

1994

# An analysis of cosolvent effects in the solvolysis of bridgehead sulfonates

Ewa F. Nauka  
*San Jose State University*

Follow this and additional works at: [https://scholarworks.sjsu.edu/etd\\_theses](https://scholarworks.sjsu.edu/etd_theses)

---

## Recommended Citation

Nauka, Ewa F., "An analysis of cosolvent effects in the solvolysis of bridgehead sulfonates" (1994). *Master's Theses*. 855.  
DOI: <https://doi.org/10.31979/etd.njtt-pb69>  
[https://scholarworks.sjsu.edu/etd\\_theses/855](https://scholarworks.sjsu.edu/etd_theses/855)

This Thesis is brought to you for free and open access by the Master's Theses and Graduate Research at SJSU ScholarWorks. It has been accepted for inclusion in Master's Theses by an authorized administrator of SJSU ScholarWorks. For more information, please contact [scholarworks@sjsu.edu](mailto:scholarworks@sjsu.edu).

## INFORMATION TO USERS

This manuscript has been reproduced from the microfilm master. UMI films the text directly from the original or copy submitted. Thus, some thesis and dissertation copies are in typewriter face, while others may be from any type of computer printer.

**The quality of this reproduction is dependent upon the quality of the copy submitted.** Broken or indistinct print, colored or poor quality illustrations and photographs, print bleedthrough, substandard margins, and improper alignment can adversely affect reproduction.

In the unlikely event that the author did not send UMI a complete manuscript and there are missing pages, these will be noted. Also, if unauthorized copyright material had to be removed, a note will indicate the deletion.

Oversize materials (e.g., maps, drawings, charts) are reproduced by sectioning the original, beginning at the upper left-hand corner and continuing from left to right in equal sections with small overlaps. Each original is also photographed in one exposure and is included in reduced form at the back of the book.

Photographs included in the original manuscript have been reproduced xerographically in this copy. Higher quality 6" x 9" black and white photographic prints are available for any photographs or illustrations appearing in this copy for an additional charge. Contact UMI directly to order.

# U·M·I

University Microfilms International  
A Bell & Howell Information Company  
300 North Zeeb Road, Ann Arbor, MI 48106-1346 USA  
313/761-4700 800/521-0600



**Order Number 1359038**

**An analysis of cosolvent effects in the solvolysis of bridgehead  
sulfonates**

**Nauka, Ewa Faustyna, M.S.**

**San Jose State University, 1994**

**U·M·I**

300 N. Zeeb Rd.  
Ann Arbor, MI 48106



AN ANALYSIS OF COSOLVENT EFFECTS IN THE SOLVOLYSIS OF  
BRIDGEHEAD SULFONATES

A Thesis

Presented to

The Faculty of the Department of Chemistry  
San Jose State University

In Partial Fulfillment  
of the Requirements for the Degree  
Master of Science

By

Ewa F. Nauka

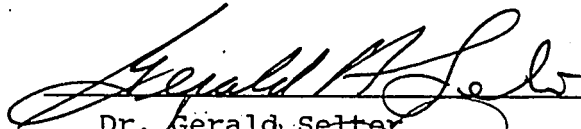
August, 1994

© 1994

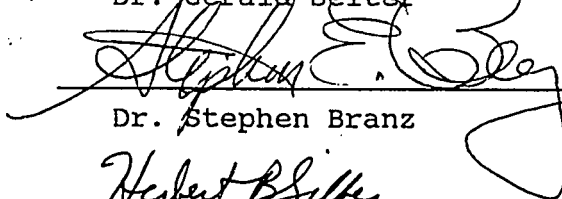
Ewa F. Nauka

ALL RIGHTS RESERVED

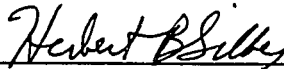
APPROVED FOR THE DEPARTMENT OF CHEMISTRY



Dr. Gerald Selzer

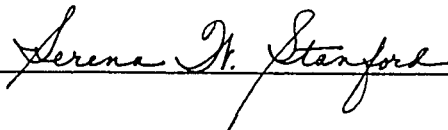


Dr. Stephen Branz



Dr. Herbert Silber

APPROVED FOR THE UNIVERSITY





## ABSTRACT

### AN ANALYSIS OF COSOLVENT EFFECTS IN THE SOLVOLYSIS OF BRIDGEHEAD SULFONATES

by Ewa F. Nauka

The effect of dilution of a binary mixture of TFE and EtOH with a series of nonreactive cosolvents (CCl<sub>4</sub>, CHCl<sub>3</sub>, hexane, acetone) on the solvolysis of 1-adamantyl mesylate (1-AdOMs), 1-bicyclo[2.2.2]octanyl tosylate ([2.2.2]-OTs) and 2-adamantyl tosylate (2-AdOTs) was investigated. It was found that reaction rates decreased with increasing concentration of cosolvent. This rate reduction is independent of the nature of the cosolvent but is related to the presence or absence of back-side pathway for product formation.

The selectivity of the TFE ether product over ethyl ether product increases with increasing CCl<sub>4</sub> and CHCl<sub>3</sub> mole fraction. Selectivity remains constant in the case of hexane, and decreases when acetone is used. These results can be explained in terms of the ability of the hydroxylic solvents to form hydrogen bonds. Selectivity behavior also can be related to the number of mechanistic pathways for product formation.

### ACKNOWLEDGMENTS

I would like to thank first and foremost Dr. Gerald Selter for constant guidance and encouragement during the course of this study. I also want to extend my thanks to Dr. Stephen Branz and Dr. Herbert Silber for help and suggestions during preparation of this thesis. Last but not least, I would like to thank my husband for his support and patience.

TABLE OF CONTENTS

INTRODUCTION.....1

EXPERIMENTAL SECTION.....13

RESULTS.....18

DISCUSSION.....22

CONCLUSIONS AND FUTURE WORK.....31

REFERENCES.....33

TABLES AND FIGURES.....35

LIST OF TABLES

Table I. Products for Solvolysis of 2-Adamantyl Tosylate in TFE-EtOH-CCl<sub>4</sub> Media at 90 °C.....35

Table II Products for Solvolysis of 2-Adamantyl Tosylate in TFE-EtOH-CHCl<sub>3</sub> Media at 90 °C.....36

Table III. Products for Solvolysis of 2-Adamantyl Tosylate in TFE-EtOH-Hexane Media at 90 °C.....37

Table IV. Products for Solvolysis of 2-Adamantyl Tosylate in TFE-EtOH-Acetone Media at 90 °C.....38

Table V. Products for Solvolysis of 1-Bicyclo[2.2.2]-octanyl Tosylate in TFE-EtOH-CCl<sub>4</sub> Media at 90 °C.....39

Table VI. Products for Solvolysis of 1-Bicyclo[2.2.2]-octanyl Tosylate in TFE-EtOH-CHCl<sub>3</sub> Media at 90 °C.....40

Table VII. Products for Solvolysis of 1-Bicyclo[2.2.2]-octanyl Tosylate in TFE-EtOH-Hexane Media at 90 °C.....41

Table VIII. Products for Solvolysis of 1-Bicyclo[2.2.2]-octanyl Tosylate in TFE-EtOH-Acetone Media at 90 °C.....42

Table IX. Products for Solvolysis of 1-Adamantyl Mesylate in TFE-EtOH-CCl<sub>4</sub> Media at 90 °C.....43

Table X. Products for Solvolysis of 1-Adamantyl Mesylate in TFE-EtOH-CHCl<sub>3</sub> Media at 90 °C.....44

Table XI. Products for Solvolysis of 1-Adamantyl Mesylate in TFE-EtOH-Hexane Media at 90 °C.....45

Table XII. Summary of Selectivities for the Solvolysis of 2-AdOTs, [2.2.2]-OTs, 1-AdOTs in tertiary mixtures of TFE-EtOH and cosolvent at 90 °C (2-AdOTs and [2.2.2]-OTs) and 25 °C (1-AdOMs).....46

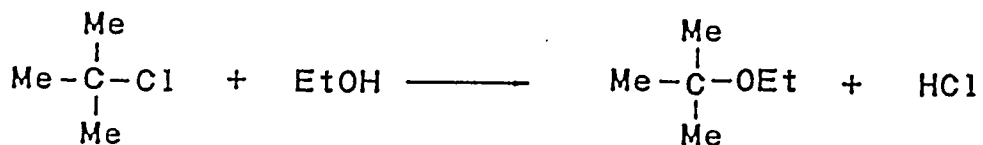
Table XIII. Summary of rate constant values for 2-AdOTs and [2.2.2]-OTs in 50:50 volume percent of EtOH-EtOH and cosolvent at 90 °C.....47

## LIST OF FIGURES

- Figure 1. Correlation of Excess Kinematic Viscosity and Product Excess for Solvolysis of 1-AdOTs in TFE-EtOH.....48
- Figure 2. Summary of Product Excesses for Adamantyl Substrates in TFE-EtOH.....49
- Figure 3. Correlation of Rate of Formation of Products and Mole Fractions for Solvolysis of 2-AdOTs and [2.2.2]-OTs in TFE-EtOH plus CCl<sub>4</sub>, CHCl<sub>3</sub>, Acetone, Hexane at 90 °C.....50

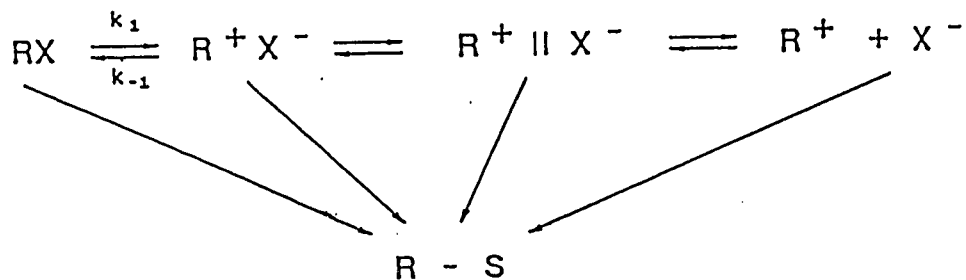
## INTRODUCTION

The effect of solvent variation on a solvolysis reaction was studied for the first time by Ingold and Hughes<sup>1</sup>. A solvolysis reaction is defined as a reaction in which substrate reacts with a solvent molecule and the solvent appears as a part of the product. An example is the solvolysis of *t*-butyl chloride in ethanol, in which *t*-butyl ethyl ether (*t*-BuOEt) is a product.



In general, the mechanism of a solvolysis reaction can be represented by the Winstein ion pair scheme (Scheme A)<sup>2</sup>.

Scheme A



According to Winstein, ionization of RX results in the formation of an internal ion pair  $[\text{R}^+ \text{X}^-]$  in which the cation and anion are adjacent. The internal ion pair can undergo either further dissociation to an external ion pair,  $\text{R}^+ \parallel \text{X}^-$ , in which at least one solvent molecule separates the

two ions, or it can collapse back to starting material (internal ion pair return). The external ion pair can either collapse back to the reactants via the internal ion pair (external return) or dissociate to free ions. The free ions also can collapse back toward reactants or can be captured by solvent. According to this scheme the solvent can attack any of the species in Scheme A (i.e., the substrate itself, the internal ion pair, the external ion pair or the free ions, to give a product).

The pathway in which solvent directly attacks substrate is called the  $S_N2$  mechanism. If the rate determining step occurs before reaction with solvent, the pathway is called  $S_N1$ . Nucleophilic attack on an intimate ion pair normally is expected to occur with inversion of configuration. This is because the leaving group shields the front side of the carbocation. At the solvent separated ion pair stage, the nucleophile can attack the ion pair from either side. This can lead to a combination of inversion and retention of configuration at the reacting carbon. Reaction via dissociated carbocations should occur with complete racemization. The extent to which reaction occurs on the intimate ion pair, solvent separated ion pair, or free ion stage can be estimated from product stereochemistry.

According to Winstein the stability of carbocation is a major factor controlling how far a substrate goes through the Winstein scheme before being captured by a solvent. Only very stable cations can survive long enough to give free ions. Usually these are the systems which can delocalize positive charge into a neighboring pi system, as for example the triphenylmethyl carbocation.

The Winstein scheme has provided a useful mechanistic model which goes a long way in explaining observed effects such as common ion rate depression<sup>3</sup>, salt effects<sup>4</sup>, product stereochemistry in optically active systems<sup>7</sup>, and equilibration of labeled oxygens in sulfonate and carboxylate leaving groups<sup>5,6</sup>. However, it poorly explains the very important role of the solvent in such a reaction. Changing the nature or the concentration of a solvent can greatly change both the rate of a reaction and the resulting product distribution. For example, when the solvent is changed from ethanol to trifluoroacetic acid in the solvolysis of 2-AdOTs the rate increases by  $2 \times 10^6$  at 25 °C<sup>8</sup>. Also, solvolysis of t-BuCl in ethanol gives 44% elimination to 2-methylpropene, whereas in the 70% aq. ethanol only 10% elimination is observed<sup>9</sup>. The above examples illustrate that the solvent can be as important as the substrate in the solvolysis reaction.



Solvent effects can be assessed either by measuring solvolysis rates, or by measuring product distributions in binary solvent systems. The first way of assessing solvent effects in this type of reaction is by measuring the substrate response to changes in the solvent ionizing power. Solvent ionizing power was defined by Winstein and Grunwald<sup>10-12</sup> when they used equation 1 to correlate solvolysis rates of *t*-butyl chloride in different solvents.

$$\text{Log}(k/k_0)_{\text{RX}} = mY \quad (\text{eq. 1})$$

In equation 1, *Y* is the solvent ionizing power, and *m* is the substrate response to the changes in solvent ionizing power. *t*-BuCl was chosen as a standard substrate (RX) with *k* referring to its solvolysis rate in any solvent and *k*<sub>0</sub> to its rate in 80% (v/v) ethanol-water at 25 °C. *t*-BuCl was assumed to solvolyze without nucleophilic solvent assistance, i.e., by an S<sub>N</sub>1 mechanism.

Solvolysis rates were measured for a number of compounds and correlated with solvent ionizing power. Since the rate increased with increasing ionizing power, it was believed that the bond breakage was a function of ionizing power and therefore was the rate determining step. When two compounds responded similarly to medium changes ("*m*" has

similar values), then it was assumed that they react by similar mechanisms and that solvent plays the same role in each solvolysis reaction. Traditionally, rates of solvolysis were correlated with solvent ionizing power (linear free energy correlation)<sup>3</sup>. However, a linear free energy correlation cannot be used for exact mechanistic conclusions, particularly with regard to solvent functions, when the standard substrate reaction mechanism and the role of the solvent are not known.

Y values were obtained via equation 1 for a large number of solvents using t-BuCl as a standard<sup>8</sup>. However, the failure of most reactions conducted in sets of binary solvent mixtures to be correlated by equation 1 (dispersion) led to conclusion that the substrate parameter "m" is solvent dependent. Also, t-BuCl reacts in some solvents, for example H<sub>2</sub>O, with weak but important nucleophilic assistance (the beta deuterium isotope effect is smaller than that for free ions)<sup>13</sup>. As a response to the above problems, Bentley, Schleyer and coworkers proposed 2-adamantyl tosylate (2-AdOTs) as a standard<sup>8</sup>. This choice was based on the assumption that 2-AdOTs solvolyses without either nucleophilic solvent assistance or significant internal return. However, it was later found that internal return occurs in such secondary substrates. From work by Bunnett

and Paradisi<sup>6</sup> it was shown that the rate of internal return is greater than the rate of solvolysis of 2-adamantyl benzenesulfonate. Thus, Bentley and others have defined  $Y_X$  scales for a variety of leaving groups, using appropriately chosen standard substrates.  $Y_X$ , as defined by Bentley, seems to be dependent on the alkyl group, the leaving group and the solvent; the  $Y$  value for 1-AdI in TFE was measured to be 2.22<sup>14</sup> ; for 1-AdOTs in TFE  $Y$  was 2.34<sup>8</sup> ; and for 2-AdOTs in TFE  $Y$  was 1.80<sup>15</sup>. Because of such variations in the  $Y$  values, rigorous application of Grunwald-Winstein correlations as a mechanistic probe is greatly weakened.

Information concerning the role of the solvent also can be obtained by studying product formation in binary solvent mixtures. In such cases at least two external ion pair species can be described. For example, in the solvolysis of 1-AdOTs in ethanol-trifluoroethanol solvent, one external ion pair can be envisioned in which ethanol lies near reacting carbon, and another external ion pair with trifluoroethanol. In binary hydroxylic media the selectivity is commonly evaluated according to equation 2<sup>16</sup>

$$S = \frac{k_{s1}}{k_{s2}} = \frac{[ROS_1] [S_2]}{[ROS_2] [S_1]} \quad (\text{eq. 2})$$

where  $k_{S_1}$  and  $k_{S_2}$  are the rate constants for formation of products  $ROS_1$  and  $ROS_2$  from solvents  $S_1$  and  $S_2$  respectively. If  $S_1$  is a better nucleophile than  $S_2$ , a selectivity value greater than unity means that the better  $S_1$  nucleophile is preferred. Thus, a selectivity value less than unity means that the poorer  $S_2$  nucleophile is preferred. A non selective model would have selectivity value equal to 1.

In a binary hydroxylic solvent system, cationic intermediates can react with either solvent component. Selectivity is the ratio of the second-order rate constants for product formation resulting from the bimolecular reaction of a cationic intermediate with each of the hydroxylic solvent molecules. If it is assumed that the cation has a long enough lifetime to choose the better nucleophile, then selectivity values greater than unity are expected. However, observed selectivities for the solvolysis of adamantyl compounds and other bridgehead systems are usually inverted. This means that the poorer nucleophile is preferred<sup>26</sup>.

Harris and his collaborators<sup>18</sup> studied the solvolyses of a series of 2-adamantyl arenesulfonates in the binary solvent, EtOH-H<sub>2</sub>O, where EtOH is the better nucleophile. However, they observed inverted selectivity. They attributed

this phenomenon to the ability of H<sub>2</sub>O to form two hydrogen bonds in the solvent separated ion pair, with two of the oxygen atoms of the arenesulfonate leaving group. EtOH, on the contrary, can form only one hydrogen bond.

Ando and Tsukamoto<sup>17</sup> reported that selectivities ( $k_{\text{TFE}}/k_{\text{EtOH}}$ ) for 2-adamantyl and 1-adamantyl systems in 50/50 (v/v) TFE-EtOH mixtures are 1.35 and 1.74 respectively which means that TFE, the poorer nucleophile, is preferred. Ando and Tsukamoto explained their results by assuming that products were formed by front-side collapse of solvent separated ion pairs. Thus, TFE separated ion pairs were preferred. They concluded that the electrophilicity of the solvent is an important factor and that the collapse of the solvent separated ion pair is the product forming step.

Kaspi and Rapport<sup>16</sup> reported selectivities for 1-AdBr in TFE-EtOH and in TFE-H<sub>2</sub>O. For the TFE-EtOH solvent mixtures, TFE is favored at low [ $X(\text{TFE}) < 0.35$ ] and high [ $X(\text{TFE}) > 0.65$ ] concentrations. Ethanol is favored at the intermediate concentrations. For the solvolysis in TFE-H<sub>2</sub>O they found that TFE was favored over H<sub>2</sub>O at  $X(\text{TFE})$  less than ca. 0.25, and H<sub>2</sub>O was favored at  $X(\text{TFE})$  greater than 0.25.

Karton and Pross<sup>19</sup> reported selectivity values, ( $k_{\text{water}}/k_{\text{EtOH}}$ ), between 1.6 and 2.2 for the solvolysis of 1- and 2-adamantyl bromide and chloride and 2-adamantyl tosylate in EtOH-H<sub>2</sub>O. The selectivity behavior described above cannot be explained in terms of ionizing power and nucleophilicity.

Inverted selectivities also were observed by Ferla<sup>20</sup> in the 1- and 2-adamantyl sulfonates solvolysed in EtOH-TFE media. In all cases TFE, the poorer nucleophile, was favored in the reaction. This observation was explained using the following ground state argument and viscosity/diffusion hypothesis<sup>20</sup>.

#### The ground state argument

TFE is approximately 2500 times more acidic than EtOH. Therefore, in the ground state it forms hydrogen bonds with the leaving group to a greater extent than does EtOH. Since in the ground state the micro-solvent composition near the leaving group is TFE-rich, the carbocation is able to react with TFE in higher proportion than with EtOH. This leads to the possibility that products may be formed by nucleophilic attack on the internal ion pair. Those products are a

function of micro solvent composition and not carbocation stability.

#### Viscosity/diffusion model

Another parameter, an excess function, is also defined<sup>20</sup> to determine the excess quantity of one product relative to the molar composition of the solvent. The excess is simply the deviation in the amount of product formed compared to that expected in a non-selective model. This function is complementary to the selectivity function:

$$XS = X(1-AdOTFE) - X(TFE) \quad (\text{eq. 3})$$

where XS is the excess TFE product and X(1-AdOTFE) relative to X(1-AdOEt) and X(TFE) relative to X(EtOH) are the mole fractions of 1-AdOTFE and TFE, respectively. If the 1-AdOTFE product is formed in the same amount as the mole fraction of TFE in the solvent then the excess TFE is zero, which means that there is no selectivity. Otherwise, a positive excess indicates that 1-AdOTFE is formed in larger percentage than the TFE fraction in the solvent.

The excess functions for 1-AdOTs and 2-AdOTs are plotted versus mole fraction of TFE (Figure 2). In the 1-AdOTs plot the excess function is parabolic. The curve for

2-AdOTs has a lower maximum excess value (0.10) than 1-AdOTs (0.14) and the excess plot is not symmetric. This observation suggests that in the case of 2-AdOTs the products result from both front-side and back-side mechanisms. In the back-side mechanism there is no hydrogen bond effect and therefore the better nucleophile is favored. Thus, the excess function (eq. 3) for 2-AdOTs actually represents a composite of product formation from the front-side of the reacting carbon, where TFE is favored, and back-side reaction where EtOH is favored.

There is a strong correlation between product formation and solvent viscosity<sup>20</sup>. An excess viscosity plot can be generated by calculating the difference between the observed viscosity at any composition and the mole fraction average of the viscosity of the pure solvents. In other words, the excess viscosity is the deviation of the observed viscosity from the linear (ideal) behavior. Both the excess viscosity and the excess kinematic viscosity (viscosity divided by density) of TFE-EtOH correlate inversely with the product excess value (eq. 3) of bridgehead compounds (Figure 1). Since viscosity is inversely proportional to diffusion, it was concluded that product formation is diffusion controlled. It was also shown<sup>6</sup> that the rate of internal return is faster than the rate of solvolysis. This suggests



that during the time domain of bond breakage and reformation, the bulk solvent is essentially frozen (rotation is thousand times faster than diffusion)<sup>3</sup> and the diffusional separation of the cation and the leaving group is relatively slow. Thus, in these relatively simple alkyl systems, the cation does not have a long enough lifetime to reach the solvent separated stage. Therefore, it can undergo internal return or react with whichever nucleophile is present as the leaving group begins to diffuse into the solvent.

The arguments presented above suggest that the anomalous product selectivities cited previously may be rationalized on the basis of other mechanistic parameters besides solvent ionizing power and nucleophilicity.

The purpose of this study was to extend our present understanding of the ground state theory and the proposed diffusion/viscosity model. It was shown that in [2.2.2]-OTs solvolysis, TFE was favored over EtOH in the products even at mole fractions as low as 0.05 of TFE in TFE-EtOH. It was of interest to us to measure product distributions even for lower TFE concentrations in TFE-EtOH media. In order to perform experiments at such low TFE-EtOH concentrations it was convenient to dilute the TFE-EtOH with a third

nonreactive cosolvent. Holding the ratio of TFE to EtOH constant, we were able to observe how different concentrations of cosolvent affect product ratios. Both the product distributions in the ternary solvent mixture and reaction rates were measured. We expected that data from these two independent experiments would be complementary. In order to support the hypothesis that 2-AdOTs reacts by both front-side and back-side mechanisms, 2-AdOTs was compared to [2.2.2]-OTs and 1-AdOMs, which can only react by the front-side pathway.

#### EXPERIMENTAL SECTION

Infrared spectra were recorded with a Perkin-Elmer IR-257 spectrophotometer using 10% solutions in chloroform against the pure reference solvent. Melting points were determined with a Fischer-Johns melting point apparatus and they are uncorrected. Gas chromatographic and mass spectroscopic data were obtained on Finnigan 1020B GC/MS.

**Synthesis of 1-Adamantyl Mesylate.** 1-Adamantyl alcohol in methylene chloride (30.4g, 0.2 M ) containing a 50% molar excess of triethylamine was treated with methanesulfonyl chloride using the procedure of Crossland and Servis<sup>21</sup>. The

product, 1-AdOMs in CH<sub>2</sub>Cl<sub>2</sub>, was washed in succession with ice water, 10% hydrochloric acid, saturated sodium bicarbonate solution, and brine. The organic layer was dried over MgSO<sub>4</sub>. A 10 uL sample of 1-AdOMs in CH<sub>2</sub>Cl<sub>2</sub> was injected into pure, dried, and distilled TFE using a Hamilton microliter gas tight syringe. The resulting solution was analyzed by GC/MS, which indicated that there was 95.6% conversion to 1-AdOMs with 4.4% of unreacted 1-AdOH remaining.

**Synthesis of 1-Bicyclo[2.2.2]octanyl Tosylate.** Bicyclo[2.2.2]octan-1-ol (1.0 g, 0.0079 mol), 10 mL of dry pyridine (BaO), and p-toluenesulfonyl chloride (2.5 g, 0.013 mol, m.p. 66.3-67.1 °C) were sealed in an ampule and kept at 40 °C for 78 hours. After cooling, the red-brown solution was poured into ice-water (30 mL). The solid tosylate was removed by filtration and dried in vacuum. Recrystallization from petroleum ether (30-60) at 0 °C gave pure product: m.p. 65.8-67.3 °C (lit<sup>21</sup>. m.p. 65 °C). IR (CHCl<sub>3</sub>) 3300 (Ar-H), 1600 (Ar), 1350 (asym O=S=O), 1170 (sym O=S=O) cm<sup>-1</sup>.

2-Adamantyl Tosylate was prepared by the same method as that used for 1-bicyclo[2.2.2]octanyl tosylate. IR (CHCl<sub>3</sub>)

1600 and 1460 (Ar), 1350 (asym O=S=O), 1180 (sym O=S=O);  
m.p. 81.6-82.2 °C.

### Solvent purification

TFE and EtOH. Dry TFE and EtOH were each prepared by refluxing over dried type 4A molecular sieves for 24 hours followed by distillation. The first few drops of the distillate were discarded. Molecular sieves (type 4A) were dried in an oven at 100 °C for several days before use.

Acetone and hexane. Analytical grade absolute acetone and hexane were stored over 4A molecular sieves and used directly.

Dichloromethane, chloroform and carbon tetrachloride. Reagent grade solvents were obtained from commercial sources.

### Product studies

Each substrate (1-AdOMs, 2-AdOTs and [2.2.2]-OTs) was solvolyzed in a mixture of 50/50 volume percent TFE-EtOH and a third nonreactive solvent (carbon tetrachloride, chloroform, hexane, or acetone).

Product studies for 1-AdOMs in TFE/EtOH containing CCl<sub>4</sub>, CHCl<sub>3</sub>, acetone or hexane. These studies were performed in duplicate at room temperature. A mixture of 50 volume percent of TFE and 50 volume percent of EtOH was prepared and used as a stock solution. CCl<sub>4</sub> (x volume percent) was mixed with the TFE-EtOH stock mixture (100-x) volume percent; (x = 10, 20, 40, 60, 80). Naphthalene (0.12g, 1 mM), used here as internal standard, was added to the freshly prepared 1-AdOMs in CH<sub>2</sub>Cl<sub>2</sub> (5 mL). The choice of naphthalene is discussed in the "Results" section. The solution was buffered with ca. 2 mM 2,4,6-trimethyl pyridine and 10 uL samples of this solution were added to the ampules containing the TFE-EtOH/CCl<sub>4</sub> solvents. The ampules were sealed, solvolyzed for 20 minutes, and analyzed by GC/MS. The constant volume injections were made with a Hamilton microliter gas tight syringe. Product studies for 1-AdOMs in TFE-EtOH/CHCl<sub>3</sub>, TFE-EtOH/hexane, and TFE-EtOH/acetone were done by the same procedure as described above.

Product studies for 2-AdOTs and [2.2.2]-OTs in TFE-EtOH containing CCl<sub>4</sub>, CHCl<sub>3</sub>, acetone or hexane. These studies were done at 90 °C. 2-AdOTs and naphthalene (internal standard) were added to a mixture of TFE-EtOH (50/50 volume percent) to make a 2 mM stock solution in each substrate. The solution was buffered with ca. 2 mM 2,4,6-trimethyl

pyridine.  $\text{CCl}_4$  was mixed with 2-AdOTs to make a 2 mM solution which also was buffered with ca. 2 mM 2,4,6-trimethyl pyridine. The 2-AdOTs in TFE-EtOH solution and 2-AdOTs in  $\text{CCl}_4$  were mixed in the following way: x volume percent of  $\text{CCl}_4$  solution was mixed with (100-x) volume percent of the TFE-EtOH stock solution (x = 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, 95). Aliquots (ca. 1 mL) of the resulting solutions were placed in ampules which were then sealed and solvolyzed for approximately 10 half-lives or longer at 90 °C in an oil bath. Product studies for 2-AdOTs and [2.2.2]-OTs in TFE-EtOH/ $\text{CHCl}_3$ , TFE-EtOH/hexane, TFE-EtOH/acetone, and for [2.2.2]-OTs in TFE-EtOH/ $\text{CCl}_4$  were done using the same procedure as described above.

#### Solvolysis rate studies

These studies were done for x = 50 volume percent of TFE-EtOH and x = 50 volume percent of cosolvent.

Solvolysis rate studies for 2-AdOTs and [2.2.2]-OTs in TFE-EtOH containing  $\text{CCl}_4$ ,  $\text{CHCl}_3$ , acetone or hexane. 2-AdOTs and naphthalene (an internal standard) were added to a mixture of TFE-EtOH (50/50 volume percent) to make a 1 mM stock solution in each substrate. The solution was buffered with ca. 2 mM 2,4,6-trimethyl pyridine. A 2 mM solution of

both 2-AdOTs and naphthalene in a cosolvent (e.g., CCl<sub>4</sub>) was prepared, which also was buffered with ca. 2 mM 2,4,6-trimethyl pyridine. The stock solutions of alcohol and cosolvent were combined in a ratio of 1:1 by volume. Approximately 1 mL aliquots of the resulting mixture were sealed in 1 mL ampules and solvolyzed in an oil bath at 90 °C. Samples were withdrawn at 1, 3, 6, 10, and 24 hr. All samples were analyzed using GC/MS. The relative percents of naphthalene and the reaction products (as determined by ion counts) were obtained from the GC/MS quantitation reports. The concentration of the products was then calculated relative to the 2 mM naphthalene standard, and the resulting values were used to calculate the first-order rate constant. Solvolysis rate studies for 2-AdOTs and [2.2.2]-OTs in TFE-EtOH/CHCl<sub>3</sub>, TFE-EtOH/hexane, TFE-EtOH/acetone, and for [2.2.2]-OTs in TFE-EtOH/CCl<sub>4</sub> were done using the same procedure.

## RESULTS

Both the kinetic and the product samples were analyzed using the Finnigan 1020B GC/MS. All data discussed here were obtained from the GC/MS scans. Naphthalene was used in all solvolysis reactions as an internal standard because it gave

a well defined, sharp peak, did not undergo any decomposition, did not react with substrates, and had a convenient retention time. For all substrates used in the experiments, GC/MS peaks of unreacted sulfonate were never observed. This was probably due to their decomposition in the injector of the GC. The internal standard was used in the product studies to ensure that the product analyses were determined on samples that had reacted for at least three half-lives (87%) in media where the rate constant was unknown. In the kinetic samples, the concentration of the solvolysis products was determined by reference to the known concentration of the internal naphthalene standard. Thus, unreacted substrate concentration could be calculated along with the percent of substrate that underwent reaction.

#### Product studies

The samples were prepared by mixing x volume percent of 50/50 volume percent TFE-EtOH with (100-x) volume percent of cosolvent, where x = 5, 10.....80, 90, 95. All samples were buffered with 2 mM of 2,4,6-trimethyl pyridine and also contained 2 mM of naphthalene. The sample concentration in these studies was ca. 2 mM. Product studies were done using a sealed ampule technique. The reactions were run for at least ten half-lives. It was observed that the products



were formed in a constant ratio independent of how far the reaction had progressed. Each sample was analyzed by GC/MS with at least three separate injections. The solvolysis products were the ethyl and the 2,2,2-trifluoroethyl ethers of the corresponding sulfonate ester. The results for solvolysis of 2-AdOTs in TFE-EtOH-cosolvent are presented in Tables I-IV. Results for [2,2,2]-OTs are summarized in Tables V-VIII, and those for the 1-AdOMs are presented in Tables IX-XI. The first column in Tables I to XI present volume percent of TFE-EtOH. Columns two and three (percent of relative ion counts for ROTFE and ROEt) were taken directly from the GC/MS reports. The mole fraction of the products is shown in column four of Tables I to IX. The mole fractions of the solvents were calculated from the solvent volumes prior to mixing, and are shown in columns five and six of Tables I to XI. Selectivity values were calculated using eq. 2 and are summarized in Table XII. Selectivity values for all solvolysis reactions except 2-AdOTs in TFE-EtOH-acetone are greater than one. This indicates that TFE is preferred over EtOH for all solvent compositions. Also, selectivity values for all solvolysis reactions except 2-AdOTs and [2,2,2]-OTs in TFE-EtOH/acetone increase with decreasing mole fraction of TFE. For [2,2,2]-OTs in TFE-EtOH/acetone selectivity is greater than one; however, it decreases with increasing acetone (decreasing mole fraction

of TFE). Selectivity for 2-AdOTs in TFE-EtOH/acetone is greater than one only for two highest (0.42 and 0.40) mole fractions of TFE. For the mole fractions of 0.36 to 0.02 selectivities are less than one.

### Kinetic studies

Kinetic studies were performed with 2-AdOTs and [2.2.2]-OTs. The solvolysis rates for 1-AdOMs are 10 to 100 times faster than for 1-AdOTs<sup>27</sup>. Thus, the half-life for 1-AdOMs under the conditions used is too short to perform such studies. The rates were determined for 50 volume percent TFE-EtOH and 50 volume percent of cosolvent at 90 °C. All samples were buffered with 2 mM of 2,4,6-trimethyl pyridine and contained naphthalene (2 mM). Kinetic solutions were ca. 1 mM in initial sulfonate concentration. Product concentrations were determined relative to the naphthalene internal standard. The rate constants were calculated from the time and concentration data using LSKIN1 program and are listed in Table XIII<sup>23</sup>. The observed correlations between the mole fraction of the alcohols and the logarithm of the rate constants are shown in Figure 3.

## DISCUSSION

Ferla showed<sup>20</sup> that even for TFE concentrations as low as 0.05 mole percent in a TFE-EtOH mixture, TFE was favored over EtOH in the observed solvolysis products. The objective of this work was to study the effect of dilution of TFE-EtOH with third, non-reactive, solvent. Four different solvents (CCl<sub>4</sub>, CHCl<sub>3</sub>, hexane and acetone) and three substrates (2-AdOTs, [2.2.2]-OTs and 1-AdOMs) were selected. These systems were chosen for two main reasons. First, they cannot undergo elimination reactions since the olefin formed would violate Bredt's rule<sup>24</sup>. Second, 1-AdOMs and [2.2.2]-OTs are both incapable of either back-side solvation or back-side nucleophilic attack, so that all products are necessarily formed by a front-side reaction<sup>25</sup>. 2-AdOTs may have back-side nucleophilic solvation in the transition state, but the ratio of back-side to front-side reaction is much lower than in the case of acyclic secondary tosylates<sup>20</sup>. The substrates discussed here can be evaluated with respect to the following differences and similarities:

A. 2-AdOTs vs. [2.2.2]-OTs. Both substrates have the same leaving group; however, 2-AdOTs is a secondary system and [2.2.2]-OTs is a tertiary, bridgehead system. Both have similar reactivity under the conditions used in this study.

B. 2-AdOTs vs. 1-AdOMs. 2-AdOTs is a secondary system and 1-AdOMs is a tertiary, bridgehead system. Also, they have different leaving groups: tosylate and mesylate (for mesylate the absence of steric hindrance from the phenyl ring increases the availability of the sulfonate to participate in hydrogen bonding by the solvent in the ground state).

C. 1-AdOMs vs. [2.2.2]-OTs. Both of these compounds are tertiary, bridgehead systems, but they differ in leaving group.

The reacting solvents (TFE and EtOH) were selected because of the previous extensive studies<sup>20</sup>. TFE and EtOH have the same functionality (primary alcohols), similar molecular volume and dielectric constants. Significant differences can be found when their nucleophilicities, ionizing power and acidities<sup>25</sup> are compared. Studies of solvolysis reactions of 1-AdOMs, 2-AdOTs and [2.2.2]-OTs in 50/50 volume percent TFE-EtOH were reported by Ferla<sup>20</sup>. Ferla's data can be compared with that obtained in the present study where the solvolyses are run in 50/50 volume percent TFE-EtOH-cosolvent. The choice of cosolvent was based on the fact that they are all non-hydroxylic while they differ significantly in functionality and polarity. The main parameter introduced in this work is the

concentration of cosolvent, since the ratio of TFE to EtOH remains constant. Any observed differences in kinetic behavior and product selectivity can be evaluated in terms of changes in total alcohol concentration and differences in cosolvent properties.

### Product studies

In the Winstein mechanistic model, the anticipation that product selectivity be governed by the better solvent nucleophile is predicated on the existence of cationic intermediates with lifetimes significantly longer than the diffusional limit of the reaction medium. In other words, in TFE-EtOH media, selectivity favoring the better nucleophile, EtOH, in the bridgehead substrates requires that the system reach a solvent separated ion pair having a sufficient lifetime to select the better nucleophile. This was not observed. For all the solvolyses we studied in ternary media, except 2-AdOTs in TFE-EtOH-acetone, the TFE ether was preferred over the ethyl ether (i.e.,  $k_{ROTFE}/k_{ROEt} > 1$ ). From the above observation we conclude that the nucleophilicity of the solvent is not the major factor determining the selectivity in the ternary solvent mixtures used in this study. If nucleophilicity determined the selectivity, EtOH would be the favored nucleophile in TFE-EtOH mixtures. The

preference for TFE during product formation can be explained in terms of a ground state solvation effect<sup>20</sup> and a diffusional model. TFE is approximately 2500 times stronger acid than EtOH. Therefore, in the ground state, TFE can more readily bind with the sulfonate leaving group due to its greater facility to form hydrogen bonds. Thus, the solvent pool in the vicinity of the leaving group would be expected to be richer in TFE than is the bulk solvent.

From the work of Bunnett and Paradisi<sup>6</sup> it is known that the rate of internal return is greater than the rate of solvolysis for 2-adamantyl benzenesulfonate. This means collapse of the internal ion pair is faster than the separation of the cation and the leaving group. If the lifetime of the catanoid intermediate involved in the product forming step is governed by the diffusional separation of the leaving group and the reacting carbon, it follows that the same solvent molecules that surround the leaving group in the ground state must also be present in the transition state of the product forming step. As a result, the product distribution will show a higher selectivity toward the TFE ether compared to ethyl ether.

### 2-AdOTs vs. [2.2.2]-OTs

Solvolysis rate constants for 2-AdOTs ( $5.55 \times 10^5$ ) and [2.2.2]-OTs ( $36.3 \times 10^5$ ) in mixtures of 50/50 TFE-EtOH at 90 °C are similar. For both substrates when solvolyzed in CCl<sub>4</sub> and CHCl<sub>3</sub> cosolvents, selectivity values favoring the TFE ether increase as the mole fraction of TFE-EtOH was decreased. For the 2-AdOTs selectivity values ranged between 1.68 and 2.30 for CCl<sub>4</sub>, and between 1.70 and 2.60 for CHCl<sub>3</sub>. For [2.2.2]-OTs selectivity values were 2.01-3.26 and 1.78-3.60, respectively, for these same cosolvents. The lower values are almost the same for both substrates in both solvents. However, at the higher concentrations of cosolvents [2.2.2]-OTs showed higher selectivity values than the corresponding 2-AdOTs. The selectivities for [2.2.2]-OTs are very similar for both cosolvents and so they are for 2-AdOTs, but selectivity values are different for these two substrates. Selectivity values are the same at the lower concentrations of cosolvent. With increasing concentrations of cosolvent, selectivity increases more slowly for 2-AdOTs than for [2.2.2]-OTs. One would expect selectivity to be higher for 2-AdOTs than for [2.2.2]-OTs because 2-AdOTs reacts more slowly. In fact, the reverse situation was observed. This cannot be explained as resulting from differences between the cosolvents. Both cosolvents, CCl<sub>4</sub>

and  $\text{CHCl}_3$ , are similar in structure and both exhibit similar weak interactions with alcohols. However, it can be explained by the back-side mechanism of 2-AdOTs. [2.2.2]-OTs can only react by the front-side mechanism and therefore TFE is the preferred nucleophile. In the case of 2-AdOTs, reaction takes place at the secondary carbon. This reaction is likely to be a combination of front-side and back-side pathways. In the case of the back-side mechanism, the solvent molecules are too far away to interact with leaving group. EtOH, the better nucleophile, is favored. The combination of front-side and back-side mechanisms is probably responsible for the lower selectivity for 2-AdOTs.

The selectivity values decrease with decreasing mole fraction of acetone. For 2-AdOTs the selectivity values are greater than unity only for two lowest concentrations of acetone (0.05 and 0.09). For acetone concentrations between 0.18 and 0.95 the selectivity values are less than one. This indicates that EtOH, the better nucleophile, is preferred. However, acetone is the only cosolvent used in this study which can form hydrogen bonds with TFE and EtOH. Hydrogen bonds between acetone and TFE are probably favored over those of acetone and EtOH because TFE is a stronger acid. The more the TFE-EtOH mixture is diluted with acetone, the less TFE is present in the solution and the higher is the



fraction of TFE hydrogen-bonded with acetone. This process takes TFE away from the reaction and allows EtOH to react in higher proportions. Thus, in the case of acetone as a cosolvent, the selectivity of TFE relative to EtOH is lower than the selectivity with other cosolvents. In the case of 2-AdOTs an additional decrease of selectivity is observed. 2-AdOTs reacts not only by front-side, but also by the back-side mechanism. In the back-side attack there would not be a hydrogen bond. The solvent composition is the same in the vicinity of reaction, and further in the solution. Thus, in the back-side mechanism the better nucleophile is favored. These two effects could lead to selectivity lower than unity for reaction of 2-AdOTs in TFE-EtOH/acetone.

Selectivity values for reactions of tosylates in TFE-EtOH/hexane are almost constant. Hexane is the only cosolvent used in this study that cannot interact with alcohols. Acetone can interact with alcohols via hydrogen bonds. The chloride lone pairs of electrons of  $\text{CCl}_4$  and  $\text{CHCl}_3$  may also weakly interact with alcohols. However, hexane as a nonpolar solvent can be involved in the hydrophobic effect. "Hydrophobic affect is defined as a tendency of nonpolar species to aggregate in water solution so the hydrocarbon-water interfacial area is decreased"<sup>22</sup>. It is likely that hexane does not take any part in the

reaction. Since the alcohols are present in a constant 50/50 volume percent ratio in every tertiary solvent mixture, and hexane does not interact either with the alcohols or with the leaving group, the selectivity remains constant.

#### Tosylates vs. mesylates

Although, in the present work, reaction conditions were not the same for both tosylates and mesylate (temperature of 90 °C and 25 °C, respectively) higher selectivity values were obtained for the mesylates. Solvolytic rates are approximately 10 to 100 times faster for mesylates than for tosylates<sup>27</sup>. For mesylates, the absence of steric hindrance from the phenyl ring increases the availability of the sulfonate to participate in hydrogen bonding in the ground state. This additional increase of TFE near the leaving group (compared to tosylates) results in higher selectivity values for mesylates (than for tosylates). Similar behavior was observed by Ferla<sup>20</sup>. The selectivity and the excess values are higher for 1-AdOMs than for 1-AdOTs<sup>20</sup>.

#### Reaction rate studies

For both tosylates, 2-AdOTs and [2.2.2]-OTs, reactions were slower when the solutions were more diluted with

cosolvent. The slower reaction was accompanied by greater selectivity.

Logarithms of the rate constants for 2-AdOTs and [2.2.2]-OTs versus the mole fraction of total alcohol are plotted (Figure 3). Both plots are linear suggesting that the rate decrease with increasing cosolvent concentration is roughly independent of the nature of the cosolvent. However, the slope for 2-AdOTs is 4.84 (correlation coefficient, 0.98), and that for [2.2.2]-OTs is 7.66 (correlation coefficient, 0.99). The slope of 2-AdOTs is about 1.6 times less steep than that of [2.2.2]-OTs. Similar results were previously reported<sup>26</sup>. The slope of correlations between solvent mole fraction and log k for substrates which can react only by a front-side pathway is greater than those of substrates which can react via back-side solvent attack. For the substrates which react by both a front-side and a back-side pathway, slopes of intermediate value are observed. These results are consistent with Ferla's observations<sup>20</sup> for the solvolyses of adamantly sulfonates in TFE-EtOH (Figure 2), where the maximum in the plot of product excess vs. solvent mole fraction is significantly greater in the case of bridgehead substrates (ca. 0.15) compared to a maximum of 0.10 for 2-AdOTs. Although Ferla's studies were conducted at different

temperatures, we believe that the observed differences are due to the possibility of both back-side and front-side mechanisms for 2-AdOTs. It should be noted that all reaction rates and product studies for 2-AdOTs and [2.2.2]-OTs presented in this work were carried out at the same temperature (90 °C).

For 1-AdOMs, reaction rates are very fast for all solvent compositions investigated, and rate studies were not performed.

#### CONCLUSIONS AND FUTURE WORK

The results of the present work are in agreement with the previous results of Ferla<sup>20</sup>. They suggest that 2-AdOTs, 1-AdOMs and [2.2.2]-OTs, solvolyze by rate limiting attack on specifically solvated internal ion pairs.

It has been shown for the solvolyses of 2-AdOTs, 1-AdOMs and [2.2.2]-OTs, in ternary mixtures of TFE, EtOH and a non-hydroxylic cosolvent, that TFE is the preferred nucleophile. It is consistent that 2-AdOTs reacts by both, front-side and back-side mechanisms. The better nucleophile is favored in the back-side mechanism. Reaction rates were

lower when cosolvent was added. This is due to decrease in medium polarity.

Future work should include parallel studies on the solvolyses of 2-AdOMs and [2.2.2]-OMs. We expect that the different leaving group will not affect the observed trends. Also, it would be interesting to study all of these solvolyses with new cosolvents which, like acetone, can interact via hydrogen bonds with TFE and EtOH.

### REFERENCES

1. Ingold, C.K.; *J. Chem. Soc.* 1953, 2745.
2. March, J., "Advanced Organic Chemistry"; Third Edition: John Wiley & Sons: New York, 1985, p.263-268.
3. Lowry, T. and Richardson, K. "Mechanism and Theory in Organic Chemistry, Third Edition: Harper and Row: New York, 1987, sections 4.1 & 2.2.
4. Winstein, S.; Appel, B.; Baker; R. *J. Am. Chem. Soc.* 1954, 76, 2597.
5. Goering, H.L.; Levy, J.L.; *J. Am. Soc. Chem.* 1964, 86, 120.
6. Paradisi, C.; Bunnett, J.F.; *J. Am. Chem. Soc.* 1985, 107, 8223.
7. Allen, A.D.; Kanagasabapathy, V.M.; Tidwel, T.T.; *J. Am. Chem. Soc.* 1985, 107, 4513.
8. Bentley, T.W.; Schleyer, P.v.R.; *J. Am. Chem. Soc.* 1976, 98, 7660.
9. Cociver, M.; Winstein, S.; *J. Am. Chem. Soc.* 1963, 85, 3458.
10. Bentley, T.W.; Schleyer, P.v.R.; *Adv. Phys. Org. Chem.* 1977, 14, 1.
11. Grunwald, E.; Winstein, S.; *J. Am. Chem. Soc.* 1948, 70, 846.
12. Winstein, S.; Grunwald, E ; Jones, H.W.; *J. Am. Chem. Soc.* 1951, 73, 2700.
13. Carey, F.A.; Sundberg, R.J.; "Advanced Organic Chemistry"; Third Edition, Plenum Press, New York, 1990, section 4.5.
14. Bentley, T.W.; Carter, G.E.; Robert, K.; *J. Org. Chem.* 1984, 49, 5183.
15. Schadt, F.L.; Bentley, T.W.; Schleyer, P.v.R.; *J. Am. Chem. Soc.* 1976, 98, 7667.
16. Kaspi, J.; Rapport, Z.; *J. Am. Chem. Soc.* 1980, 102, 3830.

17. Ando, T.; Tsukamoto, S.I.; *Tetrahedron Lett.* 1977, 2776.
18. Harris, J.M.; Becker, A.; Fagan, J.F.; Walden, F.A.; *J. Am. Chem. Soc.* 1974, 96, 4484.
19. Karton, Y.; Pross, A.; *J. Chem. Soc. Perkin Trans.* 1978, 2, 59.
20. Ferla, S.W.; Master Thesis, San Jose State University, 1990
21. Crossland, R.; Servis, K.; *J. Org. Chem.* 1970, 35, 3195.
22. Grob, C.A.; Kostka, K.; Kuhnen, F.; *Helvetica Chimica Acta*, 1970, 53, 608.
23. Computer Program by Selter, G.A.; San Jose State University.
24. Quinn, C.B.; Wiseman, J.R.; Calabrese, J.C.; *J. Am. Chem. Soc.* 1973, 95, 6121.
25. Kevill, D.N.; Kolwyck, K.C.; Weitzl, F.; *J. Am. Chem. Soc.* 1970, 92, 7300.
26. Mukherjee, L.M.; Grunwald, E.; *J. Phys. Chem.* 1958, 62, 1311.
27. Bentley, T.W.; Carter, C.W.; *J. Org. Chem.* 1983, 48, 579.

Table I. Products for Solvolysis of 2-Adamantyl Tosylate<sup>a</sup>  
in TFE-EtOH-CCl<sub>4</sub> Media at 90 °C.

Volume % of TFE- EtOH <sup>b</sup>	% of Relative Ion Counts			Calculated mole fractions <sup>c</sup>				S <sup>d</sup>
	AdOTFE	AdOEt	AdOTFE	AdOTFE	X (TFE)	X (EtOH)		
5	29.14	22.28	0.57	0.42	0.54		1.70	
10	30.07	22.46	0.57	0.41	0.52		1.68	
20	30.35	22.53	0.57	0.37	0.48		1.72	
30	31.68	22.71	0.58	0.34	0.43		1.72	
40	31.02	22.78	0.58	0.30	0.38		1.75	
50	33.23	22.68	0.59	0.26	0.33		1.83	
80	34.97	23.20	0.60	0.17	0.15		1.88	
90	31.86	19.59	0.62	0.06	0.08		2.18	
95	6.87	3.93	0.64	0.03	0.04		2.30	

<sup>a</sup>Determined in triplicate. <sup>b</sup>Volume % of CCl<sub>4</sub> = 1 - Volume % of TFE-EtOH;  
<sup>c</sup>X(CCl<sub>4</sub>) = 1 - [X(TFE) + X(EtOH)]; X(AdOEt) = 1 - X(AdOTFE). <sup>d</sup>Selectivity,  
k<sub>T</sub>/k<sub>E</sub>.



Table II. Product for Solvolysis of 2-Adamantyl Tosylate<sup>a</sup>  
in TFE-EtOH-CHCl<sub>3</sub> Media at 90 °C.

Volume % of TFE- EtOH <sup>b</sup>	% of Relative Ion Counts		Calculated mole fractions <sup>c</sup>				S <sup>d</sup>
	AdOTFE	AdOEt	AdOTFE	X (TFE)	X (EtOH)	X (EtOH)	
5	26.85	20.00	0.57	0.42	0.54	0.54	1.70
10	28.29	20.95	0.57	0.40	0.52	0.52	1.72
20	28.16	21.00	0.57	0.36	0.47	0.47	1.73
30	28.21	19.69	0.59	0.32	0.42	0.42	1.89
40	29.23	18.90	0.61	0.28	0.36	0.36	2.01
50	29.57	20.00	0.60	0.24	0.31	0.31	1.93
60	29.69	18.31	0.62	0.20	0.25	0.25	2.04
70	29.92	17.48	0.63	0.15	0.19	0.19	2.16
80	30.17	16.06	0.65	0.10	0.13	0.13	2.41
90	23.23	12.55	0.65	0.05	0.07	0.07	2.60
95	14.71	8.34	0.64	0.03	0.03	0.03	1.78

<sup>a</sup>Determined in triplicate. <sup>b</sup>Volume % of CHCl<sub>3</sub> = 1 - Volume % of TFE-EtOH;  
<sup>c</sup>X(CHCl<sub>3</sub>) = 1 - [X(TFE) + X(EtOH)]; X(AdOEt) = 1 - X(AdOTFE). <sup>d</sup>Selectivity,  
k<sub>T</sub>/k<sub>E</sub>.

Table III. Product for Solvolysis of 2-Adamantyl Tosylate<sup>a</sup>  
in TFE-EtOH-Hexane Media at 90 °C.

Volume % of TFE- EtOH <sup>b</sup>	% of Relative Ion Counts		Calculated mole fractions <sup>c</sup>				S <sup>d</sup>
	AdOTFE	AdOEt	AdOTFE	X (TFE)	X (EtOH)		
5	23.46	17.25	0.58	0.43	0.55		1.77
10	23.11	17.01	0.58	0.41	0.53		1.78
20	23.76	16.74	0.58	0.39	0.50		1.77
30	23.16	16.24	0.59	0.36	0.46		1.84
40	21.98	15.57	0.59	0.33	0.42		1.83
50	21.61	15.19	0.59	0.29	0.37		1.84
60	21.83	14.17	0.61	0.25	0.32		2.00
70	21.61	13.53	0.62	0.20	0.26		2.12
80	18.69	11.66	0.62	0.14	0.19		2.21
90	12.53	7.66	0.62	0.08	0.10		2.04
95	8.77	5.43	0.62	0.04	0.05		2.04

<sup>a</sup>Determined in triplicate. <sup>b</sup>Volume % of Hexane = 1 - Volume % of TFE-EtOH;  
<sup>c</sup>X(Hexane) = 1 - [X(TFE) + X(EtOH)]; X(AdOEt) = 1 - X(AdOTFE). <sup>d</sup>Selectivity,  
k<sub>T</sub>/k<sub>E</sub>.

Table IV. Product for Solvolysis of 2-Adamantyl Tosylate<sup>a</sup>  
in TFE-EtOH-Acetone Media at 90 °C.

Volume % of TFE- EtOH <sup>b</sup>	% of Relative Ion Counts			Calculated mole fractions <sup>c</sup>				S <sup>d</sup>
	AdOTFE	AdOEt	AdOTFE	AdOTFE	X (TFE)	X (EtOH)	X (EtOH)	
5	31.46	27.61	0.53	0.42	0.54	0.54	1.45	
10	30.57	28.95	0.51	0.40	0.51	0.51	1.33	
20	29.16	32.12	0.48	0.36	0.46	0.46	1.18	
30	27.78	34.77	0.44	0.32	0.41	0.41	1.01	
40	24.25	37.93	0.39	0.27	0.35	0.35	0.83	
50	23.19	39.68	0.37	0.23	0.30	0.30	0.77	
60	15.96	34.73	0.35	0.19	0.24	0.24	0.68	
70	10.41	26.00	0.29	0.14	0.18	0.18	0.53	
80	6.42	18.72	0.26	0.10	0.12	0.12	0.42	
95	2.27	8.93	0.20	0.02	0.03	0.03	0.38	

<sup>a</sup>Determined in triplicate. <sup>b</sup>Volume % of Acetone = 1 - Volume % of TFE-EtOH;  
<sup>c</sup>X(Acetone) = 1 - [X(TFE) + X(EtOH)]; X(AdOEt) = 1 - X(AdOTFE). <sup>d</sup>Selectivity,  
k<sub>T</sub>/k<sub>E</sub>.

Table V. Product for Solvolysis of 1-Bicyclo[2.2.2]octanyl Tosylate<sup>a</sup> in TFE-EtOH-CCl<sub>4</sub> Media at 90 °C.

Volume % of TFE- EtOH <sup>b</sup>	% of Relative Ion Counts			Calculated mole fractions <sup>c</sup>				S <sup>d</sup>
	BOTFE	BOEt	BOE	BOTFE	X (TFE)	X (EtOH)	X (EtOH)	
5	22.54	14.38	0.61	0.42	0.54	2.01		
10	22.52	13.47	0.63	0.41	0.52	2.16		
20	21.95	12.93	0.63	0.37	0.48	2.21		
30	22.03	12.57	0.64	0.34	0.43	2.25		
40	21.30	11.71	0.65	0.30	0.38	2.35		
50	20.30	10.92	0.65	0.26	0.33	2.36		
60	19.76	10.55	0.65	0.21	0.27	2.39		
70	18.83	9.21	0.67	0.17	0.21	2.51		
80	20.31	9.05	0.69	0.12	0.15	2.78		
90	18.92	8.20	0.70	0.06	0.08	3.11		
95	13.41	5.47	0.71	0.03	0.04	3.26		

<sup>a</sup>Determined in triplicate. <sup>b</sup>Volume % of CCl<sub>4</sub> = 1 - Volume % of TFE-EtOH;  
<sup>c</sup>X(CCl<sub>4</sub>) = 1 - [X(TFE) + X(EtOH)]; X(BOEt) = 1 - X(BOTFE). <sup>d</sup>Selectivity, k<sub>T</sub>/k<sub>E</sub>.

Table VI. Product for Solvolysis of 1-Bicyclo[2.2.2]octanyl Tosylate<sup>a</sup> in TFE-EtOH-CHCl<sub>3</sub> Media at 90 °C.

Volume % of TFE- EtOH <sup>b</sup>	% of Relative Ion Counts			Calculated mole fractions <sup>c</sup>				S <sup>d</sup>
	BOTFE	BOEt	BOTFE	BOTFE	X (TFE)	X (EtOH)		
5	23.05	16.98	0.58	0.42	0.54		1.78	
10	22.58	16.77	0.57	0.40	0.52		1.72	
20	22.83	16.30	0.58	0.36	0.47		1.80	
30	23.05	14.90	0.61	0.32	0.42		2.05	
40	22.82	14.84	0.61	0.28	0.36		2.01	
50	22.51	11.61	0.66	0.24	0.31		2.58	
60	23.39	13.49	0.64	0.20	0.25		2.22	
70	23.28	12.87	0.64	0.15	0.19		2.25	
80	23.75	11.40	0.68	0.10	0.13		2.76	
90	21.74	8.47	0.72	0.05	0.07		3.60	
95	19.62	7.37	0.73	0.03	0.03		2.70	

<sup>a</sup>Determined in triplicate. <sup>b</sup>Volume % of CHCl<sub>3</sub> = 1 - Volume % of TFE-EtOH;  
<sup>c</sup>X(CHCl<sub>3</sub>) = 1 - [X(TFE) + X(EtOH)]; X(BOEt) = 1 - X(BOTFE). <sup>d</sup>Selectivity, k<sub>T</sub>/k<sub>E</sub>.

Table VII. Product for Solvolysis of 1-Bicyclo[2.2.2]octanyl Tosylate<sup>a</sup>  
in TFE-EtOH-Hexane Media at 90 °C.

Volume % of TFE- EtOH <sup>b</sup>	% of Relative Ion Counts		Calculated mole fractions <sup>c</sup>				S <sup>d</sup>
	BOTFE	BOEt	BOTFE	X (TFE)	X (EtOH)	X (EtOH)	
5	21.80	15.25	0.59	0.43	0.55	0.55	1.84
20	22.57	15.14	0.60	0.39	0.50	0.50	1.92
40	23.07	15.55	0.60	0.33	0.42	0.42	1.91
50	22.46	15.42	0.59	0.29	0.37	0.37	1.84
60	22.85	15.84	0.59	0.25	0.32	0.32	1.84
70	22.79	15.69	0.59	0.20	0.26	0.26	1.87
80	22.23	14.42	0.61	0.14	0.18	0.18	2.01
90	21.15	13.04	0.62	0.08	0.10	0.10	2.04
95	19.09	12.06	0.61	0.04	0.05	0.05	1.96

<sup>a</sup>Determined in triplicate. <sup>b</sup>Volume % of Hexane = 1 - Volume % of TFE-EtOH;  
<sup>c</sup>X (Hexane) = 1 - [X (TFE) + X (EtOH)]; X (BOEt) = 1 - X (BOTFE). <sup>d</sup>Selectivity,  
 $k_T/k_E$ .

Table VIII. Product for Solvolysis of 1-Bicyclo[2.2.2]octanyl Tosylate<sup>a</sup> in TFE-EtOH-Acetone Media at 90 °C.

Volume % of TFE- EtOH <sup>b</sup>	% of Relative Ion Counts			Calculated mole fractions <sup>c</sup>				S <sup>d</sup>
	BOTFE	BOEt	BOE	BOTFE	X (TFE)	X (EtOH)	S <sup>d</sup>	
5	29.71	21.06		0.59	0.42	0.54	1.85	
10	25.35	19.31		0.57	0.40	0.51	1.69	
20	23.13	18.02		0.56	0.36	0.46	1.63	
30	21.61	16.45		0.57	0.32	0.41	1.70	
40	19.92	14.63		0.58	0.27	0.35	1.79	
50	18.15	14.34		0.56	0.23	0.30	1.66	
60	17.44	13.92		0.56	0.19	0.24	1.61	
70	12.09	10.47		0.54	0.14	0.18	1.51	
80	7.19	5.05		0.57	0.10	0.12	1.20	
90	2.47	2.19		0.53	0.05	0.06	1.20	
95	2.99	2.53		0.54	0.02	0.03	1.50	

<sup>a</sup>Determined in triplicate. <sup>b</sup>Volume % of Acetone = 1 - Volume % of TFE-EtOH;  
<sup>c</sup>X (Acetone) = 1 - [X (TFE) - X (EtOH)]; X (BOEt) = 1 - X (BOTFE). <sup>d</sup>Selectivity,  
 $k_T/k_E$ .

Table IX. Product for Solvolysis of 1-Adamantyl Mesylate<sup>a</sup>  
in TFE-EtOH-CCl<sub>4</sub> Media at 90 °C.

Volume % of TFE- EtOH <sup>b</sup>	% of Relative Ion Counts			Calculated mole fractions <sup>c</sup>			S <sup>d</sup>
	AdOTFE	AdOEt	AdOTFE	X (TFE)	X (EtOH)	X (EtOH)	
10	25.81	13.02	0.67	0.41	0.52	0.52	2.58
20	25.67	11.51	0.69	0.37	0.48	0.48	2.89
40	28.11	12.90	0.68	0.29	0.38	0.38	2.78
60	28.69	10.42	0.73	0.21	0.27	0.27	3.48
80	26.33	10.56	0.71	0.12	0.15	0.15	3.06

<sup>a</sup>Determined in triplicate. <sup>b</sup>Volume % of CCl<sub>4</sub> = 1 - Volume % of TFE-EtOH;  
<sup>c</sup>X(CCl<sub>4</sub>) = 1 - [X(TFE) + X(EtOH)]; X(AdOEt) = 1 - X(AdOTFE). <sup>d</sup>Selectivity,  
k<sub>T</sub>/k<sub>E</sub>.



Table X. Product for Solvolysis of 1-Adamantyl Mesylate<sup>a</sup>  
in TFE-EtOH-CHCl<sub>3</sub> Media at 90 °C.

Volume % of TFE- EtOH <sup>b</sup>	<u>% of Relative Ion Counts</u>			<u>Calculated mole fractions<sup>c</sup></u>				S <sup>d</sup>
	AdOTFE	AdOEt	AdOTFE	X (TFE)	X (EtOH)	X (EtOH)	X (EtOH)	
10	24.29	10.27	0.70	0.40	0.52	0.52	0.52	3.03
20	24.69	12.23	0.67	0.36	0.47	0.47	0.47	2.65
40	24.66	11.10	0.69	0.28	0.36	0.36	0.36	2.86
60	26.92	11.24	0.71	0.20	0.25	0.25	0.25	3.06
80	30.13	9.14	0.77	0.10	0.13	0.13	0.13	4.35

<sup>a</sup>Determined in triplicate. <sup>b</sup>Volume % of CHCl<sub>3</sub> = 1 - Volume % of TFE-EtOH;  
<sup>c</sup>X(CHCl<sub>3</sub>) = 1 - [X(TFE) + X(EtOH)]; X(AdOEt) = 1 - X(AdOTFE). <sup>d</sup>Selectivity,  
k<sub>T</sub>/k<sub>E</sub>.

Table XI. Product for Solvolysis of 1-Adamantyl Mesylate<sup>a</sup>  
in TFE-EtOH-Hexane Media at 90 °C.

Volume % of TFE- EtOH <sup>b</sup>	% of Relative Ion Counts			Calculated mole fractions <sup>c</sup>				S <sup>d</sup>
	AdOTFE	AdOEt	AdOTFE	AdOTFE	X (TFE)	X (EtOH)	X (EtOH)	
10	16.09	8.63	0.65	0.65	0.53	0.59	0.59	1.86
20	15.64	8.76	0.64	0.64	0.50	0.58	0.58	1.78
40	15.10	8.21	0.65	0.65	0.42	0.59	0.59	1.86
60	16.03	8.40	0.66	0.66	0.32	0.60	0.60	1.94
80	17.13	9.24	0.65	0.65	0.19	0.59	0.59	1.76

<sup>a</sup>Determined in triplicate. <sup>b</sup>Volume % of Hexane = 1 - Volume % of TFE-EtOH;  
<sup>c</sup>X (Hexane) = 1 - [X (TFE) + X (EtOH)]; X (AdOEt) = 1 - X (AdOTFE). <sup>d</sup>Selectivity,  
k<sub>T</sub>/k<sub>E</sub>.

Table XII. Summary of Selectivities<sup>a</sup> for the Solvolysis of 2-AdOTs, [2.2.2]-OTs, 1-AdOTs in tertiary mixtures of TFE-EtOH and cosolvent at 90 °C (2-AdOTs and [2.2.2]-OTs) and 25 °C (1-AdOMs).

Cosolvent <sup>b</sup>	Substrate:		
	2-AdOTs <sup>c</sup>	[2.2.2]-OTs <sup>c</sup>	1-AdOMs <sup>d</sup>
10	10.27	0.40	0.52
20	12.23	0.36	0.47
40	11.10	0.28	0.36
60	11.24	0.20	0.25
80	9.14	0.10	0.13

<sup>a</sup>Selectivity,  $k_T/k_E$ . <sup>b</sup>Cosolvent / (TFE-EtOH) 50/50 volume percent. <sup>c</sup>Range of mole fractions;  $X(\text{TFE}) = (0.42 - 0.03)$ ,  $X(\text{EtOH}) = (0.54 - 0.03)$ ,  $X(\text{cosolvent}) = 1 - [X(\text{TFE}) + X(\text{EtOH})]$ . <sup>d</sup>Range of mole fractions:  $X(\text{TFE}) = (0.53 - 0.10)$ ,  $X(\text{EtOH}) = (0.53 - 0.13)$ ,  $X(\text{cosolvent}) = 1 - [X(\text{TFE}) + X(\text{EtOH})]$ .

Table XIII. Summary of rate constant<sup>a</sup> values for 2-AdOTs and [2.2.2]-OTs in 50:50 volume percent of EtOH-TFE and cosolvent at 90 °C.

Cosolvent	Mole fraction of EtOH-TFE <sup>b</sup>	10 <sup>5</sup> k s <sup>-1</sup>	
		2-AdOTs	[2.2.2]-OTs
CCl4	0.58	0.74	2.40
CHCL3	0.55	0.53	1.40
hexane	0.66	1.60	9.60
acetone	0.53	0.35	0.96

<sup>a</sup>LSKINI program<sup>23</sup>. <sup>b</sup>X(cosolvent) = 1 - X(TFE - EtOH).

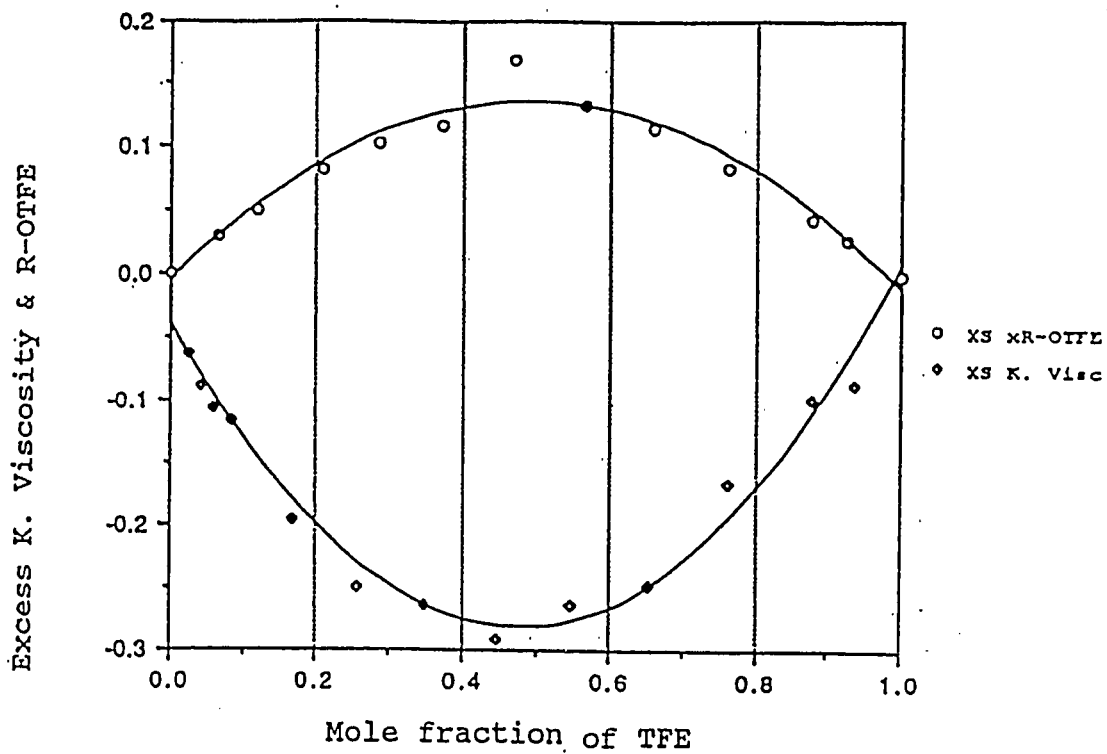


Figure 1. Correlation of Excess Kinematic Viscosity and Product Excess for Solvolysis of 1-AdOTs in TFE-EtOH (From Ferla<sup>20</sup>).

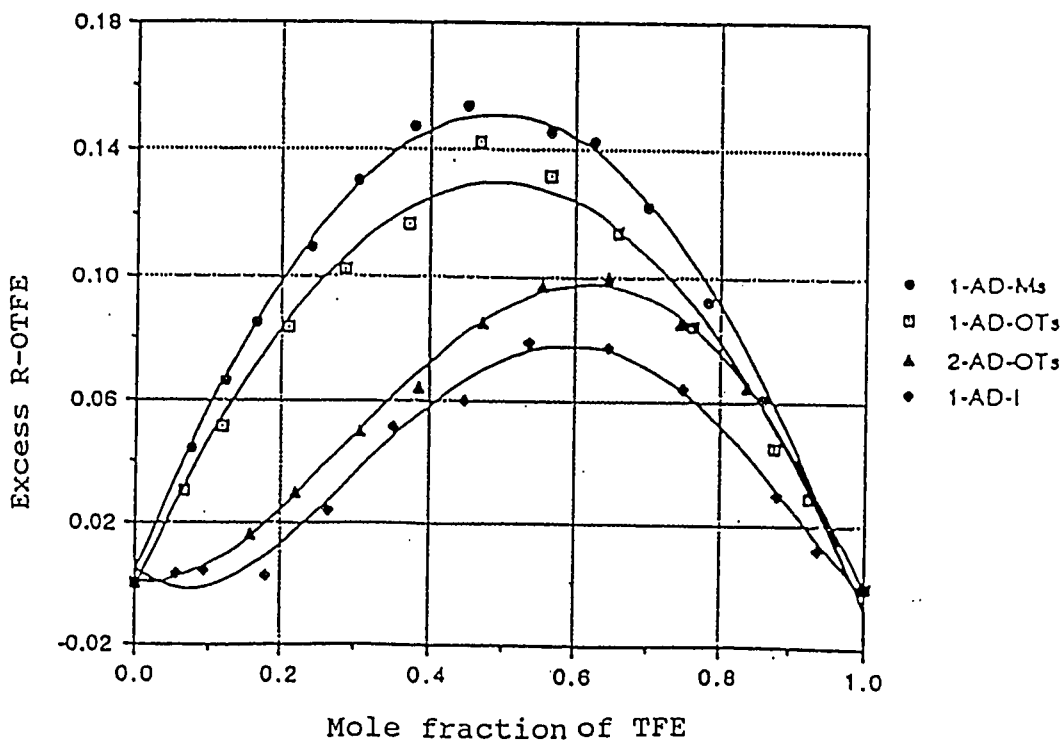


Figure 2. Summary of Product Excesses for Adamantyl Substrates in TFE-EtOH (From Ferla<sup>20</sup>).

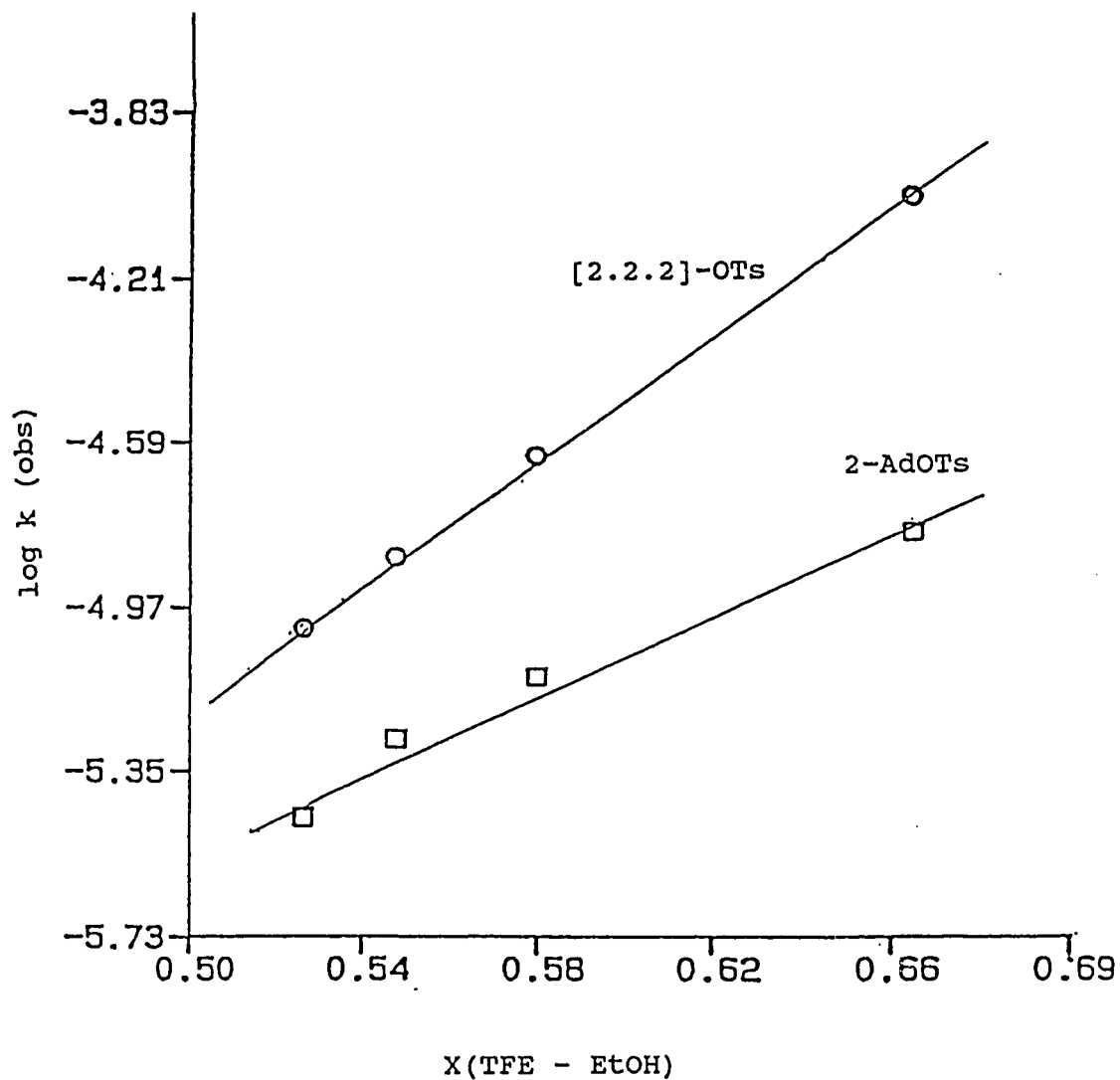


Figure 3. Correlation of Rate of Formation of Products and Mole Fractions for Solvolysis of 2-AdOTs and [2.2.2]-OTs in TFE-EtOH plus  $\text{CCl}_4$ ,  $\text{CHCl}_3$ , Acetone, Hexane at  $90^\circ\text{C}$ .