecular orbitals energies (έHOMO-έLUMO) of the reactants and products using density functional theory (DFT) with B3LYP level, def2-SVP basis sets, and def2-SVP/C as auxiliary basis sets. Also, RIJCOSX "chain of spheres" COSX approximation was used to speed DFT calculations[14]. A surface scan was done in order to start optimization from a point near the transition state (TS). Imaginary frequencies were obtained from the Hessian calculations. Then the energies of the molecular orbitals of the TS were computed. The hardness and the polarizability of the reactant, product, and the transition state were calculated from the obtained molecular orbital energies and the diagonalized tensor using equations 2 and 3 respectively. A linear regression was performed to obtain linear correlations between the temperature of isomerization and hardness, energies of orbitals, using SPSS statistical program. The credibility of the correlations obtained depend on the significance value (sig.< .05 considered), R2, t-test(as the value move away from zero the significance of the correlation increase), and F-test (the higher the F-value the better the correlation).

Result and Discussion

The hardness and polarizabilities of all the BCBs, o-QDMs and the TSs were shown in Table 1. The best single correlation obtained was for the regression of the difference between the hardness of TS (H) and that of the product (H_p) and EG (H-$H_{p)}$ with the isomerization temperature (IT):

$$IT = 899.738 – 28099.264\ EG \ldots\ldots\ldots\ldots (4)$$
$$R^2 = 0.756,\ sig. = 0.005,\ t = -4.308$$

The predicted ITs are shown in Table 2.

Also, the hardness of the product (H_p) showed a significant correlation with IT and the predicted values of ITs are shown in Table 2:

$$IT = 47841.35\ H_p – 2139.172 \ldots\ldots\ldots\ldots (5)$$
$$R^2 = 0.845,\ sig. = 0.008,\ t = 3.871$$

Since electron-releasing groups involve the interaction of σ and π* orbitals and electron-withdrawing groups the interaction of σ* and π orbitals separate regressions were done for each. On single regression of these parameters with the experimental IT the following equations were obtained:

$$IT = 1712.511 – 21307.85\ H \ldots\ldots\ldots\ldots (6)$$
$$R^2 = 1.0,\ sig. = 0.012\quad t = -52.098.$$

where H is the hardness of TS.

The above equation indicates an excellent correlation of the hardness of the TS with the isomerization temperature for the electron-withdrawing groups. The calculated values of IT are shown in Table 2. On the other hand hardness of the TS of the electron-releasing groups showed poor correlation with the isomerization temperature.

However a correlation of the difference H -Hp (EG) with the isomerization temperature is shown below:

$$IT = 662.383 – 19708.395\ EG \ldots\ldots\ldots\ldots (7)$$
$$R^2 = 0.996,\ sig. = 0.039,\ t = -16.386$$
$$IT = 1375.333 – 44654.531\ EG \ldots\ldots\ldots\ldots (8)$$
$$R^2 = 0.922,\ sig. = 0.009,\ t = -5.952$$

Equations 6 and 7 represent the single parameter correlation for the prediction of IT for benzocyclobutenes substituted with electron-withdrawing or electron-releasing groups respectively.

However, on multiple regressions the following equation was obtained:

$$IT = 29109.159\ H_p - 18483.124\ EG – 743.865 \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (9)$$
$$R^2 = 0.932,\ sig. =0.001,\ F =34.018$$

The predicted values are also shown in Table 2.

Other useful correlation obtained was between the energies of the σ, σ* and π* orbitals (Table3) and the isomerization temperature IT:

$$IT = -1011.814-163.059\ σ + 132.196\ σ* – 108.304\ π* \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots (10)$$
$$R^2 = 0.961,\ sig. = 0.058,\ F = 16.514$$

The predicted ITs are shown in Table2.

A closer look at Table 2 shows that most of the compounds with substitution adjacent to π bond such as –CN, –CH=CH₂, -Ph, CHO showed anomaly. Unlikely compounds with substitution adjacent to a lone pair such as –NH₂, -OH, OCH₃, Cl, Br showed good correlation since the lone pair delocalized with C-C σ* in the transition state.

Table 1: Hardness and Polarizabilities of the Reactant, Transition State and the Product.

Substituent	Hr	Pr	H	P	Hp	Pp
H	0.114065	78.6921	0.075665	88.2634	0.049231	90.5063
CH₃	0.11352	90.37909	0.074804	-	0.04831	106.2492
OCH₃	0.111955	94.06988	0.075439	-	0.04655	114.32396
OH	0.112775	82.26175	0.0766245	-	0.0474	97.33571
NH₂	0.11301	86.54088	0.075356	-	0.045725	104.6009
Cl	0.11134	87.41711	0.073372	-	0.047515	103.8129

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CN	0.113055	90.29933	0.066729	-	0.04577	111.7488
Br	0.108315	94.64172	0.071897	110.15433	0.047325	112.3879
OTMS	0.08033	140.618646	0.075633	-	0.04708	158.528606
NO₂	0.086285	91.20616	0.065575	-	0.04353	116.6538
-CH=CH₂	0.110165	99.377303	0.062637	121.87008	0.043705	126.87378
-CHO	0.10202	90.100993	0.063611	104.20755	0.043735	112.85843
F	0.11221	78.137653	0.0772015	88.81935	0.048675	90.920843
Ph	0.10943	140.38854	0.0607155	169.48339	0.044135	179.58731
CF₃	0.113405	88.703996	0.0729655	97.11433	0.04804	104.763116
2CH₃	0.113755	101.88542	0.049729	117.785713	0.052215	119.67187
2CN	0.113155	101.60529	0.058938	123.65009	0.042025	136.018323
2NH₂	0.111095	94.05098	0.0690815	109.64964	0.039355	119.50328
CN, NH₂	0.103355	97.67138	0.0708145	115.84723	0.044035	129.32406

Table 2: Predication of Isomerization Temperature IT by the Correlations Obtained.

Substituent	IT (oC)a	IT3 (oC)b	IT4 (oC)c	IT5 (oC)d	IT6 (oC)e	IT7 (oC)f	IT8 (oC)g	IT9 (oC)h	IT (oC)i
NH₂	25	67	48	107	78	52	39	27	113
OH	80	79	129	80	86	70	96	96	-
OCH₃	110	88	88	105	93	85	77	95	-
CH₃	180	155	172	119	140	192	173	145	170
H	200	157	216	100	141	195	201	152	-
Cl	150	173	134	149	153	-	161	139	-
CN	155	311	51	291	249	-	201	159	-
Br	180	209	125	181	178	-	180	184	-
OTMS	100	97	113	101	100	100	99	106	-
CHO	150	341	- 46	357	271	-	162	157	123
F	-	98	190	68	100	101	146	207	143
CF₃	-	199	159	158	171	-	194	211	156
-CH=CH₂	-	368	- 48	378	289	-	178	142	132
Ph	-	434	- 28	419	336	-	234	83	154
NH₂, NH₂	-	64	- 256	241	77	48	- 148	95	15
CN, CN	-	424	- 129	457	329	-	167	417	60
CN, NH₂	-	147	- 32	204	135	180	43	130	18
NO₂	-	280	- 57	315	228	-	116	153	109

a: experimental values taken from literature reference 5,6,7,8.   b,c,d,e,f,g: values predicted by equations 3,4,5,6,7,8,9 respectively   i: values predicted by reference 5.

Table 3: Energies of σ, σ*, π and π* orbitals of the substituted benzocyclo butenes.

Substituent	σ	σ*	π	π*
Cl	- 6.804	- 0.286	- 7.077	- 0.728
CN	- 7.038	- 0.459	- 7.284	- 0.773
NH₂	- 6.279	- 0.08	- 6.775	- 0.238
NO₂	- 7.008	- 0.511	- 7.308	- 0.825
OH	- 6.583	- 0.058	- 6.884	- 0.386
OCH₃	- 6.583	- 0.065	- 6.884	- 0.389
Br	- 6.911	- 0.309	- 6.948	- 1.017
CF₃	- 7.121	- 0.219	- 7.012	- 0.84
Ph	- 6.577	- 0.344	- 6.726	- 0.622
OTMS	- 6.562	- 0.096	- 6.699	- 0.56
F	- 7.076	- 0.173	- 7.076	- 0.813
NH₂, NH₂	- 6.508	- 0.033	- 6.667	- 0.461
CN, NH₂	- 6.698	- 0.502	- 7.274	- 1.073
H	- 6.651	+ 0.225	- 6.642	- 0.46
CH₃	- 6.647	+ 0.189	- 6.618	- 0.439
-CH=CH₂	- 6.678	- 0.024	- 6.623	- 0.627
CHO	- 6.842	- 0.599	- 6.842	- 1.222

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Conclusion

All the methods of prediction obtained were successfully applied to benzocyclobutenes in which substituent has a lone pair in the allyl position.

Conflicts of interest

There are no conflicts to declare.

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