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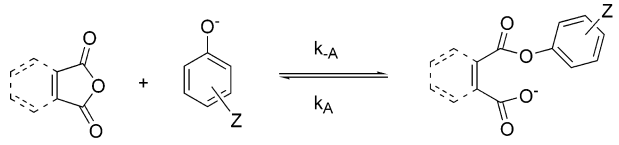
Kinetics and Mechanistic Study of the Reaction of Cyclic Anhydrides with Substituted Phenols. Structure−Reactivity Relationships

Gabriel O. Andrés and Rita H. de Rossi*

Instituto de Investigaciones en Físico Química de Córdoba (INFIQC), Facultad de Ciencias Químicas,
Departamento de Química Orgánica, Universidad Nacional de Córdoba, Ciudad Universitaria,
5000 Córdoba, Argentina

ritah@dqo.fcq.unc.edu.ar

Received October 14, 2004



Z= H, m-CH$_3$, p-CH$_3$, m-Cl, p-Cl and m-CN

The kinetic of the reactions of phthalic and maleic anhydrides with different substituted phenols (Z-PhOH with Z = H, *m*-CH$_3$, *p*-CH$_3$, *m*-Cl, *p*-Cl, and *m*-CN) were studied in aqueous solution. Two kinetic processes well separated in time were observed. The fast one is attributed to the formation of the aryl ester in equilibrium with the anhydride and allows the determination of the rate of nucleophilic attack of the phenol on the anhydride (k_{-A}). From the slow kinetic process, the equilibrium constant for this reaction was determined. The Brönsted-type plots for the nucleophilic attack of substituted phenols on the anhydrides were linear with slopes β_{Nuc} of 0.45 and 0.56 for phthalic and maleic anhydride, respectively. The results are consistent with a mechanism involving rate-determining nucleophilic attack and also with a concerted mechanism. The calculated effective charge on the atoms involved in the reactions and the Brönsted β values are consistent with a mechanism involving a concerted or enforced concerted mechanism where a tetrahedral intermediate with significant lifetime is not formed along the reaction coordinate. The latter mechanism is preferred over the stepwise process.

Introduction

The detailed mechanism of addition of nucleophiles to reactive carbonyl compounds is a subject of continuing interest.[1−3] The reaction of substituted phenols with anhydrides is a common and practical approach to the synthesis of esters and it is also important for the understanding of the hydrolysis mechanism of esters.[4]

Detailed mechanistic analysis of a reaction is assisted by information from studies of the reverse reaction. The nucleophilic attack by carboxylate ion on esters is observed for aqueous solution only in the case of intramolecular reactions because the intermolecular reaction occur with a mixture of nucleophilic an general base-catalyzed mechanisms, where the different terms cannot readily be separated.[5,6]

The study of both forward and reverse reaction for the nucleophilic reaction of anhydrides with phenols (eq 1) can give relevant information regarding the mechanism of the reaction particularly concerning the discussion of concerted vs stepwise mechanisms of ester hydrolysis. This is a subject which has been widely discussed for

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(1) Castro, E. A.; Pavez, P.; Santos, J. G. *J. Org. Chem.* **2002**, *67*, 4494.

(2) Tundo, P.; Selva, M. *Acc. Chem. Res.* **2002**, *35*, 706.

(3) Castro, E. A. *Chem. Rev.* **1999**, *99*, 3505.

(4) Williams, A. *Free energy relationship in organic and bio-organic chemistry*; The Royal Society of Chemistry: Cambridge, 2003.

(5) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1987**, *109*, 6362.

(6) Ba-Saif, S.; Maude, A. B.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1994**, 2395.

(7) Stefanidis, D.; Cho, S.; Dhe-Paganon, S.; Jencks, W. P. *J. Am. Chem. Soc.* **1993**, *115*, 1650.

(8) Williams, A. *Chem. Soc. Rev.* **1994**, *23*, 93.

(9) Castro, E. A.; Angel, M.; Pavez, P.; Santos, J. G. *J. Chem. Soc., Perkin Trans. 2* **2001**, 2351.

(10) Andrés, G. O.; Granados, A. M.; de Rossi, R. H. *J. Org. Chem.* **2001**, *66*, 7653.

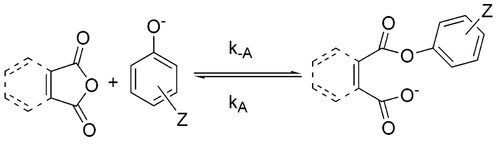
10.1021/jo048183l CCC: $30.25

TABLE 1. Effect of Phenol Concentration on the Observed Rate Constant of the Slow Kinetic Process (τ_2^{-1}) for the Reaction of Phthalic Anhydride at pH 8.90[a]

[phenol], 10^{-3} M	τ_2^{-1}, 10^{-3} s^{-1}
0.60	6.7 ± 0.1
1.46	3.3 ± 0.2
1.67	2.93 ± 0.04
1.88	2.68 ± 0.09
2.16	2.21 ± 0.05[b]

[a] Ionic strength 0.5 M, temperature 25 °C, buffer CO_3^{2-}/CO_3H^- 0.04 M. The errors are the standard deviation of the fit as calculated by the software used. [b] Phenyl hydrogen phthalate under the same conditions.

intermolecular reactions[7–9] but not so much for intramolecular reactions.[10]



(1)

We reported previously the effect of the substituents on the aryl ring of the phenol leaving group on the hydrolysis of monoesters of phthalic acid (k_A). The intramolecularly catalyzed hydrolysis of aryl esters proceeds with carboxylate assistance to give the anhydride and the substituted phenol; this reaction is quite sensitive to the pK_a of the leaving group ($\beta_{lg} = -1.15$), indicating a significant bond breaking in the transition state.[10]

In the present work, we report a study of the reactions of substituted phenoxide ions with phthalic and maleic anhydride in aqueous solution. The results are important for the determination of β_{Eq} of eq 1, and these data will be useful to interpret values of β_{Nuc} and β_{lg} for those reactions and to shed some light on the mechanism of intramolecular catalysis in esters hydrolysis. It is important to note that there have not been previously reported studies regarding the equilibrium described in eq 1.

Results and Discussion

Rate constants for the addition of substituted phenols (Z-PhOH with Z = H, p-CH_3, m-CH_3, p-Cl, m-Cl, and m-CN) to phthalic and maleic anhydrides were obtained by measuring the change in absorbance at a convenient wavelength under pseudo-first-order conditions.

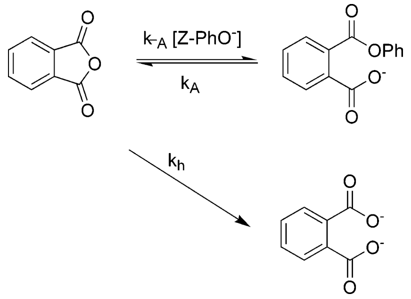
The kinetic study was carried out in the presence of substituted phenols (pK_a between 8.60 and 10.20) at constant pH. Two kinetic processes well separated in time were observed in all cases. The observed rate constant for the fast kinetic process ($1/\tau_1$) increases with the phenol concentration whereas the slow kinetic process ($1/\tau_2$) decreases (see the Supporting Information).

Slow Process. The rate constant decreases as phenol concentration increases (Table 1), and the plot of τ_2 vs phenol concentration is linear (Figure S1, Supporting Information). Similar results were obtained using m-cyanophenol as nucleophile (Table S1, Supporting Information).

We attribute this process to the reaction described in Scheme 1, where the phthalic anhydride is in steady-state concentration.

The fact that the same rate constant was obtained using phthalic anhydride or phenyl hydrogen phthalate as starting substrates under otherwise similar reaction conditions (Table 1; Figure S1, Supporting Information) confirm this proposal. The value of the observed rate constant for Scheme 1 can be derived by standard procedures[11] and is given by eq 2, which inverted give eq 3.[12]

SCHEME 1. Hydrolysis of Phthalic Anhydride in the Presence of Substituted Phenols



$$\tau_2^{-1} = \frac{k_A k_h}{k_{-A}[\text{Z-PhO}^-] + k_h} \tag{2}$$

$$\tau_2 = \frac{1}{k_h} + \frac{k_{-A}}{k_A k_h[\text{Z-PhO}^-]} \tag{3}$$

The plot of τ_2 vs phenol concentrations is linear (Figure S1, Supporting Information) and has a reasonable correlation with a slope of $(17.8 \pm 0.3) \times 10^4$ M^{-1} s. This value must be divided by the fraction of phenolate ion which was 0.095 to give k_{-A}/k_Ak_h. To check for consistency of the results, we measured k_h under otherwise similar reaction conditions. This value was 0.62 s^{-1}, and it can be combined with the slope of the plot in Figure S1 (Supporting Information) to yield $k_{-A}/k_A = 11.6 \times 10^5$ M^{-1} in good agreement with the value obtained from the fast process (see below, Table 2).

The observed rate constant for the slow process (τ_2^{-1}) was also measured for the reactions of maleic anhydride with several Z-PhOH (Z = H, p-Me, m-Cl, and m-CN) (Table S2, Supporting Information). In all cases, reasonably linear plots (not shown) were obtained when τ_2 was plotted vs Z-PhO$^-$ concentration. From the slope of these plots and the value of k_h, independently determined, the values of k_{-A}/k_A were obtained (Table 2).

Fast Process. The rate constants for the fastest observed relaxation time were linearity dependent on the phenolate ion concentration. In Figure 1 is shown representative data for phthalic anhydride, and the complete set of data is collected in Tables S3–S6 (Supporting Information).

This process is attributed to the equilibration reaction shown in eq 1; therefore, the observed rate constant (τ_1^{-1}) is given by eq 4[11]

$$\tau_1^{-1} = k_A + k_{-A}[\text{Z-PhO}^-] \tag{4}$$

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[11] Bernasconi, C. F. *Relaxation Kinetics*; Academic Press, Inc.: New York, 1976.

[12] It should be noticed that k_h in Scheme 1 represents the rate constant for the hydrolysis of phthalic anhydride. It is not an elemental rate constant, and it involves terms for HO- and buffer-catalyzed pathways.

TABLE 2. Rate and Equilibrium Constants for the Phenolysis of Anhydrides[a]

Z-phenol		phthalic anhydride			maleic anhydride	
Z	pK_a	k_{-A},[b] 10^3 s^{-1} M^{-1}	k_A,[c] s^{-1}	k_{-A}/k_A, 10^5 M^{-1}	k_{-A},[d] 10^4 s^{-1} M^{-1}	k_{-A}/k_A,[e] 10^5 M^{-1}
p-CH_3	10.26	87 ± 8	0.0228	38	23 ± 1	46 ± 7
m-CH_3	10.08	61 ± 7	0.0333	18	16.5 ± 0.9	
H	9.88	43 ± 2	0.0443	9.7	10.7 ± 0.5	11 ± 1
p-Cl	9.38	36 ± 2	0.229	1.57	9.6 ± 0.3[f]	
m-Cl	9.02	22 ± 3	0.55	0.40	3.65 ± 0.05[f]	0.37 ± 0.03[f]
m-CN[g]	8.61	13.0 ± 0.6[f]	2.1[h]	0.062	i	0.075 ± 0.009[f]

[a] pH = 8.50, ionic strength 0.5 M, temperature 25 °C, acetonitrile 4.25%. Rate constant calculated from eq 4. [b] $\lambda = 300$ nm. [c] Reference 10. [d] $\lambda = 250$ nm. [e] Value calculated from τ_2 using eq 3 and $k_h = 0.26$ s^{-1} at pH 8.5 and 0.14 at pH 8.2; both rate constants were determined independently in this work. [f] pH = 8.20. [g] $\lambda = 265$ nm. [h] Obtained as the intercept from lineal plot of τ_1^{-1} vs *m*-cyanophenol concentration. [i] Cannot be determined under these conditions (see ref 14).

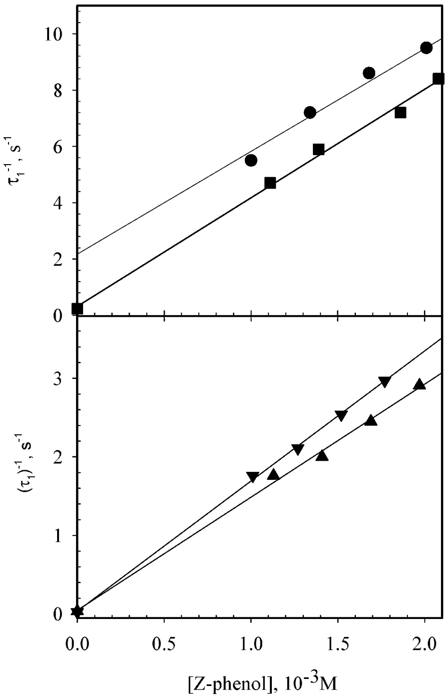

FIGURE 1. Dependence of the pseudo-first-order rate constants for the reaction of phthalic anhydride with substituted phenols on the phenol concentration. Z = ▲, *m*-CH_3, ▼, *p*-CH_3, ■, *p*-Cl, ●, *m*-CN.

The values of k_{-A} were obtained as the slope of linear plots of τ_1^{-1} vs [Z-PhO$^-$] at constant pH. The intercept of the plots represents k_A, but in most cases, these values have large errors since they are very small compared with the slope. However, for the phthalic anhydride reactions (Figure 1) they are of the same order of magnitude as the k_A determined in previous work,[10] giving support to the mechanism.[13] For the reaction of *m*-cyanophenol with phthalic anhydride the value of k_A was obtained from the intercept of the linear plot according to eq 4 (see Figure 1 and Table 2).

To determine the effect of the buffer concentration on the rate constant, the reactions were carried out at constant pH and phenol concentrations and with variable concentrations of 1,4-diazabicyclo[2.2.2]octane (DABCO), from 1 to 10 mM (Tables S3 and S5, Supporting Information, for phthalic and maleic anhydrides, respectively). The values of the second-order rate constants obtained are the same within experimental error (Table S7, Supporting Information) indicating that the buffer has no effect on the rate. These results are in good agreement with reported data on the nucleophilic reaction of phenoxide ions with methyl aryl carbonates[15] and with 4-nitrophenyl acetate,[5] which do not show evidence of general base catalysis. Therefore, the reactions of different substituted phenols have been carried out at pH 8.50 or 8.20 (when the kinetics were too fast) at 0.03 M buffer concentration for all the other Z-PhOH with phthalic and maleic anhydrides. The reaction of *m*-cyanophenol with maleic anhydride could not be measured because k_A is too high and even at the lowest *m*-cyanophenol concentration using the fast process has a very small amplitude[16] under the conditions of our studies.

In Table 2, the rate and equilibrium constants for the reactions are summarized; also included in Table 2 are the pK_a of the phenol nucleophiles taken from the literature.[17]

A Brönsted-type plot[18] (Figure 2) for k_{-A} using all the data has a reasonable correlation coefficient and gives β_{Nuc} of 0.45 ± 0.04 and 0.56 ± 0.10 for phthalic and maleic anhydride, respectively.

The values obtained are similar to those reported by Williams[6] for the concerted phenolysis reaction of acetic anhydride ($\beta_{Nuc} = 0.56 \pm 0.06$). In that case, the equilibrium constant for the reaction in water could not be determined because the reverse reaction (nucleophilic attack of acetate on phenyl ester) is a mixture of nucleophilic and general base catalysis, although the values of the reverse reaction were obtained by an indirect route. Ideally, rate constants for the forward and reverse processes need to be known for reactions under the same conditions in order to determine equilibrium constants accurately. We had determined previously[10] the rate of nucleophilic attack by the neighboring carboxylate group (k_A, eq 1) in the hydrolysis of Z-aryl hydrogen

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(13) Note that in Figure 1 the value of τ_1^{-1} at zero Z-phenol concentration is the value determined in previous work (ref 10) for Z = *m*-CH_3, *p*-CH_3, and *p*-Cl.

(14) A decrease in the pK_a of nucleophile leads a considerable increase in the value of k_A; therefore, the equilibrium constant for eq 1 lies very much on the left-hand side and the observed rate constant is completely determined by k_A which it is too high for the stopped-flow technique.

(15) Castro, E. A.; Pavez, P.; Santos, J. G. *J. Org. Chem.* **2001**, *66*, 3129.

(16) The amplitude is defined as the total change in optical density during one kinetic process. See ref 11, Chapters 6 and 7.

(17) *Handbook of Chemistry and Physics*, 72nd ed.; Lide, D. R., Ed.; CRC Press: Boca Raton, FL, 1991−1992; pp 8-30−8-35.

(18) This is not formally a Brönsted plot and the slope values are not related to general base catalysis. Jenck has used the expression "β_{Nuc}" for this parameter.[23c]

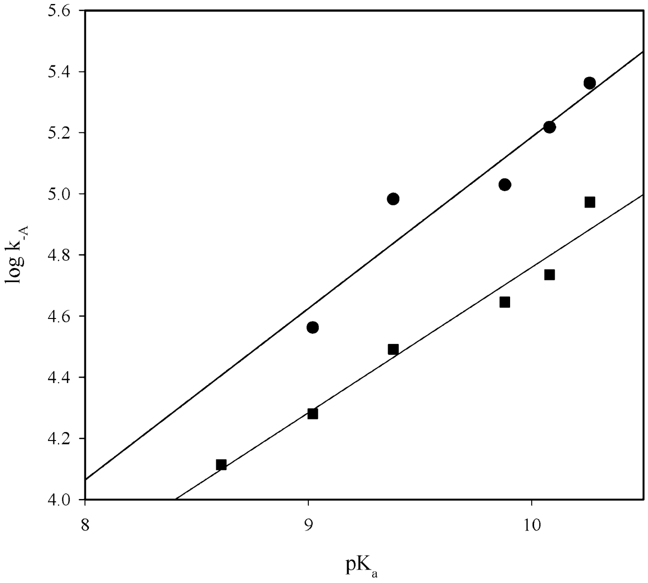


FIGURE 2. Brönsted plot for the nucleophilic attack of phenolate ions (k_{-A}) on phthalic (■) and maleic (●) anhydrides.

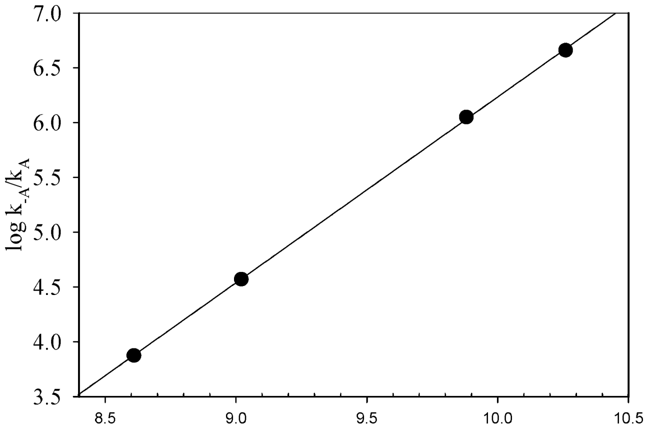
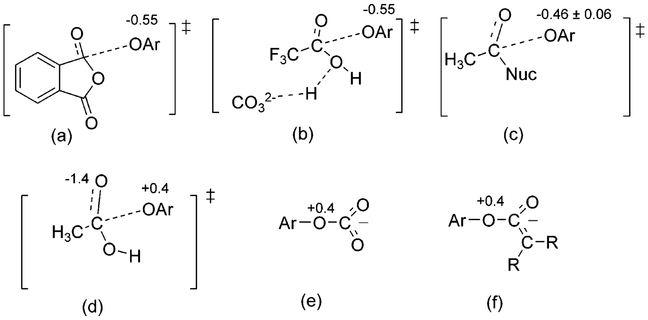


FIGURE 3. Brönsted plot for the equilibrium in the reaction of maleic anhydride with substituted phenols.

phthalates (Z = H, p-CH_3, m-CH_3, p-Cl, m-Cl) by a direct route; therefore, the equilibrium constants for formation of esters from Z-phenoxide anions and phthalic anhydride can be determined (Table 2). From a Brönsted-type correlation (plot not shown) for the equilibrium constants (k_{-A}/k_A) of phthalic anhydride a value of $\beta_{Eq} = 1.66 \pm 0.04$ was obtained. The value of β_{Eq} can also be calculated from the difference between β_{Nuc} and β_{lg}, $\beta_{Eq} = \beta_{Nuc} - \beta_{lg} = 1.6 \pm 0.1$. A similar value was reported for acyl transfer[19] ($\beta_{Eq} = 1.7$) in aqueous solution. For the reactions of maleic anhydride the Brönsted plot for k_{-A}/k_A (Figure 3) gave a slope of $\beta_{Eq} = 1.69 \pm 0.01$.

The charge on the ether oxygen atom, as measured by β_{Eq}, is +0.7 ($\beta_{Eq} - 1$). This appears not to be very indicative of reactivity at the carbonyl carbon of the ester. For instance, ethyl N-benzoylglycinate has a rate constant of 1.1 M^{-1} s^{-1} and ethyl acetate has a rate constant of 0.0061 M^{-1} s^{-1} toward the attack by hydroxide ion, and both compounds have an effective charge of +0.7 on the oxygen of the ester.[20]

SCHEME 2 [a]



[a] Key: (a) transition state for the nucleophilic attack of substituted phenol on phthalic anhydride; (b) transition state for the hydrolysis of aryl trifluoroacetates, calculated from data in ref 22; (c) transition state for the reaction of nucleophiles with aryl acetates, ref 7; (d) transition state for the hydroxyl attack on aryl esters; (e) and (f) taken from ref 19.

The Brönsted β_{Eq} value can be used to calculate the change of effective charge[19] on the phenyl oxygen from reactant to transition state relative to that from reactant to product; this is the Leffler's α parameter. The α_N value gives an estimate of the degree of bond formation between aryl oxygen and the carbonyl carbon in the transition state ($\alpha_N = \beta_{Nuc}/\beta_{Eq} = 0.27$ for k_{-A}). This result indicates a small degree of bond formation in the forward direction and agrees with the data previously published,[10] which indicates a high degree of bond rupture for the leaving group in the reverse reaction (k_A in eq 1).

The similarities between the β values for the two anhydrides indicate that the position of the transition state of the rate-determining step on the reaction coordinate does not change significantly among the two anhydrides. It is interesting to note that anhydrides of different structure such as acetic, maleic, and phthalic anhydrides have similar β_{Nuc} for the reactions with phenols, although the reactivity is quite different; for instance, the second-order rate constants for the reactions with m-chlorophenol are 626, 2.2×10^4, and 3.65×10^4 M^{-1} s^{-1} for acetic,[6] phthalic, and maleic anhydrides, respectively.

The effective charge on the oxygen of the nucleophile (Z-PhO$^-$) in the transition state is calculated as −0.55 for phthalic anhydride (a in Scheme 2). Similar effective charges were observed in the transition state of different acyl-transfer reactions.[4,21] For example, the hydrolysis of trifluoromethyl acetate esters (b in Scheme 2)[22] and the reaction of nucleophiles with aryl acetates (c in Scheme 2).[7] In all these cases a concerted or enforced concerted mechanism was proposed for the reactions.

On the other hand, the transition state for the formation of the tetrahedral intermediate was associated to asmall charge development (between 0.1 and 0.3);[23] however, a stepwise mechanism for the title reaction cannot be completely discarded.

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[19] Williams, A. *Acc. Chem. Res.* **1984**, *17*, 425.

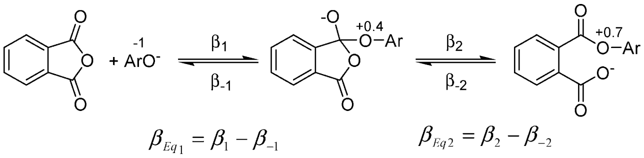
[20] Chrystiuk, E.; Jusoh, A.; Santafianos, D.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1986**, 163.

[21] Castro, E. A.; Pavez, P.; Santos, J. G. *J. Org. Chem.* **1999**, *64*, 2310.

[22] Fernandez, M. A.; de Rossi, R. H. *J. Org. Chem.* **1999**, *64*, 6000.

[23] (a) Hupe, D. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 451. (b) Satterthwait, A. C.; Jencks, W. P. *J. Am. Chem. Soc.* **1974**, *96*, 7018. (c) Gresser, M. J.; Jencks, W. P. *J. Am. Chem. Soc.* **1977**, *99*, 6963.

SCHEME 3. Effective Charge Map for the Phenolysis of Phthalic Anhydride Involving a Putative Tetrahedral Intermediate



Considering the possibility of formation of a tetrahedral intermediate with finite lifetime (Scheme 3) and assuming that leaving group expulsion is the rate-determining step,[24] the value of β_{Nuc} determined in the present work correspond to β_1. Taking into account data from the literature (see d−f in Scheme 2), the effective charge on the oxygen in the intermediate can be estimated as approximately +0.4 which leads to β_{Eq1} 1.4 and β_{-1} −0.95. Considering conservation of effective charges[4] the value of β_{Eq2} is estimated as 0.3. A small value for β_{Eq2} is reasonable because the substituent on the aryl group should not have any significant influence on either the rate of the leaving group (β_2) or the rate for nucleophilic attack by the neighboring carboxylate group (β_{-2}).[25]

The linearity of the Brönsted plots and the value of their slopes are not enough evidences to either prove or disprove a concerted mechanism. The best demonstration of a concerted process is the lack of a Brönsted break at the pK_a expected for a change in rate-determining step if the reaction were stepwise.[8,9] For the phenolysis of anhydrides the center of the Brönsted curvature (breakpoint) for a stepwise reaction should be around pK_a 3 (pK_a of aryl hydrogen phthalates[10]). Unfortunately, this pK_a is far lower than the pK_a range used in this investigation. The formation of the tetrahedral intermediate is expected to be rate limiting in the phenolysis of phenyl esters when the nucleophile has a pK_a greater than that of the leaving group.[26] It has been suggested[27] that the alkaline hydrolysis of *p*-nitrophenyl esters proceeds toward the anionic tetrahedral intermediate with a nearly tetrahedral transition-state structure, and the expulsion of the leaving group from the tetrahedral intermediate does not create a significant barrier of activation.[28] We do not have any reason to suppose that the expulsion of carboxylate with p$K_a \approx 3$ has an important barrier of activation for substituted phenoxides with pK_a higher than 7. Therefore, we think that a concerted or enforced concerted mechanism more adequately describes these reactions.

Experimental Section

Materials. Phthalic and maleic anhydrides were sublimed before use.[29] The purity of the products was also checked by comparing the UV−vis absorption spectrum of a solution containing the fully hydrolyzed anhydride in the presence of substituted phenols with one at the same concentration prepared with phthalic or maleic acid and the corresponding phenol.

Aqueous solutions were made up from water purified in a Millipore apparatus. Acetonitrile was dried on silica gel 10% p/v as described in the literature.[29]

Kinetic Procedures. Most reactions were carried out in a stopped-flow apparatus with unequal mixing. The appropriate anhydride dissolved in dry acetonitrile was placed in the smaller syringe (0.1 mL). The larger syringe (2.5 mL) was filled with a water solution containing all the other ingredients.

The slow reactions were measured in the cell, with temperature control, of a conventional spectrophotometer by adding the substrate dissolved in acetonitrile to a solution containing all of the other ingredients in the required proportions to have the same amount of the organic solvent as in the stopped-flow experiments.

The substituted phenols concentration was varied between 1 and 2×10^{-3} M. The total acetonitrile concentration was 4.25% v/v. The solutions of the substrate for the kinetic determinations were freshly prepared in dry acetonitrile in the appropriate concentration to get a final concentration of 1.2×10^{-4} M.

All reactions were run at 25.0 ± 0.1 °C and at constant ionic strength (0.5 M) using NaCl as the compensating electrolyte. The pH measurements were made with a pH meter at controlled temperature and calibrated with buffers prepared according to the literature.[30]

The observed rate constants were determined by measuring the change in absorbance at 250, 265, or 300 nm, depending on the anhydride and substituted phenol, and the wavelength was chosen so as to have the best signal-to-noise ratio. In some of the experiments, the pH of the solution was checked after the reaction by measuring it in the discarded solution, and the changes observed were always less than 0.03 pH units. The kinetic traces were fitted to one exponential equation using the software of the SF apparatus.

The pK_a of substituted phenols were taken from the literature,[17] since in previous work we found that there are few differences in the pK_a of the phenols measured at 0.5 and 1 M ionic strength.[10]

Acknowledgment. This research was supported in part by the Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), the Agencia Córdoba Ciencia, Agencia Nacional de Ciencia y Tecnología (FONCYT), Fundación Antorchas, and the Universidad Nacional de Córdoba, Argentina. G.O.A. is a grateful recipient of a fellowship from CONICET.

Supporting Information Available: Table S1 with τ_2^{-1} for the reactions of phthalic anhydride with *m*-cyanophenol, Table S2 τ_2^{-1} for the reactions of maleic anhydride with all the phenols, Tables S3 and S4 with data for phthalic anhydride with all the other Z-PhOH used, Tables S5 with τ_1^{-1} for maleic anhydride with phenol at different buffer concentrations, Table S6 with the data for all the other Z-PhOH, and Table S7 with the second-order rate constants for the reactions of maleic and phthalic anhydride with phenol at different buffer concentrations. Figure S1: plot of τ_2 vs phenol concentration for the reaction of phthalic anhydride with phenol. This material is available free of charge via the Internet at http://pubs.acs.org.

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[24] Leaving group expulsion in the reverse direction in Scheme 3 could be rate determining if bond rupture to regenerate the ester is faster that expulsion of the phenolate anion. This is a reasonable possibility since the pK_a of the carboxylate group is much lower than that of the phenol.

[25] Fife, T. H.; Hutchins, J. E. C. *J. Am. Chem. Soc.* **1981**, *103*, 4194.

[26] (a) Colthurst, M. J.; Williams, A. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1493. (b) Ba-Saif, S.; Luthra, A. K.; Williams, A. *J. Am. Chem. Soc.* **1989**, *111*, 2647. (c) Williams, A. *Acc. Chem. Res.* **1989**, *22*, 387.

[27] Shames, S. L.; Byers, L. D. *J. Am. Chem. Soc.* **1981**, *103*, 6170.

[28] This is defined as an enforced concerted mechanism.[7]

[29] Perrin, D. D.; Armarego, W. L. G. *Purification of Laboratory Chemicals*, 3rd ed.; Butterworth-Heinemann Ltd: Great Britain, 1994.

[30] See ref 17.