

TRANSITION STATE STRUCTURE FOR THE INTRAMOLECULAR CATALYSIS
BY CARBOXYLATE OF PHENYL HYDROGEN MALONATE HYDROLYSIS ¹

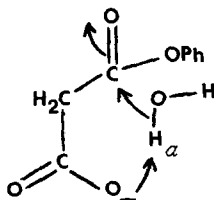
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Abstract: The intramolecular catalysis by carboxylate of phenyl hydrogen malonate hydrolysis has been shown to involve a single water molecule in a 6-membered ring transition state.

The question of the structural requirements for intramolecular proton transfers has received considerable attention. Gandour has presented a hypothesis which predicts when intramolecular proton transfer will most likely occur.² He suggested that "the highest probability for intramolecular proton transfer will occur when the cyclic transition state formed can accommodate a linear arrangement of donor-proton-acceptor of appropriate length. This most easily occurs when the ring size is eight." We wish to report that this prediction does not hold for the intramolecular catalysis by carboxylate ion of phenyl hydrogen malonate hydrolysis. This is in apparent contrast to the many examples cited by Gandour.

The hydrolysis of aryl hydrogen malonates has been previously investigated by Kirby and Lloyd as part of a study to probe the dependence on structure of the efficiency of intramolecular catalysis.³ Phenyl hydrogen malonate was found to exhibit a pH-independent reaction between pH 4.5 and 7.0. Reaction in this region was attributed to intramolecular general base catalysis of the attack of water by the carboxylate ion as in 1.³ The negative entropy of activation,



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Hammett rho value, and solvent deuterium isotope effect appeared consistent with the proposed transition state. However, the available data could not exclude a transition state involving several water molecules. We note that the involvement of two water molecules would give a cyclic

eight-membered transition state.

We have conducted a proton inventory investigation of the hydrolysis of phenyl hydrogen malonate anion at pH 4.61, or the equivalent point on the pH(D)_n rate profile, using a 1:1 acetic acid acetate buffer system. The release of phenol was monitored at 270 nm using the initial rate method. The reaction was found to be independent of the buffer concentration between 0.02 and 0.2M acetate. Our rate constant in pure protiated solvent of $8.19 \times 10^{-4} \text{ m}^{-1}$ compares favorably with the value of $8.33 \times 10^{-4} \text{ m}^{-1}$ calculated for pH 4.61 using the literature values of Kirby and Loyd.³ This comparison is based on 97% dissociation of the acid at pH 4.61 (lit.³ $\text{p}K_a=3.15$). No correction has been made in our data treatment for the small amount of undissociated acid.

A plot of the atom fraction of deuterium in the solvent system versus the rate constant, k_n , is included as Figure 1 (data in Table I). Such a plot is known as a proton inventory. The theory of the technique has been discussed many times.⁴ For the present discussion it is only necessary to note that a linear dependence of k_n on n is, under most circumstances⁵, indicative of a solvent deuterium isotope effect arising from a *single* transition state proton. Our data indicate that the proton H_α is solely responsible for the observed solvent deuterium isotope effect of $k_{\text{H}_2\text{O}/\text{D}_2\text{O}}=2.30$ (lit.³ 2.28). The linearity of a proton inventory can also be expressed in terms of the γ -value of Albery.⁶ He has shown that γ approaches unity as the proton inventory becomes linear and that γ approaches zero as the number of protons contributing to the solvent deuterium isotope effect becomes large. The calculated γ -value of 1.1 in the present study is clearly consistent with a linear inventory.

We have shown that the solvent deuterium isotope effect observed results from the transfer of a *single* proton H_α from water to carboxylate ion in an intramolecular general base catalysis mechanism as in 1. Although a linear arrangement of donor-proton-acceptor is not readily accommodated in this cyclic six-membered ring transition state the inventory is clearly not consistent with the involvement of more than one water molecule in proton transfer in the transition state. However, Gandour has pointed out that the strain imposed by the linear transfer might be better accommodated by a flexible alkyl backbone but should not be accommodated in rigid aromatic cases.² Indeed, proton inventories of the hydrolysis of *o*-dichloroacetylsalicylic acid anion⁷ and 3,5-dinitroacetylsalicylic acid anion⁸ serve as examples of the latter.

In summary, the original transition state 1 proposed by Kirby and Loyd is the correct one for phenyl hydrogen malonate anion hydrolysis.

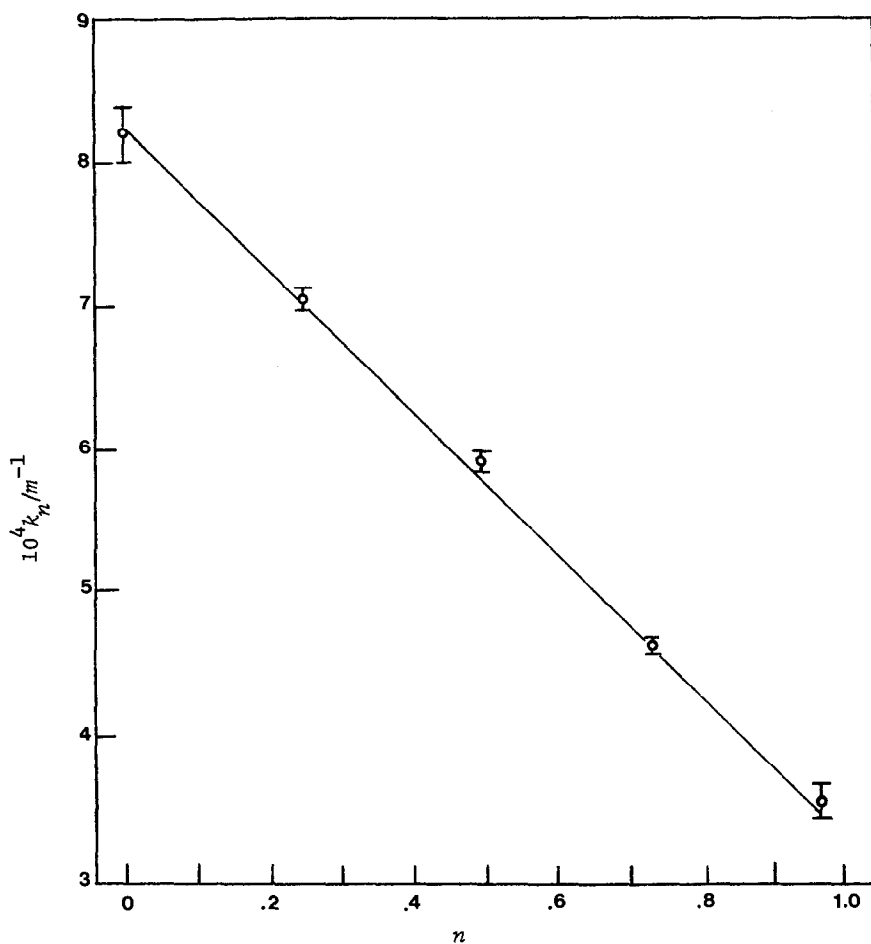


Figure 1. Plot of k_n versus the atom fraction of deuterium n for the hydrolysis of phenyl hydrogen malonate anion at pH 4.61. Data are from Table I. The solid line is the linear least squares line and obeys the equation $10^4 k_n = 8.22(1-n + 0.416n)$ which is of the general form $k_n = k_o(1-n + n\phi^*)$, the equation for a one-proton mechanism.

Table I. First Order Rate Constants for the Hydrolysis of Phenyl Hydrogen Malonate at pH 4.61, or the Equivalent Point on the $\text{pH}(D)_n$ Rate Profile, in $\text{HOAc}(\text{DOAc})/\text{OAc}^-$ Buffers at $40.0 \pm 0.1^\circ\text{C}$.^a

Atom fraction of deuterium (n)	No. of runs	$10^4 k_n / \text{m}^{-1}$
0.00	9	8.19 ± 0.20^b
0.248	6	7.05 ± 0.07
0.495 ^c	7	5.94 ± 0.07
0.730	4	4.64 ± 0.06
0.973 ^c	5	3.56 ± 0.12

^aIonic strength maintained at 1.0M with KCl. ^bError limits are standard deviations. ^cAtom fraction of deuterium in these buffer solutions was determined by Mr. Josef Nemeth, Urbana, Illinois 61801.

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