

Origin of Deactivation of Chlorobenzene in Aromatic Electrophilic Substitution

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Deactivation of chlorobenzene in aromatic electrophilic substitution may arise from the unique energy level of chlorine lone pair orbital which is *higher* than the subjacent π -molecular orbital of benzene (π_1), in sharp contrast to the widely accepted concept that inductive electron-withdrawing property ($-I$ effect) of chlorine should be responsible for ring deactivation. The role of π_1 in protonation at C-4 is found to be as important as the frontier orbital (π_2).

Anomalous reactivity of chlorobenzene in electrophilic substitution reaction is generally explained in terms of antagonistic operation of resonance and inductive effects: while the former influences regioselectivity *via* electron donation from the lone-pair into the π -system ($+M$ effect), the latter is responsible for deactivation of the benzene ring *via* reverse electron movement due to a high electronegativity of chlorine atom ($-I$ effect), thereby destabilizing the intermediate cationic σ -complex.¹

The above textbook explanation is apparently inconsistent with the reactivity of fluorobenzene which is known to be often more reactive than benzene or heavier halobenzenes (halogen = Cl, Br, I) in a variety of aromatic electrophilic substitution despite the fact that fluorine is more electronegative than chlorine.^{1, 2} It is therefore obvious that the logic of the conventional explanation was constructed ignoring the fluorobenzene cases. Furthermore the well known experimental evidence reported by Taft in 1965 that chlorine atom stabilizes methyl cation more effectively than fluorine atom³ strongly suggests that ring deactivation due to chloro substituent cannot be rationalized by destabilization of intermediate cationic σ -complex. In fact the experimental proton affinities of fluoro- and chlorobenzenes are 180.7 and 180.0 kcal mol⁻¹, respectively.⁴ These values are not much different from that of benzene (179.3 kcal mol⁻¹).⁴ In addition, the frontier orbital theory fails to explain the peculiar behavior of the halobenzenes since their first ionization potentials, which are regarded as a good measure of their highest occupied molecular orbital (HOMO) levels, are uniformly lower than that of benzene.⁵ This paper describes a new proposal based on the assumption that the subjacent (low-lying) π -molecular orbital (π -MO) should be responsible for deactivation of the benzene ring of chloro- or bromobenzene.

Ab initio calculations were performed at the Hartree-Fock level using 6-31G(d) basis set for 2nd- and 3rd-row elements and Huzinaga's 43321/4321/311* basis for Br⁶ on mono-substituted benzenes (PhX; X=H, Me, OH, F, Cl, Br) as well as the model reactions between PhX and proton as an electrophile. Benzene itself has two degenerate occupied π -MO's (π_2 and π_3) as frontier orbitals and a subjacent π -MO (π_1) with total symmetry (Figure 1). While the energy level of the latter (-13.55 eV) is lower than those of the former (-9.00 eV), its spatial extension, as quantitatively evaluated by exterior electron density (EED)⁷ (4.42%), is comparable to those of π_2 and π_3 (4.37 and 4.36%, respectively). It is hence expected that the subjacent π orbital (π_1)

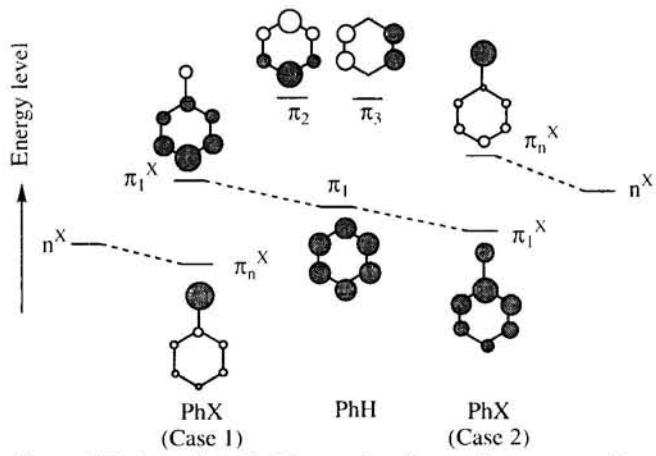


Figure 1. Schematic orbital interaction diagram between π_1 of benzene (PhH) and lone pair electrons of substituent (n^X) in mono-substituted benzene (PhX). Case 1: n^X is lower than π_1 (X = Me, OH, F). Case 2: n^X is higher than π_1 (X = Cl, Br). Phase property of MO is indicated with open or filled circles, the size of which correspond to relative contribution of p-orbitals.

should play an important role in aromatic electrophilic substitution reactions.

Driving force of a reaction is generated chiefly by orbital interaction between reactants, which depends not only on spatial expanse but also energy difference between interacting orbitals.⁸ Introduction of a substituent into benzene ring causes a unique change in energy level of the subjacent π_1 orbital. Figure 1 shows two cases of schematic orbital interaction diagram between π_1 of benzene (PhH) and lone pair electrons of substituent X (n^X) in a mono-substituted benzene (PhX). Case 1, in which n^X is lower than π_1 , leads to an energy increment of π_1 . The resulting MO (π_1^X) polarizes toward C-4 through mixing with other (occupied and vacant) π -MO's *via* secondary orbital interaction. On the other hand, Case 2, in which n^X is higher than π_1 , leads to energy reduction of π_1 . Unlike Case 1, polarization of the resulting MO (π_1^X) occurs toward C-1. It should be noted that spatial extension of π_1^X at C-4 in Case 2 should be significantly reduced, whereas in Case 1 the π electron density should reach maximum at C-4. Apparently Case 1 corresponds to X = OH, Me or F and Case 2 to X = Cl or Br. It is hence suggested that in the latter case two salient features relevant to π_1 , namely energy reduction and electron density diminution at C-4, should be responsible for ring deactivation. The energy levels of π_2 and π_3 for these mono-substituted benzenes exhibit no significant difference (-8.41 ~ -9.52 eV), while those for π_1 exhibit the trend predicted by the simple theory (-13.55, -13.20, -13.04, -13.74⁹, -14.76, and -14.33 eV for X = H, Me, OH, F, Cl and Br, respectively). It should be emphasized here that when lone pair orbital lies slightly higher than π_1 as seen in Case 2 (X = Cl and Br), relative contribution from ring π -orbital diminishes, which should cause ring deactivation.

Importance of the subjacent π -MO (π_1) to ring reactivity is further substantiated by two other quantities calculated at the 6-31G(d) level. Atomic exterior electron density⁷ at C-4 (EED(C4)) representing spatial extension of an MO at C-4 should control the magnitude of orbital overlap with an electrophile. Energy reduction of π -MO's upon proton attack at C-4 to form the corresponding σ -complex (Δ) may be a reasonable measure of the magnitude of the orbital interaction between C-4 of PhX and H⁺. Energy reduction due to electrostatic field in the reaction can be estimated by Δ of π_3 since π_3 has marginal orbital extension at C-4 (EED(C4) = ~0.12 %) and is reasonably constant for all substituents (Δ = ~ -6 eV). The values of EED(C4) for π_2 as a frontier orbital are considerably large compared to those for other π -type MO's, although slight reduction is observed for X = Cl and Br (1.07 and 0.84%, respectively), leading to appreciable reduction in Δ (-7.22 and -6.56 eV, respectively). The same argument can be applied to π_1 : EED(C4)'s for Cl and Br are much smaller than those of other substituents (0.33 and 0.48%, respectively) and so are the Δ values (-7.24 and -7.37 eV, respectively). Decrease of the latter may be attributed in part by reduction in energy level of π_1 (-14.76 and -14.33 eV for Cl and Br, respectively). Consequently reactivity reduction in π_1 and π_2 should be significant in cases for X = Cl and Br.

Table 1. Atomic exterior electron density at C-4 (EED(C4)) for substituted benzenes (PhX) and energy changes of π -type MO's for protonation at C-4 of PhX (Δ)^a

MO	Parameters ^b	Substituent (X)					
		H	Me	OH	F	Cl	Br
π_3	EED(C4)	0.13	0.12	0.12	0.12	0.12	0.12
	Δ	-6.19	-6.08	-6.19	-6.22	-5.93	-5.82
π_2	EED(C4)	1.23	1.19	1.16	1.23	1.07	0.84
	Δ	-8.40	-7.94	-7.94	-8.24	-7.22	-6.56
π_1	EED(C4)	0.71	0.77	0.83	0.74	0.33	0.48
	Δ	-8.35	-8.49	-8.37	-8.32	-7.24	-7.37

^aCalculated with 6-31G(d) basis sets for 2nd- and 3rd-row elements and Huzinaga's 43321/4321/311* basis for Br. See Figure 1 for orbital notations. ^bUnits: EED(C4) in % and Δ in eV.

It is surprising that contribution of subjacent orbital π_1 is as large as that of the frontier orbital π_2 in protonation, a representative and the simplest aromatic electrophilic substitution reaction. It should be particularly emphasized here that ring

deactivation should not occur because Cl and Br are electron-withdrawing. Rather, in sharp contrast to the conventional concept, the present theoretical investigation clearly suggested that the unique energy levels of the valence p orbitals of these elements, which are higher than that of benzene π_1 , is most likely to be the origin of ring deactivation. Namely, ring deactivation arises because Cl and Br are less electronegative than F or O.² To the best of our knowledge, this is the first example of a reaction in which a subjacent orbital is as important as a frontier orbital.

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References and Notes

- 1 R. Taylor, "Electrophilic Aromatic Substitution", John Wiley & Sons Ltd., Chichester (1990), p.46 and p.85.
- 2 L. C. Allen, *J. Am. Chem. Soc.*, **111**, 9003 (1989).
- 3 R. W. Taft, R. H. Martin, and F. W. Lampe, *J. Am. Chem. Soc.*, **87**, 2490 (1965). Stabilization energies of substituted methyl cation are 26 and 32 kcal mol⁻¹ for F and Cl, respectively.
- 4 E. P. Hunter and S. G. Lias, in NIST Standard Reference Database Number 69, Eds. W. G. Mallard and P. J. Linstrom, February 1997, National Institute of Standards and Technology, Gaithersburg MD, 20899 (<http://webbook.nist.gov>).
- 5 First ionization potentials for PhX (X = H, F, Cl, Br, I) are 9.25, 9.20, 9.10, 9.02, and 8.79 eV, respectively. K. Kimura, S. Katsumata, Y. Achiba, T. Yamazaki, and S. Iwata, "Handbook of HeI Photoelectron Spectra of Fundamental Organic Molecules", Halsted Press, New York (1981).
- 6 Structural optimizations were performed using the Gaussian 94 program (Gaussian, Inc., Pittsburgh, PA, 1997).
- 7 Exterior electron density (EED) is defined as a total electron density of an MO outside repulsive molecular surface defined by an assembly of spherical atoms having van der Waals radii (1.70 Å (C); 1.20 Å (H), 1.52 Å (O), 1.47 Å (F), 1.75 Å (Cl), 1.85 Å (Br)). Atomic EED is defined as the electron density of an MO for a specific atom integrated over the exterior subspace nearest to the van der Waals surface of the atom. Both these quantities are expressed in % unit for the sake of numerical convenience. K. Ohno, K., S. Matsumoto, and Y. Harada, *J. Chem. Phys.*, **81**, 2183 (1984).
- 8 a) G. Klopman, *J. Am. Chem. Soc.*, **90**, 223 (1968). b) L. Salem, *J. Am. Chem. Soc.*, **90**, 543 (1968). c) S. Inagaki, H. Fujimoto, and K. Fukui, *J. Am. Chem. Soc.*, **98**, 4054 (1976).
- 9 A small reduction in the energy of PhF may be attributed to electrostatic field caused by electronegative F.