

The polarisability potential as a steric index[†]

Cristopher Camacho^a and Julio F. Mata-Segreda^{b*}

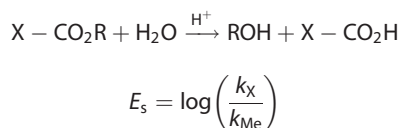
The acid-catalysed hydrolysis of carboxylic esters is the reference chemical reaction used for the empirical evaluation of steric effects. In this work, the polarisability potential (Hehre, *et al.*, *J. Am. Chem. Soc.* 1986, 108, 1711–1712) is identified as quantum-mechanical size of substituent groups. Correlation is found between this quantity and reactivity features of the reference reaction. Copyright © 2010 John Wiley & Sons, Ltd.

Keywords: acid-catalysed ester hydrolysis; moment of inertia; polarisability potential; steric effect; Taft parameter; torsional barrier

INTRODUCTION

The rate and product outcome of a chemical reaction can be influenced by the ability of a substituent group to occupy space. This observation is the phenomenological description of the so-called steric effect. The intuitive view points to situations where atom contacts between reaction sites are made more difficult by the electrostatic repulsion of moieties close to each other, that do not otherwise participate in the molecular change.

The steric parameter E_s was defined by Taft, based on a suggestion by Christopher Ingold, on the basis of kinetic measurements for the acid-catalysed hydrolysis of carboxylic esters:^[1]



This quantity was shown to be approximately insensitive to polar effects, and thus assumed to account for steric effects only (e.g. the cases where $X =$ alkyl and monohaloalkyl groups). Extensive tables have been assembled from data collected for the reference chemical reaction, in different reaction conditions.^[2]

Dubois defined the Taft–Dubois steric parameter E_s' in the same way as E_s , but the kinetic data were measured using only one standard chemical reaction: the acid-catalysed esterification of $X-CO_2H$ at 40 °C in methanol.^[3] E_s and E_s' are useful as long as no interaction exists between the X and CO_2R moieties via a mechanism such as conjugation. This is the case of phenyl and conjugated alkenyl substituents. Proposals to correct E_s parameters have been devised,^[2] but no attempt is made in this paper to review E_s .

Correlation between quantum mechanical size and steric effect has given fruitful insights. Large groups have a greater number of occupied molecular orbitals with large amplitudes in the space occupied by the moiety. This means that stronger repulsions may arise between the occupied molecular orbitals of reacting molecules or groups situated at close distances within the same molecule (or transition-state complex).

Fujimoto *et al.*^[4] studied the nature of the steric effect of alkyl groups by paired-interacting orbitals analysis. The results of these authors agreed with the known experimental observation that steric repulsion is not governed by the global size of substituents but determined principally by their local arrangement of bonds.

Hollett *et al.*^[5] explored a quantum mechanical definition of molecular size and shape, as formulated from the electronic second moment of the Hartree–Fock wave function. This quantum-mechanical quantity correlated well with E_s' for halogens and first-row hydrides, but significant positive deviations were observed for groups such as $N \equiv C$, MeO, MeS or $CH_2=CH$. The experimental $\log(k_X/k_H)$ values for HO and MeO are -0.55 and for both HS and MeS are -1.07 . This observation indicates that the acid-catalysed hydrolysis of esters is mainly affected by the oxygen and sulphur atoms, and not by the entire substituent as calculated from the electronic second moment.

In a more recent study of Liu and collaborators,^[6] the so-called *steric energy* was related to E_s' . This quantum mechanical quantity represents a hypothetical state with all electrons packed into the lowest orbital and other effects entirely excluded. Thus, it is a measure of the intrinsic space occupied by an electronic system. The quality of correlation between *steric energy* and E_s was better for this model than for the result of Hollett *et al.*^[5]

A conceptually simpler structural parameter that may correlate with steric feature is the polarisation potential of Hehre, Taft and co-workers, σ_{α} .^[7] This quantity gives the energy of interaction between a particular CH_3-X molecule and a positive charge located 3 Å away from the methyl group, along the C–X axis. The stabilisation of the system depends on how easily is electron density ‘projected’ towards the positive charge. This electron-density plasticity depends on the polarisability of X . There is a general relationship between polarisability and molar refraction. This latter quantity gives the actual volume (without free space)

* Correspondence to: J. F. Mata-Segreda, Laboratory of Bio-organic Chemistry, School of Chemistry, University of Costa Rica, 11501-2060, Costa Rica. E-mail: julio.mata@ucr.ac.cr

a C. Camacho
Department of Applied Chemistry and Institute of Molecular Science, National Chiao Tung University, Hsinchu 30010, Taiwan

b J. F. Mata-Segreda
Laboratory of Bio-organic Chemistry, School of Chemistry, University of Costa Rica, 11501-2060, Costa Rica

† This article is published in *Journal of Physical Organic Chemistry* as a special issue on Tenth Latin American Conference on Physical Organic Chemistry, edited by Faruk Nome, Dept de Química, Universidade Federal de Santa Catarina, Campus Universitario – Trindade 88040-900, Florianopolis-SC, Brazil.

of groups or molecules of various sizes, shapes and degrees of polarity.^[8] Therefore, a relation between size and σ_{α} should be expected to exist. Thus, it is an acceptable working hypothesis to state that σ_{α} can be considered as a steric index.

We aim to draw attention to the notion that steric hindrance stems from electron-density distribution in substituent groups, rather than mass distribution. This work presents an analysis of the use of σ_{α} for the correlation of the steric effect in the model hydrolysis reaction.

RESULTS AND DISCUSSION

The effect of structure on the acid-catalysed hydrolysis of carboxylic esters was proposed by Taft as the reference chemical reaction for the quantitative estimation of steric effect.^[1] For the case of *Alkyl*-CO₂R's, $\Delta^{\ddagger}H^{\circ}$ is quite insensitive to the nature of the substituent groups ($68 \pm 2 \text{ kJ mol}^{-1}$).^[9] This observation indicates that the variation of reactivity results mainly from the difference of $\Delta^{\ddagger}S^{\circ}$ values between *Alkyl*-CO₂Et and H-CO₂Et. There is evidence that considerable electrostriction of transition-state (TS) complexes occurs in the acid-catalysed hydrolysis of simple unfunctionalised esters. The observations that lead to such conclusion are: lower $\Delta^{\ddagger}H^{\circ}$ values for the hydrolysis of esters with hydrogen-bonding capability,^[10] negative activation volumes ($-9 \text{ cm}^3 \text{ mol}^{-1}$)^[11,12] and activation entropies in the range from -0.08 to $-0.12 \text{ kJ K}^{-1} \text{ mol}^{-1}$.^[9] The only conceivable difference amongst the group of esters is the loss of internal rotational freedom of the TS complex, relative to reagent molecules.^[13]

The amount of entropy associated with the internal rotation of groups in molecules can be calculated from the well-established relationships of statistical thermodynamics.^[14]

$$S_{\text{int rot}} = R \ln Q_{\text{int rot}} + RT \left(\frac{\partial \ln Q_{\text{int rot}}}{\partial T} \right)_V \quad (1)$$

$$Q_{\text{int rot}}^{\text{free}} = \left(\frac{8\pi^2 I_r k_B T}{h} \right)^{1/2} \quad (2)$$

Equation (2) gives the partition function for a free rotor, where the only structural feature that describes the nature of the substituents is the reduced moment of inertia for internal rotation of the group, I_r .

Since $\Delta^{\ddagger}H^{\circ}$ can be taken as a constant along the series, one should expect the following relation to hold:

$$\ln \left(\frac{k_X}{k_H} \right) = \frac{\Delta^{\ddagger}S^{\circ}(X) - \Delta^{\ddagger}S^{\circ}(H)}{R} \quad (3)$$

and the logical consequence would be

$$\Delta^{\ddagger}S^{\circ}(X) - \Delta^{\ddagger}S^{\circ}(H) = -S_{\text{int rot}}^{\circ}(X) \quad (4)$$

Table 1 gives the second-order rate constants for the acid-catalysed hydrolyses of the ethyl esters studied at 30.0 °C and the corresponding values of σ_{α} . Table 2 gives the calculated reduced moments of inertia for internal rotation of different groups and the corresponding values of $S_{\text{int rot}}^{\text{free}}$. Gas-phase moments of inertia must be significantly different for the more polar ester molecules in solution. Using more real values of I_r of X groups is at the present time out of the scope of this paper.

Figure 1 shows the semi-quantitative validity of the type of association given by Eqn (4), for the case of X = alkyl and mono-

Table 1. Kinetic data for the acid-catalysed hydrolysis of esters at 30.0 °C. σ_{α} values from the work of Hehre *et al.*^[7] are denoted by asterisk. The other values were obtained from the empirical relationship between σ_{α} and molar refraction (refer the Experimental section)

X	$10^5 k_2/s^{-1}$ (mol dm^{-3}) ⁻¹	$\Delta^{\ddagger}G^{\circ}$ (kJ mol^{-1})	σ_{α} (kJ mol^{-1})
H	501 ± 3	87.6	0*
Me	19.3 ± 0.4	95.8	-1.46*
Et	18.4 ± 0.3	96.2	-2.05*
<i>n</i> -Pr	8.4 ± 0.2	97.9	-2.26*
<i>i</i> -Pr ^[9]	—	100.3	-2.59*
<i>t</i> -Bu ^[9]	—	107.3	-3.10*
Bn	3.6 ± 0.1	100.0	-5.91
Cl—CH ₂	9.9 ± 0.6	97.5	-2.06
Br—CH ₂	6.5 ± 0.2	98.5	-2.58
N≡C—CH ₂	2.2 ± 0.6	101.3	-2.02
CH ₂ =CH	0.76 ± 0.07	104.0	-2.09*
Me—CH=CH	0.32 ± 0.03	106.1	-3.01
Ph ^[9]	—	110.8	-3.39*
EtO ₂ C	3.3 ± 0.1	100.2	-3.22
EtO ₂ C—CH ₂	1.28 ± 0.06	102.6	-4.01
EtO ₂ C—CH ₂ —CH ₂	1.67 ± 0.05	102.0	-4.80
Me—CH(OH)	16.2 ± 0.2	96.2	-2.27

haloalkyl. The data fit Eqn (3) adequately:

$$\Delta^{\ddagger}S^{\circ}(X) - \Delta^{\ddagger}S^{\circ}(H) = -(1.2 \pm 0.3) \times S_{\text{int rot}}^{\text{free}} \quad r = 0.95, \quad p < 0.005 \quad (5)$$

The goodness of fit given by $r = 0.95$ is good and the existence of correlation between the quantities is definitely well established. One reason for having obtained this r -value stems from the

Table 2. Reduced moments of inertia for internal rotation of different groups and the corresponding values of $S_{\text{int rot}}^{\text{free}}$ at 30.0 °C

X	I_r (kg m^2)	$S_{\text{int rot}}^{\text{free}}$ ($\text{JK}^{-1} \text{mol}^{-1}$)
H	0	0
Me	5.22×10^{-47}	19.4
Et	4.95×10^{-46}	28.8
<i>i</i> -Pr	9.02×10^{-46}	31.3
<i>t</i> -Bu	1.20×10^{-45}	32.5
Bn	2.66×10^{-45}	35.8
Cl—CH ₂	1.12×10^{-45}	32.2
Br—CH ₂	1.64×10^{-45}	33.8
N≡C—CH ₂	1.20×10^{-45}	32.5
CH ₂ =CH	3.38×10^{-46}	27.2
Ph	1.04×10^{-45}	31.9
EtO ₂ C	1.73×10^{-45}	34.0
Me—CH(OH)	8.63×10^{-46}	31.1
HO—CH ₂	5.80×10^{-46}	29.4
MeO—CH ₂	3.73×10^{-45}	37.1

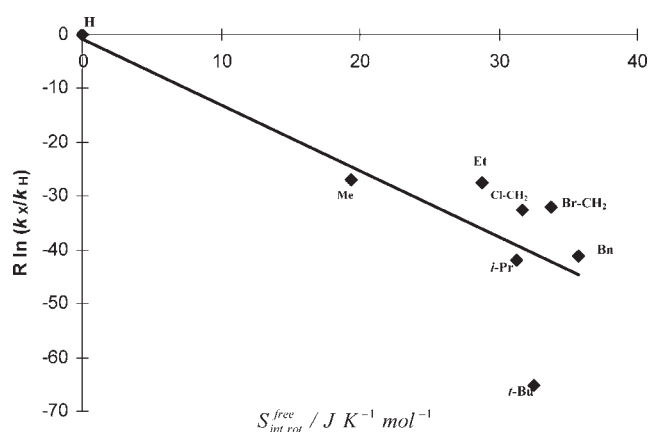


Figure 1. Reactivity of X—CO₂Et at 30.0 °C (X = alkyl and monohaloalkyl) as the result of freezing of the internal rotation of X in the transition state

inclusion of the significantly larger *t*-Bu. For the acid-catalysed hydrolysis of ethyl pivalate (X = *t*-Bu), $\Delta^\ddagger H^\circ = 77 \text{ kJ mol}^{-1}$,^[9] a value higher than the range $68 \pm 2 \text{ kJ mol}^{-1}$. Exclusion of the data point for *t*-Bu gives the expected statistically better regression equation $\Delta^\ddagger S^\circ(\text{X}) - \Delta^\ddagger S^\circ(\text{H}) = -(1.1 \pm 0.3) \times S_{\text{int rot}}^{\text{free}}$ $r = 0.98$. Nevertheless, the writers believe that the inclusion of the outlier in Fig. 1 is instructive.

From a conceptual point of view, although $S_{\text{int rot}}^\circ$ is indeed a function of I'_r , it is also a function of the barrier to free rotation about the X—CO₂Et bond.

Pitzer^[15–17] has given numerical values that allow the calculation of entropy contributions to internal rotation, as a function of the magnitude of potential-energy barriers. For example, the barrier for internal rotation in CH₃—CO₂Me is reported as 1.2 kJ mol^{-1} .^[18,19] By using the tables of Pitzer, the entropy decrease from free rotation is estimated as $0.2 \text{ J K}^{-1} \text{ mol}^{-1}$ ($S_{\text{int rot}}^{\text{free}} = 19.4 \text{ J K}^{-1} \text{ mol}^{-1}$). An analogous calculation was done for *i*-Pr—CO₂Me. Its barrier for internal rotation is 4.2 kJ mol^{-1} ,^[20] and the correction turns out to be $2 \text{ J K}^{-1} \text{ mol}^{-1}$ ($S_{\text{int rot}}^{\text{free}} = 31.3 \text{ J K}^{-1} \text{ mol}^{-1}$). Corrections to $S_{\text{int rot}}^{\text{free}}$ can be done whenever values of torsional barriers are available, but one may expect that corrections for X = Alkyl are not significant in carboxylic ester molecules.

Despite this first approximation assumed as valid, one can recognise in Eqn (5) the qualitative rule of Price and Hammett.^[13] The rule states that for reactions that involve highly polar TS complexes, the more entropy is contributed to reactant molecules by the substituent groups, the more entropy becomes frozen out in the TS.

This result indicates that structure-reactivity effects in the hydrolysis of Alkyl-CO₂Et have an entropy origin that can be calculated approximately from the inertial characteristics of X. Since the moment of inertia I' is the second moment of mass, $I' = \int_V r^2 dm$, one can finally conclude that the steric effect of alkyl and monohaloalkyl groups stems mainly from a mass-distribution effect in the group X.

Phenyl, *trans*-1-propenyl and vinyl groups in ester molecules (groups conjugated to the carboxyl moiety) fail to fit the simple inertial model. The corrections needed for phenyl and vinyl groups are much more significant than for alkyl groups. For the case of ethyl acrylate (X = vinyl), the internal rotational barrier is reported as 25 kJ mol^{-1} ^[21] and the corresponding correction is $9 \text{ J K}^{-1} \text{ mol}^{-1}$ ($S_{\text{int rot}}^{\text{free}} = 27.2 \text{ J K}^{-1} \text{ mol}^{-1}$). The Gibbs-energy barrier in Ph—CO₂Me has been determined by ¹³C NMR experiments to be equal to 20.6 kJ mol^{-1} .^[22] One may take this value as close

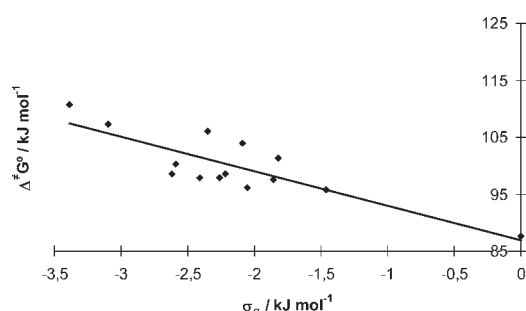


Figure 2. Polarisation potential as steric-effect index for the acid-catalysed hydrolysis of X—CO₂Et at 30.0 °C. X are alkyl, phenyl, alkenyl conjugated to the carboxylic moiety and groups with non-bonding electron pairs

to the actual torsional potential-energy barrier (mean ratio of $|\Delta^\ddagger S^\circ|/\Delta^\ddagger H^\circ = 0.2$ at 300 K for a series of interconversions of rotamers^[23]). Thus, correction results as $8 \text{ J K}^{-1} \text{ mol}^{-1}$ ($S_{\text{int rot}}^{\text{free}} = 31.9 \text{ J K}^{-1} \text{ mol}^{-1}$). This observation is understood in terms of the theoretical requirement that there must be a single interaction mechanism, in order for a simple extra-thermodynamic relationship to exist.^[24] For these three cases at hand, there are two effects: the inertial effect and the delocalisation of electron density from X to the carboxyl moiety.

Esters with the more polar unconjugated X groups other than haloalkyl also fail quantitatively the free-rotor inertial model with $r = 0.61$, $p < 0.5$ (X = NC—CH₂, EtO₂C, Me—CH(OH), HO—CH₂^[25] and MeO—CH₂^[25]). This leads to the formulation of the following question: Does the steric effect stem from electron-density distribution in the X moieties, rather than mass distribution? For the case X = alkyl, all atoms are C and H. Thus, variations in mass distribution run in parallel to electron-density distribution.

Figure 2 shows an acceptable correlation between activation barriers and the corresponding values of σ_α :

$$\Delta^\ddagger G^\circ = 87.2 - 5.5 \sigma_\alpha \quad r = -0.81 \quad p < 0.0002 \quad n = 14 \quad (6)$$

Three groups grossly fail the correlation: Bn (+20% deviation), EtO₂C—CH₂ (+8.3% deviation) and EtO₂C—CH₂—CH₂ (+13% deviation). These data points are not included in the graph. This can be explained in terms of the inaccuracy in determining their σ_α values from molar refraction calculations (*vide infra*). It is reasonable to think that not all of the structure of X contributes significantly to σ_α the same way as the case of the electronic second moment of the Hartree–Fock wave function, discussed above.^[5]

A test of validity of Eqn (6) is the prediction of $\Delta^\ddagger G^\circ$ values, for substituents of known σ_α from the work of Hehre and co-workers.^[7] The observed $\Delta^\ddagger G^\circ$ for the hydrophobic ester ethyl cyclohexylcarboxylate ($\sigma_\alpha = -4.0 \text{ kJ mol}^{-1}$) is $104.1 \text{ kJ mol}^{-1}$.^[9] Equation (6) gives the value $109.1 \text{ kJ mol}^{-1}$ (+4.8% error). For ethyl methoxyacetate ($\sigma_\alpha = -1.8 \text{ kJ mol}^{-1}$), the observed value is 96.9 kJ mol^{-1} , and Eqn (6) predicts 97.1 kJ mol^{-1} (+0.2% error).

A further test of validity is the prediction of $\Delta^\ddagger G^\circ$ values for simple X groups, small enough to guarantee accuracy in their calculated σ_α from molar refraction: (a) FCH₂—CO₂Et, $\sigma_\alpha = -1.15 \text{ kJ mol}^{-1}$, $\Delta^\ddagger G^\circ(\text{obs}) = 98.4 \text{ kJ mol}^{-1}$,^[25] $\Delta^\ddagger G^\circ(\text{calc}) = 93.5 \text{ kJ mol}^{-1}$ (+3.2% error); (b) HOCH₂—CO₂Et, $\sigma_\alpha = -1.43 \text{ kJ mol}^{-1}$, $\Delta^\ddagger G^\circ(\text{obs}) = 95.4 \text{ kJ mol}^{-1}$,^[25] $\Delta^\ddagger G^\circ(\text{calc}) = 95.1 \text{ kJ mol}^{-1}$ (+0.3% error).

A note of caution was pointed out by a Reviewer, concerning the intermingling of the rate data of this work in aqueous HCl

and data taken from Reference [9], determined in 70% aqueous acetone ($X = i\text{-Pr}, t\text{-Bu}, c\text{-Hx}$ and Ph). The consideration of the data put together is useful, because the difference in activation barriers in the two media is relatively small.

For example, the activation barriers in this work for the acid-catalysed hydrolyses of ethyl acetate, ethyl propionate and ethyl phenylacetate in aqueous HCl differ from those in 70% aqueous acetone^[9] by 2.7, 2.3 and 1.4% (mean difference 2.1% equivalent to 2.1 kJ mol^{-1}). Seventy per cent aqueous acetone implies $[\text{H}_2\text{O}] \sim 21 \text{ mol dm}^{-3}$. This means that $\Delta^\ddagger G^\circ$ should increase in the H_2O -acetone mixture by $RT \ln(55/21) = 2.4 \text{ kJ mol}^{-1}$. This crude estimate checks well enough, considering that a medium dielectric effect also plays a role.

This relative success in the use of σ_α for the assessment of the steric effect in the hydrolysis of esters prompts to inquire about the validity of the model for the esterification of $X\text{—CO}_2\text{H}$. Correlation of rate data for the Fischer esterification of five carboxylic acids with methanol at 40°C gives the following result:^[26]

$$\Delta^\ddagger G^\circ / \text{kJ mol}^{-1} = 26.3 - 5.1 \sigma_\alpha \quad r = -0.81 \quad p < 0.04 \quad n = 5 \quad (7)$$

This value of $(\partial\Delta^\ddagger G^\circ / \partial\sigma_\alpha) = -5.1$ is similar to the value -5.5 in Eqn (6), as expected from the mechanistic corollary of the principle of microscopic reversibility.

The results of this work support the hypothesis that the polarisation potential can be regarded as an index of quantum mechanical size and that steric hindrance arises as an electron-density distribution effect, rather than a mass-distribution effect in the substituent groups.

Limitations of using σ_α : Modern thinking in chemistry is based on establishing associations (correlations) between molecular features and observed reactivity or equilibrium properties of materials. We have presented in this paper an empirical approach to the nature of steric hindrance, based on a simple working hypothesis that stems from observation and intuition.

The association between effective quantum size of substituent groups (measured by σ_α) and $\Delta^\ddagger G^\circ$ was well established at $p < 0.0002$ for the acid-catalysed hydrolysis of carboxylic esters, the reference chemical reaction proposed by Taft for the quantitative estimation of steric hindrance. On the other hand, the quality of the regression equation found to describe the $\sigma_\alpha\text{—}\Delta^\ddagger G^\circ$ association can be assessed as fair, with an $r = -0.81$, though it yields values of activation barriers within a mean error range of $\pm 2.5\%$.

Limitations of using gas-phase σ_α values for reactions in solution are subjected to the effect of the microenvironment on the polarisability potential of groups, because compression of the bonding electrons in X by the solvating molecules increases their electron density.^[27]

CONCLUSION

The degree of steric hindrance of substituent groups in the acid-catalysed hydrolysis of ethyl carboxylates (HCl, 30°C) and the Fischer esterification of $X\text{—CO}_2\text{H}$ (MeOH, 40°C) are fairly accounted for by the polarisation potential of Hehre, Taft and co-workers, σ_α .^[7] The groups included in this study were alkyl, monohaloalkyl, phenyl, alkenyl conjugated to the carboxyl moiety, as well as unconjugated groups with non-bonding electron pairs. The proposed model in this work produces Gibbs

activation barriers within $\pm 2.5\%$ error, for the acid-catalysed hydrolysis of carboxylic esters.

As a general result, steric hindrance is the result not of mass-distribution effect but of electron-density distribution in X moieties.

EXPERIMENTAL

Materials: All esters were common chemicals from different commercial sources. Small quantities were distilled prior to each kinetic series.

Rate measurements: The reaction mixtures were made by dissolving 2 or 3 cm^3 of a particular ester in 100 cm^3 of aqueous 0.3 mol dm^{-3} HCl. The rates were measured by titration of free $X\text{—CO}_2\text{H}$ at suitable reaction times with 0.1 mol dm^{-3} NaOH – phenolphthalein in 3.00 cm^3 aliquot portions withdrawn from the reaction flask. In all experiments, data points were collected up to at least 90% of the total extent of reaction.

The data were fitted to the first-order kinetic scheme $[\text{NaOH}]/\text{cm}^3 = A - B \exp(-k_1 t)$, by using a nonlinear least-squares computer programme. The reported uncertainty limits are standard deviations from the mean obtained from at least three experiments. Second-order specific rates were obtained by dividing the observed k_1 by the corresponding value of $[\text{HCl}]$. The k_2 values for the three diesters in Table 1 include the $1/2$ statistical correction.

Polarisation potentials: The σ_α values of groups not given by Hehre, Taft and collaborators^[7] were estimated by the linear correlation found between σ_α and molar refraction calculated from atom contributions^[28] ($\sigma_\alpha/\text{kJ mol}^{-1} = -0.16 [R] - 0.28, r = -0.86, n = 22$).

Reduced moments of inertia of the X groups, I'_r : The experimentally determined geometries of the corresponding $X\text{—H}$ were obtained from the Computational Chemistry and Benchmark Database of NIST (<http://cccbdb.nist.gov>). For each case, the 'connecting carbon atom' in $X\text{—H}$ ($X\text{—CO}_2\text{Et}$) was translated to the Cartesian origin and then a 3D rotation was done in order to have the chosen C—H bond placed on the x -axis. After such a geometrical transformation is done, the moment of inertia for internal rotation of substituent X is reduced to the calculation of $I_{xx}(X\text{—H})$. The I'_r values were then calculated as $1/I'_r(X) = 1/I_{xx}(X) + 1/I_{xx}(\text{CO}_2\text{Et})$. The procedure applied to obtain $I_{xx}(\text{CO}_2\text{Et})$ was the same described, but applied to ethyl formate.

Acknowledgements

The authors wish to thank Prof. Henryk Witek, National Chiao Tung University, for his interest in this work. JFM-S wishes to thank the Vice-Rector for Research of University of Costa Rica (project No. 115-A8-190) and the National Council of Scientific and Technological Research and the Ministry of Science and Technology of Costa Rica.

REFERENCES

- [1] R. W. Taft, Jr, *J. Am. Chem. Soc.* **1952**, *74*, 2729–2732, 3120–3128.
- [2] Many sources offer E_s data. For example refer: S. H. Unger, C. Hansch, *Prog. Phys. Org. Chem.* **1976**, *12*, 91–118.
- [3] J. A. MacPhee, A. Panaye, J.-E. Dubois, *Tetrahedron Lett.* **1978**, 3293–3296.

- [4] H. Fujimoto, Y. Mitzutani, J. Endo, Y. Jinbu, *J. Org. Chem.* **1989**, *54*, 2568–2573.
- [5] J. W. Hollett, A. Kelly, R. Poirier, *J. Phys. Chem. A* **2006**, *110*, 13884–13888.
- [6] M. Torrent-Sucarrat, S. Liu, F. De Proft, *Ibid.* **2009**, *113*, 3698–3702.
- [7] W. J. Hehre, C.-F. Pau, A. D. Headley, R. W. Taft, Jr, *J. Am. Chem. Soc.* **1986**, *108*, 1711–1712.
- [8] T. Brinck, J. S. Murray, P. Politzer, *J. Chem. Phys.* **1993**, *98*, 4305–4306.
- [9] A. J. Kirby, in *Comprehensive Chemical Kinetics*, Vol. 10 (Eds: C. H. Bamford, C. H. F. Tipper), Elsevier, Amsterdam, **1972**, 57–207.
- [10] J. F. Mata-Segreda, *J. Phys. Org. Chem.* **2004**, *17*, 567–571.
- [11] A. R. Osborn, E. Whalley, *Can. J. Chem.* **1961**, *39*, 1094–1100.
- [12] E. Whalley, *Adv. Phys. Org. Chem.* **1964**, *2*, 93–161.
- [13] E. K. Thornton, E. R. Thornton, in *Transition States of Biochemical Processes*, (Eds: R. Gandour, R. L. Schowen), Plenum, New York, **1978**, pp. 31–34.
- [14] K. J. Laidler, *Chemical Kinetics*, 3rd edn, Harper & Row, New York, **1987**, p. 95.
- [15] K. S. Pitzer, *Quantum Chemistry*, Prentice-Hall, New York, **1953**, section 9h and appendix 18.
- [16] G. N. Lewis, M. Randall, Revised by K. S. Pitzer, L. Brewer, *Thermodynamics*, 2nd edn, McGraw-Hill, New York, **1961**, p. 446.
- [17] S. W. Benson, *Thermochemical Kinetics*, Wiley, New York, **1968**, p. 213.
- [18] G. Williams, N. L. Owen, J. Sheridan, *Trans. Faraday Soc.* **1971**, *67*, 922–949.
- [19] J. Sheridan, W. Bossert, A. Bauder, *J. Mol. Spectrosc.* **1980**, *80*, 1–11.
- [20] A. N. Krasovskii, K. K. Kalnin'sh, B. S. Zhorov, *J. Appl. Spectrosc.* **1978**, *29*, 1212–1216.
- [21] X. Yu, J. Pfaendtner, L. J. Broadbelt, *J. Phys. Chem. A* **2008**, *112*, 6772–6782.
- [22] D. M. Pawar, K. K. Wilson, E. A. Noe, *J. Org. Chem.* **2000**, *65*, 1552–1553.
- [23] J. E. Leffler, E. Grunwald, *Rates and Equilibria of Organic Reactions*, Dover, New York, **1989**, 116–117.
- [24] J. E. Leffler, E. Grunwald, *Rates and Equilibria of Organic Reactions*, Dover, New York, **1989**, 141.
- [25] Second-order rate constants for the acid-catalysed hydrolysis of HO—CH₂—CO₂Et and MeO—CH₂—CO₂Et at 25°C are $1.20 \times 10^{-4} \text{ s}^{-1} (\text{mol dm}^{-3})^{-1}$ and $6.55 \times 10^{-5} \text{ s}^{-1} (\text{mol dm}^{-3})^{-1}$ in water solvent, respectively. The corresponding value for H—CO₂Et is $3.00 \times 10^{-3} \text{ s}^{-1} (\text{mol dm}^{-3})^{-1}$. National Bureau of Standards. *Tables of Chemical Kinetics – Homogeneous Reactions*, NBS, Washington, DC, **1951**.
- [26] M. S. Newman, in *Steric Effects in Organic Chemistry*, (Ed.: M. S. Newman), Wiley, New York, **1956**, 205.
- [27] W. J. Glover, R. E. Larsen, B. J. Schwartz, *J. Phys. Chem. Lett.* **2010**, *1*, 165–169.
- [28] S. A. Wildman, G. M. Crippen, *J. Chem. Inf. Comput. Sci.* **1999**, *39*, 868–873. The empirical correlation found is $\sigma_{\alpha}/\text{kJ mol}^{-1} = -0.16 [R] - 0.28$, $r = -0.81$, $n = 22$.