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Correlation of the rates of solvolysis of α -bromoisobutyrophenone using both simple and extended forms of the Grunwald-Winstein equation and the application of correlation analysis to related studies

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RESEARCH ARTICLE

ABSTRACT



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A Grunwald-Winstein treatment of the specific rates of solvolysis of α -bromoisobutyrophenone in 100% methanol and in several aqueous ethanol, methanol, acetone, 2,2,2-trifluoroethanol (TFE), and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) mixtures gives a good logarithmic correlation against a linear combination of N_T (solvent nucleophilicity) and Y_{Br} (solvent ionizing power) values. The l and m sensitivity values are compared to those previously reported for α -bromoacetophenone and to those obtained from parallel treatments of literature specific rate values for the solvolyses of several tertiary mesylates containing a C(=O)R group attached at the α -carbon. Kinetic data obtained earlier by Pasto and Sevenair for the solvolyses of the same substrate in 75% aqueous ethanol (by weight) in the presence of silver perchlorate and perchloric acid are analysed using multiple regression analysis.

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1. Introduction

Several years ago, we reported [1] on the application of the Grunwald-Winstein equations [2-6] to the specific rates of solvolysis (k_i) of the primary alpha-bromoketone α -bromoacetophenone ($C_6H_5COCH_2Br$, **1**) (Scheme 1). An S_N2 process had previously been proposed [7] for this process based on a study in three aqueous ethanol solvents leading to a very low m value of 0.20 ± 0.01 when the one-term (simple) Grunwald-Winstein equation [2,3] (Equation 1) was applied to the specific rates (first-order rate coefficients) at three temperatures in the 55-80 °C range, coupled with a very low Hammett ρ value [7] of +0.35 being obtained for solvolyses in 80% ethanol at 70 °C of the parent and five *meta*- and *para*-substituted derivatives.

$$\log(k/k_o)_{RX} = mY_X + c \quad (1)$$

In Equation (1), k and k_o represent the specific rates of solvolysis of a substrate RX in a given solvent and in the

standard solvent (80% ethanol), m is the sensitivity to changes in the solvent ionizing power (Y_X for a leaving group X) and c is a constant (residual) term.

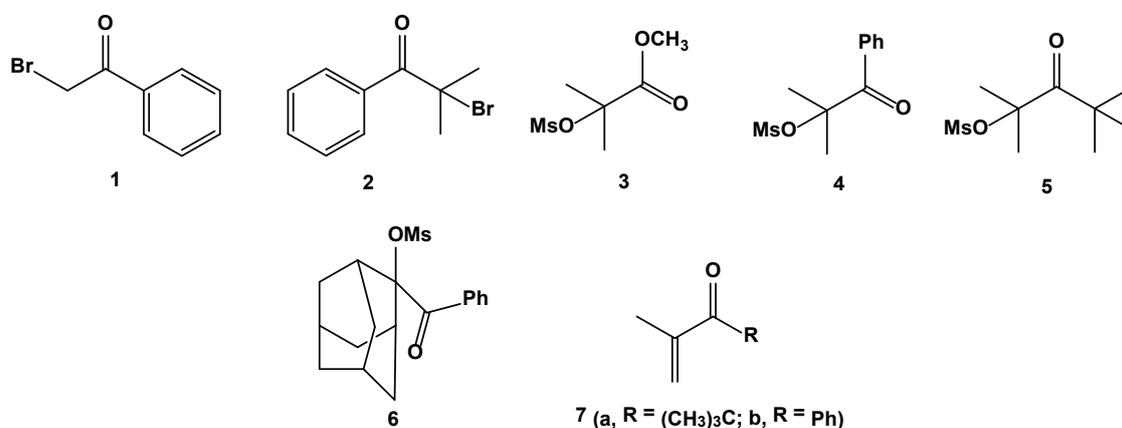
In our determination [1], at 62.5 °C, of the specific rates of solvolysis of **1** in a much wide range of solvent type, Equation (1) was inadequate and the two-term (extended) Grunwald-Winstein equation [8,9] was required (Equation 2), where the additional term involves the sensitivity l to changes in solvent nucleophilicity (N_T). Tables of N_T values are available for a wider variety of pure and binary solvents [6,9].

$$\log(k/k_o)_{RX} = lN_T + mY_X + c \quad (2)$$

It is of interest to investigate the corresponding solvolysis of the tertiary alpha-bromoketone α -bromoisobutyrophenone (2-benzoyl-2-bromopropane, $C_6H_5COC(CH_3)_2Br$, **2**) (Scheme 1) to see whether it follows the same pathway as **1** or whether there is a partial or complete movement towards a unimolecular path-way involving formation of a carbocation, as has

Table 1. Specific rates of solvolysis (k_2) for the solvolysis of α -bromoisobutyrophenone (**2**) at 62.5 °C together with the N_T and Y_{Br} values for the solvents and the ratio of the k_2 values relative to the corresponding values for **1** (k_2/k_1).

Solvent ^a	$10^7 k_2$ (s ⁻¹) ^b	N_T ^c	Y_{Br} ^d	(k_2/k_1) ^e
90% EtOH	1.79±0.05	0.16	-0.84	(0.038) ^f
80% EtOH	3.70±0.08	0.00	0.00	0.090
60% EtOH	12.1±0.6	-0.39	1.26	0.154
40% EtOH	43.5±1.5	-0.74	2.62	0.316
100% MeOH	2.29±0.08	0.17	-1.12	0.082
90% MeOH	6.58±0.13	-0.01	-0.14	^g
80% MeOH	11.7±0.4	-0.06	0.70	0.187
60% MeOH	37.8±0.8	-0.54	2.04	0.332
40% MeOH	106±5	-0.87	3.14	0.632
80% Acetone	0.735±0.017	-0.37	-0.7	0.036
60% Acetone	5.88±0.21	-0.52	1.03	0.104
80% TFE	5.22±0.22	-2.19	2.67	2.03
60% TFE	16.0±0.3	-1.85	2.91	1.55
90% HFIP	2.93±0.14	-3.84	3.91 ^h	^g
70% HFIP	13.8±0.3	-2.94	3.59 ^h	4.35

^a On volume-volume basis at 25.0 °C, except for TFE-H₂O and HFIP-H₂O, which are on a weight-weight basis.^b With associated standard deviation.^c From Ref. [6].^d Unless otherwise stated, from Ref. [5].^e Ratio of the specific rates of solvolysis for **2** and **1** at 62.5 °C (k_1 values from Ref. [1]).^f Using the averaged value for k_1 (see footnote *h* to Table 1 of Ref. [1]).^g The k_1 value is not available.^h From Ref. [20].

Scheme 1

been proposed for the solvolyses of several tertiary ketones related to **2** but with a considerably more effective leaving group (nucleofuge) such as methanesulfonate (mesylate) or trifluoromethanesulfonate (triflate) [10–12]. An alternative approach for generating carbocations, with the charge primarily at the α -carbon, is to use tertiary α -halo ketones in the presence of silver-ion [13], with the complexation of the chlorine, bromine or iodine with the silver-ion providing an alternative route to an effective leaving group [14].

In an earlier study, Pasto and Sevenair [15] found that the solvolyses of **2** proceeded extremely slowly in 75% aqueous ethanol (by weight), with less than 2% reaction after 13 days at 25 °C. We have found, however, that, with the use of sealed ampoules, the specific rates can be obtained for solvolyses in a wide variety of solvents when the temperature is elevated to 62.5 °C.

2. Experimental

The α -bromoisobutyrophenone (Aldrich, 98%, **2**) was used as received. The purifications of acetone [12], ethanol [16], methanol [16], 2,2,2-trifluoroethanol (TFE) [17], and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP)[18] were as previously described. All kinetic runs were performed with 5×10^{-3} M substrate in the appropriate solvent contained within sealed tubes at 62.5 °C, usually with 5 mL aliquots, but with 2 mL aliquots for the runs in HFIP-H₂O mixtures. At appropriate

time intervals, the aliquots were removed and quenched by addition to 20 mL of acetone maintained at solid CO₂-acetone slush temperature and containing resorcinol blue (Lacmoid) as indicator. The acid produced was then determined by titration against a standardized solution of triethylamine in toluene. For the runs in 100% MeOH, loss of HBr by reaction with the solvent, was prevented by the addition of 5.5×10^{-3} M lutidine (2,6-dimethylpyridine, Aldrich 99%) [1].

The determinations of the specific rates (first-order rate coefficients) for solvolysis were as previous described [9]. The regression analyses were carried out using commercially available statistical packages.

3. Results and discussion

The specific rates of solvolysis of α -bromoisobutyrophenone (**2**) in a variety of solvents at 62.5 °C are presented in Table 1. All of the integrated values from the, at least, duplicate runs are averaged and the average values together with the standard deviation are reported. Also presented within the table are the relevant solvent nucleophilicity (N_T)[6] and ionizing power (Y_{Br}) [5,19,20] values used in the simple and multiple regression analyses, together, when both specific rates are available, with the ratio of the specific rate for the solvolysis of **2** relative to that for the corresponding solvolysis of **1** [1]. These ratios vary from 0.038 in 90% ethanol to 4.35 in 70% HFIP, a relatively small range considering the large varia-

Table 2. Correlation of the specific rates of solvolysis for α -bromoacetophenone (**1**) and α -bromoisobutyrophenone (**2**), using equations (1) and (2) and tertiary alpha-ketomesylates (**3** - **6**), using equations (3) and (4).^{a,b}

Compound	n^c	l^d	m^e	$(c + \log k_0)$	r	F
1	15	1.02±0.08	0.44±0.04	0.10±0.06 ^f	0.967	85.8
2	15	0.63±0.06	0.58±0.04	0.11±0.05 ^f	0.970	92.7
3	6	0.45±0.23	0.22±0.13	-7.783	0.632	2.7
	5 ^g		0.64±0.24	-6.946	0.859	4.3
	5 ^g		0.40±0.14	-8.394	0.852	7.9
4	5 ^g	0.37±0.14	0.71±0.14	-7.593	0.968	14.9
	5 ^h		0.58±0.09	-7.395	0.966	41.7
	5 ^h		0.10±0.17	0.65±0.17	-7.184	0.971
5	6	0.04±0.12	0.62±0.05	-6.142	0.990	190
	6		0.66±0.12	-6.073	0.990	73.6
6	5 ⁱ	0.03±0.04	0.96±0.02	-5.096	0.999	2237
	5 ⁱ		0.96±0.04	-5.038	0.999	941

^a The absence of an l value indicates that the correlation is against only Y_{S} values.

^b For compounds **1** and **2**, the Y scale is the Y_{Br} scale and, for compounds **3** through **6** (specific rate data from Ref. [10]), it is the Y_{OTs} scale.

^c Number of solvents.

^d Sensitivity to changes in solvent nucleophilicity, with associated standard error.

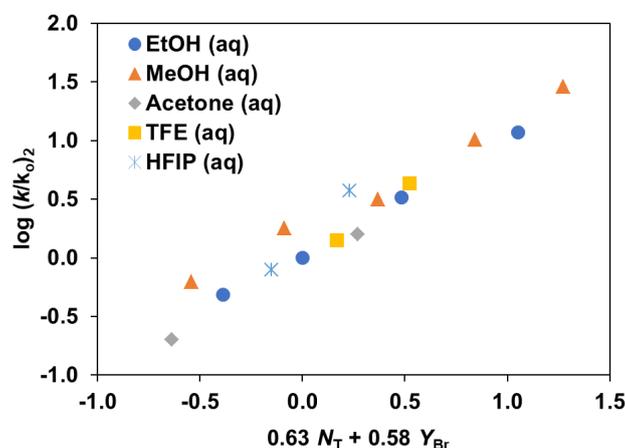
^e Sensitivity to changes in solvent ionizing power, with associated standard error.

^f Since k_0 values are available, these correlations are against $\log(k/k_0)$ values, such that these values are the c values.

^g Omitting the EtOH values.

^h Specific rate not available for solvolysis in EtOH.

ⁱ Specific rate not available for solvolysis in trifluoroacetic acid (TFA).

**Figure 1.** Plot of $\log(k/k_0)$ for the solvolyses of α -bromoisobutyrophenone (**2**) in 15 solvents against $(0.63 N_T + 0.58 Y_{\text{Br}})$; multiple correlation coefficient of 0.970.

tions in both N_T and Y_{Br} values. Since the solvolyses of **1** were considered to show a Grunwald-Winstein equation behavior typical of that to be expected for an S_N2 process over the full range of solvents [1], it is reasonable to assign the variations in the k_2/k_1 ratio to the solvolyses of the tertiary alpha-bromoketone **2** showing considerably increased unimolecular character, which will be especially favored in the fluoroalcohol-containing solvents.

When the extended Grunwald-Winstein equation is applied to the specific rates for the solvolyses of **2** reported in Table 1, values are obtained for l of 0.63 ± 0.06 and for m of 0.58 ± 0.04 , with a small residual c value of 0.11 ± 0.05 and with a correlation coefficient of 0.970 (Table 2). The plot of $\log(k/k_0)$ against $(0.63 N_T + 0.58 Y_{\text{Br}})$ is shown in Figure 1. The corresponding values for the solvolyses of **1**, with the expected higher l value and lower m value being coupled with a correlation coefficient and an F -test value essentially identified to those presently reported for **2** are also reported within Table 2. The extended Grunwald-Winstein equation comparison of **1** with **2** suggests a movement away from an essentially pure S_N2 reaction for **1** on going to the solvolyses of **2**. However, the l -value is somewhat higher and the m -value somewhat lower than one would expect for an S_N1 reaction. In the extreme, the behavior in S_N1 solvolyses is illustrated by studies of the solvolyses of 1-adamantyl and 2-adamantyl derivatives [5], which show a negligible dependence on solvent nucleophilicity and (by definition) an m value of unity.

A typical solvolysis of a non-caged structure tertiary halide, *tert*-butyl chloride, does show a small dependence on solvent nucleophilicity and a mechanism, described as S_N2 (intermediate), has been proposed in order to explain values for l of 0.30 and for m of 0.76 [19]. The mechanism is considered to be bimolecular but with reduced bond formation and more extensive bond breaking than in the traditional S_N2 situation. An extension from 11 solvents [19] to 46 solvents and with use of N_T and Y_{Cl} values led [21] to very similar correlation sensitivities of 0.38 for l and 0.86 for m . It has been suggested that values for l as large as 0.3 can be accommodated by nucleophilic solvation of the incipient carbocation [22] but, thinking in terms of the detailed structure of the activated complex, the structures for the S_N2 (intermediate) pathway and for the S_N1 with a moderate solvation of the developing carbocation can be considered as essentially identical. The values for solvolysis of **2** show appreciably larger l values and lower m values, suggesting a tighter transition state for the solvolyses of **2** than for *t*-butyl chloride.

Also included in Table 2 are values which have been calculated from specific rate values reported for five or six pure solvents by Creary [10]. Using N_T and Y_{OTs} values, we have used both the simple (Equation 1) and extended (Equation 2) forms of the Grunwald-Winstein equation for the solvolyses of four α -ketomesylates, which are designated as structures 3-6, where OMs represents the mesylate group ($-\text{OSO}_2\text{CH}_3$). Although several Y_{OMs} values are available [23], we

have used the Y_{OTS} values for a tosylate leaving group ($-\text{OSO}_2\text{C}_6\text{H}_4\text{-}p\text{-CH}_3$) [5]. It has been suggested [5] that, to avoid a proliferation of Y scales, the solvolyses of sulfonate esters similar to the *p*-toluenesulfonate (such as mesylate [24]) be correlated using Y_{OTS} values.

Creary found that for solvolysis of **5** in ethanol, acetic acid, formic acid, TFE, HFIP, and trifluoroacetic acid, the major product (94-100%) was the alkene **7a**, with 0-6% of the direct substitution product. For the solvolyses of **4**, related to **2** but with the bromine atom replaced by the mesylate group, for solvolysis in acetic acid, formic acid, HFIP, and trifluoroacetic acid, 81-97% of the product was **7b**, with 3-19% being the direct substitution product. With $\text{R}=\text{OCH}_3$ (**3**), 94% of the product was the alkene in HFIP as solvent, but appreciable amounts of both the elimination and substitution product were found in the other solvents. For the mesylate **6**, formation of a double bond at the bridgehead would be strongly disfavored and the substitution product was the major product, accompanied by small amounts of the 1,3-elimination product. For more details of the product formation, the reader is referred to the original report [10] and to a subsequent review article [11].

Creary [10] presented plots of $\log k$ against Y_{OTS} for compounds **3** - **6**, indicating slopes of 0.63 for **4**, 0.66 for **5**, and 1.01 for **6**. For **3**, with the electron withdrawing methoxy group on the carbonyl carbon, a scattered plot was observed, with a particularly large deviation for the specific rate for ethanolysis.

We have analyzed the specific rates of solvolysis of **3** through **6** by simple and multiple regression analyses. While the 5 or 6 data points available for the solvolyses of **3** through **6** are low for a multiple regression analysis, a review [25] has suggested a minimum of five data points for each variable, they do cover a wide range of solvent type and, hence, they represent a favorable variety of N_T and Y_{OTS} combinations. The m and the l plus m values obtained are reported in Table 2.

Since the Creary data for the solvolysis of **3** - **6** do not indicate a value for the specific rate of solvolysis in 80% ethanol [the k_0 value for insertion into Equations (1) and (2)], the equations were rearranged to give, respectively:

$$\log k = mY_x + (c + \log k_0) \quad (3)$$

$$\text{and } \log k = lN_T + mY_x + (c + \log k_0) \quad (4)$$

such that in both instances, with correlation of $\log k$, rather than $\log(k/k_0)$, the residual term is $(c + \log k_0)$ rather than c .

Correlating only against Y_{OTS} values, the m values obtained for **4-6** are similar to those reported by Creary [10] but the detailed correlations allow assessment in terms of standard error, correlation coefficient and F-test value. As expected, solvolysis of **3** gives an m -value with a largest standard error, 0.22 ± 0.13 , and a low, 0.632 correlation coefficient. The two-term correlation is also poor ($r = 0.859$). As observed by Creary, the one-term correlation is considerably improved when the data point for solvolysis in ethanol is omitted. The resultant five-point correlation against Y_{OTS} values leads to an m -value of 0.40 ± 0.14 and a correlation coefficient of 0.852. The goodness-of-fit is further improved by use of the two-term correlation with $l = 0.37 \pm 0.14$, $m = 0.71 \pm 0.14$ and $r = 0.968$, with the correlation coefficient now being only very slightly lower than those obtained for the two-term correlations of the solvolyses of **4** through **6** (Table 2).

Consistent with the proposed unimolecular processes for the solvolyses of **4** - **6**, good correlations are obtained using the one-term Grunwald-Winstein equation ($r = 0.966$ to 0.999) and the two-term equations leads to l values statistically close to zero (0.03 ± 0.04 to 0.10 ± 0.17) and with essentially no change in the r values (0.971 to 0.999).

The analyses of the solvolyses of the mesylates **4-6** reported in Table 2, strongly supports the proposal of essentially classical $S_N1 + E1$ reaction schemes. Further, the reported [10] product studies, showing the principal product to be that formed by an elimination pathway strongly indicates that the reactions are predominantly completed by proton abstraction rather than by collapse to a substitution product. Such reactions require the terminology S_N2 (intermediate) [8] to be modified to $E2$ (intermediate) when elimination strongly dominates or, in general, to $[S_N2 + E2]$ (intermediate).

One further point that should be addressed is the question as to why the replacement of the bromine in substrate **2** by the mesylate group to give substrate **4** leads to very different solvolytic behavior, as is indicated by the entries in Table 2, with the l value falling from 0.63 ± 0.06 for solvolyses of **2** to 0.10 ± 0.17 for solvolyses of **4**. It is well established that the ratio of the specific rate of solvolysis in a given solvent for a sulfonate relative to that of a halide can give useful information regarding mechanism. Initial consideration focused on the extent of charge development on the leaving group at the transition state [24,26-28]. However, it has since been proposed that in relatively crowded tertiary structures, such as with the tertiary alpha-substituted ketones **2** and **4**, the k_{OMs}/k_{Br} ratio (for example) can be raised considerably by steric factors [29] being much greater for the bulkier sulfonate leaving group than for the halide ion leaving group [30,31] especially for unimolecular solvolyses via the carbocation, when a late transition state is involved.

Inspection of the data in Table 2 shows that, with the application of equation (2), the m -values are similar for the bromide and the mesylate. However, these values cannot be directly compared because one is based on the Y_{Br} scale and the other on the Y_{OTS} scale, with the variations in Y_{Br} values being approximately 23% greater [5]. These values are coupled with l values for the solvolyses of essentially zero for **4** and of 0.63 ± 0.06 for **2**. This suggests that steric acceleration being larger for the bulkier mesylate favors this substrate reacting, as proposed earlier by Creary [10], by an essentially unimolecular ionization process ($E1$ plus S_N1) but that this pathway is considerably less favored for the presently reported corresponding bromide **2**, such that the dominant pathway becomes the $[S_N2 + E2]$ (intermediate) pathway. Supporting the belief that this a reasonable proposal to explain the differences in behavior, values of the k_{OMs}/k_{Br} ratio as large as 10^4 in 80% ethanol and 10^5 in acetic acid have been observed [30,31] for the unimolecular solvolyses of the tertiary 1-adamantyl derivatives at 25 °C. Such values could lead to the unimolecular pathway operating for the mesylate **4** to become so much slower for the corresponding bromide **2** that an alternative mechanism involving nucleophilic assistance from the solvent becomes the favored pathway.

A comparison of the specific rates under identical conditions for compounds **2** and **4** would allow the determination of the k_{OMs}/k_{Br} ratio [24]. Values close to unity would indicate considerable S_N2 character and values considerably larger than unity would suggest considerable S_N1 character. Using the Arrhenius equation, one can calculate from the Creary data [10] a specific rate for the mesylate in 100% HFIP at 62.5 °C of $1.87 \times 10^{-4} \text{ s}^{-1}$ and using the extended Grunwald-Winstein equation, with extrapolated values for 100% HFIP as solvent of -6.08 for N_T and 5.20 for Y_{Br} , one can calculate for the bromide in 100% HFIP at 62.5 °C a specific rate of $7.32 \times 10^{-8} \text{ s}^{-1}$. The k_{OMs}/k_{Br} ratio of 2.55×10^3 is consistent with appreciable unimolecular character at the transition state for the solvolysis of the mesylate.

Another interesting comparison is of compound **6** with the corresponding compound with the benzoyl group replaced by a methyl group, which has been previously studied [18] in several solvolyses, including one in 97% TFE at 25.2 °C where a specific rate of solvolysis of $2.31 \times 10^{-2} \text{ s}^{-1}$ was obtained. This

can be compared with the value determined [10] for **6** in 100% TFE at 25.0 °C of $4.33 \times 10^{-4} \text{ s}^{-1}$. The temperatures show only a small difference and the Y_{OTs} values of 1.77 for 100% TFE and 1.83 for 97% TFE [5] are also very similar. The k_{CH_3}/k_{COPh} ratio of 53 is quite low considering the expected strong electron-withdrawing influence of a benzoyl group. It is possible that the larger benzoyl group could lead to an appreciable steric acceleration of the ionization process, counteracting to a large degree the electronic influences [29].

In reactions requiring the removal of a chlorine, bromine, or iodine attached to the carbon adjacent to a carbonyl carbon, silver-ion is frequently added to promote the removal of the halide ion [13,15,32,33]. In an earlier kinetic study of the solvolysis of **2** in 75% aqueous ethanol (by weight), Pasto and Sevenair [15] found that a very slow reaction at 25.0 °C could be appreciably accelerated by the addition of silver perchlorate and the reaction could then be further accelerated by the addition of perchloric acid.

The rate could formally be expressed in terms of an apparent second-order rate coefficient (Equation (5))

$$\text{Rate} = k_{app} [\text{RBr}][\text{Ag}^+] \quad (5)$$

It was proposed that the rate could best be described by three contributions to the rate equation, with one first-order in both $[\text{Ag}^+]$ and $[\text{RBr}]$ and with the other two terms also having a contribution from $[\text{H}^+]$ or from a second $[\text{Ag}^+]$, as in Equation (6).

$$\text{Rate} = k_{\pi}[\text{Ag}^+][\text{RBr}] + k_{\text{H}}[\text{Ag}^+][\text{RBr}][\text{H}^+] + k_{\text{Ag}}[\text{Ag}^+]^2[\text{RBr}] \quad (6)$$

Combining Equations (5) and (6) we arrive at Equation (7).

$$k_{app} = k_{\pi} + k_{\text{H}}[\text{H}^+] + k_{\text{Ag}}[\text{Ag}^+] \quad (7)$$

Using graphical methods, the authors were able to extract from their rate data values for k_{π} of $0.052 \text{ l mol}^{-1} \text{ min}^{-1}$, for k_{H} of $0.062 \text{ l}^2 \text{ mol}^{-2} \text{ min}^{-1}$ (units erroneously reported [15] as $\text{l mol}^{-1} \text{ min}^{-1}$), and two different graphical methods gave values of $1.81 \text{ l}^2 \text{ mol}^{-2} \text{ min}^{-1}$ or $2.24 \text{ l}^2 \text{ mol}^{-2} \text{ min}^{-1}$ for k_{Ag} .

With the use of statistical packages for multiple regression analysis, which have since become readily available, we have reanalyzed in terms of Equation (7) the twelve sets of rate coefficients and concentrations to arrive at a rigorously derived set of values of $0.037 \pm 0.010 \text{ l mol}^{-1} \text{ min}^{-1}$ for k_{π} , $0.073 \pm 0.016 \text{ l}^2 \text{ mol}^{-2} \text{ min}^{-1}$ for k_{H} , and $2.26 \pm 0.22 \text{ l}^2 \text{ mol}^{-2} \text{ min}^{-1}$ for k_{Ag} , with a multiple correlation coefficient of 0.971. The values obtained earlier by Pasto and Sevenair are in reasonable agreement with the presently reported values and the acceptable correlation coefficient indicates that the combination of these three terms within the overall kinetic equation (Equation 6) gives a reasonable reproduction of the experimental [15] specific rates.

4. Conclusions

The extended Grunwald-Winstein equation [3-6], which has been found to be very useful in its application to the specific rates of solvolysis of a wide variety of substrates, such as phosphorus compounds [34], silicon compounds [35], acid chlorides [36], chloroformate esters [37], chlorothioformate esters [38], and heterocyclic compounds [39], is here applied to the solvolyses of tertiary alpha-substituted ketones, some of which have, contrary to earlier opinions summarized elsewhere [12], been found to be capable of forming carbocations with the charge formally adjacent to the carbonyl group under solvolytic conditions [10-12].

The correlation of the specific rates of solvolysis of the tertiary α -bromoisobutyrophenone (**2**) gave l and m sensitivity

values (Table 2) very different to those previously reported [1] for the solvolyses of the primary α -bromoacetophenone (**1**), which had given typical values for solvolysis of a primary substrate. The values were also very different to those for the corresponding tertiary mesylate **4** which gave values indicating a unimolecular (S_N1+E1) process. Further, the mesylate **4** reacted considerably faster than the bromide **2**, suggesting that this represents a further example of, for crowded tertiary structures, the relief of steric strain in an ionization process giving enhanced $k_{\text{OMs}}/k_{\text{Br}}$ leaving-group effects [31,32]. Indeed, the wide differences in l and m values suggest that the bromide a process with appreciably nucleophilic assistance from the solvent is favored over a considerably slower unassisted ionization pathway.

The scheme proposed by Pasto and Sevenair [15] for the silver-ion assisted solvolysis of **2** in 75% aqueous ethanol (by weight) involving three terms with just silver ion assistance, assistance from both silver ion and a proton, and assistance by one silver ion assisted by a second one, has been shown to be a reasonable one by the application of multiple regression analysis.

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