Solvolysis of 2-Chloro-2(3,4disubstituted) Phenylpropanes: Validity of Hammett–Brown σ^+ Constants in Assessing Additive Effects of Substituents

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ABSTRACT: The objective of this study is to test the suitability of the extended Hammett–Brown equation, log $(k_{XX}/k_{HH}) = \rho^+ \Sigma \sigma^+$, in depicting satisfactorily additive effects of electronegative atom-bearing substituents, which are known to possess diverse and multicomponent influences on the side chain reactions of polysubstituted benzenes. The equation has been used to correlate, for the first time, the additive effect of substituents in the specific rates of solvolysis of 2-chloro-2-phenylpropanes (3b-3f) having 3-F,4-Me, 3-Br,4-Me, 3-I,4-Me, 3-Me,4-Me, or 3-MeO,4-Me substituents. The rates were determined titrimetrically at 288, 298, and 308 K using 90% aqueous acetone as solvent. Measured additive effects of these substituents on the solvolysis rate and activation parameters of the parent cumyl chloride (2-chloro-2phenylpropane) are found to be well correlated using the equation given above. Plots of log (k_{XX}/k_{HH}) of **3b–3f** together with mainly di-, but also tri- and mono-substituted cumyl chlorides from previous studies against $\Sigma\sigma^+$ give a linear correlation coefficient of 0.990 as a measure of the validity of the equation to depict such systems. The halogen substituents' extent of conformity with additivity reflected in their relative (k_{obsd}/k_{calcd}) rate ratios is found to correlate with the steric size of substituents. Plots of rate ratios against Taft's steric factor of each halogen give a linear correlation coefficient of 0.994 for the 3-halo substituents. The 3,4-dimethyl substituents' relative rate ratio of 1.03 shows excellent additivity, whereas the

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3-methoxy-4-methyl ratio of 1.43 shows the methoxy group to be far less deactivating than predicted. Similar trends were found for the free energy of activation $(\Delta G^{\ddagger} - \Delta G_{0}^{\ddagger})$ differences, which correlated linearly with a coefficient of 0.983 with Taft's steric factor of halogen atoms. © 2012 Wiley Periodicals, Inc. Int J Chem Kinet 44: 514–523, 2012

INTRODUCTION

The Hammett equation [1]:

$$\log(k_{\rm X}/k_{\rm H}) = \rho\sigma \tag{1}$$

is considered to be one of the most important structureactivity relationships in organic chemistry. The equation was successful in describing specific rate constants of substituted $(k_{\rm X})$ and unsubstituted $(k_{\rm H})$ benzenoid systems in relation to a dual constant ($\rho\sigma$). σ is a substituent constant varying with the type of substituent (X), whereas ρ is a constant related to the particular type of reaction involved. By applying the Hammett equation to the solvolyses of substituted cumyl chlorides, Brown and coworkers [2] found that the equation is obeyed when ring substituents are meta to the reaction center. The equation, however, fails to describe satisfactorily solvolyses of para-substituted benzylic system in which $\pi\pi$ delocalization of the cationic charge into the benzene ring takes place. To be able to describe such systems satisfactorily, Brown used solvolysis rates of meta-substituted cumyl chlorides in 90% aqueous acetone-10% water (v/v) to derive a new set of substituent constants (σ^+) known as the Hammett– Brown equation [2]:

$$\log(k_{\rm X}/k_{\rm H}) = \rho^+ \sigma^+ \tag{2}$$

where σ^+ is the substituent's (X) contribution to the rate constant $k_{\rm X}$ and its ability to stabilize the charged carbocation intermediate. Negative values of the substituent constant σ^+ indicate rate enhancement, whereas positive values indicate deactivation by the substituent. The reaction constant ρ^+ gives a measure of the sensitivity of the reaction to perturbation by factors such as those pertaining to the substituent and the solvent; $k_{\rm H}$ is the rate constant of the parent (unsubstituted) cumyl chloride (3a). The Hammett-Brown equation proved to be useful in correlating substituents' effects in various substituted benzenes [3-5] irrespective of the substituent position in the ring (meta or para), the type of carbocation formed, or the solvent used [6]. In systems where strong deactivating groups are attached to the carbocation intermediate, such as the CF₃ group, strong departures from the Hammett-Brown linear plots take place. Such systems are expected to have an enhanced resonance demand and are better correlated with Yukawa–Tsuno equation [7]:

$$\log(k_{\rm X}/k_{\rm H}) = \rho(\sigma^+ r \Delta_{\sigma R}^+) \tag{3}$$

where *r* is a parameter characteristic of a given reaction and describes the resonance demand of the transition state, and $r\Delta_{\sigma R}^+$ is a substituent constant describing resonance capacity of the substituent and is given by $\sigma^+ - \sigma$. Correlation analyses of several solvolytic rate data of cumyl derivatives using both single parameter (the Hammett–Brown equation) and dual parameter (the Yukawa–Tsuno equation) have been made [8–11]. The Hammett–Brown scale is expected to prevail in solvolytic systems generating ordinary and relatively stable benzylic carbocations, whereas the Yukawa– Tsuno scale prevails in systems having *r* values larger or smaller than unity.

Extension of the Hammett equation to polysubstituted benzenes was shown to be feasible by Jaffé [12]. Much later, following the work of Jaffé [12] and the work of others [13], Benson [14] summarized the assumptions of the additivity principle. The principle predicts that the contribution of each substituent on the benzene ring is to be constant and simply additive. The Hammett–Brown equation hence takes the following extended form:

$$\log(k_{\rm XY}/k_{\rm HH}) = \rho^+ \Sigma \sigma^+ \tag{4}$$

where $\Sigma \sigma^+$ is the sum of the contributions of all substituents present. Apart from their classical area of application in the structure–reactivity relationship [4], the Hammett–Brown parameters or the Hammett equation on which they are based have recently found applications in various fields such as environmental toxicology, drug metabolism [15], chromatography [16], oxidation studies [17], mechanistic studies [18], mass spectrometry [19] to name but a few. Some earlier studies based on the original Hammett equation found disubstitution effects of various substituted benzoic acids to be additive [20]. Additive effects were observed in various other systems such as polyfluorinated tryptophans [21] and the electrostatic potentials of substituted benzoic acids [22].

Successful treatments of the rates of reactions of polymethylbenzenes systems were reported for mercuration, bromination, chlorination, and protodesilylation and to a lesser extent in nitration reactions [23]. On the other hand, substituents with electronegative atoms are known to possess diverse and multicomponent influences on the side chain reactions of polysubstituted benzenes [24] and as such present a serious challenge to the capabilities of linear free energy relationship and to the additivity principle on which it is based. The objective of this work was thus to test the suitability of Hammett-Brown parameters for predicting additive behavior of such type of substituents. This work therefore undertook to investigate the behavior of the electronegative atom-bearing halogeno and methoxy substituents in disubstituted cumyl chlorides under the same conditions used by Brown for deriving $\rho^+\sigma^+$ values. A fewer studies to the author's knowledge dealt with these effects of disubstitution [4,25] in such systems studied by Brown. The compounds chosen to be investigated were, namely the halogeno 3-flouro-4-methyl- (3b), 3-bromo-4-methyl- (3c), and 3-iodo-4-methyl-(3d) derivatives of cumyl chloride (2chloro-2-phenylpropane) together with the 3-methoxy-4-methyl- (3e) and 3,4-dimethyl- (3f) derivatives. The latter was chosen by a way of comparison, as previous studies indicated close adherence to additivity predictions [26]. The observed rate constants of these disubstituted cumyl chlorides are then compared with the calculated rate constants obtained from the modified Hammett-Brown equation (4) as a measure of the additivity of substituent effects. Activation energy (E_a) is obtained utilizing the Arrhenius equation:

$$k = Ae^{-E_{\rm a}/RT} \tag{5}$$

and the observed and predicted differences in the free energy of activation $(\Delta G^{\ddagger} - \Delta G_0^{\ddagger})$ can be obtained from the following equation:

$$\left(\Delta G^{\ddagger} - \Delta G_{0}^{\ddagger}\right) = -2.303 \ RT \log_{10} k/k_{o}$$
 (6)

EXPERIMENTAL

General Remark, Synthesis of Alcohols, and Rate Measurement

Boiling points and melting points were uncorrected. Starting materials and solvents were of analytical grade. Anhydrous solvents were obtained by prior distillation over a suitable drying agent and kept over molecular sieves (type 4). Et₂O was sodium-dried grade. Acetone (used for preparation of stock solutions of substrates) was purified by refluxing it first over KMnO₄ and then was distilled, dried (CaSO₄), and fractionated. 3-Substituted *p*-toluic acids, alkyl halides, and acetophenone were purchased and used as received. IR spectra were recorded using a Shimadzu IR-435 spectrophotometer on KBr windows.

Compounds **1a–1f** and **2a–2f** were synthesized according to standard procedures [27] and had elemental analysis values and spectral data consistent with their structures (Table I).

The parent alcohol (**2a**) was prepared in 80% yield by the reaction between acetone and phenylmagnesium bromide [28,30]. The alcohols **2b–2e** (Table I) were prepared by reacting the corresponding metasubstituted methyl *p*-toluate esters (**1b–1e**) with 2 molar equiv of methylmagnesium bromide or iodide [29]. The esters were prepared by refluxing the corresponding acids in MeOH/H⁺. The alcohol **2f** was prepared by reacting 4-bromomagnesium-*o*-xylene with acetone.

The stock solvent for rate measurements was prepared by mixing pure dry acetone (9 volumes) and boiled, redistilled water (1 volume); this was adjusted by adding small amounts of acetone or water to give a value of $k = (12.3 \pm 0.1) \times 10^{-5} \text{ s}^{-1}$ (0.999 correlation coefficient) at 298 K for 2-chloro-2-phenylpropane (3a) [30]. After adjustment, the solvent composition was calculated to be 90.4:9.6% (v/v) acetone to water. The rates were measured titrametrically following the procedure of Brown et al. [30]. All reactions were carried out under pseudo-first-order conditions. Rates were determined at three different temperatures for each chloride, and the activation parameters were evaluated. Temperature fluctuations were less than ± 0.05 K for the temperature range 288–308 K and less than ± 0.1 K for lower temperatures. Plots of log rate constants against 1/T gave a straight line with a linear correlation. The activation parameters were evaluated from the slopes of these lines. Data obtained were from duplicate runs within an experimental error of $\pm 3.3\%$.

Synthesis of alcohol and its chloride. The alcohols (2) were synthesized by the Grignard reaction of MeMgBr or MeMgI with the ester of benzoic acid (1) according to Scheme 1. The alcohol **2f** was prepared by the action of 3,4-dimethylphenylmagnesium bromide upon Me₂CO. Physical data and elemental analysis values are given in Table I. The chlorides R^1R^2 -C₆H₄·CMe₂Cl (**3**) were prepared from the alcohols by saturation with HCl gas in pentane. The *m*-methoxy chloride was highly unstable and was prepared at -20°C in CH₂Cl₂. Purification of the chlorides was not attempted and they were used directly in rate measurements.

Solvolysis rate. Following the procedure by Brown et al. [31], the specific rates of solvolysis of the

Compound	Melting Point (°C)	Boiling Point (°C/mmHg (Lit.))s; IR	Yield (%)	Analysis C, H, and Halogen
2a		67–68/0.2(93/11) [30]; IR (liquid film, cm ⁻¹): 3345 v(O–H); 2975 v(C–H); 1370–1365 v(–CMe2def)	80	-
1b	_	100/10; IR (liquid film, cm ⁻¹); 2975–2950 v(C–H); 1730–1715 v(C=O); 1275, 1125 v(C–O); 1110–1000 v(C–F)	75	-
2b	_	55/0.05 [27]; IR (liquid film, cm ⁻¹): 3400 v(O-H); 2975–2950 v(C-H); 1370–1365 v(-CMe ₂ def)	70	Calcd for C ₁₀ H ₁₃ OF (Found): C: 71.44 (71.14); H:7.74 (7.91)
1c	_	119/0.75(138–40/10) [28]. IR (liquid film, cm ⁻¹): 2975–2950 ν(C–H); 1730–1715 ν(C=O); 1280, 1125 ν(C–O)	70	Calcd for C ₉ H ₉ BrO ₂ (Found): C: 47.19 (47.34); H: 3.91 (4.03); Br: 34.91 (34.73)
2c	48-49	90–91/0.04; IR (liquid film, cm ⁻¹): 3400 ν(O–H); 2975–2950 ν(C–H); 1370–1365 ν(–CMe ₂ def)	87	Calcd forC ₁₀ H ₁₃ BrO (Found): C: 52.24 (52.43); H: 5.68 (5.82), Br: 34.91 (34.80)
1d	_	200/57(194/52) [29]; IR (liquid film, cm ⁻¹): 2975–2950 ν(C–H); 1730–1715 ν(C=O); 1275,1125 ν(C–O)	77	-
2d	52	100–102/0.065; IR (liquid film, cm ⁻¹): 3400 ν (O–H); 2975–2950 ν (C–H); 1370–1365 ν (–CMe ₂ def)	87	Calcd for C ₁₀ H ₁₃ OI (Found): C: 43.49 (43.32); H: 4.71 (4.91), I: 45.92 (45.54)
1e	_	85/0.15(263-5) [44]	70	Calcd for C ₁₀ H ₁₂ O ₃ (Found): C: 66.66 (66.51); H: 6.66 (6.80)
2e	64–65	102/0.25	78	Calcd for C ₁₁ H ₁₆ O ₂ (Found): C: 73.30 (72.92); H: 8.80 (8.93)
2f	-	92/0.25	65	Calcd for C ₁₁ H ₁₆ O (Found): C: 80.50 (80.12); H: 9.76 (9.82)

 Table I
 Physical Constants, Yields (%), and Elemental Analysis of Cumyl Alcohols (2) and Their Precursor Esters (1)



$$R^{3} = CO_{2}Me (1a-1e) = MgBr (1f). {}^{a}Me_{2}CO \text{ for } 1f$$

$$R^{1} = R^{2} = H (1a, 2a, 3a); R^{1} = CH_{3}, R^{2} = F (1b, 2b, 3b); R^{1} = CH_{3}, R^{2} = Br (1c, 2c, 3c)$$

$$R^{1} = CH_{3}, R^{2} = I (1d, 2d, 3d); R^{1} = CH_{3}, R^{2} = OCH_{3} (1e, 2e, 3e); R^{1} = CH_{3}, R^{2} = CH_{3} (2f, 3f)$$
Scheme 1. Synthesis and solvolysis of cumyl chlorides. $R^{1}R^{2}:C_{4}H_{4}CMe_{2}Cl (3)$.

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Substituent	Compound	$\Sigma \sigma^+$	$k_{\rm XY} (10^5 \text{ s}^{-1})$ (Observed)	Correlation Coefficient	d^a	$k_{\rm XY} \ (10^5 \ { m s}^{-1})$ (Calculated)	$k_{\rm obsd}/k_{\rm calcd}$
3-F, 4-Me	3b	+0.041	7.00 ± 0.20^{b}	0.999	0.05	8.04	0.87
3-Cl, 4-Me		+0.088	3.83^{c}	_	0.09	4.88	0.79
3-Br, 4-Me	3c	+0.094	3.36 ± 0.03	0.993	0.12	4.62	0.72
3-I, 4-Me	3d	+0.048	5.09 ± 0.05	0.999	0.16	7.47	0.68
3-Cl, 4- <i>t</i> -Bu		0.143	1.22^{c}	-	0.33	2.75	0.44
3-Me, 5-Me		-0.132	47.3^{d}	_	0.04	49.3	0.96
3-MeO, 4-Me	3e	-0.264	278 ± 2	0.995	0.08	195	1.43
3-Me, 4-Me	3f	-0.377	652 ^e	-	0.05	635	1.028
3,4,5-Me ₃		-0.437	1260^{f}		0.04	1272.5 ^g	0.990
3-Cl, 4-MeO		-0.490	2200^{f}		0.05	-	_
3-CN, 4-MeO		-0.255	184^{f}		0.03	-	-

Table IIObserved and Calculated Rates of Solvolysis of 3,4-Disubstitued and 3,4,5-Trisubstituted2-Chloro-2-phenylpropanes in 90% Aqueous Acetone at 298 K Together with Their $\Sigma \sigma^+$ Values

^{*a*}Deviation from regression line in log k_{XY}/k_{HH} units.

^bStandard error for two rate runs.

^cFrom [25].

^dFrom [34].

^eExtrapolated from values at 268 K, $k_{XY} = 20.32 \times 10^5 \text{ s}^{-1}$; at 273 K, $k_{XY} = 35.39 \times 10^5 \text{ s}^{-1}$; and at 278 K, $k_{XY} = 67.42 \times 10^5 \text{ s}^{-1}$.

^fFrom [9].

^gCalculated from data in [9].

Compound	<i>T</i> (°K)	$k_{\rm obsd} \ (10^5 \ {\rm s}^{-1}) \ ({\rm SD})$	$\Delta E_a (\text{kJ mol}^{-1})$	ΔH^{\ddagger} (kJ mol ⁻¹)	$\Delta S^{\ddagger} (\mathrm{J} \mathrm{K}^{-1} \mathrm{mol}^{-1})$
3b	288	$2.25 \pm 0.01 \ (0.14)$			
	298	$7.00 \pm 0.20 \ (0.24)$	79.7 ($r^2 = 0.999$)	77.9 ($r^2 = 1$)	-62.7
	308	$19.9 \pm 0.70 \ (0.12)$			
3c	288	$1.03 \pm 0.02 \ (0.1)$			
	298	$3.36 \pm 0.03 \ (0.04)$	86.3 ($r^2 = 1$)	$83.7 (r^2 = 0.999)$	-49.2
	308	$10.7 \pm 0.02 \ (0.07)$			
3d	288	$1.64 \pm 0.01 \ (0.02)$			
	298	$5.09 \pm 0.05 \ (0.06)$	$81.6 (r^2 = 0.999)$	79.0 ($r^2 = 1$)	-61.5
	308	$14.9 \pm 0.02 \ (0.08)$			
3e	273	$17.2 \pm 0.40 \ (0.55)$			
	288	$96.1 \pm 1.50 \ (0.25)$	75.3 ($r^2 = 1$)	72.7 ($r^2 = 1$)	-49.1
	298	$278 \pm 2.0 (1.6)$			
3f	268	$20.3 \pm 0.4 (1.1)$			
	273	$35.4 \pm 0.4 (0.40)$	74.4 ($r^2 = 0.997$)	$72.0 (r^2 = 0.997)$	-44.7
	278	$67.4 \pm 0.2 \ (1.6)$			

Table III Rate Constants (k_{XY}) and Derived Activation Parameters for the Solvolysis of Disubstituted 2-Chloro-2-phenylpropanes (**3**) in 90% Aqueous Acetone at Three Different Temperatures

Rates are average of duplicate runs. SD indicates standard deviation for $n \ge 8$. r^2 indicates correlation for the Arrhenius plot.

disubstituted chlorides R^1R^2 -C₆H₄·CMe₂Cl were measured in 90% aqueous acetone at 288, 298, and 308 K, and the values are given in Tables II and III. These measured rate constants gave excellent first-order behavior, as shown by the constancy of the rate coefficient throughout the course of a single run. Correlation coefficients were determined using an Excel least-square best-fitted line package and were in the range 0.993–0.999 for the whole series of substituents.

RESULTS AND DISCUSSION

Hammett–Brown Equation and Additive Substituent Effects

Brown [2] chose to define the new substituent constant σ^+ using solvolysis of cumyl chlorides in 90% aqueous acetone at 298 K as a model of electrondeficient systems. The values of Hammett–Brown σ^+ constants [32] and Taft's E_s constants [33] for various substituents are given in Table IV.

Substituent	4-Me	3-Me	3-F	3-Cl	3-Br	3-I	3-OMe
$\overline{\sigma^+}$	-0.311	-0.066	+0.352	+0.399	+0.405	+0.359	+0.047
E_{s}	-1.24	_	-0.46	-0.97	-1.16	-1.40	-

Table IV Values of Hammett–Brown σ^+ Constants [32] and Taft's E_s Constants [33] for Various Substituents



Figure 1 Plot of log k_{XY}/k_{HH} rate constants for the solvolysis in 90% aqueous acetone at 298 K of 2-chloro-2(3-halo-4-methyl)phenylpropanes (**3b-3d**), 2-chloro-2(3-methoxy-4-methyl) phenylpropane (**3e**), and 2-chloro-2(3-methyl)-4-methyl)phenyl propane (**3f**) against $\Sigma\sigma^+$ constants [32]. In the figure, letters in superscripts indicate references: ^a[34], ^b[25], ^c[30], ^d[31], and ^e[9]. *For monosubstituents, X = H, Y = 3-F,3-Me or 3-MeO, and $\Sigma\sigma^+ = 0^+\sigma^+$ for Ysubstituent.

Using Hammett–Brown σ^+ constants and taking the value of the reaction constant $\rho^+ = -4.54$, the calculated rate constant k_{XY} for disubstituted 2-chloro-2-phenylpropane was obtained utilizing the following Hammett–Brown equation:

$$\log(k_{\rm XY}/k_{\rm HH}) = \rho^+ \Sigma \sigma^+ \tag{7}$$

The observed and calculated rate values are given in Table II together with $\Sigma \sigma^+$ values. A plot of log $(k_{\rm XY}/k_{\rm HH})$ rate constants against $\Sigma\sigma^+$ for the solvolysis of substituted 2-chloro-2-phenylpropanes (3b-3d; Fig. 1 and Table II), together with mainly di-, but also tri- and mono-substituents from the literature, is linear with a correlation coefficient of 0.990, showing the extent of validity of Hammett-Brown $\Sigma \sigma^+$ for assessing the additive effect of these substituents. Small deviations from additivity in the observed rate constants for these compounds under investigation have been shown to be in accordance with steric requirements of the three-halogen atom (Fig. 2) and its inhibition of resonance of the adjacent 4-methyl group. The fluorine atom, being the one with the least steric demand due to its smaller size, adheres most closely to the additivity principle. A good correlation coefficient of 0.994 was obtained when $\log k_{obs}/k_{calc}$ was plotted against Taft's





Figure 2 Plot of log k_{obsd}/k_{calcd} rate constants (lower plot) and the values of free energy of activation divergences, $(\Delta\Delta G^{\ddagger})_{obsd} - (\Delta\Delta G^{\ddagger})_{calcd}$ (upper plot) for 2-chloro-2-(3-halo-4-methyl)phenylpropanes (**3b–3d**) together with 2chloro-2-(3-chloro-4-methyl)- and 2-chloro-2-(3-chloro-4-*t*butyl)phenylpropanes^a [25] against Taft's steric parameter, ΣE_{s} .

steric parameter [33], ΣE_s , (Fig. 2) computed from individual values of methyl and halogen substituents (Table IV).

Close adherence to additivity is expected to take place in cases where interaction between two adjacent substituents is minimal. Brown and Cleveland [34] reported the solvolysis of 2-chloro-2-(3,5-dimethylphenyl)propane to show excellent additivity; the observed value of k was 96% of the calculated value. However, it is striking to note that the observed rate constant of 2-chloro-2-(3,4-dimethylphenyl)propane currently examined in this work does not differ remarkably from the anticipated rate. The observed rate, within experimental error, adheres remarkably well to the calculated value. This shows that steric hindrance to free rotation of the benzene ring-Me bond and hence to resonance is negligible. Brown [26] demonstrated that the rate of solvolysis of 2-chloro-2-(3,4-dimethylphenyl)propane at 273 K is precisely predicted from the rate of 3- and 4-methyl derivatives; the predicted(calculated) and observed relative rates are 58.4 and 60.0, respectively, with a ratio of $k_{\rm obsd}/k_{\rm calcd} = 1.03$. This is similar to the ratio of $k_{\rm obsd}/k_{\rm calcd} = 1.03$ obtained in the present work for the same compound from the extrapolated observed value in Table II. Similar results were found by Hassan and coworkers [35] (ratio $k_{obsd}/k_{calcd} = 1.02$) for the chlorination of ortho-xylene at 298 K using chlorine acetate in the presence of perchloric acid catalyst.

The effect of the *m*-methoxy group on the rate of solvolysis of 2-chloro-2-(3-methoxy-4-methylphenyl)propane investigated in this work was found to be far less deactivating than that would be expected from the slightly positive σ_m^+ value for the methoxy group. This value of $\sigma_m^+ = +0.047$ obtained by Brown [26] establishes the methoxy group in the meta position as being rate retarding. The value we obtained (ratio $k_{obsd}/k_{calcd} = 1.43$) in Table II shows that the *m*-methoxy group to be unexpectedly far less rate retarding. Similar values were found by de la Mare

and Vernon [36] and by Stock and Brown [24] for the noncatalytic bromination of anisole, which leads the former to suggest the presence of a nonclassical structure resonance contribution operating from the meta position. Built-in dipole interactions could also, perhaps, contribute to this enhanced reactivity. However, none of the results obtained by direct measurement of the reactivity of the position meta to the methoxy group indicated larger activation than expected [37–39]. As it seems, the additivity principle perhaps fails to accommodate adequately the variation in π -complex character of the transition state resulting from substituent-substituent interactions, leading to larger rate values than predicted. Further work is needed to investigate this diminished retarding effect of *m*-methoxy substituent in various disubstituted benzenes observed [24,36]. Another obvious weakness of the additivity is found in the fact that, whereas Eq. (7) proposes the strength of 2,3- and 2,5-disubstituted benzoic acids should be identical, it is found that in practice they are often distinctly different. Supplementary resonance interactions in some cases can well lead to serious departures from additivity, e.g., in 2-hydroxy-3-nitrobenzoic acid [40].

There is a general tendency in processes in solution for heats and entropies to compensate one another [41]. And since the free energy of activation ΔG^{\ddagger} is equal to $\Delta H^{\ddagger} - T \Delta S^{\ddagger}$, no variation in ΔG^{\ddagger} is expected to occur in such processes. Therefore, for homologous series reactions like the one in our hand, the plots of ΔH^{\ddagger} against ΔS^{\ddagger} should give straight lines. These values of activation were obtained following Cagle and Eyring [42], and they give a straight line of approximately unit slope (0.993) (Fig. 3).

The rate constants at three different temperatures and the derived activation parameters for the



Figure 3 Plot of ΔH^{\ddagger} (kJ mol⁻¹) against ΔS^{\ddagger} (J K⁻¹ mol⁻¹) values for 2-chloro-2-(3-halo-4-methyl)phenylpropanes (**3b-3d**) together with values by Hassan for 2-chloro-2-(3-chloromethyl)phenylpropane and 2-chloro-2-(3-chloro-4-*t*-butyl)phenylpropanes [25].

Substituent	$(\Delta\Delta G^{\ddagger})^a_{\mathrm{obsd}}$ (kJ)	$(\Delta \Delta G^{\ddagger})^{b}_{calcd}$ (kJ)	$[(\Delta\Delta G^{\ddagger})_{\text{obsd}} - (\Delta\Delta G^{\ddagger})_{\text{calcd}}] \text{ (kJ)}$
3-F, 4-Me	+1.41	+1.06	+0.35
3-Cl, 4-Me	$+2.88^{c}$	+2.26	+0.62
3-Br, 4-Me	+3.23	+2.48	+0.75
3-I, 4-Me	+2.20	+1.28	+0.92
3-Cl, 4- <i>t</i> -Bu	$+5.73^{c}$	+3.77	+1.96
3-Me, 5-Me	-3.32^{d}	-3.43	+0.11
3-Me, 4-Me	-9.82	-9.78	-0.040
3-MeO, 4-Me	-7.72	-6.84	-0.88

Table VDivergences between Observed and Calculated Differences in Free Energy of Activation for the Disubstituted2-Chloro-2-phenylpropanes (**3b-3f**)

 $^{a}(\Delta\Delta G^{\ddagger})_{\text{obsd}}$ is $(\Delta G^{\ddagger} - \Delta G^{\ddagger}_{\text{o}})_{\text{obsd}}$.

 $^{b}(\Delta\Delta G^{\ddagger})_{\text{calcd}}$ is $(\Delta G^{\ddagger} - \Delta G^{\ddagger}_{o})_{\text{calcd}}$; calculated by using Eq. (8).

^cCalculated from rate constants by Hassan et al. [25].

^dCalculated from rate constants by Brown and Cleveland [34].

solvolysis of substituted 2-chloro-2-phenylpropanes in 90% aqueous acetone are given in Table V.

Additive Effects of Substituents on Free Energy of Activation

Assuming the constancy of the entropy factor, the change in the free energy of activation produced by a single substituent may be calculated by means of the relation $(\Delta \Delta^{\ddagger} - \Delta \Delta_0^{\ddagger}) = -2.303RT \log k/k_0$, and if, moreover, substituent effects are additive, the observed difference in the free energy of activation due to two substituents will be the sum of the differences due to each substituent alone, i.e. [42],

$$(\Delta G^{\ddagger} - \Delta G_0^{\ddagger})_{XY}$$

= $(\Delta G^{\ddagger} - \Delta G_0^{\ddagger})_X + (\Delta G^{\ddagger} - \Delta G_0^{\ddagger})_Y$ (8)

Within the limits of experimental error, the entropies of ionization (ΔS^{\ddagger}) of 2-chloro-2-phenylpropanes and their mono- and disubstituted derivatives appear to be constant. Consequently, the difference in free energies of activation ($\Delta G^{\ddagger} - \Delta G_{o}^{\ddagger}$; Table V) may be taken as a measure of the relative stabilities of transition states and the ability of each substituent to stabilize such transition states [43].

The differences in the free energy of activation for disubstituted 2-chloro-2-phenylpropanes are given in Table V. Figure 2, showing the divergences in additivity between observed and calculated energies of activation, summarizes the trend.

Analysis of the data given above in Table V will show the validity of assessing the role of substituent on reactivity in terms of a free energy relationship. The concept of additivity based on these assessments will

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be maintained in reactions of the type where the electrical effects of the substituent can be described with precision. However, the additivity principle perhaps tends to oversimplify the role of factors arising when two constituents are in the vicinity of each other. In such cases, deviations are bound to occur. Thus in the case of 2-chloro-2-(3-halo-4-methyl)phenylpropanes (3b-3d), divergences, albeit small, from additivity calculations for the free energy differences increase in magnitude according to the increase in the steric requirements of the halogen atom. For the *m*-methoxy derivative, the additivity calculations overestimate the deactivating effect of the *m*-methoxy group to the extent of 0.88 kJ per mol. Only the 2-chloro-2-(3-methyl-4methyl)phenylpropane rate values show a close fit to additivity calculations.

A good correlation coefficient of 0.983 was obtained when divergences from additivity in the free energy of activation of $(\Delta\Delta G^{\ddagger})_{obsd} - (\Delta\Delta\Delta G^{\ddagger})_{calcd}$ for 2-chloro-2-(3-halo-4-methyl)phenylpropanes (**3b**– **3d**) together with values by Hassan [25] for 3-chloro-4-methyl and 3-chloro-4-*t*-butyl were plotted against Taft's steric parameter, ΣE_s , values of methyl and halogen substituents, as shown in Fig. 2.

CONCLUSION

3-Halogeno, -methyl, and -methoxy derivatives of 4methylcumyl chlorides (3) when dissolved in 90% aqueous acetone undergo both solvolysis and elimination to give the corresponding alcohols (by $S_N 1$) and olefins (by E1). Since both $S_N 1$ and E1 have a common rate-determining (carbocation-forming) step, measurement of the solvolysis rate gives the overall rate of reaction. These specific rates for the various disubstituents (**3b–3f**) given in Table IV have been analyzed using, and with the purpose of testing the validity of, the extended Hammett-Brown equation, log $(k_{\rm X}/k_{\rm H}) = \rho^+ \Sigma \sigma^+$, where $\Sigma \sigma^+$ is the sum of meta- and para-substituent constants. Additive effects of disubstituents 3-F,4-Me, 3-Br,4-Me, 3-I,4-Me, 3-Me,4-Me, and 3-MeO,4-Me on the rate of solvolysis of the parent chloride (3) are well correlated using the extended Hammett-Brown equation. The plot of log $(k_{\rm X}/k_{\rm H})$ against $\Sigma\sigma^+$ has a linear correlation coefficient of 0.990, which gives a measure of the validity of the equation to depict such systems. Figure 1 includes, together with the values for present work, values for mono-, di-, and tri-substituents from the previous work. From Fig. 1, it is clear that polymethyl substituents whether in the meta or para positions show no departure from additivity, with 3,4-Me₂ (present work), 3,5-Me₂ ([34], Fig. 1), and 3,4,5-Me₃ ([9], Fig. 1) fitting nicely on the regression line. The introduction of a third methyl group does not seem to bear on their resonance demands predicted by the Hammett-Brown equation. A good fit is also seen in Fig. 1 for the 3-Cl,4-OMe and 3-CN,4-OMe disubstituents plotted values obtained from Fujio et al. [9]. However, the 3-OMe,4-Me disubstituent gives a departure toward higher values from the regression line (lower retarding effect than that predicted by the Hammett-Brown equation). It seems that the *meta*-methoxy group has a lesser steric inhibitory effect on the resonance demands of the para-methyl group than that predicted by the Hammett-Brown equation, or that the metamethoxy substituent has an unusual residual resonance contribution, resulting in a lower rate retardation than the designated $\sigma_{\rm m}^+ = +0.047$ would suggest. This role of the meta-methoxy group warrants further investigation. The relative (k_{obsd}/k_{calcd}) rate ratios of the different substituents, shown in Table II, give the extent of conformity with additivity. The small degree of departure from additivity for each substituent is found to correlate with the steric demand of the halogen substituents. Thus, plots of log of these rate ratios against Taft's steric factor of each halogen (the sum of 3-halo and 4-methyl substituents) give a linear correlation coefficient of 0.994 for the 3-halo substituents. The 3methyl substituent, which has a relative (k_{obsd}/k_{calcd}) rate ratio of 1.03, shows excellent additivity, precluding any type of steric rate retardation as a result of the proximity of the two methyl substituents. It is hypothesized that, unlike the 3-halo derivatives, the methyl group can freely rotate about the benzene–Me bond, and by doing so, militates against the steric interaction and hence rate retardation. The 3-methoxy group is found to have a relative rate ratio of 1.43. This shows the group unexpectedly to be far less deactivating than that predicted by the Hammett-Brown equation. One

explanation for this enhanced reactivity of the methoxy group lies in its ability to indulge from its meta position in a resonance electron-enrichment process at the position ortho to the reaction center (the ipso position), from which it can be relayed by induction to the reaction center. This explanation was suggested earlier by Brown et al. [30] to account for the enhanced reactivity of the monosubstituted *m*-methoxycumyl chloride. Similar trends were found for the free energy of activation $(\Delta \Delta G^{\ddagger})_{obsd} - (\Delta \Delta G^{\ddagger})_{calcd}$ differences, which correlate linearly to a coefficient of 0.983 with Taft's steric factor of halogen atoms, as shown in Fig. 2. The values obtained earlier by Hassan et al. [25] for 3chloro-4-methyl and 3-chloro-4-t-butyl derivatives fit nicely in this plot of Fig. 2 for the relationship between Taft's steric factor and the substituent bulk. As for the *m*-methoxy derivative, the free energy calculations estimate the deactivating effect of the *m*-methoxy group to the extent of 0.88 kJ per mol. This is can be recognized in terms of a second-order relay of the mesomeric effect of the methoxy from the ortho position to the reaction center mentioned above [30]. The 2-chloro-2-(3-methyl-4-methyl)phenylpropane rate values show a close fit to additivity calculations, with a deviation of 0.04 kJ per mol. As a final conclusion, it is necessary to allow for steric interactions between adjacent substituents for the additivity principle to hold true; this can be done, perhaps, by incorporating a steric factor in the extended Hammett-Brown equation (4) of the type shown in Eq. (9):

$$\log(k_{\rm XY}/k_{\rm HH}) = \rho^+ \Sigma \sigma^+ + \delta \Sigma E s \tag{9}$$

where δ is measure of the susceptibility of a particular reaction toward steric effects. However, the role of meta substituents in polysubstituted cumyl systems, such as the case of *m*-methoxy group, needs to be resolved by further work.

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