

# **Estimation of Hydrolysis Rate Constants of Carboxylic Acid Ester and Phosphate Ester Compounds in Aqueous Systems from Molecular Structure by SPARC**

# **Estimation of Hydrolysis Rate Constants of Carboxylic Acid Ester and Phosphate Ester Compounds in Aqueous Systems from Molecular Structure by SPARC**

By

S. H. Hilal  
Ecosystems Research Division  
National Exposure Research Laboratory  
Athens, Georgia

U.S. Environmental Protection Agency  
Office of Research and Development  
Washington, DC 20460

## **NOTICE**

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## **ABSTRACT**

SPARC (SPARC Performs Automated Reasoning in Chemistry) chemical reactivity models were extended to calculate hydrolysis rate constants for carboxylic acid ester and phosphate ester compounds in aqueous non- aqueous and systems strictly from molecular structure. The energy differences between the initial state and the transition state for a molecule of interest are factored into internal and external mechanistic perturbation components. The internal perturbations quantify the interactions of the appended perturber (P) with the reaction center (C). These internal perturbations are factored into SPARC's mechanistic components of electrostatic and resonance effects. External perturbations quantify the solute-solvent interactions (solvation energy) and are factored into H-bonding, field stabilization and steric effects. These models have been tested using 1471 reliable measured base, acid and general base-catalyzed carboxylic acid ester hydrolysis rate constants in water and in mixed solvent systems at different temperatures. In addition, they were tested on 397 reliably measured second order base, acid and general base-catalyzed phosphate ester hydrolysis rate constants over a range of temperatures. The RMS deviation error between predicted and measured values for carboxylic acid ester and phosphate ester compounds was close to the intralaboratory experimental error.

## **EXECUTIVE SUMMARY**

This report is in partial fulfillment of the National Exposure Research Laboratory Task number 16386, “Developing Computational Tools for Predicting Chemical Fate, Metabolism, and Markers of Exposure”, (Goal 4 and GPRA Sub-objective 4.5.2.) under subtask title “Development of computational tools and databases for screening-level modeling of the environmental fate of toxic organic chemicals”. The primary goal of this subtask is to develop computational tools to predict the identity of chemical species to which vulnerable organisms are likely to be exposed. This screening-level model will require a chemical structure as input, and will generate a set of daughter products that can form when the chemical is released into the environment.

The subtask is broadly divided into five research areas. The first area focuses on speciation of organic chemicals in aquatic systems. The second area focuses on the abiotic transformation processes hydrolysis and reduction. The third is concerned with identifying and characterizing the state variables that control the rate and extent of transformation processes in the environment. The fourth focuses on the refinement and extension of SPARC models. The area integrates 'omic tools' into environmental fate research.

The primary goal of the second research area of this subtask (this project) is to develop and implement mathematical models to estimate hydrolysis rate constants of carboxylic acid esters and organophosphate ester using SPARC. This report describes the SPARC computational modeling approach to estimate hydrolysis rate constants that are necessary to predict the environmental fate of carboxylic acid ester and organophosphate ester compounds in water. The SPARC chemical reactivity models were extended to calculate hydrolysis rate constants for the aforementioned compounds in aqueous and in non-aqueous systems as a

function of temperature in basic, acidic and neutral solution media strictly from molecular structure. The output from the hydrolysis rate constants models will inform chemists, environmentalists and toxicologists as to the chemical forms (parent or transformation products) that may be present in an ecosystem and their rates of hydrolysis transformation. The ultimate goal of this research project is to extend the SPARC solution-phase hydrolysis model to estimate the transformation rates of other chemical compounds classes of concern that may hydrolyze under environmental conditions, and to predict all possible hydrolysis pathways in aqueous and non-aqueous systems.

The SPARC chemical hydrolysis models will meet some of the needs of EPA's long term research task agenda under chemical toxicology initiative that emphasizes that EPA will have to rely heavily on predictive modeling to carry out the increasingly complex array of exposure and risk assessments necessary to develop scientifically defensible regulations. Ultimately, SPARC chemical reactivity models (ionization pKa, speciation, tautomerization, chemical hydration and chemical hydrolysis) will be integrated with the metabolic simulator TIMES (TIssue MEtabolism Simulator) and CATABOL to provide a highly reliable simulator of metabolic activity for direct application to the computational toxicology initiative.

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## **1. GENERAL INTRODUCTION**

The major differences among the behavior profiles of organic compounds in the environment are attributable to their physicochemical properties. The key properties are believed to be vapor pressure, solubility, Henry's constant in water, octanol/water distribution coefficient and transportation processes rates/equilibrium constants. Although considerable progress has been made in transportation process elucidation and modeling for chemical and physical processes, determination of the complete set of values for the fundamental thermodynamic and physicochemical properties have been achieved for only a small number of molecular structures. For most chemicals, only fragmentary knowledge exists about those properties that determine their fate in the environment. A big gap still exists between the available information and what is needed.

In fact, physical and chemical properties have only actually been measured for about 1 percent of the approximately 70,000 industrial chemicals listed by the U.S. Environmental Protection Agency's Office of Prevention, Pesticides and Toxic Substances (OPPTS) [1], with approximately 1000 new chemicals being added each year. These properties, in most instances, must be obtained from measurements or from the judgment of expert chemists. Reliable estimation techniques for these properties are therefore very cost-effective. In any case, trained technicians and adequate facilities would not be available for measurement efforts involving thousands of chemicals.

Mathematical models for predicting the fate of pollutants in the environment require reactivity parameter values--that is, the physical and chemical constants that govern reactivity. Although empirical structure-activity relationships (SAR) have been developed that allow estimation of some constants, such relationships generally hold only within limited families of chemicals. Computer programs have been under development for several years that predict

chemical reactivity parameters such as ionization pK<sub>a</sub>, electron affinity and numerous physical properties strictly from molecular structure for a broad range of molecular structures [2-14]. The prototype computer program called SPARC uses computational algorithms based on fundamental chemical structure theory to estimate a variety of reactivity parameters. This capability crosses chemical family boundaries to cover a broad range of organic compounds. SPARC costs the user minimal computer time and will provide greater accuracy and a broader scope of predicted physical and chemical parameters than is possible with other conventional estimation techniques.

## **2. QUANTITATIVE CHEMICAL THEORY**

Chemical properties describe molecules in transition, that is, the conversion of a reactant molecule to a different state or structure. For a given chemical property, the transition of interest may involve electron redistribution within a single molecule or a bimolecular union to form a transition state or distinct new product. The behavior of chemicals depends on the differences in electronic properties of the initial state of the system and the state of interest. For example, chemical equilibrium - thus ionization chemical equilibrium constants - depends on the energy differences between the protonated state and unprotonated state. Electron affinity depends on the energy differences between the LUMO (Lowest Unoccupied Molecular Orbital) state and the HOMO (Highest Unoccupied Molecular Orbital) state of the molecule. Hydrolysis reaction rates, on the other hand, depend on the energies of the transition states relative to the reactant (initial) states.

In every case, these differences are usually small compared to the overall energy. The *ab initio* methods that calculate absolute energies have a difficult time in predicting the small energy differences between the chemical states of interest. Estimation approaches based on LFER (Linear

Free Energy Relationships), QSAR (Quantitative Structure Activity Relationship) and QSP (Quantitative Structure Property) have proven to offer good prediction for a limited number of molecules and those within a particular class of molecules, but have failed to predict either chemical or physical properties for a broad range of molecular structures. In most cases, the number of data points/values does not exceed the number of the trainable parameters needed to estimate a property of interest by large amount as would be desired.

Perturbation methods, however, can be used to accurately compute the small differences in energy leading to differences in reactivity. These methods treat the final state as a perturbed initial state and the energy differences then are determined by quantifying the perturbation. These perturbation methods are ideally suited for expert system application due to their extreme flexibility and computational simplicity. The requisite conditions for applicability, as well as the selection of appropriate reference structures or reactions, can be easily built into the computation control portion of the expert system.

### **3. SPARC COMPUTATIONAL PROCEDURE**

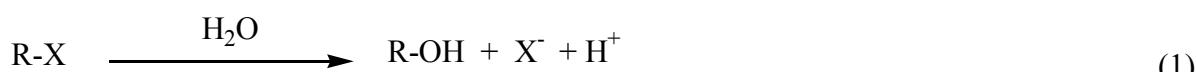
SPARC does not do "first principles" computation, but seeks to analyze chemical structure relative to a specific reactivity query in much the same manner as an expert chemist would do. For chemical properties, reaction centers with known intrinsic reactivity are identified and the impact on the reactivity of appended molecular structure (termed perturber) is quantified using mechanistic perturbation models. For physical properties, molecular structures are broken at each essential single bond and a molecular descriptor is expressed as a linear combination of fragment contributions of the property of interest. SPARC calculates the molecular descriptors and inserts them in to the physical process models developed from intermolecular interaction models to calculate a chemical and/or physical property of interest.

The computational approaches in SPARC are a blending of conventional LFER [15-17], Structure Activity Relations (SAR) [18, 19] and Perturbed Molecular Orbital (PMO) theory [20, 21]. In general, SPARC utilizes a classification scheme that defines the role of structural constituents in effecting or modifying reactivity, and quantifies the various "mechanistic" descriptions commonly utilized in physical analysis, such as resonance, electrostatic, induction and dipole effects, etc. SPARC uses LFER to compute thermodynamic or thermal properties and PMO theory to describe quantum effects such as delocalization energies or polarizabilities of  $\pi$  electrons. In reality, every chemical property involves both quantum and thermal contributions and necessarily requires the use of both perturbation methods for prediction.

A "toolbox" of mechanistic perturbation models has been developed that can be implemented where needed for a specific reactivity query. Resonance models were developed and calibrated on light absorption spectra [1, 22], whereas electrostatic models were developed and calibrated on ionization equilibrium constants [3, 4, 7-9]. Solvation models (e.g., dispersion, induction, H-bonding, deipole-dipole) have been developed and calibrated on physical properties such as vapor pressure, solubility, distribution coefficient Henry's law constant and gas chromatographic retention time [4, 5, 11, 12].

#### 4. CHEMICAL HYDROLYSIS

Hydrolysis is a chemical transformation process in which an organic compound, RX, reacts with water, forming a new carbon-oxygen bond and the cleaving of the carbon-X bond in the original molecule. The net reaction is most commonly a direct displacement of X by OH or:



Hydrolysis is likely to be the most important reaction of organic molecules with water in aqueous environments and is a significant environmental fate process for many organic chemicals. Hydrolysis under environmental conditions is actually not one reaction as shown in equation (1), but a family of reactions involving compound types as diverse as alkyl halides, carboxylic acid esters, phosphate esters, carbamates, epoxides, nitriles, amides, amines, etc [23]. However, many organic compounds have functional groups that are relatively inert with respect to chemical hydrolysis, such as alkanes, ethers, aromatic nitro compounds, etc.

The object of this study is to extend the SPARC chemical reactivity models to estimate hydrolysis rate constants for carboxylic acid esters and organophosphorus compounds from molecular structure. Based on these models, the chemical forms or species that may be present in the ecosystem can be identified (parent compounds such as carboxylic acid esters/organophosphorus or hydrolyzed products such as organic acid and alcohol). This report describes the process models and rate constants that are necessary to predict the environmental fate of these chemicals in the aqueous phase as a function of temperature in basic, acidic and neutral (general base) solution media strictly from molecular structure.

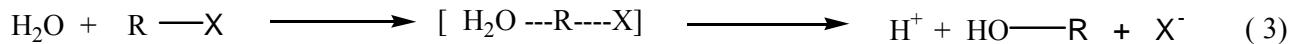
#### **4.1. Carboxylic acid Esters and Organophosphorus Hydrolysis Mechanisms and Reactions Pathway**

When an organic molecule undergoes hydrolysis, a nucleophile ( $\text{H}_2\text{O}$ ,  $\text{OH}^-$ ) attacks an electrophile (carbon or phosphorus atom) and displaces a leaving group such as phenoxide. For a long time, it has been recognized that nucleophilic displacement reactions usually fit one of two distinct substitution processes:  $\text{S}_{\text{N}}1$  (Substitution, Nucleophilic, Unimolecular) and  $\text{S}_{\text{N}}2$  (Substitution, Nucleophilic, Bimolecular) [24]. Kinetically, the  $\text{S}_{\text{N}}1$  process is characterized by

A rate independent of the concentration and nature of the nucleophile, the formation of racemic products from optically active parent chemicals, and enhancement of the rate due to an electron-donating substituent on the central atom. The rate determining step is the ionization of the RX to yield a planar carbonium ion (equation 2a), that then undergoes a relatively rapid nucleophilic attack as shown in equation 2b.



In an S<sub>N</sub>2 process, on the other hand, the rate depends on the concentration and type of the nucleophile, and an optically active starting material yields gives a product of inverted configuration. This is a one-step bimolecular process involving nucleophilic attack on the central atom at the side opposite the leaving group:



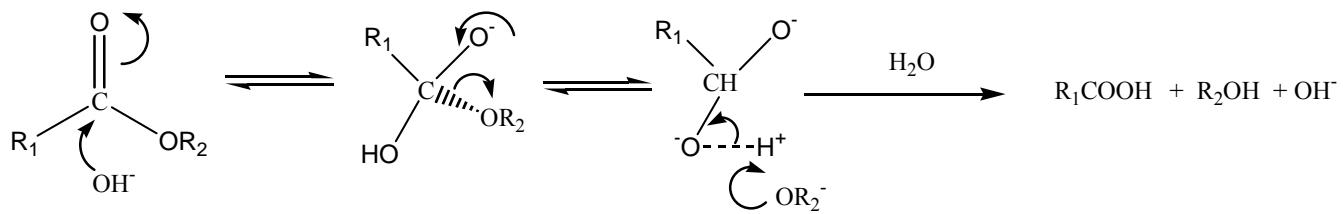
Generally, the hydrolysis of carboxylic acid esters and organophosphorus compounds involves bimolecular nucleophilic attack analogous to the S<sub>N</sub>2 (rather than S<sub>N</sub>1) mechanism on the saturated carbon. Organophosphate and carboxylic acid esters, depending on the substituents and the local environmental conditions, can undergo acid catalyzed hydrolysis, second-order alkaline hydrolysis, and neutral hydrolysis (general base). The alkaline and neutral hydrolysis pathways may not give the same products depending on the structure of the ester groups [25]. This is because hydroxide is about 10<sup>8</sup> times better as a nucleophile than water towards the phosphorous atom but only 10<sup>4</sup> times better as a nucleophile towards saturated carbon [25].

### **4.1.1. Carboxylic Acid Esters**

Ester functions are among the most common acid derivatives present in natural as well as man-made chemicals (e.g., lipids, plasticizers, pesticides). An ester bond is defined as  $\text{ROC}(=\text{O})-$ , where R is a carbon-centered substituent. The general structure of carboxylic acid esters is represented by  $\text{R}_1\text{C}(=\text{O})\text{OR}_2$ , where  $\text{R}_1$  and  $\text{R}_2$  are appended perturber structures. These perturbers can be alkyl chains, phenyl groups or heteroatoms. Carboxylic acid esters are used industrially to make flavors, soaps, herbicides and so on. Generally hydrolysis of an ester bond yields the corresponding acid and alcohols. Carboxylic acid esters undergo hydrolysis through three different mechanisms: base, acid and general base-catalyzed (neutral) hydrolysis.

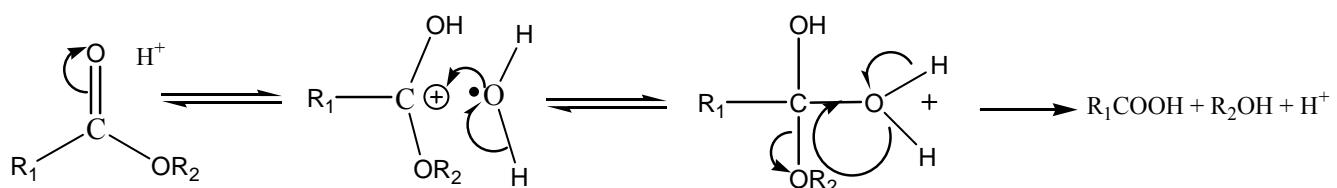
#### **4.1.1.1. Base Catalyzed Hydrolysis**

The base-catalyzed or alkaline hydrolysis of esters generally takes place via a  $\text{B}_{\text{AC}2}$  mechanism as shown in the following equation [26, 27].  $\text{B}_{\text{AC}2}$  stands for base-catalyzed, acyl-oxygen fission, bimolecular reaction. It is similar to the  $\text{S}_{\text{N}}2$  reaction, occurring when the hydroxide ion attacks the carbonyl carbon of an ester to yield a carboxylic acid and an alcohol. Alkaline hydrolysis of esters also occurs through other mechanisms, e.g.,  $\text{B}_{\text{AC}1}$  (base-catalyzed, acyl-oxygen fission, unimolecular),  $\text{B}_{\text{AL}1}$  (base-catalyzed, alkyloxygen fission, unimolecular) and  $\text{B}_{\text{AL}2}$  (base-catalyzed, alkyl-oxygen fission, bimolecular). However,  $\text{B}_{\text{AC}2}$  is the most common mechanism, and usually masks all other possible mechanisms.



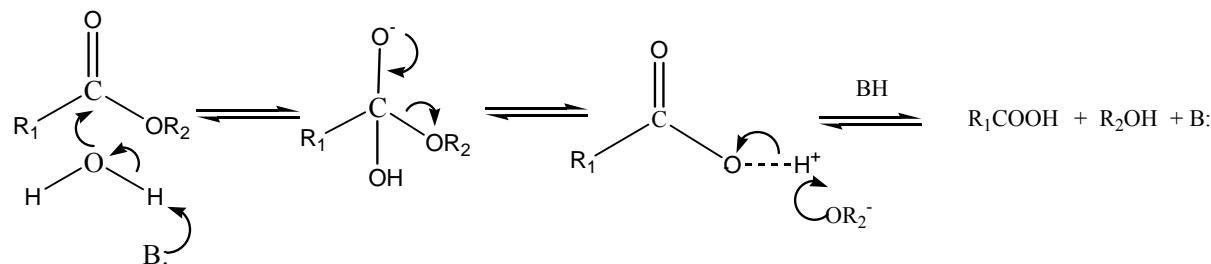
#### 4.1.1.2. Acid Catalyzed Hydrolysis

Acid catalyzed hydrolysis of esters takes place via an  $\text{A}_{\text{AC2}}$  mechanism as shown in the following equation [26, 27].  $\text{A}_{\text{AC2}}$  stands for acid-catalyzed, acyl-oxygen fission, bimolecular reaction. It is similar to the  $\text{S}_{\text{N}}2$  reaction, occurring when a positive hydrogen ion catalyzes the ester and a water molecule attacks the carbonyl carbon of the ester to produce a carboxylic acid and an alcohol. Acid-catalyzed hydrolysis of esters also takes place by other mechanisms, such as  $\text{A}_{\text{AC1}}$  (acid-catalyzed, acyl-oxygen fission, unimolecular),  $\text{A}_{\text{AL1}}$  (acid-catalyzed, alkyl-oxygen fission, unimolecular) and  $\text{A}_{\text{AL2}}$  (acid-catalyzed, alkyl-oxygen fission, bimolecular) [26, 27]. However,  $\text{A}_{\text{AC2}}$  is the general mechanism for acid-catalyzed hydrolysis of esters, and usually masks all other possible mechanisms.



#### 4.1.1.3. General Base Catalyzed Hydrolysis

The general base-catalyzed hydrolysis of esters takes place via a  $B_{AC2}$  mechanism illustrated in the following reaction [26, 27]:



As before,  $B_{AC2}$  stands for base-catalyzed, acyl-oxygen fission, bimolecular reaction. It is also similar to the  $S_N2$  reaction, occurring when a base ( $B:$ ) present extracts a hydrogen atom from a water molecule, releasing the hydroxide ion, that eventually attacks the carbonyl carbon of the ester to yield a carboxylic acid and an alcohol. The base,  $B:$  stands for any base, such as ammonia, acetate ion, pyridine, imidazole and so on. In the case of neutral hydrolysis,  $B:$  represents the water molecule.

#### 4.1.2. Phosphate ester (Organophosphorus)

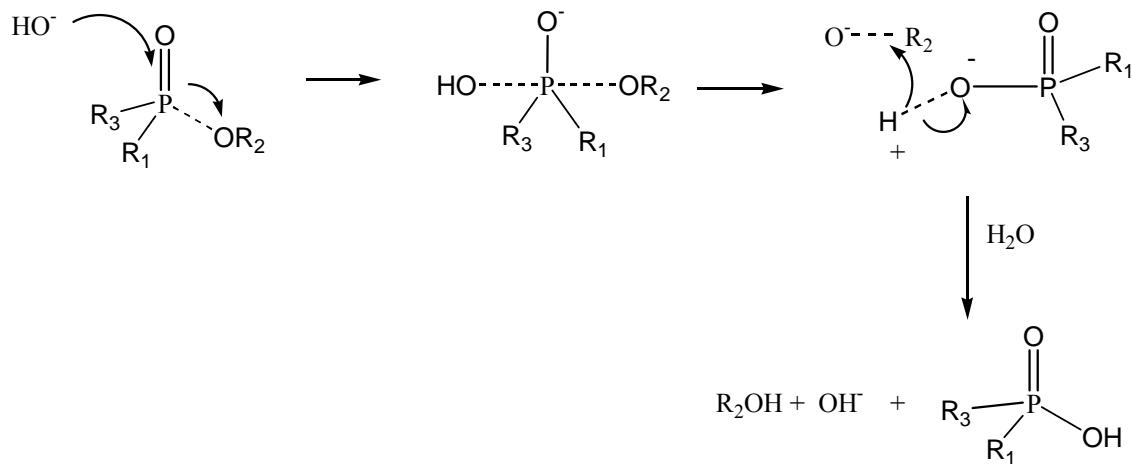
Organophosphorus compounds are of interest to many groups of chemists. Biochemists study their relationship to cholinesterase inhibition [28] ; organic chemists investigate the reaction mechanisms to improve synthetic routes to these chemicals [29]; environmental chemists are interested in these compounds for their role as pesticides, as well as their persistence and overall toxicity in the environment [25]. These compounds are widely used as insecticides for different types of cultivation and for elimination of crustaceans and mosquitoes [30]. Also, they are widely used in heavy industries as hydraulic fluid additives, and in the petrochemical

industry as plasticizers [31]. Despite the extensive production and resultant widespread exposure of environmental compartments to various amounts of these compounds, surprisingly few quantitative data on their hydrolytic reactivity are reported in the open literature. This lack of information is particularly surprising because hydrolytic transformation is proposed as an important pathway for the degradation of these compounds in aquatic ecosystems [32].

Organophosphorus or phosphate esters can be represented as  $R_1OP(=O)(R_2)(R_3)$ , where the oxygen of  $OR_1$  is bonded to a  $sp^2$  or  $sp^3$  carbon ( $R_1$ ).  $R_2$  and  $R_3$  represent additional leaving groups or substituents of the perturber structure, P. Depending on the local environment, these compounds hydrolyze via three distinct mechanisms: acid, base and neutral hydrolysis [25, 29].

#### 4.1.2.1. Base Catalyzed Hydrolysis

The base-catalyzed (alkaline) hydrolysis of phosphate esters follows the same general mechanism as carboxylic acid ester base hydrolysis, see section 4.1.1.1. This mechanism is depicted in the following [14, 29]. BP2 stands for base-catalyzed, phosphoryl-oxygen fission, bimolecular reaction, and is similar to the  $S_N2$  reaction that occurs when a hydroxide ion attacks the carbonyl carbon of an ester to yield a carboxylic acid and an alcohol.



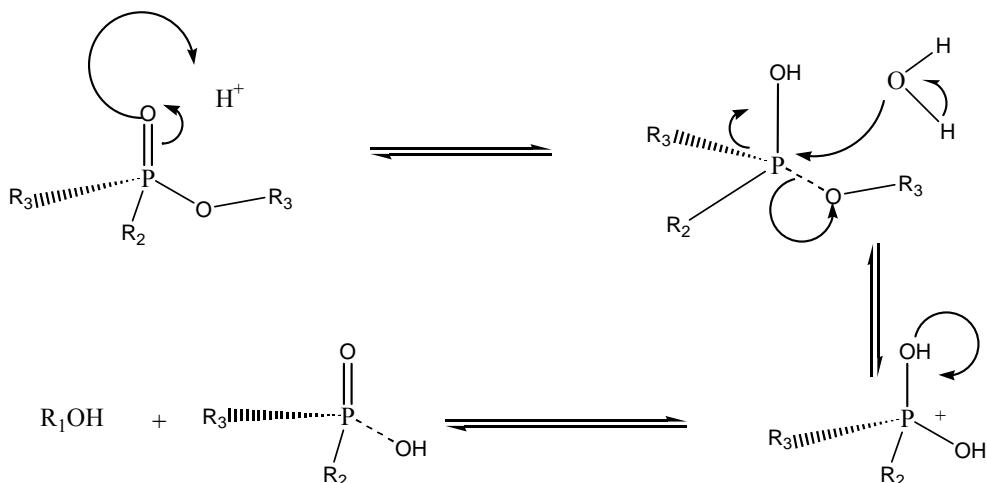
The hydroxide ion attacks the phosphorus atom in the rate-controlling step of the sequence [29]. Formation of an intermediate addition product of hydroxide ion and the ester that is in equilibrium with the reactants and decomposes to give the products is excluded by the failure of the phosphorus group to exchange oxygen with the solvent prior to chemical hydrolysis. Therefore, the reaction cannot proceed by an addition-elimination sequence analogous to that believed to represent the course of hydrolysis of carboxylic acid esters, but must consist either of a one-step process in which the leaving group is being expelled at the same time the substituent group is entering (see the above mechanism), or a two step process in which the intermediate decomposes so very rapidly that it cannot equilibrate with the solvent [33, 34].

Alkaline hydrolysis of phosphate esters also occurs through other mechanisms, such as: BP1 (base-catalyzed, phosphoryl-oxygen fission, unimolecular), B<sub>AL1</sub> (base-catalyzed, alkyl-oxygen fission, unimolecular), and B<sub>AL2</sub> (base-catalyzed, alkyl-oxygen fission, bimolecular). However, the B<sub>P2</sub> mechanism usually dominates and these other mechanisms are masked. In certain circumstances, such as when carbonyl or glycerol groups are attached to the molecule, there is no dominant pathway; this situation makes it difficult to accurately assess the rate of hydrolysis [35, 36]. Since the SPARC model was not designed to model these later situations, molecules with these types of mechanisms have not been investigated.

#### **4.1.2.2. Acid Catalyzed Hydrolysis**

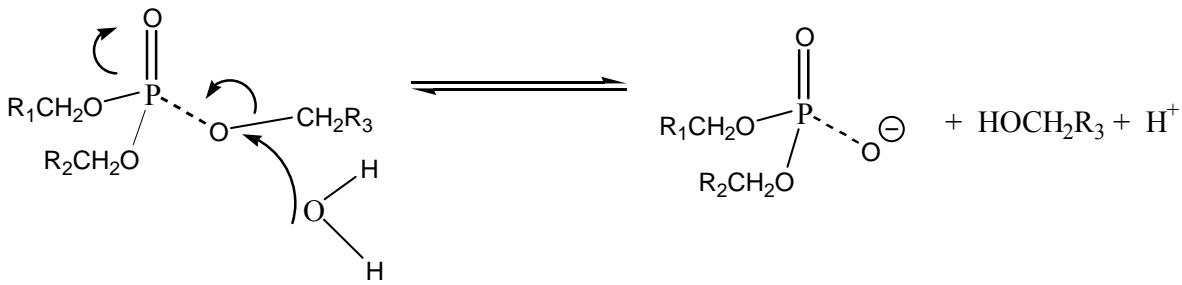
Acid-catalyzed hydrolysis of phosphoric acid esters can occur by direct nucleophilic attack at the phosphorus atom without the formation of a pentavalent intermediate. The reaction takes place via an A<sub>AC2</sub> mechanism as shown in the following equation. A<sub>AC2</sub> stands for acid-catalyzed, acyl-oxygen fission, bimolecular reaction. It is similar to the S<sub>N</sub>2 reaction, occurring

when a positive hydrogen ion catalyzes the ester and a water molecule attacks the carbonyl carbon of the ester to produce a carboxylic acid and an alcohol. Acid-catalyzed hydrolysis of esters also takes place by other mechanisms such as phosphoryl-oxygen or alkyl-oxygen fission unimolecular and alkyl-oxygen fission bimolecular [26, 27]. However,  $A_{AC2}$  is the general mechanism for acid-catalyzed hydrolysis of esters and usually masks all other possible mechanisms.



#### 4.1.2.3. General Base Catalyzed (Neutral) Hydrolysis

Neutral hydrolysis of phosphoric acid esters occurs by direct nucleophilic substitution of water at the carbon atom, causing C-O cleavage, as is the case for trialkyl phosphates such as trimethyl phosphate:



This reaction is analogous to the base catalyzed S<sub>N</sub>2 reaction; however neutral and base hydrolysis may not yield the same products. This difference in products is primarily because toward phosphorous, OH<sup>-</sup> is a better nucleophile than H<sub>2</sub>O by about a factor of 10<sup>8</sup> [37]. This usually causes the base catalyzed reaction to occur at the phosphorous atom with the hydroxide causing the best leaving group to dissociate (P-O cleavage). However, depending on the leaving groups present, the neutral (general base) reaction may occur where water acts as the nucleophilic substituent at the carbon atom (C-O cleavage). If a good leaving group is present, the reaction may proceed simultaneously by both neutral and base hydrolysis reaction mechanisms with C-O and P-O cleavage. Multiple researchers [38] have found higher temperatures cause the proportion of C-O to P-O cleavage to be greater; while at lower temperatures, P-O cleavage dominates. For example, at 70°C and pH = 5.9 parathion reacted 90% by C-O cleavage, while at a lower temperature, higher proportion of the neutral reaction occurred by P-O cleavage [39]. This observation is explained because the reaction involving C-O cleavage requires a greater activation energy than that involving P-O cleavage [40]. Even this simple thermal case demonstrates the complexity of the mechanisms involved when dealing with phosphoric acid derivatives.

## 5. HYDROLYSIS MODELING APPROACH

Hydrolysis reaction kinetics have been quantitatively modeled within the chemical equilibrium framework described in previous publications for ionization pK<sub>a</sub> in water [3, 6-9]. For this, it was assumed that a reaction rate constant could be described in terms of a pseudo equilibrium constant between the reactant (initial) and transition (final) states of the molecule undergoing hydrolysis. This reaction rate constant is expressed in the appropriate second order form inclusive of catalytic effects. For molecules susceptible to hydrolysis, reaction centers with known intrinsic reactivity were identified and the reaction rate constants expressed (energy terms) by perturbation theory as:

$$\log k_{\text{Hydrolysis}} = \log k_c + \Delta_p \log k_c \quad (4)$$

where  $\log k_{\text{Hydrolysis}}$  is the log hydrolysis rate constant of interest and  $\log k_c$  is the log of the intrinsic rate constant of the reaction center. A given reaction center may have two or more appendages or perturbing units. For example, a carboxylic acid ester reaction center has two appendages and a phosphate ester has three. The  $\log k_c$  for the reaction center can be either measured directly (if the reaction center exists as a distinct molecule) or determined via data-fit. The  $\Delta_p \log k_c$  term denotes the perturbations of the intrinsic rate constant of the reaction center due to the appended structures, P, and to solvation effects. The perturbations associated with appendages to the reaction center are factored into the mechanistic components of resonance and electrostatic effects. Likewise, the perturbations associated with the solvent are factored into steric, H-bonding, and field stabilization effects. The solvent dependence of  $\log k_c$  is expressed as a linear function of solvent properties (alpha/beta H-bonding and dipole; calculated as described later) with data-fitted coefficients. For mixed solvents, solvent descriptors that are site interactions, such as H- bonding, are the mole-fraction-weighted average when used in the

interaction models, and the interactions are summed over all solvent components [11]. Solvent properties that are essentially bulk in nature, such as the dielectricity, volume, and polarizability, are volume-fraction-averaged [11]. With the exception of steric effects, all the perturbations of the reaction center are modeled independently and simply summed.

The SPARC computational model for the hydrolysis rate constant is divided into three sub-models: reference rate, internal perturbation, and external perturbation. The reference rate sub-model calculates the hydrolysis rate constant for the smallest ester compound substructure that excludes internal perturbation and steric effects. The internal perturbation model calculates the perturbation of the reference hydrolysis rate constant due to the internal perturbation interactions between the reaction center and its appended perturber. Finally, the external perturbation model calculates the solvation contributions to changes in the hydrolysis rate constant due to solute-solvent interactions. The hydrolysis rate constant contributions from these three sub-models are then summed to give the total calculated hydrolysis rate constant for the compound under investigation according to equation:

$$\log k_{\text{Hydrolysis}} = \log k_c + \delta_{\text{IP}} \log k_c + \delta_{\text{EP}} \log k_c \quad (5)$$

where  $\log k_c$  describes the hydrolysis behavior of the reaction center (reference structure), i.e., the "reference rate", in this study the hydrolysis rate constant for the smallest ester compound structure that resemble the structure of the reaction center  $C(=O)OCH_3$  or  $P(=O)OCH_3$ . The term,  $\delta_{\text{IP}} \log k_c$  is the change in hydrolysis behavior of the reaction center brought about by internal interactions due to the perturber structure, P. SPARC computes the various internal reactivity perturbations,  $\delta_{\text{IP}} \log k_c$ , used to "correct" the hydrolysis behavior of the reaction center (reference structure) for the compound in question in terms of all the potential "mechanisms" for the interaction of the perturber structure, P, of the compound and its reaction center (reference

structure), C [3, 4, 6-9]. The last term in equation 5 describes the external perturbation of the hydrolysis rate due to the effect of the solvent on both the initial (reactant) and the final (transition) state. Specifically,  $\delta_{EP} \log k_c$  describes the change in the solvation of the initial state versus the transition state due to steric, H-bond, and field stabilization effects of the solvent.

### 5.1. Reference Rate Model

As stated earlier, the reference rate,  $\log k_c$ , is the hydrolysis rate constant for the smallest ester compound that resembles the structure of reaction center C(=O)OR or P(=O)OR (in this study). The reference rate is free of any internal perturbation interactions, such as resonance, electrostatic and steric effects. However, it is dependent upon the temperature. As the temperature increases, the reference hydrolysis rate increases. SPARC expresses the reference rate,  $\log k_c$ , as a function of the temperature and enthalpic and entropic contributions as

$$\log k_c = A + \log T_k + Ref_1 + Ref_2/T_k \quad (6)$$

where A is the log of the Arrhenius equation pre-exponential factor,  $T_k$  is the temperature in degrees Kelvin,  $Ref_1$  is the entropic contribution to the rate, and  $Ref_2$  is the enthalpic contribution. A,  $Ref_1$ , and  $Ref_2$  are all data-fitted parameters that are the same for all molecules, solvents, and temperatures.

### 5.2. Internal Perturbation Models

The internal perturbation of the hydrolysis rate constant of the reaction center (reference structure) in equation (5) for a molecule of interest can be expressed in terms of mechanistic perturbations as:

$$\delta_{\text{IP}} \log k_c = \delta_{\text{res}} \log k_c + \delta_{\text{elec}} \log k_c \quad (7)$$

where the  $\delta_{\text{res}} \log k_c$  and  $\delta_{\text{elec}} \log k_c$  describe the change in the hydrolysis rate due to the difference in the resonance and electrostatic interactions of P with the initial state versus the transition state (activation energy) of C, respectively. Electrostatic interactions are derived from local dipoles or charges in P interacting with charges or dipoles in C. The term,  $\delta_{\text{res}} \log k_c$  describes the effect on the rate due to a change in the delocalization of  $\pi$ -electrons of the two states due to P. The delocalization of  $\pi$  electrons can be into or out of the reaction center.

The modeling of the perturber effects on chemical reactivity relates to the structural representation S-R-C, where S-R is the perturber structure, P, appended to the reaction center, C. S denotes a substituent group that "instigates" the perturbation. For electrostatic effects, S contains (or can induce) electric fields; for resonance, S donates/receives electrons to/from the reaction center. R links the substituent and reaction center and serves as a conductor of the perturbation (e.g., "conducts" resonant  $\pi$  electrons or electric fields) [2-4, 7].

### 5.2.1.      **Electrostatic Effect**

Electrostatic effects on reactivity derive from charges or electric dipoles in the appended perturber structure, P, interacting through space with charges or dipoles in the reaction center, C. Direct electrostatic interaction effects (field effects) are manifested by a fixed charge or dipole in a substituent interacting through the intervening molecular cavity with a charge or dipole in the reaction center. The substituent can also "induce" electric fields in R that can interact electrostatically with C. This indirect interaction is called the "mesomeric field effect". In addition, electrostatic effects derived from electronegativity differences between the reaction center and the substituent are termed sigma induction (or  $R_\pi$  if  $\pi$ -electrons involves). These

effects are transmitted progressively through a chain of  $\sigma$ -bonds (or  $\pi$ ) bonds between atoms. For compounds containing multiple substituents, electrostatic perturbations are computed for each singly and summed to produce the total effect.

### 5.2.1.1. Direct Field Effect

For a given dipolar or charged substituent interacting with the change in the charge at the reaction center, the direct field effect is expressed as a multipole expansion

$$\delta(\Delta E)_{field} = \frac{\delta q_c q_s}{r'_{cs} D_e} + \frac{\delta q_c \mu_s \cos \theta_{cs}}{r'^2_{cs} D_e} + \frac{\delta \mu_c q_s \cos \theta_{cs}}{r'^2_{cs} D_e} + \frac{\delta \mu_c \mu_s \cos \theta_{cs'} \cos \theta_{cs}}{r^3_{cs} D_e} + \dots \quad (8)$$

where  $q_s$  is the charge on the substituent, approximated as a point charge located at point,  $s'$ ;  $\mu_s$  is the substituent dipole located at point s (this dipole includes any polarization of the anchor atom i effected by S);  $q_c$  ( $\delta\mu_c$ ) is the *change* in charge (dipole moment) of the reaction center accompanying the reaction, both presumed to be located at point c;  $\theta$  gives the orientation of the substituent dipole relative to the reaction center;  $D_e$  is the effective dielectric constant for the medium; and  $r_{cs}$  ( $r_{cs}'$ ) is the distance from the substituent dipole (charge) center to the reaction center.

In modeling electrostatic effects, only those terms containing the "leading" nonzero electric field change in the reaction center are retained. For example, acid-base ionization is a monopole reaction that is described by the first two terms of the preceding equation; electron affinity is described by only the second term, whereas the dipole change in hydrolysis rate constant or H-bond formation is described by the third and fourth terms.

In order to provide parameter "portability" and, hence, effects-model portability to other structures and to other types of chemical reactivity, the contribution of each structural component is quantified independently:

$$\delta_{\text{field}} \log k_c = \rho_{\text{elec}} \sigma_p = \rho_{\text{elec}} \sigma_{\text{cs}} F_s = \frac{\rho_{\text{elec}} F_s \cos \theta_{\text{cs}}}{r_{\text{cs}}^3 D_e} \quad (9)$$

where  $\sigma_p$  characterizes the field strength that the perturber exerts on the reaction center and has been previously calculated for estimation of ionization pK<sub>a</sub> [2-4, 7].  $\rho_{\text{elec}}$  is the susceptibility of a given reaction center to electric field effects that describes the electrostatic change accompanying the hydrolysis rate constant reaction.  $\rho_{\text{elec}}$  is presumed to be independent of the perturber. The perturber potential,  $\sigma_p$ , is further factored into a field strength parameter,  $F$  (characterizing the magnitude of the field component, charge or dipole, on the substituent), and a conduction descriptor,  $\sigma_{\text{cs}}$ , of the intervening molecular network for electrostatic interactions. This structure-function specification and subsequent parameterization of individual component contributions enables one to analyze a given molecular structure (containing an arbitrary assemblage of functional elements) and to "piece together" the appropriate component contributions to give the resultant reactivity effect.

The electrostatic susceptibility,  $\rho_{\text{elec}}$ , is a data-fitted parameter inferred directly from measured hydrolysis rate constants. This parameter is determined once for each reaction center and stored in the SPARC database. With regard to the substituent parameters, each uncharged substituent has one field strength parameter,  $F_\mu$ , characterizing the dipole field strength; whereas, a charged substituent has two,  $F_q$  and  $F_\mu$ .  $F_q$  characterizes the effective charge on the substituent and  $F_\mu$  describes the effective substituent dipole inclusive of the anchor atom i, assumed to be a

carbon atom. If the anchor atom  $i$ , is a noncarbon atom, then  $F_\mu$  is adjusted based on the electronegativity of the anchor atom relative to carbon. The effective dielectric constant,  $D_e$ , for the molecular cavity, any polarization of the anchor atom  $i$  affected by  $S$ , and any unit conversion factors for charges, angles, distances, etc. are included in the  $F$ 's.

Since the transition states for both base and general base-catalyzed hydrolysis of the reaction center are negatively charged, the substituent dipole will increase the hydrolysis rate constant of these reactions. In contrast, the transition state for acid hydrolysis of carboxylic acid esters and organophosphorus is positively charged, and the substituent dipole will decrease the hydrolysis rate constant. For example, the direct field contribution is 0.32 and -0.042 log-units for base and acid catalyzed hydrolysis of ethyl p-nitrobenzoate respectively, while it is 0.346 log-unit for general base catalyzed hydrolysis of p-nitrophenyl acetate. Since the transition states of the base and general base catalyzed hydrolysis of esters are negative, the field always contributes positively to the internal perturbations causing the hydrolysis rate constant to increase. In contrast, the field contributes negatively to the internal perturbations for acid catalyzed hydrolysis because of the positive transition state that occurs during the hydrolysis reaction causing the hydrolysis rate constant to decrease.

### 5.2.1.2. Mesomeric Field Effect

A mesomeric field,  $MF$ , ( $\pi$ -induction or indirect field) is generated when either an electron withdrawing or electron donating substituent induces electric fields or charges on the molecular conductor  $R$  that can interact electrostatically with the reaction center,  $C$ . An electron-withdrawing substituent creates positive charges on the conductor, while an electron-donating substituent creates negative charges. Since the transition states in both base and general base-

catalyzed hydrolysis of carboxylic acid and phosphate esters are negatively charged, the electron-withdrawing substituents will increase the hydrolysis rate constant because the induced positive charges on the molecular conductor will stabilize the negative charges of the reaction center. However, electron-donating substituents induce negative charges on the molecular conductor and have an opposite effect on the hydrolysis rate constant.

In SPARC, this mesomeric field effect ( $\pi$ -induction or indirect field) is treated as a collection of discrete charges,  $q_R$ , with the contribution of each described by the following equation. The MF effect on the log of the hydrolysis rate constant due to either the electron-withdrawing or electron-donating substituents is given as

$$\delta_{MF} \log k_c = \rho_{elec} \text{MF}_S \sum_k \frac{q_{ik}}{r_{kc}^2} A_{MF} \quad (10)$$

where as before,  $\rho_{elec}$  is the intrinsic susceptibility of the reference reaction center to electrostatic effects independent of the substituent;  $\text{MF}_S$  is the mesomeric field constant of the substituent that describes its ability to induce charges on the molecular conductor, R, and generate the mesomeric field.  $\text{MF}_S$  gauges the ability or strength of a given S to induce a field in  $R_\pi$ . It describes the  $\pi$ -induction ability of a particular substituent relative to the  $\text{CH}_2^-$ .  $A_{MF}$  is a data-fitted parameter and has the same value for all molecules in this study. Substituent  $\text{MF}_S$  values have been calculated and presented in previous work [4];  $q_{ik}$  is the charge induced at atom k in R calculated using PMO (Perturbed Molecular Orbital) theory [4, 20, 21]; and  $r_{kc}$  is the through-cavity distance between the charge on atom k and C.

An electron-withdrawing substituent creates positive charges on the conductor, while an electron-donating substituent creates negative charges. Since the transition states in both base and general base-catalyzed hydrolysis of carboxylic acid and phosphate esters are negatively charged, the electron-withdrawing substituents will increase the hydrolysis rate constant because the induced positive charges on the molecular conductor will stabilize the negative charges of the reaction center. However, electron-donating substituents induce negative charges on the molecular conductor and have an opposite effect on the hydrolysis rate constant. For example, the mesomeric field (MF) contribution is 0.65 and 0.147 log-units for hydrolysis of ethyl p-nitrobenzoate in base and acid catalyzed media respectively and it is 0.513 log unit for hydrolysis of p-nitrophenyl acetate in general base catalyzed medium. The MF contributions are positive in all three catalyzed media and increase the hydrolysis rate constant because the induced positive charges on the phenyl ring stabilize the charged transition states. In addition, we see large positive values for the base and general base catalyzed hydrolysis because of the negative transition states that occur during the hydrolysis reactions for these mechanisms. The induced positive charges on the phenyl ring enhance the stabilization of the negative transition states more. In contrast, the small positive value for acid catalyzed hydrolysis is due to the positive transition state that occurs during the hydrolysis reaction and diminishing stabilization of it.

### **5.2.1.3. Sigma Induction Effect**

Sigma induction occurs due to the difference in electronegativity between C and S. For base and general base-catalyzed hydrolysis of carboxylic acid and phosphate esters, the reaction center has a large electronegativity. Therefore, methyl substituents, for example, will move charge or electrons into the reaction center and decrease the hydrolysis rate constant. The acid

hydrolysis reaction center is less electronegative and the substituent-induced perturbations are always quite small. Sigma induction is a short range effect. Calculated effects due to substituents beyond two atoms from C were considered negligible. The sigma induction effects are given as:

$$\delta_{\text{Sigma}} \log k_c = \rho_{\text{elec}} \sum (\chi_c - \chi_s) NB \quad (11)$$

where  $\chi_c$  and  $\chi_s$  are the electronegativities of the reaction center and the appended substituent, respectively, and NB is a data-fitted parameter that depends on the number of appended substituents. Values of  $\chi_s$  and NB have been calculated using ionization pK<sub>a</sub> data [4, 7].

#### 5.2.1.4. R<sub>π</sub> effect

The R<sub>π</sub> effect is similar to sigma induction, except that it involves π-electrons instead of σ-electrons. The magnitude of the reactivity perturbation,  $\delta_\pi \log k_c$ , depends upon the difference in the electronegativity of the substituent atom π group and that of the reaction center to which it is attached. Since the differential induction capability of carboxylic acid and phosphate esters is highly correlated with  $\rho_{\text{elec}}$ , SPARC uses a simple model, requiring a minimum of computation and only one extra parameter to estimate the R<sub>π</sub> effect on the hydrolysis rate constant as follows:

$$\delta_\pi \log k_c = \rho_{\text{elec}} P_{jc} \sigma_\pi \quad (12)$$

where  $P_{jc} = \cos^2 \Theta_{jc}$ ,  $\Theta_{jc}$  is the dihedral angle of C and R-π unit (describing the π orbital alignment), and is set to 1 for this study.  $\sigma_\pi$  is a data-fitted parameter; currently  $\sigma_\pi$  is 0.008 and 0.1 for aromatic and ethylenic R-π units, respectively. When an R-π unit is attached to a carbonyl carbon or P=O (electron withdrawing group), the R<sub>π</sub> effect contributes negatively or

lowers the hydrolysis rate constant. In contrast, when the  $\pi$ -system is attached to an acyl oxygen (electron donating group), the  $R_\pi$  effect increases the hydrolysis rate constant.

### 5.2.2. Resonance Effect

Resonance is a phenomenon of  $\pi$ -electrons moving in or out of the reaction center. Resonance stabilization energy in SPARC is a differential quantity, related directly to the extent of electron delocalization in the initial state versus the transition state of the reaction center. The  $\pi$ -electron source, or sink, in P may be either from a substituent, S, or R- $\pi$  units contiguous to the reaction center. Substituents that withdraw electrons from a reference point,  $\text{CH}_2^-$ , are designated S+ and those that donate electrons are designated S-. The R- $\pi$  units can either withdraw or donate electrons or may serve as "conductors" of  $\pi$ -electrons between resonance units. Reaction centers are likewise classified as C+ (C=O or P=O) and C- (alkyl oxygen), denoting the withdrawing and donating of electrons, respectively. The distribution of NBMO (Non-Bonded Molecular Orbital) charge from the surrogate donor,  $\text{CH}_2^-$ , is used to quantify the acceptor potential for P, the perturber structure [4, 20, 21]. The resonance reactivity perturbation is given by:

$$\delta_{\text{res}} \log k_c = \rho_{\text{res}} \Delta q_c + \rho'_{\text{res}} \Delta q'_c \quad (13)$$

where  $\rho_{\text{res}}$  and  $\rho'_{\text{res}}$  are the susceptibilities of the alkyloxygen (donating electrons) and C=O/P=O (withdrawing electrons), respectively, of the ester to resonance interactions.  $\rho_{\text{res}}$  ( $\rho'_{\text{res}}$ ) quantifies the differential "donor" ability of the initial and transition states of the alkyl oxygen (C=O and P=O) of the reaction center relative to  $\text{CH}_2^-$ .  $\Delta q_c$  ( $\Delta q'_c$ ) is the fraction loss of NBMO charge from the alkyl oxygen (C=O or P=O) surrogate reaction center calculated based on PMO theory [4,

21]. Resonance plays different roles in carboxylic acid ester and organophosphorus hydrolysis. The major impact is that of resonance stabilization of the leaving group. Thus, the R- $\pi$  unit attached to the oxygen of the ester (alkyl oxygen) reaction center has a pronounced effect, greatly increasing the hydrolysis rate constant. Conversely, the R- $\pi$  unit attached to the C=O or P=O (electron-withdrawing group) tends to destabilize the leaving group, thereby decreasing the hydrolysis rate constant.

### **5.3. External Perturbation (Solvation Effect) Model**

Hydrolysis reactions (involve reactants, intermediates and/or products), are affected by changes in the solvating power of the reaction medium. The presence of organic solvents can affect the solvating power and thus alter the hydrolysis rate. The presence of water as solvent influences the rate and mechanism of hydrolysis reactions in a number of ways; as a nucleophilic reagent, as a high dielectric-constant continuum in which reaction takes place; and as a specific solvating agent for organic reactants and products (leaving group).

The external reactivity perturbation (solvation effects) model, i.e., for  $\delta_{EP} \log k_c$ , describes the hydrogen bonding, dielectric field stabilization and steric effects of the solvent on the transition (final) state versus the reactant (initial) state of the molecule. The hydrogen bonding calculation gauges both the hydrogen acceptor effect (alpha) and hydrogen donor effect (beta) of the esters, while the field stabilization calculation describes the effect of dielectric constant of the solvent on the ester hydrolysis rate constant.

### 5.3.1. Hydrogen Bonding Effect

The hydrogen bonding interaction is a direct, site-coupling of a proton-donating site of one molecule with a proton-accepting site of another molecule. The total H-bonding energy is resolved into a proton-donating site,  $\alpha$ , and proton-accepting site,  $\beta$  that in the SPARC models are presumed to be independently quantifiable [4, 6-9]. If the transition state of the ester is better solvated or stabilized by the H-bonding than the initial state, the hydrolysis rate constant increases. The negatively charged transition states of base and general base-catalyzed ester hydrolysis are strongly stabilized by solvent alpha sites, while the solvent beta sites play a minor role. Thus, it might appear that  $\alpha$  the sites of the solvent should increase carboxylic acid and phosphate esters hydrolysis rate constants. However, the  $\alpha$  sites do not only solvate the transition states, but also the attacking hydroxide ion. The latter tends to stabilize the initial state more than the transition state as shown in Figure 1. The net effect is that the solvent  $\alpha$  sites tend to decrease the carboxylic acid and phosphate esters hydrolysis rate constants. On the other hand, the  $\beta$  site of the solvent can interact with an  $\alpha$  site, freeing-up hydroxide ions to react with an ester thereby tending to increase the base and neutral hydrolysis rate constant. For acid-catalyzed carboxylic acid and phosphate esters hydrolysis, both the  $\alpha$  and the  $\beta$  sites of the solvent stabilize the initial state more than the transition state. Therefore, both solvent site types decrease the acid-catalyzed hydrolysis rate constant. SPARC expresses the alpha and beta site H-bond contribution as:

$$\text{alpha} = \frac{\rho_A \alpha}{T_k} \quad \text{beta} = \frac{\rho_B \beta}{T_k} \quad (14)$$

where alpha (beta) is the hydrogen accepter (donor) effect of the solute ester and  $\alpha$  ( $\beta$ ) is the hydrogen donating (accepting) value of the solvent.  $\rho_A$  and  $\rho_B$  are data-fitted parameters

quantifying the susceptibility of the  $\alpha$  and  $\beta$  values of the solvent, respectively.  $T_k$  is the temperature in degrees Kelvin. Both  $\alpha$  and  $\beta$  of the solvent are calculated as pseudo pK<sub>a</sub>'s, with the electrostatic component treated as a dipole transition [4, 7, 11, 12].

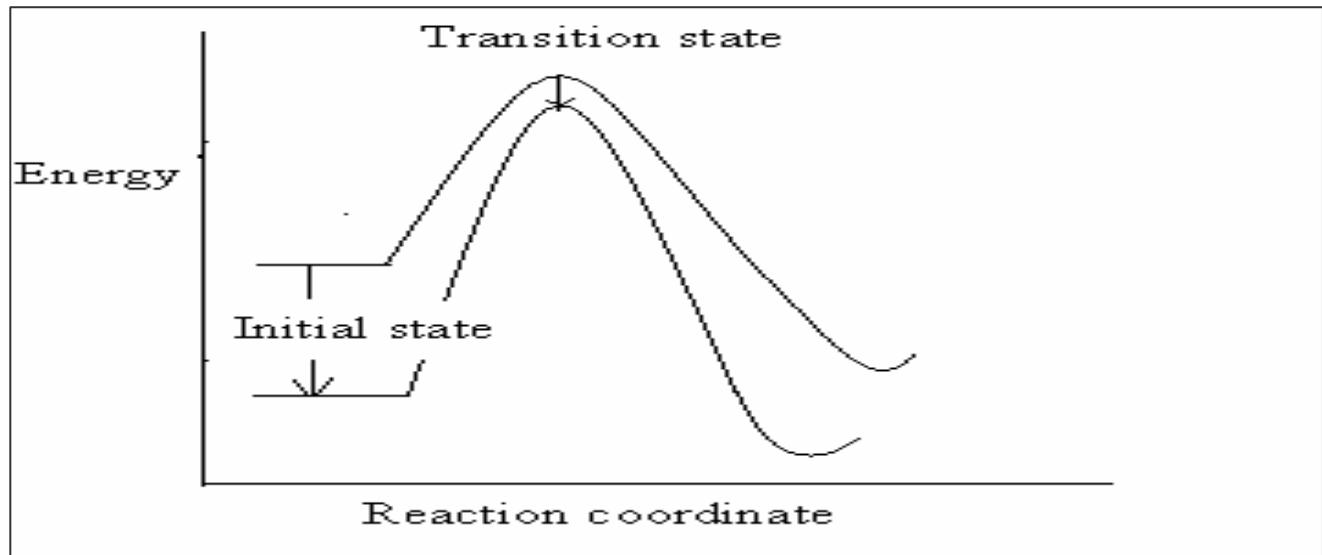


Figure 1. The effect of solvent alpha sites on the initial and transition states in carboxylic acid ester or phosphate ester hydrolysis rate. The alpha sites solvate the hydroxide ion and stabilize the initial state more than the transition state. As a result, the alphas decrease the hydrolysis rate constant during ester hydrolysis.

### 5.3.2. Field Stabilization Effect

The field stabilization effect describes the perturbation of the log of the hydrolysis rate constant by dielectric stabilization of the transition state by the solvent. It is expressed as a function of both the temperature of reaction and the dielectric constant of the solvent:

$$FS = \frac{\rho_{FS}}{T_k D_e} \quad (15)$$

where  $D_e$  is the nonlinear temperature dielectric constant of the solvent, and  $\rho_{FS}$  is the intrinsic susceptibility of the hydrolysis rate constant to the solvation effect due to the dielectric properties of the solvent, and is a data-fitted parameter. It describes the susceptibility of the transition state to dielectric stabilization. Equation 15 quantifies the differential solvation of initial (reactant) versus the transition states of the reactants in the hydrolysis reaction due to the dielectric constant of the solvent. The dielectric constant of solvents solvates or stabilizes the initial state of ester hydrolysis reactants more than the transition states. Thus, the field stabilization effect always decreases the hydrolysis rate constant. Comparing the dielectric effect on the ester hydrolysis rate constant in various mixed solvents, we observe that the decrease in the rate constant is less in pure water than in mixed aqueous-organic solvents. This is because to the higher dielectric of pure water compared to the organic solvent component of the mixed solvent relatively enhances the stability of the transition state. Thus, the hydrolysis rate constant reduction is greater in mixed aqueous-organic solvents.

For example, The field stabilization effects are  $-2.843$  and  $-0.297$  log-units for hydrolysis of ethyl p-nitrobenzoate in base and acid media respectively, while it is  $-4.530$  log-units for hydrolysis of p-nitrophenyl acetate in general base catalyzed medium. The field stabilization effect involves the dielectric constant of the solvent and in general it rises the energy of the transition state more than the initial state. As a result, it lowers the hydrolysis rate constant [41].

### 5.3.3. Steric Effect

The normal trend for a steric effect is as the bulkiness of the substituent increases, the steric effect also increases. Thus, the steric effect always decreases the hydrolysis rate constant.

Comparing the relative steric effect on carboxylic acid ester or phosphate ester hydrolysis rate constant for various solvents, we observe there is much less steric effect in pure water than in mixed solvents. The reason for this is that pure water more efficiently solvates the solute molecule and aligns the structure of the solute ester for the attacking hydroxide ion or water molecule. Conversely, the mixed-organic aqueous solvents only partially solvate the solute molecule and deform the ester structure, creating a hindrance to attack from the hydroxide ion or water molecule. Thus, the reaction does not proceed as rapidly as it does in pure water, and the hydrolysis rate constant decreases. Steric effects include both steric blockage of reaction site access and strain in achieving the transition state. SPARC expresses the steric effect on the log hydrolysis rate constant as:

$$Steric = \frac{\rho_{steric} (V_s + V_{ex} - V_{thresh})}{T_k D_e} \quad (16)$$

where:  $V_s$  is the sum of the appended substituent sizes,  $V_{thresh}$  is a threshold size for onset of steric effects;  $V_{ex}$  is the excluded (cavity) volume between pairs of appended substituents;  $\rho_{steric}$  is the intrinsic steric susceptibility, and  $D_e$  is the dielectric constant of the solvent.

For example, The steric effects are  $-1.29$  and  $-1.5$  log-units for hydrolysis of ethyl pnitrobenzoate in base and acid media respectively and it is  $-0.781$  log-unit for neutral hydrolysis of p-nitrophenyl acetate. The normal trend of steric effect is that bulkier the substituents lower the hydrolysis rate constants. Since both ethyl p-nitrobenzoate and p-nitrophenyl acetate have bulky phenyl rings, the steric effects display huge negative values [41].

## 5.4. Temperature Effect

The quantitative relationship between the rate constant and temperature is frequently expressed by the Arrhenius equation as:

$$k = A e^{-\left(\frac{E_a}{RT}\right)} \quad (17)$$

where  $k$  is the hydrolysis rate constant,  $A$  is the pre-exponential or frequency factor,  $E_a$  is the activation energy (the minimum energy required to form a product from the reactants),  $R$ , is the gas constant, and  $T$  is the absolute temperature in degrees Kelvin. This temperature dependence relationship is incorporated in the reference rate model, the field stabilization effect, the alpha/beta H-bond effect, and the steric effect.

The observed rates of hydrolysis of organic compounds, including the carboxylic acid phosphate esters, increases with temperature (see Figure 2). Figure 2 also illustrates the predictive power of the SPARC model versus measured values for three esters undergoing alkaline hydrolysis in three different solvents.

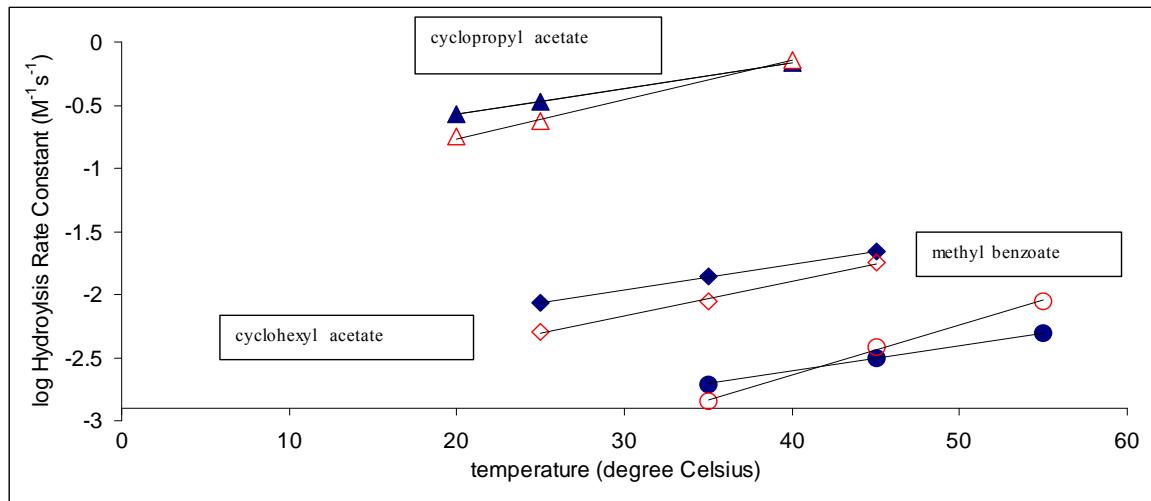


Figure 2. Log hydrolysis rate constants vs temperature for alkaline hydrolysis of methyl benzoate in 80% methanol-water (circles), cyclopropyl acetate in pure water (triangles), and cyclohexyl acetate in 70% acetone (diamonds). Solid symbols are observed values, empty symbols represent calculated values.

## 6. RESULTS AND DISCUSSIONS

SPARC's computational methodology is based on structure query and analysis. This involves combining the perturbation potentials of perturber units with the susceptibilities of the reaction center. The reaction parameters that describe a given reaction center are constant, regardless of the appended molecular structure. The same is true of substituents; the parameters that describe their mechanistic contributions are independent of the rest of the molecule. This structure factorization and mechanistic specification enables the construction of virtually any molecule and computation of its properties.

Thus, in the estimation of any molecular property via SPARC, the contributions of the structural components C, S, and R are quantified independently. For example, the strength of a substituent, S, in creating an electrostatic field effect depends only on the substituent, regardless of the reaction center, C, the appended molecular conductor, R, or the property of interest. Likewise, R is modeled so as to be independent of the identities of S, C, or the property being estimated. Hence, S and R parameters for hydrolysis rate are the same as those for pK<sub>a</sub> or electron affinity. The susceptibility of a C to an electrostatic effect quantifies only the differential interaction of the initial state versus the final state with the electrostatic fields. The susceptibility gauges only the reaction C<sub>initial</sub> – C<sub>transition state</sub>, and is completely independent of R or S. Thus, no modifications in any of the previously developed pK<sub>a</sub> models in SPARC or any extra parameterization for either S or R, were needed to calculate the hydrolysis rate constant using the pK<sub>a</sub> models, other than inferring the electronegativity and the susceptibilities of carboxylic acid ester and phosphate ester hydrolysis rate constants to electrostatic, resonance, steric and solvation effects.

Table 1 displays the aggregate statistical performance of the SPARC-calculated versus observed hydrolysis rate constants for all tests of the hydrolysis rate models to date. Figures 3-5 present observed versus SPARC-calculated values of carboxylic acid ester hydrolysis rate constants undergoing base, acid and general base catalyzed hydrolysis, respectively. These carboxylic acid ester test sets represent 321, 416 and 50 unique esters undergoing base, acid and general-base catalyzed hydrolysis, respectively. Because several of the esters were measured under different conditions (solvents, temperatures, etc) there were 654, 667 and 150 base, acid and general base-catalyzed calculations performed. The RMS deviations between the SPARC-calculated and observed values for each of these reaction mechanisms were 0.37, 0.37 and 0.39  $\log M^{-1}s^{-1}$ , respectively. A sample calculation of the acid hydrolysis rate constant for p-nitrophenyl acetate is shown in the appendix.

The same chemical hydrolysis models were used to estimate base, acid and neutral organophosphorus hydrolysis rate constants in water as a function of temperature from molecular structure. Results were tested against 225 base, 83 acid and 89 neutral measured organophosphorus hydrolysis rate constants. The RMS deviation error between the observed and SPARC-calculated values were 0.40, 41 and 1.08  $\log M^{-1}s^{-1}$  for the base, acid and neutral hydrolysis organophosphate ester rate constants, respectively also as is reported in Table 1B.

We discovered that to expand our model to fluorine leaving groups on organophosphate esters base hydrolysis, all that was required was a single addition to the reference rate model. This addition took the form of redefining the  $Ref_1$  constant. The remaining portions of the model use the parameters of the group that will hydrolyze after the fluorine-containing group. For example, if the compound has two additional leaving groups and one is an aromatic group and

the other is aliphatic, then the aromatic parameters will be used. This resulted in a fluorine-containing organophosphate esters hydrolysis model with a RMS of  $0.268 \text{ log M}^{-1}\text{s}^{-1}$ .

The organophosphate ester base-catalyzed hydrolysis calculator was initially trained on 15 compounds (29 data points), chosen by visual inspection to span all hydrolysis mechanisms. This training set had a RMS deviation of  $0.403 \text{ log M}^{-1}\text{s}^{-1}$  and a  $R^2$  value of 0.97. The calculator was then tested on 78 other compounds (196 data points) with a RMS deviation of  $0.50 \text{ log M}^{-1}\text{s}^{-1}$  and a  $R^2$  value of 0.95.

Acid catalyzed and neutral hydrolysis rate constants have been measured by many groups [37, 42-47]. Unfortunately, the interlab agreement between measurements of the same compounds is low. This experimental data varies by a much greater amount than that reported for base catalyzed hydrolysis. The variance is partially due to the slow hydrolysis rate of acid and neutral solutions as compared to alkaline hydrolysis. Slow hydrolysis rates (hundreds of years) require sensitive instruments to detect any change in the composition of the solution. Also, these compounds are usually synthesized as inorganic species or complexes and accurate measurements depend on being able to measure the transformation of a single species. Acid catalyzed hydrolysis doesn't really begin to occur until a pH of 2 or lower is reached and for many compounds, it doesn't begin until the solution is at a negative pH. Further complicating matters is the ionization or multiple ionization of the compound that occurs. This can lead to different concentrations of various species, obscuring the overall hydrolysis rate. In neutral hydrolysis, much of the same is true, with the pH range being from 2-8. For most components in this range, the hydrolysis rate is only approximately constant. This is due to competing mechanisms which occur at the same time. A complete listing of the compounds used to develop these models can be found in Tables 18 and 19. These compounds represent the best

experimentally measured data available for these types of phosphate ester hydrolysis. SPARC's acid catalyzed hydrolysis model is robust and accurately represents the mechanisms influencing the hydrolysis rate constant. In order to determine the parameters for the mechanisms that describe acid catalyzed hydrolysis, the model was trained on all the data found in the literature: 28 compounds, at a variety of temperatures (83 data points). The neutral model is not as accurate as most SPARC models, however, as the disparity of measurements as reported in the literature preclude a more accurate model. The same procedure was repeated for neutral hydrolysis model as for acid: 36 compounds (89 data points) were found in the literature and used to train the parameters.

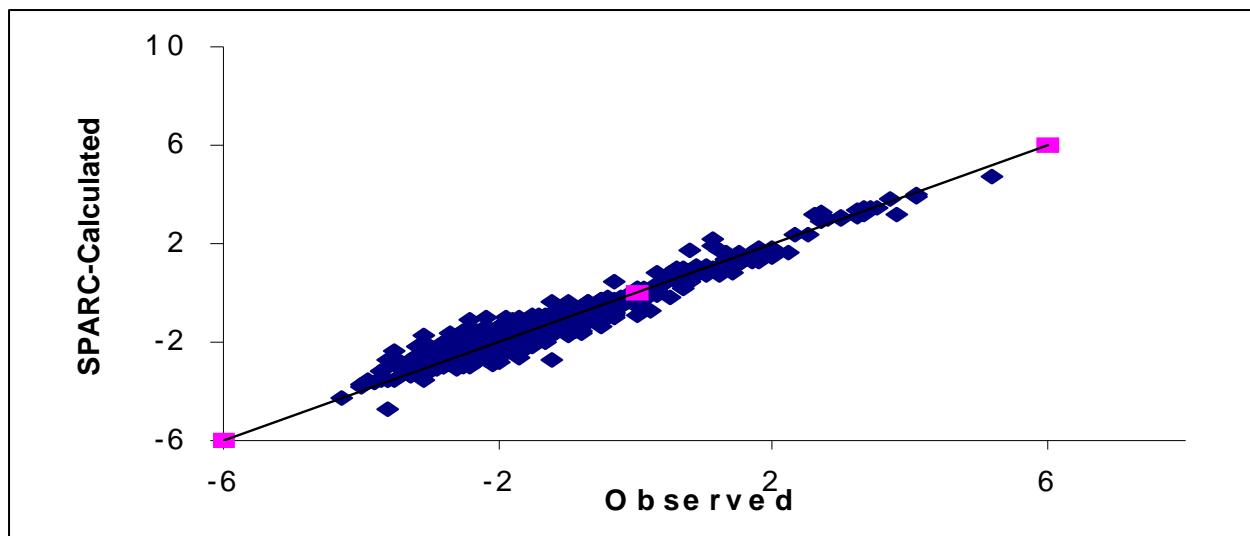


Figure 3. SPARC-calculated vs. observed log hydrolysis rate constants for alkaline hydrolysis of carboxylic acid esters in six different solvents. The RMS deviation error of the log values is  $0.37 \text{ M}^{-1}\text{s}^{-1}$  and  $R^2$  is 0.97. See Tables 2-7.

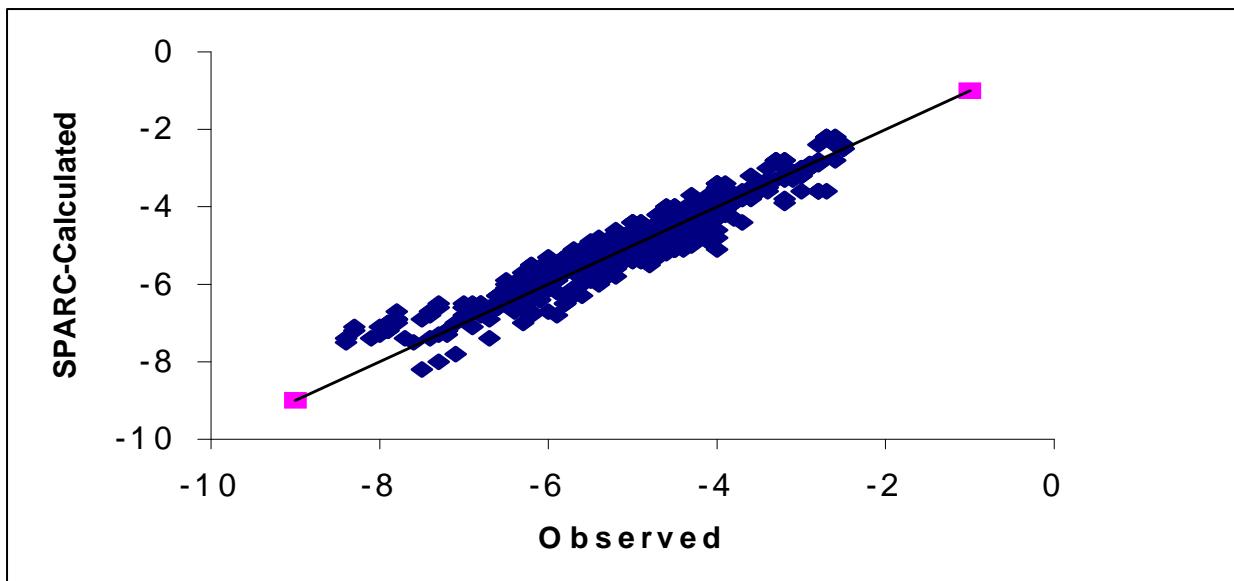


Figure 4. SPARC-calculated vs. observed log hydrolysis rate constants for acid hydrolysis of carboxylic acid esters in five solvents and at different temperatures. The RMS deviation error of the log values is  $0.37 \text{ M}^{-1}\text{s}^{-1}$  and  $R^2$  is 0.97. See Tables 8-12.

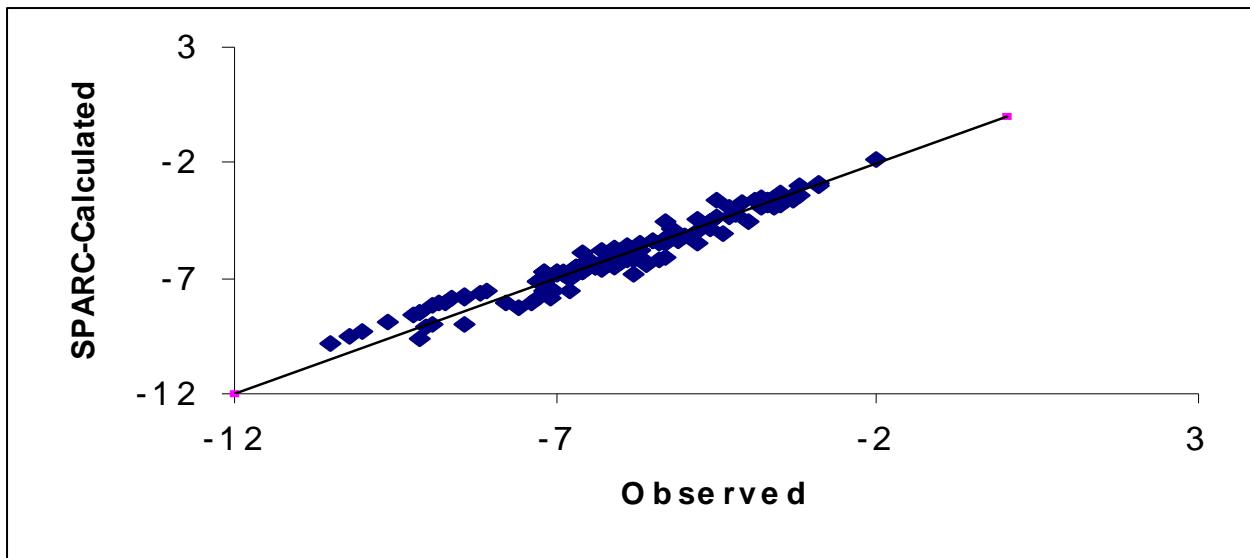


Figure 5. SPARC-calculated vs. observed log hydrolysis rate constants for general alkaline base hydrolysis of carboxylic acid esters in four different solvents and at different temperatures. The RMS deviation error of the log values is  $0.39 \text{ M}^{-1}\text{s}^{-1}$  and  $R^2$  is 0.97. See Tables 13-16.

Table1A. Statistical comparison of SPARC-calculated to observed<sup>a</sup> values of log hydrolysis rate constants of carboxylic acid ester in water and in mixed solvent systems

Training Set			Test Sets										
All Mechanisms (Base, Acid, Neutral)			Solvent	Total. Comp	Base Catalyzed			Acid Catalyzed			Neutral Catalyzed		
No	RMS	R <sup>2</sup>			No	RMS	R <sup>2</sup>	No	RMS	R <sup>2</sup>	No	RMS	R <sup>2</sup>
705	0.33	0.98	Water	576	142	0.39	0.98	383	0.36	0.98	51	0.34	0.98
			Acetone /Water	424	143	0.34	0.83	208	0.33	0.96	73	0.36	0.96
			Ethanol /Water	153	105	0.29	0.83	39	0.17	0.98	9	0.1	0.99
			Methanol /Water	172	150	0.36	0.78	22	0.22	0.95	N/A	N/A	N/A
			Dioxnae/ Water	122	90	0.47	0.75	15	0.16	0.87	17	0.47	0.67
			Acetonitrile /Water	24	24	0.3	0.97	N/A	N/A	N/A	N/A	N/A	N/A
			Total	1471	654	0.37	0.96	667	0.37	0.97	150	0.39	0.97

a: Observed values are from many sources, see Tables 2-16. Units are (L/mole) s<sup>-1</sup>

Table1B. Statistical comparison of SPARC-calculated to observed<sup>a</sup> values of log hydrolysis rate constants of organophosphorus in water

Training Set			Test Sets									
All Mechanisms (Base, Acid, Neutral)			Total. Comp	Base-Catalyzed			Acid-Catalyzed			Neutral -Catalyzed		
No	RMS	R <sup>2</sup>	397	No	RMS	R <sup>2</sup>	No	RMS	R <sup>2</sup>	No	RMS	R <sup>2</sup>
278 <sup>b</sup>	0.38	0.94		225	0.40	0.93	83	0.41	0.81	89	1.08	0.51

a: Observed values are from many sources, see Tables 17-19. Units are (L/mole) s<sup>-1</sup>

b: The training set include all acid, neutral and 197 base hydrolysis data points

## **7. MODELS VERIFICATION AND VALIDATION**

In chemistry, as with all physical sciences, one can never determine the “validity” of any predictive model with absolute certainty. This is a direct consequence of the empirical nature of science. Because SPARC is expected to predict reaction parameters for processes for which little data exists, “validity” must drive the efficiency of the model constructs in “capturing” or reflecting the existing knowledge base of chemical reactivity. In every aspect of SPARC development, from choosing the programming environment to building model algorithms or rule bases, system validation and verification were important criteria. The basic mechanistic models in SPARC were designed and parameterized to be portable to any type of chemistry or organic chemical structure. This extrapolability impacts system validation and verification in several ways. First, as the diversity of structures and the chemistry that is addressable increases, so does the opportunity for error. More importantly, however, in verifying against the theoretical knowledge of reactivity, specific situations can be chosen that offer specific challenges. This is important when verifying or validating performance in areas where existing data are limited or where additional data collection may be required. Finally, this expanded prediction capability allows one to choose, for exhaustive validating, the reaction parameters for which large and reliable data sets do exist to validate against.

In SPARC, the experimental data for physicochemical properties (such as hydrolysis rate constant, or ionization  $pK_a$ ) are not used to develop (or directly impact) the model that calculates that particular property. Instead, physicochemical properties are predicted using a few models that quantify the underlying phenomena that drive all types of chemical behavior (e.g., resonance, electrostatic, induction, dispersion, H-bonding interactions, etc.).

These mechanistic models were parameterized using a very limited set of experimental data, but not data for the end-use properties that will subsequently be predicted. After verification, the mechanistic models were used in (or ported to) the various software modules that calculate the various end-use properties (such as chemical reduction or hydrolysis rate constant). It is critical to recognize that the same mechanistic model (e.g., H-bonding model) will appear in all of the software modules that predict the various end-use properties (e.g., chemical hydrolysis rate constant or ionization pKa) for which that phenomenon is important. Thus, any comparison of SPARC-calculated physicochemical properties to an adequate experimental data set is a true model validation test -- there is no training (or calibration) data set in the traditional sense for that particular property. The SPARC physical properties and chemical reactivity parameters models have been tested and validated on more than 10,000 data points [48].

A quality assurance (QA) plan was developed to recalculate all the hydrolysis rate constants reported in Tables 2-19 and compare each calculation to an originally-calculated-value stored in the SPARC databases. Under this plan, every quarter, two batch files that contain all the hydrolysis rate constants data recalculate various hydrolysis rate constants. The QA software compares every single “new” output to the SPARC originally-calculated-value in earlier date (stored in SPARC database). In this way, we ensure that existing parameter models still work correctly after new capabilities and improvements are added to SPARC. This also ensures that the computer code for hydrolysis rate constants and other mechanistic models are fully operational.

## **8. TRAINING AND MODEL PARAMETER INPUT**

All quantitative chemical models require, at some point, calibration or parameterization. The quality of computational output necessarily reflects the quality of the calibration parameters. For this reason, a self-training complement (TRAIN) to SPARC was developed. Although a detailed description of TRAIN will not be given at this time, the following is a general review. For a given set of targeted model parameters, the program takes initial “guesstimates” (and the appropriate boundary constraints) together with a set of designated training data and provides an optimized set of model parameters. TRAIN cycles once or iteratively through Jacobian optimization procedure that is basically a non-linear, least square matrix method. TRAIN sets-up and executes the optimization specifics according to user prescription.

Table 2. SPARC-calculated vs. observed log base-catalyzed hydrolysis rate constants for carboxylic acid esters in water as a function of temperature in M<sup>-1</sup>s<sup>-1</sup>

Num	Esters	Obs	Calc	Temp	Ref
1	Methyl formate	1.4	1.1	25	[49]
2	Ethyl formate	1.4	1.1	25	[49]
3	Propyl formate	1.2	1.1	25	[49]
4	Butyl formate	1.3	1.1	25	[49]
5	Methyl dichloroacetate	3.2	3.1	25	[49]
6	Ethyl difluoroacetate	3.7	3.8	25	[49]
7	Ethyl methyl sulfoxide acetate	0.6	0.5	25	[49]
8	Ethyl methyl sulfone acetate	1.1	2.2	25	[49]
9	Methyl acetate	-0.7	-0.4	25	[50]
10	Ethyl acetate	-1	-0.6	25	[51]
11	Propyl acetate	-1.1	-0.7	25	[51]
12	Butyl acetate	-1.1	-0.7	25	[51]
13	Isopropyl acetate	-1.5	-0.9	25	[51]
14	Cyclopropyl acetate	-0.6	-0.5	25	[51]
15	Cyclopentyl acetate	-1.4	-0.9	25	[51]
16	b-Methoxyethyl acetate	-0.7	-0.4	25	[51]
17	b-Chloroethyl acetate	-0.4	-0.2	25	[51]
18	Chloromethyl acetate	1.8	1.8	25	[51]
19	Dichloromethyl acetate	3.2	3.4	25	[51]
20	Trichloromethyl acetate	4.1	3.9	25	[51]
21	Bromomethyl acetate	2	1.7	25	[51]
22	Dimethyl-amino-ethyl acetate	-1	-0.4	25	[51]
23	Ethyl propionate	-1	-1	25	[51]
24	Ethyl butyrate	-1.3	-1.2	25	[51]
25	Ethyl sec-butyrate	-1.5	-1.4	25	[51]
26	Ethyl neopentate	-2.8	-2	25	[51]
27	Ethyl fluoroacetate	1.1	1.9	25	[51]
28	Ethyl chloroacetate	1.5	1.5	25	[51]
29	Methyl chloroacetate	1.8	1.6	25	[51]
30	Ethyl dichloroacetate	2.8	3	25	[51]
31	Ethyl trichloroacetate	3.4	3.5	25	[51]
32	Isopropyl trichloroacetate	2.6	3.2	25	[51]
33	Ethyl bromoacetate	1.7	1.3	25	[51]
34	Methyl bromoacetate	2	1.5	25	[51]
35	Ethyl dibromoacetate	2.3	2.4	25	[51]
36	Ethyl bromopropionate	1	0.8	25	[51]
37	Ethyl iodoacetate	1.2	1.1	25	[51]
38	Ethyl methoxyacetate	0.1	0.2	25	[51]
39	Ethyl oxyacetate	0	-0.1	25	[51]
40	Ethyl methyl thioacetate	0	0.2	25	[51]

Num	Esters	Obs	Calc	Temp	Ref
41	Ethyl aminoacetate	-0.2	-0.3	25	[51]
42	Acetic acid, 1-Pentene, 3-methyl- ester	-2.4	-1.1	25	[51]
43	Vinyl acetate	0.6	1	25	[51]
44	Ethyl acrylate	-1.1	-0.7	25	[51]
45	2-Butenoic acid, ethyl ester	-1.9	-2.1	25	[51]
46	Ethyl 2-butynoate	-0.3	-1.2	25	[51]
47	Ethyl propiolate	0.7	0.6	25	[51]
48	p-Nitrophenyl chloroacetate	3.8	3.2	25	[51]
49	Phenyl dichloroacetate	4.1	4	25	[51]
50	Ethyl benzoate	-1.5	-1.3	25	[51]
51	Ethyl p-aminobenzoate	-2.6	-2.8	25	[51]
52	Ethyl p-nitrobenzoate	-0.1	-0.3	25	[51]
53	Ethyl p-fluorobenzoate	-1.4	-1.3	25	[51]
54	Ethyl m-aminobenzoate	-1.6	-1.8	25	[51]
55	Methyl benzoate	-1.1	-1.1	25	[51]
56	Isopropyl benzoate	-2.2	-1.5	25	[51]
57	p-Tolyl benzoate	-0.5	-0.3	25	[51]
58	m-cyanophenyl benzoate	0.3	0.4	25	[51]
59	p-Nitrophenyl benzoate	0.4	0.5	25	[51]
60	2,4-dinitrophenyl benzoate	1.2	1.7	25	[51]
61	Phenyl acetate	-0.3	0.5	25	[51]
62	Phenyl propionate	0.1	0	25	[51]
63	Phenyl butyrate	-0.1	-0.1	25	[51]
64	Phenyl sec-butyrate	-0.2	-0.4	25	[51]
65	Phenyl pentate	-0.2	-0.2	25	[51]
66	Phenyl sec-pentate	-0.6	-0.9	25	[51]
67	Phenyl neopentate	-0.9	-1	25	[51]
68	Phenyl (t-butyl)acetate	-0.3	-0.9	25	[51]
69	p-Methoxyphenyl acetate	0	0.2	25	[51]
70	p-Methoxyphenyl propionate	-0.1	-0.2	25	[51]
71	p-Methoxyphenyl butyrate	-0.1	-0.4	25	[51]
72	p-Methoxyphenyl sec-butyrate	-0.3	-0.6	25	[51]
73	p-Methoxyphenyl pentate	-0.2	-0.4	25	[51]
74	p-Methoxyphenyl sec-pentate	-0.6	-1.1	25	[51]
75	p-Methoxyphenyl neopentate	-0.9	-1.2	25	[51]
76	o-Nitrophenyl acetate	1.3	1.1	25	[50]
77	p-Nitrophenyl acetate	1.5	1.2	25	[50]
78	p-Nitrophenyl propionate	0.9	0.7	25	[50]
79	p-Nitrophenyl butyrate	0.8	0.5	25	[50]
80	p-Nitrophenyl sec-butyrate	0.7	0.3	25	[50]
81	p-Nitrophenyl pentate	0.7	0.5	25	[50]
82	p-Nitrophenyl sec-pentate	0.5	-0.2	25	[50]

Num	Esters	Obs	Calc	Temp	Ref
83	p-Nitrophenyl neopentate	0.1	-0.3	25	[50]
84	o-Fluorophenyl acetate	0.9	0.9	25	[50]
85	o-Chlorophenyl acetate	0.7	1	25	[50]
86	o-Bromophenyl acetate	0.8	0.9	25	[50]
87	o-Iodophenyl acetate	0.7	0.9	25	[50]
88	o-Methylphenyl acetate	0.1	0	25	[50]
89	o-Ethylphenyl acetate	0.1	-0.2	25	[50]
90	o-Isopropylphenyl acetate	0	-0.5	25	[50]
91	o-(t-Butyl)phenyl acetate	-0.3	-0.8	25	[50]
92	o-Methoxyphenyl acetate	0.3	0.3	25	[50]
93	o-Nitrophenyl acetate	1.3	1.6	25	[50]
94	o-Cyanophenyl acetate	1.5	1.6	25	[50]
95	m-Fluorophenyl acetate	0.9	0.7	25	[50]
96	m-Bromophenyl acetate	0.9	0.8	25	[50]
97	m-Methylphenyl acetate	0.4	0.4	25	[50]
98	m-Ethylphenyl acetate	0.4	0.4	25	[50]
99	m-Methoxyphenyl acetate	0.6	0.5	25	[50]
100	m-Nitrophenyl acetate	1	1.1	25	[50]
101	m-Cyanophenyl acetate	1.2	1	25	[50]
102	p-Fluorophenyl acetate	0.6	0.6	25	[50]
103	p-Chlorophenyl acetate	0.8	0.6	25	[50]
104	p-Bromophenyl acetate	0.7	0.6	25	[50]
105	p-Ethylphenyl acetate	0.3	0.3	25	[50]
106	p-(t-Butyl)phenyl acetate	0.3	0.3	25	[50]
107	p-Cyanophenyl acetate	1.3	1.1	25	[50]
108	(p-Ethanal)phenyl acetate	1	0.7	25	[50]
109	Isopropyl acetate	-0.8	-0.6	20	[52]
110	Cyclopropyl acetate	-0.1	-0.2	40	[52]
111	Vinylic acetate	-0.2	0.5	0.2	[52]
112	Vinylic acetate	0.5	0.9	20	[52]
113	Isopropenyl acetate	-1.2	0.3	0.2	[52]
114	Isopropenyl acetate	-0.5	0.6	20	[52]
115	Cyclopentenyl acetate	-0.1	0	0.2	[52]
116	Cyclopentenyl acetate	0.4	0.3	20	[52]
117	Cyclohexyl acetate	-0.8	-1.2	20	[52]
118	Cyclohexyl acetate	-0.3	-0.8	40	[52]
119	Cyclopentyl acetate	-1.6	-1.1	20	[52]
120	Cyclopentyl acetate	-1	-0.7	40	[52]
121	Butyl acetate	-1.2	-0.8	20	[52]
122	Ethyl chloroacetate	1.3	1.4	15	[53]
123	Ethyl chloroacetate	1.7	1.6	35	[53]
124	Ethyl dichloroacetate	2.7	2.9	15	[53]

Num	Esters	Obs	Calc	Temp	Ref
125	Ethyl dichloroacetate	3	3	35	[53]
126	Ethyl trichloroacetate	3.3	3.5	15	[53]
127	Ethyl trichloroacetate	3.5	3.5	35	[53]
128	Ethyl bromoacetate	1.5	1.2	15	[53]
129	Ethyl bromoacetate	1.8	1.4	35	[53]
130	Ethyl iodoacetate	1.1	1	15	[53]
131	Ethyl iodoacetate	1.4	1.2	35	[53]
132	Ethyl dibromoacetate	2.5	2.4	35	[53]
133	Methyl chloroacetate	1.5	1.5	15	[53]
134	Methyl chloroacetate	2	1.8	35	[53]
135	Methyl bromoacetate	1.8	1.3	15	[53]
136	Methyl bromoacetate	2.2	1.6	35	[53]
137	Methyl dichloroacetate	3	3.1	15	[53]
138	Methyl dichloroacetate	3.3	3.2	35	[53]
139	Ethyl trifluoroacetate	5.2	4.7	15	[53]
140	Isopropyl trichloroacetate	2.7	3.3	35	[53]
141	Chloromethyl acetate	0.8	1.7	15	[53]
142	Ethyl 2-pyridine-carboxylate	-0.3	0.3	25	[49]

Table 3. SPARC-calculated vs. observed log base-catalyzed hydrolysis rate constants for carboxylic acid esters in water-acetone mixture as a function of temperature in M<sup>-1</sup>s<sup>-1</sup>

Num	Esters	Obs.	Calc.	Temp	Solvent.	Ref.
1	Methyl formate	1.2	0.8	25	37% Acetone	[54]
2	Ethyl formate	1	0.8	25	37% Acetone	[54]
3	Propyl formate	0.9	0.8	25	37% Acetone	[54]
4	Isopropyl formate	0.5	0.8	25	37% Acetone	[54]
5	Butyl formate	0.8	0.8	25	37% Acetone	[54]
6	sec-Butyl formate	0.3	0.8	25	37% Acetone	[54]
7	Isobutyl formate	0.8	0.8	25	37% Acetone	[54]
8	Pentyl formate	0.7	0.8	25	37% Acetone	[54]
9	Isopentyl formate	0.7	0.8	25	37% Acetone	[54]
10	Methyl acetate	-0.8	-0.8	25	37% Acetone	[54]
11	Methyl propionate	-1	-1.3	25	37% Acetone	[54]
12	Methyl butyrate	-1.3	-1.5	25	37% Acetone	[54]
13	Methyl isobutyrate	-1.4	-1.5	25	37% Acetone	[54]
14	Ethyl acetate	-1.2	-1	25	37% Acetone	[54]
15	propyl acetate	-1.3	-1	25	37% Acetone	[54]
16	Butyl acetate	-1.4	-1.1	25	37% Acetone	[54]
17	sec-Butyl acetate	-2.2	-1.9	25	37% Acetone	[54]
18	Isobutyl acetate	-1.5	-1.1	25	37% Acetone	[54]
19	Pentyl acetate	-1.5	-1.1	25	37% Acetone	[54]
20	Isopentyl acetate	-1.5	-1.6	25	37% Acetone	[54]
21	Hexyl acetate	-1.5	-1.1	25	37% Acetone	[54]
22	Ethyl propionate	-1.3	-1.5	25	37% Acetone	[54]
23	Ethyl butyrate	-1.7	-1.7	25	37% Acetone	[54]
24	Methyl acetate	-1	-1.1	25	70% Acetone	[55]
25	Ethyl acetate	-1.3	-1.3	25	70% Acetone	[55]
26	propyl acetate	-1.6	-1.4	25	70% Acetone	[55]
27	Isopropyl acetate	-2.2	-1.8	25	70% Acetone	[55]
28	sec-Butyl acetate	-1.7	-1.5	25	70% Acetone	[55]
29	Butyl acetate	-1.6	-1.5	25	70% Acetone	[55]
30	sec-Butyl acetate	-2.5	-2.6	25	70% Acetone	[55]
31	t-Butyl acetate	-3.6	-2.7	25	70% Acetone	[55]
32	Cyclohexyl acetate	-2.3	-2.1	25	70% Acetone	[55]
33	Methyl propionate	-1.2	-1.7	25	70% Acetone	[55]
34	Ethyl propionate	-1.7	-2	25	70% Acetone	[55]
35	Isopropyl propionate	-2.5	-2.4	25	70% Acetone	[55]
36	Butyl propionate	-2	-2.1	25	70% Acetone	[55]
37	Benzyl benzoate	-2.2	-1.9	25	70% Acetone	[55]
38	p-Methylbenzyl benzoate	-2.3	-2	25	70% Acetone	[55]
39	m-Methylbenzyl benzoate	-2.2	-2	25	70% Acetone	[55]

Num	Esters	Obs.	Calc.	Temp	Solvent	Ref.
40	p-Ethylbenzyl benzoate	-2.3	-2	25	70% Acetone	[55]
41	p-Isopropylbenzyl benzoate	-2.3	-2	25	70% Acetone	[55]
42	p-(t-Butyl)benzyl benzoate	-2.3	-2	25	70% Acetone	[55]
43	p-Methoxylbenzyl benzoate	-2.3	-2.1	25	70% Acetone	[55]
44	p-Phenoxybenzyl benzoate	-2.1	-1.9	25	70% Acetone	[55]
45	(p-Methiol)benzyl benzoate	-2.1	-1.9	25	70% Acetone	[55]
46	(m-Methiol)benzyl benzoate	-2	-1.8	25	70% Acetone	[55]
47	p-Phenylbenzyl benzoate	-2.1	-1.8	25	70% Acetone	[55]
48	2-Naphthylcarbinyl benzoate	-2.1	-1.8	25	70% Acetone	[55]
49	p-Fluorobenzyl benzoate	-2	-1.8	25	70% Acetone	[55]
50	p-Chlorobenzyl benzoate	-1.9	-1.7	25	70% Acetone	[55]
51	m-Chlorobenzyl benzoate	-1.8	-1.6	25	70% Acetone	[55]
52	p-Bromobenzyl benzoate	-1.9	-1.7	25	70% Acetone	[55]
53	m-Bromobenzyl benzoate	-1.8	-1.6	25	70% Acetone	[55]
54	p-Nitrobenzyl benzoate	-1.4	-1.2	25	70% Acetone	[55]
55	m-Nitrobenzyl benzoate	-1.5	-1.3	25	70% Acetone	[55]
56	p-Cyanobenzyl benzoate	-1.5	-1.2	25	70% Acetone	[55]
57	m-Cyanobenzyl benzoate	-1.5	-1.3	25	70% Acetone	[55]
58	p-methylsulfoxide benzyl benzoate	-1.6	-1.4	25	70% Acetone	[55]
59	p-methylsulfone benzyl benzoate	-1.4	-1.3	25	70% Acetone	[55]
60	m-methylsulfone benzyl benzoate	-1.5	-1.3	25	70% Acetone	[55]
61	2-Fluorenylcarbinyl benzoate	-2.2	-1	25	70% Acetone	[55]
62	1-Naphthylcarbinyl benzoate	-2.1	-1.9	25	70% Acetone	[55]
63	2-Phenanthrylcabinyl benzoate	-2	-1.8	25	70% Acetone	[55]
64	3-Phenanthrylcabinyl benzoate	-2.1	-1.7	25	70% Acetone	[55]
65	9-Phenanthrylcabinyl benzoate	-2	-1.9	25	70% Acetone	[55]
66	9-Anthrylcabinyl benzoate	-2.2	-1.7	25	70% Acetone	[55]
67	Ethyl phenylacetate	-1.4	-1.4	25	60% Acetone	[56]
68	Ethyl o-fluorophenylacetate	-1.5	-1.8	25	60% Acetone	[56]
69	Ethyl o-chlorophenylacetate	-1.8	-1.9	25	60% Acetone	[56]
70	Ethyl o-bromophenylacetate	-1.9	-2	25	60% Acetone	[56]
71	Ethyl o-iodophenylacetate	-1.9	-2.1	25	60% Acetone	[56]
72	Ethyl m-iodophenylacetate	-1.1	-1.3	25	60% Acetone	[56]
73	Ethyl o-methylphenylacetate	-2	-2.1	25	60% Acetone	[56]
74	Ethyl o-butylphenylacetate	-2.8	-2.5	25	60% Acetone	[56]
75	Ethyl 1,6-dichlorophenylacetate	-2.9	-2.4	25	60% Acetone	[56]
76	Ethyl p-(t-butyl)phenylacetate	-1.7	-1.6	25	60% Acetone	[57]
77	Ethyl p-dimethylaminophenylacetate	-1.6	-1.9	25	60% Acetone	[57]
78	Ethyl o-nitrophenylacetate	-1.6	-2	25	60% Acetone	[57]
79	Ethyl p-aminophenylacetate	-1.5	-1.9	25	60% Acetone	[57]
80	Ethyl m-methoxyphenylacetate	-1.3	-1.5	25	60% Acetone	[57]

Num	Esters	Obs.	Calc.	Temp	Solvent	[57]
81	Ethyl (3,4-biphenyl)phenylacetate	-1.3	-1.4	25	60% Acetone	[57]
82	Ethyl (p-phenyl)phenylacetate	-1.5	-1.4	25	60% Acetone	[57]
83	Ethyl p-iodophenylacetate	-1.2	-1.3	25	60% Acetone	[57]
84	Ethyl m-chlorophenylacetate	-1	-1.4	25	60% Acetone	[57]
85	Ethyl m-fluorophenylacetate	-1	-1.4	25	60% Acetone	[57]
86	Ethyl p-cyanophenylacetate	-0.7	-1.1	25	60% Acetone	[57]
87	Ethyl p-nitrophenylacetate	-0.6	-1.1	25	60% Acetone	[57]
88	Ethyl m-nitrophenylacetate	-0.8	-1.2	25	60% Acetone	[57]
89	Ethyl p-bromophenylacetate	-1	-1.4	25	60% Acetone	[57]
90	Ethyl p-chlorophenylacetate	-1	-1.4	25	60% Acetone	[57]
91	Ethyl p-fluorophenylacetate	-1.2	-1.4	25	60% Acetone	[57]
92	Ethyl p-methoxyphenylacetate	-1.4	-1.7	25	60% Acetone	[57]
93	Ethyl p-methylphenylacetate	-1.6	-1.6	25	60% Acetone	[57]
94	Methyl phenylacetate	-0.9	-1.5	25	75% Acetone	[58]
95	Methyl 9-anthrylacetate	-1.8	-2.3	25	75% Acetone	[58]
96	Methyl 9-phenanthrylacetate	-1.4	-1.7	25	75% Acetone	[58]
97	Methyl 1-naphthylacetate	-1.3	-1.7	25	75% Acetone	[58]
98	Methyl p-methylbenzoate	-1	-1.7	25	75% Acetone	[58]
99	Methyl 2-naphthylacetate	-0.8	-1.4	25	75% Acetone	[58]
100	Methyl 4-biphenylacetate	-0.8	-1.4	25	75% Acetone	[58]
101	Methyl 2-anthrylacetate	-0.8	-1.4	25	75% Acetone	[58]
102	Methyl 3-phenanthrylacetate	-0.8	-1.4	25	75% Acetone	[58]
103	Methyl 2-phenanthrylacetate	-0.8	-1.5	25	75% Acetone	[58]
104	Methyl acetate	-1	-1.2	20	70% Acetone	[55]
105	Ethyl acetate	-1.5	-1.4	20	70% Acetone	[55]
106	Ethyl acetate	-1.3	-1.1	35	70% Acetone	[55]
107	Ethyl acetate	-0.9	-0.9	44.7	70% Acetone	[55]
108	Propyl acetate	-1.7	-1.5	20	70% Acetone	[55]
109	Propyl acetate	-1.3	-1.2	35	70% Acetone	[55]
110	Propyl acetate	-1	-1	44.7	70% Acetone	[55]
111	Isopropyl acetate	-2.3	-1.9	20	70% Acetone	[55]
112	Isopropyl acetate	-1.9	-1.6	35	70% Acetone	[55]
113	Isopropyl acetate	-1.6	-1.4	44.7	70% Acetone	[55]
114	Isobutyl acetate	-1.9	-1.6	20	70% Acetone	[55]
115	Isobutyl acetate	-1.4	-1.3	35	70% Acetone	[55]
116	Isobutyl acetate	-1.2	-1.1	44.7	70% Acetone	[55]
117	n-Butyl acetate	-1.8	-1.6	20	70% Acetone	[55]
118	n-Butyl acetate	-1.6	-1.3	35	70% Acetone	[55]
119	n-Butyl acetate	-1.1	-1.1	44.7	70% Acetone	[55]
120	sec-Butyl acetate	-2.6	-2.7	20	70% Acetone	[55]
121	sec-Butyl acetate	-2.2	-2.3	35	70% Acetone	[55]
122	sec-Butyl acetate	-1.9	-2.2	44.7	70% Acetone	[55]

Num	Esters	Obs.	Calc.	Temp	Solvent	Ref.
123	t-Butyl acetate	-3.2	-2.5	35	70% Acetone	[55]
124	t-Butyl acetate	-3	-2.3	44.7	70% Acetone	[55]
125	Cyclohexyl acetate	-2	-1.9	35	70% Acetone	[55]
126	Cyclohexyl acetate	-1.8	-1.7	44.7	70% Acetone	[55]
127	Methyl propionate	-1.3	-1.8	20	70% Acetone	[55]
128	Methyl propionate	-1	-1.5	35	70% Acetone	[55]
129	Methyl propionate	-0.8	-1.3	44.7	70% Acetone	[55]
130	Ethyl propionate	-1.8	-2.1	20	70% Acetone	[55]
131	Ethyl propionate	-1.4	-1.8	35	70% Acetone	[55]
132	Ethyl propionate	-1.2	-1.6	44.7	70% Acetone	[55]
133	Isopropyl propionate	-2.7	-2.6	20	70% Acetone	[55]
134	Isopropyl propionate	-2.2	-2.2	35	70% Acetone	[55]
135	Isopropyl propionate	-1.9	-2	44.7	70% Acetone	[55]
136	n-Butyl propionate	-2.1	-2.2	20	70% Acetone	[55]
137	n-Butyl propionate	-1.7	-1.9	35	70% Acetone	[55]
138	n-Butyl propionate	-1.5	-1.7	44.7	70% Acetone	[55]
139	Ethyl picolinate	-0.7	-0.9	25	60% acetone	[59]
140	Ethyl isonicotinate	-0.2	-1.1	25	60% acetone	[59]
141	Ethyl nicotinate	-0.9	-1.2	25	60% acetone	[59]

Table 4. SPARC-calculated vs. observed log base-catalyzed hydrolysis rate constants of carboxylic acid esters in ethanol-water mixtures as a function of temperature in M<sup>-1</sup>s<sup>-1</sup>

Num	Esters	Obs	Calc	Temp.	Solvent	Ref
1	Ethyl 1-naphthoate	-3.6	-3	25	85% Ethanol	[60]
2	Ethyl 3-chloro-1-naphthoate	-2.7	-2.7	25	85% Ethanol	[60]
3	Ethyl 3-bromo-1-naphthoate	-2.7	-2.7	25	85% Ethanol	[60]
4	Ethyl 4-bromo-1-naphthoate	-3	-2.9	25	85% Ethanol	[60]
5	Ethyl 5-bromo-1-naphthoate	-3	-2.9	25	85% Ethanol	[60]
6	Ethyl 4'-methoxy-p-biphenyl carboxylate	-3.5	-2.9	25	91% Ethanol	[60]
7	Ethyl 4'-methyl-p-biphenyl carboxylate	-3.4	-2.8	25	91% Ethanol	[60]
8	Ethyl p-biphenyl carboxylate	-3.3	-2.7	25	91% Ethanol	[60]
9	Ethyl 4'-chloro-p-biphenyl carboxylate	-3.1	-2.7	25	91% Ethanol	[60]
10	Ethyl 4'-bromo-p-biphenyl carboxylate	-3.1	-2.7	25	91% Ethanol	[60]
11	Ethyl 3'-bromo-p-biphenyl carboxylate	-3	-2.7	25	91% Ethanol	[60]
12	Ethyl 4'-nitro-p-biphenyl carboxylate	-2.8	-2.5	25	91% Ethanol	[60]
13	Ethyl benzoate	-3	-2.5	25	75% Ethanol	[60]
14	Ethyl phenylacetate	-1.9	-1.7	25	85% Ethanol	[56]
15	Ethyl o-iodophenyl acetate	-2.3	-2.5	25	85% Ethanol	[56]
16	Ethyl p-iodophenylacetate	-1.5	-1.6	25	85% Ethanol	[56]
17	Ethyl p-nitrophenylacetate	-1	-1.3	25	85% Ethanol	[56]
18	Ethyl o-methylphenylacetate	-2.4	-2.5	25	85% Ethanol	[56]
19	Ethyl p-methylphenylacetate	-2	-1.8	25	85% Ethanol	[56]
20	Ethyl phenylacetate	-1.8	-1.6	25	75% Ethanol	[56]
21	Ethyl o-iodophenylacetate	-2.2	-2.3	25	75% Ethanol	[56]
22	Ethyl p-iodophenylacetate	-1.4	-1.4	25	75% Ethanol	[56]
23	Ethyl p-nitrophenylacetate	-0.9	-1.2	25	75% Ethanol	[56]
24	Ethyl o-methylphenylacetate	-2.3	-2.3	25	75% Ethanol	[56]
25	Ethyl p-methylphenylacetate	-1.9	-1.7	25	75% Ethanol	[56]
26	Ethyl phenylacetate	-1.7	-1.4	25	65% Ethanol	[56]
27	Ethyl o-chlorophenylacetate	-2.1	-1.8	25	65% Ethanol	[56]
28	Ethyl o-chlorophenylacetate	-1.3	-1.3	25	65% Ethanol	[56]
29	Ethyl o-bromophenylacetate	-2.1	-2	25	65% Ethanol	[56]
30	Ethyl o-iodophenylacetate	-2.2	-2	25	65% Ethanol	[56]
31	Ethyl p-iodophenylacetate	-1.3	-1.3	25	65% Ethanol	[56]
32	Ethyl o-nitrophenylacetate	-1.9	-1.9	25	65% Ethanol	[56]
33	Ethyl m-nitrophenylacetate	-0.9	-1.1	25	65% Ethanol	[56]
34	Ethyl p-nitrophenylacetate	-0.8	-1	25	65% Ethanol	[56]
35	Ethyl o-methylphenylacetate	-2.2	-2.1	25	65% Ethanol	[56]
36	Ethyl p-methylphenylacetate	-1.8	-1.5	25	65% Ethanol	[56]
37	Ethyl p-(t-butyl)phenylacetate	-1.8	-1.5	25	65% Ethanol	[56]
38	Ethyl phenylacetate	-2	-1.7	25	90% Ethanol	[56]
39	Ethyl o-fluorophenylacetate	-2.1	-2.2	25	90% Ethanol	[56]
40	Ethyl p-fluorophenylacetate	-1.8	-1.7	25	90% Ethanol	[56]

Num	Esters	Obs.	Calc.	Temp	Solvent.	Ref.
41	Ethyl o-chlorophenylacetate	-2.3	-2.3	25	90% Ethanol	[56]
42	Ethyl m-chlorophenylacetate	-1.6	-1.6	25	90% Ethanol	[56]
43	Ethyl p-chlorophenylacetate	-1.6	-1.6	25	90% Ethanol	[56]
44	Ethyl o-bromophenylacetate	-2.4	-2.4	25	90% Ethanol	[56]
45	Ethyl p-bromophenylacetate	-1.6	-1.6	25	90% Ethanol	[56]
46	Ethyl o-iodophenylacetate	-2.4	-2.5	25	90% Ethanol	[56]
47	Ethyl m-iodophenylacetate	-1.6	-1.6	25	90% Ethanol	[56]
48	Ethyl p-iodophenylacetate	-1.6	-1.6	25	90% Ethanol	[56]
49	Ethyl o-nitrophenylacetate	-2.1	-2.4	25	90% Ethanol	[56]
50	Ethyl m-nitrophenylacetate	-1.1	-1.4	25	90% Ethanol	[56]
51	Ethyl p-nitrophenylacetate	-1.1	-1.3	25	90% Ethanol	[56]
52	Ethyl o-methylphenylacetate	-2.5	-2.5	25	90% Ethanol	[56]
53	Ethyl p-methylphenylacetate	-2.1	-1.9	25	90% Ethanol	[56]
54	Ethyl o-(t-butyl)phenylacetate	-3.3	-3.4	25	90% Ethanol	[56]
55	Ethyl p-(t-butyl)phenylacetate	-2.1	-1.9	25	90% Ethanol	[56]
56	Ethyl o-methoxyphenylacetate	-2.8	-2.8	25	90% Ethanol	[56]
57	Ethyl m-methoxyphenylacetate	-2	-1.8	25	90% Ethanol	[56]
58	Ethyl p-methoxyphenylacetate	-2.1	-2	25	90% Ethanol	[56]
59	Ethyl p-nitrophenylacetate	-2.3	-2.1	25	90% Ethanol	[56]
60	Ethyl 1,6-dichlorophenylacetate	-3.4	-2.9	25	90% Ethanol	[56]
61	Ethyl 3,4-dimethoxyphenylacetate	-2	-2.1	25	90% Ethanol	[56]
62	Ethyl 1-naphthoate	-3.1	-2.8	35	85% Ethanol	[60]
63	Ethyl 1-naphthoate	-2.8	-2.6	45	85% Ethanol	[60]
64	Ethyl 1-naphthoate	-2.5	-2.4	55	85% Ethanol	[60]
65	Ethyl 1-naphthoate	-2.1	-2.3	65	85% Ethanol	[60]
66	Ethyl 3-chloro-1-naphthoate	-2.7	-2.5	35	85% Ethanol	[60]
67	Ethyl 3-chloro-1-naphthoate	-2	-2.3	45	85% Ethanol	[60]
68	Ethyl 3-chloro-1-naphthoate	-1.6	-2.2	55	85% Ethanol	[60]
69	Ethyl 4-chloro-1-naphthoate	-2.6	-2.8	35	85% Ethanol	[60]
70	Ethyl 4-chloro-1-naphthoate	-2.2	-2.6	45	85% Ethanol	[60]
71	Ethyl 4-chloro-1-naphthoate	-1.9	-2.4	55	85% Ethanol	[60]
72	Ethyl 4-chloro-1-naphthoate	-2.5	-2.2	65	85% Ethanol	[60]
73	Ethyl 3-bromo-1-naphthoate	-2	-2.3	45	85% Ethanol	[60]
74	Ethyl 3-bromo-1-naphthoate	-1.3	-2	65	85% Ethanol	[60]
75	Ethyl 4-bromo-1-naphthoate	-2.6	-2.7	35	85% Ethanol	[60]
76	Ethyl 4-bromo-1-naphthoate	-1.9	-2.4	55	85% Ethanol	[60]
77	Ethyl 4-bromo-1-naphthoate	-1.5	-2.2	65	85% Ethanol	[60]
78	Ethyl 5-bromo-1-naphthoate	-2.3	-2.5	45	85% Ethanol	[60]
79	Ethyl 5-bromo-1-naphthoate	-1.9	-2.3	55	85% Ethanol	[60]
80	Ethyl 5-bromo-1-naphthoate	-1.6	-2.1	65	85% Ethanol	[60]
81	Ethyl 4-methyl-1-naphthoate	-3.1	-3.2	45	85% Ethanol	[60]
82	Ethyl 4-methyl-1-naphthoate	-2.8	-3	55	85% Ethanol	[60]

Num	Esters	Obs.	Calc.	Temp	Solv.	Ref.
83	Ethyl 4-methyl-1-naphthoate	-2.4	-2.8	65	85% Ethanol	[60]
84	Ethyl 4-methyl-1-naphthoate	-2	-2.6	75	85% Ethanol	[60]
85	Ethyl 3-methyl-1-naphthoate	-2.9	-2.7	45	85% Ethanol	[60]
86	Ethyl 3-methyl-1-naphthoate	-2.6	-2.5	55	85% Ethanol	[60]
87	Ethyl 3-methyl-1-naphthoate	-2.2	-2.4	65	85% Ethanol	[60]
88	Ethyl 3-methyl-1-naphthoate	-1.9	-2.2	75	85% Ethanol	[60]
89	Ethyl 4'-methoxy-p-biphenyl carboxylate	-2.8	-2.6	40	91% Ethanol	[61]
90	Ethyl 4'-methyl-p-biphenyl carboxylate	-2.7	-2.5	40	91% Ethanol	[61]
91	Ethyl p-biphenyl carboxylate	-2.6	-2.4	40	91% Ethanol	[61]
92	Ethyl 4'-chloro-p-biphenyl carboxylate	-2.5	-2.4	40	91% Ethanol	[61]
93	Ethyl 4'-bromo-p-biphenyl carboxylate	-2.5	-2.4	40	91% Ethanol	[61]
94	Ethyl 3'-bromo-p-biphenyl carboxylate	-2.4	-2.4	40	91% Ethanol	[61]
95	Ethyl 3'-nitro-p-biphenyl carboxylate	-2.2	-2.3	40	91% Ethanol	[61]
96	Ethyl 4'-nitro-p-biphenyl carboxylate	-2.2	-2.2	40	91% Ethanol	[61]
97	Ethyl picolinate	-1.5	-1.1	17	75% Ethanol	[62]
98	Ethyl nicotinate	-1.7	-1.5	17	75% Ethanol	[62]
99	Ethyl isonicotinate	-0.9	-1.4	17	75% Ethanol	[62]
100	Ethyl picolinate	-1.2	-1	25	75% Ethanol	[62]
101	Ethyl nicotinate	-1.4	-1.3	25	75% Ethanol	[62]
102	Ethyl isonicotinate	-0.7	-1.2	25	75% Ethanol	[62]
103	Ethyl picolinate	-0.9	-0.8	35	75% Ethanol	[62]
104	Ethyl nicotinate	-1.1	-1.1	35	75% Ethanol	[62]
105	Ethyl isonicotinate	-0.4	-1	35	75% Ethanol	[62]

Table 5. SPARC-calculated vs. observed log base-catalyzed hydrolysis rate constants for carboxylic acid esters in methanol-water mixtures as a function of temperature in M<sup>-1</sup>s<sup>-1</sup>

Num	Esters	Obs.	Calc	Temp.	Solvent	Ref.
1	Methyl o-fluorobenzoate	-2.6	-2.7	25	80% Methanol	[63]
2	Methyl m-nitrobenzoate	-1.6	-2.2	25	80% Methanol	[63]
3	Methyl m-chlorobenzoate	-2.4	-2.7	25	80% Methanol	[63]
4	Methyl benzoate	-2.7	-2.2	25	60% Methanol	[63]
5	Methyl p-bromobenzoate	-2.3	-2.2	25	60% Methanol	[63]
6	Methyl p-nitrobenzoate	-1.1	-1.4	25	60% Methanol	[63]
7	Methyl m-bromobenzoate	-2	-2	25	60% Methanol	[63]
8	Methyl m-nitrobenzoate	-1.3	-1.6	25	60% Methanol	[63]
9	Methyl 9-anthrylacetate	-3.3	-2.9	25	85% Methanol	[58]
10	Methyl 6-chryslacetate	-2.9	-2.4	25	85% Methanol	[58]
11	Methyl 9-phenanthrylacetate	-2.9	-2.4	25	85% Methanol	[58]
12	Methyl 1-naphthylacetate	-2.9	-2.4	25	85% Methanol	[58]
13	Methyl 1-pyrenylacetate	-2.7	-2.3	25	85% Methanol	[58]
14	Methyl p-methylphenylacetate	-2.6	-2.3	25	85% Methanol	[58]
15	Methyl 2-fluorenylacetate	-2.6	-1.7	25	85% Methanol	[58]
16	Methyl phenylacetate	-2.5	-2.1	25	85% Methanol	[58]
17	Methyl 2-naphthylacetate	-2.4	-2.1	25	85% Methanol	[58]
18	Methyl 4-biphenylacetate	-2.4	-2.1	25	85% Methanol	[58]
19	Methyl 2-anthrylacetate	-2.4	-2	25	85% Methanol	[58]
20	Methyl 3-phenanthrylacetate	-2.4	-2.4	25	85% Methanol	[58]
21	Methyl 2-phenanthrylacetate	-2.4	-2.1	25	85% Methanol	[58]
22	Methyl benzoate	-2.3	-2.1	25	50% Methanol	[64]
23	Methyl p-nitrobenzoate	-1.9	-2.3	25	88% Methanol	[63]
24	Methyl m-nitrobenzoate	-2.1	-2.5	25	88% Methanol	[63]
25	Methyl m-bromobenzoate	-2.9	-2.9	25	88% Methanol	[63]
26	Methyl p-bromobenzoate	-3.2	-3.1	25	88% Methanol	[63]
27	Methyl m-methoxybenzoate	-3.6	-3.5	25	88% Methanol	[63]
28	Methyl benzoate	-3.7	-3.2	25	88% Methanol	[63]
29	Methyl m-methylbenzoate	-3.9	-3.5	25	88% Methanol	[63]
30	Methyl m-dimethylaminobenzoate	-4	-3.7	25	88% Methanol	[63]
31	Methyl p-methylbenzoate	-4	-3.8	25	88% Methanol	[63]
32	Methyl p-methoxybenzoate	-4.3	-4.3	25	88% Methanol	[63]
33	Methyl benzoate	-2.8	-2.7	34.8	80% Methanol	[63]
34	Methyl benzoate	-2.4	-2.5	44.8	80% Methanol	[63]
35	Methyl benzoate	-2.3	-2.4	49.8	80% Methanol	[63]
36	Methyl benzoate	-2	-2.3	55.2	80% Methanol	[63]
37	Methyl o-methylbenzoate	-3.7	-3.5	35	80% Methanol	[63]
38	Methyl o-methylbenzoate	-3.3	-3.3	45	80% Methanol	[63]
39	Methyl o-methylbenzoate	-2.9	-3.1	55	80% Methanol	[63]
40	Methyl o-methylbenzoate	-2.3	-2.8	70.2	80% Methanol	[63]

Num	Esters	Obs.	Calc.	Temp	Solvent	Ref.
41	Methyl o-ethylbenzoate	-3.6	-3.5	45	80% Methanol	[63]
42	Methyl o-ethylbenzoate	-3.2	-3.3	55	80% Methanol	[63]
43	Methyl o-ethylbenzoate	-2.5	-3	70.2	80% Methanol	[63]
44	Methyl o-ethylbenzoate	-2.1	-2.9	80.4	80% Methanol	[63]
45	Methyl o-isopropylbenzoate	-2.6	-3.1	71.6	80% Methanol	[63]
46	Methyl o-isopropylbenzoate	-2.4	-3	78.4	80% Methanol	[63]
47	Methyl o-isopropylbenzoate	-2	-2.8	89.9	80% Methanol	[63]
48	Methyl o-isopropylbenzoate	-1.7	-2.6	100.2	80% Methanol	[63]
49	Methyl o-(t-butyl)benzoate	-3.5	-2.4	119.8	80% Methanol	[63]
50	Methyl o-(t-butyl)benzoate	-3.2	-2.2	129.8	80% Methanol	[63]
51	Methyl o-(t-butyl)benzoate	-3	-2.2	134	80% Methanol	[63]
52	Methyl o-(t-butyl)benzoate	-1.8	-2.1	140	80% Methanol	[63]
53	Methyl o-fluorobenzoate	-3	-2.9	15.4	80% Methanol	[63]
54	Methyl o-fluorobenzoate	-2.2	-2.5	35	80% Methanol	[63]
55	Methyl o-fluorobenzoate	-1.8	-2.3	44.8	80% Methanol	[63]
56	Methyl o-chlorobenzoate	-2.5	-2.4	35	80% Methanol	[63]
57	Methyl o-chlorobenzoate	-2.2	-2.2	44.8	80% Methanol	[63]
58	Methyl o-chlorobenzoate	-2	-2.1	50	80% Methanol	[63]
59	Methyl o-chlorobenzoate	-1.8	-2	55	80% Methanol	[63]
60	Methyl o-bromobenzoate	-2.7	-2.5	35	80% Methanol	[63]
61	Methyl o-bromobenzoate	-2.3	-2.3	45	80% Methanol	[63]
62	Methyl o-bromobenzoate	-2.1	-2.2	50	80% Methanol	[63]
63	Methyl o-bromobenzoate	-2	-2.1	55	80% Methanol	[63]
64	Methyl o-iodobenzoate	-2.9	-2.5	34.8	80% Methanol	[63]
65	Methyl o-iodobenzoate	-2.5	-2.3	44.8	80% Methanol	[63]
66	Methyl o-iodobenzoate	-2.3	-2.2	49	80% Methanol	[63]
67	Methyl o-iodobenzoate	-2.1	-2.1	54.9	80% Methanol	[63]
68	Methyl m-nitrobenzoate	-2.6	-2.6	4.6	80% Methanol	[63]
69	Methyl m-nitrobenzoate	-2.1	-2.4	15	80% Methanol	[63]
70	Methyl m-nitrobenzoate	-1.3	-2	34.5	80% Methanol	[63]
71	Methyl m-chlorobenzoate	-2.9	-2.9	15	80% Methanol	[63]
72	Methyl m-chlorobenzoate	-2	-2.5	34.5	80% Methanol	[63]
73	Methyl m-chlorobenzoate	-1.6	-2.3	45.2	80% Methanol	[63]
74	Methyl m-methylbenzoate	-3.1	-3.1	30.1	80% Methanol	[63]
75	Methyl m-methylbenzoate	-2.7	-2.8	40.7	80% Methanol	[63]
76	Methyl m-methylbenzoate	-2.3	-2.6	50	80% Methanol	[63]
77	Methyl m-methylbenzoate	-2	-2.4	59.8	80% Methanol	[63]
78	Methyl 9-anthrylacetate	-2.9	-2.8	32.5	85% Methanol	[58]
79	Methyl 9-phenanthrylacetate	-2.6	-2.2	32.5	85% Methanol	[58]
80	Methyl 1-naphthylacetate	-2.6	-2.2	32.5	85% Methanol	[58]
81	Methyl 6-chrysylacetate	-2.4	-2.2	32.5	85% Methanol	[58]
82	Methyl p-methylphenylacetate	-2.3	-2.2	32.5	85% Methanol	[58]

Num	Esters	Obs.	Calc.	Temp	Solvent	Ref.
83	2-Fluorenyl phenylacetate	-2.2	-1.6	32.5	85% Methanol	[58]
84	Methyl phenylacetate	-2.2	-2	32.5	85% Methanol	[58]
85	Methyl 2-naphthylacetate	-2.1	-1.9	32.5	85% Methanol	[58]
86	Methyl p-biphenylacetate	-2.1	-1.9	32.5	85% Methanol	[58]
87	Methyl 3-phenanthrylacetate	-2	-1.9	32.5	85% Methanol	[58]
88	Methyl 2-phenanthrylacetate	-2.1	-1.9	32.5	85% Methanol	[58]
89	Methyl phenylacetate	-2	-1.9	40	85% Methanol	[58]
90	Methyl 2-naphthylacetate	-1.9	-1.8	40	85% Methanol	[58]
91	Methyl p-biphenylacetate	-1.9	-1.8	40	85% Methanol	[58]
92	Methyl 2-phenanthrylacetate	-1.8	-1.8	40	85% Methanol	[58]
93	Methyl 9-anthrylacetate	-2.3	-2.4	50	85% Methanol	[58]
94	Methyl 9-phenanthrylacetate	-2	-1.9	50	85% Methanol	[58]
95	Methyl 1-naphthylacetate	-2	-1.9	50	85% Methanol	[58]
96	Methyl 6-chrysylacetate	-1.8	-1.9	50	85% Methanol	[58]
97	Methyl p-methylphenylacetate	-1.7	-1.8	50	85% Methanol	[58]
98	2-Fluorenyl phenylacetate	-1.6	-1.3	50	85% Methanol	[58]
99	Methyl phenylacetate	-1.6	-1.7	50	85% Methanol	[58]
100	Methyl 2-naphthylacetate	-1.5	-1.6	50	85% Methanol	[58]
101	Methyl p-biphenylacetate	-1.5	-1.6	50	85% Methanol	[58]
102	Methyl 3-phenanthrylacetate	-1.5	-1.6	50	85% Methanol	[58]
103	Methyl 2-phenanthrylacetate	-1.5	-1.6	50	85% Methanol	[58]
104	Methyl 9-anthrylacetate	-1.9	-2.2	60.2	85% Methanol	[58]
105	Methyl 9-phenanthrylacetate	-1.6	-1.7	60.2	85% Methanol	[58]
106	Methyl 2-naphthylacetate	-1.6	-1.7	60.2	85% Methanol	[58]
107	Methyl 6-chrysylacetate	-1.4	-1.7	60.2	85% Methanol	[58]
108	Methyl p-methylphenylacetate	-1.4	-1.6	60.2	85% Methanol	[58]
109	2-Fluorenyl phenylacetate	-1.3	-1.2	60.2	85% Methanol	[58]
110	Methyl 3-phenanthrylacetate	-1.1	-1.4	60.2	85% Methanol	[58]
111	2-Carbomethoxyquinoline	-0.5	-0.6	25	50% Methanol	[64]
112	Methyl 2-nitropicolinate	-0.6	-1	25	88% Methanol	[65]
113	Methyl 2-bromopicolinate	-1.5	-1.5	25	88% Methanol	[65]
114	Methyl 2-methylpicolimates	-2.3	-2	25	88% Methanol	[65]
115	Methyl 2-dimethylnitropicolinate	-2.9	-2.3	25	88% Methanol	[65]
116	Methyl nicotinate	-1.4	-1.2	25	88% Methanol	[49]
117	Methyl picolinate	-1.2	-0.9	25	88% Methanol	[49]
118	Methyl isonicotinate	-0.7	-1.1	25	88% Methanol	[49]
119	Methyl 5-nitropicolinate	-0.4	-0.8	25	88% Methanol	[65]
120	Methyl 5-bromopicolinate	-1.5	-1.7	25	88% Methanol	[65]
121	Methyl picolinate	-2	-1.8	25	88% Methanol	[65]
122	Methyl 5-methylpicolinate	-2.4	-2.3	25	88% Methanol	[65]
123	Methyl 5-methoxypicolinate	-2.8	-2.8	25	88% Methanol	[65]
124	Methyl 5-dimethylnitropicolinate	-3.7	-3.3	25	88% Methanol	[65]

Num	Esters	Obs.	Calc.	Temp	Solvent	Ref.
125	Methyl 4-nitropicolinate	-0.7	-1	25	88% Methanol	[65]
126	Methyl 4-bromopicolinate	-1.3	-1.5	25	88% Methanol	[65]
127	Methyl 4-methylpicolinate	-2.2	-2	25	88% Methanol	[65]
128	Methyl 4-methoxypicolinate	-2	-2.1	25	88% Methanol	[65]
129	Methyl 5-bromonicotinate	-1.5	-1.8	25	88% Methanol	[65]
130	Methyl nicotinate	-2.3	-2.1	25	88% Methanol	[65]
131	Methyl 5-methylnicotinate	-2.3	-2.3	25	88% Methanol	[65]
132	Methyl 5-methoxynicotinate	-2.1	-2.4	25	88% Methanol	[65]
133	Methyl 5-dimethylnitronicotinate	-2.7	-2.6	25	88% Methanol	[65]
134	Methyl 2-bromonicotinate	-1.8	-2	25	88% Methanol	[65]
135	Methyl 2-methylnicotinate	-2.6	-2.7	25	88% Methanol	[65]
136	Methyl 2-methoxynicotinate	-3.2	-3.2	25	88% Methanol	[65]
137	Methyl 2-dimethylnitronicotinate	-4.3	-3.8	25	88% Methanol	[65]
138	Methyl 2-nitroisonicotinate	0.2	-1.2	25	88% Methanol	[65]
139	Methyl 2-bromoisonicotinate	-0.9	-1.7	25	88% Methanol	[65]
140	Methyl isonicotinate	-1.5	-2	25	88% Methanol	[65]
141	Methyl 2-methylisonicotinate	-1.7	-2.2	25	88% Methanol	[65]
142	Methyl 2-methoxyisonicotinate	-1.8	-2.2	25	88% Methanol	[65]
143	Methyl 2-dimethylnitroisonicotinate	-2.3	-2.5	25	88% Methanol	[65]
144	3-Carbomethoxyquinoline	-1.1	-0.9	25	50% Methanol	[64]
145	4-Carbomethoxyquinoline	-0.8	-1.1	25	50% Methanol	[64]
146	5-Carbomethoxyquinoline	-1.7	-1.4	25	50% Methanol	[64]
147	6-Carbomethoxyquinoline	-1.6	-1.2	25	50% Methanol	[64]
148	7-Carbomethoxyquinoline	-1.5	-1.2	25	50% Methanol	[64]
149	8-Carbomethoxyquinoline	-2.4	-1.4	25	50% Methanol	[64]

Table 6. SPARC-calculated vs. observed log base-catalyzed hydrolysis rate constants for carboxylic acid esters in dioxane-water mixtures as a function of temperature in M<sup>-1</sup>s<sup>-1</sup>

Num	Esters	Obs	Calc	Temp.	Solvent	Ref.
1	Ethyl benzoate	-2.1	-1.6	30	33% dioxane	[49]
2	p-Nitrobenzyl benzoate	-1.5	-1.2	25	67% dioxane	[66]
3	p-Chlorobenzyl benzoate	-2	-1.4	25	67% dioxane	[67]
4	p-Chlorobenzyl benzoate	-1.7	-1	25	67% dioxane	[67]
5	Benzyl benzoate	-2.3	-1.5	25	67% dioxane	[67]
6	p-Methoxybenzyl benzoate	-2.4	-1.5	25	67% dioxane	[67]
7	Methyl benzoate	-1.6	-1.5	25	33% dioxane	[67]
8	Methyl p-aminobenzoate	-2.9	-3	25	33% dioxane	[67]
9	Methyl p-methylbenzoate	-2	-2	25	33% dioxane	[67]
10	Methyl p-chlorobenzoate	-1.2	-1.4	25	33% dioxane	[67]
11	Methyl p-nitrobenzoate	-0.2	-0.5	25	33% dioxane	[67]
12	Methyl acetate	-0.5	-0.3	35	40% dioxane	[68]
13	Methyl propionate	-0.6	-0.9	35	40% dioxane	[68]
14	Methyl isobutyrate	-1.1	-1.1	35	40% dioxane	[68]
15	Methyl n-butyrate	-0.9	-1.1	35	40% dioxane	[68]
16	Methyl n-pentate	-1	-1.2	35	40% dioxane	[68]
17	Methyl isopentate	-1.5	-1.2	35	40% dioxane	[68]
18	Methyl sec-pentate	-1.6	-2.1	35	40% dioxane	[68]
19	Methyl neopentate	-2	-1.4	35	40% dioxane	[68]
20	Methyl phenylacetate	-0.4	-0.4	35	40% dioxane	[68]
21	Methyl benzoate	-1.5	-1.7	35	60% dioxane	[69]
22	Methyl p-methylbenzoate	-1.9	-2.2	35	60% dioxane	[69]
23	Methyl m-methylbenzoate	-1.8	-1.9	35	60% dioxane	[69]
24	Methyl p-methoxybenzoate	-2.2	-2.7	35	60% dioxane	[69]
25	Methyl p-aminobenzoate	-3	-3.2	35	60% dioxane	[69]
26	Methyl p-bromobenzoate	-1	-1.6	35	60% dioxane	[69]
27	Methyl m-iodobenzoate	-0.9	-1.3	35	60% dioxane	[69]
28	Methyl m-chlorobenzoate	-0.8	-1.4	35	60% dioxane	[69]
29	Methyl m-bromobenzoate	-0.8	-1.4	35	60% dioxane	[69]
30	Methyl m-nitrobenzoate	0	-0.9	35	60% dioxane	[69]
31	Methyl p-nitrobenzoate	0.2	-0.7	35	60% dioxane	[69]
32	Ethyl benzoate	-2	-1.9	35	60% dioxane	[69]
33	Propyl benzoate	-2.2	-2	35	60% dioxane	[69]
34	Propyl p-chlorobenzoate	-1.6	-2	35	60% dioxane	[69]
35	Isopropyl benzoate	-2.8	-2.4	35	60% dioxane	[69]
36	Isopropyl p-methoxybenzoate	-3.4	-3.4	35	60% dioxane	[69]
37	Isopropyl p-nitrobenzoate	-0.9	-1.5	35	60% dioxane	[69]
38	Butyl benzoate	-2.3	-2.1	35	60% dioxane	[69]
39	Butyl p-aminobenzoate	-3.8	-3.6	35	60% dioxane	[69]
40	Isobutyl benzoate	-2.4	-2.1	35	60% dioxane	[69]

Num	Esters	Obs.	Calc.	Temp	Solvent	Ref.
41	Isobutyl p-aminobenzoate	-3.8	-3.6	35	60% dioxane	[69]
42	sec-Butyl benzoate	-3.1	-3.2	35	60% dioxane	[69]
43	sec-Butyl m-methylbenzoate	-3.3	-3.4	35	60% dioxane	[69]
44	Isopentyl benzoate	-2.4	-1.8	35	60% dioxane	[69]
45	Isopentyl p-chlorobenzoate	-1.8	-1.7	35	60% dioxane	[69]
46	Benzyl benzoate	-1.8	-1.1	35	60% dioxane	[69]
47	Benzyl p-methylbenzoate	-2.2	-1.7	35	60% dioxane	[69]
48	1-Phenyl-ethyl benzoate	-2.1	-2.8	35	60% dioxane	[69]
49	1,1-Biphenyl-methyl benzoate	-3.6	-4.7	35	60% dioxane	[69]
50	Ethyl p-methoxybenzoate	-2.7	-2.9	35	60% dioxane	[69]
51	Ethyl p-fluorobenzoate	-1.8	-1.9	35	60% dioxane	[69]
52	Ethyl m-nitrobenzoate	-0.5	-1.2	35	60% dioxane	[69]
53	Ethyl p-nitrobenzoate	-0.3	-1	35	60% dioxane	[69]
54	Ethyl 3,4-dinitrobenzoate	-1.2	-0.4	35	60% dioxane	[69]
55	Ethyl p-aminobenzoate	-3.5	-3.5	35	60% dioxane	[69]
56	Methyl benzoate	-2.4	-2.4	10	60% dioxane	[65]
57	Methyl m-bromobenzoate	-1.7	-2.1	10	60% dioxane	[65]
58	Methyl p-bromobenzoate	-1.8	-2.3	10	60% dioxane	[65]
59	Methyl p-methoxybenzoate	-3.1	-3.5	10	60% dioxane	[65]
60	Methyl m-methoxybenzoate	-2.3	-2.7	10	60% dioxane	[65]
61	Methyl p-methylbenzoate	-2.8	-3	10	60% dioxane	[65]
62	Methyl m-methylbenzoate	-2.6	-2.7	10	60% dioxane	[65]
63	Methyl p-nitrobenzoate	-0.5	-1.4	10	60% dioxane	[65]
64	Methyl m-nitrobenzoate	-0.8	-1.6	10	60% dioxane	[65]
65	Methyl p-trifluoromethylbenzoate	-1.2	-2.7	10	60% dioxane	[65]
66	Methyl benzoate	-2.5	-2.2	10	60% dioxane	[63]
67	Methyl benzoate	-1.9	-1.9	25	60% dioxane	[63]
68	Methyl o-methylbenzoate	-2.8	-2.8	25	60% dioxane	[63]
69	Methyl o-methylbenzoate	-2.3	-2.5	40.2	60% dioxane	[63]
70	Methyl o-methylbenzoate	-2	-2.3	50.4	60% dioxane	[63]
71	Methyl o-ethylbenzoate	-3.1	-2.9	30	60% dioxane	[63]
72	Methyl o-ethylbenzoate	-2.7	-2.7	40	60% dioxane	[63]
73	Methyl o-ethylbenzoate	-2.4	-2.5	50	60% dioxane	[63]
74	Methyl o-isopropylbenzoate	-2.9	-2.8	40.9	60% dioxane	[63]
75	Methyl o-isopropylbenzoate	-2.5	-2.6	49.9	60% dioxane	[63]
76	Methyl o-isopropylbenzoate	-2.3	-2.4	60	60% dioxane	[63]
77	Methyl o-isopropylbenzoate	-2	-2.3	70	60% dioxane	[63]
78	Methyl o-(t-butyl)benzoate	-3.1	-1.7	114.6	60% dioxane	[63]
79	Methyl o-(t-butyl)benzoate	-2.7	-1.6	124.1	60% dioxane	[63]
80	Methyl o-(t-butyl)benzoate	-2.5	-1.5	133.7	60% dioxane	[63]
81	Methyl o-(t-butyl)benzoate	-2.2	-1.4	144.3	60% dioxane	[63]
82	Ethyl benzoate	-2	-1.7	30	60% dioxane	[59]

Num	Esters	Obs.	Calc.	Temp	Solvent	Ref.
83	Ethyl benzoate	-2.3	-2.2	30	70% dioxane	[59]
84	Ethyl p-nitrobenzoate	-1.2	-1.1	30	60% dioxane	[59]
85	Ethyl p-nitrobenzoate	-1.3	-1.2	30	70% dioxane	[59]
86	Benzyl benzoate	-1.9	-1	30	50% dioxane	[59]
87	Benzyl benzoate	-2.1	-1.5	30	70% dioxane	[59]
88	Methyl nicotinate	-0.9	-1	10	65% dioxane	[59]
89	Methyl picolinate	-0.7	-0.7	10	65% dioxane	[59]
90	Methyl isonicotinate	-0.1	-0.9	10	65% dioxane	[59]

Table 7. SPARC-calculated vs. observed log base-catalyzed hydrolysis rate constants for carboxylic acid esters in acetonitrile-water mixtures as a function of temperature in  $M^{-1}s^{-1}$

	Esters	Obs.	Calc.	Temp.	Solvent	Ref.
1	p-Tolyl p-dimethylaminobenzoate	-3.1	-2.6	25	33% Acetonitrile	[70]
2	p-Tolyl p-methylbenzoate	-1.9	-1.6	25	33% Acetonitrile	[70]
3	p-Tolyl benzoate	-1.5	-1	25	33% Acetonitrile	[70]
4	p-Tolyl p-chlorobenzoate	-1	-1	25	33% Acetonitrile	[70]
5	p-Tolyl p-nitrobenzoate	0.2	-0.1	25	33% Acetonitrile	[70]
6	Phenyl p-dimethylaminobenzoate	-2.9	-2.5	25	33% Acetonitrile	[70]
7	Phenyl p-methylbenzoate	-1.6	-1.5	25	33% Acetonitrile	[70]
8	Phenyl benzoate	-1.3	-0.9	25	33% Acetonitrile	[70]
9	Phenyl p-chlorobenzoate	-0.8	-0.8	25	33% Acetonitrile	[70]
10	Phenyl p-nitrobenzoate	0.3	0.1	25	33% Acetonitrile	[70]
11	p-Chlorophenyl p-methylbenzoate	-1.3	-1.3	25	33% Acetonitrile	[70]
12	p-Chlorophenyl benzoate	-0.9	-0.8	25	33% Acetonitrile	[70]
13	p-Chlorophenyl p-chlorobenzoate	-0.5	-0.7	25	33% Acetonitrile	[70]
14	p-Chlorophenyl p-nitrobenzoate	0.7	0.2	25	33% Acetonitrile	[70]
15	m-Nitrophenyl p-dimethylaminobenzoate	-2.1	-1.9	25	33% Acetonitrile	[70]
16	m-Nitrophenyl p-methylbenzoate	-0.7	-0.9	25	33% Acetonitrile	[70]
17	m-Nitrophenyl benzoate	-0.3	-0.3	25	33% Acetonitrile	[70]
18	m-Nitrophenyl p-chlorobenzoate	0.1	-0.2	25	33% Acetonitrile	[70]
19	m-Nitrophenyl p-nitrobenzoate	1.2	0.7	25	33% Acetonitrile	[70]
20	p-Nitrophenyl p-dimethylaminobenzoate	-1.8	-1.8	25	33% Acetonitrile	[70]
21	p-Nitrophenyl p-methylbenzoate	-0.5	-0.8	25	33% Acetonitrile	[70]
22	p-Nitrophenyl benzoate	-0.1	-0.2	25	33% Acetonitrile	[70]
23	p-Nitrophenyl p-chlorobenzoate	0.3	-0.1	25	33% Acetonitrile	[70]
24	p-Nitrophenyl p-nitrobenzoate	1.4	0.8	25	33% Acetonitrile	[70]

Table 8. SPARC-calculated vs. observed log acid-catalyzed hydrolysis rate constants for carboxylic acid esters in water as a function of temperature in M<sup>-1</sup>s<sup>-1</sup>

Num	Esters	Obs.	Calc.	Temp.	Ref.
1	Ethyl acetate	-4	-3.9	25	[27, 71]
2	Ethyl propionate	-4	-4.3	25	[27, 71]
3	Ethyl cyclo-butyl carboxylate	-4	-4.7	25	[27, 71]
4	Ethyl butyrate	-4.3	-4.4	25	[27, 71]
5	Ethyl pentate	-4.4	-4.5	25	[27, 71]
6	Ethyl hexanoate	-4.4	-4.5	25	[27, 71]
7	Ethyl iso-hexanoate	-4.3	-4.4	25	[27, 71]
8	Ethyl (heptyl)acetate	-4.3	-4.5	25	[27, 71]
9	Ethyl (t-butyl)propionate	-4.3	-4.9	25	[27, 71]
10	Ethyl sec-butyrate	-4.4	-4.6	25	[27, 71]
11	Ethyl cyclopentate	-4.5	-5	25	[27, 71]
12	Ethyl cyclohexanoate	-4.8	-5.1	25	[27, 71]
13	Ethyl iso-pentate	-4.9	-4.6	25	[27, 71]
14	Ethyl cyclohexyl-acetate	-4.9	-4.8	25	[27, 71]
15	Ethyl sec-pentate	-5.1	-5.1	25	[27, 71]
16	Ethyl cycloheptyl-carboxylate	-5	-5.1	25	[27, 71]
17	Ethyl neopentate	-5.5	-5.2	25	[27, 71]
18	Ethyl (t-butyl) acetate	-5.7	-5.4	25	[27, 71]
19	Ethyl (t-butyl)-sec-butyrate	-5.8	-5.7	25	[27, 71]
20	Ethyl (2-ethyl)butyrate	-5.9	-5.9	25	[27, 71]
21	Ethyl (2-propyl)pentate	-6.1	-6.2	25	[27, 71]
22	Ethyl (2-isobutyl-4-methyl)pentate	-6.4	-6.7	25	[27, 71]
23	Ethyl (t-butyl)neopentate	-6.5	-6.5	25	[27, 71]
24	Ethyl (2-neopentyl-4,4-dimethyl)pentate	-7.2	-7.1	25	[27, 71]
25	Ethyl (t-butyl)isopropionate	-7.3	-6.6	25	[27, 71]
26	Ethyl (t-butyl)t-butyrate	-7.9	-7.1	25	[27, 71]
27	Ethyl (2,2-diethyl)butyrate	-7.8	-6.8	25	[27, 71]
28	Ethyl (methyl )(neopentyl) (t-butyl) acetate	-8	-8.4	25	[27, 71]
29	Isopropyl formate	-3	-3.5	25	[27, 71]
30	Isopropyl acetate	-4.2	-4.2	25	[27, 71]
31	Isopropyl propionate	-4.3	-4.5	25	[27, 71]
32	Isopropyl chloroacetate	-4.4	-4.8	25	[27, 71]
33	Isopropyl butyrate	-4.6	-4.7	25	[27, 71]
34	Isopropyl pentate	-4.6	-4.7	25	[27, 71]
35	Isopropyl hexanoate	-4.6	-4.8	25	[27, 71]
36	Isopropyl iso-hexanoate	-4.6	-4.7	25	[27, 71]
37	Isopropyl phenylacetate	-4.6	-4.8	25	[27, 71]
38	Isopropyl phenylpropionate	-4.6	-4.8	25	[27, 71]
39	Isopropyl phenylbutyrate	-4.7	-4.7	25	[27, 71]
40	Isopropyl isobutyrate	-4.7	-4.9	25	[27, 71]

Num	Esters	Obs.	Calc.	Temp.	Ref.
41	Isopropyl cyclohexyl-carboxylate	-5	-5.3	25	[27, 71]
42	Isopropyl isopentate	-5.1	-4.9	25	[27, 71]
43	Isopropyl cyclohexylacetate	-5.2	-5	25	[27, 71]
44	Isopropyl (2-ethyl) propionate	-5.3	-5.4	25	[27, 71]
45	Isopropyl (2,2-methyl-phenyl) acetate	-5.4	-5.6	25	[27, 71]
46	Isopropyl (2,2-ethyl-phenyl) acetate	-5.7	-6.1	25	[27, 71]
47	Isopropyl neopentate	-5.8	-5.4	25	[27, 71]
48	Isopropyl (2,2-diphenyl) acetate	-6	-6.7	25	[27, 71]
49	Isopropyl (2-ethyl) butyrate	-6.2	-6.1	25	[27, 71]
50	Isopropyl (3-phenyl)-2-propenoate	-6.2	-5.9	25	[27, 71]
51	Isopropyl trichloroacetate	-6.3	-5.8	25	[27, 71]
52	Isopropyl benzoate	-6.8	-6.2	25	[27, 71]
53	Isopropyl cyclobutyl-carboxylate	-4.3	-5	25	[27, 71]
54	Isopropyl methoxyacetate	-4.4	-4.9	25	[27, 71]
55	Isopropyl bromoacetate	-4.5	-4.9	25	[27, 71]
56	Isopropyl thiolpropionate	-4.6	-4.9	25	[27, 71]
57	Isopropyl iodoacetate	-4.6	-4.9	25	[27, 71]
58	Isopropyl nonoate	-4.5	-4.8	25	[27, 71]
59	Isopropyl (4,4-dimethyl)pentate	-4.6	-5.1	25	[27, 71]
60	Isopropyl phenoxy-acetate	-4.5	-4.9	25	[27, 71]
61	Isopropyl cyclopentyl-carboxylate	-4.7	-5.2	25	[27, 71]
62	Isopropyl difluoroacetate	-4.9	-5.1	25	[27, 71]
63	Isopropyl methoxypropionate	-5	-4.8	25	[27, 71]
64	Isopropyl chloropropionate	-5.1	-4.7	25	[27, 71]
65	Isopropyl trifluoroacetate	-5.4	-5.6	25	[27, 71]
66	Isopropyl cycloheptyl-carboxylate	-5.3	-5.3	25	[27, 71]
67	Isopropyl dichloracetate	-5.8	-5.2	25	[27, 71]
68	Isopropyl neopentate	-5.9	-5.4	25	[27, 71]
69	Isopropyl (2-neopentyl)propionate	-6.1	-5.9	25	[27, 71]
70	Isopropyl dibromoacetate	-6.1	-5.6	25	[27, 71]
71	Isopropyl (2-propyl)pentate	-6.3	-6.5	25	[27, 71]
72	Isopropyl tribromoacetate	-6.6	-6.4	25	[27, 71]
73	Isopropyl (3,3-methyl-neopentyl)acetate	-6.8	-6.7	25	[27, 71]
74	Isopropyl (3-neopentyl-4,4-dimethyl)pentate	-7.4	-7.4	25	[27, 71]
75	Isopropyl (2-t-butyl)propionate	-7.5	-6.8	25	[27, 71]
76	Isopropyl (2,2-methyl-t-butyl)propionate	-8.1	-7.4	25	[27, 71]
77	Isopropyl (2,2-diethyl)butyrate	-8	-7.1	25	[27, 71]
78	Isopropyl (methyl) (neopentyl) (t-butyl)acetate	-8.2	-8.6	25	[27, 71]
79	n-Butyl formate	-2.8	-3.5	25	[27, 71]
80	n-Butyl acetate	-4	-4	25	[27, 71]
81	n-Butyl propionate	-4.1	-4.3	25	[27, 71]
82	n-Butyl chloroacetate	-4.2	-4.6	25	[27, 71]

Num	Esters	Obs.	Calc.	Temp.	Ref.
83	n-Butyl butyrate	-4.4	-4.5	25	[27, 71]
84	n-Butyl pentate	-4.4	-4.5	25	[27, 71]
85	n-Butyl hexanoate	-4.4	-4.6	25	[27, 71]
86	n-Butyl iso-hexanoate	-4.4	-4.5	25	[27, 71]
87	n-Butyl phenylacetate	-4.4	-4.6	25	[27, 71]
88	n-Butyl phenylpropionate	-4.5	-4.6	25	[27, 71]
89	n-Butyl phenylbutyrate	-4.5	-4.5	25	[27, 71]
90	n-Butyl isobutyrate	-4.5	-4.7	25	[27, 71]
91	n-Butyl cyclohexyl-carboxylate	-4.8	-5.1	25	[27, 71]
92	n-Butyl isopentate	-5	-4.7	25	[27, 71]
93	n-Butyl cyclohexylacetate	-5	-4.8	25	[27, 71]
94	n-Butyl (2-ethyl)propionate	-5.2	-5.2	25	[27, 71]
95	n-Butyl (2,2-methyl-phenyl)acetate	-5.2	-5.4	25	[27, 71]
96	n-Butyl (2,2-ethyl-phenyl)acetate	-5.5	-5.9	25	[27, 71]
97	n-Butyl neopentate	-5.6	-5.2	25	[27, 71]
98	n-Butyl (2,2-diphenyl)acetate	-5.8	-6.5	25	[27, 71]
99	n-Butyl (2-ethyl)butyrate	-6	-5.9	25	[27, 71]
100	n-Butyl (3-phenyl)2-propenoate	-6	-5.7	25	[27, 71]
101	n-Butyl trichloroacetate	-6.1	-5.6	25	[27, 71]
102	n-Butyl benzoate	-6.6	-6	25	[27, 71]
103	n-Butyl cyclobutyl-carboxylate	-4.1	-4.8	25	[27, 71]
104	n-Butyl methoxyacetate	-4.2	-4.7	25	[27, 71]
105	n-Butyl bromoacetate	-4.3	-4.7	25	[27, 71]
106	n-Butyl thiolpropionate	-4.4	-4.7	25	[27, 71]
107	n-Butyl iodoacetate	-4.4	-4.7	25	[27, 71]
108	n-Butyl nonoate	-4.4	-4.6	25	[27, 71]
109	n-Butyl (4,4-dimethyl) pentate	-4.4	-5	25	[27, 71]
110	n-Butyl phenoxy-acetate	-4.4	-4.7	25	[27, 71]
111	n-Butyl cyclopentyl-carboxylate	-4.5	-5	25	[27, 71]
112	n-Butyl difluoroacetate	-4.7	-4.9	25	[27, 71]
113	n-Butyl methoxypropionate	-4.8	-4.6	25	[27, 71]
114	n-Butyl chloropropionate	-4.9	-4.5	25	[27, 71]
115	n-Butyl trifluoroacetate	-5.2	-5.4	25	[27, 71]
116	n-Butyl cycloheptyl-carboxylate	-5.1	-5.1	25	[27, 71]
117	n-Butyl dichloracetate	-5.6	-5	25	[27, 71]
118	n-Butyl neopentate	-5.8	-5.2	25	[27, 71]
119	n-Butyl (2-neopentyl)propionate	-5.9	-5.7	25	[27, 71]
120	n-Butyl dibromoacetate	-5.9	-5.4	25	[27, 71]
121	n-Butyl (2-propyl) pentate	-6.1	-6.3	25	[27, 71]
122	n-Butyl tribromoacetate	-6.5	-6.2	25	[27, 71]
123	n-Butyl (3,3-methyl-neopentyl)acetate	-6.6	-6.5	25	[27, 71]
124	n-Butyl (3-neopentyl-4,4-dimethyl)pentate	-7.2	-7.2	25	[27, 71]

Num	Esters	Obs.	Calc.	Temp.	Ref.
125	n-Butyl (2-t-butyl) propionate	-7.4	-6.7	25	[27, 71]
126	n-Butyl (2,2-methyl-t-butyl) propionate	-7.9	-7.2	25	[27, 71]
127	n-Butyl (2,2-diethyl) butyrate	-7.8	-6.9	25	[27, 71]
128	(methyl) (neopentyl) (t-butyl)CC(=O)OCCCC	-8	-8.4	25	[27, 71]
129	Propyl formate	-2.8	-3.5	25	[27, 71]
130	Propyl acetate	-4	-4	25	[27, 71]
131	Propyl propionate	-4.1	-4.3	25	[27, 71]
132	Propyl chloroacetate	-4.2	-4.6	25	[27, 71]
133	Propyl butyrate	-4.4	-4.5	25	[27, 71]
134	Propyl pentate	-4.4	-4.5	25	[27, 71]
135	Propyl hexanoate	-4.4	-4.5	25	[27, 71]
136	Propyl iso-hexanoate	-4.4	-4.5	25	[27, 71]
137	Propyl phenylacetate	-4.4	-4.6	25	[27, 71]
138	Propyl phenylpropionate	-4.5	-4.6	25	[27, 71]
139	Propyl phenylbutyrate	-4.5	-4.5	25	[27, 71]
140	Propyl isobutyrate	-4.5	-4.7	25	[27, 71]
141	Propyl cyclohexyl-carboxylate	-4.8	-5.1	25	[27, 71]
142	Propyl isopentate	-5	-4.7	25	[27, 71]
143	Propyl cyclohexylacetate	-5	-4.8	25	[27, 71]
144	Propyl (2-ethyl)propionate	-5.2	-5.2	25	[27, 71]
145	Propyl (2,2-methyl-phenyl)acetate	-5.2	-5.4	25	[27, 71]
146	Propyl (2,2-ethyl-phenyl)acetate	-5.5	-5.9	25	[27, 71]
147	Propyl neopentate	-5.6	-5.2	25	[27, 71]
148	Propyl (2,2-diphenyl)acetate	-5.8	-6.5	25	[27, 71]
149	Propyl (2-ethyl)butyrate	-6	-5.9	25	[27, 71]
150	Propyl (3-phenyl)2-propenoate	-6	-5.7	25	[27, 71]
151	Propyl trichloroacetate	-6.1	-5.6	25	[27, 71]
152	Propyl benzoate	-6.6	-6	25	[27, 71]
153	Propyl cyclobutyl-carboxylate	-4.1	-4.8	25	[27, 71]
154	Propyl methoxyacetate	-4.2	-4.7	25	[27, 71]
155	Propyl bromoacetate	-4.3	-4.7	25	[27, 71]
156	Propyl thiolpropionate	-4.4	-4.7	25	[27, 71]
157	Propyl iodoacetate	-4.4	-4.7	25	[27, 71]
158	CCCCCC(=O)OCCC	-4.4	-4.6	25	[27, 71]
159	Propyl (4,4-dimethyl)pentate	-4.4	-4.9	25	[27, 71]
160	Propyl phenoxy-acetate	-4.4	-4.7	25	[27, 71]
161	Propyl cyclopentyl-carboxylate	-4.5	-5	25	[27, 71]
162	Propyl difluoroacetate	-4.7	-4.9	25	[27, 71]
163	Propyl methoxypropionate	-4.8	-4.6	25	[27, 71]
164	Propyl chloropropionate	-4.9	-4.5	25	[27, 71]
165	Propyl trifluoroacetate	-5.2	-5.4	25	[27, 71]
166	Propyl cycloheptyl-carboxylate	-5.1	-5.1	25	[27, 71]

Num	Esters	Obs.	Calc.	Temp.	Ref.
167	Propyl dichloracetate	-5.6	-5	25	[27, 71]
168	Propyl neopentate	-5.8	-5.2	25	[27, 71]
169	Propyl (2-neopentyl)propionate	-5.9	-5.7	25	[27, 71]
170	Propyl dibromoacetate	-5.9	-5.4	25	[27, 71]
171	Propyl (2-propyl)pentate	-6.1	-6.3	25	[27, 71]
172	Propyl tribromoacetate	-6.5	-6.2	25	[27, 71]
173	Propyl (3,3-methyl-neopentyl)acetate	-6.6	-6.5	25	[27, 71]
174	Propyl (3-neopentyl-4,4-dimethyl)pentate	-7.2	-7.2	25	[27, 71]
175	Propyl (2-t-butyl)propionate	-7.4	-6.6	25	[27, 71]
176	Propyl (2,2-methyl-t-butyl)propionate	-7.9	-7.2	25	[27, 71]
177	Propyl (2,2-diethyl)butyrate	-7.8	-6.9	25	[27, 71]
178	(methyl) (neopentyl) (t-butyl)CC(=O)OCCC	-8	-8.4	25	[27, 71]
179	Methyl formate	-2.7	-3.5	25	[27, 71]
180	Methyl acetate	-4	-3.8	25	[27, 71]
181	Methyl propionate	-4	-4.1	25	[27, 71]
182	Methyl chloroacetate	-4.2	-4.4	25	[27, 71]
183	Methyl butyrate	-4.3	-4.3	25	[27, 71]
184	Methyl pentate	-4.3	-4.3	25	[27, 71]
185	Methyl hexanoate	-4.4	-4.4	25	[27, 71]
186	Methyl iso-hexanoate	-4.3	-4.3	25	[27, 71]
187	Methyl phenylacetate	-4.3	-4.4	25	[27, 71]
188	Methyl phenylpropionate	-4.4	-4.4	25	[27, 71]
189	Methyl phenylbutyrate	-4.4	-4.3	25	[27, 71]
190	Methyl isobutyrate	-4.4	-4.5	25	[27, 71]
191	Methyl cyclohexyl-carboxylate	-4.8	-4.9	25	[27, 71]
192	Methyl isopentate	-4.9	-4.5	25	[27, 71]
193	Methyl cyclohexylacetate	-4.9	-4.6	25	[27, 71]
194	Methyl (2-ethyl)propionate	-5.1	-5	25	[27, 71]
195	Methyl (2,2-methyl-phenyl)acetate	-5.2	-5.2	25	[27, 71]
196	Methyl (2,2-ethyl-phenyl)acetate	-5.5	-5.7	25	[27, 71]
197	Methyl neopentate	-5.5	-5	25	[27, 71]
198	Methyl (2,2-diphenyl)acetate	-5.7	-6.3	25	[27, 71]
199	Methyl (2-ethyl)butyrate	-5.9	-5.7	25	[27, 71]
200	Methyl (3-phenyl)2-propenoate	-5.9	-5.5	25	[27, 71]
201	Methyl trichloroacetate	-6	-5.4	25	[27, 71]
202	Methyl benzoate	-6.5	-5.8	25	[27, 71]
203	Methyl cyclobutyl-carboxylate	-4	-4.6	25	[27, 71]
204	Methyl methoxyacetate	-4.2	-4.5	25	[27, 71]
205	Methyl bromoacetate	-4.2	-4.5	25	[27, 71]
206	Methyl thiolpropionate	-4.3	-4.5	25	[27, 71]
207	Methyl iodoacetate	-4.3	-4.5	25	[27, 71]
208	CCCCCCCCC(=O)OC	-4.3	-4.4	25	[27, 71]

Num	Esters	Obs.	Calc.	Temp.	Ref.
209	Methyl (4,4-dimethyl)pentate	-4.3	-4.7	25	[27, 71]
210	Methyl phenoxy-acetate	-4.3	-4.5	25	[27, 71]
211	Methyl cyclopentyl-carboxylate	-4.5	-5	25	[27, 71]
212	Methyl difluoroacetate	-4.6	-4.7	25	[27, 71]
213	Methyl methoxypropionate	-4.7	-4.4	25	[27, 71]
214	Methyl chloropropionate	-4.9	-4.3	25	[27, 71]
215	Methyl trifluoroacetate	-5.1	-5.2	25	[27, 71]
216	Methyl cycloheptyl-carboxylate	-5.1	-4.9	25	[27, 71]
217	Methyl dichloroacetate	-5.5	-4.8	25	[27, 71]
218	Methyl neopentate	-5.7	-5	25	[27, 71]
219	Methyl (2-neopentyl)propionate	-5.8	-5.5	25	[27, 71]
220	Methyl dibromoacetate	-5.8	-5.2	25	[27, 71]
221	Methyl (2-propyl)pentate	-6.1	-6.1	25	[27, 71]
222	Methyl tribromoacetate	-6.4	-6	25	[27, 71]
223	Methyl (3,3-methyl-neopentyl)acetate	-6.5	-6.3	25	[27, 71]
224	Methyl (3-neopentyl-4,4-dimethyl)pentate	-7.1	-7	25	[27, 71]
225	Methyl (2-t-butyl)propionate	-7.3	-6.4	25	[27, 71]
226	Methyl (2,2-methyl-t-butyl)propionate	-7.9	-7	25	[27, 71]
227	Methyl (2,2-diethyl)butyrate	-7.8	-6.7	25	[27, 71]
228	(methyl) (neopentyl) (t-butyl)CC(=O)OC	-8	-8.2	25	[27, 71]
229	Chloroethyl formate	-2.8	-3.6	25	[27, 71]
230	Chloroethyl acetate	-4.1	-4.1	25	[27, 71]
231	Chloroethyl propionate	-4.2	-4.5	25	[27, 71]
232	Chloroethyl chloroacetate	-4.3	-4.7	25	[27, 71]
233	Chloroethyl butyrate	-4.4	-4.6	25	[27, 71]
234	Chloroethyl pentate	-4.5	-4.7	25	[27, 71]
235	Chloroethyl hexanoate	-4.5	-4.7	25	[27, 71]
236	Chloroethyl iso-hexanoate	-4.4	-4.6	25	[27, 71]
237	Chloroethyl phenylacetate	-4.5	-4.7	25	[27, 71]
238	Chloroethyl phenylpropionate	-4.5	-4.7	25	[27, 71]
239	Chloroethyl phenylbutyrate	-4.5	-4.6	25	[27, 71]
240	Chloroethyl isobutyrate	-4.6	-4.8	25	[27, 71]
241	Chloroethyl cyclohexyl-carboxylate	-4.9	-5.3	25	[27, 71]
242	Chloroethyl isopentate	-5	-4.8	25	[27, 71]
243	Chloroethyl cyclohexylacetate	-5.1	-4.9	25	[27, 71]
244	Chloroethyl (2-ethyl)propionate	-5.2	-5.3	25	[27, 71]
245	Chloroethyl (2,2-methyl-phenyl)acetate	-5.3	-5.5	25	[27, 71]
246	Chloroethyl (2,2-ethyl-phenyl)acetate	-5.6	-6	25	[27, 71]
247	Chloroethyl neopentate	-5.6	-5.4	25	[27, 71]
248	Chloroethyl (2,2-diphenyl)acetate	-5.8	-6.6	25	[27, 71]
249	Chloroethyl (2-ethyl)butyrate	-6.1	-6	25	[27, 71]
250	Chloroethyl (3-phenyl)2-propenoate	-6.1	-5.8	25	[27, 71]

Num	Esters	Obs.	Calc.	Temp.	Ref.
251	Chloroethyl trichloroacetate	-6.1	-5.7	25	[27, 71]
252	Chloroethyl benzoate	-6.6	-6.1	25	[27, 71]
253	Chloroethyl cyclobutyl-carboxylate	-4.1	-4.9	25	[27, 71]
254	Chloroethyl methoxyacetate	-4.3	-4.8	25	[27, 71]
255	Chloroethyl bromoacetate	-4.3	-4.8	25	[27, 71]
256	Chloroethyl thiolpropionate	-4.4	-4.8	25	[27, 71]
257	Chloroethyl iodoacetate	-4.4	-4.8	25	[27, 71]
258	Chloroethyl nonatae	-4.4	-4.7	25	[27, 71]
259	Chloroethyl (4,4-dimethyl)pentate	-4.4	-5.1	25	[27, 71]
260	Chloroethyl phenoxy-acetate	-4.4	-4.8	25	[27, 71]
261	Chloroethyl cyclopentyl-carboxylate	-4.6	-5.1	25	[27, 71]
262	Chloroethyl difluoroacetate	-4.8	-5	25	[27, 71]
263	Chloroethyl methoxypropionate	-4.8	-4.7	25	[27, 71]
264	Chloroethyl chloropropionate	-5	-4.7	25	[27, 71]
265	Chloroethyl trifluoroacetate	-5.2	-5.5	25	[27, 71]
266	Chloroethyl cycloheptyl-carboxylate	-5.2	-5.3	25	[27, 71]
267	Chloroethyl dichloracetate	-5.6	-5.1	25	[27, 71]
268	Chloroethyl neopentate	-5.8	-5.4	25	[27, 71]
269	Chloroethyl (2-neopentyl)propionate	-5.9	-5.9	25	[27, 71]
270	Chloroethyl dibromoacetate	-5.9	-5.5	25	[27, 71]
271	Chloroethyl (2-propyl)pentate	-6.2	-6.4	25	[27, 71]
272	Chloroethyl tribromoacetate	-6.5	-6.3	25	[27, 71]
273	Chloroethyl (3,3-methyl-neopentyl) acetate	-6.7	-6.6	25	[27, 71]
274	Chloroethyl (3-neopentyl-4,4-dimethyl) pentate	-7.3	-7.3	25	[27, 71]
275	Chloroethyl (2-t-butyl)propionate	-7.4	-6.8	25	[27, 71]
276	Chloroethyl (2,2-methyl-t-butyl)propionate	-8	-7.3	25	[27, 71]
277	Chloroethyl (2,2-diethyl)butyrate	-7.9	-7	25	[27, 71]
278	(methyl) (neopentyl) (t-butyl)CC(=O)OCCl	-8.1	-8.6	25	[27, 71]
279	Methoxymethyl formate	-3.2	-3.8	25	[27, 71]
280	Methoxymethyl acetate	-4.5	-4.3	25	[27, 71]
281	Methoxymethyl propionate	-4.5	-4.6	25	[27, 71]
282	Methoxymethyl chloroacetate	-4.7	-4.9	25	[27, 71]
283	Methoxymethyl butyrate	-4.8	-4.8	25	[27, 71]
284	Methoxymethyl pentate	-4.9	-4.8	25	[27, 71]
285	Methoxymethyl hexanoate	-4.9	-4.8	25	[27, 71]
286	Methoxymethyl iso-hexanoate	-4.8	-4.8	25	[27, 71]
287	Methoxymethyl phenylacetate	-4.8	-4.9	25	[27, 71]
288	Methoxymethyl phenylpropionate	-4.9	-4.9	25	[27, 71]
289	Methoxymethyl phenylbutyrate	-4.9	-4.7	25	[27, 71]
290	Methoxymethyl isobutyrate	-4.9	-5	25	[27, 71]
291	Methoxymethyl cyclohexyl-carboxylate	-5.3	-5.4	25	[27, 71]
292	Methoxymethyl isopentate	-5.4	-4.9	25	[27, 71]

Num	Esters	Obs.	Calc.	Temp.	Ref.
293	Methoxymethyl cyclohexylacetate	-5.4	-5.1	25	[27, 71]
294	Methoxymethyl (2-ethyl)propionate	-5.6	-5.5	25	[27, 71]
295	Methoxymethyl (2,2-methyl-phenyl)acetate	-5.7	-5.7	25	[27, 71]
296	Methoxymethyl (2,2-ethyl-phenyl)acetate	-6	-6.2	25	[27, 71]
297	Methoxymethyl neopentate	-6	-5.5	25	[27, 71]
298	Methoxymethyl (2,2-diphenyl)acetate	-6.2	-6.8	25	[27, 71]
299	Methoxymethyl (2-ethyl)butyrate	-6.4	-6.2	25	[27, 71]
300	Methoxymethyl (3-phenyl)2-propenoate	-6.5	-6	25	[27, 71]
301	Methoxymethyl trichloroacetate	-6.5	-5.9	25	[27, 71]
302	Methoxymethyl benzoate	-7	-6.3	25	[27, 71]
303	Methoxymethyl cyclobutyl-carboxylate *	-4.5	-5.1	25	[27, 71]
304	Methoxymethyl methoxyacetate	-4.7	-5	25	[27, 71]
305	Methoxymethyl bromoacetate	-4.7	-5	25	[27, 71]
306	Methoxymethyl thiolpropionate	-4.8	-4.9	25	[27, 71]
307	Methoxymethyl iodoacetate	-4.8	-5	25	[27, 71]
308	CCCCCCCC(=O)OCOC	-4.8	-4.9	25	[27, 71]
309	Methoxymethyl (4,4-dimethyl)pentate	-4.8	-5.2	25	[27, 71]
310	Methoxymethyl phenoxy-acetate	-4.8	-5	25	[27, 71]
311	Methoxymethyl cyclopentyl-carboxylate	-5	-5.3	25	[27, 71]
312	Methoxymethyl difluoroacetate	-5.1	-5.2	25	[27, 71]
313	Methoxymethyl methoxypropionate	-5.2	-4.9	25	[27, 71]
314	Methoxymethyl chloropropionate	-5.4	-4.8	25	[27, 71]
315	Methoxymethyl trifluoroacetate	-5.6	-5.7	25	[27, 71]
316	Methoxymethyl cycloheptyl-carboxylate	-5.6	-5.4	25	[27, 71]
317	Methoxymethyl dichloroacetate	-6	-5.3	25	[27, 71]
318	Methoxymethyl neopentate	-6.2	-5.5	25	[27, 71]
319	Methoxymethyl (2-neopentyl)propionate	-6.3	-6	25	[27, 71]
320	Methoxymethyl dibromoacetate	-6.3	-5.7	25	[27, 71]
321	Methoxymethyl (2-propyl)pentate	-6.6	-6.6	25	[27, 71]
322	Methoxymethyl tribromoacetate	-6.9	-6.4	25	[27, 71]
323	Methoxymethyl (3,3-methyl-neopentyl)acetate	-7	-6.8	25	[27, 71]
324	CC(C)(C)CC(CC(C)(C)C(=O)OCOC	-7.7	-7.5	25	[27, 71]
325	Methoxymethyl (2-t-butyl)propionate	-7.8	-6.9	25	[27, 71]
326	Methoxymethyl (2,2-methyl-t-butyl)propionate	-8.4	-7.5	25	[27, 71]
327	Methoxymethyl (2,2-diethyl)butyrate	-8.3	-7.2	25	[27, 71]
328	(methyl) (neopentyl) (t-butyl)CC(=O)OCOC	-8.4	-8.9	25	[27, 71]
329	Chloromethyl formate	-3.2	-4	25	[27, 71]
330	Chloromethyl acetate	-4.4	-4.4	25	[27, 71]
331	Chloromethyl propionate	-4.5	-4.8	25	[27, 71]
332	Chloromethyl chloroacetate	-4.6	-5.1	25	[27, 71]
333	Chloromethyl butyrate	-4.8	-4.9	25	[27, 71]
334	Chloromethyl pentate	-4.8	-5	25	[27, 71]

Num	Esters	Obs.	Calc.	Temp.	Ref.
335	Chloromethyl hexanoate	-4.8	-5	25	[27, 71]
336	Chloromethyl iso-hexanoate	-4.8	-4.9	25	[27, 71]
337	Chloromethyl phenylacetate	-4.8	-5.1	25	[27, 71]
338	Chloromethyl phenylpropionate	-4.9	-5.1	25	[27, 71]
339	Chloromethyl phenylbutyrate	-4.9	-4.9	25	[27, 71]
340	Chloromethyl isobutyrate	-4.9	-5.2	25	[27, 71]
341	Chloromethyl cyclohexyl-carboxylate	-5.2	-5.6	25	[27, 71]
342	Chloromethyl isopentate	-5.4	-5.1	25	[27, 71]
343	Chloromethyl cyclohexylacetate	-5.4	-5.3	25	[27, 71]
344	Chloromethyl (2-ethyl)propionate	-5.6	-5.6	25	[27, 71]
345	Chloromethyl (2,2-methyl-phenyl)acetate	-5.6	-5.8	25	[27, 71]
346	Chloromethyl (2,2-ethyl-phenyl)acetate	-5.9	-6.4	25	[27, 71]
347	Chloromethyl neopentate	-6	-5.7	25	[27, 71]
348	Chloromethyl (2,2-diphenyl)acetate	-6.2	-6.9	25	[27, 71]
349	Chloromethyl (2-ethyl)butyrate	-6.4	-6.4	25	[27, 71]
350	Chloromethyl (3-phenyl)2-propenoate	-6.4	-6.2	25	[27, 71]
351	Chloromethyl trichloroacetate	-6.5	-6	25	[27, 71]
352	Chloromethyl benzoate	-7	-6.4	25	[27, 71]
353	Chloromethyl cyclobutyl-carboxylate*	-4.5	-5.2	25	[27, 71]
354	Chloromethyl methoxyacetate	-4.6	-5.1	25	[27, 71]
355	Chloromethyl bromoacetate	-4.7	-5.1	25	[27, 71]
356	Chloromethyl thiolpropionate	-4.8	-5.1	25	[27, 71]
357	Chloromethyl iodoacetate	-4.8	-5.2	25	[27, 71]
358	Chloromethyl nonatae	-4.8	-5	25	[27, 71]
359	Chloromethyl (4,4-dimethyl) pentate	-4.8	-5.4	25	[27, 71]
360	Chloromethyl phenoxy-acetate	-4.8	-5.1	25	[27, 71]
361	Chloromethyl cyclopentyl-carboxylate	-5	-5.5	25	[27, 71]
362	Chloromethyl difluoroacetate	-5.1	-5.3	25	[27, 71]
363	Chloromethyl methoxypropionate	-5.2	-5	25	[27, 71]
364	Chloromethyl chloropropionate	-5.3	-5	25	[27, 71]
365	Chloromethyl trifluoroacetate	-5.6	-5.9	25	[27, 71]
366	Chloromethyl cycloheptyl-carboxylate	-5.6	-5.6	25	[27, 71]
367	Chloromethyl dichloracetate	-6	-5.5	25	[27, 71]
368	Chloromethyl neopentate	-6.2	-5.7	25	[27, 71]
369	Chloromethyl (2-neopentyl)propionate	-6.3	-6.2	25	[27, 71]
370	Chloromethyl dibromoacetate	-6.3	-5.9	25	[27, 71]
371	Chloromethyl (2-propyl)pentate	-6.6	-6.8	25	[27, 71]
372	Chloromethyl tribromoacetate	-6.9	-6.6	25	[27, 71]
373	Chloromethyl (3,3-methyl-neopentyl)acetate	-7	-7	25	[27, 71]
374	Chloromethyl (3-neopentyl-4,4-dimethyl)pentate	-7.6	-7.6	25	[27, 71]
375	Chloromethyl (2-t-butyl)propionate	-7.8	-7.1	25	[27, 71]
376	Chloromethyl (2,2-methyl-t-butyl)propionate	-8.4	-7.6	25	[27, 71]

Num	Esters	Obs.	Calc.	Temp.	Ref.
377	Chloromethyl (2,2-diethyl)butyrate	-8.3	-7.3	25	[27, 71]
378	(methyl) (neopentyl) (t-butyl)CC(=O)OCCl	-8.4	-8.9	25	[27, 71]
379	p-Nitrophenyl acetate	-3.9	-3.9	30	[72]
380	p-Nitrophenyl propionate	-3.9	-4.3	30	[72]
381	p-Nitrophenyl butyrate	-4.1	-4.4	30	[72]
382	p-Nitrophenyl isobutyrate	-4.1	-4.6	30	[72]
383	p-Nitrophenyl 3,3-dimethylbutyrate	-4.8	-5.4	30	[72]

Table 9. SPARC-calculated vs. observed log acid-catalyzed hydrolysis rate constants for carboxylic acid esters in water-acetone mixtures as a function of temperature in M<sup>-1</sup>s<sup>-1</sup>

Num	Esters	Obs	Calc	Temp	Solvent	Ref.
1	Ethyl m-nitrobenzoate	-7	-6.4	25	60% acetone	[73]
2	Ethyl benzoate	-6.9	-6.3	25	60% acetone	[73]
3	Ethyl dichloroacetate	-4.9	-5.2	25	60% acetone	[73]
4	Ethyl iso-butyrate	-4.7	-4.9	25	60% acetone	[73]
5	Ethyl chloroacetate	-4.4	-4.7	25	60% acetone	[73]
6	Methyl acetate	-4.3	-3.7	25	60% acetone	[73]
7	Ethyl phenylacetate	-4.8	-5	25	70% acetone	[74]
8	Ethyl phenylpropionate	-4.9	-4.9	25	70% acetone	[74]
9	Ethyl phenylbutyrate	-4.9	-4.6	25	70% acetone	[74]
10	Ethyl phenylpentate	-4.8	-4.7	25	70% acetone	[74]
11	Ethyl phenylisopropionate	-6.6	-6.3	25	70% acetone	[74]
12	Ethyl (2-ethyl)phenylacetate	-6.9	-7.1	25	70% acetone	[74]
13	Ethyl (2,2-diphenyl)acetate	-7.3	-8	25	70% acetone	[74]
14	Ethyl cyclohexylacetate	-5.3	-5.2	25	70% acetone	[74]
15	Chloromethyl acetate	-4.5	-4.4	25	70% acetone	[74]
16	Chloromethyl acetate	-4.6	-4.4	25	70% acetone	[74]
17	Chloromethyl acetate	-4.7	-4.4	25	70% acetone	[74]
18	Chloromethyl propionate	-4.7	-4.9	25	70% acetone	[74]
19	Chloromethyl butyrate	-5	-5.1	25	70% acetone	[74]
20	Ethyl acetate	-4.3	-3.8	25	70% acetone	[74]
21	Ethyl propionate	-4.4	-4.4	25	70% acetone	[74]
22	Ethyl butyrate	-4.7	-4.7	25	70% acetone	[74]
23	Ethyl pentate	-4.7	-4.8	25	70% acetone	[74]
24	Ethyl hexanoate	-4.8	-4.8	25	70% acetone	[74]
25	Ethyl heptanoate	-4.8	-4.8	25	70% acetone	[74]
26	Ethyl octanoate	-4.8	-4.8	25	70% acetone	[74]
27	Ethyl isobutyrate	-4.9	-5	25	70% acetone	[74]
28	Ethyl isopentate	-5.2	-4.9	25	70% acetone	[74]
29	Ethyl hexanoate	-4.8	-4.7	25	70% acetone	[74]
30	Ethyl sec-hexanoate	-5.4	-6	25	70% acetone	[74]
31	Ethyl neopentate	-5.9	-5.9	25	70% acetone	[74]
32	Ethyl (2-ethyl)butyrate	-5.9	-6.8	25	70% acetone	[74]
33	Ethyl fluoroacetate	-4.6	-4.7	25	70% acetone	[74]
34	Ethyl fluoroacetate	-4.1	-4.3	35	70% acetone	[74]
35	Ethyl fluoroacetate	-3.6	-3.8	50	70% acetone	[74]
36	Ethyl difluoroacetate	-4	-5	25	70% acetone	[74]
37	Ethyl p-methoxybenzoate	-5.7	-5.3	60	60% acetone	[75]
38	Ethyl p-methoxybenzoate	-4.9	-4.7	80.2	60% acetone	[75]
39	Ethyl p-methoxybenzoate	-4.2	-4.2	99.2	60% acetone	[75]
40	Ethyl p-methoxybenzoate	-3.6	-3.6	119.9	60% acetone	[75]

Num	Esters	Obs.	Calc.	Temp	Solvent	Ref.
41	Ethyl p-methoxybenzoate	-3	-3.2	138.5	60% acetone	[75]
42	Ethyl p-hydroxybenzoate	-5	-4.7	80.2	60% acetone	[75]
43	Ethyl p-hydroxybenzoate	-4.3	-4.1	99.8	60% acetone	[75]
44	Ethyl p-hydroxybenzoate	-3.7	-3.6	120.2	60% acetone	[75]
45	Ethyl p-hydroxybenzoate	-3.2	-3.2	138.9	60% acetone	[75]
46	Ethyl p-methylbenzoate	-4.8	-4.5	80.3	60% acetone	[75]
47	Ethyl p-methylbenzoate	-4.1	-4	100.05	60% acetone	[75]
48	Ethyl p-methylbenzoate	-3.5	-3.5	120.5	60% acetone	[75]
49	Ethyl p-methylbenzoate	-3	-3	138.9	60% acetone	[75]
50	Ethyl benzoate	-4.7	-4.4	80.3	60% acetone	[75]
51	Ethyl benzoate	-4	-3.9	100.2	60% acetone	[75]
52	Ethyl benzoate	-3.4	-3.4	120.9	60% acetone	[75]
53	Ethyl benzoate	-2.9	-2.9	139.3	60% acetone	[75]
54	Ethyl p-chlorobenzoate	-4.7	-4.5	80.3	60% acetone	[75]
55	Ethyl p-chlorobenzoate	-4.1	-3.9	99.85	60% acetone	[75]
56	Ethyl p-chlorobenzoate	-3.4	-3.4	120.2	60% acetone	[75]
57	Ethyl p-chlorobenzoate	-2.9	-3	139.4	60% acetone	[75]
58	Ethyl p-bromobenzoate	-5.5	-5.1	60.05	60% acetone	[75]
59	Ethyl p-bromobenzoate	-4.7	-4.5	80.2	60% acetone	[75]
60	Ethyl p-bromobenzoate	-4.1	-4	100.15	60% acetone	[75]
61	Ethyl p-bromobenzoate	-3.5	-3.5	120.2	60% acetone	[75]
62	Ethyl p-bromobenzoate	-3	-3	139.2	60% acetone	[75]
63	Ethyl p-nitrobenzoate	-5.3	-5	60	60% acetone	[75]
64	Ethyl p-nitrobenzoate	-4.6	-4.3	80.2	60% acetone	[75]
65	Ethyl p-nitrobenzoate	-4	-3.8	99.4	60% acetone	[75]
66	Ethyl p-nitrobenzoate	-3.4	-3.3	120	60% acetone	[75]
67	Ethyl p-nitrobenzoate	-2.8	-2.9	138.5	60% acetone	[75]
68	Ethyl m-nitrobenzoate	-5.4	-5.1	60	60% acetone	[75]
69	Ethyl m-nitrobenzoate	-4.7	-4.4	80.2	60% acetone	[75]
70	Ethyl m-nitrobenzoate	-4.1	-3.9	99.9	60% acetone	[75]
71	Ethyl m-nitrobenzoate	-3.4	-3.4	120.4	60% acetone	[75]
72	Ethyl m-nitrobenzoate	-2.9	-3	139	60% acetone	[75]
73	Ethyl o-nitrobenzoate	-5.8	-5.2	80.3	60% acetone	[75]
74	Ethyl o-nitrobenzoate	-5.2	-4.6	99.85	60% acetone	[75]
75	Ethyl o-nitrobenzoate	-4.5	-4.1	120.7	60% acetone	[75]
76	Ethyl o-nitrobenzoate	-4	-3.7	139.2	60% acetone	[75]
77	Ethyl butyrate	-4.9	-4.9	20	70% acetone	[74]
78	Ethyl butyrate	-4.5	-4.5	30	70% acetone	[74]
79	Ethyl butyrate	-4.2	-4.1	40	70% acetone	[74]
80	Ethyl butyrate	-3.8	-3.8	50	70% acetone	[74]
81	Ethyl pentate	-4.9	-4.9	20	70% acetone	[74]
82	Ethyl pentate	-4.6	-4.6	30	70% acetone	[74]

Num	Esters	Obs.	Calc.	Temp	Solvent	Ref.
83	Ethyl pentate	-4.2	-4.2	40	70% acetone	[74]
84	Ethyl pentate	-3.8	-3.9	50	70% acetone	[74]
85	Ethyl isobutyrate	-5.1	-5.2	20	70% acetone	[74]
86	Ethyl isobutyrate	-4.7	-4.8	30	70% acetone	[74]
87	Ethyl isobutyrate	-4.3	-4.5	40	70% acetone	[74]
88	Ethyl isobutyrate	-3.9	-4.1	50	70% acetone	[74]
89	Ethyl sec-hexanoate	-5.6	-6.2	20	70% acetone	[74]
90	Ethyl sec-hexanoate	-5.2	-5.8	30	70% acetone	[74]
91	Ethyl sec-hexanoate	-4.8	-5.5	40	70% acetone	[74]
92	Ethyl sec-hexanoate	-4.4	-5.1	50	70% acetone	[74]
93	Ethyl iso-hexanoate	-5	-4.9	20	70% acetone	[74]
94	Ethyl iso-hexanoate	-4.6	-4.5	30	70% acetone	[74]
95	Ethyl iso-hexanoate	-4.2	-4.2	40	70% acetone	[74]
96	Ethyl iso-hexanoate	-3.8	-3.8	50	70% acetone	[74]
97	Ethyl cyclohexyl-carboxylate	-5.3	-5.7	20	70% acetone	[74]
98	Ethyl cyclohexyl-carboxylate	-4.9	-5.4	30	70% acetone	[74]
99	Ethyl cyclohexyl-carboxylate	-4.6	-5	40	70% acetone	[74]
100	Ethyl cyclohexyl-carboxylate	-4.2	-4.7	50	70% acetone	[74]
101	Ethyl acetate	-3.6	-3.2	44.7	70% acetone	[74]
102	Ethyl propionate	-3.7	-3.7	44.7	70% acetone	[74]
103	Ethyl butyrate	-4	-4	44.7	70% acetone	[74]
104	Ethyl pentate	-4	-4.1	44.7	70% acetone	[74]
105	Ethyl hexanoate	-4	-4.1	44.7	70% acetone	[74]
106	Ethyl isobutyrate	-4.1	-4.3	44.7	70% acetone	[74]
107	Ethyl isopentate	-4.5	-4.3	44.7	70% acetone	[74]
108	Ethyl t-butyrate	-4.9	-5.1	44.7	70% acetone	[74]
109	Ethyl phenylacetate	-4	-4.4	44.7	70% acetone	[74]
110	Ethyl acetate	-4	-3.5	35	70% acetone	[74]
111	Ethyl propionate	-4	-4.1	35	70% acetone	[74]
112	Ethyl butyrate	-4.3	-4.3	35	70% acetone	[74]
113	Ethyl pentate	-4.3	-4.4	35	70% acetone	[74]
114	Ethyl hexanoate	-4.4	-4.4	35	70% acetone	[74]
115	Ethyl isobutyrate	-4.5	-4.6	35	70% acetone	[74]
116	Ethyl isopentate	-4.8	-4.6	35	70% acetone	[74]
117	Ethyl t-butyrate	-5.4	-5.5	35	70% acetone	[74]
118	Ethyl phenylacetate	-4.1	-4.7	35	70% acetone	[74]
119	Ethyl phenylacetate	-5	-5.2	20	70% acetone	[74]
120	Ethyl phenylpropionate	-5.1	-5.1	20	70% acetone	[74]
121	Ethyl phenylbutyrate	-5.1	-4.8	20	70% acetone	[74]
122	Ethyl phenylpentate	-5.1	-4.9	20	70% acetone	[74]
123	Ethyl phenylisopropionate	-6.8	-6.5	20	70% acetone	[74]
124	Ethyl 2-ethyl-2-phenylacetate	-7.2	-7.3	20	70% acetone	[74]

Num	Esters	Obs.	Calc.	Temp	Solvent	Ref.
125	Ethyl 2,2-diphenylacetate	-7.5	-8.2	20	70% acetone	[74]
126	Ethyl cyclohexylacetate	-5.5	-5.4	20	70% acetone	[74]
127	Ethyl phenylacetate	-4.6	-4.8	30	70% acetone	[74]
128	Ethyl phenylpropionate	-4.7	-4.8	30	70% acetone	[74]
129	Ethyl phenylbutyrate	-4.7	-4.5	30	70% acetone	[74]
130	Ethyl phenylpentate	-4.6	-4.5	30	70% acetone	[74]
131	Ethyl phenylisopropionate	-6.3	-6.1	30	70% acetone	[74]
132	Ethyl 2-ethyl-2-phenylacetate	-6.7	-6.9	30	70% acetone	[74]
133	Ethyl 2,2-diphenylacetate	-7.1	-7.8	30	70% acetone	[74]
134	Ethyl cyclohexylacetate	-5.1	-5	30	70% acetone	[74]
135	Ethyl phenylacetate	-4.3	-4.5	40	70% acetone	[74]
136	Ethyl phenylpropionate	-4.3	-4.4	40	70% acetone	[74]
137	Ethyl phenylbutyrate	-4.3	-4.1	40	70% acetone	[74]
138	Ethyl phenylpentate	-4.3	-4.1	40	70% acetone	[74]
139	Ethyl phenylisopropionate	-6	-5.7	40	70% acetone	[74]
140	Ethyl 2-ethyl-2-phenylacetate	-6.4	-6.6	40	70% acetone	[74]
141	Ethyl 2,2-diphenylacetate	-6.7	-7.5	40	70% acetone	[74]
142	Ethyl cyclohexylacetate	-4.7	-4.7	40	70% acetone	[74]
143	Ethyl phenylacetate	-4.2	-4.2	50	70% acetone	[74]
144	Ethyl phenylpropionate	-3.9	-4.1	50	70% acetone	[74]
145	Ethyl phenylbutyrate	-4	-3.8	50	70% acetone	[74]
146	Ethyl phenylpentate	-3.9	-3.8	50	70% acetone	[74]
147	Ethyl phenylisopropionate	-5.6	-5.4	50	70% acetone	[74]
148	Ethyl 2-ethyl-2-phenylacetate	-6	-6.2	50	70% acetone	[74]
149	Ethyl 2,2-diphenylacetate	-6.3	-7.1	50	70% acetone	[74]
150	Ethyl cyclohexyl-acetate	-4.3	-4.3	50	70% acetone	[74]
151	Benzyl acetate	-4.9	-4.4	15	60% acetone	[76]
152	Benzyl acetate	-4.5	-4	25	60% acetone	[76]
153	Benzyl acetate	-3.9	-3.5	40	60% acetone	[76]
154	Benzyl acetate	-3.2	-2.9	60	60% acetone	[76]
155	Benzyl acetate	-2.6	-2.3	80	60% acetone	[76]
156	m-Methylbenzyl acetate	-5	-4.4	15	60% acetone	[76]
157	m-Methylbenzyl acetate	-4.5	-4	25	60% acetone	[76]
158	m-Methylbenzyl acetate	-4	-3.5	40	60% acetone	[76]
159	m-Methylbenzyl acetate	-3.3	-2.9	60	60% acetone	[76]
160	m-Methylbenzyl acetate	-2.7	-2.3	80	60% acetone	[76]
161	p-Methylbenzyl acetate	-4.5	-4	25	60% acetone	[76]
162	p-Methylbenzyl acetate	-3.9	-3.5	40	60% acetone	[76]
163	p-Methylbenzyl acetate	-3.2	-2.9	60	60% acetone	[76]
164	p-Methylbenzyl acetate	-2.6	-2.4	80	60% acetone	[76]
165	m-Nitrobenzyl acetate	-5	-4.4	15	60% acetone	[76]
166	m-Nitrobenzyl acetate	-4.6	-4	25	60% acetone	[76]

Num	Esters	Obs.	Calc.	Temp	Solvent	Ref.
167	m-Nitrobenzyl acetate	-4	-3.5	40	60% acetone	[76]
168	m-Nitrobenzyl acetate	-3.3	-2.9	60	60% acetone	[76]
169	m-Nitrobenzyl acetate	-2.7	-2.4	80	60% acetone	[76]
170	p-Nitrobenzyl acetate	-5	-4.4	15	60% acetone	[76]
171	p-Nitrobenzyl acetate	-4.6	-4	25	60% acetone	[76]
172	p-Nitrobenzyl acetate	-4	-3.5	40	60% acetone	[76]
173	p-Nitrobenzyl acetate	-3.3	-2.9	60	60% acetone	[76]
174	p-Nitrobenzyl acetate	-2.7	-2.4	80	60% acetone	[76]
175	Phenyl acetate	-5	-4.6	15	60% acetone	[76]
176	Phenyl acetate	-4.6	-4.3	25	60% acetone	[76]
177	Phenyl acetate	-3.9	-3.8	40	60% acetone	[76]
178	Phenyl acetate	-3.2	-3.1	60	60% acetone	[76]
179	Phenyl acetate	-2.6	-2.6	80	60% acetone	[76]
180	m-Methylphenyl acetate	-5	-4.7	15	60% acetone	[76]
181	m-Methylphenyl acetate	-4.6	-4.3	25	60% acetone	[76]
182	m-Methylphenyl acetate	-4	-3.8	40	60% acetone	[76]
183	m-Methylphenyl acetate	-3.2	-3.2	60	60% acetone	[76]
184	m-Methylphenyl acetate	-2.6	-2.6	80	60% acetone	[76]
185	p-Methylphenyl acetate	-4.5	-4.3	25	60% acetone	[76]
186	p-Methylphenyl acetate	-3.9	-3.8	40	60% acetone	[76]
187	p-Methylphenyl acetate	-3.2	-3.2	60	60% acetone	[76]
188	p-Methylphenyl acetate	-2.5	-2.6	80	60% acetone	[76]
189	m-Nitrophenyl acetate	-5.2	-4.8	15	60% acetone	[76]
190	m-Nitrophenyl acetate	-4.7	-4.4	25	60% acetone	[76]
191	m-Nitrophenyl acetate	-4.1	-3.9	40	60% acetone	[76]
192	m-Nitrophenyl acetate	-3.4	-3.2	60	60% acetone	[76]
193	m-Nitrophenyl acetate	-2.8	-2.7	80	60% acetone	[76]
194	Ethyl dibromoacetate	-4.7	-5.2	35	35% acetone	[77]
195	Ethyl dibromoacetate	-4.8	-5.2	35	44% acetone	[77]
196	Ethyl dibromoacetate	-4.9	-5.3	35	51.5% acetone	[77]
197	Ethyl dibromoacetate	-5.1	-5.4	35	62% acetone	[77]
198	Ethyl dibromoacetate	-5.3	-5.6	35	82.5% acetone	[77]
199	Ethyl dibromoacetate	-4.3	-4.8	45	35% acetone	[77]
200	Ethyl dibromoacetate	-4.4	-4.9	45	42.5% acetone	[77]
201	Ethyl dibromoacetate	-4.6	-4.9	45	52% acetone	[77]
202	Ethyl dibromoacetate	-4.7	-5	45	62% acetone	[77]
203	Ethyl dibromoacetate	-4.9	-5.2	45	82% acetone	[77]
204	Ethyl dibromoacetate	-4.1	-4.6	55	35% acetone	[77]
205	Ethyl dibromoacetate	-4.2	-4.7	55	42.5% acetone	[77]
206	Ethyl dibromoacetate	-4.3	-4.7	55	52% acetone	[77]
207	Ethyl dibromoacetate	-4.2	-4.8	55	62% acetone	[77]
208	Ethyl dibromoacetate	-4.6	-5	55	81.5% acetone	[77]

Table 10. SPARC-calculated vs. observed log acid-catalyzed hydrolysis rate constants for carboxylic acid esters in water-methanol mixtures as a function of temperature in M<sup>-1</sup>s<sup>-1</sup>

Num	Ester	Obs	Calc	Temp.	Solvent	Ref.
1	Ethyl p-methoxybenzoate	-4	-4.2	99.85	60% methanol	[75]
2	Ethyl p-methoxybenzoate	-3.4	-3.6	120.45	60% methanol	[75]
3	Ethyl p-methoxybenzoate	-3	-3.2	138.5	60% methanol	[75]
4	Ethyl p-methoxybenzoate	-2.6	-2.9	153.9	60% methanol	[75]
5	Ethyl benzoate	-3.8	-3.9	100.2	60% methanol	[75]
6	Ethyl benzoate	-3.3	-3.4	121.2	60% methanol	[75]
7	Ethyl benzoate	-2.8	-3	139.2	60% methanol	[75]
8	Ethyl benzoate	-2.5	-2.6	153.9	60% methanol	[75]
9	Ethyl p-nitrobenzoate	-3.8	-3.8	100.12	60% methanol	[75]
10	Ethyl p-nitrobenzoate	-3.2	-3.3	120.75	60% methanol	[75]
11	Ethyl p-nitrobenzoate	-2.8	-2.9	138.4	60% methanol	[75]
12	Ethyl p-nitrobenzoate	-2.5	-2.6	153	60% methanol	[75]
13	Methyl benzoate	-3.7	-3.9	100.8	80% methanol	[63]
14	Methyl o-methylbenzoate	-4.4	-4.5	100.8	80% methanol	[63]
15	Methyl o-ethylbenzoate	-4.7	-4.6	100.8	80% methanol	[63]
16	Methyl o-fluorobenzoate	-3.7	-4.4	100.8	80% methanol	[63]
17	Methyl o-chlorobenzoate	-4.2	-4.5	100.8	80% methanol	[63]
18	Methyl o-bromobenzoate	-4.3	-4.6	100.8	80% methanol	[63]
19	Methyl o-iodobenzoate	-4.6	-4.7	100.8	80% methanol	[63]
20	Methyl m-methylbenzoate	-3.8	-3.9	100.8	80% methanol	[63]
21	Methyl m-chlorobenzoate	-3.8	-3.9	100.8	80% methanol	[63]
22	Methyl m-nitrobenzoate	-3.9	-3.9	100.8	80% methanol	[63]

Table 11. SPARC-calculated vs. observed log acid-catalyzed hydrolysis rate constants for carboxylic acid esters in water-ethanol mixtures as a function of temperature in M<sup>-1</sup>s<sup>-1</sup>

Num	Esters	Obs	Calc	Temp	Solvent	Ref
1	Ethyl p-methoxybenzoate	-5.7	-5.5	60	60% ethanol	[75]
2	Ethyl p-methoxybenzoate	-4.8	-4.8	80.2	60% ethanol	[75]
3	Ethyl p-methoxybenzoate	-4.2	-4.3	99.4	60% ethanol	[75]
4	Ethyl p-methoxybenzoate	-3.6	-3.7	119.9	60% ethanol	[75]
5	Ethyl p-methoxybenzoate	-3.1	-3.3	138.1	60% ethanol	[75]
6	Ethyl p-hydroxybenzoate	-5	-4.8	80.2	60% ethanol	[75]
7	Ethyl p-hydroxybenzoate	-4.4	-4.3	99.5	60% ethanol	[75]
8	Ethyl p-hydroxybenzoate	-3.7	-3.7	120	60% ethanol	[75]
9	Ethyl p-hydroxybenzoate	-3.2	-3.3	138.5	60% ethanol	[75]
10	Ethyl p-methylbenzoate	-5.5	-5.3	60.05	60% ethanol	[75]
11	Ethyl p-methylbenzoate	-4.8	-4.7	80.25	60% ethanol	[75]
12	Ethyl p-methylbenzoate	-4.1	-4.1	99.9	60% ethanol	[75]
13	Ethyl p-methylbenzoate	-3.5	-3.6	120.3	60% ethanol	[75]
14	Ethyl p-methylbenzoate	-3	-3.1	139.7	60% ethanol	[75]
15	Ethyl benzoate	-5.4	-5.2	60	60% ethanol	[75]
16	Ethyl benzoate	-4.7	-4.5	80.2	60% ethanol	[75]
17	Ethyl benzoate	-4.1	-4	99.6	60% ethanol	[75]
18	Ethyl benzoate	-3.5	-3.5	120.2	60% ethanol	[75]
19	Ethyl benzoate	-2.9	-3.1	138.6	60% ethanol	[75]
20	Ethyl p-chlorobenzoate	-4.7	-4.6	80.3	60% ethanol	[75]
21	Ethyl p-chlorobenzoate	-4.1	-4.1	100	60% ethanol	[75]
22	Ethyl p-chlorobenzoate	-3.5	-3.5	120.6	60% ethanol	[75]
23	Ethyl p-chlorobenzoate	-3.1	-3.1	139.3	60% ethanol	[75]
24	Ethyl p-bromobenzoate	-4.7	-4.6	80.2	60% ethanol	[75]
25	Ethyl p-bromobenzoate	-4.1	-4.1	100	60% ethanol	[75]
26	Ethyl p-bromobenzoate	-3.5	-3.6	120.2	60% ethanol	[75]
27	Ethyl p-bromobenzoate	-3	-3.1	139.4	60% ethanol	[75]
28	Ethyl p-nitrobenzoate	-4.5	-4.5	80.2	60% ethanol	[75]
29	Ethyl p-nitrobenzoate	-4	-3.9	98.9	60% ethanol	[75]
30	Ethyl p-nitrobenzoate	-3.5	-3.4	119.3	60% ethanol	[75]
31	Ethyl p-nitrobenzoate	-3	-3	138	60% ethanol	[75]
32	Ethyl m-nitrobenzoate	-4.7	-4.6	80.2	60% ethanol	[75]
33	Ethyl m-nitrobenzoate	-4.1	-4	99.45	60% ethanol	[75]
34	Ethyl m-nitrobenzoate	-3.5	-3.5	119.9	60% ethanol	[75]
35	Ethyl m-nitrobenzoate	-3	-3.1	138.3	60% ethanol	[75]
36	Ethyl o-nitrobenzoate	-5.8	-5.3	80.3	60% ethanol	[75]
37	Ethyl o-nitrobenzoate	-5.2	-4.7	100	60% ethanol	[75]
38	Ethyl o-nitrobenzoate	-4.6	-4.2	120.6	60% ethanol	[75]
39	Ethyl o-nitrobenzoate	-4.1	-3.8	138.9	60% ethanol	[75]

Table 12. SPARC-calculated vs. observed log acid-catalyzed hydrolysis rate constants for carboxylic acid esters in water-dioxane mixtures as a function of temperature in M<sup>-1</sup>s<sup>-1</sup>

Num	Esters	Obs	Calc	Temp	Solvent	Ref.
1	Chloromethyl acetate	-4.4	-4.4	25	10% dioxane	[78]
2	Chloromethyl acetate	-4	-4.1	35	10% dioxane	[78]
3	Chloromethyl acetate	-3.6	-3.7	45	10% dioxane	[78]
4	Chloromethyl acetate	-4.5	-4.5	25	25% dioxane	[78]
5	Chloromethyl acetate	-4.1	-4.1	35	25% dioxane	[78]
6	Chloromethyl acetate	-3.7	-3.8	45	25% dioxane	[78]
7	Chloromethyl acetate	-4.7	-4.6	25	50% dioxane	[78]
8	Chloromethyl acetate	-4.3	-4.2	35	50% dioxane	[78]
9	Chloromethyl acetate	-3.9	-3.9	45	50% dioxane	[78]
10	Chloromethyl acetate	-4.9	-4.8	25	75% dioxane	[78]
11	Chloromethyl acetate	-4.5	-4.5	35	75% dioxane	[78]
12	Chloromethyl acetate	-4.1	-4.1	45	75% dioxane	[78]
13	Methyl benzoate	-3.8	-4.1	100	60% dioxane	[79]
14	Methyl o-methylbenzoate	-4.4	-4.8	100	60% dioxane	[79]
15	Methyl o-ethylbenzoate	-4.7	-5	100	60% dioxane	[79]

Table 13. SPARC-calculated vs. observed log neutral hydrolysis rate constants for carboxylic acid esters in water as a function of temperature using different catalysts in M<sup>-1</sup>s<sup>-1</sup>

Num	Esters	Obs	Calc	Catalyst	Temp	Ref
1	Ethyl acetate	-11.3	-12.1	water	25	[53]
2	Vinyl acetate	-8.7	-9	water	25	[53]
3	Chloromethyl formate	-5.8	-6.5	water	25	[53]
4	Methyl chloroacetate	-8.4	-8.5	water	25	[53]
5	Methyl dichloroacetate	-6.6	-6.9	water	25	[53]
6	Ethyl dichloroacetate	-7	-7	water	25	[53]
7	Chloroethyl dichloroacetate	-6.2	-6.4	water	25	[53]
8	Methoxyethyl dichloroacetate	-6.7	-6.7	water	25	[53]
9	Methyl trichloroacetate	-4.8	-5.5	water	25	[53]
10	Methoxyethyl trichloroacetate	-5	-5.3	water	25	[53]
11	Ethyl difluoroacetate	-6	-5.9	water	25	[49]
12	Methyl trifluoroacetate	-4.2	-4.1	water	25	[49]
13	Ethyl trifluoroacetate	-4.3	-4.2	water	25	[49]
14	Isopropyl trifluoroacetate	-4.2	-4.2	water	25	[49]
15	t-Butyl trifluoroacetate	-4.6	-4.4	water	25	[49]
16	Chloromethyl chloroacetate	-5.7	-5.6	water	25	[53]
17	Phenyl acetate	-9	-9.1	water	25	[53]
18	p-Methylphenyl acetate	-9.1	-9.4	water	25	[49]
19	p-Chlorophenyl acetate	-8.9	-8.9	water	25	[49]
20	p-Nitrophenyl acetate	-7.8	-8.2	water	25	[49]
21	3,4-Dinitrophenyl acetate	-7.1	-7.5	water	25	[49]
22	2,4-Dinitrophenyl acetate	-6.7	-6.5	water	25	[80]
23	2,6-Dinitrophenyl acetate	-6.6	-5.8	water	25	[49]
24	p-Nitrophenyl chloroacetate	-5.2	-4.7	water	25	[80]
25	Phenyl dichloroacetate	-4.5	-4	water	25	[80]
26	Ethyl trifluoroacetate	-4.6	-4.4	water	10	[49]
27	Ethyl difluoroacetate	-3.8	-3.5	aniline	25	[81]
28	Ethyl difluoroacetate	-3.2	-3	acetate	25	[81]
29	Ethyl difluoroacetate	-2	-2	imidazole	25	[81]
30	Ethyl dichloroacetate	-4.5	-4.5	formate	25	[81]
31	Ethyl dichloroacetate	-4.8	-4.6	aniline	25	[81]
32	Ethyl dichloroacetate	-3.7	-3.9	pyridine	25	[81]
33	Ethyl dichloroacetate	-3.5	-3.5	picoline4	25	[81]
34	Ethyl dichloroacetate	-4.3	-4.1	acetate	25	[81]
35	Ethyl dichloroacetate	-3.6	-3.7	succinate	25	[81]
36	Ethyl dichloroacetate	-2.9	-3.1	imidazole	25	[81]
37	Ethyl chloroacetate	-6.1	-5.7	acetate	25	[81]
38	Ethyl chloroacetate	-4.4	-4.7	imidazole	25	[81]
39	Ethyl trichloroacetate	-2.8	-2.3	aniline	25	[80]
40	p-Nitrophenyl chloroacetate	-1.9	-1.6	pyridine	25	[80]

Num	Esters	Obs	Calc	Catalyst	Temp	Ref
41	p-Nitrophenyl chloroacetate	0.2	-0.1	imidazole	25	[80]
43	2,6-dinitrophenyl acetate	-2.9	-2.9	acetate	25	[82]
44	2,4-dinitrophenyl acetate	-3.3	-3.6	acetate	25	[82]
45	2,3-dinitrophenyl acetate	-3.6	-3.8	acetate	25	[82]
46	3,4-dinitrophenyl acetate	-4	-4.6	acetate	25	[82]
47	p-Nitrophenyl acetate	-5.2	-5.3	acetate	25	[82]
48	o-Nitrophenyl acetate	-5.3	-4.5	acetate	25	[82]
49	m-Nitrophenyl acetate	-5.5	-5.4	acetate	25	[82]
50	p-Chlorophenyl acetate	-6	-6.1	acetate	25	[82]
51	p-Methylphenyl acetate	-6.6	-6.6	acetate	25	[82]

Table 14. SPARC-calculated vs. observed log neutral hydrolysis rate constants for carboxylic acid esters in water-acetone mixtures as a function of temperature using different catalysts in M<sup>-1</sup>s<sup>-1</sup>

Num	Esters	Obs	Calc	Catalysts	Temp.	Solvent	Ref.
1	Chloromethyl chloroacetate	-7.2	-7	water	25	50% acetone	[53]
2	Chloromethyl dichloroacetate	-5.3	-5.4	water	25	50% acetone	[80]
3	Methyl trifluoroacetate	-5.6	-6.4	water	25	70% acetone	[83]
4	Ethyl trifluoroacetate	-6.1	-6.5	water	25	70% acetone	[83]
5	Propyl trifluoroacetate	-6.3	-6.5	water	25	70% acetone	[83]
6	Butyl trifluoroacetate	-6.4	-6.5	water	25	70% acetone	[83]
7	Pentyl trifluoroacetate	-6.4	-6.5	water	25	70% acetone	[83]
8	Hexyl trifluoroacetate	-6.5	-6.5	water	25	70% acetone	[83]
9	Isopropyl trifluoroacetate	-7	-6.6	water	25	70% acetone	[65]
10	sec-Butyl trifluoroacetate	-7.2	-6.8	water	25	70% acetone	[65]
11	sec-Pentyl trifluoroacetate	-7.3	-6.9	water	25	70% acetone	[65]
12	sec-Hexyl trifluoroacetate	-7.3	-7	water	25	70% acetone	[65]
13	Phenyl trifluoroacetate	-3.5	-3.6	water	25	70% acetone	[65]
14	m-Methyl trifluoroacetate	-3.7	-3.7	water	25	70% acetone	[65]
15	p-Methyl trifluoroacetate	-3.8	-3.9	water	25	70% acetone	[65]
16	o-Methyl trifluoroacetate	-4.1	-3.7	water	25	70% acetone	[65]
17	Ethyl pentafluoroacetate	-7.3	-8	water	25	70% acetone	[83]
18	Ethyl heptafluoropropionate	-7.6	-8.3	water	25	70% acetone	[83]
19	Chloromethyl dichloroacetate	-6.3	-6	water	-6.23	50% acetone	[80]
20	Chloromethyl dichloroacetate	-6.1	-5.9	water	0	50% acetone	[80]
21	Chloromethyl dichloroacetate	-5.9	-5.8	water	5	50% acetone	[80]
22	Chloromethyl dichloroacetate	-5.7	-5.7	water	12	50% acetone	[80]
23	Chloromethyl dichloroacetate	-5.5	-5.5	water	18	50% acetone	[80]
24	Chloromethyl dichloroacetate	-5	-5.3	water	35	50% acetone	[80]
25	Chloromethyl dichloroacetate	-4.8	-5.1	water	45	50% acetone	[80]
26	Ethyl trifluoroacetate	-4.6	-4.4	Water	10	70% acetone	[83]
27	Isopropyl trifluoroacetate	-6.7	-6.4	Water	35	70% acetone	[84]
28	Isopropyl trifluoroacetate	-6.5	-6.2	Water	45	70% acetone	[84]
29	sec-Butyl trifluoroacetate	-6.9	-6.6	Water	35	70% acetone	[84]
30	sec-Butyl trifluoroacetate	-6.7	-6.5	Water	45	70% acetone	[84]
31	sec-Pentyl trifluoroacetate	-7.1	-6.7	Water	35	70% acetone	[84]
32	sec-Pentyl trifluoroacetate	-6.9	-6.5	Water	45	70% acetone	[84]
33	sec-Hexyl trifluoroacetate	-7.1	-6.8	water	35	70% acetone	[84]
34	sec-Hexyl trifluoroacetate	-6.8	-6.6	water	45	70% acetone	[84]
35	Phenyl trifluoroacetate	-3.3	-3.5	water	35	70% acetone	[84]
36	Phenyl trifluoroacetate	-3.2	-3.4	water	45	70% acetone	[84]
37	m-Methylphenyl trifluoroacetate	-3.6	-3.6	water	35	70% acetone	[84]
38	m-Methylphenyl trifluoroacetate	-3.4	-3.6	water	45	70% acetone	[84]
39	p-Methylphenyl trifluoroacetate	-3.7	-3.8	water	35	70% acetone	[84]
40	p-Methylphenyl trifluoroacetate	-3.5	-3.7	water	45	70% acetone	[84]

Num	Esters	Obs	Calc	Catalysts	Temp.	Solvent	Ref.
41	o-Methylphenyl trifluoroacetate	-3.9	-3.7	water	35	70% acetone	[84]
42	o-Methylphenyl trifluoroacetate	-3.7	-3.6	water	45	70% acetone	[84]
43	Methyl trifluoroacetate	-5.4	-6.2	water	35	70% acetone	[83]
44	Methyl trifluoroacetate	-5.3	-6	water	45	70% acetone	[83]
45	Ethyl trifluoroacetate	-6	-6.3	water	35	70% acetone	[83]
46	Ethyl trifluoroacetate	-5.8	-6.1	water	45	70% acetone	[83]
47	Propyl trifluoroacetate	-6.1	-6.3	water	35	70% acetone	[83]
48	Propyl trifluoroacetate	-5.9	-6.1	water	45	70% acetone	[83]
49	Butyl trifluoroacetate	-6.2	-6.3	water	35	70% acetone	[83]
50	Butyl trifluoroacetate	-6	-6.1	water	45	70% acetone	[83]
51	Pentyl trifluoroacetate	-6.3	-6.3	water	35	70% acetone	[83]
52	Pentyl trifluoroacetate	-6	-6.1	water	45	70% acetone	[83]
53	Hexyl trifluoroacetate	-6.3	-6.3	water	35	70% acetone	[83]
54	Hexyl trifluoroacetate	-6.1	-6.1	water	45	70% acetone	[83]
55	Ethyl pentafluoroacetate	-7.1	-7.8	water	35	70% acetone	[83]
56	Ethyl pentafluoroacetate	-6.8	-7.6	water	45	70% acetone	[83]
57	Ethyl heptafluoroacetate	-7.4	-8.1	water	35	70% acetone	[83]
58	Ethyl heptafluoroacetate	-7.1	-7.9	water	45	70% acetone	[83]
59	Ethyl dibromoacetate	-8.4	-8	water	35	36% acetone	[77]
60	Ethyl dibromoacetate	-8.8	-8.3	water	35	44% acetone	[77]
61	Ethyl dibromoacetate	-9.1	-8.7	water	35	53% acetone	[77]
62	Ethyl dibromoacetate	-10.5	-10	water	35	83% acetone	[77]
63	Ethyl dibromoacetate	-9.6	-9.1	water	35	63% acetone	[77]
64	Ethyl dibromoacetate	-8.2	-7.8	water	45	36% acetone	[77]
65	Ethyl dibromoacetate	-8.6	-8.1	water	45	44% acetone	[77]
66	Ethyl dibromoacetate	-8.9	-8.4	water	45	53% acetone	[77]
67	Ethyl dibromoacetate	-9.2	-8.8	water	45	63% acetone	[77]
68	Ethyl dibromoacetate	-10.2	-9.7	water	45	83% acetone	[77]
69	Ethyl dibromoacetate	-8.1	-7.7	water	51	36% acetone	[77]
70	Ethyl dibromoacetate	-8.4	-7.9	water	51	44% acetone	[77]
71	Ethyl dibromoacetate	-8.7	-8.3	water	51	53% acetone	[77]
72	Ethyl dibromoacetate	-9.1	-8.6	water	51	63% acetone	[77]
73	Ethyl dibromoacetate	-10	-9.5	water	51	83% acetone	[77]

Table 15. SPARC-calculated vs. observed log neutral hydrolysis rate constants for carboxylic acid esters in water-ethanol mixtures using different catalysts in M<sup>-1</sup>s<sup>-1</sup>

No	Esters	Obs	Calc	Catalysts	Temp.	Solvent	Ref.
1	Ethyl trichloroacetate	-6.3	-6.3	water	25	40% ethanol	[81]
2	Ethyl difluoroacetate	-5.8	-5.9	water	25	3% ethanol	[81]
3	Ethyl difluoroacetate	-5.9	-6	water	25	7 % ethanol	[81]
4	Ethyl difluoroacetate	-6	-6.1	water	25	12% ethanol	[81]
5	Ethyl difluoroacetate	-6.3	-6.2	water	25	22% ethanol	[81]
6	Ethyl difluoroacetate	-6.4	-6.4	water	25	32% ethanol	[81]
7	Ethyl difluoroacetate	-6.8	-6.8	water	25	52% ethanol	[81]
8	Ethyl difluoroacetate	-7.1	-7.1	water	25	72% ethanol	[81]
9	Ethyl trichloroacetate	-3.7	-3.4	acetate	25	40% ethanol	[81]

Table 16. SPARC-calculated vs. observed log neutral hydrolysis rate constants for carboxylic acid esters in water-dioxane mixtures as a function of temperature using different catalysts in M<sup>-1</sup>s<sup>-1</sup>

No	Esters	Obs	Calc	Catalysts	Temp.	Solv	Ref.
1	Methyl trichloroacetate	-6.3	-7.7	water	25	50% dioxane	[53]
2	Trichloroethyl dichloroacetate	-6.3	-6.6	water	25	50% dioxane	[53]
3	Methyl trifluoroacetate	-5.3	-5.5	water	25	60% dioxane	[53]
4	Methyl trifluoroacetate	-5.7	-5.8	water	10	70% dioxane	[53]
5	Ethyl trichloroacetate	-7	-6.7	water	25	50% dioxane	[53]
6	Propyl trichloroacetate	-7.2	-6.7	water	25	50% dioxane	[53]
7	Butyl trichloroacetate	-7.2	-6.8	water	25	50% dioxane	[53]
8	Isopropyl trichloroacetate	-7.8	-6.9	water	25	50% dioxane	[53]
9	Chloroethyl trichloroacetate	-6.1	-6.2	water	25	50% dioxane	[53]
10	Methoxyethyl trichloroacetate	-6.6	-6.4	water	25	50% dioxane	[53]
11	Methyl trifluoroacetate	-5.3	-5.5	water	25	60% dioxane	[53]
12	Methyl trifluoroacetate	-5.7	-5.8	water	25	70% dioxane	[53]
13	Methyl trifluoroacetate	-6.5	-6.2	water	0	70% dioxane	[85]
14	Methyl trifluoroacetate	-5.4	-5.4	water	44.6	70% dioxane	[85]
15	Methyl trifluoroacetate	-6	-5.9	water	0	60% dioxane	[85]
16	Methyl trifluoroacetate	-5.1	-5.3	water	34.8	60% dioxane	[85]
17	Methyl trifluoroacetate	-4.9	-5.2	water	44.6	60% dioxane	[85]

Table 17. SPARC-calculated vs. observed log hydrolysis rate constants for organophosphorus in water in basic media in M<sup>-1</sup>s<sup>-1</sup>

No	Ester	Obs	Calc	Temp	Ref.
1	Methyl-o-isopropylphosphonofluoride	1.35	1.018	20	[86]
2		1.412	1.146	25	[86]
3		1.56	1.271	30	[86]
4		1.627	1.393	35	[86]
5	Phosphonofluoridic acid, methyl-, methyl ester	2.025	2.501	25	[86]
6		2.274	2.722	35	[86]
7	Phosphonofluoridic acid, methyl-, 3,3-dimethylbutyl ester	1.693	1.574	25	[86]
8		1.979	1.807	35	[86]
9	Phosphonofluoridic acid, (1-methylethyl)-, 1-methylethyl ester	0.307	0.731	25	[86]
10		0.525	0.959	35	[86]
11	Phosphonofluoridic acid, methyl-, ethyl ester	1.783	1.84	25	[86]
12		2.049	2.076	35	[86]
13	Phosphonofluoridic acid, methyl-, 2-bromoethyl ester	2.21	1.98	25	[86]
14		2.479	2.21	35	[86]
15	Phosphonofluoridic acid, methyl-, propyl ester	1.732	1.791	25	[86]
16		1.979	2.026	35	[86]
17	Phosphonofluoridic acid, ethyl-, 1-methylethyl ester	0.971	0.949	25	[86]
18		1.225	1.187	35	[86]
19	Diethyl ethylphosphonate	-4.691	-4.59	30	[45]
20		-4.36	-4.29	40	[45]
21		-4.065	-4.01	50	[45]
22		-3.05	-3.5	69.5	[45]
23		-2.941	-3.39	73.9	[45]
24		-2.675	-3.13	84.7	[45]
25		-2.51	-2.97	91.3	[45]
26	Phosphoric acid, diethyl 4-nitrophenyl ester	-1.96	-2.01	25	[87]
27		-1.787	-1.91	30	[87]
28		-1.574	-1.79	37	[87]
29		-1.336	-1.64	45	[87]
30	Phosphoric acid, trimethyl ester	-3.951	-3.64	35	[45]
31		-3.603	-3.37	44.7	[45]
32		-3.162	-2.97	60	[45]
33		-2.952	-2.83	65.5	[45]
34		-2.798	-2.74	69.3	[45]
35		-2.706	-2.65	73	[45]

No	Ester	Obs	Calc	Temp	Ref.
36	Diethyl methylphosphonate	-3.796	-4.31	30	[45]
37		-3.483	-4.01	40	[45]
38		-3.194	-3.72	50	[45]
39		-2.886	-3.44	60	[45]
40		-2.717	-3.18	70	[45]
41		-2.484	-2.92	80	[45]
42		-2.249	-2.68	90	[45]
43	Phosphonic acid, methyl-, dimethyl ester	-2.136	-2.99	49.8	[45]
44		-1.906	-2.71	60	[45]
45		-1.65	-2.46	70	[45]
46		-1.363	-2.21	79.8	[45]
47	Phosphoric acid, ethyl bis(4-nitrophenyl) ester	-1.446	-1.75	25	[45]
48	Phosphoric acid, dimethyl 4-nitrophenyl ester	-1.706	-1.99	15	[88]
49		-1.409	-1.78	25	[88]
50		-1.244	-1.69	30	[88]
51		-1.039	-1.55	37	[88]
52		-0.845	-1.41	45	[88]
53	Phosphoric acid, diethyl 6-methyl-2-(1-methylethyl)-4-pyrimidinyl ester	-1.45	-1.55	10	[89]
54		-1.12	-1.38	20	[89]
55		-0.607	-1.05	40	[89]
56		0.039	-0.75	60	[89]
57	Phosphoric acid, 4-nitrophenyl dipropyl ester	-2.526	-2.08	25	[88]
58		-2.342	-1.99	30	[88]
59		-2.176	-1.86	37	[88]
60		-1.911	-1.72	45	[88]
61	Phosphinic acid, dibutyl-, 4-nitrophenyl ester	-0.119	-0.56	15	[90]
62		0	-0.49	20	[90]
63		0.149	-0.43	25	[90]
64	Diisopropyl methylphosphonate	-4.116	-3.71	80	[45]
65		-3.941	-3.47	90	[45]
66	Phosphonic acid, phenyl-, diethyl ester	-2.651	-2.58	59.8	[45]
67		-2.499	-2.46	65.7	[45]
68		-2.298	-2.29	74.9	[45]
69		-2.201	-2.21	79.4	[45]
70		-2.038	-2.11	84.8	[45]
71		-1.99	-2.03	89.1	[45]

Num	Ester	Obs	Calc	Temp	Ref.
72	Phosphonic acid, propyl-, dipropyl ester	-3.747	-3.15	95	[45]
73	Phosphoric acid, dibutyl 4-nitrophenyl ester	-2.559	-2.11	25	[88]
74		-2.342	-2.02	30	[88]
75		-2.156	-1.89	37	[88]
76		-1.933	-1.75	45	[88]
77	Phosphonic acid, butyl-, diethyl ester	-3.434	-3.34	80.3	[45]
78		-3.233	-3.09	91.2	[45]
79		-3.018	-2.92	99	[45]
80		-2.735	-2.9	100	[45]
81	O,O-Diethyl-O-phenylphosphate	-3.51	-2.96	25	[91]
82	Phosphoric acid, diethyl 4-(methylthio) phenyl ester	-3.306	-2.94	25	[91]
83	Phosphonic acid, (chloromethyl)-, diethyl ester	-2.901	-2.55	20	[90]
84		-2.604	-2.32	30	[90]
85		-2.313	-2.09	40	[90]
86	Bis(1-methylethyl)phosphoric acid 4-nitrophenyl ester	-3.177	-2.27	25	[88]
87		-2.978	-2.18	30	[88]
88		-2.767	-2.06	37	[88]
89		-2.505	-1.92	45	[88]
90	Phosphonic acid, methyl-, 1-methylethyl 4-nitrophenyl ester	-0.714	-1.42	24.9	[86]
91		-0.577	-1.33	29.9	[86]
92		-0.367	-1.2	37	[86]
93		-0.164	-1.06	45	[86]
94	Phosphonic acid, methyl-, ethyl 4-nitrophenyl ester	-2.222	-1.82	0	[45]
95		-1.741	-1.5	15	[45]
96		-1.398	-1.31	25	[45]
97	Phosphoric acid, diethyl 2-nitrophenyl ester	-1.654	-2.48	25	[91]
98	Phosphoric acid, diethyl 3-nitrophenyl ester	-2.195	-2.75	25	[91]
99	Phosphinic acid, diethyl-, ethyl ester	-3	-2.27	70	[92]
100		-2.824	-2.05	80	[92]
101		-2.67	-1.84	90	[92]
102		-2.535	-1.68	98	[92]
103	Phosphoric acid, 4-chlorophenyl diethyl ester	-2.939	-2.9	25	[91]
104	Phosphoric acid, diethyl 4-methoxyphenyl ester	-3.553	-2.98	25	[91]
105	Phosphoric acid, 4-cyanophenyl diethyl ester	-2.196	-2.12	25	[91]
106	Phosphoric acid, bis(2-methylpropyl) 4-nitrophenyl ester	-2.204	-1.98	25	[88]
107		-2.036	-1.88	30	[88]
108		-1.825	-1.76	37	[88]

No	Ester	Obs	Calc	Temp	Ref.
109		-1.591	-1.62	45	[88]
110	Phosphoric acid, bis(1-methylpropyl) 4-nitrophenyl ester	-3.317	-3.27	25	[88]
111		-3.137	-3.19	30	[88]
112		-2.914	-3.07	37	[88]
113		-2.651	-2.94	45	[88]
114	Phosphonic acid, ethyl-, isopropyl p-nitrophenyl ester	-1.432	-1.68	24.9	[86]
115		-1.28	-1.59	29.9	[86]
116		-1.069	-1.47	37	[86]
117		-0.867	-1.34	45	[86]
118	Phosphonic acid, propyl-, isopropyl p-nitrophenyl ester	-1.479	-1.82	24.9	[86]
119		-1.345	-1.74	29.9	[86]
120		-1.155	-1.62	37	[86]
121		-0.954	-1.49	45	[86]
122	Phosphonic acid, isopropyl-, isopropyl p-nitrophenyl ester	-2.654	-1.95	24.9	[86]
123		-2.504	-1.87	29.9	[86]
124		-2.278	-1.75	37	[86]
125		-2.05	-1.63	45	[86]
126	Phosphonic acid, butyl-, isopropyl p-nitrophenyl ester	-1.502	-1.87	24.9	[86]
127		-1.384	-1.79	29.9	[86]
128		-1.19	-1.67	37	[86]
129		-0.957	-1.54	45	[86]
130	Phosphonic acid, isobutyl-, isopropyl p-nitrophenyl ester	-1.706	-1.99	24.9	[86]
131		-1.569	-1.9	29.9	[86]
132		-1.375	-1.79	37	[86]
133		-1.175	-1.66	45	[86]
134	Phosphonic acid, sec-butyl-, isopropyl p-nitrophenyl ester	-2.741	-2.36	24.9	[86]
135		-2.596	-2.27	29.9	[86]
136		-2.377	-2.16	37	[86]
137		-2.147	-2.04	45	[86]
138	Phosphonic acid, pentyl-, isopropyl p-nitrophenyl ester	-1.54	-1.89	24.9	[86]
139		-1.393	-1.81	29.9	[86]
140		-1.198	-1.69	37	[86]
141		-0.979	-1.56	45	[86]
142	Phosphinic acid, dipropyl-, 4-nitrophenyl ester	-0.004	-0.46	15	[86]
143		0.059	-0.39	20	[86]
144		0.192	-0.32	25	[86]
145	Phosphinic acid, diisopropyl-, p-nitrophenyl ester	-0.944	-0.38	25	[86]

No	Ester	Obs	Calc	Temp	Ref.
146		-0.774	-0.32	30	[86]
147		-0.548	-0.24	37	[86]
148		-0.322	-0.15	45	[86]
149	Phosphinic acid, diisobutyl-, p-nitrophenyl ester	-0.452	-0.79	15	[86]
150		-0.329	-0.72	20	[86]
151		-0.206	-0.66	25	[86]
152	Phosphinic acid, dipentyl-, 4-nitrophenyl ester	-0.167	-0.6	15	[86]
153		-0.058	-0.53	20	[86]
154		0.031	-0.46	25	[86]
155	Phosphinic acid, di-sec-butyl-, p-nitrophenyl ester	-1.19	-1.26	25	[86]
156		-1.025	-1.2	30	[86]
157		-0.8	-1.13	37	[86]
158		-0.574	-1.06	45	[86]
159	Phosphonic acid, methyl-, diphenyl ester	-2.475	-2.68	0.1	[45]
160		-1.927	-2.35	15	[45]
161		-1.771	-2.22	21.5	[45]
162	Phosphinic acid, diethyl-, 4-nitrophenyl ester	0.13	-0.18	15	[86]
163		0.189	-0.1	20	[86]
164		0.329	-0.04	25	[86]
165	Phosphinic acid, dimethyl-, 4-nitrophenyl ester	-0.244	0.111	15	[86]
166		-0.087	0.194	20	[86]
167		0.059	0.275	25	[86]
168	Phosphinic acid, methylpropyl-, 4-nitrophenyl ester	-0.548	-0.18	15	[86]
169		-0.394	-0.11	20	[86]
170		-0.26	-0.03	25	[86]
171		-0.106	0.043	30	[86]
172	Phosphinic acid, isopropylmethyl-, p-nitrophenyl ester	-0.714	-0.07	25	[86]
173		-0.577	-0	30	[86]
174		-0.367	0.09	37	[86]
175		-0.164	0.195	45	[86]
176	Phosphinic acid, butylmethyl-, p-nitrophenyl ester	-0.555	-0.23	15	[86]
177		-0.402	-0.16	20	[86]
178		-0.269	-0.08	25	[86]
179		-0.144	-0.01	30	[86]
180	Phosphinic acid, isobutylmethyl-, p-nitrophenyl ester	-0.62	-0.35	15	[86]
181		-0.473	-0.27	20	[86]
182		-0.331	-0.2	25	[86]

No	Ester	Obs	Calc	Temp	Ref.
183		-0.173	-0.13	30	[86]
184	Phosphinic acid, sec-butylmethyl-, p-nitrophenyl ester	-1.037	-0.58	20	[86]
185		-0.901	-0.51	25	[86]
186		-0.753	-0.45	30	[86]
187		-0.571	-0.36	37	[86]
188	Phosphoric acid, diethyl 3-methoxyphenyl ester	-3.206	-2.9	25	[91]
189	Phosphoric acid, diethyl 3-methylphenyl ester	-3.452	-2.98	25	[91]
190	Phosphinic acid, ethylmethyl-, 4-nitrophenyl ester	-0.424	-0.04	15	[86]
191		-0.278	0.038	20	[86]
192		-0.15	0.114	25	[86]
193		-0.031	0.188	30	[86]
194	Phosphinic acid, methylpentyl-, p-nitrophenyl ester	-0.591	-0.25	15	[86]
195		-0.396	-0.17	20	[86]
196		-0.26	-0.1	25	[86]
197		-0.112	-0.03	30	[91]
198	Phosphoric acid, 4-aminophenyl diethyl ester	-3.614	-3.08	25	[91]
199	Phosphoric acid, diethyl 4-ethylphenyl ester	-3.488	-2.93	25	[91]
200	Phosphoric acid, diethyl 4-(1-methylethyl)phenyl ester	-3.473	-2.96	25	[91]
201	Phosphoric acid, diethyl 4-iodophenyl ester	-2.889	-2.9	25	[91]
202	Phosphoric acid, 3-bromophenyl diethyl ester	-2.781	-2.83	25	[91]
203	Phosphoric acid, o-(dimethylamino)phenyl diethyl ester	-3.829	-3.39	25	[91]
204	Phosphoric acid, diethyl o-ethylphenyl ester	-3.717	-3.3	25	[91]
205	Phosphoric acid, diethyl 2-iodophenyl ester	-2.717	-2.92	25	[91]
206	Phosphoric acid, 2-bromophenyl diethyl ester	-2.623	-2.89	25	[91]
207	Phosphoric acid, 2-chlorophenyl diethyl ester	-2.585	-2.83	25	[91]
208	Phosphoric acid, diethyl 2-methoxyphenyl ester	-3.436	-3.13	25	[91]
209	Phosphoric acid, 4-(dimethylamino)phenyl diethyl ester	-3.555	-3.07	25	[91]
210	Phosphoric acid, 4-bromophenyl diethyl ester	-2.899	-2.9	25	[91]
211	Phosphoric acid, diethyl 2-(1-methylethyl)phenyl ester	-3.765	-3.45	25	[91]
212	Phosphoric acid, 4-acetylphenyl diethyl ester	-2.49	-2.9	25	[91]
213	Phosphonic acid, methyl-, mono(4-nitrophenyl) ester, ion(1-)	-4.632	-4.68	30	[93]
214		-4.206	-4.38	39.4	[93]
215		-3.848	-4.05	50	[93]
216		-3.495	-3.76	60	[93]
217	Phosphonic acid, methyl-, monophenyl ester, ion(1-)	-5.745	-5.3	39	[93]
218		-4.9	-4.65	58.8	[93]
219		-4.533	-4.35	68.5	[93]

No	Ester	Obs	Calc	Temp	Ref.
220		-4.206	-4.07	78	[93]
221	Phosphoric acid, 3-chlorophenyl diethyl ester	-2.806	-2.84	25	[91]
222	Phosphoric acid, diphenyl ester, ion(1-)	-5.456	-4.23	75	[93]
223	Phosphonic acid, methyl-, bis(2,2-dimethylpropyl) ester	-4.319	-3.69	88	[45]
224	Benzoic acid, monoanhydride with phosphoric acid, ion(2-)	-2.141	-1.71	37	[94]
225	Benzoic acid, dianhydride with phosphoric acid, ion(1-)	0.404	1.073	37	[94]

Table 18. SPARC-calculated vs. observed log acid hydrolysis rate constants of organophosphorus in water in M<sup>-1</sup>s<sup>-1</sup>

No	Esters	Temp.	Obs.	Calc.	Ref
1	Phosphoric acid, diethyl 1-phenylethyl ester	25	-4.68	-4.66	[44]
2		41.5	-4.05	-4.13	[44]
3		54.7	-3.50	-3.74	[44]
4		70.2	-2.73	-3.32	[44]
5	Phosphoric acid, diethyl 1-(4-methoxyphenyl)ethenyl ester	25	-3.24	-3.24	[44]
6		41.4	-2.46	-2.79	[44]
7		54.4	-2.02	-2.46	[44]
8	Phosphoric acid, diethyl 1-(4-methylphenyl)ethenyl ester	25	-4.03	-4.05	[44]
9		41.5	-3.18	-3.56	[44]
10		54.7	-2.83	-3.19	[44]
11		70.2	-2.26	-2.79	[44]
12	Phosphoric acid, diethyl 1-(4-bromophenyl)ethenyl ester	25	-5.03	-4.36	[44]
13		41.5	-4.30	-3.85	[44]
14		54.2	-3.72	-3.49	[44]
15		54.7	-3.60	-3.47	[44]
16		70.2	-3.21	-3.06	[44]
17	Phosphoric acid, diethyl 1-(4-nitrophenyl)ethenyl ester	69.8	-4.45	-3.81	[44]
18		84.9	-3.80	-3.41	[44]
19		99	-3.19	-3.06	[44]
20	Phosphoric acid, diethyl 1-(3-nitrophenyl)ethenyl ester	69.8	-4.16	-3.56	[44]
21		85	-3.50	-3.16	[44]
22		99	-2.92	-2.83	[44]
23	Phosphonic acid, (1,1-dimethylethyl)-, dimethyl ester	120	-3.95	-2.98	[45]
24	Phosphonic acid, methyl-, bis(2,2-dimethylpropyl) ester	103	-4.33	-3.83	[45]
25		120	-3.66	-3.40	[45]
26	Phosphonic acid, butyl-, bis(1-methylethyl) ester	96	-3.79	-3.81	[45]
27		101	-3.68	-3.68	[45]
28		114.7	-3.07	-3.34	[45]
29	Phosphonic acid, (1,1-dimethylethyl)-, bis(1-methylethyl) ester	115.2	-2.79	-2.28	[45]
30	Phosphonic acid, methyl-, ethyl 4-nitrophenyl ester	110.4	-4.12	-4.56	[45]
31	Phosphonic acid, propyl-, bis(1-methylethyl) ester	96	-3.77	-3.81	[45]
32		101	-3.56	-3.68	[45]
33		107.3	-3.33	-3.52	[45]
34		114	-3.04	-3.36	[45]
35		114.7	-3.06	-3.34	[45]
36	Phosphonic acid, butyl-, diethyl ester	110	-4.58	-3.45	[45]
37		119.5	-4.17	-3.22	[45]
38	Phosphonic acid, phenyl-, diethyl ester	105.2	-4.61	-4.49	[45]
39		110.2	-4.45	-4.35	[45]
40		114.7	-4.18	-4.23	[45]
41		120.3	-3.98	-4.09	[45]
42		122.6	-3.96	-4.03	[45]

43	Diisopropyl methylphosphonate	93.6	-3.49	-4.07	[45]
44		100.6	-3.20	-3.88	[45]
45		109.9	-2.93	-3.64	[45]
46		110	-2.85	-3.64	[45]
47		115	-2.69	-3.52	[45]
48	Phosphonic acid, ethyl-, bis(1-methylethyl) ester	92.5	-3.80	-3.91	[45]
49		101	-3.40	-3.69	[45]
50		105.3	-3.31	-3.58	[45]
51		110.4	-3.11	-3.45	[45]
52		114.7	-2.88	-3.35	[45]
53	Phosphonic acid, methyl-, dimethyl ester	99.8	-4.72	-4.59	[45]
54		104.4	-4.52	-4.47	[45]
55		110	-4.29	-4.32	[45]
56		114.3	-3.94	-4.20	[45]
57		119.6	-3.77	-4.07	[45]
58	Diethyl methylphosphonate	101	-4.75	-4.21	[45]
59		108.8	-4.46	-4.00	[45]
60		109.9	-4.25	-3.97	[45]
61		115.3	-4.21	-3.84	[45]
62		116.9	-4.10	-3.80	[45]
63		119.5	-3.96	-3.73	[45]
64	Diphosphoric acid	39.8	-4.93	-4.94	[46]
65		42.07	-4.81	-4.86	[46]
66		44.79	-4.67	-4.77	[46]
67		49.77	-4.44	-4.61	[46]
68	Triphosphoric acid	39.59	-4.43	-4.36	[46]
69		42.04	-4.29	-4.29	[46]
70		44.71	-4.20	-4.21	[46]
71		48.95	-3.98	-4.08	[46]
72	Phosphoric acid, monophenyl ester	100	-5.42	-5.95	[42]
73	Phosphoric acid, mono(4-methylphenyl) ester	100	-5.22	-5.15	[42]
74	Phosphoric acid, diethyl 4-nitrophenyl ester	70	-3.98	-4.58	[95]
75	Phosphoric acid, diethyl 4-(methylsulfonyl)phenyl ester	70	-4.01	-3.48	[95]
76	1,2,3-Propanetriol, 1-(dihydrogen phosphate)	72.3	-6.81	-6.41	[96]
77		85.5	-6.28	-5.96	[96]
78		100	-5.70	-5.50	[96]
79	1,2-Propanediol, 1-(dihydrogen phosphate)	72	-6.82	-6.75	[96]
80		87.7	-6.11	-6.21	[96]
81		100	-5.37	-5.81	[96]
82	1,2,3-propanetriol, 2-(dihydrogen phosphate)	100	-5.70	-4.90	[96]
83	D-Glucose, 2-(dihydrogen phosphate)	100	-3.38	-3.95	[97]

Table 19. SPARC-calculated vs. observed log neutral hydrolysis rate constants of organophosphorus in water in M<sup>-1</sup>s<sup>-1</sup>

No	Esters	Temp.	Obs.	Calc.	Ref
1	Triethyl phosphate	79.6	0.63	-0.15	[98]
2		101	1.45	0.34	[98]
3	Phosphoramidic acid, (1-methylethyl)-, ethyl 3-methyl-4-(methylthio)phenyl ester	5	-3.96	-2.66	[99]
4		22	-3.33	-2.03	[99]
5		32	-2.10	-1.68	[99]
6		50	-1.66	-1.10	[99]
7	Serine dihydrogen phosphate (ester)	80	-1.46	-1.12	[100]
8		90	-0.97	-0.90	[100]
9		100	-0.37	-0.70	[100]
10	Benzoic acid, 4-methoxy-, monoanhydride with phosphoric acid	39	2.68	1.73	[101]
11		39	-1.20	-0.15	[101]
12	Benzoic acid, 3,5-dinitro-, anhydride with H <sub>3</sub> PO <sub>4</sub>	39	-0.65	-2.63	[101]
13	Phosphoric acid, mono(4-methylphenyl) ester	39	2.84	1.54	[101]
14		39	-1.12	-0.34	[101]
15		73	-0.82	0.38	[42]
16		80	-0.49	0.52	[42]
17		89	0.01	0.68	[42]
18		100	0.50	0.88	[42]
19	Phosphoric acid, monophenyl ester	39	2.91	0.83	[101]
20		39	-1.09	-1.05	[101]
21		73	-0.71	-0.26	[42]
22		75.6	-0.49	-0.20	[102]
23		80	-0.39	-0.11	[42]
24		89	0.09	0.07	[42]
25		100	0.58	0.28	[42]
26	Phosphoric acid, trimethyl ester	44.7	-0.27	-0.61	[37]
27		65.5	0.72	-0.12	[37]
28		73	1.04	0.04	[37]
29		80	1.34	0.19	[37]
30		100.1	2.09	0.59	[37]
31	Phosphoric acid, mono (4-nitrophenyl) ester	39	3.87	2.42	[101]
32		25	-2.94	0.25	[103]
33		39	-0.97	0.54	[101]
34		73	-0.20	1.17	[103]
35	Phosphoric acid, mono(2-nitrophenyl) ester	25	-3.30	-1.38	[103]
36		73	-0.43	-0.14	[103]
37		100	2.53	0.44	[103]
38	Phosphoric acid, mono (3-nitrophenyl) ester	25	-2.80	-2.24	[103]
39		39	-0.96	-1.84	[101]
40		73	-0.50	-0.97	[103]

41		100	0.76	-0.38	[103]
42	Phenol, 2-(1,1-dimethylethyl)-, dihydrogen phosphate	100	-0.30	-1.13	[103]
43	Phenol, 2,6-dimethyl-, dihydrogen phosphate	73	-1.06	-0.56	[103]
44		100	0.31	0.10	[103]
45	Phenol, 2,6-bis(1,1-dimethylethyl)-4-methyl-, dihydrogen phosphate	100	-0.38	0.97	[103]
46	Phosphoric acid, mono (4-chlorophenyl) ester	39	3.24	0.73	[101]
47		39	-1.13	-1.14	[101]
48		100	0.58	0.20	[103]
49	Phenol, 4-(1,1-dimethylethyl)-, dihydrogen phosphate	100	0.35	0.68	[103]
50	Phosphoric acid, mono (2-chlorophenyl) ester	73	-0.78	-1.01	[103]
51		100	0.46	-0.38	[103]
52	a-D-Glucopyranose, 1-(dihydrogen phosphate)	82	0.94	-0.22	[104]
53		100.1	1.92	0.14	[104]
54		82	-1.21	-1.84	[104]
55		100.1	-0.29	-1.40	[104]
56	Phosphoric acid, monomethyl ester	80	-1.97	-0.15	[105]
57		89	-1.50	0.01	[105]
58		100.1	-0.92	0.20	[105]
59		109.7	-0.43	-0.62	[105]
60		117.2	-0.09	0.47	[105]
61	2-(Phosphonoxy) benzoic acid	25	2.36	2.23	[43]
62		37.2	0.88	-0.16	[106]
63		42	1.13	-0.04	[106]
64		47.4	1.48	0.09	[106]
65	Phosphoric acid, diethyl 6-methyl-2-(1-methylethyl)-4-pyrimidinyl ester	20	0.84	1.02	[32]
66	Diisopropyl methylphosphonate	70	-0.17	1.37	[47]
67		81	0.38	1.58	[47]
68		90	0.79	1.74	[47]
69		98	1.12	1.88	[47]
70	Phosphoric acid, monoethyl ester	100	-2.12	-0.55	[107]
71	Phosphoric acid, diethyl 4-nitrophenyl ester	20	0.15	0.43	[32]
72		70	1.03	1.61	[95]
73	Phosphoric acid, diethyl 4-(methylsulfonyl)phenyl ester	70	1.10	1.30	[95]
74	Dimethyl-2,2-dichlorovinyl phosphate	70	-0.20	-0.36	[95]
75	Trichlorfon	70	3.14	2.78	[95]
76	Phosphoric acid, dimethyl 4-nitrophenyl ester	24	0.74	0.15	[108]
77		32	0.92	0.35	[108]
78		40	1.90	0.55	[108]
79	Phosphoric acid, mono(1-methylethyl) ester	72.2	-2.39	-1.63	[109]
80		84.6	-1.58	-1.34	[109]
81		100	-0.77	-1.00	[109]
82	1,2-Propanediol, 1-(dihydrogen phosphate)	100	-0.66	-0.62	[96]
83	Phenol, 2,4-dinitro-, dihydrogen phosphate (ester)	25	1.92	1.72	[103]
84		39	0.70	-1.08	[110]
85	1-Naphthalenol, dihydrogen phosphate	80	-1.01	-0.24	[106]

86	2-Naphthalenol, dihydrogen phosphate	80.6	-0.57	0.91	[106]
87	Benzoic acid, 3-(phosphonoxy)-	80	0.33	-0.14	[106]
88	Benzoic acid, 4-(phosphonoxy)-	80	1.09	1.38	[106]
89	1-Naphthoic acid, 8-hydroxy-, phosphate	80	-2.39	-0.42	[106]

## 9. CONCLUSION

SPARC's chemical reactivity models, which are used to calculate both ionization pK<sub>a</sub> (in water, non-aqueous liquid and gases) and electron affinity, have been extended to calculate hydrolysis rate constants for carboxylic acid and organophosphate esters. These reactivity models have been tested to the maximum extent possible in a single and in a mixed solvent (organophosphorus only in water) as a function of temperature using all the reliable data found in the literature.

The strength of the SPARC calculator is its ability to estimate the hydrolysis rate constants (as well many other properties) of interest for almost any molecular structure within an acceptable error, especially for molecules that are difficult to measure. However, the real test of SPARC does not lie in testing the predictive capability for hydrolysis rate constants, pK<sub>a</sub>'s, or activity coefficient, but is determined by its extrapolability to other types of chemistry. Further extension of the SPARC chemical reactivity models will be under development soon to calculate hydrolysis rate constants for other classes of organic compounds as a function of solvent and temperature.

Finally, SPARC is an important tool in designing chemicals for specific properties, for use in preliminary evaluation of the risks associated with chemical release into the environment, and in chemical fate-modeling applications in the absence of experimentally measured values. The development of the SPARC chemical hydrolysis models (as well as its other physical and chemical properties estimation) directly address the EPA Office of Research and Development (ORD) long term research agenda for the agency's Chemical Toxicology Initiative that emphasizes that EPA will rely heavily on predictive modeling to carry out the increasingly

complex array of exposure and risk assessments necessary to develop scientifically defensible regulations.

**SPARC is online and can be used at <http://ibmlc2.chem.uga.edu/sparc>**

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## APPENDIX

Figure 6. Sample calculations of log hydrolysis rate constant in acid catalyzed media for p-nitrophenyl acetate in water at 25°C. Only the reaction center parameters are trained on hydrolysis rate constant (at the top). The substituent, molecular conductor parameters and distances (r's) between the various components are the same as of ionization  $pK_a$

### Carboxylic Acid Ester Hydrolysis Rate Constant Reaction Center Characteristic Parameters

Reaction Center	$\rho_{ele}$	$\rho^a_{res}$	$\rho^b_{res}$	$\chi_c$	$A_{MF}$	$A_{3.36}$	Ref <sup>1</sup>	Ref <sup>2</sup>	$\rho_{FS}$	$\rho_{Steric}$	$\rho_\alpha$	$\rho_\beta$	$\sigma_\pi^c$	$\sigma_\pi^d$
Acid Hydrolysis	-0.87	-0.4	1.11	1.80	-0.67	3.36	3.886	-3070.8	$-3.0 \times 10^5$	-310935	-1821	944.6	0.008	0.1
Base Hydrolysis			3.90	2.55	-0.67	3.36	-3.522	-1443.4	$* 10^7$	-328642	-4205	2119	0.008	0.1
GBase Hydrolysis	4.5 5.2 -0.8	2.59 -0.6	2.65 -0.67		3.36	-5.249		-3479.7	$0.18 * 10^7$	-114969	-373	5598	0.008	0.1

$$\log k_c = 3.36 + \log (298.15) + 3.886 + (-3070.8 / 298.15) = -0.59$$

$$\delta_{IPd} \log k_c = \rho_{ele} \left[ NB (\chi_c - \chi_s) + \frac{F_s \cos \theta_{cs}}{r_{cs}^3} + MF_s A_{MF} \sum_k \frac{q_{ik}}{r_{kc}^2} + P_{jc} \sigma_\pi \right] + \rho_{res} \Delta q_c$$

$$\delta_{IP} \log k_c = -0.87 \left[ 0.65(2.3 - 1.8) + \frac{7.746 \times 1}{(1.3 + 2 + 1)^3} + 2.515 (-0.67) \left( \frac{2 \times 0.078}{(1.73 + 1.3)^2} + \frac{0.078}{1.3^2} - \frac{3 \times 0.078}{(1.3 + 2)^2} \right) + 1 \times 0.008 \right] + 0.28 \times 1.11 = -0.07$$

$r_{jc}$      $r$      $r_{14}$  (p-benzene)     $r_{is}$      $r_{13}$  (m-benzene)

$$\delta_{EP} \log k_c = \frac{\rho_{FS}}{T_k D_e} + \frac{\rho_{steric} (V_s + V_{ex} - V_{thresh})}{T_k D_e} + \frac{\rho_A \alpha}{T_k} + \frac{\rho_B \beta}{T_k}$$

$damp -$   
 $T_k + \frac{1}{D_e}$

$$\delta_{EP} \log k_c = \frac{-3 \times 10^5}{298.15 \times 78.54} + \frac{-310935 \times 0.0687}{298.15 \times 78.54} + \frac{-1821 \times 0.384}{298.15} + \frac{944.6 \times 0.382}{298.15} = -3.333$$

$$\text{Log } k_{\text{Hydrolysis}} = -0.59 + (-0.075) + (-3.33) = -3.995 \quad (\text{Observed is } 3.9)$$

a: for carbonyl of C, b: for the oxygen of C, c: for aromatic R- $\pi$  unit, d: for ethylenic R- $\pi$  unit.