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Electrostatic Potential Minimum of the Aromatic Ring as a Measure of Substituent Constant

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The molecular electrostatic potential minimum (V_{min}) observed for the arene π system of a substituted benzene derivatives is found to correlate linearly with the substituent constant $\sigma_p°$. The use of V_{min} as a measure of substituent effect is further confirmed by obtaining a linear correlation between V_{min} and a thermodynamic measure of the substituent effect obtained from an isodesmic reaction scheme involving benzene derivatives. V_{min} and the recently proposed electrostatic potential value at the nucleus of the para carbon atom (V_c) show a nearly identical trend toward quantification of substituent effects. Both quantities have been compared at three different density functional theory methods, viz. B3LYP/6-311+G(2d,2p), BPW91/6-311G(d,p), and B3LYP/aug-cc-pvtz, as well as the at the MP2/6-31+G(d,p) level of theory, showing remarkable consistency among them.

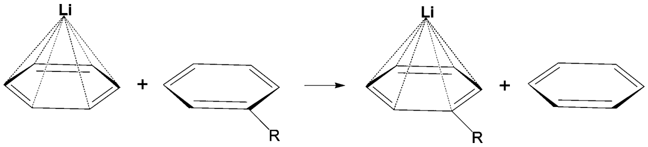
Introduction

In earlier studies we have shown that the electron-donating and -withdrawing effects of substituents as well as their orientation effects in electrophilic substitution reactions can be well understood in terms of the molecular electrostatic potential (MESP) minimum (V_{min}) observed for the arene π system.[1,2] For instance, the V_{min} values near the meta and para carbon atoms, derived from topography mapping of the electrostatic potential, showed good linear correlations with the Hammett σ_m and σ_p constants, respectively. Bobadova-Parvanova and Galabov[3,4] earlier attempted to correlate the hydrogen-bond energy of the HF molecule with carbonyl[3,4] and cyano[3] compounds with the electrostatic potential at the oxygen and nitrogen nuclei, respectively. They found a very good correlation coefficient (> 0.990 in all the cases) between these two quantities. In a similar spirit, Galabov, Elieva, and Schaefer[5] in a recent study employed the electrostatic potential at the para carbon atom of substituted benzenes (V_c) as a descriptor of the substituent effect. The V_c values showed a good linear correlation with respect to the $\sigma_p°$ values.[6] In the present work, we undertake a theoretical study to compare the V_{min} and V_c values of a variety of substituted benzene systems using different levels of theory.

Method

For the present study, benzene and its 14 monosubstituted derivatives, viz. $-NH_2$-, $-OCH_3$-, $-CF_3$-, $-CH_3$-, $-CHF_2$-, −Cl-, −F-, −CN-, −CCH-, −COCl-, −COF-, −CHO-, −COOH-, and $-NO_2$-substituted systems, have been selected. All calculations have been performed with density functional theory (DFT) and second-order Møller−Plesset perturbation theory (MP2) methods. The three different DFT methods considered in the present work are (i) B3LYP/6-311+G(2d,2p),[7,8] (ii) BPW91/6-311G(d,p),[9,10] and (iii) B3LYP/aug-cc-pvtz,[11] with MP2/6-31+G(d,p)[12,13] being the forth method. All of the above systems were fully optimized within these methods, and subsequently the corresponding wave functions were used for analysis of the three-dimensional (topographical) features of MESP.[14−16] In this study the most negative-valued MESP point (designated as V_{min}) for the arene π system is located. It may be noted that for systems with a plane of symmetry passing through the aromatic ring, a same-valued V_{min} will appear on both faces of the π system. Further, interaction of these benzene derivatives with the Li^+ cation is modeled at the B3LYP/6-311+G(2d,2p) level of theory. The energetics of the cation−π interaction obtained in terms of an isodesmic reaction[17,18] given in Scheme 1 is also used as a model for understanding the substituent effects.

SCHEME 1



Results and Discussion

(a) Results Obtained Using the B3LYP/6-311+G(2d,2p) Method. First, the results obtained using this method will be presented. The MESP features of benzene and its $-NH_2$-, $-OCH_3$-, $-CH_3$-, −F-, −CCH-, −Cl-, and $-CHF_2$-substituted derivatives are presented in Figure 1. Figure 2 depicts the MESP features of −COOH-, −CHO-, $-CF_3$-, −COCl-, −COF-, and −CN-substituted benzene systems. The V_{min} point located for the arene π system is also plotted for each system depicted in Figures 1 and 2. In the case of nitrobenzene, no negative potential is observed for the arene ring. In Table 1 the V_{min} values, the distance of V_{min} from the nearest two atoms on the arene ring, the relative V_c values with respect to benzene, and the $\sigma_p°$ values are also displayed. The relative values of V_c are

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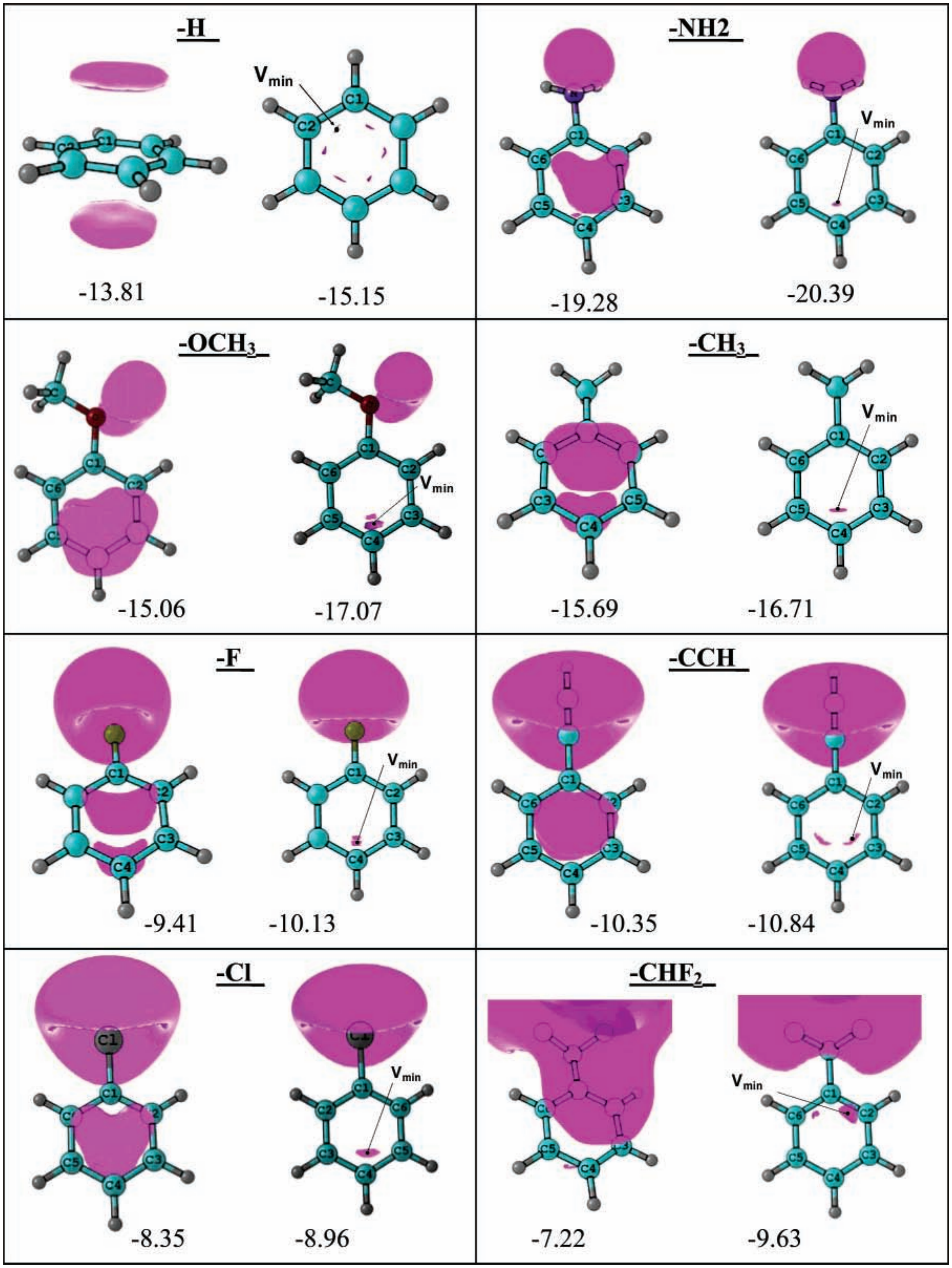

Figure 1. Two different MESP isosurface values of benzene and some substituted benzenes (each isosurface value in kcal/mol is given at the bottom of the structure). Location of the most negative-valued point $V_{\min}$ is also depicted. See also Table 1 for these $V_{\min}$ values and distances of the MESP minimum position from the nearest two atoms.

used because their absolute values are much larger than the $V_{\min}$ values. The absolute value of V_c for benzene is −9271.89 kcal/mol at the B3LYP/6-311++G(2d,2p) level of theory.

The 3-D plots of MESP given in Figures 1 and 2 are useful for obtaining a quick view of the direction of electron flow in the system as a result of various substitutions. As expected, the electron-donating groups $-NH_2$, $-CH_3$, and $-OCH_3$ show electron flow toward the arene ring as these systems have a more negative $V_{\min}$ than that of benzene. On the other hand, the rest of the substituents have a net electron-withdrawing effect on the arene ring. The electron-donating substituents and the halogen-substituted systems show the location of $V_{\min}$ near the para carbon atom. On the other hand, except the $-CHF_2$-substituted system, all remaining systems with electron-

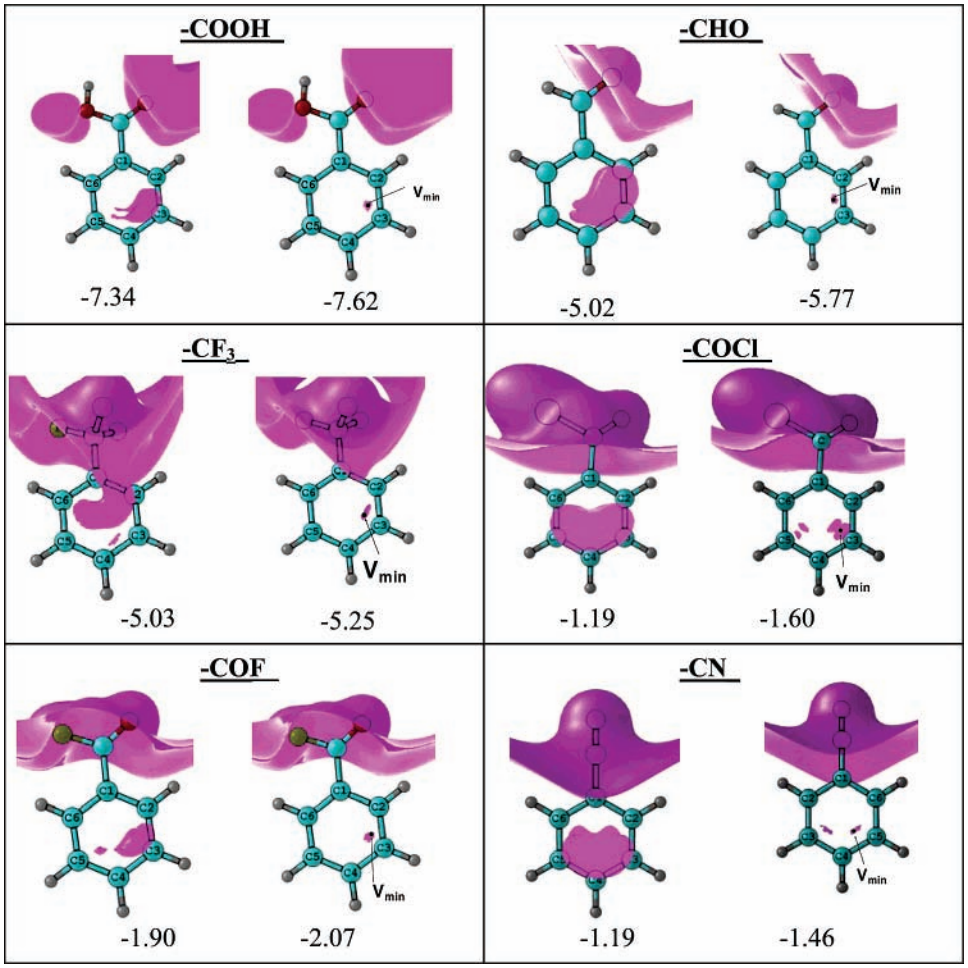

Figure 2. Two different MESP isosurface values of substituted benzenes (each isosurface value in kcal/mol is given at the bottom of the structure). Location of the most negative-valued point $V_{\min}$ is also depicted. See also Table 1 for $V_{\min}$ values and distances of the MESP minimum position from the nearest two atoms.

TABLE 1. $V_{\min}$ (in kcal/mol) and the Distances of the $V_{\min}$ Point from the Nearest Two Atoms (in Angstroms) at the B3LYP/6-311++G(2d, 2p) Level[a]

R	$V_{\min}$	distance 1	distance 2	V_c	$\sigma_p°$
$-NH_2$	−20.39	1.9270 (p-C)	2.1789 (m-C)	−3.15	−0.33
$-OCH_3$	−17.13	1.9350 (p-C)	2.1809 (m-C)	−0.71	−0.13
$-CH_3$	−16.77	1.9972 (p-C)	2.1803 (m-C)	−2.02	−0.12
−H	−15.15	2.1032 (C1)	2.1032 (C2)	0.00	0.00
−CCH	−10.89	2.1256 (m-C)	2.1820 (p-C)	5.41	0.22
−F	−10.17	2.0208 (p-C)	2.2716 (m-C)	8.69	0.20
$-CHF_2$	−9.73	2.2212 (o-C)	2.2844 (i-C)	8.11	0.35
−Cl	−9.05	2.0843 (p-C)	2.3001 (m-C)	9.19	0.24
−COOH	−7.64	2.1151 (m-C)	2.2312 (o-C)	8.40	0.44
−CHO	−5.81	2.1505 (m-C)	2.1831 (o-C)	10.97	0.47
$-CF_3$	−5.30	2.2202 (m-C)	2.3312 (o-C)	12.70	0.53
−COF	−2.12	2.2001 (m-C)	2.3609 (o-C)	15.32	0.70
−COCl	−1.67	2.2292 (m-C)	2.3737 (o-C)	15.92	0.69
−CN	−1.46	2.2714 (m-C)	2.3578 (p-C)	17.08	0.71
$-NO_2$				19.42	0.81

[a] p-C, m-C, and o-C are the para, meta, and ortho carbon atoms, respectively. V_c (in kcal/mol) and $\sigma_p°$ values are also depicted. See the Supporting Information for the geometry of the systems and coordinates of the $V_{\min}$ points.

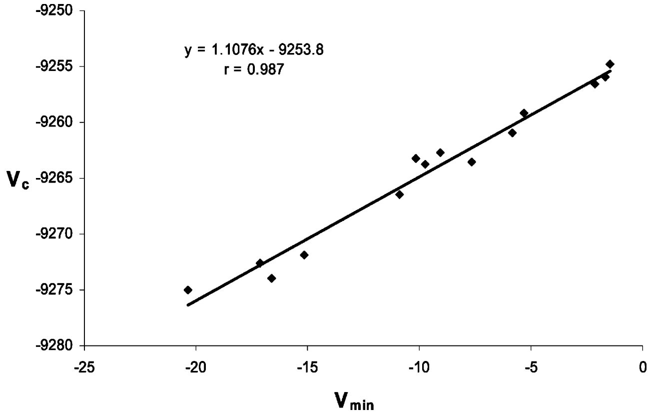

Figure 3. Relationship between $V_{\min}$ and V_C values.

withdrawing groups show the $V_{\min}$ position close to the meta carbon atom.

Both $V_{\min}$ and V_c show nearly the same trend as these two quantities can be correlated using a linear equation with a correlation coefficient $r = 0.987$ (Figure 3). Moreover, similar to the linear correlation of V_c and $\sigma_p°$ obtained by Schaefer et al.,[5] $V_{\min}$ also shows a very good linear relationship with the substituent constant $\sigma_p°$ (Figure 4). The $\sigma_p°$ values were taken from the compilation of Exner.[6] These correlations suggest that both quantities have almost equal potential to be used as a measure of the substituent effect. However, compared to a nuclei-centered quantity V_c, $V_{\min}$ gives a more quantitative knowledge about the π character of the system as the visual inspection of MESP around the vicinity of a $V_{\min}$ (Figures 1 and 2) brings out the electron-rich regions of a molecule. Such regions are often considered as centers of electrophilic attack.[15,19,20] In formation of weak intermolecular complexes

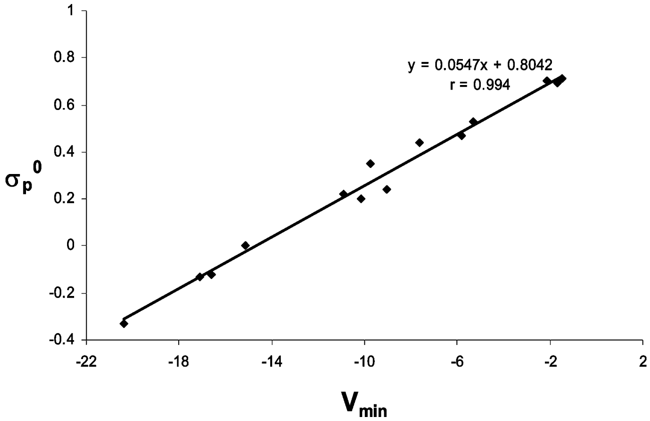

Figure 4. Relationship between V_{min} and $\sigma_p°$ constants.

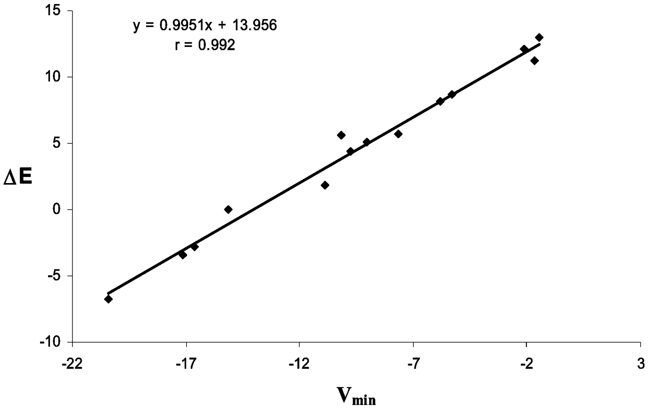

Figure 5. Relationship between V_{min} and ΔE values.

TABLE 2. Energetics of the Reactions (in kcal/mol) Presented in Scheme 1 at the B3LYP/6-311++G(2d, 2p) Level[a]

R	ΔE	d_{arene}	$d_{p-C}/d_{m-C}/d_{o-C}/d_{i-C}$
$-NH_2$	−6.76	1.825	2.239 (d_{p-C})
$-OCH_3$	−3.41	1.835	2.253 (d_{p-C})
$-CH_3$	−2.83	1.823	2.283 (d_{p-C})
$-H$	0.00	1.836	2.308
$-CCH$	1.82	1.847	2.308 (d_{p-C})
$-F$	5.58	1.874	2.293 (d_{p-C})
$-CHF_2$	4.38	1.871	2.319 (d_{i-C})
$-Cl$	5.13	1.859	2.307 (d_{p-C})
$-COOH$	5.74	1.859	2.322 (d_{m-C})
$-CHO$	8.19	1.867	2.323(d_{o-C})
$-CF_3$	8.71	1.885	2.328(d_{i-C})
$-COF$	12.12	1.882	2.340 (d_{m-C})
$-COCl$	11.26	1.876	2.337 (d_{m-C})
$-CN$	12.97	1.892	2.344(d_{p-C})
$-NO_2$	14.94	1.900	2.342(d_{p-C})

[a] The distance of Li^+ (in Ångstroms) from the centroid of the arene ring (d_{arene}) and the nearest carbon atom (d_{p-C}, d_{m-C}, d_{o-C}, and d_{i-C} for para, meta, ortho, and ipso carbon atoms, respectively).

comprising C−H···π and O−H···π interactions as well as in formation of water-linked hydrogen-bonded complexes, the location and magnitude of V_{min} is found to correlate with the strength and direction of the hydrogen-bond interactions.[21−24] In other words, to understand the interactive behavior of electron-rich molecules, the 3-D feature of MESP is more effective when V_{min} is used as a descriptor than V_c because the latter is confined only to the nuclei.

To further confirm the interactive behavior of the molecules and its relationship with the V_{min} values, the energy change (ΔE = sum of the energy of products − sum of the energy of reactants) associated with the isodesmic reaction presented in Scheme 1 is calculated. This reaction is expected to give a very good measure of the substituent effect as it compares the binding of Li^+ to benzene with that of the arene ring of a substituted benzene. The calculated ΔE values are presented in Table 2, which shows that in the case of systems with electron-donating substituents Li^+ binds more strongly than benzene, whereas in the case of halogens and electron-withdrawing systems, the binding of Li^+ is weaker than that found in benzene. In fact, these ΔE values show a very neat linear correlation (Figure 5) with the calculated V_{min} values ($r = 0.992$). This further confirms that V_{min} can be used as a substituent constant or a measure of the substituent effect.

In general, the distance of Li^+ from the center of arene ring (d_{arene}) follows a linear correlation with the ΔE values ($r = 0.954$). The most electron-rich arene ring of aniline shows the shortest d_{arene} value of 1.825 Å, while the most electron-deficient nitrobenzene showed a d_{arene} value of 1.900 Å. In Table 2 the distance of Li^+ from the nearest carbon atoms is also depicted, and as we can see, aniline has the shortest distance (2.239 Å), while the longest distance (2.344 Å) is found for acetonitrile. It may be noted that the distance of V_{min} from the nearest carbon atom (Table 1) follows a very similar trend as it shows the shortest distance of 1.927 Å in aniline while the longest distance of 2.271 Å in acetonitrile. In fact, the distance between Li^+ and the nearest carbon atom and that between V_{min} and the nearest carbon atom showed a good linear relationship ($r = 0.946$). Moreover, in most of the systems the position of Li^+ as well as the position of V_{min} with respect to the nearest carbon atom was the same (R = $-CHF_2$, $-CF_3$, $-CCH$, and $-CN$ are exceptions). In the case of $-CHF_2$- and $-CF_3$-substituted systems, Li^+ is nearest to the ipso carbon atom, which can be attributed to the attractive interactions from the lone pair electrons of fluorine atoms. Since the para position is between the two meta positions and Li^+ is equidistant from both meta positions, the shorter distance of Li^+ to the para carbon atom in $-CCH$- and $-CN$-substituted systems can be mainly attributed to a geometrical effect rather than an electronic effect. The above results on V_{min} suggest that the electronic effect of a substituted aromatic ring is most felt at around 2.0 Å away from the ring plane. Therefore, a small cationic species such as Li^+ prefers to coordinate to the aromatic ring at around the same distance.

(b) Results Obtained Using Other Methods. The V_{min} and relative V_c values obtained using methods (ii) (BPW91/6-311G-(d,p)), (iii) (B3LYP/aug-cc-pvtz), and (iv) (MP2/6-31+G(d,p)) are presented in Table 3. In all cases V_{min} and V_c follow a linear trend as the r value is found to be 0.995, 0.993, and 0.991 for methods ii, iii, and iv, respectively. Both the B3LYP/6-311+G-(2d,2p) (method i) and the B3LYP/aug-cc-pvtz (method iii) methods show nearly the same values for both V_{min} and V_c. However, in general, the higher level method iii gives a slightly less negative V_{min} and V_c compared to method i.[25] On the other hand, compared to method i, V_{min} values obtained from methods ii and iv are more negative. For instance, between method i and method ii, V_{min} values show a maximum difference of 3.96 kcal/mol in the case of aniline, whereas between method i and method iv, toluene shows the highest deviation of 3.75 kcal/mol. The V_{min} values obtained using the DFT method BPW91/6-311G(d,p) and the ab initio method MP2/6-31+G(d,p) are very close for all systems, whereas these two methods differ in their V_c values by an average amount of 38.00 kcal/mol. The V_{min} values obtained from methods ii, iii, and iv also show very

TABLE 3. V_{min} and Relative V_c Values (in kcal/mol) Obtained Using Different Methods[a]

	BPW91/6-311G(d,p)		B3LYP/aug-cc-pvtz		MP2/6-31+G(d,p)	
R	V_{min}	V_c	V_{min}	V_c	V_{min}	V_c
$-NH_2$	−24.35	−10.32	−19.14	−9.03	−23.47	−8.54
$-OCH_3$	−20.02	−5.55	−15.88	−5.23	−20.02	−4.96
$-CH_3$	−19.26	−2.98	−15.37	−3.19	−20.52	−3.64
−H	−17.44	0.00	−13.74	0.00	−18.64	0.00
−CCH	−13.18	5.73	−9.79	5.57	−13.99	6.95
−F	−12.74	3.99	−9.10	4.23	−12.17	5.89
$-CHF_2$	−12.74	7.43	−8.91	7.90	−13.11	9.36
−Cl	−11.11	7.36	−7.84	6.62	−11.80	7.89
−COOH	−10.60	9.87	−6.71	10.77	−10.29	13.56
−CHO	−8.09	13.46	−4.96	13.68	−8.97	15.18
$-CF_3$	−8.03	12.26	−4.39	12.77	−7.53	15.38
−COF	−4.71	17.29	−1.38	17.81	−4.08	21.26
−COCl	−3.01	19.84	−1.00	18.50	−4.89	20.42
−CN	−3.83	17.70	−0.63	17.63	−3.77	20.53
$-NO_2$	−2.38	19.59		20.25	−0.75	25.20

[a] The absolute V_c values of benzene at BPW91/6-311G(d,p), B3LYP/aug-cc-pvtz, and MP2/6-31+G(d,p) are −9272.11, −9266.28, and, −9236.03 kcal/mol, respectively.

good linear correlations with the $\sigma_p°$ values (r value is 0.989, 0.992, and 0.989 for methods ii, iii, and iv, respectively). This means that V_{min} and the corresponding 3-D features of MESP show remarkable consistency among the different levels of theory used in the present work.

Conclusions

The MESP minimum (V_{min}) values located for the arene π system of several substituted benzene systems are analyzed with three DFT methods and one ab initio (MP2) method. In all cases the V_{min} value gives a very good measure of the electron-donating/withdrawing power of a substituent on the arene ring as it exhibits a very good linear relationship with the substituent constant $\sigma_p°$. Both V_{min} and V_c follow nearly the same trend in various substituted benzene derivatives. Although both quantities can be used as a measure of the substituent effect, V_{min} has an added advantage as it reflects the location of the electron-rich centers of the molecules in three dimensions.

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Supporting Information Available: Cartesian coordinates and absolute energies of optimized structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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