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Analysis of medium effects in the solvolysis of adamantyl compounds

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compounds**

Ferla, Steven William, M.S.

San Jose State University, 1990

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ANALYSIS OF MEDIUM EFFECTS
IN THE SOLVOLYSIS OF ADAMANTYL COMPOUNDS

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

Steven W. Ferla

May, 1990

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ABSTRACT

ANALYSIS OF MEDIUM EFFECTS IN THE SOLVOLYSIS OF ADAMANTYL COMPOUNDS

by Steven W. Ferla

Solvolysis studies, conducted on 1 and 2-adamantyl systems as well as 1-bicyclo[2.2.2]octanyl tosylate and *cis*-4-*t*-butylcyclohexyl tosylate, are evaluated by an alternate treatment in contrast to the traditional Grunwald-Winstein approach. Correlation of product composition versus solvent viscosity demonstrates diffusional control of the reaction. A ground state argument is presented to account for observed selectivities of different compounds. Products are shown to be regulated by solvent viscosity and solvent sorting in front-side reactions. Evidence is presented to show that product formation occurs as a result of capture of an internal ion pair. In addition, back-side reactions are demonstrated for 2-adamantyl tosylate and *cis*-4-*t*-butylcyclohexyl tosylate in which the better nucleophile is favored. Linear free energy correlations are observed for all tosylate compounds. Excess values are defined, calculated, and used as a mechanistic probe.

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INTRODUCTION

The widely accepted mechanism for solvolysis reactions is built on the Grunwald-Winstein ion pair scheme.²⁴ This model says that a substrate with leaving group "X" undergoes bond breakage, in the rate determining step, to form an internal ion pair. The internal ion pair is still enclosed in a solvent cage and can undergo further dissociation to form an external (or solvent separated) ion pair, in which at least one solvent molecule separates the two ions. The external ion pair can further dissociate to form free ions that do not interact with one another.

Scheme I

At any of the steps in the Scheme I, a solvent nucleophile can react to produce the product, R-S. The reaction is termed an S_N2 type if the nucleophile attacks the substrate, RX, concerted with bond breakage and the reaction is termed an S_N1 type if the nucleophile attacks the external ion pair in step 3. It is at this step that most researchers believe the product is formed in the solvolysis of adamantyl compounds.^{1,2}

There are three key points regarding this mechanistic model.

First, the model states that bond breakage is the rate determining step. Reaction rates have been measured and

correlated with solvent ionizing power, Y , according to the Grunwald-Winstein equation:^{23,13,15}

$$\log(k/k_0) = mY + lN \quad \text{Eq. (1)}$$

where k = solvolysis rate constant of substrate in solvent of interest.

k_0 = solvolysis rate constant of substrate in 80% aqueous EtOH.

m = sensitivity of substrate to solvent ionizing power.

Y = solvent ionizing power; rate constant of *t*-butyl chloride in solvent of interest/rate constant in 80% aqueous EtOH.

l = sensitivity of substrate to nucleophile.

N = nucleophilicity of the respective solvent molecule.

Note: all rate constants are measured at 25 °C.

Since rates increase with increasing ionizing power, it is believed that bond breakage is a function of ionizing power and is therefore rate determining. This concept was put forth by Grunwald and Winstein²³ and has been accepted as the model by which all solvolysis reactions are interpreted. A large body of research has been done to develop more accurate Y scales. Bentley and Schleyer¹³ are the leading proponents of this model and have developed Y scales based on 2-adamantyl tosylate (**2-Ad-OTs**) that are the most commonly used. More recently, Y scales have been developed based on 1-adamantyl tosylate (**1-Ad-OTs**).⁵

Second, the model predicts that for a mixed nucleophilic solvent system, there are two external ion pair species, one for each solvent nucleophile. For example, for an ethanol-trifluoroethanol (EtOH-TFE) solvent, an external ion pair exists for both EtOH and TFE.

Third, the model implicitly assumes that a catanoid intermediate is produced (in the external ion pair) that is stable and can selectively react with the better solvent nucleophile. In mixed solvents of high ionizing power, therefore, the equilibrium of the ion pair scheme should be shifted to the right (Scheme I), thereby allowing increased selectivity by the substrate carbocation to discriminate in favor of the better nucleophile.

Nucleophilicity (N) is treated as an independent parameter in the Grunwald-Winstein equation. Indeed, Bentley and Schleyer¹³ have developed scales of solvent nucleophilicities (as well as scales for ionizing power) based on a rearrangement of the Grunwald-Winstein equation using methyl tosylate as the standard substrate:

$$N = \log [(k/k_0) - 0.23Y] / 1 \quad \text{Eq. (2)}$$

where k = solvolysis rate constant of methyl tosylate in solvent of interest.

k₀ = solvolysis rate constant of methyl tosylate in 80% aqueous EtOH.

Note: all rate constants are measured at 50 °C.

With this method, they have calculated that EtOH is approximately 1000 times stronger a nucleophile than TFE, presumably due to the electron rich oxygen on EtOH versus the electron deficient oxygen on TFE. See Table III.

Kevill and Rissman¹⁴ realized that charge development in the transition state, Eq. (3), could lead to electrophilic solvent

assistance, hence, inaccurate N values. They developed an N scale using Et_3O^+ as the standard substrate to reduce this effect. Et_3O^+ shows charge dispersal in the transition state, Eq.(4), thereby resulting in a scale showing EtOH to be

relatively 500 times a stronger nucleophile than TFE. Regardless of the scale used, the better nucleophile would be expected to dominate in solvolysis reactions and this would be reflected in the selectivity values.

Selectivities are not defined in terms of a mechanism but are simply a measure of the dominance of a nucleophile in a reaction product. For an EtOH-TFE solvent system, selectivities are defined in terms of TFE by the following relationship:

$$S = \frac{(\text{xR-OTFE}) (\text{xEtOH})}{(\text{xTFE}) (\text{xR-OEt})} = \frac{k_t}{k_e} \quad \text{Eq. (5)}$$

where S = selectivity.

R = substrate (i.e., respective ether product).

k = second order bimolecular rate constants for the formation of the respective ether products.

Consistent with Scheme I, selectivities would be expected to favor the better nucleophile and have values of less than 1. Therefore, using Kevill's scale, a 1:1 mix of EtOH-TFE should give a 500:1 ratio of the ethyl ether:trifluoroethyl ether products resulting in $S = 0.002$. Selectivities favoring TFE, the poorer nucleophile, would have values greater than 1. A non-selective process would have a selectivity value of 1.

However, selectivities for the solvolysis of adamantyl compounds and other bridgehead systems are inverted; that is, the poorer nucleophile is favored in the reaction. Ando² reported selectivities for the solvolysis of various 1 and 2-adamantyl benzenesulfonates in EtOH-TFE (1:1 mixes by volume) varying from 1.35 to 1.74. Pross¹ reported selectivities of 1.6 to 2.2 (in terms of H₂O) for the EtOH-H₂O solvolysis of 1 and 2-adamantyl bromide (**1-Ad-Br**, **2-Ad-Br**) and chloride, and 2-adamantyl tosylate (**2-Ad-OTs**). Rappoport¹⁶ reported variable selectivities for the EtOH-TFE solvolysis of **1-Ad-Br** in which TFE was favored at low and high concentrations and EtOH was favored at intermediate concentrations. Such results are inconsistent with the predictions of the Grunwald-Winstein ion pair scheme.

In addition, Paradisi and Bunnett³ have shown that the rate of ¹⁸O scrambling for 2-adamantyl compounds, presumably via internal return (k_{-1} in Scheme I), is greater than the rate of solvolysis. This casts doubt as to the validity of ionizing power as a mechanistic tool and suggests that bond breakage is not the rate determining step.

It can only be concluded that the Grunwald-Winstein treatment does not adequately explain the data.

In this study, an alternate treatment of the data is developed for the solvolysis of bridgehead compounds in EtOH-TFE. This treatment is based on the correlation of product studies with intrinsic properties of the solvent medium and with interactions of the solvent and various leaving groups.

For example, in a non-selective model, products would be formed in the same ratio as the respective solvent composition. Product studies for the adamantyl compounds

deviate from the non-selective model by favoring the poorer nucleophile. This deviation can be measured and is called the "excess." Excess plots for EtOH-TFE solvolyses of adamantyl compounds show maxima and curve shapes that are characteristic of the respective compounds. There appear to be correlations in these curves with the viscosities¹⁰ of the solvent mixtures.

It is the objective of this research to evaluate solvent effects by an alternative treatment of the data in terms of measurable properties intrinsic to the solvent composition. Adamantyl and bicyclo[2.2.2-octyl] compounds will be used because they show no rearrangement or elimination products, thereby simplifying the study. The basic reactions studied, therefore, are as follows:

Scheme II

TREATMENT OF THE DATA

Throughout this paper, the solvent composition is presented in terms of the mole fraction of TFE (xTFE) or the mole fraction of EtOH (xEtOH). The product distribution is in terms of the relative mole fractions of the respective ether solvolysis products; i.e., the trifluoroethyl ether (xR-OTFE) or the ethyl ether (xR-OEt).

Excess (XS) values are calculated as follows:

$$XS = (xR-OTFE) - (xTFE) \quad \text{Eq. (6)}$$

Therefore, the excess value is simply the deviation of the triflouroethyl ether product from the non-selective model. Excess values are plotted versus solvent composition.

From the data, selectivities are calculated using Eq.(5).

A rearrangment of Eq.(5) results in a linear expression that correlates product ratios with solvent ratios in which the selectivity is the slope of the line:

$$\frac{(xR-OTFE)}{(xR-OEt)} = \frac{k_t}{k_e} \frac{(xTFE)}{(xEtOH)} \quad \text{Eq. (7)}$$

Therefore, solvent ratios versus product ratios are plotted. Eq.(7) also represents a ratio of the first-order rate constants for the formation of the respective products. Taking the logarithms of both sides of the equation results in linear free energy expression correlating product formation with solvent composition.²⁵

RESULTS

1-Adamantyl Tosylate

The results for the solvolysis of **1-Ad-OTs** are summarized in Table I.

A plot of product versus solvent composition is shown in Figure 1. The excess calculation, plotted in Figure 2, is analytically parabolic and indicates that TFE is favored at all mole fractions of solvent composition. This deviation from the non-selective model, then, is symmetrical and reaches a maximum of about 0.14 at about 0.5 mole fraction of TFE.

Calculated selectivity values for the individual data points, showing that TFE is favored, are in conflict with the predictions of the Grunwald-Winstein ion pair scheme; i.e., they are inverted. Though the selectivity values are variable, plots of the product ratios versus the solvent ratios (Figure 3) are linear, indicating constant selectivity. This apparent disagreement of constant versus variable selectivity is not crucial and may be explained within the limits of experimental error. The importance of Figure 3 is that the slope of the "line" is 1.68, indicating that selectivity is favoring TFE. A linear free energy correlation exists for product formation versus solvent composition as exhibited in Figure 4.

EtOH-TFE Viscosities and Densities

The measured viscosities and densities of EtOH-TFE solutions are summarized in Table II and Figure 5. The data approximately agrees with data by Grunwald.¹⁰ The kinematic viscosity, which is the measured viscosity divided by the solvent density, is shown in Figure 6. An excess plot can be generated by assuming linearity between mole fractions 0.0 and 1.0. The observed kinematic viscosity represents the deviation from the linear model. This deviation is termed the "excess viscosity" and is shown in Figure 7.

The excess plots for the solvolysis of **1-Ad-OTs** and the kinematic viscosity are combined in Figure 8. Both curves are parabolic, indicating a correlation between product formation and solvent viscosity.

1-Adamantyl Iodide

The results for the solvolysis of 1-adamantyl iodide (**1-Ad-I**) are summarized in Table IV.

A plot of product formation versus solvent composition is shown in Figure 9. The excess plot (Figure 10) indicates that TFE is favored at all solvent compositions until about 0.18 mole fraction of TFE at which point the excess becomes approximately zero. A maximum excess of about 0.08 is indicated.

The selectivity values, reflecting the excess curve, have values greater than 1.0 until 0.18 mole fraction of TFE when they become approximately 1.0, thereby indicating a non-selective situation at these mole fractions of TFE.

Although a plot of product ratios versus solvent ratios (Figure 11) is approximately linear, a strict evaluation shows that it is slightly curved, indicating variable selectivity. The key point, again, is that TFE is favored throughout most of the solvent composition range.

1-Adamantyl Mesylate

The results for the solvolysis of 1-adamantyl mesylate (**1-Ad-Ms**) are summarized in Table V.

A plot of product formation versus solvent composition is shown Figure 13. The excess plot (Figure 14) is parabolic and shows that TFE is favored at all mole fractions, reaching a maximum excess of about 0.15.

The selectivity values reinforce the dominance of TFE at all mole fractions, again with variable selectivity. The trends that product ratios are formed proportionately with solvent ratios is shown in Figure 15. A linear free energy correlation exists for product formation versus solvent composition as shown in Figure 16.

2-Adamantyl Tosylate

The results for the solvolysis of **2-Ad-OTs** are summarized in Table VI.

A plot of product formation versus solvent composition is shown in Figure 17. TFE is favored at all mole fractions with a maximum excess of approximately 0.10 as shown in Figure 18

(excess plot). In contrast to **1-Ad-OTs** and **1-Ad-Ms**, the excess is not parabolic and tends to flatten out at low concentrations of TFE. Both the loss of symmetry and the lower excess value can only be attributed to the nature of the reacting carbon.

The loss of symmetry is also reflected in the plot of product ratios versus solvent ratios (Figure 19) which shows a small but distinct curvature. As with **1-Ad-OTs** and **1-Ad-Ms** a linear free energy correlation exists for product formation versus solvent composition as shown in Figure 20.

1-Bicyclo[2.2.2]octanyl Tosylate

The results for the solvolysis of 1-bicyclo[2.2.2]octanyl tosylate (**2.2.2-OTs**) are summarized in Table VII.

The product formation versus the solvent composition is shown in Figure 21. The excess plot (Figure 22) is parabolic and indicates that TFE is favored at all mole fractions reaching a maximum of about 0.16.

Selectivity values are slightly variable but reflect the dominance of TFE over EtOH. The plots of product ratios versus solvent ratios (Figures 23 and 24) continue the previous trends for the sulfonates and again show a linear free energy correlation between products and solvent composition.

***cis*-4-*t*-Butylcyclohexyl Tosylate**

The results for the EtOH-TFE solvolysis of *cis*-4-*t*-butylcyclohexyl tosylate (***cis*-4-OTs**) are summarized in Tables VIII and IX. The results shown are the normalized uncorrected data points as analyzed by GC/MS using selected ion monitoring. Due to the multiplicity of products, it was impossible to prepare standards for sensitivity correction of the samples. Normally, this technique favors the trifluoroethyl ether products by as much as 5% (absolute) prior to correction. In this light, the results can only be viewed as indications of the trends in the reactions and cannot be interpreted as absolute values.

The *cis* and *trans*-1,4 ethyl and trifluoroethyl ethers were observed, as expected. An unexpected result was the formation of, presumably, *cis* and *trans*-1,3-trifluoroethyl ether products.²⁶ No such ethyl ethers were observed.

A plot of elimination products versus solvent composition is shown in Figure 31. Elimination was by far the dominant reaction in the solvolysis. As can be seen, elimination increased with increasing TFE concentration.

The back-side reaction at the tosylate bearing carbon results in the formation of the respective *trans*-4-*t*-butylcyclohexyl ethers. The plot of product ratios versus solvent ratios is shown in Figure 27. Within the error of the experiment, the plot is linear with a slope corresponding to the selectivity. It can be seen that the selectivity for the backside reaction overwhelmingly favors EtOH over TFE. Additionally, a free energy correlation is observed (Figure 28).

The front-side reaction results in the formation of the respective *cis*-1,4 ethers and the presumed *cis*-1,3 ethers. For purposes of simplicity, only the *cis*-1,4 trifluoroethyl ether products were tabulated in Table VIII. The plot of product ratios versus solvent ratios is shown in Figure 29. From both the calculated selectivities and the slope of the line in Figure 29, it appears that EtOH is favored over TFE.

DISCUSSION

In the discussion, **1-Ad-OTs** is presented as the model compound upon which an alternative treatment of the data is based. From this treatment, a cohesive interpretation of other adamantyl systems is developed that is supported by the observed and measured data. It is acknowledged in this treatment that nucleophiles can react with 1-adamantyl compounds only through a front-side attack on a carbocation intermediate.

1-Adamantyl Tosylate

From Table I and Figure 2 (excess plot) it is clearly seen that TFE is favored over EtOH throughout the entire solvent composition range. This observation can be explained by two arguments: a ground state argument and a viscosity/diffusion model.

Ground State Argument:

TFE is a thousand times more acidic than EtOH (Table III) leading to coordination with the leaving group in the ground

state, via hydrogen bonding, much more effectively than can EtOH. Therefore, solvent sorting results in a microscopic solvent composition around the leaving group that is much richer in TFE than is the bulk solvent composition. The carbocation, therefore, is able to react with TFE in higher proportions than would be expected on the basis of nucleophilicity values. This is the case across the entire range of solvent composition as shown by the excess plot (Figure 2). The excess plot reaches a maximum at 0.5 mole fraction of TFE and then diminishes as the bulk concentration moves away from 0.5 in either direction. This is probably due to the decreased need for solvent sorting at the higher TFE concentrations and the increased difficulty for solvent sorting at the lower TFE concentrations.

This electrophilic solvent assistance by TFE stabilizes the tosylate leaving group better than EtOH, which forms weaker hydrogen bonds, and explains why the rates are faster as the solvent composition increases in TFE concentration.

Additional evidence for solvent sorting comes from Figure 3. In a non-selective model where product formation is diffusion controlled, product ratios plotted against solvent ratios would give a straight line with a slope of unity. Any deviation from unity would indicate a selective process taking place. In Figure 3, the slope of 1.68 is consistent with solvent sorting which would lead to greater selectivity of TFE.

It also follows that the products (R-OTFE and R-OEt) are not formed by nucleophilic capture of the solvent separated ion pair. The Grunwald-Winstein model implies that a stable carbocation should reach the solvent separated ion pair stage where it can then select the better nucleophile. This is not

observed. However, there are no such constraints on the internal ion pair. Products formed from capture of the internal ion pair are a function of the microscopic solvent composition and not of the stability of the adamantyl carbocation.

Viscosity/Diffusion Model:

The excess kinematic viscosity of TFE-EtOH correlates inversely with the excess values for 1-Ad-OTFE as shown in Figure 8. This is strong evidence that product formation is diffusion controlled.

From Ficke's First Law of diffusion

$$\text{Rate of Diffusion} = -D \frac{dc}{dx} \quad \text{Eq. (8)}$$

where: D = the coefficient of diffusion
 dc/dx = the change in concentration along the diffusion direction; i.e., the concentration gradient

The coefficient of diffusion, D, is defined as

$$D = \frac{kT}{6\pi r\eta} \quad \text{Eq. (9)}$$

where: k = Boltzmann constant
 T = temperatur
 r = radius for a spherical molecule
 η = coefficient of viscosity

Therefore, viscosity is inversely proportional to diffusion.

From work by Paradisi and Bunnet³ it was shown that the rate of internal return is greater than the rate of solvolysis for

2-adamantyl benzenesulfonate. This suggests that in the time frame of bond breakage and reformation (internal return) the bulk solvent is frozen. The diffusion of the leaving group away from the substrate is, then, relatively slow. The lifetime of the cation is not long enough to allow diffusion of the ion pair to reach the solvent separated stage. The cation, therefore, can do one of two things: it can (internal) return or it can react with whatever nucleophile is present. The lifetime of the carbocation is simply not long enough to choose the better nucleophile. As a result, assuming S_N1 kinetics, anything faster than diffusion is allowed and anything slower than diffusion is not allowed.

Formation of the internal ion pair is allowed since it is formed automatically with bond breakage. The internal ion pair is enclosed in a TFE rich solvent cage from which nucleophilic capture of the carbocation occurs.

Internal return is allowed. Since internal return has been shown to occur at a faster rate than solvolysis, it must be faster than diffusion of the solvent nucleophiles.

Formation of the solvent separated ion pair is not allowed since the time required would demand a carbocation stable enough to select the better nucleophile.

Both the ground state argument and the viscosity/diffusion model are consistent with the experimental observations and lead to the following mechanistic scheme: solvent sorting creates a TFE rich pool around the leaving group. When bond breakage occurs, products are formed in a diffusion controlled process by a front-side nucleophilic capture of the internal ion pair. Product formation, not bond breakage, is the rate determining step.

In summary, **1-Ad-OTs** is used as the model compound for this thesis but as will be seen, steric and size considerations play a role in influencing the above stated arguments.

1-Adamantyl Iodide

The results for the solvolysis of **1-Ad-I** are consistent with the ground state argument and the viscosity/diffusion model. As seen in Figures 10 and 11 the excess trifluoroethyl ether products show that TFE is the selected nucleophile across the range of solvent composition except at low mole fractions of TFE.

It would seem that at low TFE concentrations, the microscopic solvent composition is not appreciably different than the bulk solvent composition. This is due to the reduced ability of the iodide to be an effective electron donator for hydrogen bonding in the ground state; i.e., halides are less basic than sulfonates by virtue of their 3 available electron pairs compared to 6 (on the 3 oxygens) for the sulfonates. The iodide is also much smaller than tosylate, thereby reducing the number of molecules in the solvent cage. As a consequence, for **1-Ad-I**, product formation reflects the bulk solvent composition at low TFE concentrations. This is reflected in both the excess values (approximately 0.0) and selectivity values (approximately 1.0), both of which indicate that a non-selective pathway is being followed at these solvent compositions.

Indeed, for **1-Ad-I** in general, the less overall selectivity for TFE, as reflected in the lower maximum excess values, is consistent with a microscopic solvent composition across the

entire range that is not as TFE rich relative to the sulfonates.

1-Adamantyl Mesylate

The solvolysis of **1-Ad-Ms** results in the same behavior as for the **1-Ad-OTs**: TFE is favored as a nucleophile at all mole fractions of TFE.

One noticeable difference, however, is that the maximum excess is at 0.16 as compared to 0.14 for **1-Ad-OTs**. Within the calculated error of these studies, it can be said that these values are different. Apparently for the 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 further increases the microscopic solvent concentration of TFE relative to the tosylates and **1-Ad-I** and results in higher excess and selectivity values. This result is consistent with and supported by the ground state argument and the viscosity/diffusion model.

The decrease in steric hindrance also supports the fact that the solvolytic rates are approximately 10 to 100 times faster for **1-Ad-Ms** than for **1-Ad-OTs**.⁹

2-Adamantyl Tosylate

Up to this point, the discussion has been confined to the 1-adamantyl systems where the reacting carbon is tertiary and the reaction can only take place from a front-side nucleophilic attack on the carbocation. It is upon this basis

that both the ground state argument and the viscosity/diffusion model are based.

Many researchers, among them Bentley, Carter, and Schleyer, have maintained that **2-Ad-OTs** is also restricted to a front-side nucleophilic attack^{1,12,22} even though the reacting carbon is secondary. However, evidence is shown in Table VI and Figure 20 that **2-Ad-OTs** is also subject to what will be called a "back-side" attack.¹⁷ This is reflected in the observation that **2-Ad-OTs** has a lower maximum excess value of 0.10 (compared to 0.14 for **1-Ad-OTs**) and the excess plot shows a distinct loss of symmetry.

In a back-side attack, the ground state argument would not apply; that is, there would be no hydrogen bonding effect. The microscopic solvent composition would be the same as the bulk solvent composition. A back-side attack would, therefore, favor the better nucleophile and the nucleophile is involved in the transition state so that there is an S_N2 component to the mechanism. This leads to inversion of configuration in "back-side" products. However, due to the symmetry of the respective 2-adamantyl ethers, it is impossible to distinguish "front-side products" from "back-side" products since they are stereochemically identical.

In **2-Ad-OTs**, the products, then, are the result of both the front-side and back-side reactions. TFE is favored from the front side and EtOH is favored from the back side. The excess and selectivity values, therefore, are a composite value of both front and back-side reactions and are depressed from those of **1-Ad-OTs** due to the back-side contribution.

1-Bicyclo[2.2.2]octanyl Tosylate

The solvolysis of **2.2.2-OTs** results in the same behavior as for the **1-Ad-OTs**: TFE is favored as a nucleophile at all mole fractions of TFE. The maximum excess is at 0.16 as compared to 0.14 for **1-Ad-OTs** and is symmetrical.

Ring strain in the eight carbon bicyclo structure is greater than that in the ten carbon 1-adamantyl structure resulting in a carbocation that is less easily formed, compared to the adamantyl structure. **2.2.2-OTs** is, therefore, less reactive than **1-Ad-OTs**. As a consequence, **2.2.2-OTs** requires greater electrophilic solvent assistance, via increased solvent sorting, to cause bond breakage. This is evident from the greater slope for **2.2.2-OTs** in Figure 23 (compared to **1-Ad-OTs**, Figure 3). The resulting bicyclo carbocation is less stable than the 1-adamantyl cation and has an even richer TFE solvent pool with which to react. This results in even greater selectivity and excess values favoring TFE.

The symmetry of the excess plot indicates that **2.2.2-OTs**, solvolyzing via a front-side reaction at the bridgehead carbon, shows the same behavior as **1-Ad-OTs**. Product formation is still the result of interactions between the solvent and the leaving group.

cis-4-t-Butylcyclohexyl Tosylate

In **2-Ad-OTs** evidence was found that both front-side and back-side reactions were taking place and that EtOH was favored from the back-side. To test this hypothesis, **cis-4-OTs** was solvolyzed since the products would be *cis* or *trans* to the *t*-butyl substituent and this could be used to

distinguish between the respective front and back-side reactions.

However, the solvolysis of ***cis*-4-OTs** represents a more complex situation wherein several competing reactions (and mechanisms) are simultaneously taking place.

As seen in Figure 31, elimination was the dominant reaction and was shown to increase with increasing TFE. Elimination is favored because the tosylate and axial α -H are coplanar. An E2 elimination can then take place, especially when EtOH is under the ring²⁷ in position to act as a base. TFE can also abstract a proton but is less basic than EtOH.

Four trifluoroethyl ether products were observed: *cis* and *trans*-1,4 ethers and presumably *cis* and *trans*-1,3 ethers. The *cis* and *trans*-1,4 ethers were formed by nucleophilic attack at the tosylate bearing carbon. The presumed *cis* and *trans*-1,3 ethers were probably formed by a nucleophilic attack at an adjacent carbon (adjacent to the tosylate bearing carbon) with an accompanying hydride transfer of the axial proton, thereby replacing the tosylate leaving group. This was an unexpected side reaction that further complicates the situation.

Only two ethyl ether products were observed: *cis* and *trans*-1,4 ethyl ethers formed by nucleophilic attack at the tosylate bearing carbon.

The following generalizations can therefore be made: when EtOH is under the ring, elimination (favored) or nucleophilic substitution at the tosylate bearing carbon can take place. When TFE is on top of the ring,²⁷ it can substitute at two

different positions but must compete with elimination (which is favored) from solvent under the ring.

Simplifying the dynamics of the this system is difficult given the complexity of the product mixture and the fact that the observed products could not be sensitivity corrected with standards.

However, it was definitely observed that EtOH is favored over TFE from the back-side for **cis-4-OTs**. The selectivity values in Table IX (in terms of EtOH) reflect overwhelming dominance of EtOH. From the back-side, solvent sorting is no longer important so the solvent composition is more reflective of the bulk composition. In such a case, the better nucleophile, EtOH, is selected.

This, then, supports the contention that **2-Ad-OTs** is subject to both front and back-side reactions.

CONCLUSIONS

The objectives of this thesis were to explain the observed products for the solvolysis of adamantyl compounds in terms of an alternative point of view; that is , that solvent sorting and solvent viscosity are important regulators in the solvolysis mechanism. With this in mind, the following mechanistic conclusions are reached.

First, in front-side reactions, products are formed in a diffusion controlled (rate determining) step that does not allow the carbocation enough time to select the better

nucleophile. The cation simply reacts with whatever nucleophile is proximate. Since solvent sorting adjusts the microscopic solvent concentration to favor TFE, TFE is favored as a nucleophile.

Second, nucleophilic substitution occurring as a result of capture of the internal ion pair is consistent with the data. Carbocation lifetimes are not long enough to survive formation of an external (solvent separated) ion pair. Such a complex would favor the better nucleophile and this is not observed.

Third, back-side reactions in secondary systems (**2-Ad-OTs** and **cis-4-OTs**) favor the better nucleophile. The microscopic solvent composition from the backside is reflective of the bulk composition so that the better nucleophile can dominate. In these systems there is an S_N2 component.

Fourth, excess plots and plots of product ratios versus solvent composition are mechanistic probes that allow solvent effects to be measured.

EXPERIMENTAL SECTION

General Procedures. All solvents were dried (molecular sieves) and distilled prior to use. All ampules were pre-cleaned, dried, and weighed. Solutions were prepared by volume percent using a Hamilton 1000 µL gas tight syringe. After each addition, the ampules were weighed and the mole fractions of the solvents were calculated. All samples were

buffered with collidine at twice the molarity of the substrate.

The samples and standards were analyzed on a Finnigan 1020 Automated GC/MS using selected ion monitoring with at least three injections per sample and standard. A graph of observed mole fraction R-OTFE versus actual mole fraction R-OTFE (for the standards) was plotted and used for sensitivity correction of the samples.

Substrates were characterized on a Varian T-60 NMR Spectrometer, Analect RFX 20 infrared spectrophotometer, and Fisher-Johns melting point apparatus.

Solvolysis of 1-Adamantyl Tosylate. Solutions of EtOH-TFE were prepared at 5, 10, 20...90,95 volume percent intervals by mixing 0.05(X) mL of one solvent with [0.5 - 0.05(X)] mL of the other solvent (X= 0.5, 1, 2, 3...9, 9.5). This was done in duplicate.

A stock solution of **1-Ad-OTs** (0.115 g) was prepared in hexane (20 mL) resulting in a 0.0188M solution. A 1 mL aliquot was then buffered with collidine (5.3 μ L, 40 mM). A 5 μ L aliquot of the buffered solution was injected into each of the EtOH-TFE ampules to give approximately 0.2 mM **1-Ad-OTs** solutions. The ampules were sealed and solvolyzed at 25 °C for 10 half-lives.¹⁸

Standards were prepared as follows: ca. 2 mM **1-Ad-I** was prepared in diethyl ether (20 mL). Aliquots (10 mL) of the ether solution were pipetted into two 100 mL round bottom flasks and the ether was removed by roto-evaporation. Next, 10 mL of EtOH was pipetted into one flask and 10 mL of TFE was pipetted into the other. Each solution was buffered with

collidine (ca. 4 mM), sealed and solvolyzed at 90 °C for 10 half-lives⁷ to give the pure stock solutions of the respective ethers. Standard solutions were then prepared at 5, 10, 20...90, 95 volume percent intervals by mixing the pure ether stock solutions in the same way as described for the samples.

Synthesis of 1-Adamantyl Iodide. 1-Adamantyl alcohol (**1-Ad-OH**, 1.0678 g, 7.0 mmol) was treated with 15 mL of 47% HI acid using the procedure of Schleyer and Nicholas.⁶ Recrystallization from methanol at -70 °C gave 0.23 g of the pure white product: mp 74-75 °C (lit.⁶ mp 75-76 °C).

Solvolysis of 1-Adamantyl Iodide. The solvolysis of **1-Ad-I** was conducted at 35 °C, 50 °C, and 75 °C using the procedure by Anwarul Haque.⁷

Synthesis of 1-Adamantyl Mesylate. **1-Ad-OH** in methylene chloride (0.2M) was treated with methanesulfonyl chloride using the procedure of Crossland and Servis.⁴ The product, **1-Ad-Ms** in CH₂Cl₂, was purified and 8 µL was added to TFE (0.5 mL). The resulting 1-Ad-OTFE ether solution was analyzed by GC/MS. The results showed 98.8% 1-Ad-OTFE (therefore, 98.8% pure **1-Ad-Ms**) and 1.2% 1-Ad-OH. The **1-Ad-Ms** was further characterized: IR (CDCl₃) 1340 (asym. O=S=O), 1180 (sym. O=S=O), 1050 and 990 (C-O-S stretches) cm⁻¹.

Solvolysis of 1-Adamantyl Mesylate. Solutions of EtOH-TFE were prepared at 3, 5, 10, 20...90, 95 volume percent intervals by mixing 0.05(X) mL of one solvent with [0.5 -

0.05(X)] mL of the other solvent (X= 0.3, 0.5, 1, 2, 3...9, 9.5). All ampules were then buffered with collidine (0.26 μ L, 0.004M). This was done in triplicate.

A stock solution of **1-Ad-Ms** (0.1047 g) in methylene chloride (11 mL) was prepared to give a 41.32 mM solution. Aliquots (24 μ L) of the stock solution were injected into the EtOH-TFE ampules to give 1.983 mM **1-Ad-Ms** solutions. The ampules were sealed and solvolized at 25 °C for 10 half-lives.⁹

Standards were prepared as follows: ca. 2 mM **1-Ad-I** was prepared in diethyl ether (20 mL). Aliquots (10 mL) of the ether solution were pipetted into two 100 mL round bottom flasks and the ether was removed by roto-evaporation. Next, 10 mL of EtOH was pipetted into one flask and 10 mL of TFE was pipetted into the other. Each solution was buffered with collidine (ca. 4mM), sealed, and solvolized at 90 °C for 10 half-lives⁷ to give the pure stock solutions of the respective ethers. Standard solutions were then prepared at 5, 10, 20...90, 95 volume percent intervals by mixing the pure ether stock solutions in the same way as described for the samples.

Solvolysis of 2-Adamantyl Tosylate. **2-Ad-OTs** (0.0303 g, 0.09888 mmol) was dissolved in 50.0 mL of dry ether to give a 1.98 mM solution. Aliquots (20.0 mL) of the mixture were pipetted into two 100 mL round bottom flasks and the ether was removed by roto-evaporation. Next, 20.0 mL of EtOH was pipetted into one flask and 20.0 mL of TFE was pipetted into the other flask to give two respective stock solutions of 2.0 mM concentration. These solutions were used to prepare samples for solvolysis.

Samples were prepared in duplicate at 10, 20, 30...90 volume percent concentrations of TFE by mixing 0.1(X) mL of the TFE stock solution with [1.0 - 0.1(X)] mL of the EtOH stock solution (X = 1, 2, 3...9) in 1 mL pre-weighed ampules. The ampules were sealed and solvolized for at 90 °C for 10 half-lives.¹⁸ The remaining stock solutions were also sealed and solvolized in the same manner to give the respective pure ethers which were used to prepare standard solutions.

Standards were prepared by mixing the pure ether stock solutions in the same way as described for the samples.

Synthesis of 1-Bicyclo[2.2.2]-octanyl Tosylate.

1-Bicyclo[2.2.2]-octanyl alcohol (0.49 g, 3.9 mmol) was dissolved in 5 mL of dry pyridine (BaO) with p-toluenesulfonyl chloride (1.3 g, 67 mmol), sealed in an ampule, and reacted at 40 °C for 120 hours. After cooling, the red brown solution was poured in 30 mL of ice water. The crystallized **2.2.2-OTs** was removed by filtration and dried overnight in vacuo. Recrystallization from 30-60 petroleum ether at 0 °C gave the pure white product: mp 66-68 °C (lit.¹⁸ mp 65 °C), IR (nujol) 1600 and 1458 (Ar), 1332 (asym.O=S=O), 1177 (sym. O=S=O)cm⁻¹.

Solvolysis of 1-Bicyclo[2.2.2]-octanyl Tosylate.

2.2.2-OTs (14.4 mg) was dissolved in 50.0 mL of dry ether. Aliquots (20.0 mL) of the tosylate/ether solution were pipetted into two 100 mL round bottom flasks and the ether was removed by roto-evaporation. Next, 22.0 mL of dried and distilled EtOH was pipetted into one flask and 22.0 mL of dried and distilled TFE was added to the other flask to give two stock solutions of identical concentration (1.0 mM). Each

solution was then buffered with collidine (6 μ L, 2.0 mM). Samples were prepared in duplicate at 5, 10, 20...90, 95 volume percent intervals by mixing 0.1(X) mL of one stock solution with [1.0 - 0.1(X)] mL of the other (X= 0.5, 1, 2, 3...9, 9.5). The ampules were sealed and solvolized at 90 °C for 3 half-lives.¹⁸ The remaining stock solutions were sealed and solvolized for 10 half-lives¹⁸ to give the respective pure ethers which were used to prepared standard solutions.

Standards were prepared by mixing the pure ether stock solutions in the same way as described for the samples.

Synthesis of *cis*-4-*t*-Butylcyclohexanol. The procedure by Krishnamurthy and Brown⁸ was adapted to reduce 4-*t*-butylcyclohexanone: Under a stream of dry nitrogen, 28.1 mL of Selectride (lithium trisiamylborohydride, 1 M) was injected into a 100 mL round bottom flask and cooled to -78 °C (dry ice, isopropanol). Then, 4-*t*-butylcyclohexanone (3.6508 g, 0.95 M) in THF (dried and distilled) at 0 °C was slowly injected into the flask, allowed to react with stirring for 2 hours, and then allowed to equilibrate at room temperature for 1 hour. The product was hydrolyzed with 4 mL H₂O followed by 15 mL EtOH (distilled). Sodium hydroxide (10mL, 6M) and H₂O₂ (15 mL, 30%) were slowly added to oxidize the organoborane. After 1 hour, the solution was saturated with solid anhydrous potassium carbonate. The organic phase was separated and the aqueous phase was extracted with two 10 mL aliquots of Et₂O/THF (1:1), which were combined with the organic phase. The combined solution was extracted with brine (10 mL) and dried (MgSO₄). The solvent was removed by roto-evaporation and the purified product was recrystallized in hexane. The recrystallized product was characterized as follows: GC/MS (>99% *cis* product, <1% unreacted ketone), MS

(70 eV) m/z 156 (1, m^+), 57 (100, $(CH_3)_3C^+$) ; IR (nujol mull) 3350 (O-H stretch), 975 (C-O-H stretch) cm^{-1} ; 1H -NMR (60 MHz, CCl_4) δ 3.48 (1H, quintet, $J = 6$ Hz), 4.02 (1H, s), 1.6 (9H, m), 0.85 (9H, s); mp 79-80 °C (lit.⁸ mp 82 °C)

Synthesis of *cis*-4-*t*-Butylcyclohexyl Tosylate.

cis-4-*t*-butylcyclohexanol (0.1062 g, 0.0006796 mol) was dissolved in pyridine (0.5 mL, BaO) and *p*-toluenesulfonyl chloride (0.1815 g, 0.9520 mmol) was added. The mixture was stoppered in a 50 mL Ehrlenmeyer flask under an N_2 blanket and allowed to react at room temperature for 21 hours, with stirring. The mixture was then transferred to a separatory funnel with the aid of diethyl ether and extracted with ice water (3x5 mL), cold HCl (10%, 3x5 mL), $NaHCO_3$ (saturated, 3x5 mL), and brine (3x5 mL). The organic layer was then dried ($MgSO_4$) and the Et_2O removed by roto-evaporation. The resulting white ***cis*-4-OTs** crystals were characterized: IR (CCl_4) 1602 and 1447 (Ar), 1372 (asymm. S=O stretch), 1192 (sym. S=O), 915 (S-O-C stretch), 2958 (asym. CH_3), 2870 (sym. CH_3), 2847 (sym. CH_2), 2916 (asym. CH_2) cm^{-1} ; 1H -NMR (60 MHz, CCl_4) δ 0.85 (9H, s), 2.43 (3H, s) 4.63 (1H, m), 7.27 (2H, d, $J = 8$ Hz), 7.73 (2H, d, $J = 8$ Hz), $\approx$ 1.5 (9H, m).

Solvolysis of *cis*-4-*t*-Butylcyclohexyl Tosylate.

Solutions of EtOH-TFE were prepared at 0, 5, 10, 20...90, 95, 100 volume percent intervals by mixing 0.05(X) mL of one solvent with [0.5 - 0.05(X)] mL of the other solvent (X= 0.0, 0.5, 1, 2, 3...9, 9.5) in 1 mL pre-weighed ampules. All ampules were then buffered with collidine (0.26 μ L, 4 mM). This was done in duplicate.

A stock solution of **cis-4-OTs** (0.0124 g) in THF (0.50 mL) was prepared to give a 79.88 mM solution. Aliquots (12.5 μ L) of the stock solution were injected into the above prepared ampules to give approximately 2.0 mM **cis-4-OTs** solutions. The ampules were sealed and solvolyzed at 70 $^{\circ}$ C for 10 half-lives.

The following products were characterized by GC/MS: *cis*-4-*t*-butylcyclohexyl ethyl ether (70 eV) m/z 57 (100, $(\text{CH}_3)_3\text{C}^+$), 184 (5, M^+), 138 (15, $\text{M} - \text{EtOH}$); *trans*-4-*t*-butylcyclohexyl ethyl ether (70 eV) m/z 57 (100 $(\text{CH}_3)_3\text{C}^+$), 138 (45, $\text{M} - \text{EtOH}$); *trans*-4-*t*-butylcyclohexyl trifluoroethyl ether (70 eV) m/z 57 (100, $(\text{CH}_3)_3\text{C}^+$), 138 (10, $\text{M} - \text{TFE}$), 181 (5, $\text{M} - t\text{-butyl}$). Additionally, retention times of the pure ethyl ethers showed the *cis*-ether to elute before the *trans*-ether.

Reaction Rates for *cis*-4-*t*-Butylcyclohexyl Tosylate.

Stock solutions (2 mL) of EtOH-TFE were prepared at 20, 50 and 80 volume percent TFE intervals and buffered with collidine (1.1 μ L, 4 mM). *p*-Xylene (1.1 μ L, 4 mM) was added to each solution as an internal standard. **cis-4-OTs** (ca. 1.4 mg, 2 mM) was added to each solution. The solutions were sealed in ampules and solvolyzed for 0, 15, 30, 60, 120, 180, and 240 minutes at 70 $^{\circ}$ C. Rates were measured by analyzing elimination product formation using GC/MS. Rate constants were calculated using LSKIN kinetic software.

Viscosity Measurements for EtOH-TFE. Solutions of EtOH-TFE were prepared at 0, 3, 5, 7, 10, 20, 30...90, 95, 100 volume percent TFE intervals by mixing 20.0(X) mL of EtOH with [20.0 - 20.0(X)] mL of TFE ($X = 1, 0.97, 0.95, 0.93, 0.90, 0.80, 0.70...0.10, 0.05, 0.0$) into pre-weighed air

tight bottles. The bottles were weighed after each addition and the mole fractions were calculated.

The viscosity of the solutions was measured using a Rheometrics Mechanical Spectrometer (RMS-800) with the couette geometry. Measurements were obtained at the following dynamic shear rates: 100 radians/sec, 215.4 radians/sec, 464.2 radians/sec, 1000 radians/sec, and 81.6 radians/sec. At least three measurements were taken for each solution and the results averaged. The temperature of the solutions was maintained at 25 °C. The couette dimensions were as follows:

cup radius = 17 mm
bob radius = 16 mm
bob length = 32 mm

Density Measurements for EtOH-TFE. Solutions of EtOH-TFE were prepared at 0, 3, 5, 7, 10, 20, 30...90, 95, 100 volume percent TFE intervals by mixing 20.0(X) mL of EtOH with [20.0 - 20.0(X)] mL of TFE (X = 1, 0.97, 0.95, 0.93, 0.90, 0.80, 0.70...0.10, 0.05, 0.0) into pre-weighed air tight bottles. The bottles were weighed after each addition and the mole fractions were calculated.

Densities of the above solutions were measured in triplicate at 25 °C using 10 mL Weld pycnometers. The pycnometers were calibrated with triple distilled water immediately prior to use.

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when the tosylate is axial and an axial attack when the tosylate is equatorial. It does not imply that the nucleophile can pass inside the adamantyl cage structure and react from there.

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25. The first order rate constants for the formation of the respective products is simply the k_{obs} multiplied by the respective product mole fractions. In Eq.(6), k_{obs} drops out leaving only the corresponding product ratios which represent the ratio of the energy barriers leading to the products. The logarithm of the ratio represents the free energy change leading to the products. Therefore, a plot of the log (products ratios) versus log (solvent ratios) is a free energy correlation.
26. Four trifluoroethyl ethers were positively observed but only two could be assigned with any degree of certainty: the *cis* and *trans*-1,4 ethers. This is based on their mass spectra and relative retention times. It is postulated that the remaining two ethers are *cis* and *trans*-1,3 ethers.
27. As we have routinely written this structure, "under the ring" refers to the solvent in a position *trans* to the *t*-butyl substituent and "on top of the ring" refers to the solvent in a position *cis* to the *t*-butyl substituent.

Table I: EtOH-TFE Solvolysis of 1-Adamantyl Tosylate^a at 25 °C

xTFe ^b	xR-OTFe ^c	Excesse	xTFe/ xEtOH	x1-Ad-OTFe/ x1-Ad-OEt	S ^f	log (xTFe/ xEtOH)	log (xR-OTFe/ xR-OEt)
0.000	0.000	0.000	0.000	0.000			
0.065	0.095	0.031	0.069	0.105	1.520	-1.159	-0.978
0.120	0.170	0.051	0.136	0.205	1.510	-0.867	-0.688
0.210	0.293	0.083	0.266	0.415	1.562	-0.576	-0.382
0.286	0.389	0.103	0.401	0.636	1.588	-0.397	-0.197
0.373	0.490	0.117	0.595	0.961	1.616	-0.226	-0.017
0.472	0.614 ^d	0.142	0.894	1.593	1.782	-0.049	0.202
0.565	0.698	0.133	1.299	2.306	1.775	0.114	0.363
0.659	0.774	0.115	1.930	3.416	1.770	0.286	0.534
0.765	0.849	0.084	3.250	5.626	1.731	0.512	0.750
0.879	0.923	0.044	7.278	12.051	1.656	0.862	1.081
0.928	0.956	0.028	12.802	21.638	1.690	1.107	1.335
1.000	1.000	0.000					

^aThe concentration of 1-Ad-OTs was 0.2 mM with respect to the solvent. All samples were buffered with collidine at twice the substrate concentration. ^bThe solvents were dried and distilled immediately prior to use. The value shown is the mole fraction of TFE relative to EtOH. The solutions were prepared by volume percent, weighed after each addition, and the mole fractions calculated. ^cThe value shown is the mole fraction of 1-Ad-OTFE relative to 1-Ad-OEt. The results are the average of two independent sets of data. Each set, with standards, was analyzed by GC/MS using selected ion monitoring. A graph of observed xR-OTFE versus actual xR-OTFE for the standards was plotted for sensitivity correction of the samples. The experimental error was 2%. ^dData point is the result of 1 set of data only. ^eExcess values are calculated as defined in Eq. (6). ^fSelectivities are calculated as defined in Eq. (5).

Figure 1: Solvolysis Products for 1-Ad-OTs

Figure 2: Excess Plot for 1-Ad-OTs

Figure 3: Product Ratios for 1-Ad-OTs

Figure 4: log of Product Ratios for 1-Ad-OTs

Table II: Viscosities and Densities of EtOH-TFE at 25 °C

Mole Fraction of TFE	Viscosity, cps	Density, g/mL	Kinematic		Excess K. Viscosity
			Viscosity, cs	Viscosity, cs	
0.000	1.101	0.788	1.398	1.398	0.000
0.025	1.072	0.805	1.333	1.333	-0.062
0.042	1.064	0.816	1.305	1.305	-0.088
0.059	1.061	0.827	1.284	1.284	-0.107
0.085	1.073	0.844	1.272	1.272	-0.116
0.167	1.059	0.896	1.182	1.182	-0.197
0.257	1.066	0.953	1.119	1.119	-0.250
0.350	1.105	1.011	1.093	1.093	-0.264
0.446	1.127	1.069	1.055	1.055	-0.293
0.547	1.210	1.129	1.072	1.072	-0.264
0.653	1.280	1.190	1.076	1.076	-0.248
0.763	1.432	1.252	1.144	1.144	-0.167
0.877	1.576	1.315	1.199	1.199	-0.099
0.937	1.623	1.347	1.205	1.205	-0.087
1.000	1.773	1.381	1.284	1.284	0.000

Table III: Physical Properties of Solvents

Nucleophile	Dielectric Constant	Relative		pKa	Relative Volume
		N	Y		
EtOH	24.32	1000	1	15.9	3.3
H ₂ O	78.5	389	5 x 10 ⁵	15.7	1
TFE	26.14	1	3500	12.4	4

Figure 5: Viscosity of EtOH-TFE Solutions
at 25 °C

Figure 6: Kinematic Viscosity of EtOH-TFE
at 25 °C

Figure 7: Excess Kinematic Viscosity of EtOH-TFE at 25 °C

Figure 8: Correlation of Excess Kinematic Viscosity & Excess for 1-Ad-OTs

Table IV: EtOH-TFE Solvolysis of 1-Adamantyl Iodide^a

xTfE ^b	xR-OTfE ^{b,c}	Excess ^b	xTfE/ xEtOH	x1-Ad-OTfE/ x1-Ad-OEt	S ^b	log (xTfE/ xEtOH)	log (xR-OTfE/ xR-OEt)
0.000	0.000	0.000	0.000	0.000			
0.055	0.058	0.003	0.058	0.061	1.057	-1.237	-1.213
0.095	0.100	0.004	0.105	0.111	1.049	-0.977	-0.956
0.178	0.180	0.002	0.216	0.220	1.017	-0.665	-0.658
0.263	0.287	0.024	0.358	0.402	1.126	-0.447	-0.395
0.352	0.403	0.051	0.542	0.674	1.244	-0.266	-0.171
0.448	0.508	0.059	0.813	1.032	1.269	-0.090	0.014
0.537	0.616	0.079	1.160	1.605	1.384	0.064	0.205
0.645	0.722	0.077	1.816	2.601	1.432	0.259	0.415
0.750	0.814	0.064	2.999	4.370	1.457	0.477	0.640
0.881	0.911	0.030	7.418	10.202	1.376	0.870	1.009
0.938	0.950	0.012	15.111	19.027	1.259	1.179	1.279
1.000	1.000	0.000					

^aThe concentration of 1-Ad-I was 1 mM with respect to the solvent. All samples were buffered with collidine at twice the substrate concentration. ^bSee Table I for the appropriate explanation. ^cDue to the excellent reproducibility of the results, the data shown is the average for the solvolyses at 35 °C, 50 °C, and 75 °C.

Figure 9: Solvolysis Products for 1-Ad-I

Figure 10: Excess Plot for 1-Ad-I

Figure 11: Product Ratios for 1-Ad-I

Figure 12: log of Product Ratios for 1-Ad-I

Table V: EtOH-TFE Solvolysis of 1-Adamantyl Mesylate^a at 25 °C

xTfE ^b	xR-OTfE ^{b,c}	Excess ^b	xTfE/ xEtOH	x1-Ad-OTfE/ x1-Ad-OEt	S ^b	log (xTfE/ xEtOH)	log (xR-OTfE/ xR-OEt)
0.0000	0.0000	0.0000	0.0000	0.0000			
0.0751	0.1191	0.0441	0.0811	0.1352	1.6666	-1.0907	-0.8689
0.1232	0.1890	0.0658	0.1405	0.2330	1.6579	-0.8522	-0.6326
0.1637	0.2492	0.0854	0.1958	0.3318	1.6951	-0.7083	-0.4791
0.2395	0.3492	0.1097	0.3149	0.5365	1.7038	-0.5019	-0.2705
0.3038	0.4344	0.1305	0.4364	0.7679	1.7594	-0.3601	-0.1147
0.3794	0.5271	0.1476	0.6114	1.1144	1.8228	-0.2137	0.0471
0.4545	0.6086	0.1540	0.8333	1.5546	1.8656	-0.0792	0.1916
0.5662	0.7123	0.1461	1.3051	2.4757	1.8969	0.1157	0.3937
0.6227	0.7649	0.1422	1.6505	3.2536	1.9711	0.2176	0.5124
0.7002	0.8230	0.1228	2.3357	4.6506	1.9910	0.3684	0.6675
0.7831	0.8750	0.0920	3.6098	7.0030	1.9399	0.5575	0.8453
0.8609	0.9214	0.0605	6.1884	11.7220	1.8943	0.7916	1.0690
1.0000	1.0000	0.0000					

^aThe concentration of 1-Ad-Ms was 2 mM with respect to the solvent. All samples were buffered with collidine at twice the substrate concentration. ^bSee Table I for the appropriate explanation. ^cThe value shown is the average of three independent sets of data.

Figure 13: Solvolysis Products for 1-Ad-Ms

Figure 14: Excess Plot for 1-Ad-Ms

Figure 15: Product Ratios for 1-Ad-Ms

Figure 16: log of Product Ratios for 1-Ad-Ms

Table VI: EtOH-TFE Solvolysis of 2-Adamantyl Tosylate^a at 90 °C

xTfE ^b	xR-OTfE ^{b,c}	Excess ^b	xTfE/ xEtOH	x2-Ad-OTfE/ x2-Ad-OEt	S ^b	log (xTfE/ xEtOH)	log (xR-OTfE/ xR-OEt)
0.000	0.000	0.000	0.000	0.000			
0.156	0.171	0.016	0.184	0.207	1.123	-0.735	-0.684
0.220	0.249	0.029	0.282	0.332	1.176	-0.550	-0.479
0.306	0.356	0.050	0.441	0.552	1.251	-0.355	-0.258
0.388	0.451	0.064	0.634	0.823	1.299	-0.198	-0.085
0.475	0.560	0.085	0.903	1.272	1.409	-0.044	0.105
0.555	0.653	0.098	1.247	1.877	1.505	0.096	0.274
0.645	0.745	0.100	1.814	2.916	1.608	0.259	0.465
0.745	0.830	0.085	2.918	4.882	1.673	0.465	0.689
0.838	0.903	0.065	5.184	9.295	1.793	0.715	0.968
1.000	1.000	0.000					

^aThe concentration of 2-Ad-OTs was 2 mM with respect to the solvent. All samples were buffered with collidine at twice the substrate concentration. ^bSee Table I for the appropriate explanation. ^cThe value shown is the mole fraction of 2-Ad-OTfE relative to 2-Ad-OEt.

Figure 17: Solvolysis Products for 2-Ad-OTs

Figure 18: Excess Plot for 2-Ad-OTs

Figure 19: Product Ratios for 2-Ad-OTs

Figure 20: log of Product Ratios for 2-Ad-OTs

Table VII: EtOH-TFE Solvolysis of 1-Bicyclo[2.2.2]octanyl Tosylate^a at 90 °C

xTfE ^b	xR-OTfE ^{b,c}	Excess ^b	xTfE/ xEtOH	x222-OTfE/ x222-OEt	S ^b	log (xTfE/ xEtOH)	log (xR-OTfE/ xR-OEt)
0.000	0.000	0.000	0.000	0.000			
0.052	0.074	0.022	0.055	0.080	1.456	-1.259	-1.096
0.098	0.140	0.043	0.108	0.163	1.508	-0.966	-0.788
0.179	0.253	0.074	0.218	0.339	1.557	-0.662	-0.470
0.264	0.373	0.109	0.359	0.595	1.656	-0.444	-0.225
0.358	0.493	0.136	0.557	0.974	1.748	-0.254	-0.012
0.451	0.611	0.160	0.820	1.569	1.913	-0.086	0.196
0.542	0.690	0.148	1.185	2.229	1.881	0.074	0.348
0.642	0.788	0.146	1.794	3.707	2.066	0.254	0.569
0.745	0.864	0.119	2.915	6.325	2.170	0.465	0.801
0.855	0.930	0.075	5.906	13.247	2.243	0.771	1.122
0.922	0.963	0.041	11.804	25.937	2.197	1.072	1.414
1.000	1.000	0.000					

^aThe concentration of 2.2.2-OTs was 1 mM with respect to the solvent. All samples were buffered with collidine at twice the substrate concentration. ^bSee Table I for the appropriate explanation. ^cThe value shown is the mole fraction of 2.2.2-OTfE relative to 2.2.2-OEt.

Figure 21: Solvolysis Products for 2.2.2-OTs

Figure 22: Excess Plot for 2.2.2-OTs

Figure 23: Product Ratios for 2.2.2-OTs

Figure 24: log of Product Ratios for 2.2.2-OTs

Figure 25: Summary of Excesses for Adamantyl Compounds

Figure 26: Summary of Product Ratios for Bridgehead Compounds

Table VIII: EtOH-TFE Solvolysis of *cis*-4-*t*-Butylcyclohexyl Tosylate^a at 70 °C

xTFE ^e	xElim. ^b	Backside Reaction ^{b,c}		Frontside Reaction ^{b,d}		Rate Data @ 70 °C k x 10 ⁴ , sec ⁻¹	
		xR-OTFE ^f	xR-OET	xR-OTFE ^f	xR-OET	xTFE	
0.000	0.595	0.000	0.174	0.000	0.212	0.166	0.49
0.048	0.649	0.002	0.149	0.007	0.193	0.443	1.78
0.107	0.659	0.004	0.143	0.011	0.179	0.768	25.20
0.187	0.685	0.010	0.122	0.019	0.155		
0.265	0.693	0.011	0.111	0.027	0.130		
0.354	0.710	0.018	0.104	0.042	0.137		
0.434	0.723	0.027	0.079	0.049	0.112		
0.543	0.754	0.027	0.057	0.057	0.072		
0.627	0.754	0.037	0.058	0.065	0.058		
0.742	0.772	0.037	0.029	0.072	0.044		
0.843	0.783	0.042	0.017	0.076	0.041		
0.923	0.795	0.048	0.009	0.074	0.033		
1.000	0.755	0.053	0.000	0.091	0.000		

^aThe concentration of *cis*-4-OTs was 2 mM with respect to the solvent. All samples were buffered with collidine at twice the substrate concentration. ^bThe values shown are the mole fractions of the respective products relative to all products formed. ^cThe backside reaction results in the respective *trans*-1,4-*t*-butylcyclohexyl ethers. ^dThe frontside reaction results in the respective *cis*-1,4-*t*-butylcyclohexyl ethers. ^eSee Table I. ^fOnly the 1,4-trifluoroethyl ethers are listed and not the presumed 1,3-trifluoroethyl ethers.

Table IX: Selectivities^a for Solvolysis *cis*-4-*t*-Butylcyclohexyl Tosylate^b

		Backside Reaction				Frontside Reaction			
		log		log		log		log	
xTfE	xEtOH/ xTfE	(xEtOH/ xTfE)	xR-OEt/ xR-OTfE	xR-OEt/ xR-OTfE	(xR-OEt/ xR-OTfE)	xR-OEt	xR-OTfE	(xR-OEt/ xR-OTfE)	S ^a
0.000	19.817								
0.048	8.310	1.297	78.157	1.893	3.944	26.455		1.423	1.333
0.107	4.354	0.920	32.960	1.518	3.966	16.000		1.204	1.926
0.187	2.775	0.639	12.793	1.107	2.938	8.052		0.906	1.849
0.265	1.825	0.443	10.123	1.005	3.648	4.766		0.678	1.718
0.354	1.302	0.261	5.881	0.769	3.223	3.279		0.516	1.797
0.434	0.843	0.115	2.955	0.471	2.269	2.268		0.356	1.742
0.543	0.595	-0.074	2.109	0.324	2.503	1.255		0.099	1.490
0.627	0.349	-0.226	1.552	0.191	2.961	0.894		-0.049	1.502
0.742	0.187	-0.458	0.771	-0.113	2.211	0.616		-0.210	1.767
0.843	0.083	-0.729	0.416	-0.391	2.227	0.544		-0.264	2.912
0.923	0.000	-1.081	0.176	-0.756	2.115	0.449		-0.348	5.414
1.000			0.000						

^aselectivities are calculated in terms of EtOH by taking the reciprocal of Eq.(5).

Therefore a selectivity greater than 1 indicates that EtOH is the favored nucleophile.

^bSee Table VIII for the appropriate explanations.

Figure 27: Backside Product Ratios for
cis-4-t-Butylcyclohexyl-OTs

Figure 28: log of Backside Product Ratios for
cis-4-t-Butylcyclohexyl-OTs

Figure 29: Frontside Product Ratios for
cis-4-t-Butylcyclohexyl-OTs

Figure 30: log of Frontside product Ratios
for cis-4-t-Butylcyclohexyl-OTs

Figure 31: Elimination Products for
cis-4-t-Butylcyclohexyl-OTs