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# Occurrence of an Elongated *p*-Oxo Ketene Intermediate in the Dissociative Alkaline Hydrolysis of Aryl (2*E*,4*E*)-5-(4′-Hydroxyphenyl)pentadienoates

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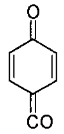
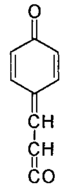
The alkaline hydrolysis of title esters possessing acidic leaving groups follows an E1cB mechanism involving the participation of an “extra extended” *p*-oxo ketene intermediate. For the hydrolysis of the 2,4-dinitrophenyl ester kinetic data, activation parameters and trapping of the intermediate clearly indicate that the dissociative pathway carries the reaction flux. Break in the Brønsted plot of the apparent second-order rate constants versus the p$K_a$ of the leaving group suggests that the reaction mechanism changes from E1cB to $B_{Ac}2$ for esters having p$K_a$ higher than about 6.

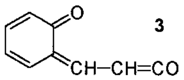
In the course of our studies on acyl transfer reactions we have at first provided evidence that alkaline hydrolysis of aryl esters of 4-hydroxybenzoic acid occurs through either associative ($B_{Ac}2$) or dissociative (E1cB, via intermediate **1**) mechanisms, depending on the basicity of the leaving group.[1] We have subsequently shown that the hydrolyses of aryl 4-hydroxycinnamates[2] and 2-hydroxycinnamates[3] in dioxane-water mixtures follow the same mechanism with the participation, in their dissociative paths, of the “extended” oxo ketene intermediates 2 and 3, respectively.



**1**



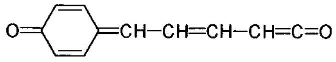
**2**



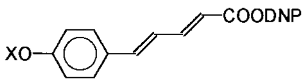
We have thus found that the dissociative mechanism carries the reaction flux when the internal nucleophile (the hydroxyl group) is $\pi$-conjugated with the reaction center in esters of the type HO-$\pi$-COOAr: the intervening backbone being a single $\pi$-system, the aromatic ring in the case of 4-hydroxybenzoates, or two $\pi$-units in the case of hydroxycinnamates. Interposition of an extra vinylene group between the internal nucleophile and the reaction center seems to favor the dissociative mechanism. We suggested that the observed reactivity enhancement could be due to an increased stability of the “extended” intermediates which, in turn, can be ascribed to a more extended delocalization of $\pi$ electrons. Analogous results come from our recent studies[4] on dissociative sulfonyl group transfer reactions where “extended” sulfoquinone intermediates are involved.

To improve the understanding of the effects of structural modifications of the $\pi$ backbone on the hydrolytic pathways, aiming to increase our knowledge on the factors that control the reaction flux (associative vs. dissociative) in ester hydrolysis (*inter alia*, stability of the putative unsaturated intermediate), we have successively directed our attention toward other esters possessing different molecular architecture such as two aromatic $\pi$ systems linked by Z = Y $\pi$-conjugated systems, with Z and Y being N or CH. In other words we have further enlarged the $\pi$-conjugated backbone, these substrates possessing indeed three $\pi$ units in the bridge. In all cases our results indicate that these substrates react through the usual associative $B_{Ac}2$ mechanism,[5] and this outcome has been tentatively ascribed to an exceedingly large loss of aromaticity on going from substrate to the transition state when two *p*-phenylene units are present in the $\pi$-conjugated bridge.

Finally, in a recent communication[6] we have reported the first observation of the occurrence of the dissociative route in the hydrolysis of an acyl derivative with three $\pi$ systems (a single *p*-phenylene unit and two vinylenic groups) in its bridge: kinetic data and trapping experiments strongly support the intervention of a dissociative, E1cB-type mechanism with the participation of a new, “elongated” oxo ketene intermediate (**4**, here depicted in the *s-trans* form) in the hydrolysis of 2,4-dinitrophenyl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoate (**5b**).



**4**



**5b**: X = H; **6**: X= Me

DNP = 2,4-dinitrophenyl

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[1] (a) Cevasco, G.; Guanti, G.; Hopkins A. R.; Thea, S.; Williams, A. *J. Org. Chem.* **1985**, *50*, 479−484. (b) Thea, S.; Cevasco, G.; Guanti, G.; Kashefi-Naini, N.; Williams, A. *J. Org. Chem.* **1985**, *50*, 1867−1872.

[2] Cevasco, G.; Thea, S. *J. Org. Chem.* **1994**, *59*, 6274−6278.

[3] Cevasco, G.; Thea, S. *J. Org. Chem.* **1995**, *60*, 70−73.

[4] Cevasco, G.; Thea, S. *J. Org. Chem.* **1998**, *63*, 2125−2129.

[5] Cevasco, G.; Thea, S. *J. Org. Chem.* **1999**, *64*, 5422−5426.

[6] Cevasco, G.; Vigo, D.; Thea, S. *Org. Lett.* **1999**, *1*, 1165−1167.

10.1021/jo0008439 CCC: $19.00

**Table 1. Hydrolysis of Aryl (2*E*,4*E*)-5-(4′-Hydroxyphenyl)pentadienoates (5a−h) in 40% Dioxane at 25 °C $\mu$ and = 0.1 ($pK_w$ = 15.00)'**

| subs. | leaving substituted phenoxides | $pK_{LG}$[a] | $k_a$, $s^{-1}$ | $k_b$, $M^{-1}$ $s^{-1}$ | $k_{app}$, $M^{-1}$ $s^{-1}$ | $\log k_{app}$[b] | $N$[c] | pH[d] |
|---|---|---|---|---|---|---|---|---|
| **5a** | 2,6-dinitro | 3.71[e] | $(7.08 \pm 0.22) \times 10^{-3}$ | $(5.78 \pm 0.93) \times 10^{-2}$ | 810.89 | 2.909 | 9 | 8.71−13.99 |
| **5b** | 2,4-dinitro | 4.11 | $(1.14 \pm 0.04) \times 10^{-2}$ | $(5.25 \pm 0.41) \times 10^{-1}$ | 1418.27 | 3.152 | 11 | 8.28−13.99 |
| **5c** | 2-methyl-4,6-dinitro | 4.35[e] | $(2.65 \pm 0.04) \times 10^{-3}$ | $(2.60 \pm 0.18) \times 10^{-2}$ | 260.00 | 2.415 | 9 | 8.71−13.99 |
| **5d** | 2,5-dinitro | 5.22[e] | $(2.04 \pm 0.12) \times 10^{-4}$ | $(2.09 \pm 0.13) \times 10^{-1}$ | 22.77 | 1.357 | 8 | 8.80−13.99 |
| **5e** | 2-chloro-4-nitro | 5.45 | $(5.32 \pm 0.39) \times 10^{-5}$ | $(1.28 \pm 0.11) \times 10^{-1}$ | 3.90 | 0.592 | 8 | 9.75−13.99 |
| **5f** | 4-chloro-2-nitro | 6.46 | $(7.35 \pm 0.79) \times 10^{-6}$ | $(5.62 \pm 0.57) \times 10^{-2}$ | 0.61 | −0.212 | 8 | 9.74−13.99 |
| **5g** | 4-nitro | 7.14 | | $(1.06 \pm 0.08) \times 10^{-1}$ | | | 3 | 12.69−13.99 |
| **5h** | 4-cyano | 7.95 | $(5.96 \pm 0.58) \times 10^{-6}$ | $(6.59 \pm 0.57) \times 10^{-2}$ | 0.45 | −0.351 | 8 | 9.74−13.99 |

[a] Jencks, W. P.; Regestein, J. *Handbook of Biochemistry and Molecular Biology* 3rd ed.; Fasman, G., Ed.; Chemical Rubber Co.: Cleveland, 1976. [b] See text, $K_a$ values are taken from Table 2. [c] Number of data points, not including duplicates. [d] pH range employed. [e] Kortum, G.; Vogel, W.; Andrussov, K. *Dissociation Constants of Organic Acids in Aqueous Solution*; Butterworths: London, 1961.

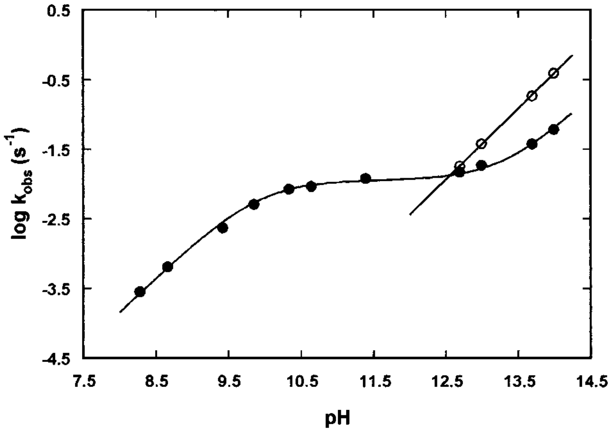

**Figure 1.** pH-rate profiles for the hydrolysis of 2,4-dinitrophenyl esters **5b** (solid circles) and **6** (open circles) in 40% (v/v) dioxane−water at 25 °C and 0.1 M ionic strength made up with KCl. Lines are calculated from eqs 1 and 2, respectively.

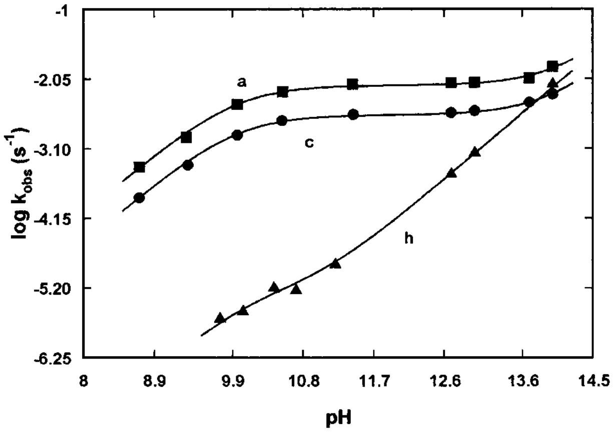

**Figure 2.** pH-rate profiles for the hydrolysis of aryl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoates in 40% (v/v) dioxane−water at 25 °C and 0.1 M ionic strength made up with KCl. Lines are calculated from eq 1; the identity of the points is given in Table 1.

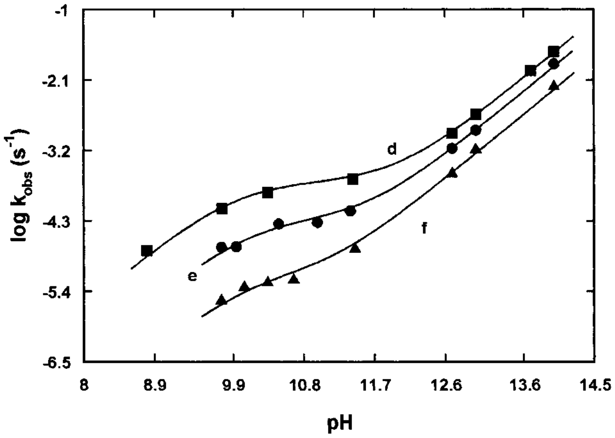

**Figure 3.** pH-rate profiles for the hydrolysis of aryl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoates in 40% (v/v) dioxane−water at 25 °C and 0.1 M ionic strength made up with KCl. Lines are calculated from eq 1; the identity of the points is given in Table 1.

We now report our results in greater detail together with new data relative to more esters suggesting the occurrence of a changeover from E1cB to $B_{Ac}2$ mechanism in the alkaline hydrolysis of aryl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoates as the $pK_a$ of the leaving phenol increases.

## Results and Discussion

The observed pseudo-first-order rate constants for the alkaline hydrolysis of aryl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoates (**5a**−**h**, see Table 1), in 40% dioxane−water (v/v) solvent at 25 °C and ionic strength 0.1 M (KCl), were found to follow eq 1.

$$k_{obs} = (k_a + k_b[OH^-])/(1 + a_H/K_a) \qquad (1)$$

The pH-rate profile for the hydrolysis of ester **5b** is illustrated in Figure 1 (●) and similar plots (Figures 2 and 3) were obtained for the other esters. In eq 1, $a_H$ is the proton activity, $k_a$ is the pseudo-first-order rate constant in the plateau region of pH, $K_a$ is the ionization constant of the hydroxyl group of the ester, and $k_b$ refers to the bimolecular attack of hydroxide ion on the ionized ester and gives rise to an upward curvature in the pH-rate profile at high pH values. In Table 1 are collected experimental conditions and the values of the kinetic parameters, obtained from primary kinetic data by iterative nonlinear curve-fitting performed with the Fig.P program,[7] for the hydrolysis of the substrates **5a**−**h**. If the reactivity of the ester under examination allows the construction of a sufficiently detailed pH-rate profile (in particular in and below the plateau region of pH) this program provides, together with the rate constants, the $K_a$ values. Table 2 indicates that the kinetic $pK_a$ values are in good agreement with those spectroscopically measured.

The dependence on pH of the pseudo-first-order rate constants for the hydrolysis of 2,4-dinitrophenyl (2*E*,4*E*)-5-(4′-methoxyphenyl)pentadienoate (**6**) is also shown in

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[7] Fig. P from Biosoft, Cambridge, UK, 1991.

**Table 2. Ionization Constants of Aryl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoates (5a−h) in 40% Dioxane at 25 °C and $\mu$ = 0.1**

| subs. | leaving substituted phenoxides | $\lambda$,[a] nm | $10^{11}K_a$, M | p$K_a$ | p$K_a$[b] |
|---|---|---|---|---|---|
| **5a** | 2,6-dinitro | 430 | 11.75 ± 0.30 | 9.93 ± 0.01 | 9.97 ± 0.04 |
| **5b** | 2,4-dinitro | 426 | 12.68 ± 0.10 | 9.90 ± 0.02 | 9.93 ± 0.04 |
| **5c** | 2-methyl-4,6-dinitro | 430 | 10.41 ± 0.40 | 9.98 ± 0.02 | 9.98 ± 0.02 |
| **5d** | 2,5-dinitro | 430 | 11.42 ± 0.20 | 9.94 ± 0.01 | 9.76 ± 0.04 |
| **5e** | 2-chloro-4-nitro | 420 | 7.51 ± 0.18 | 10.12 ± 0.01 | |
| **5f** | 4-chloro-2-nitro | 430 | 8.55 ± 0.18 | 10.07 ± 0.01 | |
| **5g** | 4-nitro | 420 | 7.79 ± 0.17 | 10.11 ± 0.01 | |
| **5h** | 4-cyano | 420 | 7.66 ± 0.22 | 10.12 ± 0.01 | |

[a] Wavelength employed for the spectroscopic determination. [b] Measured from the kinetics.

Figure 1 and indicates, as expected, a simple second-order rate law in hydroxide ion and ester concentrations (eq 2).

$$k_{\mathrm{obs}} = k_{\mathrm{OH}}[\mathrm{OH}^-] \qquad (2)$$

The $k_{\mathrm{OH}}$ value for the unambiguous $\mathrm{B_{Ac}2}$ attack of hydroxide ion on this ester, in 40% dioxane−water (v/v) solvent at 25 °C and ionic strength 0.1 M (KCl), is 3.9 ± 0.1 $\mathrm{M^{-1}\ s^{-1}}$.

The apparent second-order rate constant ($k_{\mathrm{app}} = k_aK_a/K_w$ = ca. $1.4 \times 10^3\ \mathrm{M^{-1}\ s^{-1}}$, Table 1) calculated for the attack of hydroxide ion on neutral **5b** (the p$K_w$ value of 15.00 has been reported[8] for the medium employed in this work) is larger, rather than smaller as expected ($\sigma_p$ values for OH and OMe are −0.37 and −0.27, respectively), than the second-order rate constant related to the $\mathrm{B_{Ac}2}$ attack of hydroxide ion on **6**, thus suggesting that the reactions of these esters could occur through different pathways. A better assessment, however, can be achieved by computing the rate constant ($k_{\mathrm{calc}}$) for the bimolecular attack of hydroxide ion on neutral **5b** from the Hammett relationship $\log k/k_0 = 1.97\Sigma\sigma$ for the alkaline hydrolysis of substituted 2,4-dinitrophenyl benzoates.[1a] If the attenuation factor of 0.54 related to the vinylene group[9] is taken into account, since the overall attenuation factor is given roughly by the product of those of the intervening groups,[10] the relationship becomes $\log k/k_0 = 0.57\Sigma\sigma$ and is now valid for the $\mathrm{B_{Ac}2}$ hydrolysis of substituted 2,4-dinitrophenyl (2*E*,4*E*)-5-(X-phenyl)pentadienoates. Now, from the $k_{\mathrm{OH}}$ value for **6**, using the $\sigma_p$ values for the hydroxy and methoxy groups (−0.37 and −0.27, respectively) we finally obtain $k_{\mathrm{calc}} = 3.4\ \mathrm{M^{-1}\ s^{-1}}$. The apparent second-order rate costant ($k_aK_a/K_w$, ca. 1420 $\mathrm{M^{-1}\ s^{-1}}$) for **5b** is therefore in excess of this $k_{\mathrm{calc}}$ by about 420-fold, thus confirming the suggestion that the mechanism for the $k_a$ term cannot be the associative one, and the simplest hypothesis is that an E1cB process involving the participation of the “elongated” oxo ketene **4** intermediate occurs.

Further evidence that the hydrolysis of these two esters follows different pathways is provided by the evaluation of activation entropy of the reactions (Table 3). For the hydrolysis of **5b** the value of $\Delta S^{\ddagger}$ for the $k_a$ term (measured at pH 12.69) is large and positive as expected for a unimolecular reaction, whereas the negative value of $\Delta S^{\ddagger}$ for the hydrolysis of **6** (at the same pH) is consistent with an associative process.[11]

**Table 3. Activation Parameters for the Hydrolysis of 2,4-Dinitrophenyl Esters in KOH 5 × $10^{-3}$ M, 40% Dioxane, $\mu$ = 0.1 M, pH 12.69 (at 25 °C)[a]**

| ester | $\Delta H^{\ddagger}$, kcal/mol | $\Delta S^{\ddagger}$,[b] cal/mol K |
|---|---|---|
| **5b** | 23.1 ± 0.1 | 10.4 ± 0.4 |
| **6** | 12.8 ± 0.4 | −23.8 ± 1.4 |

[a] Temperature range: 16.5−40.6 °C. [b] Calculated at 25 °C.

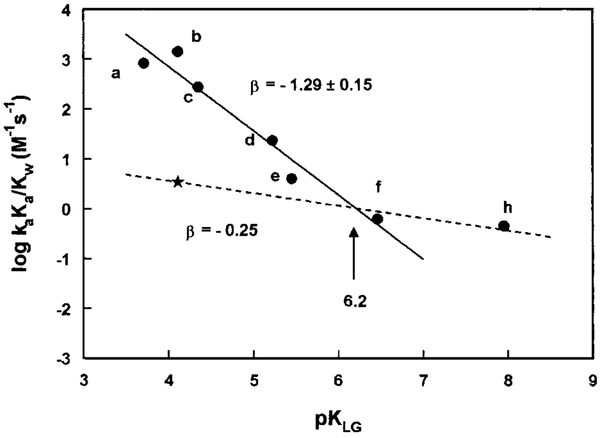

**Figure 4.** Brønsted plot for the hydrolysis of aryl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoates. The line is calculated from eq 3; for the dashed line see text; the identity of the points is given in Table 1.

The intervention of a dissociative mechanism in the hydrolysis of **5b** is also confirmed by trapping experiments carried out with added nitrogen nucleophiles. In the presence of 0.03 M *p*-toluidine, which has no effect on reaction rate, ca. 30% of *N*-(4-methylphenyl) 5-(4′-hydroxyphenyl)penta-2(*E*),4(*E*)-dienamide (**7**) was found in the hydrolysis products. This result is clearly in agreement with the proposed dissociative mechanism: the intermediate **4** is trapped by the added nucleophile after the rate-determining release of the leaving group.

The effect of the leaving group variation on reactivity was also investigated. The plot of the logarithms of the apparent second-order rate constants ($k_{\mathrm{app}} = k_aK_a/K_w$) against the p$K_a$ of the leaving substituted phenoxide (p$K_{\mathrm{LG}}$) is shown in Figure 4 (data taken from Table 1). It appears that the point **h**, corresponding to the *p*-cyanophenyl ester deviates from the Brønsted equation (eq 3) correlating the other substrates.

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(8) Arned, H. S.; Fallon, L. *J. Am. Chem. Soc.* **1931**, *61*, 2374−2378.

(9) Williams, A. *Chemistry of Enzyme Action*; Page, M. I., Ed.; Elsevier: Amsterdam, 1984; p 145.

(10) Page, M.; Williams, A. *Organic and Bioorganic Mechanisms*; Addison-Wesley Longman: Harlow, 1997; p 57.

(11) Schaleger, L. L.; Long, F. A. *Adv. Phys. Org. Chem.* **1963**, *1*, 1. Jencks, W. P. *Catalysis in Chemistry and Enzymology*; McGraw-Hill: New York, 1969. Douglas, K. T. *Prog. Bioorg. Chem.* **1976**, *4*, 194. Vlasak, P.; Mindl, J. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1401−1403. Safraoui, A.; Calmon, M.; Calmon, J.-P. *J. Chem. Soc., Perkin Trans. 2* **1991**, 1349−1352. Broxton, T. J. *Aust. J. Chem.* **1985**, *38*, 77−83.

$$\log (k_a K_a/K_w) = (8.0 \pm 0.7) - (1.3 \pm 0.2)\mathrm{p}K_{LG} \quad (3)$$

The high $\beta_{LG}$ value (−1.29) is consistent with a dissociative process,[12] thus indicating that such esters can hydrolyze through intermediate **4**, and is in good agreement with those we previously found for the E1cB hydrolysis of aryl 4-hydroxybenzoates (−1.33),[1a] 4-hydroxycinnamates (−1.32),[2] and 2-hydroxycinnamates (−1.11).[3]

Since in our previous studies we have observed a break in linearity in the Brønsted plots with upward curvature, suggesting the occurrence of a change in mechanism from E1cB to $B_{Ac}2$ as the nucleofugality of the leaving group decreases, we believe that the presently investigated substrates could behave similarly. Were this hypothesis correct, the deviation of **5h** could be simply due to the fact that the hydrolysis of this ester occurs via the associative mechanism rather than the E1cB route.

This proposal can be verified as follows. It is well-known that associative processes in acyl group transfer reactions involving carboxylic acid derivatives have $\beta_{LG}$ values restricted in a narrow range (−0.20 to −0.25). Now, if a line with a slope of −0.25 is drawn (dashed line in Figure 4) through the point indicated as (★), which represents the calculated value of the second-order rate constant ($k_{calc} = 3.4$ M$^{-1}$ s$^{-1}$, see above) for the $B_{Ac}2$-type attack of hydroxide ion on the neutral 2,4-dinitrophenyl ester **5b**, it will go across the experimental line at p$K_{LG}$ ca. 6.2 (changeover point) and the point corresponding to ester **5h** falls on this line. This strongly suggests that **5h** actually hydrolyzes through the associative pathway, thus confirming a change in mechanism. A further outcome of this finding is that in the region around the breakpoint both mechanisms can take place concurrently. Unfortunately, for practical reasons it was not possible to determine the $k_a$ value, and thus $k_{app}$, for the 4-nitrophenyl ester **5g** (p$K_{LG}$ = 7.14). Resort to the initial rates technique, dictated by the exceedingly low reactivity of this ester at pH values lower than about 12, was indeed prevented by spectral characteristics of both substrate and products. Finally, it is noteworthy that the changeover point is close in value to those previously found for related systems (i.e., 6.2 for 4-hydroxybenzoates,[1a] 6.7 for 4-hydroxycinnamates,[2] and 6.0 for 2-hydroxycinnamates[3]).

The parameter $k_b$ (see eq 1), representing the bimolecular attack of hydroxide ion on the conjugate base of the esters, fits (omitting the two esters in which the 2,6-positions of the phenolic moieties are substituted) a Brønsted equation with a slope ($\beta_{LG} = -0.21 \pm 0.06$, data from Table 1) consistent with an associative process.

It is interesting to note that the logarithms of $k_{app}$ values for aryl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoates relate very well with those of the corresponding 4-hydroxycinnamates, as shown in Figure 5. The value of the slope (0.89 ± 0.02) is less than unity thus suggesting that, for a given leaving group, the fission of the C−OAr bond in the transition state of the rate-determining step is more advanced in the case of 4-hydroxycinnamates as compared with the present system, reflecting the fact that the shorter is the π system the stronger is the interaction between internal nucleophile and reaction center. Closer inspection of this plot indicates that all the points fall nicely on the regression line, although the original Brønsted plots are somewhat scattered (see Figure 4 and ref 2). Since this behavior was observed in the cases of 4-hydroxybenzoates[1] and 2-hydroxycinnamates[3] as well, we infer that the standard equilibrium usually employed in these Brønsted-type LFER's (phenol dissociation equilibrium) may not be fully adequate, in particular when 2,6-disubstituted phenols are involved.

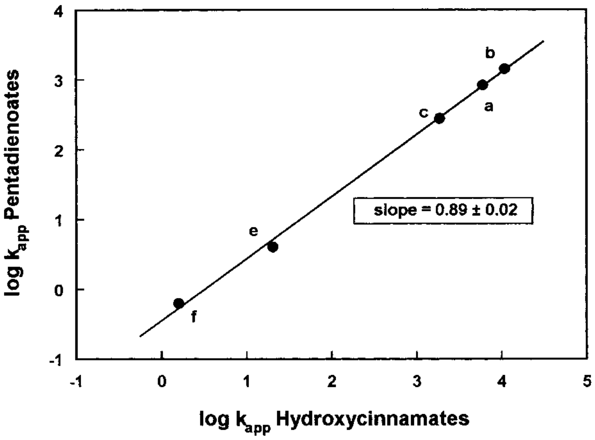

**Figure 5.** Plot of the apparent second-order rate constants for the hydrolysis of aryl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoates (this work) and the corresponding aryl 4-hydroxycinnamates (data taken from ref 2). The identity of the points is given in Table 1.

In the preliminary communication[6] we have reported that reactivity comparisons between 2,4-dinitrophenyl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoates and 4′-hydroxybenzoate indicate that the presence of additional vinylenic groups favors the hydrolytic process occurring via the dissociative pathway. Analogous results were found for 2,4-dinitrophenyl 4′-hydroxycinnamate,[2] and it was suggested that the higher reactivity of the latter (with respect to 4′-hydroxybenzoate) could be due to extra stabilization of the intermediate **2** with respect to intermediate 1, owing to a more extended delocalization of π electrons in the former.

Theoretical calculations are now planned in order to obtain additional information on the stability of the transition states leading to the intermediates **1**, **2**, and **4**.

## Experimental Section

**General.** Starting reagents and solvents were purified and/or distilled before use. Buffer materials were of analytical reagent grade. Water was double distilled and preboiled to free it from dissolved carbon dioxide. Dioxane was purged of peroxides by passage of the analytical-grade product through an activated alumina column under nitrogen; the absence of peroxides was checked by the KI test. The $^1$H NMR spectra were recorded with a 200 MHz spectrometer with TMS as internal standard and acetone-$d_6$ as solvent.

**Synthesis.** Esters **5a**−**h**, and **6** and the amide **7** were prepared starting from the corresponding acids. The acids were obtained through a Wittig-type reaction under phase-transfer conditions[13] from 4-hydroxybenzaldehyde (protected with the

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[12] Williams, A.; Douglas, K. T. *Chem. Rev.* **1975**, *75*, 627−649. Gordon, I. M.; Maskill, H.; Ruasse, M. F. *Chem. Soc. Rev.* **1989**, *18*, 123−151. Thatcher, G. R. J.; Kluger, R. *Adv. Phys. Org. Chem.* **1989**, *25*, 99−265.

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*tert*-butyldimethylsilyl group)[14] or 4-methoxybenzaldehyde, and 3-ethoxycarbonylallylidenetriphenylarsonium bromide, prepared from triphenylarsine and commercial (Aldrich) ethyl 4-bromocrotonate as described.[15] These reactions furnished, in good yield, nearly a 4:1 mixture of the *E*,*E*/*E*,*Z* isomers, as previously reported,[13] and confirmed by $^1$H NMR spectroscopy (the stereoisomers have well-resolved spectra in acetone-$d_6$, and the peak assignments and the attribution of the configurations have been conveniently carried out by a simple decoupling technique) but our attempts to obtain total conversion of the mixture of isomers into the *E*,*E* isomer by treatment with iodine in daylight[5,13] failed. The mixtures of isomers were subsequently hydrolyzed in aqueous sodium hydroxide (10%) at reflux overnight. Such prolonged heating afforded, as confirmed by $^1$H NMR spectroscopy, complete conversion to the desired *E*,*E* isomer (as stated in the preliminary communication,[6] this stereoisomer is required to ensure $\pi$ system planarity), and removal of the silyl group. The cooled solutions were washed with dichloromethane and then acidified affording the acids as crystalline precipitates which were collected and dried. Ester **6** was finally prepared from the so obtained (2*E*,4*E*)-5-(4′-methoxyphenyl)pentadienoic acid by condensation with 2,4-dinitrophenol in the presence of DCC. (2*E*,4*E*)-5-(4′-Hydroxyphenyl)pentadienoic acid was reacted with *tert*-butyldimethylchlorosilane,[14] and the bissilylated compound was subsequently treated with oxalyl chloride −DMF[16] to give, in very good yield, the acid chloride. The reaction of this chloride with the appropriate phenol or amine furnished, after removal of silyl group carried out by aqueous hydrofluoric acid,[17] the desired compounds **5a**−**h** and **7**.

The characteristics of the new compounds, purified through column chromatography and recrystallized from toluene (unless otherwise stated), were as follows; mp is given together with analytical data.

**2,6-Dinitrophenyl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoate (5a):** mp 149−150 °C (from methanol/water); 8.86 (s, 1), 8.50 (d, 2, $J$ = 8.23 Hz), 7.86 (t, 1, $J$ = 8.34 Hz), 7.74 (dd, 1, $J$ = 10.18; 15.18 Hz), 7.53 (d, 2, $J$ = 8.63 Hz), 7.14 (m, 2), 6.90 (d, 2, $J$ = 8.67 Hz), 6.24 (d, 1, $J$ = 15.18 Hz). Anal. Calcd for $C_{17}H_{12}N_2O_7$: C, 57.3; H, 3.4; N, 7.9. Found: C, 57.3; H, 3.4; N, 7.5. **2,4-Dinitrophenyl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoate (5b):** mp 207−8 °C; $\delta$ 9.01 (s, 1), 8.93 (d, 1, $J$ = 2.69 Hz), 8.69 (dd, 1, $J$ = 2.85; 9.12 Hz), 7.84 (d, 1, $J$ = 8.95 Hz), 7.74 (dd, 1, $J$ = 10.14; 15.22 Hz), 7.52 (d, 2, $J$ = 8.67 Hz), 7.21 (d, 1, $J$ = 15.31 Hz), 7.07 (dd, 1, $J$ = 10.46; 15.42 Hz), 6.90 (d, 2, $J$ = 8.75 Hz), 6.24 (d, 1, $J$ = 15.26 Hz). Anal. Calcd for $C_{17}H_{12}N_2O_7$: C, 57.3; H, 3.4; N, 7.9. Found: C, 57.4; H, 3.5; N, 7.8. **2-Methyl-4,6-dinitrophenyl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoate (5c):** mp 178−9 °C; $\delta$ 8.86 (s, 1), 8.75 (d, 1, $J$ = 2.93 Hz), 8.60 (d, 1, $J$ = 2.93 Hz), 7.77 (dd, 1, $J$ = 10.01; 15.14 Hz), 7.53 (d, 2, $J$ = 8.67 Hz), 7.14 (m, 2), 6.90 (d, 2, $J$ = 8.67 Hz), 6.28 (d, 1, $J$ = 15.14 Hz), 2.48 (s, 3). Anal. Calcd for $C_{18}H_{14}N_2O_7$: C, 58.4; H, 3.8; N, 7.5. Found: C, 58.8; H, 3.9; N, 7.2. **2,5-Dinitrophenyl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoate (5d):** mp 170−2 °C; 8.83 (s, 1), 8.41 (s, 3), 7.73 (dd, 1, $J$ = 10.06; 15.18 Hz), 7.53 (d, 2, $J$ = 8.67 Hz), 7.13 (m, 2), 6.90 (d, 2, $J$ = 8.71 Hz), 6.23 (d, 1, $J$ = 15.02 Hz). Anal. Calcd for $C_{17}H_{12}N_2O_7$: C, 57.3; H, 3.4; N, 7.9. Found: C, 57.5; H, 3.4; N, 7.5. **2-Chloro-4-nitrophenyl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoate (5e):** mp 155−6 °C; $\delta$ 8.84 (s, 1), 8.43 (d, 1, $J$ = 2.65 Hz), 8.31 (dd, 1, $J$ = 2.68; 8.96 Hz), 7.74 (dd, 1, $J$ = 10.06; 15.27 Hz), 7.67 (d, 1, $J$ = 8.91 Hz), 7.52 (d, 2, $J$ = 8.63 Hz), 7.12 (m, 2), 6.90 (d, 2, $J$ = 8.62 Hz), 6.25 (d, 1, $J$ = 15.18 Hz). Anal. Calcd for $C_{17}H_{12}NO_5Cl$: C, 59.1; H, 3.5; N, 4.1. Found: C, 59.1; H, 3.5; N, 4.0. **4-Chloro-2-nitrophenyl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoate (5f):** mp 176−7 °C; $\delta$ 8.83 (s, 1), 8.18 (d, 1, $J$ = 2.52 Hz), 7.88 (dd, 1, $J$ = 2.57; 8.75 Hz), 7.68 (dd, 1, $J$ = 10.01; 15.10 Hz), 7.54 (d, 1, $J$ = 8.75 Hz), 7.52 (d, 2, $J$ = 8.63 Hz), 7.10 (m, 2), 6.89 (d, 2, $J$ = 8.67 Hz), 6.21 (d, 1, $J$ = 15.18 Hz). Anal. Calcd for $C_{17}H_{12}NO_5Cl$: C, 59.1; H, 3.5; N, 4.1. Found: C, 59.5; H, 3.6; N, 4.0. **4-Nitrophenyl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoate (5g):** mp 196−7 °C; $\delta$ 8.83 (s, 1), 8.35 (d, 2, $J$ = 9.20 Hz), 7.70 (dd, 1, $J$ = 10.26; 15.38 Hz), 7.51 (m, 4), 7.11 (m, 2), 6.89 (d, 2, $J$ = 8.67 Hz), 6.20 (d, 1, $J$ = 15.26 Hz). Anal. Calcd for $C_{17}H_{13}NO_5$: C, 65.6; H, 4.2; N, 4.5. Found: C, 66.0; H, 4.3; N, 4.2. **4-Cyanophenyl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoate (5h):** mp 190−1 °C; $\delta$ 8.82 (s, 1), 7.88 (d, 2, $J$ = 8.67 Hz), 7.67 (dd, 1, $J$ = 9.85; 15.39 Hz), 7.51 (d, 2, $J$ = 8.67 Hz), 7.45 (d, 2, $J$ = 8.75 Hz), 7.10 (m, 2), 6.89 (d, 2, $J$ = 8.63 Hz), 6.19 (d, 1, $J$ = 15.10 Hz). Anal. Calcd for $C_{18}H_{13}NO_3$: C, 74.2; H, 4.5; N, 4.8. Found: C, 74.4; H, 4.6; N, 4.7. **2,4-Dinitrophenyl (2*E*,4*E*)-5-(4′-methoxyphenyl)pentadienoate (6):** mp 147−8 °C; $\delta$ 8.94 (d, 1, $J$ = 2.77 Hz), 8.69 (dd, 1, $J$ = 2.52; 8.79 Hz), 7.84 (d, 1, $J$ = 8.87 Hz), 7.75 (dd, 1, $J$ = 9.89; 14.81 Hz), 7.61 (d, 2, $J$ = 8.96 Hz), 7.17 (m, 2), 7.00 (d, 2, $J$ = 8.87 Hz), 6.27 (d, 1, $J$ = 15.10 Hz), 3.85 (s, 3). Anal. Calcd for $C_{18}H_{14}N_2O_7$: C, 58.4; H, 3.8; N, 7.5. Found: C, 58.7; H, 4.0; N, 7.4. ***N*-(4-Methylphenyl) (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienamide (7):** mp 207−8 °C; $\delta$ 9.17 (s, 1), 8.67 (s, 1), 7.63 (d, 2, $J$ = 8.47 Hz), 7.43 (m, 3), 7.11 (d, 2, $J$ = 8.43 Hz), 6.88 (m, 4), 6.25 (d, 1, $J$ = 14.77 Hz), 2.27 (s, 3). Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.4; H, 6.1; N, 5.0. Found: C, 77.6; H, 6.2; N, 5.0.

**Methods. Product Analysis.** The products of ester hydrolyses were identified as phenol and acid by comparison of the UV−vis spectra after completion of the reactions with authentic samples of these compounds under the same conditions.

**Kinetics.** The hydrolyses of esters **5a**−**h** and **6** in 40% v/v dioxane−water solvent were followed spectrophotometrically: the choice of the appropriate wavelength was dictated by the pH of the buffers employed in the particular kinetic run since the ionization of the hydroxyl group of both substrates and liberated acid in alkaline solutions causes large shift in the UV−Vis spectra. The buffered solution (2.5 mL) was equilibrated to the required temperature (± 0.1 °C) in a 1-cm path-length quartz cell placed in the thermostated cell holder of the spectrophotometer. The reaction was initiated by adding 10 $\mu$L of a stock solution of the substrate ca. 0.01 M in dioxane to the buffer, and automated acquisition of 50−200 data points for each kinetic run was performed. Reactions were carried out with potassium hydroxide at different concentrations and with phosphate, borate, carbonate, ammonia, and Tris buffers. In all cases at least three different buffer concentrations, at constant pH, were employed: when buffer effects were observed the rate constants at zero buffer concentration were obtained by extrapolation. The ionic strength was kept at 0.1 M with KCl. The pH of the buffered solutions were measured before and after each kinetic run using a Ross combined electrode, calibrated with standard buffers. All pH values quoted for the dioxane−water solutions are relative values measured directly, no further corrections being applied. The pseudo-first-order rate constants ($k_{obs}$) were obtained by NLLSQ fitting of absorbance vs time data, and the values reported are the averages of at least duplicate runs. Reactions were normally followed over about seven half-lives. The rate constants for the hydrolysis of **5f** and **5h** at pH values below 11 were obtained by initial rates: they were measured for each run up to ca. 10% of the total reaction and were converted to pseudo-first-order rate constants using infinity values calculated from the known extinction coefficients of the products.

**Trapping.** The hydrolysis of 2,4-dinitrophenyl (2*E*,4*E*)-5-(4′-hydroxyphenyl)pentadienoate in 0.05 M carbonate buffer (fraction of base = 0.5, 40% dioxane, ionic strength kept at 0.1 M with KCl, pH 11.40) was kinetically investigated at 364 nm in the presence of variable amounts of added *p*-toluidine: no effect on the rate of hydrolysis was observed varying the amine concentration in the range 0−0.03 M at constant pH. The UV−vis spectra taken at the end of the reactions carried out in the presence of the amine were significantly different

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from that obtained in the absence of added amine, in particular in the range 380−420 nm. The values of the molar extinction coefficients at 400 and 415 nm of the amide, phenol, and acid were determined employing authentic samples under the same conditions, and the amide yield (ca. 30%) was calculated from the absorbances measured at these wavelengths at the end of the reaction carried out in the presence of 0.03 M *p*-toluidine.

**Ionization Constants.** The determinations of p$K_a$ values were carried out by spectrophotometric titration of the ionizable substrates employing at least seven buffered solutions for each determination and extrapolating the absorption to zero time.

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