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Understanding the Holleman Rule in the Electrophilic Substitution Reaction Using Parr Functions

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ABSTRACT

The regioselectivity in electrophilic substitution reactions of phenol, iodine benzene, and some other analogues were studied out using density functional theory with B3LYP/6-31G(d). Positional selectivity namely o, m and p were predicted using local nucleophilic Parr functions and the Holleman rule has been examined by the Parr functions. The result obtained is in good agreement with this rule and is correctly predicted by Parr functions.

Keywords: Holleman rule, Regioselectivity, DFT, B3LYP/6-31 (d), Electrophilic substitution reactions, Parr functions

INTRODUCTION

Although benzene is an unsaturated compound, it gives difficulty in addition reactions. On the other hand, substitution reactions are easy [1]. Experience shows that these reactions does not depend on the incoming substituent (E) but depends on the fixed substituent (Y) [2].



A group that enriches the aromatic nucleus with electrons (electron donor) and makes the cycle more reactive than benzene (faster reaction) is called the activating group [3]. A grouping which reduces the electron density on the aromatic nucleus (electron attractor) and which makes the cycle less reactive than benzene (smaller speed) is called a deactivating group [4-6]. According to rules of Holleman: An electron donor group is activating, ortho- and para-orienting, the para orientation being generally favored. An electron withdrawing group is deactivating, meta-orienting. Halogens are deactivating, ortho- and para-orienting (Table 1).

Table 1. Wain groups activating and deactivating						
	Substitute	Electronic effect				
	-R	+I	activation			
Ortho and para	-OR, $-NR_2$ (R= H or alkyl)	-I and +M				
	-F, -Cl, -Br, -I	-I and +M				
meta	-COOR (R=H, alkyl, OH, OR) -CN, -NO ₂ , -SO ₃ H	H, OR) H -I and -M				
	-NR,	-I				

 Table 1: Main groups activating and deactivating

Our research has focused on the study of the molecular mechanism of electrophilic substitution reactions in order to shed light on the factors controlling the regioselectivity. Herein, a DFT study of the electrophilic substitution reactions in benzoic compounds (Figure 1) has been carried out in order to explain the experimental outcomes observed. In addition, the rule of Holleman has been also examined in order to investigate the role of the groups activating and deactivating in these reactions.



Figure 1: The benzene compounds studied

COMPUTATIONAL METHODOLOGY

All computations were carried out with the Gaussian 09 suite of programs [7], using the B3LYP functional [8,9] together with the standard 6-31G(d) basis set [10]. The optimizations were carried out using the Berny analytical gradient optimization method [11,12]. The global electrophilicity index [13], ω , is given by the following expression, $\omega = (\mu^2/2\eta)$, in terms of the electronic chemical potential, μ , and the chemical hardness, η . Both quantities may be approached in terms of the one-electron energies of the frontier molecular orbitals HOMO and LUMO, $\varepsilon_{\rm H}$ and $\varepsilon_{\rm L}$, as $\mu = (\varepsilon_{\rm H} - \varepsilon_{\rm L})/2$ and $\eta = (\varepsilon_{\rm L} - \varepsilon_{\rm H})$, respectively [14,15]. The empirical (relative) nucleophilicity index [16,17] *N*, based on the HOMO energies obtained within the Kohn–Sham scheme [18], is defined as N=E_{HOMO} (*Nu*) - E_{HOMO} (*TCE*), where tetracyanoethylene (TCE) is the reference, because it presents the lowest HOMO. This choice allows conveniently to hand a nucleophilicity scale of positive values. Nucleophilic P_k^+ and electrophilic P_k^+ Parr functions [19-25] were obtained through the analysis of the Mulliken atomic spin density (ASD) of the corresponding radical cations or anions, respectively. The local nucleophilicity indices were evaluated using the following expression: N_x = NP_x⁻.

RESULTS

The present work has been study aromatic electrophilic substitution reactions of the benzene substituted to understand high regioselectivity using Parr functions.

The global DFT indices, namely the electronic chemical potential μ , chemical hardness η , electrophilicity ω and nucleophilicity N, are given in Table 2 and the nucleophilic P_k^- Parr functions for the benzene compounds 1-15, are included in Table 3.

System	μ	η	Ν	ω				
1	-3.23	6.47	2.64	0.80				
2	-3.58	6.17	2.44	1.04				
3	-3.46	6.24	2.53	0.96				
4	-3.53	6.37	2.90	0.98				
5	-3.42	6.38	2.50	0.92				
6	-3.12	6.54	2.71	0.74				
7	-4.04	5.36	2.90	1.52				
8	-4.08	5.15	2.97	1.61				
9	-4.07	5.26	2.41	1.57				
10	-4.32	5.23	2.17	1.90				
11	-4.19	5.77	2.03	1.52				
12	-4.24	6.32	1.70	1.42				
13	-2.92	5.84	1.86	0.73				
14	-5.16	5.16	2.09	2.43				
15	-1.70	5.87	4.98	0.24				
NO ₂ ⁺	-5.17	5.99	1.35	2.23				

 Table 2: B3LYP/6-31G(d) electronic chemical potential, chemical hardness , electrophilicity and nucleophilicity in eV, of the benzene substituted compounds 1-15

Table 3: B3LYP/6-31G(d) the nucleophilic Parr function and the local nucleophilicity in eV, of the benzene compounds 1-15

System	P_o^-	P_m^-	P_p^-	No	N _m	N_p
1	0.12	-0.04	0.45	0.49	-0.12	1.21
2	0.14	-0.07	0.34	0.28	-0.19	0.85
3	0.08	-0.03	0.38	0.20	-0.07	0.96
4	0.07	-0.02	0.39	0.21	-0.06	1.13
5	0.08	-0.03	0.48	0.22	-0.07	1.22
6	0.07	-0.02	0.46	0.21	-0.08	1.27
7	-0.05	0.18	0.06	-0.17	0.53	0.20
8	-0.02	0.15	0.15 O-(0.53)	0.05	0.44	0.44
9	-0.05	0.19	0.10	-0.15	0.57	0.31
10	-0.10	0.22	0.18	-0.22	0.49	0.39
11	-0.04	-0.06	-0.008 O-(0.53)	-0.09	-0.14	-0.01
12	-0.08	0.14	0.11	-0.13	0.25	0.18
13	0.02	-0.005	0.39	0.03	-0.009	0.72
14	0.21	0.29	-0.12	0.51	0.59	-0.25
15	0.36	0.45	-0.09	1.81	2.25	-0.47

DISCUSSION

Analysis of the reactivity indices of the reactants and local Parr functions

The electronic chemical potential of the benzene compounds 1-15, μ =-3.23, μ =-3.58, μ =-3.46, μ =-3.53, μ =-3.42, μ =-3.12, μ =-4.04, μ =-4.08, μ =-4.07, μ =-4.32, μ =-4.19, μ =-4.24, μ =-2.92, μ =-5.16 and μ =-1.70 (eV), are higher than that of NO₂⁺, μ =-5.17 (eV), indicating that along these polar electrophilic aromatic substitution reaction (EASR), the GEDT will flux from the benzene compounds 1-15 toward nitro.

The electrophilicy ω index of the benzene compounds 1-15, varies between 0.24 and 1.9 and the nucleophilicity *N* index varies between 1.70 and 4.98, the electrophilicy ω index of the nitro 2.23 and the nucleophilicity *N* index 1.35. Consequently, the benzene compounds 1-15 are classified as a strong nucleophiles and nitro as electrophile.

Recently, Domingo proposed the electrophilic P_k^+ and nucleophilic P_k^- Parr functions, derived from the changes of spin electron density reached via the GEDT process from the nucleophile to the electrophile, as powerful tools for the study of local reactivity in polar processes. Accordingly, the nucleophilic P_k^- Parr functions for the benzene compounds 1-15, are included in Table 2.

Analysis of the nucleophilic P_p^- Parr functions of the benzene compounds 1-6 indicates that the carbon atom in position para is the most nucleophilic centre, $P_p^-=0.45$ (1), $P_p^-=0.45$ (1), $P_p^-=0.34$ (2), $P_p^-=0.38$ (3), $P_p^-=0.39$

(4), $P_o^-=0.48$ (5) and $P_o^-=0.46$ (6) being several times as electrophilically activated than the P_o^- and P_k^- positions. On the other hand, analysis of the nucleophilic P_k^- Parr functions at compounds 7-10, 14-15 indicates that the carbon in position meta is the most nucleophilic center, $P_m^-=0.40$, is very as nucleophilically activated as the P_p^- and $P_p^$ positions. But for compounds 11, 12 the acid group is very reactive than aromatic positions, in clear agreement with the experimental observation.

CONCLUSION

The regioselectivity of aromatic electrophilic substitution reactions of the benzene substituted compounds **1-15** were studied using DFT/B3LYP/6-31(d). Analysis of the global electrophilicity and nucleophilicity indices showed that of the benzene compounds 1-15 behaves as a nucleophile. The regioselectivity found experimentally was confirmed by local Parr functions, in clear agreement with the Holleman rule.

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