

TRANSMISSION OF SUBSTITUENT EFFECTS IN HETEROCYCLIC SYSTEMS.  
VARIATION OF THE HAMMETT  $\rho$  WITH THE AROMATIC SUBSTRATE.

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In a recent paper Clementi and Marino treated substituent effect data for trifluoroacetylation of 2-substituted furans, thiophenes, and pyrroles by correlation with  $\sigma_p^+$  in the Hammett equation.<sup>2</sup> The magnitudes of  $\rho$  values obtained were discussed as being related to differences in positions of the transition states along the reaction coordinates. We report here evidence which suggests that the variation in  $\rho$  values for different aromatic substrates is closely related to differences between the substrates in the distribution of charge developed in the transition state. Our proposal of this relationship is based on data from our studies of substituent effects in the solvolysis of heteroaryl derivatives and on results from CNDO/2 molecular orbital calculations.

Several recent investigations<sup>3,4</sup> have demonstrated that equations which take into account variations in the balance of field and resonance effects describe aromatic substituent effects more accurately than the simple use of substituent constants, such as  $\sigma_p^+$ , defined from the benzene series. However, satisfactory use may often be made of  $\sigma_p^+$  constants when there is mutual conjugation between the substituent and the reaction center. A list of situations in the solvolysis of substituted 1-arylethyl derivatives for which we have found  $\sigma_p^+$  constants to correlate adequately with solvolytic reactivity is presented in Table 1, accompanied by the  $\rho$  values found in the correlations.

Table 1 clearly shows that each ring system has a different sensitivity to substituent effects. There is no correlation between the magnitude of  $\rho$  and the reactivity of the unsubstituted ring systems relative to benzene; therefore, it is improbable that the magnitudes of  $\rho$  reflect differences between ring systems in the development of the transition state. However, the sensitivity to substituent effects does appear to be directly related to the amount of transition state charge,  $\Delta q$ , delocalized to the site of substituent attachment. The relationship between  $\rho$  and  $\Delta q$  is illustrated in Figure 1. The quantity  $\Delta q$  is the difference in regional charge<sup>5</sup> at the substituent site between the unsubstituted, neutral molecule and the cationic transition state. The  $\Delta q$  values listed in Table 1 were obtained from CNDO/2 calculations<sup>6</sup> performed for the parent arylmethanes,  $\text{ArCH}_3$ , as models for the neutral molecules, and the arylmethylene cations,  $\text{ArCH}_2^+$ , as models for the transition states.

In the MO calculations, each model molecule gains a full unit of positive

TABLE I

Solvolysis of Substituted 1-Arylethyl Derivatives,  
ArCHXCH<sub>3</sub>, in 80% Ethanol-H<sub>2</sub>O at 25°. <sup>a</sup>

Aryl Group	Sidechain Position	Substituent Position	Leaving Group (X)	$\rho$	$\Delta q$
Benzo[b]thiophene (1)	2	6	OPNB	-3.96	.1246
Benzofuran (2)	2	6	OPNB	-4.41 <sup>b</sup>	.1377
Benzene (3)	1	4	Cl	-5.82	.2109
Pyridine (4)	2	5	Cl	-6.05 <sup>c</sup>	.2212
Thiophene (5)	2	5	OPNB	-7.06	.2051
Thiazole (6)	5	2	Cl	-6.14	.2030
Thiazole (7)	2	5	Cl	-6.68	.2268
Furan (8)	2	5	OPNB	-7.42	.2763

<sup>a</sup>Solvolysis rate data from D. S. Noyce and G. V. Kaiser, *J. Org. Chem.*, **34**, 1008 (1969), and unpublished data of D. S. Noyce, B. Bartman, S. A. Pike, D. A. Forsyth, C. A. Lipinski, R. W. Nichols, and J. A. Virgilio. Many individual rates were extrapolated from other temperatures using the individual activation parameters. <sup>b</sup> Extrapolated from  $\rho = -3.61$  at 75°, using the factor of the observed change in  $\rho$  for benzo[k]thiophene between 75° and 25°. <sup>c</sup> Extrapolated from  $\rho = -4.71$  at 25° for the 2-(pyridyl)propyl chlorides, using the factor of the change in  $\rho$  between the *t*-cumyl chlorides ( $\rho = -4.54$ , H. C. Brown and Y. Okamoto, *J. Am. Chem. Soc.*, **80**, 4979 (1958)) and the  $\alpha$ -phenethyl chlorides,  $\rho = -5.82$ .

charge in the transition state, thus creating a model in which the reaction for each aromatic substrate is considered to have progressed to the same extent along the reaction coordinates. The relationship between  $\rho$  values and  $\Delta q$  values suggests strongly that the dominant factor in the variation of  $\rho$  with the nature of the aromatic substrate is the pattern of charge distribution within each ring system, which determines the extent of substituent interaction with the charge developed in the transition state. The increase in magnitude of  $\rho$  with increasing  $\Delta q$  reinforces the concept of the magnitude of  $\rho$  as a measure of both the magnitude of the developing charge and of the extent to which it is able to interact with the substituents<sup>7</sup>. Changes in demand for charge stabilization by substituents can arise through varying the aromatic substrate, as reported here, or through differences in charge developed in the transition state, as is most easily observed by changing from one reaction to another<sup>8</sup>. Clearly, the charge distribution within different substrates should be considered before drawing any conclusions regarding the relationship of  $\rho$  to the nature of the transition state.

The five-membered rings which contain a sulfur atom obviously deviate from the line in Figure 1, although the two thiazole points follow the general trend of increasing  $\rho$  with increasing  $\Delta q$ . One possible explanation is that the CNDO/2 calculations may place too much charge on the sulfur atom, thereby draining charge from the rest of the system. For example, the substituent effects in

thiophene correlate very well against substituent effects in furan (corr. coef. = .995)<sup>9</sup> with a similar magnitude of  $\rho$ , and this should be reflected in similar charge distributions. However, as shown below in the diagrams of regional charge distribution (Figure 2), thiophene differs significantly from furan. Benzo(b)-thiophene and benzofuran also have similar substituent effects<sup>9</sup>, but in this larger system, excessive charge placed on sulfur has only a small effect on charge distribution in the benzo ring to which the substituents are attached.

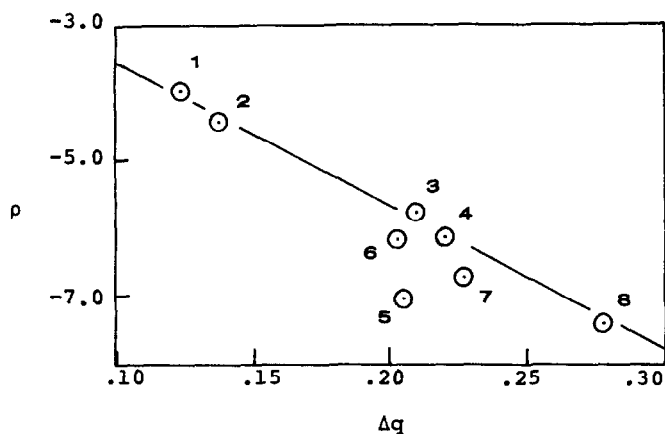


Figure 1. Variation of  $\rho$  with  $\Delta q$ .

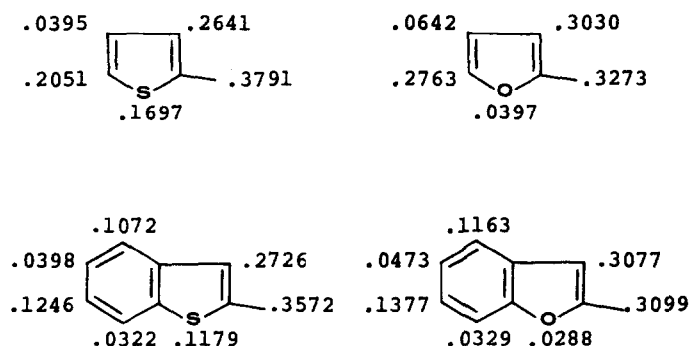


Figure 2. Differences in regional charge,  $\Delta q$ , calculated for various positions in O and S Heterocycles.

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- 9) Correlations include substituents at positions other than those reported in Table 1.