## Example Problems
Applications of Hammett Equation: Substituent and Reaction Constants

1. Predict the pK_a for the following phenols using the appropriate substituent constants, a pK_a for unsubstituted phenol of 9.90 and a ρ-value of 2.25.
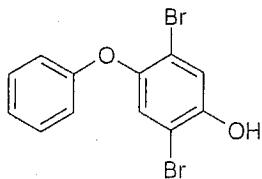
hydrolysis pdt of a PBDE   degradation pdt of gadusol
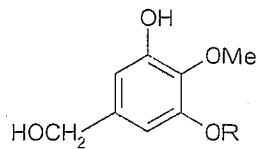
$$pK_{a(x)} = pK_{a(H)} - \rho \sum \sigma_i$$

para	Ph-O-	$\sigma_p^- = -0.20$
meta	Br-	$\sigma_m = +0.39$
ortho	Br-	$\sigma_{ortho}^{-phenol} = 0.70$

$$\therefore pK_a = 9.90 - 2.25 \left(-0.20 + 0.39 + 0.70\right)$$
$$= 7.88$$

ortho	CH_3-O-	$\sigma_{ortho}^{phenol} = 0.00$
meta	R-O-	$\sigma_{meta} = 0.11$
meta	$HO-CH_2-$	$\sigma_{meta} = 0.07$

$$\therefore pK_a = 9.90 - 2.25 \left(0.11 + 0.07\right)$$
$$= 9.50$$

2,4,5 - T $pKa(x) = 3.05 - 0.30 (0.37 + 0.23)$

$= 3.05 - 0.18$

$= 2.87$

fraction in ionized form $HA \rightleftharpoons H^+ + A^-$
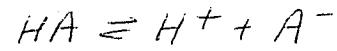
$$\alpha_{A^-} = \frac{[A^-]}{[A^-] + [HA]}$$ $Ka = \frac{[H^+][A^-]}{[HA]}$

$[A^-] = \frac{Ka\,[HA]}{[H^+]}$

$$= \frac{Ka\,[HA]/[H^+]}{Ka\,[HA]/[H^+] + [HA]}$$

$$= \frac{Ka/[H^+]}{Ka/[H^+] + 1}$$

where $[H^+] = 1.00 \times 10^{-6}\, M$ (pH 6)

$Ka = 10^{-2.87} = 1.35 \times 10^{-3}$

$$\alpha_{A^-} = \frac{(1.35 \times 10^{-3}/1.00 \times 10^{-6})}{(1.35 \times 10^{-3}/1.00 \times 10^{-6}) + 1}$$

$$= \frac{1349}{1349 + 1} = 0.999$$

2. Predict the pK$_a$ of the following compounds and calculate the fraction present in ionized form at pH 6.00.

NH$_2$ (3,4-DMA structure)

O–CH$_2$CO$_2$H with Cl substituents (2,4,5-T structure)
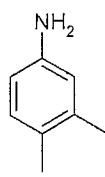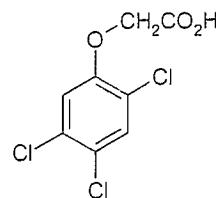
3,4-DMA   2,4,5-T (herbicide)

	pK$_a$	ρ
aniline	4.63	2.89
2-chlorophenoxyacetic acid	3.05	0.30

3,4-DMA

$$pK_a(x) = 4.63 - 2.89\,(-0.07 + (-0.17))$$
$$= 4.63 - 2.89\,(-0.24)$$
$$= 5.32$$

(structure of $NH_3^{\oplus}$ on ring)
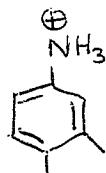
fraction in ionized form $HA^+ \rightleftharpoons H^+ + A$

$$\alpha_{HA^+} = \frac{[HA^+]}{[HA^+] + [A]}$$
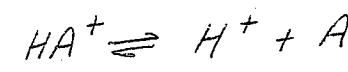
$$K_a = \frac{[H^+][A]}{[HA^+]}$$

$$\therefore [HA^+] = \frac{[H^+][A]}{K_a}$$

$$\therefore \alpha_{HA^+} = \frac{[H^+][A]/K_a}{\frac{[H^+][A]}{K_a} + [A]}$$

$$= \frac{[H^+]/K_a}{[H^+]/K_a + 1}$$

where $[H^+] = 1.00 \times 10^{-6}\,M$ (pH 6)

$$K_a = 10^{-5.32} = 4.79 \times 10^{-6}$$

So $\alpha_{HA^+} = \dfrac{1.00 \times 10^{-6} / 4.79 \times 10^{-6}}{\dfrac{1.00 \times 10^{-6}}{4.79 \times 10^{-6}} + 1}$

$$= \frac{1.00/4.79}{1.00/4.79 + 1} = \frac{0.209}{0.209 + 1} = 0.173$$

3. Consider the substitution reaction and the kinetic data given below.
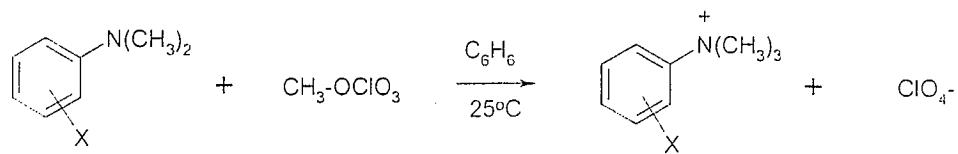
Substituent (X)	k (M^{-1} s^{-1})	Substituent (X)	k (M^{-1} s^{-1})
4-OCH$_3$	3.01 x 10^{-2}	4-Br	6.12 x 10^{-4}
4-CH$_3$	1.12 x 10^{-2}	3-Cl	2.66 x 10^{-4}
3-CH$_3$	6.00 x 10^{-3}	3-NO$_2$	2.86 x 10^{-5}
H	3.44 x 10^{-3}	4-NO$_2$	?

a) Comment on the use of σ or σ^+ for this reaction.
b) Determine the reaction constant ρ for this reaction and propose a mechanism.
c) Comment on the structure of the transition state.
d) Predict the rate constant for N,N-dimethyl *para*-nitroaniline (X = 4-NO$_2$)

Hammett Eqn for Substitution Rates of MeOClO3 with Dimethylanilines

$y = -3.0412x + 0.0268$
$R^2 = 0.9976$

a)

Nu ↓   E ↓

$\ddot{N}$-CH₃   +   →CH₃-$\ddot{O}$-Cl=O
|
CH₃

(benzene ring with X substituents)

→

(benzene ring with X) -$\overset{\oplus}{N}$(CH₃)(CH₃)-CH₃
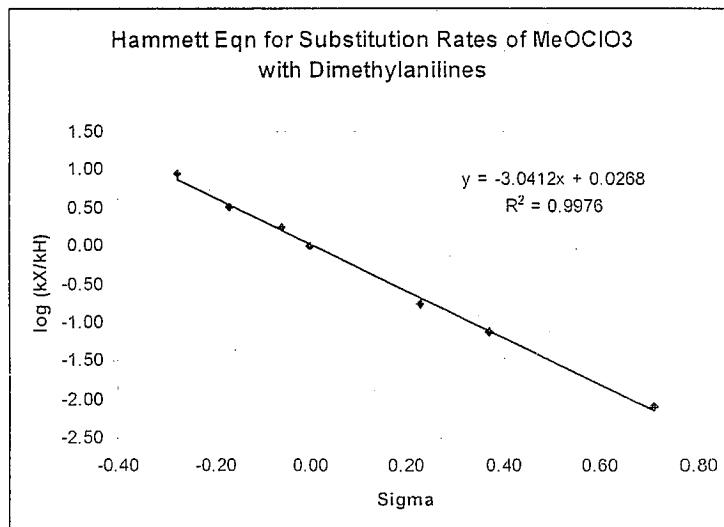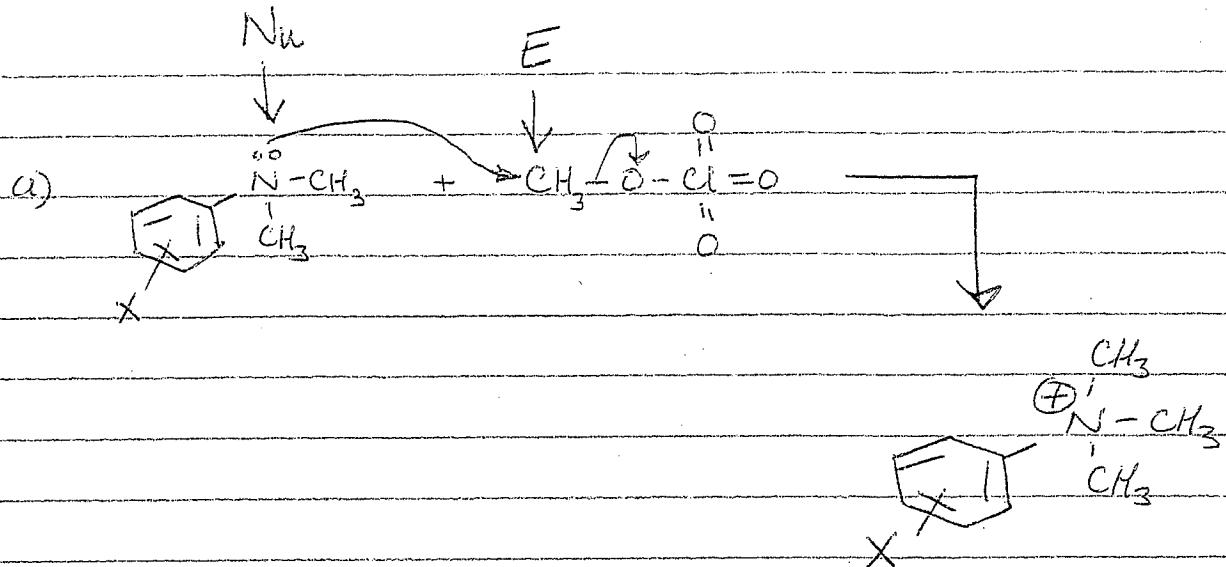
positive charge adjacent
to phenyl ring ∴
check for resonance
contribution from
substituents

i.e.

CH₃-$\ddot{O}$ (attached to benzene ring with) $\overset{\oplus}{N}$(CH₃)-CH₃ — crossed out
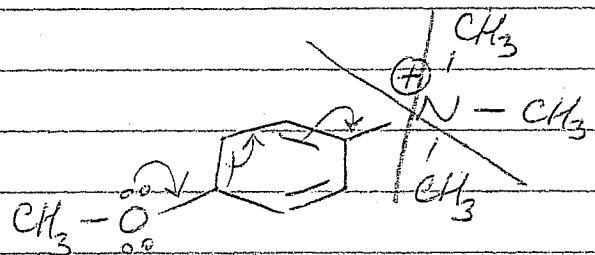
cannot resonance stabilize
the positive charge on
nitrogen directly because
of the octet rule.

Therefore use σ
NOT σ⁺

b) From the slope of the Hammett plot the reaction susceptibility constant (ρ) is determined from the slope to be -3.04

$\log\left(\dfrac{k_x}{k_H}\right)$

slope $= -3.04$ (ρ)

σ
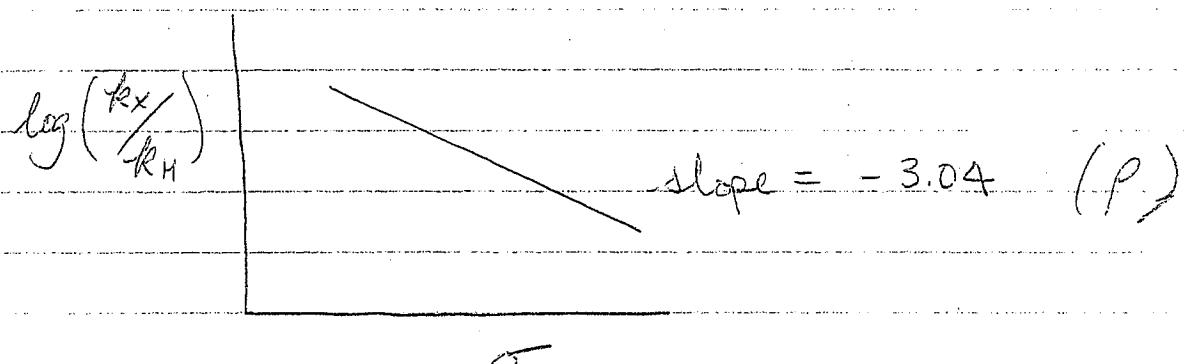
The negative sign of ρ indicates a decrease in electron density at the reaction centre. This is consistent with the lone pair electrons on nitrogen acting in a nucleophilic displacement reaction.

$CH_3 - O - ClO_3$ S_N2
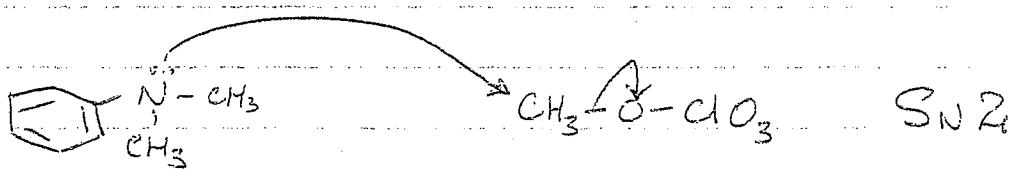
note: cannot be S_N1 since substituents on nucleophile effect the rate of reaction.

c) The relatively large magnitude of ρ suggests a substantial build up of positive charge on the nitrogen as the reaction progresses (ie. a late $\ddagger$).

$$\left[\; CH_3 \;\;\; H \;\;\; \delta^- \atop CH_3 \searrow N\ddot{\;} \overset{\delta^+}{\cdots} C \cdots\cdots\cdots O-ClO_3 \right]^{\ddagger}$$

$$H\;\;H$$
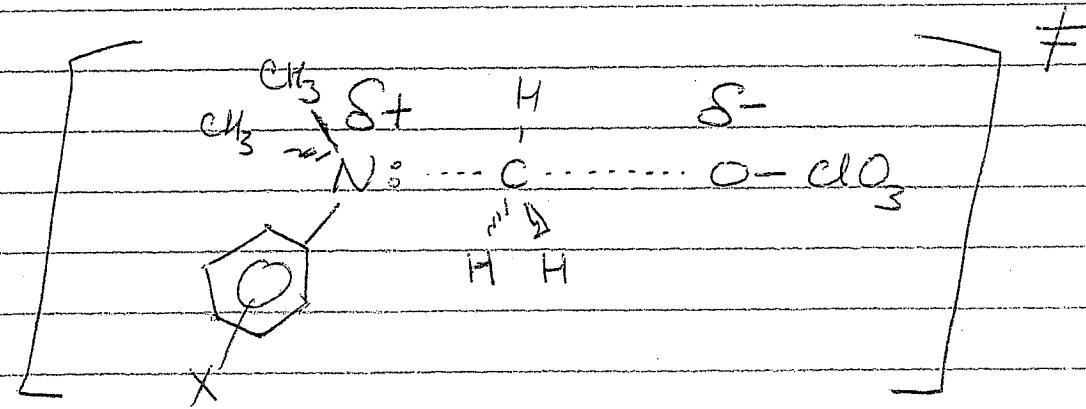
d) $\log k_{(x)} = \log k_{(H)} + \rho \sigma$

$$= \log(3.44 \times 10^{-3}) + (-3.04)(0.78)$$

$$= -2.46 - 2.37 = -4.83$$

$$\therefore k_{(x)} = 1.47 \times 10^{-5} \; M^{-1} s^{-1}$$

$$\text{for } X = p\text{-}NO_2 \quad (\sigma = 0.78)$$

4. For the following Hammett plot and reaction below, two reaction (susceptibility) constants (ρ) are obtained, one for EDG and another for EWGs. Explain the magnitude and sign of each of the two reaction constants and provide mechanism/s consistent with these observations.

$\rho(\sigma^+) = -5.58$

$\rho(\sigma^+) = -2.81$
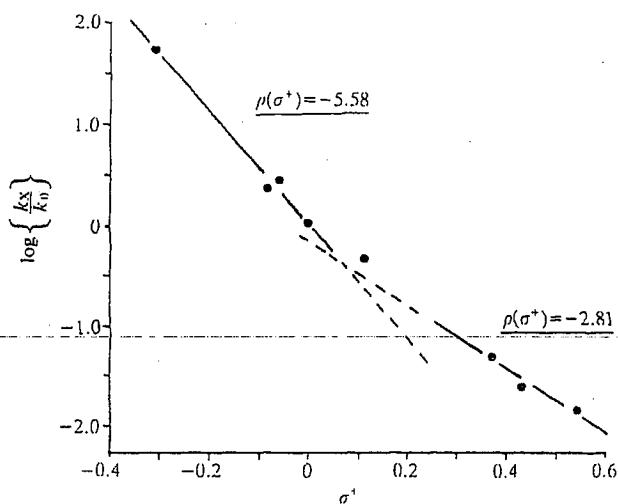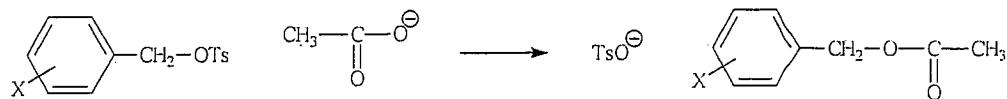
Concave up
∴ change in mechanism

Sn1 → Sn2

4. This is a substitution reaction in which –OTs is the leaving group and the acetate ion is the incoming nucleophile. There appears to be two linear regions in the Hammett plot with different slopes (i.e., differing susceptibilities to substituent effects). For a series of electron donating groups ($\sigma+ < 0$), the value of $\rho = -5.58$ suggests a large decrease in the electron density at the reaction centre (build up of positive charge). This is consistent with the formation of a carbocation like transition state such as one encountered in an S_N1 type mechanism.
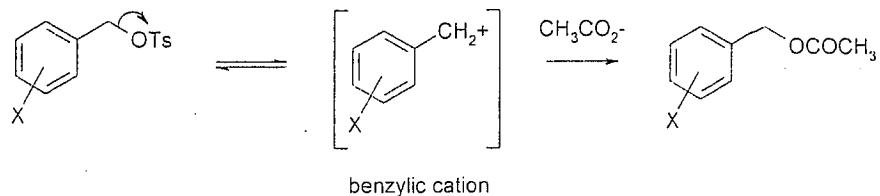

benzylic cation

Note the direct resonance capability of benzylic cation with substituents, hence the use of $\sigma+$.

As the substituents become increasingly electron withdrawing ($\sigma+ > 0$), the reaction constant seems to shift to a new value of -2.81. Although this again indicates a decrease in electron density at the reaction centre, it is not nearly as sensentive to the substituent effects. This is consistent with a change in mechanism which occurs as substituents become increasingly withdrawing, they slow the S_N1 mechanism (by destabilizing the carbocation intermediate) to the point to where the S_N2 reaction predominates.
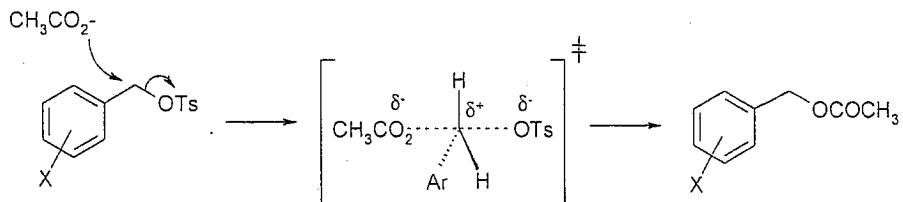
5. 4. The following rate data are for the solvolysis of substituted benzyl azoxyarenesulfonates (I) at 25°C in aqueous trifluoroethanol.
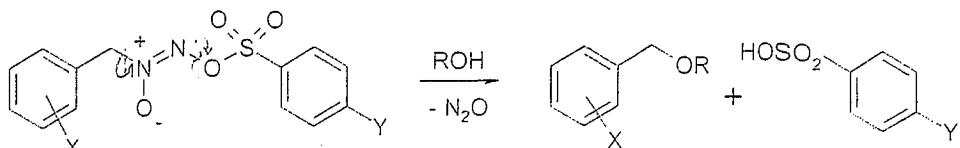
a) Calculate the reaction constants for the effects of substituents X and Y using the appropriate substituent constants.

Table 1: Substituent Effects on Benzyl Ring

X (for Y=CH₃)	$10^5 k$ (s⁻¹)
3-Cl	0.031
4-Cl	0.23
H	0.47
3-CH₃	0.76
4-CH₃	6.0
4-OCH₃	170

The X (for Y=CH₃) column header uses X and $Y=CH_3$; the rate column is $10^5 k$ (s⁻¹).

Table 2: Substituent Effects on the Arenesulfonate

Y (for X=4-CH₃)	k (s⁻¹)
OCH₃	4.24
CH₃	6.0
Br	19.1
CN	46.5

b) Using the following information, what may be deduced from the ρ-values for the solvolysis of I regarding its mechanism?
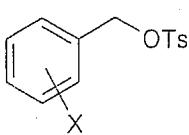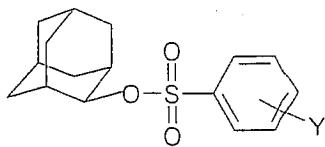

II   III

For the S_N1 solvolysis of substituted benzyl tosylates (II), ρ (vs σ+) = -5.6 and for 2-adamantyl arenesulfonates (III), ρ (vs σ) = 1.9.

a)

ROH
− N₂O
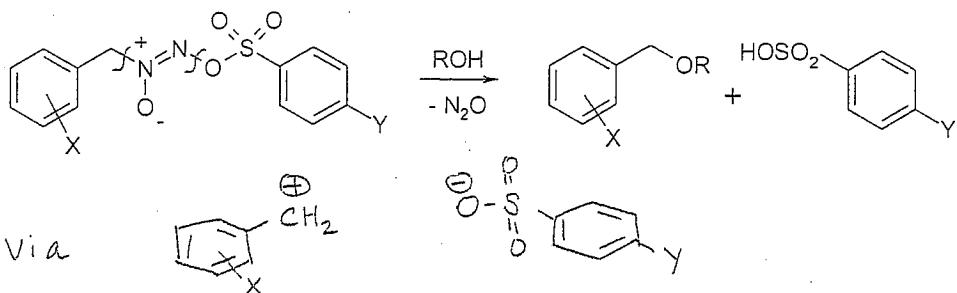
Via
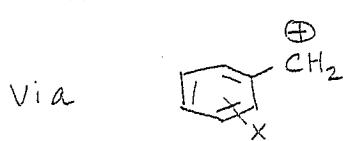
Hammett Plot for Changing X in Cmpd I

$y = -3.306x + 0.105$
$R^2 = 0.9719$

log (kX/kH)

sigma +
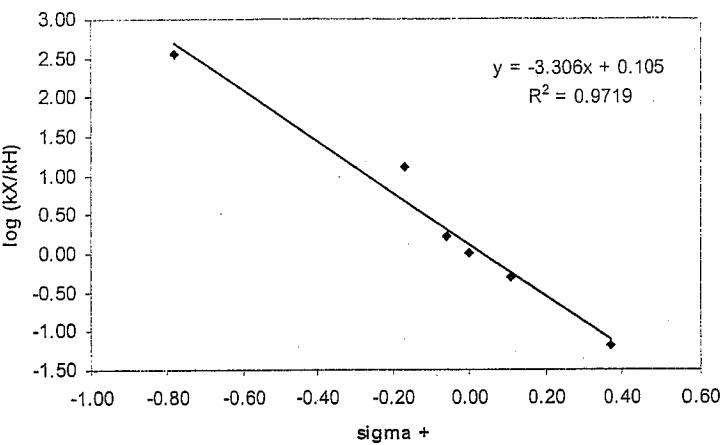
$\rho = -3.31$
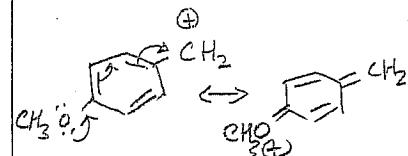
resonance stabilized
onto EDG
∴ use σ^+

Hammett Plot for Changing Y in Cmpd I

$y = 1.0655x - 4.0394$
$R^2 = 0.9876$

log kX

sigma

$\rho = 1.07$
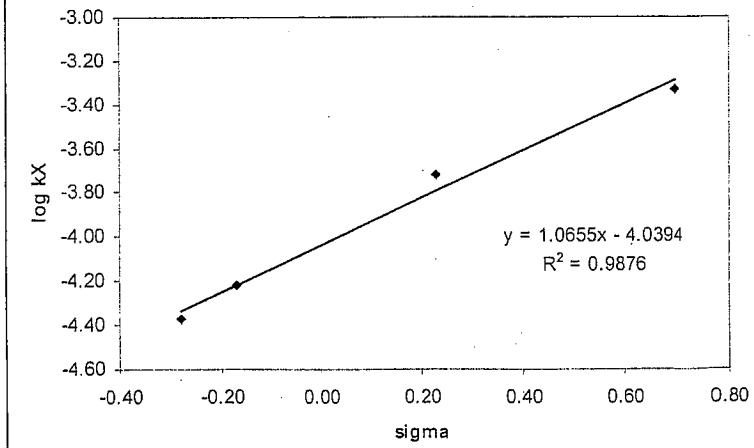
b) ρ for X substituents is large negative value indicating substantial decrease in electron density of reaction centre in close proximity to X groups. Therefore, suggests benzyl cation like

$$\require{cancel}\cancel{\ddagger}$$

$$\overset{\delta+}{CH_2}-N-\overset{\oplus}{N}=N-O-$$

(with ring bearing X substituent attached to the CH_2, and $\overset{\ominus}{O}$ below)
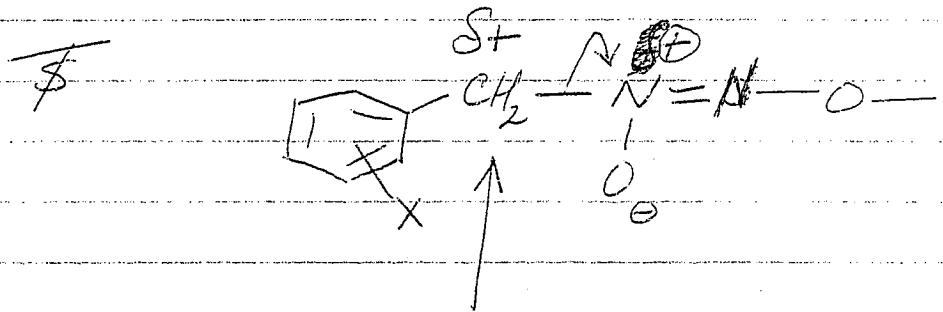
↑ build up of positive charge here since EDG's on X enhance reaction

(Compare -3.31 for this rxn to -5.6 for S_N1 solvolysis rxn (given)

in S_N1 solvolysis the $\oplus$ charge on benzyl carbon is fully formed as reaction proceeds via
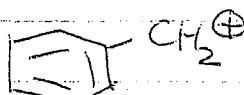
$$\overset{CH_2^{\oplus}}{\bigcirc}\ \text{intermediate}$$

∴ charge is less fully developed than in $Ph-CH_2-OTs$

ρ for Y substituents is positive value
similar in magnitude to the reference
reaction (ionization of benzoic acids).
EWG's improve leaving group ability of
phenyl sulfonates by stabilizing negative
charge.

Compare 1.07 for this rxn to $\rho = 1.9$
for Sn1 solvolysis. Therefore, negative charge
is less fully developed than adamantyl $- SO_3 - Ph$