

A Study of Solvolyses of *ortho*- and *para* Carboxybenzyl Bromides Using the Extended Grunwald-Winstein Equation

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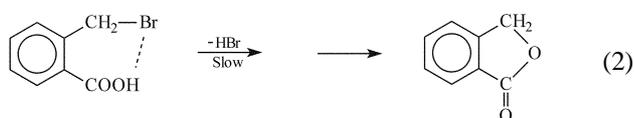
Solvolyses of benzyl halides have been studied extensively.¹ However, the reaction mechanism of the isomeric carboxybenzyl halides is not well established. Accordingly, a study of the mechanism of the isomeric carboxybenzyl bromides under solvolytic conditions is one of the subject of continuing interest.

Recently, the extended Grunwald-Winstein equation [eqn. (1)] has been applied to a very useful mechanistic tool for solvolysis reactions.²⁻⁵

$$\log(k/k_o) = lN_T + mY_X + c \quad (1)$$

In equation (1), k and k_o are the specific rates of solvolysis in a given solvent and in the standard solvent (80% ethanol), respectively; l is the sensitivity towards changes in solvent nucleophilicity (N_T);⁶ m is the sensitivity towards changes in solvent ionizing power (Y_X);^{3,7} c is a residual term. The equation is a very useful indicator of the extent of nucleophilic participation by the solvent, as expressed in the parameter, l , which, in turn, is directly related to whether a substitution reaction is unimolecular (S_N1) or bimolecular (S_N2). Also, there is a general tendency for a decrease in m values as l values increase.

For *para* carboxybenzyl bromide (*p*-isomer, I), it is to be expected that the electron withdrawing carboxylic acid group will favor S_N2 reaction, which is already known to be the favored pathway for benzyl bromide in the absence of substituents. Applying the extended Grunwald-Winstein equation [eqn. (1)] using N_T and Y_{Br} values, one would expect an l value approaching unity and an m value in the 0.4 to 0.5 range.⁸ There are indications that, in 80% aqueous dioxane as solvent, the *ortho* carboxybenzyl bromide (*o*-isomer, II) reacts about 80 times faster than the *p*-isomer(I), which suggests the possibility of an intramolecular assistance to the substitution process.⁹ If intramolecular assistance operates, it would be expected to operate as in eqn. (2):



If the mechanism operates according to eqn. (2), or some closely related variant, one would expect the influence of ionizing power (ion-pair-like species). If intramolecular

assistance should not operate for solvolyses of *o*-isomer(II), one would predict an l -value close to that operating for solvolyses of *p*-isomer(I), reflecting extensive nucleophilic assistance from a solvent molecule.

In the present study, we report concerning the application of the extended Grunwald-Winstein equation [eqn. (1)] to the solvolyses of *para* and *ortho* carboxybenzyl bromides in wide variety of hydroxylic solvents. This is the first time that this eqn. (1) has been used as a tool in a study of possible intramolecular nucleophilic participation during solvolyses.

Results and Discussion

The specific rate constants, k_{obs} , of solvolyses for *p*-isomer (I) and *o*-isomer(II), at 25.0 °C or 45.0 °C, in binary solvent mixtures are reported in Table 1, together with the N_T and Y_{Br} values. The solvents consisted of ethanol (EtOH), binary mixtures of water with ethanol, methanol (MeOH), 2,2,2-trifluoroethanol (TFE) and acetone. As shown in Table 1, the k_{obs} for reaction of the *o*-isomer(II) in all the solvents is solvolyzed much more rapidly than its *p*-isomer(I). The high reactivity of *o*-isomer(II) reverses the usual order of reactivity among isomers of this type. Andrews and co-workers⁹ have demonstrated that the high reactivity of the *o*-isomer(II) is rationalized in terms of internal participation by a neighboring carboxylic acid group (*o*-COOH). Such participation is not possible for *p*-isomer(I) because of unfavorable molecular geometry.

An analysis in terms of the simple Grunwald-Winstein equation [eqn. (1) without the lN_T term] to the specific rates of solvolysis of *p*-isomer(I) (from Table 1) leads to an extremely poor correlation with value of 0.170 for the correlation coefficient(r). Again, analysis of the data using the extended Grunwald-Winstein equation [eqn. (1)] leads to a good linear correlation with values of 1.24 ± 0.09 for l , 0.59 ± 0.05 for m , 0.10 ± 0.05 for c , 0.973 for the correlation coefficient, and 107 for the F-test value (Figure 1). These l and m values (or l/m ratio) are similar to those obtained to reflect the bimolecular pathway within the analyses of the solvolyses of *p*-nitrobenzyl *p*-toluenesulfonates¹⁰ and haloformates.^{5(c)}

Application of the equation (1) to solvolyses of *o*-isomer(II) leads to a poor correlation with values of 0.90 ± 0.14 for l , 0.49 ± 0.10 for m , 0.007 ± 0.14 for c , 0.933 for the

Table 1. Specific rate constants (k_{obs}) for the solvolyses of *p*-carboxybenzyl bromide^a(I) (at 45.0 °C) and *o*-carboxybenzyl bromide^b(II) (at 25.0 °C) in binary hydroxylic solvents

Solvent ^c	$10^5 k_{obs} (\text{sec}^{-1})_p$	$10^4 k_{obs} (\text{sec}^{-1})_o$	N_T^d	Y_{Br}^e
100EtOH ^f	0.188 ± 0.003	3.04 ± 0.1	0.37	-2.40
90EtOH	0.455 ± 0.02	4.92 ± 0.06	0.16	-0.84
80EtOH ^f	0.752 ± 0.03 ^h	15.1 ± 0.2 ⁱ	0.00	0.00
70EtOH	1.09 ± 0.04	27.1 ± 0.2	-0.20	0.68
50EtOH ^f	2.45 ± 0.08	-	-0.58	1.88
90MeOH	0.853 ± 0.02	3.93 ± 0.2	-0.01	-0.14
80MeOH	1.46 ± 0.01	10.7 ± 0.3	-0.06	0.70
60MeOH	3.76 ± 0.09	47.7 ± 0.4	-0.54	2.04
50MeOH	5.21 ± 0.2	-	-0.75	2.61
80Acetone	0.127 ± 0.009	4.25 ± 0.1	-0.37	-0.70
60Acetone	0.606 ± 0.02	25.3 ± 0.2	-0.52	1.03
50Acetone	1.06 ± 0.08	-	-0.7	1.74
97TFE ^g	-	0.275 ± 0.03	-3.3	2.53
90TFE ^g	0.0127 ± 0.002	0.385 ± 0.02	-2.55	2.58
70TFE ^g	0.210 ± 0.01 ⁱ	11.3 ± 0.3 ^k	-1.98	2.79
50TFE ^g	0.781 ± 0.03	-	-1.73	3.04

^aSubstrate concentration of ca. 5.40×10^{-4} M. ^bSubstrate concentration of ca. 5.00×10^{-4} M. ^cVolume/volume basis at 25.0 °C, except for TFE-H₂O mixtures, which are on a weight/weight basis. ^dBased on the specific rates of solvolysis of the S-methyldibenzothiophenium ion, from ref. 6 and ref. 8. ^e Y_{Br} values of 1-adamantyl bromide from ref. 3 and ref. 7. ^fPercentage of products for the solvolysis of these substrates: *p*-isomer, 100%EtOH; *p*-carboxybenzyl ethyl ether (retention time: 44.86 min. 100%), 80%EtOH; *p*-carboxybenzyl ethyl ether (retention time: 44.86 min. 4.70%), *p*-carboxybenzyl alcohol (retention time: 71.24 min. 95.3%), *o*-isomer: 100%EtOH; *o*-carboxybenzyl ethyl ether (retention time: 41.61 min. 8.52%), phthalide (retention time: 49.11 min. 91.5%), 80%EtOH; *o*-carboxybenzyl ethyl ether (retention time: 41.61 min), phthalide (retention time: 49.11 min. 97.7%), 50%EtOH; phthalide (retention time: 49.11 min. 100%). ^gTFE is 2,2,2-trifluoroethanol. ^hAt 55 °C, 68 °C, and 73 °C, values of $1.87 \times 10^{-5} \text{ sec}^{-1}$, $5.76 \times 10^{-5} \text{ sec}^{-1}$, and $8.97 \times 10^{-5} \text{ sec}^{-1}$, respectively, were obtained. $\Delta H^\ddagger = 19.6 \text{ kcal}\cdot\text{mol}^{-1}$ and $\Delta S^\ddagger = -20.7 \text{ cal}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$. ⁱAt 55 °C, 68 °C, and 73 °C, values of $0.602 \times 10^{-5} \text{ sec}^{-1}$, $1.09 \times 10^{-5} \text{ sec}^{-1}$, and $1.43 \times 10^{-5} \text{ sec}^{-1}$, respectively, were obtained. $\Delta H^\ddagger = 13.8 \text{ kcal}\cdot\text{mol}^{-1}$ and $\Delta S^\ddagger = -41.3 \text{ cal}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$. ^jAt 35 °C and 45 °C, values of $30.6 \times 10^{-4} \text{ sec}^{-1}$ and $44.2 \times 10^{-4} \text{ sec}^{-1}$ were obtained. $\Delta H^\ddagger = 9.49 \text{ kcal}\cdot\text{mol}^{-1}$ and $\Delta S^\ddagger = -39.6 \text{ cal}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$. ^kValue of $33.0 \times 10^{-4} \text{ sec}^{-1}$ at 45 °C was obtained. $\Delta H^\ddagger = 9.52 \text{ kcal}\cdot\text{mol}^{-1}$ and $\Delta S^\ddagger = -40.1 \text{ cal}\cdot\text{K}^{-1}\cdot\text{mol}^{-1}$.

correlation coefficient, and 20 for the F-test value. Accordingly, we applied the use of a new term, aromatic ring parameter *I*, together with N_T and Y_X in the extended Grunwald-Winstein equation to examine the solvolytic behavior of benzylic substrates.¹¹ To study the nucleophilic solvent participation in benzylic solvolysis, a three-term equation [eqn. (3)] should be applied.

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

h is the sensitivity to changes in aromatic ring parameter values. Application of eqn. (3) shows a good linear correlation [$\log(k/k_o) = 0.73N_T + 0.41Y_{Br} - 0.78I$, $r = 0.952$] for the specific rates of solvolysis of *o*-isomer(II) in a variety of binary solvent mixtures. This result can also be predicted that the delocalization of the developing positive charge on the methylene (α -carbon) of the *o*-isomer(II) will be larger than in the case of the *p*-isomer(I). Accordingly, it is shown that the solvolysis of *o*-isomer(II) in the transition state can

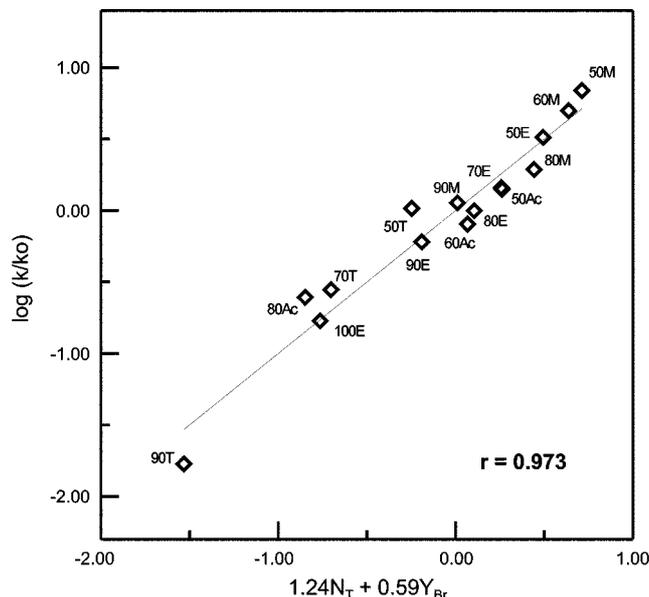


Figure 1. Plot of $\log(k/k_o)$ for solvolysis of *p*-carboxybenzyl bromide against $(1.24N_T + 0.59Y_{Br})$ in binary solvents.

be affected not only by the structure of the R-group (RX) and the nature of the leaving group but also by the effects involving changes in solvation of the aromatic ring (the *hI* term).

The values of the enthalpies and entropies of activation for the solvolyses of *p*-isomer(I) and *o*-isomer(II) in 80% aqueous ethanol and 70% aqueous 2,2,2-trifluoroethanol are reported in the footnotes to Table 1. These values are consistent with the finding by Andrews,⁹ Priebat¹² and our previous study^{13,14}, with the very negative entropies of activation, and with the bimolecular nature of the proposed rate-determining step. From the data of ΔH^\ddagger for *p*-isomer(I) and *o*-isomer(II), it appears the energy barrier for reaction of *o*-isomer(II) is significantly less than *p*-isomer(I), and this is presumed to reflect the contribution of the *o*-carboxylic acid group.

For reactions of *p*-isomer(I) and *o*-isomer(II), product studies were carried out in ethanol, 80% and 50% aqueous ethanol with the analyses employing gas chromatography and those results are reported in the footnotes to Table 1. The fact that the product obtained from the *o*-isomer(II) was identified as phthalide supports the possibility of an intramolecular participation due to assistance of the carboxyl group. From *p*-isomer(I), *p*-carboxylbenzyl ethyl ether and alcohol were obtained.

In conclusion, the specific rates of solvolyses of *p*-isomer(I) and *o*-isomer(II) are very well correlated by the equation (1) and (3) over a wide range of solvents, respectively. The solvolysis of *p*-isomer(I) ($l = 1.24$, $m = 0.59$, $l/m = 2.1$), where bond making (*l*-value) is more progressed than bond breaking (*m*-value), is indicated to proceed by the bimolecular pathway (associated S_N2), reflecting nucleophilic assistance from a solvent molecule. The bond making (*l*-value) of *o*-isomer(II) ($l/m = 1.8$) is less progressed than *p*-isomer(I) ($l/m = 2.1$). Therefore, the solvolysis of *o*-isomer(II) is

considered to reflect the operation of both the intramolecular assistance of *o*-carboxylic acid group (ion-pair like species) and the nucleophilic assistance from a solvent molecule.

Experimental Section

o-Carboxybenzyl bromide (*o*-HOOC₆H₄CH₂Br) was prepared from the corresponding *o*-toluic acid (Aldrich, *o*-HOOC₆H₄CH₃) according to previously published procedures.¹⁵ *p*-Carboxybenzyl bromide (Aldrich, *p*-HOOC₆H₄CH₂Br) was recrystallized from benzene (Aldrich) before using. Solvents were purified and the kinetic runs carried out as previously described.¹³ All runs were performed at least in duplicate. The *l*, *m* and *h* values were calculated using the multiple regression analyses. The products were directly analyzed by gas chromatography as previously described.^{5(b)}

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