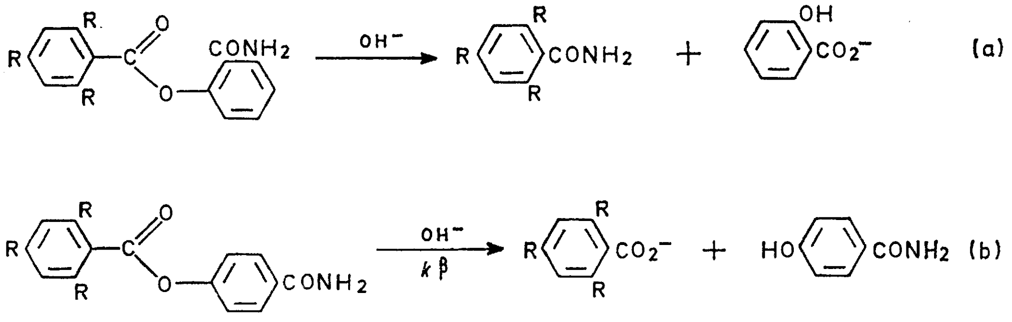
Kinetic Comparison of the Relative Susceptibility to Steric Hindrance of an Intra- and an Inter-molecular Cleavage of the Ester Bond in a Series of 2- and 4-Carbamoylphenyl Esters of 2,4,6-Trialkylated Benzoic Acids

By **Peter L. Russell** and **Richard M. Topping,*** School of Molecular Sciences, University of Sussex, Falmer, Brighton BN1 9QJ, Sussex

The rates of intramolecular nucleophilic attack by the amide group and of intermolecular nucleophilic attack by hydroxide ion on the ester carbonyl group of a series of carbamoylphenyl esters of 2,4,6-trialkylated benzoic acids have been determined. Both the intra- and inter-molecular processes showed a closely similar response to progressive increase of steric hindrance about the ester carbonyl group. An excellent correlation of rates along both reaction series with the steric substituent constants (E_s) derived by Taft from hydrolyses of esters of *aliphatic* acids indicated that progressive decoupling of the aromatic ring and the ester group with increasing 2,6-substitution was negligible (except when the substituent is hydrogen).

In the kinetic measurement of the effects of steric hindrance upon reaction rate it is usual to observe mechanistic changes (or the incursion of different reactions) in reaction series which involve large variations in steric effects. For example, methyl mesitoate is hydrolysed *via* acyl–oxygen fission in 65% dioxan–water under alkaline conditions while methyl 2,4,6-tri-t-butylbenzoate is hydrolysed *via* alkyl–oxygen fission under the same conditions.[1] The basis of a system which avoids this difficulty by repressing potential side-reactions in parallel with the principal reaction and which provides unequivocal evidence of consistency of mechanism has recently been investigated in this laboratory [2] [Scheme 1(a)]. This paper describes a kinetic investigation of this rearrangement for the series R = H, Me, Et, Pr^i, and Bu^t and makes a comparison of the results with Taft's aliphatically derived E_s values and also with the intermolecular alkaline hydrolysis of esters of similarly substituted acids [Scheme 1(b)].



Scheme 1

RESULTS

Topping and Tutt [2] have shown that 2-carbamoylphenyl mesitoate (Ic) treated with alkali under vigorous conditions (2M-NaOH for 3 days at 100°) yielded only mesitamide (IIIc) and salicylic acid. Under milder conditions [10^{-4}M-(Ic); pH 10 (carbonate buffer); 9.5% ethanol–water, μ 1.0M; 30°] we observed spectrophotometrically (200—

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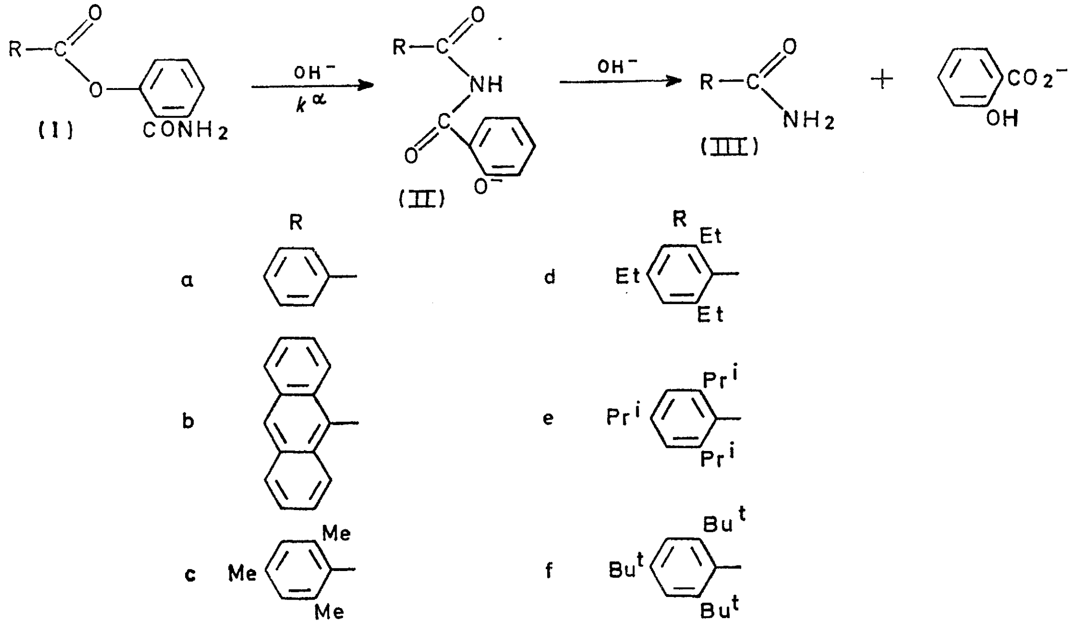
[1] L. R. C. Barclay, N. D. Hall, and G. A. Cooke, *Canad. J. Chem.*, 1962, **40**, 1981.

[2] R. M. Topping and D. E. Tutt, *J. Chem. Soc.* (*B*), 1967, **1346**; 1969, 104.

450 nm) the formation of the intermediate imide (IIc) followed by its much slower conversion to a mixture of mesitamide (10^{-4}M) and salicylic acid (10^{-4}M). This reaction sequence is shown in Scheme 2.

An analogous sequence of reactions was observed for the esters (Ib—f) resulting in complete conversion to amide (IIIb—f) and salicylic acid only. For ester (Ia), formation of salicylamide (13%) was also observed as a consequence of concurrent attack at both carbonyl groups of the precursor (IIa). From a knowledge of the half-lives of reactants and intermediate imides it was possible to isolate quantitatively the dicarbonylimines (IIa—e). The ester (If) however did not undergo observable reaction at 30° even in 1M-KOH and at the higher temperatures (80—125°) at which reaction occurred, hydrolysis of the dicarbonylimine (IIf) was rapid compared with its formation. The final spectrum was however always exactly superimposed by the spectrum of a corresponding mixture of 2,4,6-tri-t-butylbenzamide and salicylic acid under the same conditions. The nature of the products thus indicates that as in all other cases under all conditions the reaction must have proceeded entirely through the dicarbonylimine.



Scheme 2

Rearrangement of Esters (Ia—e).—The rates of formation of the dicarbonylimines (IIa—e) (Scheme 2) were followed by measuring the increase in absorbance at 365 nm (corresponding to formation of the dicarbonylimine anion) as a function of time [10^{-4}M-(Ia—e); various pH* † values; constant buffer concentration (0.1M); solvent 47.5% or 9.5% ethanol–water; μ 1.0M; 30°]. The rates of dicarbonylimine formation and hydrolysis were shown to be independent of the nature and concentration of buffer species. Values of pH were chosen such that the half-lives of the esters varied typically between 5 and 100 min. The rates of appearance of dicarbonylimines obeyed apparent first-order rate laws often to more than 90% reaction. Exact superimposition of the spectrum (250—450 nm) of the reaction mixture upon the spectrum of the appropriate dicarbonylimine indicated 100% conversion of ester. A selection of typical first-order plots for conversion of (Ia—e) to (IIa—e) is shown in Figure 1. Plots of the logarithms of the observed pseudo-first-order rate constants (log k^{α}_{obs}) for formation of (IIa—e) against pH* are shown in Figure 2. These plots reveal a first order dependence in hydroxide ion in each case, resulting in an overall rate law as in equation (1). Values of k^{α}_{II}, the second-order rate

$$d[(\text{IIa—e})]/dt = k^{\alpha}_{\text{II}}[(\text{Ia—e})][\text{OH}^-] \qquad (1)$$

constants for dicarbonylimine formation are listed in the Table.

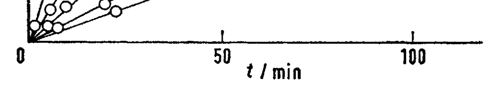


FIGURE 1 First-order plots for the formation of dicarbonylimines (II) from esters (I) at various pH* in 47.5% ethanol–water (μ 1.0M; 30°)

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† For the purpose of this work pH* values refer to the observed pH readings (glass–calomel electrode) obtained from test solutions [47.5% ethanol–water; buffer 0.1M; μ 1.0M; 30°] after calibrating the pH-meter using standard aqueous buffer solutions. A plot of pH* against measured pH in water is linear and follows the equation pH = pH* − 0.91. Second-order rate constants are calculated using pH values derived from this equation.

Rearrangement of Ester (If).—As noted above the rearrangement of the very severely hindered ester (If) is undetectable at 30° even at high pH. This reaction was therefore studied at higher temperatures [2×10^{-4}M-(If); 1M-KOH; 47.5% ethanol–water; $\mu = 1.0$M; 80—125°] utilising silver-lined stainless steel reaction vessels. Spectrophotometric analysis of the reacting mixture indicated only transient existence of the intermediate (IIf) and the reaction was therefore followed by measuring increasing absorbance at 300 nm (salicylic acid) at various temperatures. Imprecise isosbestic points were observed at 279 and 343 nm and the measured rates showed small deviations from apparent first-order rate laws. The deviations were greatest at the higher temperatures when the maximum intensity of a peak at 365 nm indicative of intermediate dicarbonylimine was also greatest. On the basis of the measured extinction coefficients of the (IIa—e), the maximum likely extinction coefficient at 365 nm of (IIf) is 6 600 giving a maximum concentration of (IIf) in any run of 2.2×10^{-5}M [2×10^{-4}M-(If); 124°]. This represents only *ca.* 11% of the original ester concentration. Recalculation of the rate of rearrangement of (If) in terms of formation of [salicylic acid + (IIf)] resulted in close adherence to pseudo-first-order kinetics. A least squares plot of the logarithm of the observed first-order rate constants for rearrangement of (If) against $1/T$ gave an apparent first-order rate constant (k^{α}_{obs}) at 30° of $(4.1 \pm 2.6) \times 10^{-6}$ min^{-1}, a calculated second-order rate constant of $(5.6 \pm 3.7) \times 10^{-6}$ l mol^{-1} min^{-1} and an activation energy (E_a) of 23.9 ± 1.6 kcal mol^{-1}.

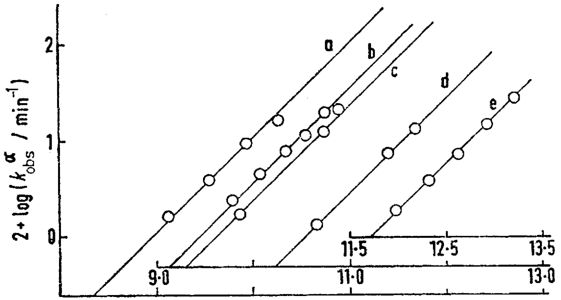


FIGURE 2 Linear dependence on pH* of the logarithms of the pseudo-first-order rate constants (log k^{α}_{obs}) for the rearrangement of esters (Ia—e) to dicarbonylimines (IIa—e) in 47.5% ethanol–water (μ 1.0M; 30°)

Second-order rate constants (47.5% ethanol–water; μ 1.0M; 30°) for the cleavage of esters (Ia—f) and (IVa—f)

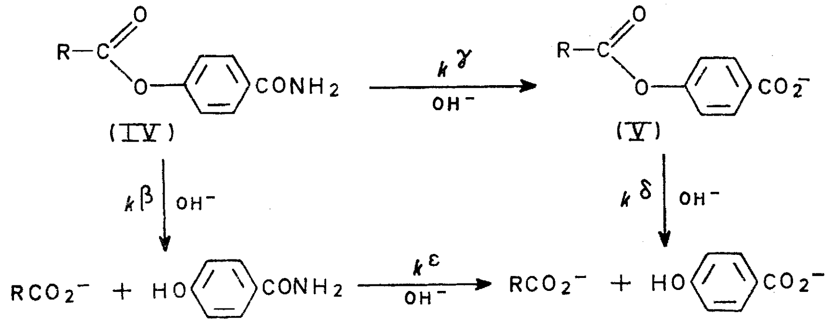
Ester series	Second-order rate constants for formation of dicarbonylimines (II) (k^{α}_{II}/l mol^{-1} min^{-1})	Second-order rate constants for formation of *p*-hydroxybenzamide (k^{β}_{II}/l mol^{-1} min^{-1})
a	$(6.8 \pm 0.4) \times 10^{5}$	50 ± 2
b	$(20.3 \pm 0.7) \times 10^{2}$	$(1.56 \pm 0.08) \times 10^{-2}$
c	$(14 \pm 0.9) \times 10^{2}$	$(5.6 \pm 0.3) \times 10^{-3}$
d	$(16.6 \pm 0.5) \times 10$	$(8.6 \pm 0.5) \times 10^{-4}$
e	10.4 ± 0.4	$(6.8 \pm 6) \times 10^{-5}$
	$(5.6 \pm 3.7) \times 10^{-6}$	(1.5×10^{-9}) *

* Estimated maximum value.

Rearrangement of the esters (Ic—e) was also examined in 9.5% ethanol–water at various pH. The reactions proceeded in an analogous manner to that observed using 47.5% ethanol–water. Again first-order dependences in ester and hydroxide ion were observed and a linear-free energy relationship was realised between rates in the two solvent systems with a rate factor of 1.9 in favour of the solvent with higher ethanol content.

Hydrolysis of 4-Carbamoylphenyl Esters (IVa—f).—The rates of hydrolysis of 4-carbamoylphenyl esters (IVa—f) were studied under comparable conditions to those used for the rearrangement of esters (Ia—f) [*e.g.* 2.5×10^{-5}M-(IVa—f); various pH* values; 47.5% ethanol–water; μ 1.0M; various temperatures]. A general reaction scheme which covers the behaviour of all six esters is shown in Scheme 3.

Hydrolysis of esters (IVa—c) resulted in 100% conversion into the corresponding acid and *p*-hydroxybenzamide only. These rates were followed by measuring the increase in absorbance at 295 nm (*p*-hydroxybenzamide anion) with time at 30°; half-lives varied typically between 60 and 700 min. No hydrolysis of *p*-hydroxybenzamide was observed during the course of these reactions and its rate of appearance obeyed an apparent first-order rate law (often to >80% reaction). First-order plots for hydrolysis of esters (IVa—c) are shown in Figure 3, and the first-order dependence in hydroxide ion is shown by the plot of log k^{β}_{obs} *versus* pH* in Figure 4. Values of k^{β}_{II}, the second-order rate constants for hydrolysis of these esters are listed in the Table.



SCHEME 3 R as in Scheme

Hydrolysis of Ester (IVd).—The hydrolysis of ester (IVd) [2.5×10^{-5}M-(IVd); 1M-KOH; 47.5% ethanol–water; μ 1.0M; 30°] gave rise to a change in the u.v. spectrum (225—325 nm) through an isosbestic point at 261 nm (complete after 130 h) followed by a slower change (isosbestic point at 256 nm), complete after *ca.* 900 h. The final spectrum corresponded to the formation of both *p*-hydroxybenzamide and *p*-hydroxybenzoic acid which were independently monitored at 270 and 303 nm respectively and shown to obey an apparent first-order rate law (to >90% reaction) in both cases. Second-order rate constants for formation of *p*-hydroxybenzamide (k^{β}_{II}) and *p*-hydroxybenzoic acid (k^{δ}_{II}) were 8.60×10^{-4} and 1.11×10^{-4} l mol^{-1} min^{-1} respectively.

The formation of *p*-hydroxybenzoic acid from *p*-hydroxybenzamide by direct hydrolysis was shown to be negligibly slow compared with the other reactions of Scheme 3, both by kinetic inference and by direct measurement. Using this observation and a knowledge of the final distribution of products, the second-order rate constant for formation of ester (Vd) (k^{γ}_{II}) was calculated as 9.6×10^{-4} l mol^{-1} min^{-1}.

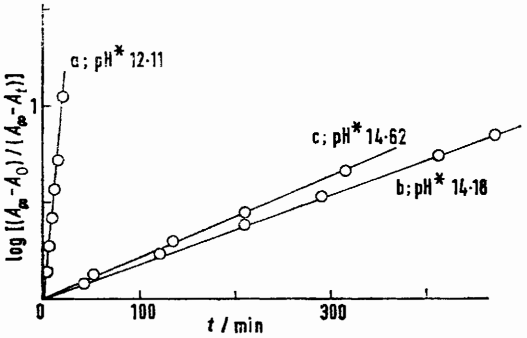


FIGURE 3 First-order plots for the hydrolysis of esters (IVa—c) at various pH* in 47.5% ethanol–water (μ 1.0M; 30°)

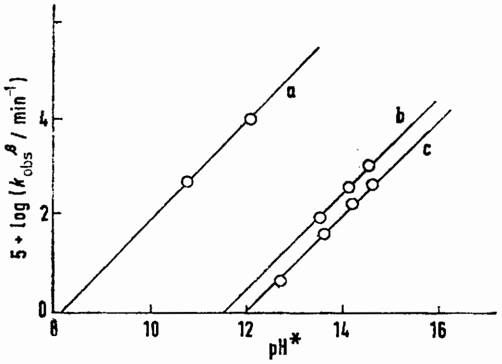


FIGURE 4 Linear dependence on pH* of the logarithms of the pseudo-first-order rate constants (log k^{β}_{obs}) for the hydrolysis of esters (IVa—c) in 47.5% ethanol–water (μ 1.0M; 30°)

Hydrolysis of Ester (IVe).—The hydrolysis of ester (IVe) was too slow to measure at 30°, even in the presence of 1M-KOH, and the same procedure was adopted as used for ester (Ie) [*i.e.* 2.5×10^{-5}M-(IVe); 1M-KOH; 47.5% ethanol–water; μ = 1.0M; various temperatures between 98 and 140° using silver-lined reaction vessels].

The formation of *p*-hydroxybenzoic acid (279 nm) followed an apparent first-order rate law over the temperature range studied (often to >80% reaction) and no *p*-hydroxybenzamide was detected. This indicated hydrolysis of amide-ester (IVe) to acid-ester (Ve) which then undergoes a slower hydrolysis to *p*-hydroxybenzoic acid and 2,4,6-tri-isopropylbenzoic acid.

A plot of the logarithm of the observed apparent first-order rate constants for formation of *p*-hydroxybenzoic acid (log k^{δ}_{obs}) against $1/T$ gave an apparent first-order rate constant (k^{δ}_{obs}) at 30° of $(6.4 \pm 4.9) \times 10^{-6}$ min^{-1}, a calculated second-order rate constant of $(8.7 \pm 6.6) \times 10^{-6}$ l mol^{-1} min^{-1} and activation energy (E_a) of 20 ± 1.7 kcal mol^{-1}.

Application of the Hammett postulate to the reactions of Scheme 3 (assuming the same reaction constant ρ for the k^{β} and k^{δ} steps) leads to expression (2) and to a value for

$$\log (k^{\delta}_{\text{II}}/k^{\beta}_{\text{II}})_{\text{Et}} = \log (k^{\delta}_{\text{II}}/k^{\beta}_{\text{II}})_{\text{Pr}^i} \qquad (2)$$

the second-order rate constant for formation of *p*-hydroxybenzamide from ester (IVe) or $(6.8 \pm 6) \times 10^{-5}$ l mol^{-1} min^{-1} (Table).

Hydrolysis of Ester (IVf).—The hydrolysis of ester (IVf) was too slow to measure conveniently under comparable conditions to the previous esters, even at 200°. Imprecise temperature control and incursion of a background absorption made the accurate measurement of reaction rate impossible. However, based upon the absorbance at 279 nm (*p*-hydroxybenzoic acid dianion) and assuming an activation energy for the hydrolysis of ester (IVf) comparable with that of (IVe), a maximum value for the second-order rate constant k^{β}_{II} for hydrolysis at 30° is 1.5×10^{-9} l mol^{-1} min^{-1}.

DISCUSSION

A kinetic evaluation of relative steric effects on intramolecular and intermolecular processes has been made using the reactions outlined in Scheme 1. The second-order rate constants for (intramolecular) dicarbonyl imine formation from the 2-carbamoylphenyl esters (Ia—f) and for the much slower (intermolecular) formation of *p*-hydroxybenzamide from the 4-carbamoylphenyl esters (IVa—f) are given in the Table.

For both reaction series there is a progressive decrease in rate with an increase in the spatial requirements of the 2,6-alkyl substituents, R. The change R = Me to R = Et to R = Pr^i results in a successive decrease in rate roughly by a factor of 10. The profound rate effect ($>10^6$) resulting from substitution of the final α-H (to give R = Bu^t) presumably arises from the consequent inability of the Bu^t substituent to rotate through a conformation in which only a proton is presented to the incoming nucleophile.[3]

In the intramolecular reaction series consistency of mechanism over a rate variation of 1.2×10^{11} is indicated by 100% conversion of the esters (Ia—f) to the corresponding dicarbonylimines. In the intermolecular reaction series, competitive hydrolysis of the amide group to carboxylic acid, which is not subject to steric hindrance, becomes important for esters (IVd and e) and the same reaction is not preserved throughout the series. Thus the second-order rate constant for hydrolysis of 4-carbamoylphenyl 2,4,6-triethylbenzoate (IVd) to 4-carboxyphenyl 2,4,6-triethylbenzoate (Vd) is 9.6×10^{-4} l mol^{-1} min^{-1}, comparable with the rate constant for hydrolysis of the ester linkage, in this case

[3] B. M. Wepster, *Progr. Stereochem.*, 1958, **2**, 110.

of 8.6×10^{-4} l mol^{-1} min^{-1}. The rates of the several pathways of Scheme 3 have, however, been separately determined, and the second-order constants quoted in the Table refer to the k^β hydrolysis step to produce *p*-hydroxybenzamide. With reference to these figures, the (extrapolated) second-order rate constant at 30° for rearrangement of 2-carbamoylphenyl 2,4,6-tri-t-butylbenzoate (If) is 5.6×10^{-6} l mol^{-1} min^{-1}. Since no hydrolysis of the 2-carbamoyl group is observed in this ester, this hydrolysis must be at least 170 times more difficult than the hydrolysis of the 4-carbamoyl groups of the esters (IVa—f), presumably for steric reasons.

A plot of the logarithms of the second-order rate constants for dicarbonylimine formation from esters (Ia—e) (log k^α_{II}) *versus* the logarithms of the second-order rate constants for formation of *p*-hydroxybenzamide from esters (IVa—e) (5 + log k^β_{II}) is given in Figure 5. All points (except a which corresponds to the unhindered benzoate esters) are close to a straight line of slope +1.0. In order to allow for any variation in polar effects in moving along a given series a ' polar ' correction factor has been applied to the rate constants of the Table and the results plotted in Figure 6. The correction was computed on the basis of a composite substituent constant for the combined polar effects of the three alkyl groups [$\Sigma\sigma$ values: H, 0; anthryl, −0.83; Me, −0.61; Et, −0.55; Pr^i, −0.55; Bu^t, −0.71 (see ref. 4 for method of calculation)] and the application of the Taft [5] equation using ρ^* +2.5 (derived for the alkaline hydrolysis of *ortho*-substituted benzoates). The composite constants $\Sigma\sigma$ were calculated using Hammett σ_p values for the alkyl groups and consequently probably overestimate polar effects, but the *variation* in the total contribution of polar effects throughout a given series is so small as not to constitute a serious source of error.

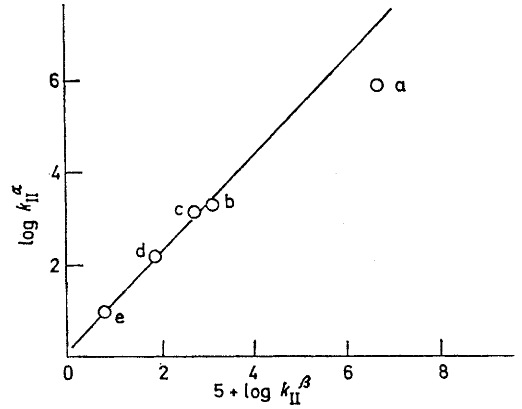


FIGURE 5 Plot of the logarithms of the second-order rate constants for dicarbonylimine formation from esters (Ia—e) (log k^α_{II}) *versus* the logarithms of the second-order rate constants for formation of *p*-hydroxybenzamide from esters (IVa—e) (5 + log k^β_{II})

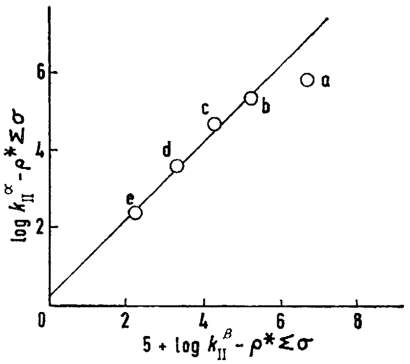


FIGURE 6 Plot of corrected values of the logarithms of the second-order rate constants for dicarbonylimine formation from esters (Ia—e) (log $k^\alpha_{\text{II}} - \rho^*\Sigma\sigma$) *versus* the logarithms of the second-order rate constants for formation of *p*-hydroxybenzamide from esters (IVa—e), similarly corrected for polar effects (5 + log $k^\beta_{\text{II}} - \rho^*\Sigma\sigma$)

As before all points (except a) lie close to a straight line of unit slope indicating that a linear steric energy relationship exists between the two series and that the relative susceptibility of both series to steric effects is identical. Such an identical response even between an intramolecular rearrangement leading to the formation of a dicarbonylimine and an intermolecular ester hydrolysis supports the general contentions of transition state theory but was observed only because in both series the increasing bulk about the ester carbonyl group in no way disturbed the essential geometry of the reaction. The obvious exceptions are the unhindered esters (Ia) and (IVa). Whereas for four pairs of esters [(Ib—e), (IVb—e)] the ratio of the second-order rate constants for the intra- and inter-molecular processes has an approximately constant value of $10^{5.2}$, the corresponding ratio for the 2- and 4-carbamoylphenyl esters of benzoic acid [(Ia) and (IVa)] falls by a factor of twelve to $10^{4.13}$ and as a result these esters do not obey the linear relationships of Figures 5 and 6. The reason probably lies in the basic differences in conformational stability between esters (Ia) and (IVa) and (Ib—f) and (IVb—f). In the former, the ester carbonyl group can lie close to the plane of the aromatic ring which carries it and addition to the carbonyl group can take place with minimal interference from *ortho*-hydrogen. In the latter the carbonyl group has rotated and approaches orthogonality to the plane of the aromatic ring. As a result resonance interactions between carbonyl group and ring remain virtually constant * for series (b—f) while steric effects are maximised by direct obstruction of the

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* The energy due to mesomerism in a species as a function of the angle of twist between two groups taking part in the mesomerism can be approximated by a $\cos^2$ function.[6] Thus even at rotation angles as low as 70°, more than 90% of resonance decoupling has taken place.

[4] J. Hine, ' Physical Organic Chemistry,' McGraw-Hill, New York, 1962, 2nd edn., p. 92.

[5] R. W. Taft, jun., in M. S. Newman, ' Steric Effects in Organic Chemistry,' Wiley, New York, 1956, ch. 13 and references therein.

[6] Ref. 3, p. 99.

preferred line of attack at carbonyl carbon by the 2,6-substituents.

Support for this interpretation is given by a plot of log k^{α}_{II} (the rate of intramolecular rearrangement to dicarbonylimine) against corresponding steric substituent constants (E_s) derived by Taft [5] from the groups R^1 in the hydrolysis of esters of *aliphatic* acids $R^1CO_2R^2$ (Figure 7).

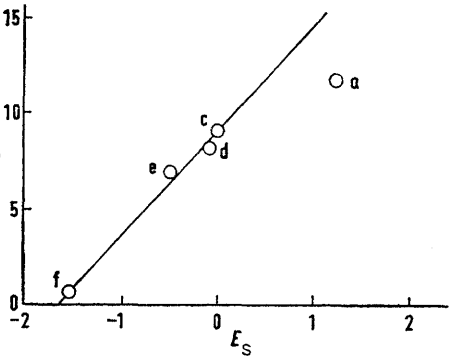

FIGURE 7 Plot of the logarithms of the second-order rate constants for dicarbonylimine formation from esters (Ia—f) ($6 + \log k^{\alpha}_{\text{II}}$) *versus* Taft E_s values

The linear relationship holds reasonably well for all points (except R = H) and covers a range of 10^8 in rate. It follows from Figure 6 that a similar relationship is followed for the intermolecular hydrolysis of esters (IV). The slope of both plots is the same and gives a value for the steric reaction constant (δ) for both reactions of +5.44, indicating an equivalent and very large dependence of rate in both reaction series upon steric factors.†

EXPERIMENTAL

2- and 4-Carbamoylphenyl benzoates,[8,9] 2- and 4-carbamoylphenyl 2,4,6-trimethylbenzoates,[2,10] *N*-salicyloylbenzamide,[8] 2,4,6-trimethyl-*N*-salicyloylbenzamide,[2,10] 4-hydroxybenzamide,[11] and 2-cyanophenol [12] were prepared according to the literature.

Preparation of 2-*Carbamoylphenyl* 2,4,6-*Trialkylbenzoates* (Id *and* e).—A mixture of 2,4,6-trialkylbenzoyl chloride (0.03 mol) and salicylamide (0.13 mol) in anhydrous pyridine was set aside at room temperature for 7—10 days before acidifying with 2N-hydrochloric acid. After separation of the aqueous phase the residual red oil was dissolved in ethyl acetate [for (Id)] or benzene [for (Ie)], passed down a silica gel column, and washed with cold 2N-sodium hydroxide and water. Solvent was removed and the crude ester recrystallised from benzene–light petroleum (b.p. 60—80°): *ester* (Id), m.p. 134—136° (Found: C, 73.8; H, 7.1; N, 4.5. $C_{20}H_{23}NO_3$ requires C, 73.8; H, 7.1; N, 4.3%), *m/e* 325 (M^+); *ester* (Ie), m.p. 217—218° (Found: C, 75.2; H, 7.9; N, 3.8. $C_{23}H_{29}NO_3$ requires C, 75.2; H, 7.95; N, 3.8%), *m/e* 367 (M^+).

Preparation of 2-*Carbamoylphenyl* 2,4,6-*Tri-t-butylbenzoate* (If).—Application of the method used in the preparation of esters (Id and e) to the preparation of (If) failed. The method was successfully applied, however, to the preparation of 2-cyanophenyl 2,4,6-tri-t-butylbenzoate which was converted to (If) by treatment with alkaline hydrogen peroxide. A mixture of 2,4,6-tri-t-butylbenzoyl chloride (3.6 g, 0.012 mol) and 2-cyanophenol (2 g, 0.017 mol) in anhydrous pyridine (25 ml) was heated at 170° for 4 h, set aside at room temperature overnight, acidified with concentrated hydrochloric acid. The crude ester was removed by filtration and washed with cold 2N-sodium hydroxide and water. The resultant 2-*cyanophenyl* 2,4,6-*tri-t-butylbenzoate* was recrystallised from aqueous alcohol followed by light petroleum (b.p. 80—100°) to give needles, m.p. 160—162° (Found: C, 80.1; H, 8.8; N, 3.6. $C_{26}H_{33}NO_2$ requires C, 79.8; H, 8.5; N, 3.6%), *m/e* 392 (M^+). A mixture of this ester (0.005 mol), acetone (350 ml), water (50 ml), 2N-sodium hydroxide (20 ml), and 30% hydrogen peroxide (70 ml) was set aside at room temperature for 14 days. Addition of water (400 ml) and removal of acetone gave a solid which was dissolved in ether, washed with 2N-sodium hydroxide and water, dried ($MgSO_4$), and after removal of ether, recrystallised from light petroleum (b.p. 80—100°) to give *ester* (If), m.p. 172—173° (Found: C, 76.3; H, 8.7; N, 3.45. $C_{26}H_{35}NO_3$ requires C, 76.3; H, 8.6; N, 3.4%), *m/e* 409 (M^+).

Preparation of 4-*Carbamoylphenyl* 2,4,6-*Trialkylbenzoates* (IVd—f).—Esters (IVd and e) were prepared by essentially the same procedures as used for the 2-isomers. *Ester* (IVd) had m.p. 182—183° (from toluene) (Found: C, 73.8; H, 7.1; N, 4.4. $C_{20}H_{23}NO_3$ requires C, 73.8; H, 7.1; N, 4.3%), *m/e* 324 (M^+). *Ester* (IVe) had m.p. 202—204° [from benzene–light petroleum (b.p. 60—80°)] (Found: C, 75.5; H, 8.0; N, 3.9. $C_{23}H_{29}NO_3$ requires C, 75.2; H, 7.95; N, 3.8%), *m/e* 367 (M^+).

4-Carbamoylphenyl and 4-cyanophenyl 2,4,6-tri-t-butylbenzoates were prepared by analogous procedures to the corresponding 2-isomers. *Ester* (IVf) had m.p. 225—227° (from alcohol) (Found: C, 75.9; H, 8.8; N, 3.5. $C_{26}H_{35}NO_3$ requires C, 76.3; H, 8.7; N, 3.45%), *m/e* 409 (M^+). The *cyano-ester* had m.p. 138—140° (from alcohol) (Found: C, 80.4; H, 8.6; N, 3.7. $C_{26}H_{33}NO_2$ requires C, 78.8; H, 8.5; N, 3.6%), *m/e* 392 (M^+).

Preparation of 2,4,6-*Trialkyl*-N-*salicyloylbenzamides* (IId *and* e).—Compounds (IId and e) were prepared by rearrangement of esters (Id and e) respectively in absolute alcohol at pH* 13.7 (KOH) and room temperature. After completion of the reaction [(Id) 3 min; (Ie) 30 min], concentrated hydrochloric acid was added to pH 2, the solvent was removed under reduced pressure, and the residual solid was extracted into benzene and finally recrystallised from benzene–light petroleum (b.p. 60—80°): (IId) m.p. 124—125° (Found: C, 74.1; H, 7.0; N, 4.45. $C_{20}H_{23}NO_3$ requires C, 73.8; H, 7.1; N, 4.3%), *m/e* 325 (M^+). (IIe) m.p. 195—198° (Found: C, 75.4; H, 8.0;

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† The largest steric reaction constant derived from kinetic data listed by Taft [5] is for the reaction of methyl iodide with 2-alkylpyridines [7] and has a value of 2.065.

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N, 4.1. $C_{23}H_{29}NO_3$ requires C, 75.2; H, 7.95; N, 3.8%), *m/e* 367 (M^+). Both (IId and e) gave clear spectroscopic evidence of tautomeric behaviour which is being further investigated.

Solvents.—The solvent used for kinetic measurements was either 47.5% ethanol–water, prepared by diluting 47.5 ml of pure dry ethanol with 52.5 ml of water (deionised, followed by distillation under nitrogen in all glass apparatus) or 9.5% ethanol–water.

Apparatus.—The u.v. spectrometers and pH-meters and electrode assembly have been described previously.[2] Reactions studied at elevated temperatures (75—200°) could not be followed satisfactorily in either alkali-resistant glass or stainless steel reaction vessels owing to the incursion of a background absorption in the region of interest (200—450 nm). Similar interference has been noted previously.[13-15] The problem was overcome by using stainless steel ampoules (*ca.* 5 ml) lined with silver shells when even at the higher temperatures and base concentrations no significant background absorption developed. Constant temperatures were maintained using a thermostatted oil-bath filled with Shell Voluta oil.

Kinetic Procedure.—All kinetic experiments at 30 ± 0.1° were carried out in the solvents described at a calculated ionic strength of 1.0M (with KCl). Buffers [carbonate (0.1M) or phosphate (0.05 or 0.1M)] were used to control pH (or pH*) below pH 12, and pH measurements were checked before and after each run. The experiments at high temperatures and high pH were initiated by mixing an aliquot portion of the appropriate ester solution with an aliquot portion of the proper potassium hydroxide solution. A measured sample of this reaction mixture was pipetted into each of eight silver-lined ampoules and the vessels were sealed and completely immersed in the oil-bath at the required temperature. The time of immersion was reckoned as zero. Ampoules were removed at appropriate intervals, quenched in an ice-bath, and the contents analysed spectrophotometrically. General kinetic procedures and methods for the calculation of rate constants are as described previously.[2]

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