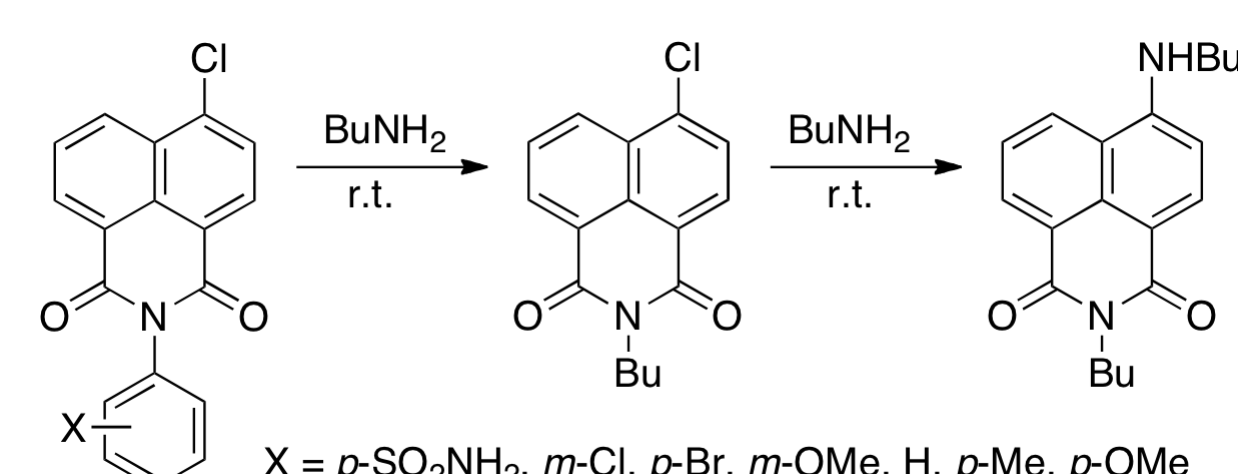
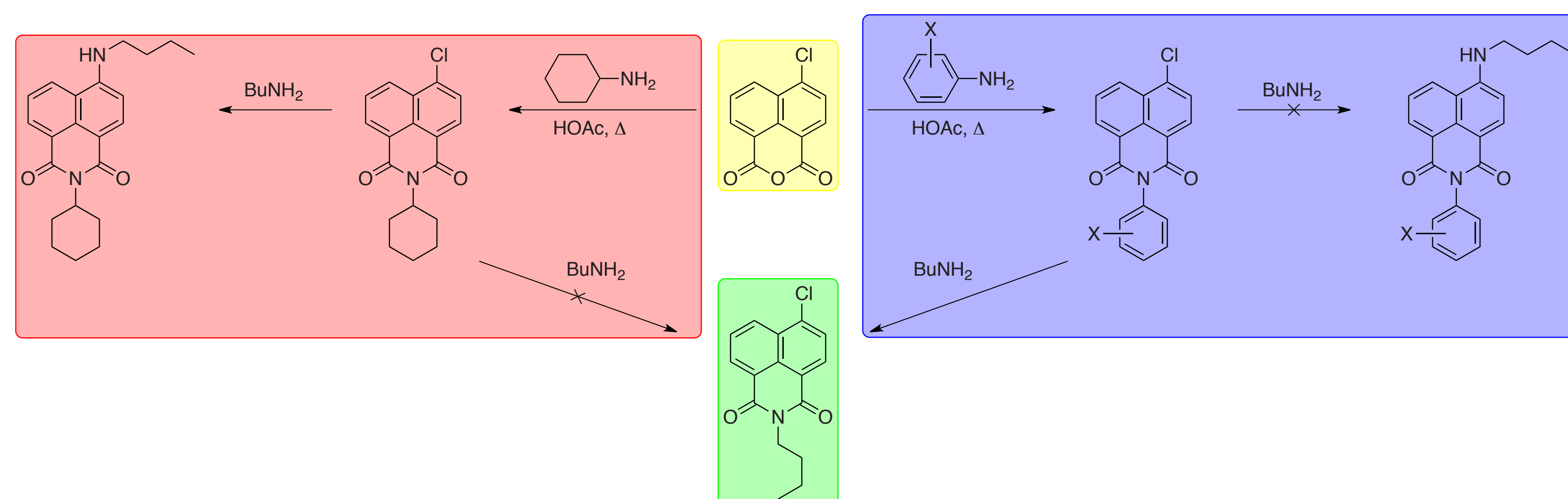


Kinetics of Naphthalimide Aminolysis

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(Faculty Mentor: David E. Lewis)

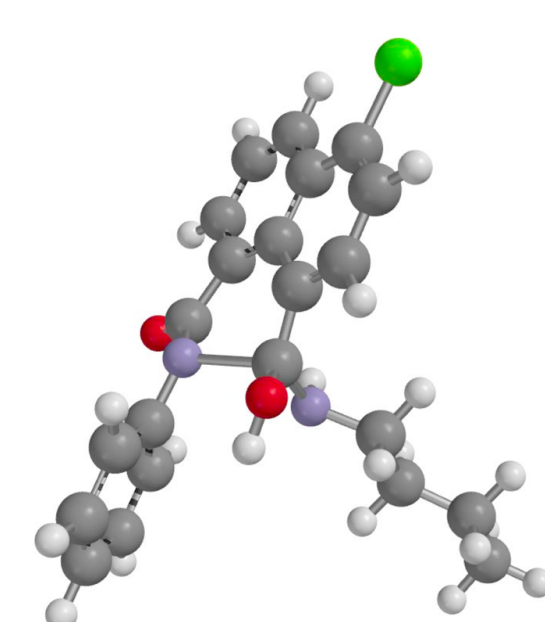
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- Displacement of arylamine is faster for electron-withdrawing substituents
- Displacement of halogen becomes competitive with displacement of the arylamine for electron-releasing substituents
- Even with electron-releasing substituents, displacement of the arylamine precedes halogen displacement

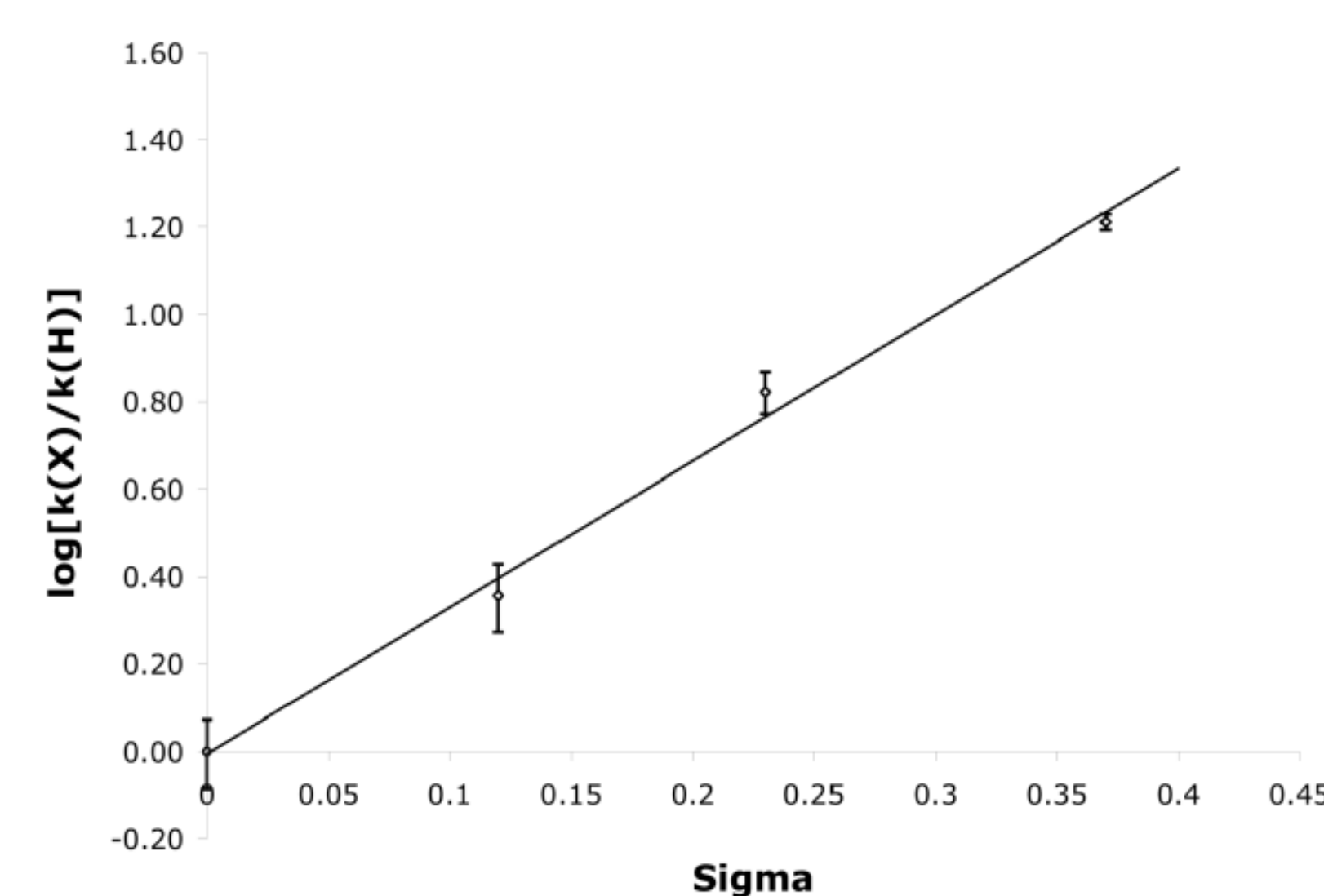
Deductions from Kinetic Data

- Hammett ρ constant = +3.3
 - significant negative charge development at N
 - comparable to Hofmann elimination (E1cb-like E2)



Bond	Reactant	Activated Complex
a	1.404	1.345
b	1.475	1.413
c	1.462	1.416
d	1.443	1.404
e	1.389	1.362
f	1.225	1.234

Hammett Plot for Reaction ($\sigma \geq 0$)



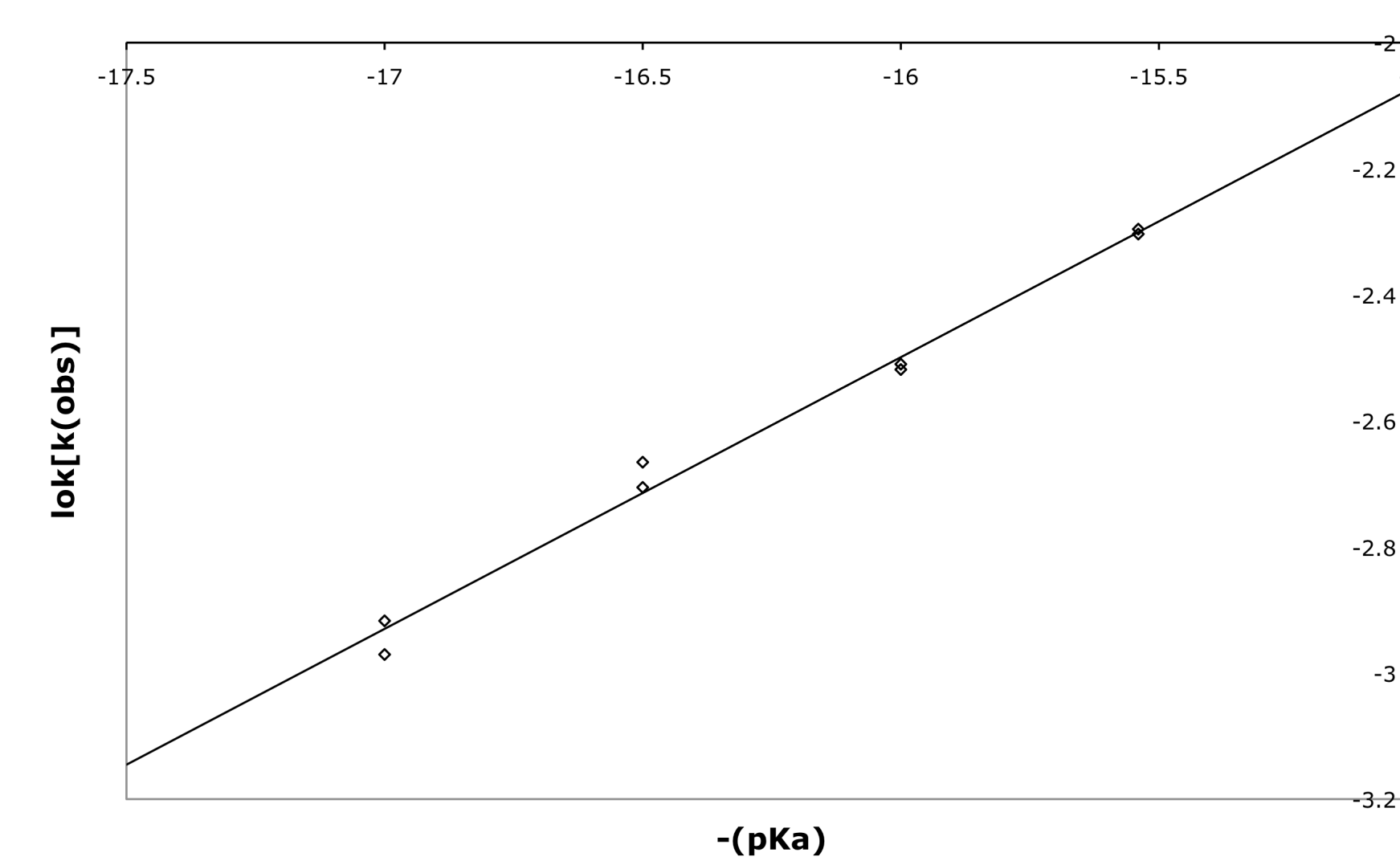
Substituent effects

- N-Substituent**
 - must be aryl for reaction to occur at the heterocyclic ring
 - cyclohexyl analogue does not undergo aminolysis
- 4-Substituent**
 - reaction is suppressed by electron-releasing groups capable of conjugating with the imide carbonyl groups (e.g. dimethylamino)
 - these compounds react slowly by transamination at the 4-position

Attempts to Determine Kinetic Order with Respect to Butylamine

- Reactions were to be carried out at 7.5 M, 5.0 M, and 2.5 M butylamine (all pseudo-first order conditions)
- Using dichloromethane (dielectric constant close to that of butylamine) as a cosolvent gave very complex kinetics
- Using methanol as cosolvent resulted in an *increase* in the value of the observed rate constant
 - hydrogen bonding?
 - something else?
- Used a series of alcohols as cosolvents
- Tested results using a Brønsted Law plot: $\log(k_{obs}) = C - \alpha(pK_a)$

Brønsted Law Plot for Alcohol Cosolvents



Effects of Solvent

- Attempts to explore effect of the concentration of the amine using alcohol cosolvents resulted in *acceleration* of the displacement reaction.
- We studied four alcohols to examine the solvent effects:
 - methanol (pK_a 15.54)
 - 1-propanol (pK_a 16.0)
 - 2-propanol (pK_a 16.5)
 - tert*-butyl alcohol (pK_a 17.0)
- The trend in reaction rates appears to correlate with the alcohols' ability to act as a hydrogen bond donor

Brønsted Law Results

- Specific Acid Catalysis
 - $\alpha = 1$
- General Acid Catalysis
 - $-0 < \alpha < 1$
- Our results:
 - Slope = +0.43
 - $R^2 = 0.993$
 - Consistent with General Acid Catalysis

Conclusions

- The aminolysis of *N*-substituted 4-chloro-1,8-naphthalimides occurs only when the substituent is an aryl group
- The reaction exhibits a second order rate law
 - Rate = $k[\text{imide}][\text{BuNH}_2]$
- N*-alkyl-4-chloro-1,8-naphthalimides react by displacement of the halogen
- An electron-releasing group at position 4 suppresses the aminolysis of the imide

Future studies

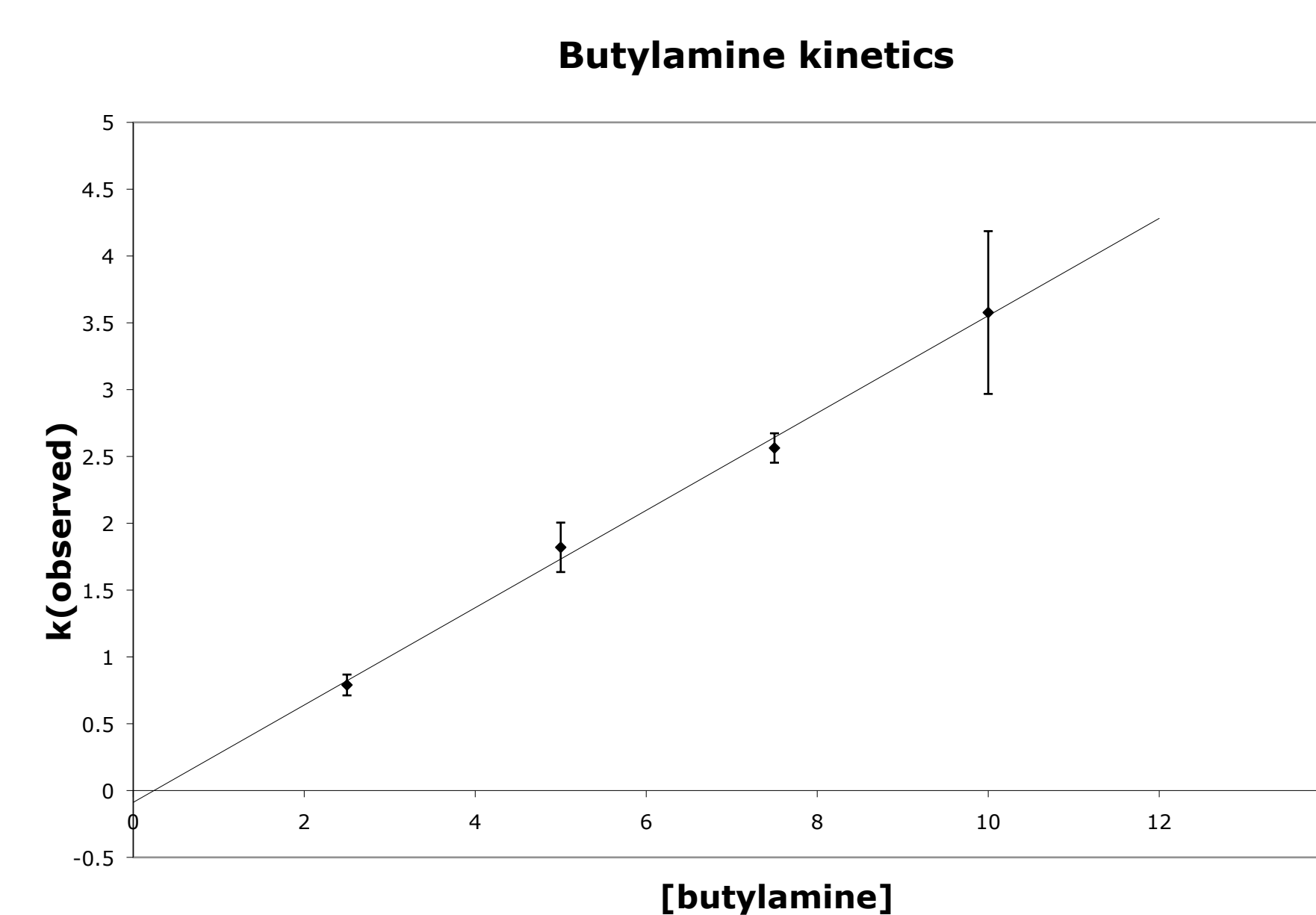
- The effects of the basic cosolvent will be measured with a view to determining whether the reaction is subject to general base catalysis
- The activation parameters of the reaction in 10 M butylamine will be determined by means of an Arrhenius plot

Kinetic order in butylamine

- Cosolvent must meet the following requirements:
 - it must be a tertiary amine
 - primary amines will compete with the butylamine
 - secondary amines will react with the imide (but reversibly)
 - it must have a pK_a close to that of butylamine
 - cosolvents has potential to lead to general base catalysis
- triethylamine has a pK_a close to butylamine

Kinetics in triethylamine cosolvent

- reaction was carried out at four different concentrations of butylamine in triethylamine
 - 10.0 M (neat butylamine), 7.5 M, 5.0 M, 2.5 M
 - all reactions gave good pseudo-first order plots
 - the pseudo-first order rate constants showed a linear dependence on butylamine concentration
- The reaction is first order in butylamine
- THE REACTION IS SECOND ORDER AND BIMOLECULAR



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