

Employing NMR Spectroscopy To Evaluate Transmission of Electronic Effects in 4-Substituted Chalcones

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In introductory college-level chemistry courses, the concepts of polarity and resonance are typically introduced to students by means of Lewis structures. Later on, the effect electron-donating or withdrawing substituents exert on a benzene ring and other conjugated systems is emphasized in organic chemistry classes. Although several experiments demonstrating the reactivities of monosubstituted benzenes toward electrophiles have been published in this *Journal* and elsewhere (1), few organic laboratory experiments quantitatively investigate the transmission of substituent effects in highly conjugated systems. Spectroscopic methods are especially useful for demonstrating the effectiveness of electronic transmission by substituents in conjugated π systems. Delocalization of the π electrons of α,β -unsaturated carbonyl compounds and its effect on the polarization of the carbonyl group are readily observed by infrared spectroscopy (2). Alternatively, perturbations in electron distribution result in changes in chemical shifts of protons or carbons investigated by nuclear magnetic resonance spectroscopy (2).

Transmission of electronic effects by substituents conjugated with α,β -unsaturated ketones can be quantitatively evaluated by observing changes in either the infrared stretching frequencies of the carbonyl group or the shielding/deshielding effects on the electronic environment of the vinylic protons or carbons. Chalcones (1,3-diphenyl-2-propen-1-ones) are easily accessible to undergraduate students by aldol condensation reactions between substituted acetophenones and benzaldehydes. The resulting α,β -unsaturated ketones are extensively conjugated, and the effects of substituents on the styryl ring can be measured by plotting chemical shift changes versus published Hammett substituent values (3–6). Alternatively, students in introductory courses can readily evaluate a substituent's ability to donate or withdraw electron density from the vinylic protons simply by comparing the chemical shift of the α -hydrogen of the 4-substituted system to that of *trans*-chalcone.

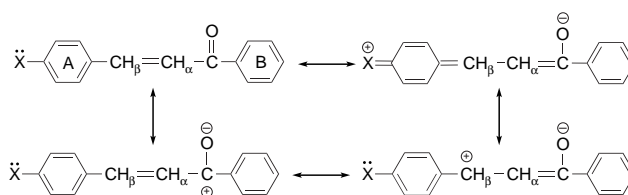
Table 1. ^1H Chemical Shifts of 4-Substituted Chalcones in CDCl_3

X	δH_α	δH_β
H	7.52	7.80
$\text{N}(\text{CH}_3)_2$	7.31	7.78
OCH_3	7.40	7.78
Cl	7.48	7.73
Br	7.50	7.72
CN	7.62	7.76
NO_2	7.66	7.82

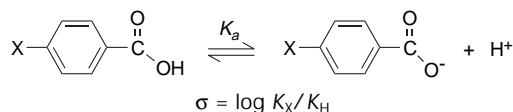
NOTE: Data represent ppm from TMS.

Theory

Substitution at the para-position of ring A by electron donors or electron acceptors will affect the electronic environment of the vinylic protons, H_α and H_β , as well as the vinylic and carbonyl carbons. Delocalization of the π electrons usually results in increased electron density on the carbonyl oxygen and in lower electron density at the β carbon. As a result, the β proton appears further downfield than the α proton (2).



The Hammett free-energy relationship has been used to evaluate transmission of electronic effects by para substituents on the styryl ring of chalcones (3–6). The Hammett substituent constant, σ_{para} , is a measure of the ease of ionization of para-substituted benzoic acids relative to the dissociation of benzoic acid (7).



Electron-withdrawing substituents will increase the rate of ionization and therefore have positive values of σ , whereas electron donors will impede the dissociation and have negative σ values. When electron-donating substituents are introduced at the para position of the styryl ring the shielding effect is enhanced: the α proton's signal is shifted upfield relative to the unsubstituted compound while the β proton remains relatively unperturbed (see Table 1). Electron-withdrawing substituents tend to shift the α proton's signal downfield.

Hammett electrophilic substituent constants, σ^+ , are used in systems where there is direct resonance participation by the substituent to an electron-deficient site (7). The σ^+ values have been shown to correlate very well with carbonyl stretching frequencies in IR experiments (4). Chemical shift measurements for H_α and H_β taken in CDCl_3 have similarly been reported to correlate well with Hammett σ_R values, which are considered to be more accurate at reflecting the resonance contribution of substituents (5). Carbon-13 chemical shifts of the alpha carbon are also strongly affected by resonance effects and substituent effects can be readily observed (6).

Experimental Procedure

Synthesis of 4-Substituted Chalcones

In a 25-mL Erlenmeyer flask equipped with a magnetic stir bar, dissolve 0.01 mol of the para-substituted benzaldehyde and an equimolar amount of acetophenone in 5 mL of 95% ethanol. To this solution, add 2 mL of 10% aqueous sodium hydroxide (CAUTION: sodium hydroxide is *very caustic* and can cause severe burns). Stir this mixture at room temperature for 15 to 60 min.¹ Formation of a precipitate, generally accompanied by a color change in the reaction mixture, is indicative of product formation.

When the reaction is complete, place the flask in an ice bath for 5 min. Add 25 mL of ice-cold water to the mixture and watch for precipitate formation.² Collect the colored product by filtration and wash it with small portions of cold water. Recrystallize the solid product from a minimum amount of hot 50% ethanol. Allow the solid to dry completely, weigh it, and determine its melting point. The ¹H NMR spectra are obtained from solutions of each compound in deuterated chloroform.

Physical Data for 4-Substituted Chalcones. *trans*-Chalcone, yellow crystals (mp 55–56 °C); *trans*-4-bromochalcone, yellow crystals (mp 127–128 °C); *trans*-4-chlorochalcone, yellow crystals (mp 112–114 °C); *trans*-4-cyanochalcone, yellow crystals (mp 154–56 °C); *trans*-4-*N,N*-(dimethyl)aminochalcone, orange crystals (mp 114–16 °C); *trans*-4-methoxychalcone, yellow crystals (mp 79–81 °C); *trans*-4-nitrochalcone, pale-yellow crystals (mp 164–165 °C).

Analysis of Data

Plot the difference in the chemical shifts of H_α of each substituted chalcone relative to chalcone ($\Delta \delta H_{\alpha} = \delta H_{\alpha}(X) - \delta H_{\alpha}(\text{chalcone})$) versus the appropriate Hammett substituent constant values. A linear plot should be obtained. A positive slope indicates that electron-donating groups stabilize the normal polarization of the carbonyl carbon by increasing electron density on the alpha carbon. Electron-withdrawing groups, on the other hand, cause deshielding of the protons on the alpha carbon. Little correlation is observed when $\Delta \delta H_{\beta}$ values are plotted versus σ^+ ; examination of the H_β chemical shift values presented in Table 1 suggests that the electronic environment is not significantly affected by the nature of the substituent on the styryl ring. The polarity of the carbonyl bond is, therefore, primarily responsible for polarizing the adjacent carbon-carbon double bond.

¹³C chemical shifts of *both* the α- and β-positions correlate well with Hammett substituent values, though much smaller shifts are observed for C_β. The students should also observe that the substituents have *little or no effect* on the chemical shift of the carbonyl carbon. Electron-donating groups in the para position of the styryl ring do produce slight shifts in

the carbonyl stretching vibrations to lower frequencies observed by IR spectroscopy. The carbonyl bond is therefore assumed to be more strongly polarized, but the carbonyl carbon experiences negligible *net* shielding effects by the delocalized electrons. Students could also discuss these observations with respect to the possible resonance forms of 4-substituted chalcones and their effect on the electronic environment of the carbonyl carbon.

Acknowledgments

We gratefully acknowledge The Camille and Henry Dreyfus Foundation for extending and expanding Research Corporation's Partners in Science program in the New York metropolitan area. This project was supported by a Camille and Henry Dreyfus Foundation Award of Research Corporation (grant HS0509). We would also like to thank Francis Picart, coordinator of the NMR facility at SUNY Stony Brook, for providing us with instrument time and helping us acquire the spectroscopic data. Some of the synthetic work for this project was initially performed by Hofstra undergraduate students in CHEM 134B (Chemical Synthesis), and we would particularly like to acknowledge the efforts of Pamela Vaughn. We are also grateful to Esther Sparberg and Dennis Ryan for their comments and suggestions.

Notes

1. Benzaldehydes substituted with electron-donating substituents react much more slowly than 4-nitrobenzaldehyde, which forms solid almost instantaneously. As expected, 4-*N,N*-dimethylaminobenzaldehyde required the longest reaction time. Heating the mixture, however, resulted in a dark, tarry product.

2. Some difficulty was encountered isolating 4-*N,N*-dimethylaminochalcone, which remained oily until most of the ethanol was removed from the solvent mixture. Crystallization of the crude product from cold water initially produced an orange-red solid, which, on recrystallization from 1:1 ethanol/water, yielded beautiful orange-yellow needles.

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