

Structure-Reactivity Correlations on the Kinetics of Substituted
2-Phenylethyl m-nitrobenzenesulfonates with Substituted Pyridines

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Abstract - The rates of the substituted 2-phenylethyl m-nitrobenzenesulfonate(2-PNS) with pyridines were determined in acetonitrile. The reaction was accelerated by an electron - donating substituent on both substrate and nucleophile. Substituent effects 2-PNS and pyridine are correlated by Brønsted and Hammett equations, respectively. The sensitivity parameters, β and ρ , obtained from the free-energy relationships, are inter-related and are themselves sensitive to the reactivity of the system. Thus, β varies from 0.246 for p-MeO 2-PNS to 0.284 for p-NO₂PNS, and are linearly related to the σ values for 2-PNS substituents. Likewise the ρ_Z (Z is a substituent of substrate) values are linearly related to pK_a of the pyridines and ρ_Y (Y is a substituent of pyridine) values are also correlated to the β values. These data show that electron-withdrawing substituents in 2-PNS increase bond formation between C and N atoms and such substituents in the pyridines also lead to increased bond formation relatively to bond breaking in the transition state. The More O'Ferral and Swain, Thornton, and Harris approaches were applied for the prediction of substituent effects on above interpretation.

In previous papers,¹⁻⁵ we reported on the Menschutkin-type S_N2 reaction for 2-phenethyl arenesulfonates with pyridine in acetonitrile. It was shown that substituent effects in the leaving group and nucleophile could be correlated by Hammett and Brønsted equations respectively. To investigate the effect of structure on reactivity in nucleophilic substitution at carbon, the rate constants for the reactions of substituted 2-phenethyl m-nitrobenzenesulfonates(2-PNS) with substituted pyridines have been determined in acetonitrile at various temperature. This reaction, which occurs according to eq.(1), was chosen because of its expected possibilities of introducing substituents both in nucleophile and substrate.

In this paper we report the result of the relationships between ρ_Z , ρ_Y , and Brønsted β values to obtain more detailed informations for Menschutkin S_N2 reactions.⁶ In addition we comment on the interpretation of transition state variation in the More O'Ferral approach⁷ and compare above all results with the predictions of Thornton,⁸ Harris, and Kurtz⁹ for a transition state structure in an S_N2 reaction.

Experimental

All materials used were commercially available(Wako, Japan). Acetonitrile was purified by distillation after standing with anhydrous potassium carbonate for three days at room temperature. Pyridine dried over NaOH pellet was fractionated twice, bp 115-115.5°C. Other liquid pyridines were distilled under nitrogen, but solid ones recrystallized before use. All purified pyridines were stored in brown ampoule or bottle filled with nitrogen gas.

IR spectra were recorded on a Hitachi EPI-2G infrared Grating Spectrophotometer, ¹H NMR spectra were taken with a Varian 60 MHz Spectrometer and conductance measurements were carried out with a Conductivity-Meter LBR (West Germany).

m-Nitrobenzenesulfonyl chloride was obtained by chlorination of sodium m-nitrobenzenesulfonate with chlorosulfonic acid. Recrystd. from ligroin (59%), mp 61°C (81-62°C).

Phenethyl m-Nitrobenzenesulfonate. By the Tipson's procedure¹¹, while stirring the temperature was kept at 0°C in a ice-water bath, 2-phenethyl alcohol(8.32g, 0.068mol) was dissolved in pure pyridine(30ml) and subsequently m-nitrobenzenesulfonyl chloride(14.92g, 0.068mol) was gradually added at above temperature. After stirring for 2 h at 0°C, the mixture was poured into ice-water and then light brown crystals were collected(10.73g, 60%). Recrystallization from hexane : mp 72°C (72-72.5°C)⁵. Other substituted phenethyl m-nitrobenzenesulfonate were obtained by above the same method.

The identification of synthesized esters were performed by mp, ¹H NMR spectra, and GLC peak : (Z, yield(%), mp) : CH₃O, 40, 78-79¹²; Br, 38, 99-101. Found : C, 43.55 ; S, 8.20 ; N, 3.59%. C₁₄H₁₂SO₅NBr requires C, 43.53 ; H, 3.10 ; S, 8.27 ; N, 3.62% (CDCl₃) 3.0 (2H, t, β-H), 4.3(2H, t, α-H). 7.15(4H, q, phenyl), 8.0(3H, t, phenyl), 8.5(1H, s, phenyl), a single peak by GLC ; NO₂, 30, 112. Found : C, 47.68 ; H, 3.44 ; S, 9.08 ; N, 7.88%.

C₁₄H₁₂SO₇N₂ requires C, 47.33 ; H, 3.43 ; S, 9.10 ; N, 7.95%. (CDCl₃) 3.0 (2H, t, β-H), 4.3(2H, t, α-H), 7.2(4H, q, phenyl), 8.6(1H, d, phenyl), a single peak by GLC.

N-Phenethylpyridinium m-Nitrobenzenesulfonate. Pyridine(0.554g, 0.007mol) was added in a solution of phenethyl m-nitrobenzenesulfonate(2.15g, 0.007mol) in anhydrous acetonitrile(80ml). The reaction mixture was heated under reflux for 4 h and then allowed to stand over night at room temperature. The product thus obtained was washed with anhydrous ether. Recrystallization from 2-propanol gave colorless crystals (40%), mp 122-123°C, ¹H NMR (CDCl₃) 3.25(2H, t, β-H), 5.15(2H, t, α-H), 9.00(2H, d, α-H of pyridine), 8.7(1H, s, r-H of pyridine); IR(nujol) 3300, 1600, 1355, 1200, 1050, 835cm⁻¹. Found : C, 59.52 ; H, 4.94 ; N, 7.33%. C₁₉H₁₈N₂O₅S requires C, 59.06 ; H, 4.70 ; N, 7.25%

Rate Measurements. Rate measurements were done conductometrically. A typical kinetic run was carried out as follows^{13,14}. Ester(0.015mol/l) in acetonitrile was prepared under nitrogen. That of pyridine(0.300M) was made similarly. A kinetic run was initiated by placing 15ml of pyridine solution in a conductivity cell and adding 15ml of the ester solution to give a reaction mixture that was 0.150M in pyridine and 0.007M in ester of final concentrations. Reactions were generally run to ca. 3-4 half-lives. Pseudo-first-order rate constants were calculated from the slopes obtained from conventional plots of log (k_∞ - k_t) against time using the least-square method. Second-order rate constants were calculated from the slopes of plots of the observed first order rate constants against pyridine concentrations. Rate constants are estimated to be accurate to ± 3%.

Results and Discussion

The observed rate of reaction were always of the first order. Plots of the observed first-order constants against concentrations of pyridine were also linear in all cases showing that the reactions are of the first-order in nucleophile. The second-order rate constants and activation parameters for the reactions of 2-PNS with various pyridines are give in Table 1. The kinetics are thus as expected from eq.(1) with the rate law (2).

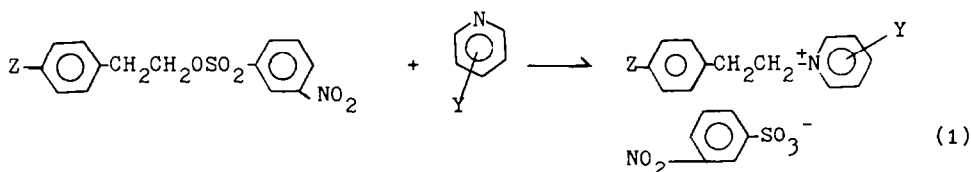
The quaternary ammonium salts were identified by recrystallization of the final reaction mixture. No other products were observed. The mechanism for the reaction of the substituted 2-PNS with various pyridines is most reasonably formulated as a bimolecular nucleophilic displacement on carbon.

Table 1. Rate Constants and Activation Parameters for the Reaction of Substituted 2-Phenethyl m-Nitrobenzenesulfonate with Substituted Pyridines in Acetonitrile

| Z Y | p-MeO | | | H | | | p-Br | | | p-NO ₂ | | | |
|---------------------|---------------------------------|-------------------|-------------------|---------------------------------|-------------------|-------------------|---------------------------------|-------------------|-------------------|---------------------------------|-------------------|-------------------|------|
| | 10 ³ k ^{a)} | ΔH ^{‡b)} | ΔS ^{‡c)} | 10 ³ k ^{a)} | ΔH ^{‡b)} | ΔS ^{‡c)} | 10 ³ k ^{a)} | ΔH ^{‡b)} | ΔS ^{‡c)} | 10 ³ k ^{a)} | ΔH ^{‡b)} | ΔS ^{‡c)} | |
| 4-NH ₂ | 50 | 187.8 | | 184.3 | | | 182.5 | | | 180.4 | | | |
| | 60 | 368.5 | 14.4 | 17.6 | 364.3 | 14.5 | 17.2 | 362.5 | 14.5 | 17.3 | 360.8 | 14.4 | 17.5 |
| | 70 | 732.5 | | | 728.6 | | | 720.6 | | | 708.8 | | |
| 3-CH ₃ | 50 | 25.0 | | 22.6 | | | 20.6 | | | 17.8 | | | |
| | 60 | 38.5 | 11.6 | 30.4 | 36.1 | 12.1 | 28.9 | 34.1 | 12.5 | 27.7 | 33.2 | 13.9 | 23.9 |
| | 70 | 75.6 | | | 71.8 | | | 68.1 | | | 66.4 | | |
| H | 50 | 11.9 | | 10.1 | | | 9.9 | | | 8.3 | | | |
| | 60 | 23.5 | 14.5 | 22.8 | 21.2 | 15.2 | 20.8 | 19.8 | 14.5 | 23.1 | 16.4 | 14.6 | 23.2 |
| | 70 | 46.8 | | | 42.5 | | | 39.0 | | | 33.0 | | |
| 3-CONH ₂ | 50 | 8.2 | | 7.8 | | | x | | | x | | | |
| | 60 | 16.3 | 11.7 | 32.0 | 13.4 | 12.1 | 30.1 | 10.6 | 15.5 | 21.4 | 9.5 | 15.0 | 23.0 |
| | 70 | 25.1 | | | 24.8 | | | 22.0 | | | 19.3 | | |
| 4-CN | 50 | 2.0 | | x | | | x | | | x | | | |
| | 60 | 5.2 | 16.4 | 20.2 | 2.20 | 14.6 | 27.0 | x | | x | | | |
| | 70 | 9.4 | | | 4.4 | | | 4.2 | | | 4.1 | | |

a) 10³k (l/mol.s.), b) ΔH[‡] (K cal/mol), c) ΔS[‡] (e. u.).

X : too slow to measure



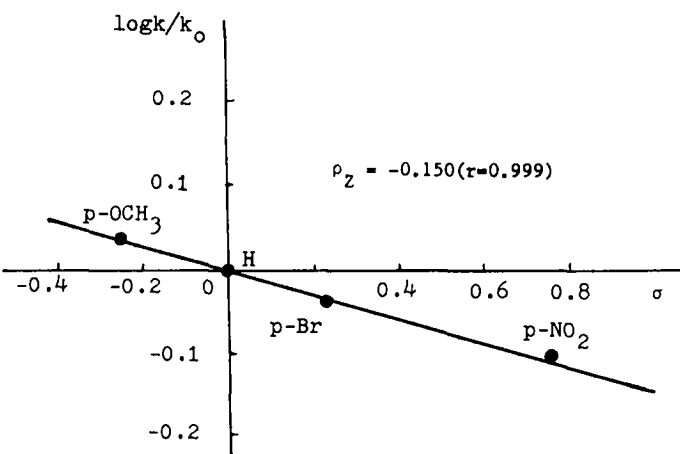
$$\text{Rate} = k [\text{2-PNS}] [\text{Pyridine}] \quad \dots \quad (2)$$

The kinetics, products, stoichiometry, and activation parameters are in agreement with such a mechanism for reason given, and a one-step S_N2 process is preferred.

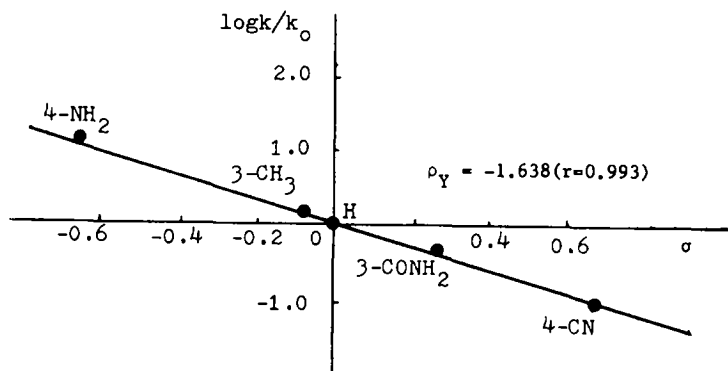
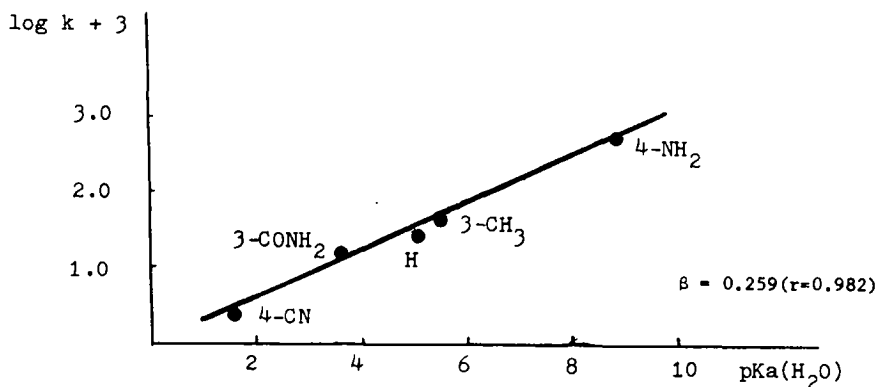
Substituent Effects - The effect of structural variations in substrate and nucleophile is apparent from the Hammett and Brønsted plots (Figure 1, 2, and 3).

The rate was increased by electron-donating substituents in both the phenethyl substrate and pyridine nucleophile. This is expected for nucleophilic attack of amines on the carbon atom. The change of rate constants are not very sensitive to the variation of substituents in the phenethyl substrate compared with that of benzyl one because of the intervention of the more -CH₂- group¹⁵. Thus the Hammett ρ_Z values for the substrate are small negative in which bond breaking have preceded relatively to bond making in the transition state.

The increasing tendencies of bond breaking are 3-CONH₂ > H > 3-Me > 4-NH₂ in pyridines as given in Table 2.

Table 2. ρ_2 Values of Substituted 2-PNS with Substituted Pyridines

| Y | ρ_2 | r |
|---------------------|----------|-------|
| 4-NH ₂ | -0.008 | 0.923 |
| 4-Me | -0.060 | 0.930 |
| H | -0.150 | 0.999 |
| 3-CONH ₂ | -0.222 | 0.942 |

Figure 1. Hammett plot for the reaction of substituted 2-phenethyl *m*-nitrobenzenesulfonates with pyridine in acetonitrile at 60°CFigure 2. Hammett plot for the reaction of 2-phenethyl *m*-nitrobenzenesulfonate with pyridines in acetonitrile at 60°CFigure 3. Brønsted plot for the reaction of 2-phenethyl *m*-nitrobenzenesulfonate with pyridines in acetonitrile at 60°C

The rates are correlated well with the Hammett equation, as shown in Figure 1. The sign and magnitude of the slope (ρ_Z) indicate development of a positive charge at the reaction center in the transition state. This is consistent with the mechanism and influence of substituents on reaction rates as discussed above. The ρ_Z values which become more negatively with decreasing reactivity of the pyridine, are linearly related to pK_a of the pyridine as shown in figure 4, in agreement with that found in the reactions of substituted benzenesulfonyl chlorides with pyridines¹⁶.

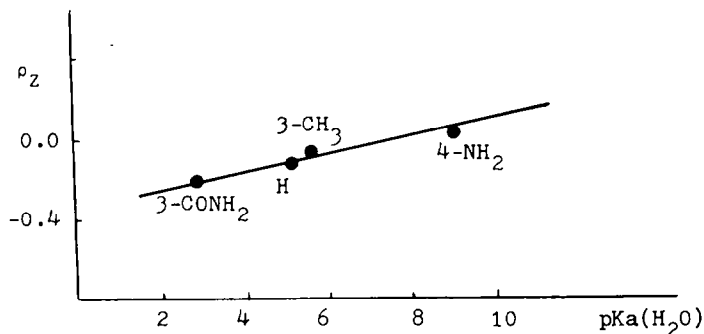


Figure 4. Dependence of the Hammett ρ_Z values upon the basicity of the pyridines.

As ρ_Z is related to the extent of bond breaking relative to bond formation¹⁷, the stretching and charging of the C-O bond increase relatively the formation of the C-N bond, i. e., the transition state becomes more product-like, with increasing electron-withdrawing substituents in the nucleophile. This is also in agreement with predictions of substituent effects on transition state structure for a simple S_N2 displacement⁹.

The rates of reaction between phenethyl 2,5-dichlorobenzenesulfonate and phenethyl tosylate with substitute pyridines show less sensitivity to basicity (2,5-dichloro¹⁸, $\rho = 0.200$; tosylate, $\rho = 0.220$) than does 2-PNS. This probably reflects the former two compounds are not so larger positive charge on the carbon atom of reaction center than the *m*-nitro one in the transition state, resulting in a decreased bonding and charge transfer.

The reaction constant, ρ_Y which may be a measure of the change in charge on the N atom of pyridines is related to the extent of bond formation and bond breaking in the transition state⁹. The larger $|\rho_Y|$ is, the more bond making have preceeded relatively to bond breaking.

Table 3. ρ_Y and β Values of Substituted Pyridines

| Z | MeO | H | Br | NO ₂ |
|----------|-------------------------|-----------------------|-----------------------|-----------------------|
| ρ_Y | -1.381 ($r=0.985$) | -1.638 (0.993) | -1.682 (0.992) | -1.740 (0.088) |
| β | 0.246 ($r=0.987$) | 0.259 (0.982) | 0.275 (0.989) | 0.284 (0.985) |

Table 3 shows that bond making increases increasingly with electron-attracting substituents in the phenethyl substrate, in agreement with prediction of substituent effects on S_N2 transition state^{8,9}. The variable ρ_Y value is thus consistent with a concerted mechanism

with the transition state occurring progressively further along the reaction coordinate from electron-donating substituent to electron-attracting one in substrate. The ρ_Y value for the reactions of 2-PNS with pyridines is more negative than those of phenethyl 2,5-dichlorobenzenesulfonate¹⁸ ($\rho_Y = -1.255$) and phenethyl tosylate¹ ($\rho_Y = -1.330$). From the result, 2-PNS is more bond breaking than the later two compounds in the transition state.

Since β provides a measure of the degree of bond formation in the transition state, it is apparent from Table 3 that bond formation increases increasingly with electron-attracting substituents in the phenethyl substrate. The direction of increasing β value is same with that of $|\rho_Y|$ value. Thus β is correlated with σ as shown in Figure 5.

A similar conclusion was reached for the reaction of pyridine catalyzed hydrolysis of arenesulfonyl chlorides¹⁶.

All the above results agreed to the structure of the S_N2 transition state predicted by Swain, Thornton⁸, and Harris and Kurtz⁹.

The linearity of the Brønsted plots also suggests that there are no significant change in transition-state structure from the most reactive to the least reactive pyridine (Figure 3).

A synchronous one step process is thus preferred.

Multiple Structure-Reactivity Correlation - The Hammett and Brønsted equations which correlate with structural change in 2-PNS and pyridine, respectively, can be combined to give an expression(3) which shows that various ρ 's and β 's are interrelated,^{19,20}

$$\frac{pka^1 - pka^2}{\rho_1 - \rho_2} = \frac{\sigma_1}{\beta_1 - \beta_0} = C \quad (3)$$

where C is a constant.

Equation(3) predicts a linear variation of pKa with ρ and of σ with β . This is the case as shown in figures 4 and 5.

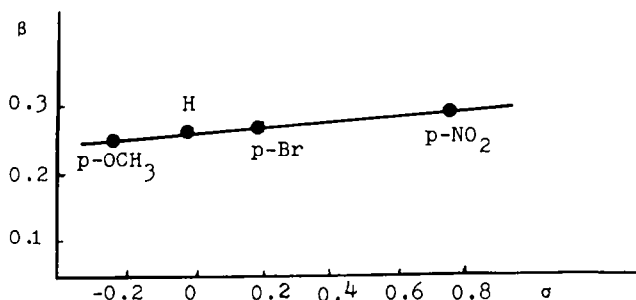


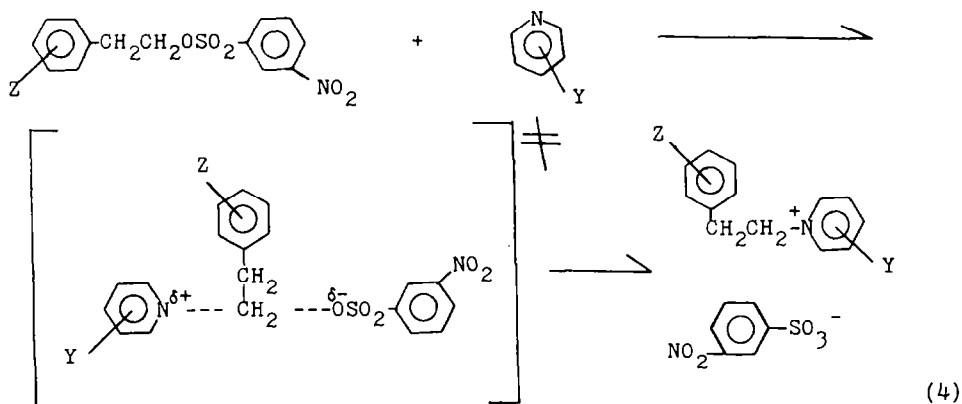
Figure 5. Dependence of the Brønsted slopes β upon the σ values for substituents of the 2-phenethyl *m*-nitrobenzenesulfonate.

The value of C, evaluated from the slope of the plots in Figure 4 or 5 is 0.035. Its positive value means that an increase in the nucleophilic reactivity of the nucleophile increases the sensitivity of the reaction to substituent effects. Likewise, the selectivity to the nucleophilic reagents increases with the reactivity of substrate.

Activation Parameters - Table 1 illustrates the activation parameters and the negative values of the entropy of activation is as expected for bimolecular reactions with polar transition state. The fairly large enthalpy of activation shown that C---O bond stretching is very important. This is consistent with the assumption that this reaction has the dissociative S_N2 transition state structure.

Application of More O'Ferrall Model⁷.

In this section we apply the More O'Ferrall approach and examine the predictions for the effects of variations of Z and Y on the S_N2 transition state, eq.(4).



As we have already concluded, the reaction of 2-PNS with pyridine in acetonitrile proceeds via a dissociative S_N2 path, which will be located between S_N1 and S_N2 paths as presented in Figure 6. An electron-donating substituent on the substrate (Z), will stabilize the R^+X^- , the upper left corner of the More O'Ferrall diagram, and the transition state T will move to point B in accordance with the Thornton's rule⁷. Judging from the accelerating effects of electron-donating substituent (Z), (Table 1), this reaction proceeds via transition state in which there is significantly positive charge development of carbon, and such transition state results when R-X bond cleavage proceeds more rapidly than N-R bond formation. In this case, the reaction coordinate will lie somewhere between S_N1 and S_N2 processes as shown in Figure 6.

The More O'Ferrall approach does lead to the prediction that this transition state variation will cause the decrease in bond formation and increase in bond breaking. Our experimental results in Table 3 show that $|\rho_Y|$ and β values are decreased by electron-donating substituents on substrate. This is consistent with the prediction of the More O'Ferrall Model since the decrease in $|\rho_Y|$ and β values can be taken as the decrease in bond formation. The large rate constant of electron-donating substituent in Table 1 can be explained as an indication of an increased C---O bond breaking at the transition state.

Alternately, the substitution of electron-withdrawing substituents in the pyridine derivative would destabilize the right corner and move the transition state T to D, which is the resultant of vectors to points T_B and T_C , caused by lowering the upper left and upper right corners, respectively. The new transition state will have no change in bond formation and increased bond breaking. This is in accord with the experimental results, as Table 2 shows the $|\rho_Z|$ value is increased by electron-withdrawing substituents on pyridine.

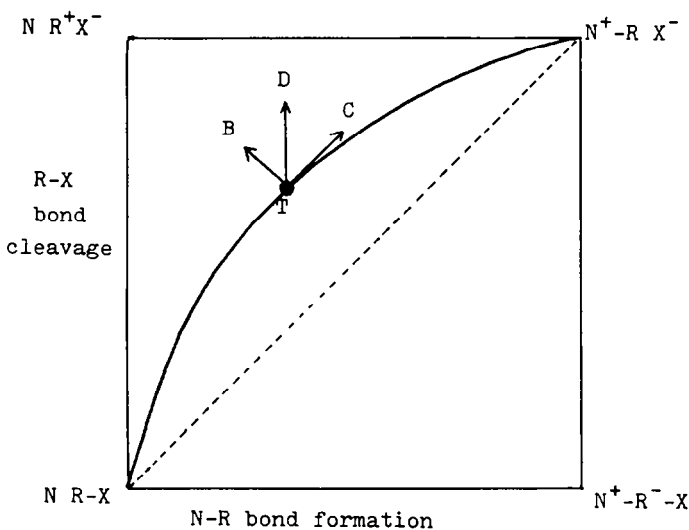


Figure 6. A More O'Ferral plot for the nucleophilic substitution reaction of substituted 2-phenethyl *m*-nitrobenzenesulfonates

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