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KINETICS OF DEHYDRATION OF THE DIASTEREOMERIC (±)2,3-DIPHENYL-3-HYDROXYPROPIONIC ACIDS IN ACETIC ANHYDRIDE AND TRIETHYLAMINE

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The Perkin reaction of benzaldehyde with phenylacetic acid, carried out in the presence of acetic anhydride and triethylamine, yields predominantly the trans isomer of α-phenylcinnamic acid (1). With the view to clarify the stereochemistry and mechanism of this reaction Zimmerman and Ahramjian(2) studied in a preparative manner the dehydration of the diastereomeric (±)2,3-diphenyl-3-hydroxypropionic acids (I), which in this case are assumed as intermediates. Using lower concentrations of the reactants they achieved a still higher stereoselectivity - a 98±2% yield of the trans isomer from both diastereomers. The autors assumed that the hydroxy acids are first converted into the mixed anhydrides (II) of the respective diastereomeric 3-acetoxy-2,3-diphenylpropionic acids with acetic acid. Under the action of triethylamine an α-proton is then cleaved. The carbanion formed eliminates spontaneously an acetate anion from a conformation allowing maximum conjugation between the carboxyl group, the double bond being formed in the transition state and the phenyl group at the β-carbon atom ("overlap control").

With the view to study the kinetics and mechanism of the Perkin reaction in all its steps, we reported earlier a preparative and kinetic investigation on the dehydration of the diastereomers I on heating in acetic anhydride in the presence of different amounts of acetic acid(3). Our present communication deals with the kinetic measurements of the dehydration of the same diastereomers in a mixture of acetic anhydride and triethylamine (1:1), carried out in the range of 5 to 25°C.

The samples for the kinetic runs were prepared in advance, in order to convert I into II, by heating for 5 hours at 70°C solutions of I (0,200 %) in acetic anhydride containing 0,5 % acetic acid(3). Equal volumes of these solutions and triethylamine were mixed at the desired temperature in brown reagent vessels in order to avoid the photochemical reaction between triethylamine and acetic anhydride. A check solution containing equal volumes of triethylamine and acetic anhydride was run simultaneously. For each diastereomer were carried out two runs at each temperature (±0,05°C). The course of the reaction was followed by the concentrations of the α-phenyl-trans-cinnamic acid, measured spectrophotometrically at λ=280 mμ, the samples of the reaction mixtures being diluted(1:50 till 1:100) with methanol, which quenches the elimination reaction. The data for calculating the rate constants were obtained by correcting the extinction values of the samples with that of the respective value for the check sample (the largest correction did not exceed 10 %).

The reaction was first order in respect to the initial hydroxy acid as may be seen from the linear relationship of $\log(k-x)$ from t (fig.1). Plots of $\log\frac{K}{T}$ against $\frac{1}{T}$ were also linear(fig.2) which allowed us to calculate the activation parameters in the temperature interval studied. The values of the rate constants and the activation parameters are given in table 1. The standard deviation is given for 99 % statistical certainty.

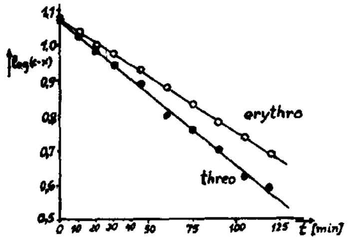


FIG. 1

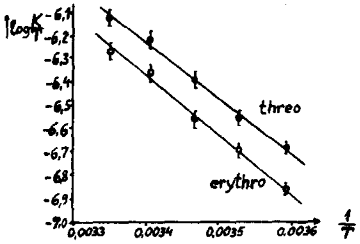
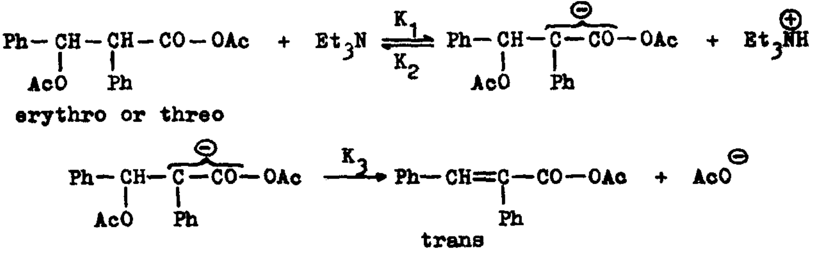


FIG. 2

TABLE 1

	Rate Constants $K.10^5$ $[sec^{-1}]$					Activation Parameters		
	T [°K]					H^* $\left[\frac{kcal}{mole}\right]$	S^* [e. u.]	F^* $\left[\frac{kcal}{mole}\right]$ at 288,2°K
	278,2	283,2	288,2	293,3	298,2			
Erythro	3,8± ±0,3	5,6± ±0,3	7,8± ± 0,8	12,7± ± 0,7	15,9± ± 0,8	11,8± ±0,04	-36,2± ±0,03	22,2± ±0,04
Threo	5,6± ±0,4	7,8± ±0,5	11,6± ±1,1	17,2± ±1,0	22,2± ±1,0	11,2± ±0,04	-37,5± ±0,03	22,0± ±0,04

First of all we wish to pay attention to the fact, that inspite of the great change in the experimental conditions in comparison to those used earlier (3), the entropies of activation are only slightly higher (more significantly with the erythro isomer - with c.a. 4 e.u.). This shows that in this case also the slowest step is the formation of a carbanion. The strong increase in the basicity of the medium has lead as main result to strong decrease in the enthalpies of activation (3,6 kcal/mole for the erythro isomer and 5,7 kcal/mole for the threo one). The latter effect determines mainly the observed increase in the rate. The mechanism of the reaction may be presented as follows:



$$\underset{\text{AcO}}{\text{Ph-CH}}\text{-}\underset{\text{Ph}}{\text{CH}}\text{-CO-OAc} + Et_3N \underset{K_2}{\overset{K_1}{\rightleftharpoons}} \text{Ph-}\underset{\text{AcO}}{\text{CH}}\text{-}\underset{\text{Ph}}{\overset{\ominus}{\text{C}}}\text{-CO-OAc} + Et_3\overset{\oplus}{N}H$$

erythro or threo

$$\text{Ph-}\underset{\text{AcO}}{\text{CH}}\text{-}\underset{\text{Ph}}{\overset{\ominus}{\text{C}}}\text{-CO-OAc} \xrightarrow{K_3} \text{Ph-CH=}\underset{\text{Ph}}{\text{C}}\text{-CO-OAc} + AcO^{\ominus}$$

trans

The steady-state approximation gives:

$$V = \frac{K_1 . K_3 . [PhCH(OAc)CH(Ph)COOAc] . [Et_3N]}{K_2 . [Et_3\overset{\oplus}{N}H] + K_3}$$

As our investigation was carried out in the presence of a large excess of triethylamine and acetic acid, i.e. under the conditions recommended for preparative work (1), the above equation may be simplified to a first order rate one:

$$V = K_{exp} . [PhCH(OAc)CH(Ph)COOAc]$$

The following experiment was also carried out: A solution of 0,5 g phenylacetic acid in 2,0 ml acetic anhydride were heated for one hour at 105°C. After cooling the reaction mixture, 2 ml benzaldehyde and 2 ml triethylamine were added and the homogenous solution obtained was allowed to stand for 24 hours in a sealed tube at room temperature. 0,5 g (61%) α-phenyl-trans-cinnamic acid were isolated according to the procedure described by Fieser(1).This result confirms the conclusion of Buckles and Bremer(4) drawn from the kinetic data,that the slowest step of the Perkin reaction is the condensation step. It follows that the method used in this paper may be utilized to study the kinetics of the Perkin reaction.

References

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