A Thesis

Entitled

STUDIES ON THE RATE OF HYDROLYSIS OF SOME UNSATURATED HALF-ESTERS

PRESENTED By :

Mervat Hakim Abdou Hassan
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University College for Girls
AIN SHAMS UNIVERSITY
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بسم الله الرحمن الرحيم

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The candidate passed successfully the examination in the following courses:

1. Kinetics..
2. Spectroscopy.
3. Photochemistry.
4. Organometallic Compounds.
5. Quantum Chemistry.
6. Thermodynamics.
7. Microanalysis.

Prof. Dr. ESSAM M. EZZO
Head of Department of Chemistry.

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Thesis Advisors	Thesis Approved
Dr. Boshra M. Awad	Boshra M. Awad
Dr. Nadia R. Guirguis	N. Guirguis
Dr. Halima A. Hefny	Halima A. Hefny

Prof. Dr. ESSAM M. EZZO
Head of Chemistry Department.

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SUMMARY

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The rates of hydrolysis of the isomeric hemiesters (E)-4-methoxycarbonyl-5-(3,4-dimethoxyphenyl)-pent-4-enoic acid (1c), (E)-4-methoxycarbonyl-5-(3,4-methylenedioxyphenyl)-pent-4-enoic acid (1d), methyl (E)-4-carboxy-5-phenyl-pent-4-enoate (2a), methyl (E)-4-carboxy-5-(4-methoxyphenyl)-pent-4-enoate (2b), methyl (E)-4-carboxy-5-(3,4-dimethoxyphenyl)-pent-4-enoate (2c) and methyl (E)-4-carboxy-5-(3,4-methylenedioxyphenyl)-pent-4-enoate (2d) were studied in alkaline medium at temperatures 10-35°C in different acetone-water and dioxane-water mixtures (v/v).

Application of the differential method shows that the rate follows the second-order kinetic equation overall, first-order with respect to both the hemiester and the hydroxide ion, and the reaction proceeds by $B_{Ac}2$ mechanism, with an intramolecular general base-catalysis.

The increase in the rate of hydrolysis by increasing the dielectric constant of the medium and the linear plots between log k_1 and $\frac{1}{D}$ with negative slope for the two aquo-organic mixtures indicate that the reaction takes place between ion-dipolar molecule and the activated complex is preferentially solvated and less polar than one or two of the reactants.

The increase in the rate of hydrolysis of hemiesters with the increase of water content of the medium indicates

that water must play an important role in the rate of hydrolysis.

The dependence of the reaction rate on water concentration of the mixed solvent is represented by plotting of log k_1 against several powers of $[H_2O]$. The best linear plots with definite intercepts are obtained with $[H_2O]^2$, indicating that the reaction proceeds simultaneously along two mechanistic paths with different rate constants, i.e., the overall rate constant of hydrolysis of the hemiesters splits into two paths:

$$k_1 = k_1' + k_2[H_2O]^2 = k_1' + k_2'$$

k_1' represents the rate constant of the water independent "true second order bimolecular mechanism" in which if water is involved, it should be either in a step prior to or after the rate-determining step and k_2' represents the rate constant of the water dependent mechanism, i.e., apparent second-order termolecular mechanism in which two water molecules are involved in the rate-determining step or alternatively "apparent second-order termolecular process" in which a water molecule participates in the rate-determining step. The low values of the frequency factor, log A, calculated from the Arrhenius equation and its independency on temperature indicate that the second term is preferable for k_2'. The results obtained show that the "true second-order bimolecular mechanism" becomes less effective by increasing the dielectric constant of the medium.

The role of water in the reaction is substantiated by the linear plots of log k_1 against log $[H_2O]$ with slope equals to 2. This indicates that two water molecules participate in the rate-determining step. It seems likely that one molecule of water acts as a general base catalyst in facilitating nucleophilic attack by the other.

The large negative values of entropy of activation $\Delta S^{\neq}$ indicate the formation of a more organised transition state with less degrees of freedom in the rate-determining step. This can be arrived at by the formation of the anhydride as a cyclic intermediate. Thus a mechanism is proposed in which an anchimeric assistance by the neighbouring group, i.e., an intramolecular nucleophilic catalysis by the carboxylate ion, takes place to form such anhydride as a cyclic intermediate in the rate-determining step.

The increase in the rate of hydrolysis of hemiesters by increasing their concentration is attributed to the increase in the ionisation of the hemiester where the carboxylate anion being a stronger nucleophile than the carboxyl group. The formation of the anhydrides and not their hydrolysis to the acids is the rate-determining step, since their rates of hydrolysis were found to be very fast with respect to the corresponding hemiesters.

The linear plots between $\Delta H^{\neq}$ and $T\Delta S^{\neq}$ with slopes equal to unity show that there is no variation of $\Delta G^{\neq}$ due largely to the general compensation effect between $\Delta H^{\neq}$ and $\Delta S^{\neq}$.

The linear plots of log k_1 against $E^{\neq}$ with slopes not equal to 2.303 RT indicate that changes in $E^{\neq}$ are not alone responsible for changes in reaction velocities but also P factor has an effect on the velocity of hydrolysis. The linear relationship between $E^{\neq}$ and log A with slopes equal to 1.8 establishes the close correlation between the two parameters $E^{\neq}$ and PZ where PZ = A.

However, the differences in $E^{\neq}$ are not large, but the general tendency is in harmony with the effect which is expected on the basis of mesomeric and hyperconjugation interactions.

Effect of Structure of the Hemiesters on the Rate of Hydrolysis :-

The experimental results show that the rates of hydrolysis of the hemiesters studied 1c, 1d and 2a-d fall in the order :

2a > 2b > 2d > 2c, 2c > 1c, 2d > 1d, and 1d > 1c

With regard to the hemiester 2b, the conjugative interaction exerts between the para-methoxy substituted group in the phenyl ring and the carboxyl group through the α, β-olefinic linkage leads to a decrease in the ionisation of the carboxyl group in the hemiester, i.e., its anchimeric assistance by the neighbouring carboxylate ion decreases results in lowering of its rate of hydrolysis than the unsubstituted one (2a).

The lower rate of hydrolysis of hemiester 2c than 2b leads us to assume that the difference in rates of anhydride formation is due to steric effect only since if electronic effect exerts, hemiester 2c with its two methoxy groups situated at 3 and 4 positions with their -I and +R $>$ -I effects, respectively should hydrolyse faster than hemiester 2b which has only one methoxy group in position 4. However, in anhydride solvolysis, the rate of nucleophilic attack will be controlled both by the $\delta(+)$ character of the anhydride carbonyl groups and the various steric influences of the substituents. In hemiester 2c the decrease in rate of anhydride formation is due to an increase in the probability of the unprofitable rotamer distribution in which the reacting groups have rotated away from each other. For hemiesters 1d and 2d the ester group and carboxylate ion are fixed in an eclipsed conformation and the participation rate is increased than that for hemiesters 1c and 2c, respectively. This means that complete restriction of rotation of the reacting carboxylate ion and carbomethoxy group away from each other has a profound rate enhancement effect on anhydride formation, but does not decrease the rate of anhydride solvolysis which is very fast.

The higher rates of hydrolysis of (E)-4-methoxycarbonyl-5-(3,4-dimethoxyphenyl)-pent-4-enoic acid (1c), (E)-4-methoxycarbonyl-5-(3,4-methylenedioxyphenyl)-pent-4-enoic acid (1d) than the corresponding (E)-4-methoxycarbonyl-4-(3,4-dimethoxyphenyl)-but-4-enoic acid (1e) and (E)-4-methoxycarbonyl-4-(3,4-methylenedioxyphenyl)-but-4-enoic acid (1f) is attributed to the steric effect on the enhancement in rate of formation of six- or five-membered ring as a cyclic intermediate. Dreiding models show the ease of formation of pentenoic anhydrides than butenoic ones since the conformation affords maximum steric repulsion to the rotation of carboxy and ester groups away from each other. It can also be explained on the basis of hybridization in the transition state of the carbonyl group undergoing attack where in the six-membered cyclic transition state it resembles more closely the tetrahedral intermediate (sp^3 hybridized C=O) and no additional nobond interaction is involved since all bonds should be staggered but in the corresponding five-membered ring it is almostly sp^2 hybridized so that the leaving and entering groups would be eclipsed with the neighbouring methylene hydrogens.

The lower rate of hydrolysis and higher energies of activation of hemiesters (E)-4-methoxycarbonyl-5-(3,4-dimethoxyphenyl)-pent-4-enoic acid (1c) and (E)-4-methoxycarbonyl-5-(3,4-methylenedioxyphenyl)-pent-4-enoic acid (1d) than their isomeric hemiesters methyl (E)-4-carboxy-5-(3,4-dimethoxyphenyl)-pent-4-enoate (2c) and methyl (E)-4-carboxy-5-(3,4-methylenedioxyphenyl)-pent-4-enoate (2d), respectively, is ascribed to the difference in their structures where the olefinic linkage is either conjugated with the methoxycarbonyl group (hemiesters 1c and 1d) or with the carboxyl group (hemiesters 2c and 2d) and extending its conjugation with the aromatic ring. This leads to two opposite effects where in the first case, the presence of the olefinic linkage conjugated with the methoxycarbonyl group with its retarding +R effect opposes its enhancing -I effect results in a decrease in the polarisation of the carbonyl group, i.e., its susceptibility toward nucleophilic attack decreases and lowers the rate of hydrolysis of the former hemiesters (1c, 1d). In the second case, the conjugation of the olefinic linkage with the carboxyl group (hemiesters 2c and 2d) decreases its ionisation leading to a decrease in the anchimeric assistance by the neighbouring carboxylate ion, i.e., the intramolecular nucleophilic catalysis decreases and the rate lowers. However, if the only factor affecting the rate of hydrolysis is the intramolecular nucleophilic catalysis, hemiesters 1c and 1d should hydrolyse faster than 2c and 2d, respectively. The results obtained indicate that the first factor outweighs the second one, i.e., the ease of polarisation of the carbonyl group affects much more the hydrolysis than the anchimeric assistance by the neighbouring carboxylate ion to form the anhydride as a cyclic intermediate.