Structural Effect on the Base-Catalyzed Hydrolysis of (E) Methyl 3-Carboxy-4-Aryl-3-Butenoate Hemiesters, and the Isomeric (E) 3-Methoxycarbonyl-4-(2-Naphthyl)-3-Butenoic Acid

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Abstract: The structural effect on the base-catalyzed hydrolysis of (E) methyl 3-carboxy-4-phenyl-3-butenoate (1), (E) methyl 3-carboxy-4-(1-naphthyl)-3-butenoate (2), (E) methyl 3-carboxy-4-(2-naphthyl)-3-butenoate (3), and (E) 3-methoxycarbonyl-4-(2-naphthyl)-3-butenoic acid (4), at different temperatures (35-50°C) in 50% aqueous dioxane (v/v), show that the rate of reaction follows the overall second order kinetics, first order with respect to each of the hemiester and base. It decreases in the order: (1) > (2) > (3) > (4). Ratios between the values of k_2 (k_1/C_w), and also between k_3 (k_1/C_w^2) in different mixtures are less than 1, which means that the reaction is apparently independent of C_w. The activation parameters $E^{\#}$, $\Delta H^{\#}$, $\Delta S^{\#}$, $\Delta G^{\#}$, and Arrhenius frequency factor (A), confirmed the structural effect on their rates of hydrolysis. [Journal of American Science 2010;6(8):472-475]. (ISSN: 1545-1003).

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1. Introduction

Although extensive work on the kinetics of esters hydrolysis has been investigated, hydrolysis of unsaturated esters has not been much explored. Further investigations of the hydrolytic cleavage of some esters and comparison of the results with those for their isomers may provide additional insight into mechanisms which can serve as models for biological systems [1] and enzymatic processes where they are helpful in elucidating the effects of structural variation on the character of intramolecular catalysis [2]. However, Jones and Watkinson [3] found that in the hydrolysis of 28 nuclear substituted ethyl cinnamate derivatives as the ethoxy carbonyl group remains conjugated with the ring, the polar effects of nuclear substituents are qualitatively similar to those operating in the hydrolysis of benzoates.

This investigation is planned to study the structural effect of hemiesters, (E) methyl 3-carboxy-4-phenyl-3-butenoate (1), (E) methyl 3-carboxy-4-(1-naphthyl)-3-butenoate (2), and (E) methyl 3-carboxy-4-(2-naphthyl)-3-butenoate (3) on their rates of hydrolysis. Also to compare the hydrolysis of esters which contain an olefinic linkage either conjugated with the carboxyl group (hemiester 3), or with the carboxylate; (E) 3-methoxycarbonyl-4-(2-naphthyl)-3-butenoic acid (4), and extended its conjugation with the naphthyl group. The comparison between the results of hydrolysis of unsaturated and isomeric hemiesters may provide additional insight into mechanisms which can serve as models for biological systems and enzymatic processes.

2. Experimental:

The hemiesters, (E) methyl 3-carboxy-4-phenyl-3-butenoate (1) [4] ; m.p. 99°C, (E) methyl 3-carboxy-4-(1-naphthyl)-3-butenoate (2); 141°C, (E) methyl 3-carboxy-4-(2-naphthyl)-3-butenoate (3) [5]; m.p. 125°C, and its isomeric (E) 3-methoxycarbonyl-4-(2-naphthyl)-3-butenoic acid (4) [5]; m.p. 136°C, were prepared and their structures confirmed.

Kinetic Measurements

The kinetic procedure involved the hydrolysis of 0.015M hemiester with 0.150M NaOH in 50% purified dioxane [6] and doubly distilled CO_2-free water (v/v), in order to assure the reaction to become pseudo-first order. The reaction was followed by a titremetric procedure at different time intervals [7] at 35-50°C, using Diphenol Purple as an indicator until a constant reading was obtained which was always concordant with that theoretically calculated. The structure of the produced dicarboxylic acid after complete hydrolysis was extracted was found to be identical with that given in the literature. The thermostatic bath was used where the temperature could be adjusted to and controlled within $\pm$ 0.02°C. The rate constants (k_1) were obtained graphically by using the integrated form of the first order rate equation, and found to be reproducible within $\pm$ 0.01. However the concordance of the

authentically prepared dicarboxylic acids by the complete hydrolysis of hemiesters (1-4) in 50% aqueous dioxane under reflux for 4 hours, assured the proposed mechanism of the reaction.

3. Results and Discussion:

The specific rates of the base-catalyzed hydrolysis of hemiesters (1-4) follow the overall second order kinetics equation, first order with respect to each of the hemiester and the base, and takes place by $B_{Ac}2$ mechanism. A carbonyl addition mechanism involving a tetrahedral intermediate is proposed. In this mechanism, the positively charged carbonyl carbon of the ester group is supposed to be attacked by the hydroxide ion where an anchimeric assistance takes place by the neighboring carboxylate group to form transition state (I), in the rate determining step, which is less polar than one or two of the reactants (charge distribution).

Activation Parameters

The specific rate constants (k_1) of the base-catalyzed hydrolysis of hemiesters (1-4) at temperatures 35-50°C allow the calculations of the activation parameters $E^{\#}$, $\Delta H^{\#}$, $\Delta S^{\#}$, $\Delta G^{\#}$, and also the Arrhenius frequency factor (A). The results obtained are represented in Table 1.

Table 1: **Rate constants and activation parameters for the hydrolysis of the hemiesters (1-4) in 50% aqueous dioxane**

Hemiester	Temp. K	10^3 x k_2 l mole^{-1} sec^{-1}	-log k_2	$E^{\#}$ K cal mole^{-1}	$\Delta H^{\#}$ K cal mole^{-1}	$-\Delta S^{\#}$ cal deg^{-1} mole^{-1}	$\Delta G^{\#}$ K cal mole^{-1}	Log A
1	308	2.9854	3.4750	13.357	12.721	29.239	22.019	6.909
	313	4.3501	3.6385					
	318	6.1404	3.7882					
	323	8.1884	3.9132					
2	308	1.8408	3.2650	14.279	13.653	27.342	22.211	7.314
	313	2.5586	3.4080					
	318	3.4514	3.5380					
	323	4.3152	3.6350					
3	308	1.5667	3.1950	14.509	13.873	26.792	22.418	7.441
	313	2.3878	3.3780					
	318	3.4119	3.5330					
	323	4.8641	3.687					
4	308	1.4962	3.1750	14.739	14.103	26.147	22.932	7.579
	313	2.3015	3.3620					
	318	3.1281	3. 5160					
	323	4.7424	3.6760					

The magnitude of the frequency factor and the large negative entropies of activation substantiate the bimolecular mechanism in which the rate-determining step involves the formation of the anhydride as a cyclic intermediate [7, 8]. The values of $\Delta H^{\#}$, $\Delta S^{\#}$, for the hemiesters (1-4) change as the structures are changed, and the compensation effect between $\Delta H^{\#}$ and $T\Delta S^{\#}$ plays an important role in keeping $\Delta G^{\#}$ more or less constant. This is substantiated by the linear relationship between them with a slope equals to unity.

The lowest entropy of activation of hemiester (1) more than (2), (3), or (4), indicates the greatest solvation of the activated complex produced during its hydrolysis than the other hemiesters.

Structure and Reactivity

The present work aims to describe the relationship between structure of the hemiester and its reactivity towards base-catalyzed hydrolysis in 50% aqueous dioxane at different temperatures. It includes the effect of aromatic ring size of phenyl versus naphthyl (hemiesters 1-3), location of the hemiester moiety on the naphtyl ring (hemiesters 2 and 3), and the conjugation of the olefinic double bond with carboxyl versus carboxylate group (hemiesters 3 and 4). The results obtained show that reactivity falls in the order: 1> 2> 3> 4.

The higer reactivity of phenyl hemiester (1) more than (2) or (3) can be ascribed to the less conjugation exerted by the carbonyl group of the carboxylate ion with the phenyl ring compareable to that in (2) or (3), where the conjugation takes place with the naphthyl group. Such a conjugation in (1) leads to a more susceptibility of the carboxylate oxygen atom towards intramolecular nucleophilic attack on the carbonyl carbon of the ester group to form the anhydride as a cyclic intermediate. (Scheme1).

Transition State I
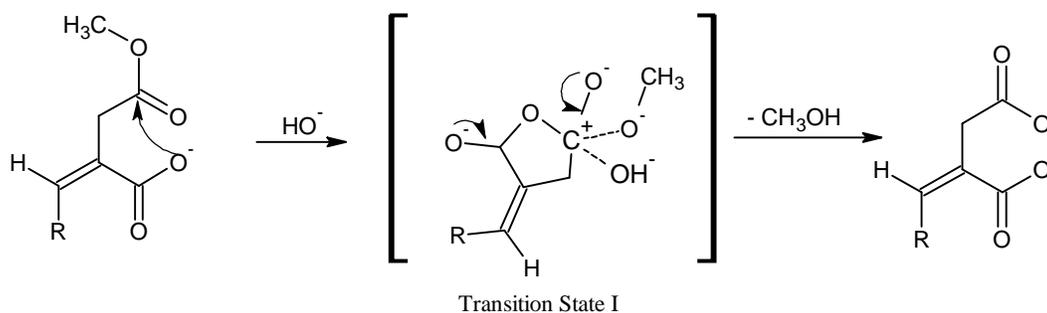
Hemiester	R
1	Phenyl
2	1-Naphthyl
3	2-Naphthyl

Scheme 1

Transition State II
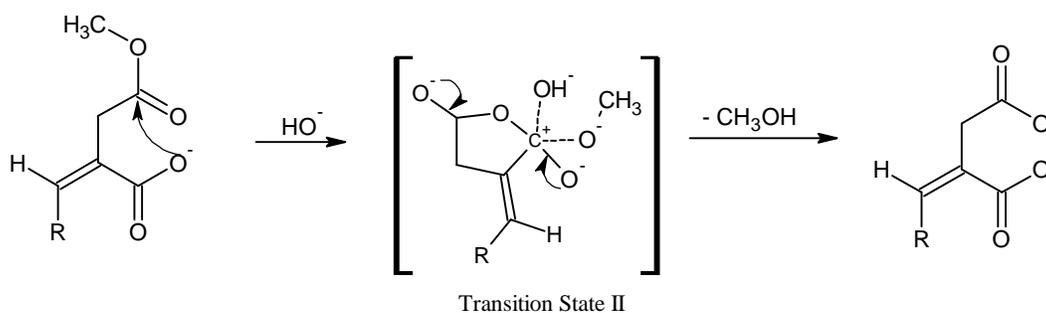
Hemiester	R
4	2-Naphthyl

Scheme 2

The higher rate of hydrolysis of isomeric hemiester (2) than (3) can be attributed to the higher reactivity of position 1 rather than position 2 in the naphthyl group. The reactivity for position 1 over 2 can be rationalized in terms of the stability of the intermediate resonating structures where for the position 1, seven resonance structures are produced, of which four preserve the aromatic ring, comparable to position 2, where the intermediate has only six resonance structures, and only two of them are aromatic. Moreover, a Dreiding model for both intermediates show that no steric hinderence exists, i.e., the electronic factor outweighs the steric factor.

The higher reactivity of hemiester (3) than (4) towards base catalysed hydrolysis can be explained on the basis of hemiester structure where in hemieser (4) the conjugation of carbomethoxy group with the olefinic double bond extended to the naphthyl group decreases the susceptibility of the carbonyl carbon in the ester group to be attcked by the carboxylat anion.

Effect of the Dielectric Constant of the Medium

The rate of base catalyzed hydrolysis of hemiester (3) was followed up, at $40^{\circ}C$ using aqueous purified dioxane (40, 50, and 60% v/v), in order to study the effect of the dielectric constant (D)[9] of the medium on the rate of hydrolysis of the

hemiester. The results obtained show that the rate follows the overall second order kinetics; first order in both of the hemiester and hydroxide ion and the rate constants decrease with the increase of the dielectric constant (D) of the medium. However, to study the role of water in the base catalyzed hydrolysis, the mole fraction of water was calculated in different dioxane-water mixtures and the values of k_1/C_w, and k_1/C_w^2, were calculated to give the rate constants k_2 and k_3, respictevly. Ratios between the values of k_2 and also between k_3 in different mixtures were found to be less than 1, which means that the reaction is apparently independent of C_w. The results obtained are given in Tables 2 and 3.

Table 2: Relation between dielectric constant of the medium and mole fractions of water on the rate of hydrolysis of hemiester (3) at 40°C

Dioxane-Water Mixture (v/v)	D 40°C	10^3 x k_1 sec^{-1}	10^4 x k_2 l mole^{-1} sec^{-1}	10^5 x k_3 l^2 mole^{-2} sec^{-1}
60:40	35.39	0.614	0.279	0.126
50:50	37.41	0.384	0.139	0.051
40:60	39.45	0.192	0.058	0.018

Table 3: Relation mole fractions of water in different dioxane-water mixtures (v/v) on the rate of hydrolysis of hemiester (3) at 40°C

Ratio	Value	Ratio	Value	Ratio	Value
k_1 (50:50)/ k_1 (60:40)	0.625	k_2 (50:50)/ k_2 (60:40)	0.500	k_3 (50:50)/ k_3(60:40)	0.406
k_1 (40:60)/ k_1 (50:50)	0.500	k_2 (40:60)/ k_2 (50:50)	0.413	k_3 (40:60)/ k_3 (50:50)	0.347
k_1 (40:60)/ k_1 (60:40)	0.313	k_2 (40:60)/ k_2 (60:40)	0.208	k_3 (40:60)/ k_3 (60:40)	0.139

4. Conclusion

- The rates of base-catalyzed hydrolysis of hemiesters (1-4), show that it follows the overall second order kinetics, first order with respect to both hemiester and base. The order of the reactivity which falls in the order 1>2>3>4 indicating that the electronic factor outweighs the steric factor.

- The highest rate of (1) is attributed to the less conjugation exerted by the carbonyl group of the carboxylate ion with the phenyl ring.

- The higher rate of hydrolysis of isomeric hemiester (2) than (3) is attributed to the higher reactivity of position 1 rather than position 2 in the naphthyl group. Dreiding models for both intermediates show that no steric hinderence exists.

- The lowest rate of base-catalyzes hydrolysis of hemieser (4) is ascribed to the conjugation of carbomethoxy group with the olefinic double bond and extended to the naphthyl group.

- The calculated values of different ratios between k_2 and between k_3 in different dioxane-water mixtures which found to be less than 1, indicae that the reaction is apparently independent of C_w.

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