Published in final edited form as:

Curr Org Chem. 2012 June 1; 16(12): 1502–1511. doi:10.2174/138527212800672592.

Nucleophilic Participation in the Solvolyses of (Arylthio)methyl Chlorides and Derivatives: Application of Simple and Extended Forms of the Grunwald-Winstein Equations

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Abstract

The specific rates of solvolysis of chloromethyl phenyl sulfide [(phenylthio)methyl chloride] and its *p*-chloro-derivative have been determined at 0.0 °C in a wide range of hydroxylic solvents, including several containing a fluoroalcohol. Treatment in terms of a two-term Grunwald-Winstein equation, incorporating terms based on solvent ionizing power (Y_{Cl}) and solvent nucleophilicity (N_T) suggest a mechanism similar to that for the solvolyses of *tert*-butyl chloride, involving in the rate-determining step a nucleophilic solvation of the incipient carbocation in an ionization process. A previous suggestion, that a third-term governed by the aromatic ring parameter (I) is required, is shown both for the new and for the previously studied related substrates to be an artifact, resulting from an appreciable degree of multicollinearity between I values and a linear combination of N_T and Y_{Cl} values.

1. INTRODUCTION

It is well-established that alkyl chlorides where derivatization involves the introduction of a substituent atom such as oxygen, sulfur, or nitrogen on the α -carbon give, on ionization, resonance stabilized carbocations (equation 1).

(1)

The formation of the carbocations, with an appreciable amount of delocalized charge, is relatively rapid [1–3]. When X = O, they are often used to protect hydroxyl groups and the resulting acetals can be easily deprotonated by a mild treatment with acid [4].

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The effect of the adjacent lone pairs of electrons can be dramatic. For example, the solvolysis of chloromethyl ethyl ether ($\text{CH}_3\text{CH}_2\text{OCH}_2\text{Cl}$) in 36% dioxane proceeds at a rate of about 10^9 times that of butyl chloride [2] and, the ethanolysis of chloromethyl methyl ether proceeds about 10^{13} times as fast as that of propyl chloride [2] and of at least 10^{14} times as fast as that of methyl chloride [5]. It is of interest that, in bimolecular reaction with ethoxide ion, the second-order rate coefficient is also considerable larger (by a factor of about 10^5) than for the methyl chloride [5].

The corresponding aryl α -chloroalkyl ethers are easily prepared and they also undergo unimolecular nucleophilic substitution in water and alcohols [6]. The replacement of an alkyl group by an aryl group leads to an appreciable reduction in the solvolysis reaction rate. For example, in 98% dioxane (2% water) at 25.0 °C, chloromethyl methyl ether reacts 1090 times as fast as chloromethyl phenyl ether [7]. Many of the more recent studies have involved cyclic substrates from the carbohydrate field [8,11]. The acetals involved in these reactions are among the most important types of biological functional groups [12].

There have also been extensive studies of the corresponding thioethers ($\text{X} = \text{S}$). Chloromethyl phenyl sulfide (**1**) is readily available and it is important [13] as a reactive electrophile, as an α -methylenating agent, as an acyl carbanion equivalent, as a source of phenylthiocarbene and the phenylthiomethyl carbanion, and as a precursor for halomethyl phenyl sulfoxides.

Indeed, the phenylthiomethyl group is so commonly encountered that it is frequently abbreviated to PTM. The compound **1**, or a ring substituted derivative, is of use as a protecting agent for alcohols or phenols [14], as an alternative to the formation of the more common methoxythiomethyl (MTM) alkyl [15–17] or aryl [18] ethers. PTMCl was found to be an excellent reagent towards phenols but not, in general, towards alcohols (where considerable amounts of side products are formed). The solvolyses of **1** can be pictured as in Scheme 1.

When the substrate is acyclic, it has been found that, in a comparison of the rates of $\text{S}_{\text{N}}1$ solvolyses of an α -chloroether with those of the corresponding α -chlorothioether, the ether reacts faster than the thioether. It was suggested that this was due to the larger sulfur atom not conjugating as well with the carbocation center [3]. In terms of stabilities, there is both experimental [19] and theoretical [20] evidence that the adjacent sulfur stabilizes a carbocation better than an adjacent oxygen. On these grounds, one might expect a faster reaction to the more stable sulfur-containing carbocation.

However, it was found for solvolyses in aqueous dioxane of both the (dichlorodimethyl) ether and sulfate and the chloromethyl ethyl ether and sulfide, that the ether reacted faster than the sulfide [21].

Also it has been found [22] that when the X atom (O or S) is within a six-membered glucopyranosyl or thioglucopyranosyl ring, the fluorides hydrolyze with the thio-derivative reacting the faster. This represents a reversal of ordering observed for the previously studied [21] acyclic equivalents. It was proposed [22] that an enhanced anomeric effect is smaller for the S-C-F system than for the O-C-F system, leading to a smaller ground state stabilization for the S-C-F system. The mechanism of reactions of substrates containing these ring substituents has been reviewed [23].

It was shown that for hydrolysis in 5 M water in dioxane at 25 °C, the phenylthiomethyl chloride (chloromethyl phenyl sulfide, **1**) reacted about 200 times slower than chloromethyl methyl sulfide [24]. The effect of the introduction of *meta*- and *para*- substituents into the aromatic ring of **1** has been studied [25] in 50% dioxane at 35 °C. Use of the Hammett σ

values (the original “normal” values) gave a better fit for the solvolyses of **1** than the σ^+ values, which would be expected to apply if considerable positive charge was being distributed into the aromatic ring [26]. The Hammett σ value was -2.6 . This is an appreciable value for a reaction governed only by inductive and field effects, with significant resonance effects ruled out by the applicability of the σ values. The lack of resonance effects was attributed to the reluctance of divalent sulfur to expand its valence shell to ten electrons [27]. It is found that, with fairly powerful nucleophiles in solvents of relatively weak ionizing power, bimolecular nucleophilic substitution (S_N2 reaction) can be observed. A study has been made [28] of the reactions of *para*-substituted phenyl chloromethyl sulfides with aniline in dimethylformamide. An Hammett plot, incorporating σ values, led to a σ value of -0.84 , indicating a modest accelerating effect of electron-supplying substituents, consistent with an S_N2 reaction with bond-breaking running modestly ahead of bond-making. Similarly, it has been found that exchange reactions of chloride ion with chloromethyl aryl sulfide in acetonitrile follow second-order kinetics [29] and involve an initial complexation [30].

Another consideration is the extent to which replacement of a hydrogen on the α -carbon carrying the halogen by some other atom or group influences the rate and mechanism of the unimolecular solvolysis reaction of an α -chloroether or α -chlorothioether.

The influence of electron-withdrawing groups was probed using a successive introduction of additional chlorines into the β -position for the solvolyses of phenyl α -chloroethyl ether. The rates of reaction fell off appreciably with each additional chlorine introduced, with the group on the α -carbon going from CH_3 , to CH_2Cl , to $CHCl_2$, to CCl_3 . The $CCl_3CHClOC_6H_5$ reacted 500,000 times slower than $CH_3CHClOC_6H_5$ [6].

In a study with thioethers [24], it was found that the solvolyses of CH_3SCH_2Cl in 1 M water in dioxane at 25 °C increased in rate by a factor of 500 on the introduction of a methyl group into the chloromethyl, to give $CH_3SCH(CH_3)Cl$. If, in turn, the introduced methyl group was replaced by a phenyl group, it was found that, for reaction with 0.2 M water in dioxane at 25 °C, there was a further 140 fold increase in rate. These quite large increases were taken as indicating that no saturation level as regards electron supply had been approached.

There have also been studies of $RSCH_2Cl$ compounds which have an electron-withdrawing benzoyl or acetyl group replacing an α -hydrogen. This would be expected to lead to a reduction in the rates of S_N1 reactions. If sufficiently powerful, it is possible that this effect could lead to the observation of contributions from a solvent-assisted S_N2 process.

In Scheme 2 are given the structures of the six substrates given consideration in this report.

Initially, 2-chloro-2-(methylthio)acetophenone (**2**), and 2-chloro-2-(phenylthio)acetophenone (**3**) were studied [31]. In a later paper, the solvolyses of 2-chloro-2-(4-methoxyphenylthio)acetophenone (**4**) and 2-chloro-2-(methylthio)acetone (**5**) were added to the study [32]. These substrates are of additional interest in that the carbocation formed in an S_N1 reaction formally has the positive charge on a carbon which is adjacent (α) to the carbonyl group. Carbocations of this type are normally difficult to form [33–35], and it is of interest to see what extent their formation is favored by having an alkylthio or arylthio substituent also at the reaction center.

The studies by Ryu et al [31,32] included a study of the effect of solvent variation on the specific rates of solvolysis (first-order rate coefficient for solvolysis) of compounds **2** – **5** (structures shown in Scheme 2). These specific rates were then analyzed using simple and extended forms of the Grunwald-Winstein equation (2). In this original [36] one-term equation, k represents the specific rates of solvolysis in a given solvent of ionizing power Y ,

k_0 represents the specific rate in the standard solvent (80% ethanol, $Y = 0$), m represents the sensitivity of the specific rates of solvolysis to changes in solvent ionizing power, and c

$$\log (k/k_o)=mY_x+c \quad (2)$$

represents a constant (residual) term. In order to take into account the nucleophilic assistance from the solvent present in S_N2 reaction (plus E2, when elimination reaction accompanies substitution) a second term, expressed as lN , was added to equation 2, to give equation 3 [37,38]. In equation 3, l represents the sensitivity of the specific rates of solvolysis towards changes in solvent nucleophilicity (N). This scale is also based on 80% ethanol being the standard solvent (both N and Y are set at zero).

$$\log (k/k_o)=lN_T+mY_x+c \quad (3)$$

It was observed early that reactions forming carbocations with aromatic substituents on the α -carbon deviated from the behavior described by equation 1 and, when several series of binary solvents of varied compositions were included in a study, dispersion into a series of linear plots was observed [39, 40]. In order to account for these aromatic ring effects, a third term, represented as hI , has been added to equation 3, to give equation 4. In equation 4, h

$$\log (k/k_o)=lN_T+mY_x+hI+c \quad (4)$$

represents the sensitivity of the solvolysis to changes in the solvent property designated as the "aromatic ring parameter", I [41]. The development and uses of the extended forms of the Grunwald-Winstein equation have recently been reviewed [42]. The scales used for solvent ionizing power (Y_X for a leaving group X) are now usually based on the solvolyses of the 1-adamantyl or 2-adamantyl derivative [43,44], as opposed to the original *tert*-butyl chloride scale [36] and scales of solvent nucleophilicity (N_T) are usually based on studies of the solvolyses of the *S*-methylidibenzothiophenium ion [38,45].

Ryu et al applied equations 2 and 3 to the solvolyses of compounds **2** through **5** and, for the two compounds with an aromatic ring at the sulfur (**3** and **4**), they also applied the three-term equation 4. We have repeated the analyses reported using equation 4, with inclusion of all of the data points available. The validity of including the hI term for these systems is given additional consideration. We have also extended the studies to the solvolyses of **1** (compound **3** without the benzoyl substituent at the α -carbon) and to chloromethyl *p*-chlorophenyl sulfide [(*p*-chlorophenylthio)methyl chloride, **6**].

The correlation analyses have been carried out using equations 2, 3, and 4. Particular attention will be paid to the sensitivities towards solvent nucleophilicity changes and towards changes in the aromatic ring parameter value, considered as a measure of solvent effects upon charge delocalization into aromatic rings.

2. EXPERIMENTAL

The chloromethyl phenyl sulfide (**1**, Sigma-Aldrich, 97%) and chloromethyl 4-chlorophenyl sulfide (**6**, Sigma-Aldrich, 97%) were used as received. Solvents were purified and the kinetic runs carried out as previously described [45]. A substrate concentration of approximately 0.007 M was used. Solubility considerations limited the range of aqueous-organic solvents which could be employed, especially for **6**. For example, specific rate values could be observed in 40% ethanol and 60% methanol for **1** but this was not possible

for **6**. The specific rates and associated standard deviations, as presented in Table 1 for each of the two substrates, are obtained by averaging all of the values obtained from, at least, duplicate runs.

Multiple regression analyses were carried out using the Excel 2010 package from the Microsoft Corporation.

3. RESULTS

The specific rates of solvolysis of chloromethyl phenyl sulfide **1** and chloromethyl *p*-chlorophenyl sulfide **6** were determined at 0 °C in ethanol-water (100–40% ethanol), methanol-water (100–60% methanol), acetone-water (80–60% acetone), TFE-water (97–70% TFE), HFIP-water (97–70% HFIP) and across the full range of TFE-ethanol mixtures. The values obtained are listed in Table 1. In a footnote to the table, values are presented at 25–55 °C for the solvolyses of **6** in 100% ethanol, together with the calculated enthalpy and entropy of activation. The solvent nucleophilicity (N_T) values [38] and solvent ionizing power (Y_{Cl}) values [44,46] used in the correlation analyses are also listed.

4. DISCUSSION

The solvolyses of **1** and **6** proceed at a convenient rate over a wide variety of hydroxylic solvents at 0.0 °C. The introduction of a *para*-chlorine atom into **1**, to give **6**, results in a reduction in rate by a factor of four to six (Table 1). Calculation of a series of Hammett σ values based on the two data points for each solvent leads to surprisingly constant values over a wide composition range for the binary solvent mixtures. In aqueous ethanol (100–60% EtOH) and aqueous methanol (100–80% MeOH), eight determinations lead to a value of -2.9 ± 0.2 and four determinations in aqueous TFE (97–80% TFE) and 90% HFIP lead to a value of -3.7 ± 0.3 . The average value of -2.9 in aqueous methanol and ethanol is in good agreement with the value of -2.6 for solvolyses of the parent and seven *meta*- and *para*-substituted derivatives in 50% dioxane [25]. While serious consideration of Hammett correlations with only two data points is, as a general rule, not recommended, the observation of constant σ values over several EtOH-H₂O and MeOH-H₂O compositions and over four TFE-H₂O and HFIP-H₂O compositions does suggest that these values have relevance.

The major aspects of the present study are to apply the various forms of the Grunwald-Winstein equation (equations 2–4) to the kinetic data reported for the solvolyses of **1** and **6** in Table 1 and to revisit the Grunwald-Winstein correlations previously reported for compounds **2** – **5** [31,32] and, in particular, to give further consideration to the significance of the analyses including the hI term (use of equation 4).

In Table 2, we present the results from the correlation analyses for the specific rates of solvolysis of **1** and **6** against Y_{Cl} (equation 2), Y_{Cl} and N_T (equation 3) and Y_{Cl} , N_T , and I (equation 4).

The analyses suffer when solvolyses in TFE-ethanol solvent mixtures are included. This is often the case (discussed elsewhere [47]), due to the data points for these solvent systems lying below the best fit correlation line. Removal of these solvents considerably improves the correlations, as determined by comparison of simple or multiple correlation coefficients, *F*-test values, and the reduced probabilities that some of the terms making a small contribution are not statistically significant as regards their contribution to the overall correlation.

The analyses using equation 3 (two-term) lead for 16 solvolyses of substrate **1** to an I value of 0.27 ± 0.08 and an m value of 0.76 ± 0.06 and for substrate **6** to an I value of 0.22 ± 0.08 and an m value of 0.67 ± 0.06 for 17 solvents. These sensitivities correspond to I/m ratios of 0.36 and 0.33, respectively. The I/m ratios are similar to those obtained for solvolyses of *tert*-butyl chloride (I/m of 0.44) [46,48]. Accordingly the original Y scale [36,44] should give reasonably good one-term correlations for the solvolyses of **1** and **6**, equivalent to using the solvolyses of *tert*-butyl chloride as a similarity model for the solvolyses [46,48,49]. It might be mentioned that the term “similarity model” in this context is often misunderstood as meaning similarity in structure. While the structures are often similar this is not a requirement. The requirement for a good similarity model is that the ratios of the sensitivities from a two-term treatment, in this case the I/m ratios are similar for the system under consideration and for the similarity model employed.

When the 16 data points for **1** and the 17 data points for **6** are plotted as $\log(k/k_0)$ against Y values, values are obtained for the solvolyses of **1** of 0.97 ± 0.08 for the slope, 0.08 ± 0.09 for the intercept, 0.958 for the correlation coefficient, and 157 for the F -test value. The corresponding values for **6** are 0.92 ± 0.08 , 0.15 ± 0.10 , 0.947, and 131. Both correlations are acceptable and the slightly better correlation for the solvolyses of **1** is consistent with the I/m value being closer to that observed for the *tert*-butyl chloride similarity model. The plots against Y values are shown in Figures 1 and 2. When the $\log(k/k_0)$ values are plotted against Y_{Cl} values, reasonably good plots are obtained for both substrates but the correlations are improved when solvent nucleophilicity is also included in the correlation (equation 3). The values in Table 2 show a considerable improvement in the correlation coefficient accompanied by a small decrease in the F -test value. The I values (sensitivities to changes in solvent nucleophilicity) have a 0.005 for solvolyses of **1** and 0.015 for solvolyses of **6** probability that the I/N term is not statistically significant in the overall correlation. Ideally, these probability values should be somewhat lower, with a value below 0.001 being considered desirable, but this is frequently the situation for low values for I , with the standard errors tending to be fairly constant, irrespective of the magnitude of the I value [38]. The two-term correlations are presented in Figures 3 and 4.

It is of interest to give further consideration to the extent of further improvement (if any) on applying the three-term equation 4 to the data. The values obtained from these correlations are also presented in Table 2. For **1**, there is a considerably improved correlation (F -test value increasing from 195 to 415) but the situation is less clear cut for **6**, with a modest increase in the correlation coefficient and a modest decrease in the F -test value. Care must be taken because of the previously demonstrated [50] relationship between the I scale and a linear combination of N_T and Y_{Cl} values. We will return to this aspect after the presentation of new analyses (more data points) for the solvolyses of substrates **2** through **5**. It was pointed out recently [51] that in consideration of multicollinearity one must consider not only collinearity between pairs of scales but also between any one scale and any linear combination of other applicable scales.

The previous studies of compounds **2–5** were analyzed in terms of the application of equations 2 and 3 and, for the two substrates **3** and **4** containing an arylthio substituent, also in terms of equation 4. The substrates **2** and **5** containing no aromatic rings were not originally analyzed in terms of equation 4 [31,32]. However, in view of Takeuchi's finding [52] of a correlation against a combination of Y and I values for the solvolyses of some highly sterically hindered tertiary alkyl derivatives, we felt that application of equation 4 to these other two substrates (**2** and **5**) would also be worthwhile. As pointed out earlier, the experimental [25] and theoretical [27] evidence against a resonance interaction of an adjacent positively charged sulfur with an attached aromatic system suggests that the hI term

may not be relevant in the correlation analyses of the solvolyses of any of the **1** through **6** substrates.

The correlation analyses of compounds **2** through **5** mimic those for **1** and **6** of Table 2, and they are reported in Table 3. In contrast to the earlier [31,32] correlations, the maximum number of data points were included in all of the correlations. Only for the solvolyses of **3** was there any indication that the analyses would be improved by omission of the specific rates measured in 100 and 90% ethanol and 100% methanol (the solvents most favorable for an S_N2 mechanism to operate). Even here, the improvement in the correlations on omission of these three data points is, at best, marginal (Table 3).

For the correlations reported in Table 3, the *m* values obtained from the simple one-term treatment (equation 2) are just slightly lower than for the solvolyses of compounds **1** and **6**. When the two-term equation (equation 3) is used, the *I* values for **3** and **4** of 0.31 and 0.33 are only slightly greater than for **1** and **6** but for substrates **2** and **5** considerably larger *I* values are obtained, reaching a value of 0.88 for **5** and at a value of 0.58 for **2**. The *m* values, however, at 0.59–0.74 are very similar to those of **1** and **6** (0.67–0.76). The larger *I* values, sensitivities to changes in solvent nucleophilicity, are in accord with the need for additional nucleophilic solvation (or increased nucleophilic participation in a loose S_N2 transition state) in the presence of the powerful electron-withdrawing acetyl or benzoyl substituent at the reaction center [33–35]. The study of **3** was at 50.0 °C [31] and in 80% ethanol a solvolysis specific rate of $4.00 \times 10^{-4} \text{ sec}^{-1}$ was reported. From specific rates at 0.0° and 25.0 °C (Table 1), a value of $24.4 \times 10^{-4} \text{ sec}^{-1}$ can be estimated at 50.0 °C for the solvolyses of **1** in 80% ethanol at 50.0 °C: the introduction of an α-benzoyl group into **1** to give **3** results in a rate reduction by a factor of 6.1. This is a relatively small influence, consistent with favorable changes in the transition state structure being the rationale for the accompanying change in the *I*/*m* ratio from 0.36 to 0.56 (Tables 2 and 3).

When equation 4 (three-term) is applied to the solvolyses of substrates **1** and **6** negative values for *h*, with large standard error, are obtained when all of the solvents are considered. The values become positive, however, when the data points for solvolyses in TFE-ethanol are excluded from the correlations (Table 2). When solvolyses of substrates **2** through **5** are considered (Table 3), positive *h* values are obtained in three cases (0.36 to 0.99) and a negative value (-0.42) when **5** is the substrate.

In a recent review in this journal [50] of the correlations of highly hindered tertiary alkyl derivatives, it was demonstrated that the *I* and *m* values of the three-term equation were always lower than those of the two-term equation when *h* was negative and always higher when *h* was positive, as one would expect if the multicollinearity as expressed in equation (5) was operative. An inspection of Tables 2 and 3 shows that this behavior is also observed for

$$I = -xN_T - yY_{Cl} - c \quad (5)$$

all nine of the analyses of the six solvolyses under consideration.

Such behavior strongly supports the conclusion previously reached [50] that the observation of an appreciable *hI* term, even for systems not containing any aromatic rings or conjugated π electron systems, is an artifact resulting from the presence of the multicollinearity as expressed in equation 5. It was also shown that, as desired, *I* correlates very poorly with *Y* values and poorly with *N_T* values (presented for *tert*-butyl chloride solvolysis previously

[50] and in Table 4), and only when correlated against both N_T and Y_{Cl} is there an important multicollinearity problem.

For each of the entries in Tables 2 and 3, the equation 5 has been applied to the set of solvents included in the correlations. It is shown in Table 4 that the multicollinearity as expressed in the equation is robust and the x , y , and c values vary only slightly with changes in the solvents included. Indeed, the average values are essentially identical to those recorded in the table for *tert*-butyl chloride solvolyses and these values ($x = 0.29$; $y = 0.14$; $c = 0.03$) have been used in our analyses. The I within the hI term of equation 4 has been replaced by the expression given in equation 5, and incorporating the x , y , and c values for the 43 solvents used in the *tert*-butyl chloride solvolyses. In this way, with a combination of terms now based on N_T and Y_{Cl} , we convert from an equation 4 representation to an equation 3 representation. In Table 5, it is shown that the values obtained in this way, except for increased standard errors, are essentially identical to those obtained directly from an application of equation 3. This exactly parallels the observations previously [50] on application to the highly hindered tertiary alkyl derivatives.

5. CONCLUSIONS

The responses of the rates of solvolysis of the (arylthio)methyl chlorides **1** and **6** to changes in the composition of a hydroxylic solvent are quantified by the application of the extended Grunwald-Winstein equation (3). This results in the observation of a high sensitivity to changes in solvent ionizing power (m value) coupled with a modest sensitivity to changes in solvent nucleophilicity (I value). We favor an S_N1 mechanism with a modest nucleophilic solvation of the developing carbocation, similar to the mechanism we proposed for *tert*-butyl chloride solvolysis [46]. An alternative description [53] involving a loose S_N2 transition state, very similar in detail, could also lead to the observed sensitivities. Indeed, for **1**, S_N2 reactions with strong nucleophiles in relatively inert solvent are well documented [28,29].

Previous analyses of the specific rates of solvolyses of compounds **2** through **5** [31,32], with an acyl substituent at the reaction center have been repeated with an increased number of data points, especially for the analyses applying the three-term equation. The sensitivities obtained in these analyses are quite similar to those reported earlier [32]. One feature of the earlier report was a claim that there was a relevant contribution from the hI term (in equation 4) for compounds **3** and **4**, which are derivatives of an (arylthio)methyl chloride. Subsequent to this claim being put forward, we have shown [50] that great care must be taken in the application of equation 4, due to a multicollinearity relationship between I values and a combination of the N_T and Y_{Cl} values for groupings of solvents. Indeed, it is now clear that the apparent utility of equation 4, not only for substrates **3** and **4** but also for **2** and **5**, is an artifact due to the presence of this multicollinearity. The lack of a need to incorporate an hI term is not surprising because the positive charge adjacent to the aromatic ring in (arylthio)methyl chloride would lie on a sulfur atom, which has been shown to be reluctant to expand its valence shell to above eight electrons [25,27] as would be required to remove electron density by resonance from the directly attached aromatic ring.

In ethanol at 50.0 °C, the introduction of a benzoyl group into **1** to give **3** leads to a six fold reduction in the specific rates of solvolysis. This is a reasonable value considering that an acetyl group in the meta position has a Hammett σ value of +0.38 and the Taft σ_1 value for the acetyl group is +0.28 [53].

Acknowledgments

This research was supported, in part, by the donors of the American Chemical Society Petroleum Research Fund (postdoctoral fellowship for BCP) and, in part, made possible by the Delaware INBRE program, supported by

grants from the National Center for Research Resources - NCRR (5P20RR016472-12) and the National Institute of General Medical Sciences - NIGMS (8 P20 GM103446-12) from the National Institutes of Health (NIH); a National Science Foundation (NSF) EPSCoR grant EPS-0814251; and a NSF ARI-R2 grant 0960503.

References

1. Ingold, CK. Structure and mechanism in organic chemistry. 2. Cornell University Press; Ithaca, New York: 1969. p. 444
2. Streitwieser, A. Solvolytic displacement reactions. McGraw Hill; New York: 1964. p. 103
3. Bunton, CA. Nucleophilic substitution at a saturated carbon. Elsevier; New York: 1963. p. 50-51.
4. March, J. Advanced organic chemistry: reactions, mechanisms, and structure. 4. Wiley; New York: 1992. p. 387
5. Ballinger P, de la Mare PDB, Kohnstam G, Prestt BM. The reaction of chlorodimethyl ether with ethanolic and with ethoxide ions. *J Chem Soc.* 1955:3641–3647.
6. Shostakovskii MF, Kalabina AV, Zikherman KKh. A study of the hydrolysis alcoholysis of α -chloroethyl aryl ethers. *Zh Organ Khim Int Ed.* 1966; 2:691–693.
7. Böhme H, Dörries A. Zur hydrolyse und alkohololyse α -chlorierter äther. *Chem Ber.* 1956; 89:719–722.
8. Banait NS, Jencks WP. Reactions of anionic nucleophiles with α -D-glucopyranosyl fluoride in aqueous solution through a concerted $A_ND_N(S_N2)$ mechanism. *J Am Chem Soc.* 1991; 113:7951–7958.
9. Zhang Y, Bommuswamy J, Sinnott ML. Kinetic isotope effect study of transition states for the hydrolyses of α - and β -glycopyranosyl fluorides. *J Am Chem Soc.* 1994; 116:7557–7563.
10. Zhu J, Bennet AJ. Solvolyses of 2-deoxy- α - and β -D-glucopyranosyl 4'-bromoisquinolinium tetrafluoroborates. *J Org Chem.* 2000; 65:4423–4430. [PubMed: 10891147]
11. Kevill DN, D'Souza MJ. Concerning the extent of nucleophilic participation in solvolyses of glucopyranosyl derivatives. *J Phys Org Chem.* 2001; 14:819–822.
12. Dwek RA. Glycobiology: Towards understanding the functions of sugars. *Chem Rev.* 1996; 96:683–720. [PubMed: 11848770]
13. Reutrakul, V.; Pohmakotr, M. Chloromethyl phenyl sulfide. In: Paquette, LA., editor. *Encyclopedia of Reagents for Organic Syntheses.* Wiley; New York: 1995. p. 1162-1165.
14. Holton RA, Nelson RV. A new protecting group for phenols: phenylthiomethyl (PTM) ethers. *Synthetic Communications.* 1980; 10:911–914.
15. Corey EJ, Bock MG. Protection of primary hydroxyl groups as methylthiomethyl ethers. *Tetrahedron Letters.* 1975:3269–3270.
16. Yamada K, Kato K, Nagase H, Hirata Y. Protection of tertiary hydroxyl groups as methylthiomethyl ethers. *Tetrahedron Letters.* 1976:65–66.
17. Rojer PM, Angyal SJ. Methylthiomethyl ethers: General synthesis and mild cleavage, protection of hydroxyl groups. *Tetrahedron Letters.* 1976:3067–3068.
18. Holton RA, Davis RG. Protection of phenols as methylthiomethyl ethers. *Tetrahedron Letters.* 1977:533–534.
19. Jagannadham V, Amyes TL, Richard JP. Kinetic and thermodynamic stabilities of α -oxygen and α -sulfur stabilized carbocations in solution. *J Am Chem Soc.* 1993; 115:8465–8466.
20. Buckley N, Oppenheimer NJ. Reactions of charged substrates. 7. The methoxymethyl carbenium ion problem. 2. A semiempirical study of kinetic and thermodynamic stabilities of linear and cyclic oxo- and thiocarbenium ions generated from aldehyde hydrates, hemiacetals, acetals, and methyl ribosides and glucosides. *J Org Chem.* 1996; 61:8048–8062. [PubMed: 11667788]
21. Böhme H. Der einfluss α -ständiger sauerstoff- und schwefelatome auf die hydrolysierungsgeschwindigkeit der kohlenstoff-halogen-bindung. *Ber dtsh chem Ges.* 1941; 74:248–256.
22. Johnston BD, Indurugalla D, Pinto BM, Bennet AJ. The 5-thioglucopyranosyl carbenium ion is a solvent-equilibrated cation. *J Am Chem Soc.* 2001; 123:12698–12699. [PubMed: 11741443]
23. Bennet AJ, Kitos TE. Mechanisms of glycopyranosyl and 5-thioglycopyranosyl transfer reactions in solution. *J Chem Soc Perkin Trans.* 2002; 2:1207–1222.

24. Böhme H, Fischer H, Frank R. Darstellung und eigenschaften der α -halogenierten thioäther. Ann. 1949; 563:54–72.
25. Bordwell FG, Cooper GD, Morita H. The hydrolysis of chloromethyl aryl sulfides. J Am Chem Soc. 1957; 79:376–378.
26. Hammett, LP. Physical Organic Chemistry. 2. Vol. Chapter 11. McGraw Hill; New York: 1970.
27. Mangini A, Passerini R. Can the sulfur bridge be considered as a relay of conjugation? Experientia. 1956; 12:49–50.
28. Nadar PA, Murugesan R. Kinetics of reaction of substituted phenyl chloromethyl sulphides with aniline in dimethylformamide. Indian J Chem. 1977; 15B:1037–1039.
29. Hayami J, Tanaka N, Kurabayashi S, Kotani Y, Kaji A. S_N2 reactions in dipolar aprotic solvents. Chlorine exchange reactions of 2-arylethyl chlorides, chloromethyl aryl ethers, and chloromethyl aryl sulfides in acetonitrile. Bull Chem Soc Jpn. 1971; 44:3091–3095.
30. Hayami J, Tanaka N, Hihara N, Kaji A. Nucleophile-substrate complex in solution. Detection of chloride-organic chloride association and the potential role of the complexes in the S_N2 reaction. Tetrahedron Letters. 1973:385–388.
31. Ryu ZH, Shin SH, Lim GT, Lee JP. Correlation of the rates of solvolysis of 2-chloro-thioacetophenones. Bull Korean Chem Soc. 2004; 25:307–310.
32. Ryu ZH, Bentley TW. Evaluation of methylthio and phenylthio group effects in the solvolyses of 2-chloro-2-(methylthio)acetone and 2-chloro-2-(phenylthio)acetophenone using extended Grunwald-Winstein equations. Bull Korean Chem Soc. 2008; 29:2145–2151.
33. Bégué JP, Charpentier-Morize M. α -Acylcarbenium ions. Acc Chem Res. 1980; 13:207–212.
34. Creary X. Carbocationic and related processes in reactions of α -keto mesylates and triflates. Acc Chem Res. 1985; 18:3–8.
35. Creary X. Electronegatively substituted carbocations. Chem Rev. 1991; 91:1625–1678.
36. Grunwald E, Winstein S. The correlation of solvolysis rates. J Am Chem Soc. 1948; 70:846–854.
37. Winstein S, Grunwald E, Jones HW. The correlation of solvolyses rates and the classification of solvolysis reactions into mechanistic categories. J Am Chem Soc. 1951; 73:2700–2707.
38. Kevill, DN. Development and uses of scales of solvent nucleophilicity. In: Charton, M., editor. Advances in Quantitative Structure-Property Relationships. Vol. 1. JAI Press; Greenwich, CT, USA: 1996. p. 81–115.
39. Fainberg AH, Winstein S. Correlation of solvolysis rates. VI. *t*-Butyl and α -phenylethyl bromides. J Am Chem Soc. 1957; 79:1602–1608.
40. Fainberg AH, Winstein S. Correlation of solvolysis rates. VII. Neophyl chloride bromide. J Am Chem Soc. 1957; 79:1608–1612.
41. Kevill DN, Ismail NHJ, D'Souza MJ. Solvolysis of the (*p*-methoxybenzyl)dimethylsulfonium ion. Development uses of a scale to correct for dispersion in Grunwald-Winstein plots. J Org Chem. 1994; 59:6303–6312.
42. Kevill DN, D'Souza MJ. Sixty years of the Grunwald-Winstein equation: development and recent applications. J Chem Res. 2008:61–66.
43. Bentley TW, Schleyer PvR. Medium effects on the rates and mechanisms of solvolytic reactions. Adv Phys Org Chem. 1977; 14:32–40.
44. Bentley TW, Llewellyn G. Y_X scales of solvent ionizing power. Prog Phys Org Chem. 1990; 17:121–158.
45. Kevill DN, Anderson SW. An improved scale of solvent nucleophilicity based on the solvolysis of the *S*-methyldibenzothiophenium Ion. J Org Chem. 1991; 56:1845–1850.
46. Kevill DN, D'Souza MJ. Additional Y_{Cl} values and correlation of the specific rates of solvolysis of *tert*-butyl chloride in terms of N_T and Y_{Cl} scales. J Chem Res Synop. 1993:174–175.
47. Kevill DN, Miller B. Application of the N_T solvent nucleophilicity scale to attack at phosphorus: Solvolyses of N,N,N',N'-prime;-tetramethyldiamidophosphorochloridate. J Org Chem. 2002; 67:7399–7406. [PubMed: 12375970]
48. Kevill DN, Abduljaber MH. Correlation of the rates of solvolysis of cyclopropylcarbinyl and cyclobutyl bromides using the extended Grunwald-Winstein equation. J Org Chem. 2000; 65:2548–2554. [PubMed: 10789470]

49. Kevill DN, D'Souza MJ. Correlation of the rates of solvolysis of benzoyl chloride and derivatives using extended forms of the Grunwald-Winstein equation. *J Phys Org Chem.* 2002; 15:881–888.
50. Kevill DN, D'Souza MJ. Use of the simple and extended Grunwald-Winstein equations in the correlation of the rates of solvolysis of highly hindered tertiary alkyl derivatives. *Cur Org Chem.* 2010; 14:1037–1049.
51. Bentley TW, Garley MS. Correlations and predictions of solvent effects on reactivity: some limitations of multi-parameter equations and comparisons with similarity models based on one solvent parameter. *J Phys Org Chem.* 2006; 19:341–349.
52. Takeuchi K, Ohga Y, Ushino T, Takasuka M. Grunwald-Winstein relations in the solvolyses of highly congested simple secondary and tertiary alkyl systems. Evidence for the Brønsted base-type solvation in the standard 1- and 2- adamantyl systems. *J Org Chem.* 1997; 62:4904–4905.
53. Shorter, J. Correlation analysis of organic reactivity. Research Studies Press; New York: 1982. p. 30p. 46

Figure 1.

Plot of $\log(k/k_0)$ for solvolyses of chloromethyl phenyl sulfide (**1**) at 0.0 °C against Y values (based on specific rates of solvolysis of *tert*-butyl chloride).

Figure 2.

Plot of $\log(k/k_0)$ for solvolyses of chloromethyl *para*-chlorophenyl sulfide (**6**) at 0.0 °C against Y values (based on specific rates of solvolysis of *tert*-butyl chloride).

Figure 3.

Plot of $\log(k/k_0)$ for solvolyses of chloromethyl phenyl sulfide (**1**) at 0.0 °C against $(0.27 N_T + 0.76 Y_{Cl})$. The data points in TFE-ethanol solvents are not included in the correlation; they are added to show the extent of their deviation from the correlation.

Figure 4.

Plot of $\log(k/k_0)$ for solvolyses of chloromethyl *para*-chlorophenyl sulfide (**6**) at 0.0 °C against $(0.22 N_T + 0.67 Y_{Cl})$. The data points in TFE-ethanol solvents are not included in the correlation; they are added to show the extent of their deviation from the correlation.

Scheme 1.

Scheme 2.

Table 1

Specific rates of solvolysis at 0.0 °C of (phenylthio)methyl chloride, **1** (k_1) and (*p*-chlorophenylthio)methyl chloride, **6** (k_6) and the literature values for (N_T) and (Y_{Cl}).

Solvent (%) ^a	$10^6 k_1, s^{-1}$	$10^6 k_6, s^{-1}$	N_T ^b	Y_{Cl} ^c
100% EtOH	0.41 ± 0.01	0.096 ± 0.004 ^d	0.37	-2.52
90% EtOH	3.83 ± 0.07	0.91 ± 0.03	0.16	-0.94
80% EtOH	18.7 ± 0.3 ^e	3.51 ± 0.05	0.00	0.00
70% EtOH	50.9 ± 1.8	10.9 ± 0.4	-0.20	0.78
60% EtOH	108 ± 5	25.7 ± 1.1	-0.38	1.38
40% EtOH	2080 ± 56		-0.74	2.75
100% MeOH	5.75 ± 0.24	1.30 ± 0.05	0.17	-1.17
90% MeOH	18.1 ± 0.3	3.53 ± 0.16	-0.01	-0.18
80% MeOH	70.8 ± 1.8	15.1 ± 0.3	-0.06	0.67
60% MeOH	540 ± 20		-0.54	2.07
80% Acetone	1.34 ± 0.08	0.46 ± 0.01 ^f	-0.37	-0.80
60 % Acetone	27.8 ± 0.6	5.32 ± 0.08	-0.52	1.00
97% TFE	296 ± 11	41.8 ± 0.8	-3.30	2.83
90% TFE	558 ± 17	76.8 ± 1.0	-2.55	2.85
80% TFE	1038 ± 79	128 ± 5	-2.19	2.90
70% TFE		219 ± 8	-1.98	2.96
80T-20E ^g	22.9 ± 0.9	4.52 ± 0.05	-2.21	2.20
60T-40E ^g	7.16 ± 0.13	1.28 ± 0.06	-1.65	1.38
40T-60E ^g	2.29 ± 0.06	0.39 ± 0.01	-0.96	0.36
20T-80E ^g	0.90 ± 0.02	<i>h</i>	-0.09	-0.92
97% HFIP		963 ± 23	-5.26	5.17
90% HFIP	3530 ± 180	615 ± 12	-3.84	4.31
70% HFIP		165 ± 4	-2.94	3.83

^a Aqueous ethanol, methanol, and acetone on a volume-volume basis at 25.0 °C; all fluoroalcohol-containing solvents on a weight-weight basis.

^b From ref [38].

^c From refs [44] and [46].

^d Extrapolated value with use of the Arrhenius equation and values of 3.11 ± 0.08 at 25.0 °C, 10.8 ± 0.2 at 35.0 °C, 32.8 ± 0.5 at 45.0 °C, and 102 ± 2 at 55.0 °C, enthalpy of activation value (ΔH_{298}) of 21.9 ± 0.2 kcal/mol and entropy of activation value (ΔS_{298}) of -10.3 ± 0.7 cal mol⁻¹ K⁻¹.

^e Also a value of 262 ± 8 at 25.0 °C.

^f Extrapolated value with use of the Arrhenius equation and values of 8.17 ± 0.09 at 25.0 °C and 36.7 ± 0.5 at 40.0 °C.

^g T-E represents TFE-ethanol mixtures; the required N_T and Y_{Cl} values for weight-weight compositions obtained by interpolation within the values reported for the pure solvents and for mixtures on a volume-volume basis.

^h A value of 6.24 ± 0.07 at 25.0 °C.

Table 2

Correlations of the specific rates of solvolysis of compounds **1** and **6** using the original (equation 2) and extended (equations 3 and 4) forms of the Grunwald-Winstein equation.^a

Substrate (Temp)	<i>n</i> ^b	<i>ρ</i> ^c	<i>m</i> ^c	<i>h</i> ^c	<i>c</i> ^c	<i>R</i> ^d	<i>F</i> ^e	<i>l/m</i>
1 (0.0°C)	20 ^f		0.60 ± 0.07		-0.29 ± 0.13	0.9045	81	
		0.43 ± 0.14 (0.007)	0.85 ± 0.10		-0.12 ± 0.12	0.9398	64	0.51
		0.35 ± 0.21 (0.111)	0.82 ± 0.13	-0.25 ± 0.48 (0.608)	-0.11 ± 0.12	0.9408	41	
6 (0.0°C)	20 ^f		0.60 ± 0.04		-0.09 ± 0.08	0.9689	215	
		0.27 ± 0.08 (0.005)	0.76 ± 0.06		-0.01 ± 0.07	0.9838	195	0.36
		0.51 ± 0.06	0.87 ± 0.04	0.92 ± 0.17	-0.02 ± 0.04	0.9952	415	
6 (0.0°C)	20 ^f		0.51 ± 0.05		-0.22 ± 0.12	0.9200	99	
		0.32 ± 0.16 (0.058)	0.75 ± 0.12		-0.09 ± 0.13	0.9362	60	0.43
		0.21 ± 0.20 (0.297)	0.70 ± 0.13	-0.42 ± 0.46 (0.372)	-0.06 ± 0.13	0.9395	40	
6 (0.0°C)	17 ^g		0.51 ± 0.03		-0.06 ± 0.07	0.9775	322	
		0.22 ± 0.08 (0.015)	0.67 ± 0.06		0.02 ± 0.07	0.9856	237	0.33
		0.33 ± 0.09 (0.002)	0.71 ± 0.06	0.51 ± 0.23 (0.050)	0.00 ± 0.06	0.9894	201	

^aThe form used is easily deduced from the sensitivity values quoted; probabilities that the term governed by the quoted parameter is not statistically significant in the overall correlation are given (below) in parenthesis when greater than 0.001; *F* values from ref. [41] (some of them obtained by interpolation).

^bNumber of solvents.

^cWith associated standard errors.

^dCorrelation coefficient.

^e*F*-test value.

^fAll available.

^gWithout TFE-EtOH data points.

Table 3

Correlations of the specific rates of solvolysis of compounds **2** through **5**, using equations 2 through 4, revisited.^a

Substrate (Temp)	<i>n</i> ^b	<i>f</i> ^c	<i>m</i> ^c	<i>h</i> ^c	<i>c</i> ^c	<i>R</i> ^d	<i>f</i> ^e	<i>l/m</i>
2 (25.0°C)	45 <i>f</i>		0.45 ± 0.04		-0.21 ± 0.12	0.8452	108	
	45 <i>f</i>	0.58 ± 0.04	0.68 ± 0.02		0.00 ± 0.05	0.9749	401	0.85
	45 <i>g</i>	0.69 ± 0.06	0.74 ± 0.03	0.36 ± 0.15 (0.024)	0.01 ± 0.05	0.9778	299	
	43 <i>h</i>		0.45 ± 0.06		0.06 ± 0.11	0.8816	143	
3 (50.0°C)	43 <i>i</i>	0.33 ± 0.06	0.59 ± 0.04		0.15 ± 0.18	0.9351	139	0.56
	43 <i>j</i>	0.55 ± 0.10	0.72 ± 0.06	0.69 ± 0.26 (0.011)	0.11 ± 0.08	0.9455	110	
	40 <i>k</i>		0.49 ± 0.04		-0.08 ± 0.13	0.8756	125	
	40 <i>k</i>	0.34 ± 0.05	0.65 ± 0.04		-0.01 ± 0.09	0.9426	147	0.52
4 (50.0°C)	40 <i>k</i>	0.60 ± 0.09	0.80 ± 0.06	0.79 ± 0.23 (0.001)	-0.07 ± 0.08	0.9574	132	
	38 <i>l</i>		0.48 ± 0.04		-0.07 ± 0.09	0.8991	152	
	38 <i>l</i>	0.31 ± 0.07	0.63 ± 0.04		0.05 ± 0.08	0.9376	127	0.49
	38 <i>m</i>	0.57 ± 0.07	0.74 ± 0.04	0.99 ± 0.18	0.04 ± 0.06	0.9670	163	
5 (25.0 °C)	39 <i>n</i>		0.46 ± 0.06		-0.35 ± 0.15	0.7741	55	
	39 <i>n</i>	0.88 ± 0.05	0.74 ± 0.03		0.04 ± 0.06	0.9749	345	1.19
	39 <i>g</i>	0.77 ± 0.07	0.69 ± 0.03	-0.42 ± 0.16 (0.012)	0.04 ± 0.05	0.9791	271	

^{a-c}See corresponding footnotes to Table 2.

^fValue of 43 in ref. [32].

^gThis correlation not reported in ref. [32].

^hValue of 42 in ref. [32].

ⁱValue of 41 in ref. [32].

^jValue of 27 in ref. [32].

^kOmitting 100, 90% ethanol and 100% methanol data points.

^lValue of 34 in ref. [32].

$m_{Y_{\text{value of 23 in ref. [32]}}$

$n_{Y_{\text{value of 35 in ref. [32]}}$

Table 4

Test for multicollinearity between the I values of equation 4 and a combination of N_T and Y_{Cl} values: Correlation of I against N_T and Y_{Cl} for the solvents used in studies of the solvolyses of **1** through **6**. ($I = -xN_T - yY_{Cl} - c$)

Substrate	n^a	x^b	y^b	c^b	R^c	F^d
$t\text{-BuCl}$ e	43 f	0.14 ± 0.04		0.14 ± 0.07	0.460	11.0
	43 g		0.03 ± 0.03	-0.07 ± 0.08	0.166	1.2
	43	0.29 ± 0.04	0.14 ± 0.02	0.03 ± 0.05	0.766	28.4
19 e,h	12	0.25 ± 0.07	0.13 ± 0.06	0.03 ± 0.07	0.790	7.5
1	20	0.31 ± 0.07	0.15 ± 0.05	-0.05 ± 0.06	0.739	10.2
	16 i	0.27 ± 0.07	0.12 ± 0.05	-0.01 ± 0.06	0.743	8.0
2	45	0.30 ± 0.04	0.15 ± 0.02	0.01 ± 0.05	0.770	30.6
3	43	0.33 ± 0.03	0.19 ± 0.02	-0.06 ± 0.05	0.846	50.5
4	38	0.26 ± 0.05	0.12 ± 0.03	-0.01 ± 0.05	0.674	14.6
5	39	0.26 ± 0.05	0.13 ± 0.03	0.00 ± 0.06	0.671	14.8
6	20	0.25 ± 0.08	0.10 ± 0.07	-0.06 ± 0.07	0.740	10.3
	17 i	0.22 ± 0.08	0.08 ± 0.06	-0.03 ± 0.07	0.776	10.6

^aNumber of solvents.

^bWith associated standard errors.

^cCorrelation coefficient.

^d F -test value.

^eFrom ref. [46].

^fOmitting the yY_{Cl} term.

^gOmitting the xN_T term.

^hSubstrate **19** in ref. [52]

ⁱOmitting data points for TFE-ethanol (T-E) solvents.

Table 5

Comparison of the I' and m' values obtained indirectly from values in Tables 2 and 3, by substituting $(-0.29 N_T - 0.14 Y_{CI} - 0.03)$ for I values within the equation 4 correlations, with those (I and m values) obtained directly by application of equation 3.

Substrate	n^a	$I' b$	$m' b$	I^c	m^c
1	20	0.42 ± 0.28	0.86 ± 0.17	0.43 ± 0.14	0.85 ± 0.10
	16	0.24 ± 0.11	0.73 ± 0.06	0.27 ± 0.08	0.76 ± 0.06
2	45	0.59 ± 0.07	0.69 ± 0.04	0.58 ± 0.04	0.68 ± 0.02
3	43	0.35 ± 0.13	0.62 ± 0.07	0.33 ± 0.06	0.59 ± 0.04
	40	0.37 ± 0.12	0.69 ± 0.08	0.34 ± 0.05	0.65 ± 0.04
4	38	0.28 ± 0.11	0.60 ± 0.08	0.31 ± 0.07	0.63 ± 0.04
5	39	0.89 ± 0.09	0.75 ± 0.04	0.88 ± 0.05	0.74 ± 0.03
6	20	0.33 ± 0.22	0.76 ± 0.14	0.32 ± 0.16	0.75 ± 0.12
	17	0.18 ± 0.11	0.64 ± 0.07	0.22 ± 0.08	0.67 ± 0.06

^aNumber of solvents.

^bCalculated by eliminating 1, using a combination of the equation 4 and equation 5 correlations; accompanied by standard errors.

^cCalculated directly using equation 3 and with standard errors (from Tables 2 and 3).