

Teaching Electrophilic Aromatic Substitution: Enthalpies of Hydrogenation of the Rings of C_6H_5X Predict Relative Reactivities; ^{13}C NMR Shifts Predict Directing Effects of X

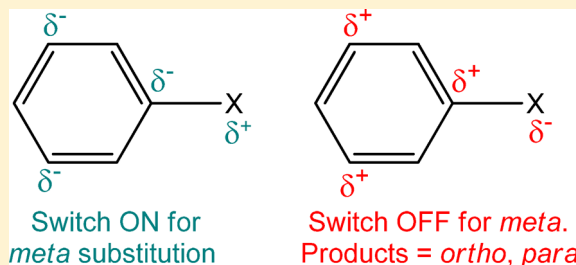
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S Supporting Information

ABSTRACT: The concept of establishing relative stabilities of alkenes by their enthalpies of hydrogenation is extended to the enthalpies of hydrogenation of the ring of substituted benzenes, C_6H_5X . Enthalpies of hydrogenation of the rings predict the ordering of their reactivities. p - ^{13}C NMR chemical shifts predict the directing effect of X, meta or ortho/para, as does the direction of the dipole of the C–X bond. Inclusion of these facts in organic chemistry curricula integrates and reinforces concepts known prior to reaching the topic on electrophilic aromatic substitutions.

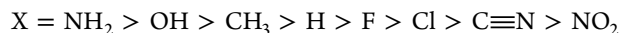
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INTRODUCTION

Undergraduate organic chemistry textbooks contain at least one chapter on electrophilic aromatic substitution. The reaction of an electrophile, E^+ , with X-substituted benzenes is generally described as proceeding via a carbocation intermediate.^{1–5} Whether the predominant products are ortho/para or meta depends on the nature of X.

The reactivity of various C_6H_5X is attributed to the electron donating or withdrawing ability of the substituent.^{1–5} Electron donating X increases the electron density of the ring and makes it more susceptible to attack by electrophiles or, the same to say, by imparting a greater tendency of the electrons of the ring to bond to the electrophile. The ordering of reactivities for various X is^{1–5}



Whether the carbocation intermediate is formed via a π or σ complex of the electrophile with the ring,^{6–8} its stability is also enhanced by electron donation by X and vice versa, and this stability affects the orientation of the substitution.

Alkenes are treated prior to the chapters on aromaticity in standard textbooks, and their enthalpies of hydrogenation (ΔH_{hyd}) are introduced at this point as a measure of stability along with heats of combustion.^{1–5} ΔH_{hyd} of benzene relative to that of three cyclohexenes is used to quantify the resonance stabilization of benzene. There are several articles related to the teaching of electrophilic aromatic substitution.^{9–13} However, until recently,¹⁴ ΔH_{hyd} of the ring of C_6H_5X had not been related to their relative reactivities, although many more complex relations have been proposed for rationalizing reactivities. These include the gap between SOMO and LUMO orbitals,¹⁵ theoretically calculated “activation hardness”

of the carbocation intermediate,¹⁶ theoretical calculations of π electron densities of the aromatic carbons,¹⁷ MO calculations,¹² and many others. Brown and Okamoto reported a good linear free energy relationship by plotting $\log(k_X/k_H)$ vs the σ_p^+ substituent constants of X.¹⁸ The σ_p^+ values were derived from rate data of reactions proceeding through carbocation intermediates, as is the case with electrophilic aromatic substitutions.

RESULTS AND DISCUSSION

Enthalpies of Hydrogenation

Class lectures on the findings presented here and in the handout (Supporting Information) expand on student knowledge of hydrogenations. ΔH_{hyd} of X-substituted benzenes to X-substituted cyclohexanes are obtained as the difference of their enthalpies of formation, $\Delta_f H^\circ$ (gas) at 298 K (eq 1).

$$\Delta H_{hyd} = \Delta_f H^\circ[C_6H_{11}X] - \Delta_f H^\circ[C_6H_5X] \quad (1)$$

The aim is to determine whether there is a correlation of ΔH_{hyd} with the ordering of reactivities of various C_6H_5X . ΔH_{hyd} cannot be obtained experimentally for some C_6H_5X . For example, nitrobenzene would be hydrogenated to cyclohexylamine rather than to nitrocyclohexane. Values of $\Delta_f H^\circ$ are available for several monosubstituted benzenes and for the similarly substituted cyclohexanes.¹⁹

The values of ΔH_{hyd} in kJ mol^{-1} , of the ring of the C_6H_5-X are ordered as follows: X = NH_2 , -185.7 ; OH, -192.4 ; CH_3 , -204.9 ; H, -208.4 ;²⁰ F, -220.5 ;¹³ Cl, -220.9 ; $C\equiv N$, -222.6 ; NO_2 , -227.8 .²¹ This ordering is identical to the ordering of

reaction rates for electrophilic aromatic substitutions (Figure 1).^{3,5} This ordering of the experimental ΔH_{hyd} was confirmed by high-level *ab initio* calculations (G4).²²

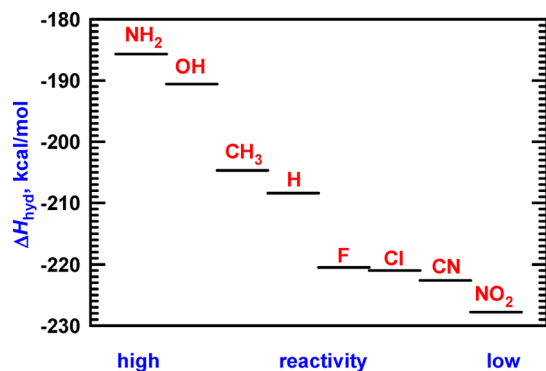


Figure 1. Plot of ΔH_{hyd} of the aromatic ring vs ordering of reactivities of $\text{C}_6\text{H}_5\text{-X}$.

Substituents other than those mentioned above are not included because $\Delta_r H^\circ$ values are not available,¹⁹ or strain is involved in the benzene and not in the cyclohexane, or there is conjugation of the substituent with the aromatic ring but not with the cyclohexane, e.g., styrene and vinylcyclohexane.

ΔH_{hyd} values reflect accurately the ring's susceptibility to reaction with an electrophile and, thus, the ordering of electron density of the ring (Figure 1). The deactivating effect of halogen substituents is often ascribed to their electronegativity. However, even though fluorine is the most electronegative, fluorobenzene is the most reactive^{10,13} and its ΔH_{hyd} value correctly predicts this.

The ΔH_{hyd} values predict the ordering of reactivities of various $\text{C}_6\text{H}_5\text{-X}$ with the same electrophile and reaction conditions, not the absolute values of relative reactivities k_X/k_H , which vary with different electrophiles.¹⁷ While reaction rates vary with different substituents, solvents, and catalysts, the ordering of reactivities remains unchanged. With eight different electrophiles, plots of $\log(k_X/k_H)$ vs σ_p^+ are linear but the slope ρ (sensitivity to the X substituent) varied dramatically from $\rho = -13.1$ to -2.4 .¹⁷ However, ρ is always negative, demonstrating that the reactivity ordering remains the same.

NMR Spectroscopy

In many undergraduate textbooks, spectroscopy is introduced prior to electrophilic aromatic substitution.²⁻⁵ Deshielding effects (lower electron density) shift ^{13}C NMR signals to higher δ (ppm) and vice versa. ΔH_{hyd} is linearly correlated to ^{13}C NMR shifts of the *para*-carbon of $\text{C}_6\text{H}_5\text{X}$ (Figure 2). All activating groups have ΔH_{hyd} less negative than -208.4 kJ mol⁻¹ of benzene and favor predominant ortho/para substitution. All others favor meta substitution, except for the halogens. F and Cl are off the line and appear unique; they are deactivating but ortho/para directing.

^{13}C NMR shifts of the *para*-carbons of various $\text{C}_6\text{H}_5\text{-X}$ are given in Table 1, along with the known directing effect of X, which is primarily ortho/para or meta. All $p\text{-}^{13}\text{C}$ NMR shifts less than δ 128.36 for benzene indicate correctly an ortho/para-directing effect of X, including that of the halogens. All others indicate correctly a meta-directing effect. For demonstrating generality, substituents not mentioned above are included in Table 1.

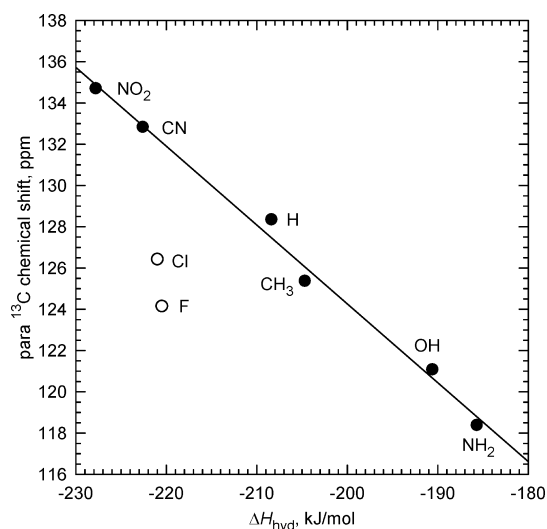


Figure 2. Plot of ^{13}C NMR chemical shifts vs ΔH_{hyd} of the aromatic ring.

Table 1. ^{13}C NMR Chemical Shifts of the *para*-Carbons and Known Directing Effects

$\text{C}_6\text{H}_5\text{-X}$	$p\text{-}^{13}\text{C}$, δ^a	Directing ^b
$\text{C}_6\text{H}_5\text{-NH}_2$	118.39	ortho/para
$\text{C}_6\text{H}_5\text{-OH}$	121.09	ortho/para
$\text{C}_6\text{H}_5\text{-CH}_3$	125.38	ortho/para
$\text{C}_6\text{H}_5\text{-F}$	124.16	ortho/para
$\text{C}_6\text{H}_5\text{-Cl}$	126.43	ortho/para
$\text{C}_6\text{H}_5\text{-Br}$	126.82	ortho/para
$\text{C}_6\text{H}_5\text{-H}$	128.36	
$\text{C}_6\text{H}_5\text{-CCl}_3$	130.24	meta
$\text{C}_6\text{H}_5\text{-CF}_3$	131.82	meta
$\text{C}_6\text{H}_5\text{-C}\equiv\text{N}$	132.84	meta
$\text{C}_6\text{H}_5\text{-CO}_2\text{CH}_3$	132.90	meta
$\text{C}_6\text{H}_5\text{-COCH}_3$	133.04	meta
$\text{C}_6\text{H}_5\text{-NO}_2$	134.71	meta

^aSource is ref 23. ^bKnown directing effects.

The direction of the dipole between the ipso carbon of benzene and the atom of the X-substituent bonded to it also predicts orientation of the substitution like an ON/OFF switch.¹⁴ When the negative end of the dipole is toward the ring, the switch is ON for predominant meta substitution, e.g., $\text{X} = -\text{NO}_2$, $-\text{CF}_3$, $-\text{C}(\text{O})\text{R}$, $-\text{CN}$, etc. It is OFF otherwise, and mostly ortho/para products are obtained, e.g., $\text{X} = -\text{NR}_2$, $-\text{OR}$, $-\text{F}$, $-\text{Cl}$, etc.

The information was presented in lectures and in a handout (Supporting Information) to two sections of introductory undergraduate organic chemistry (many majoring in pharmacy) and to one graduate-level (Master's) organic chemistry course. An assessment of student learning was performed using a survey where students were asked to provide anonymously their opinion of its impact.

Questions 1 and 6 are very general, while questions 2–5 are specific (Table 2). Apparently, this caused the difference in the ratings of the two groups. Student success in examinations for questions relevant to material treated here and in the handout was about the same as that for questions relevant to textbook material on electrophilic aromatic substitution.

Table 2. Results of Student Survey Responses

Statements for Response	Undergraduates, N = 38		Graduates, N = 10	
	Agree, %	Disagree, %	Agree, %	Disagree, %
Do you mostly agree or disagree with the following statements? I found the handout to be				
1. Confusing	42	58	10	90
2. Interesting	85	15	100	0
3. Helpful in understanding this general topic	87	13	100	0
4. Helpful in relating ΔH_{hyd} to reactivity	86	14	100	0
5. Helpful in integrating NMR and directing effects	81	19	100	0
6. Not helpful	36	62	10	90

CONCLUSIONS

Despite the large volume of research on electrophilic aromatic substitutions, the simple correlations presented here were not known until very recently and have not been used to reinforce and integrate concepts already known by undergraduates when electrophilic aromatic substitution is introduced. ΔH_{hyd} of the ring of $\text{C}_6\text{H}_5\text{X}$ correctly predict the ordering of reactivities. $p\text{-}^{13}\text{C}$ NMR shifts predict the directing effect of the substituent. The direction of the dipole of the $\text{C}_6\text{H}_5\text{-X}$ bond predicts the directing effect. By these three criteria the halogen substituents are not unique in their behavior. Thermochemistry is related to reactivity. An analytical technique (NMR spectroscopy) can be used to predict product distributions. Bond dipoles predict directing effects.

ASSOCIATED CONTENT

Supporting Information

Student handout. This material is available via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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