Mononuclear Heterocyclic Rearrangement. Note I. Kinetic Study of the Rearrangement of the Phenylhydrazone of 3-Benzoyl-5-phenyl-1,2,4-oxadiazole into 2,5-Diphenyl-4-benzoylamino-1,2,3-triazole

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The rates of the mononuclear heterocyclic rearrangement of the phenylhydrazone of 3-benzoyl-5-phenyl-1,2,4-oxadiazole (I) into 2,5-diphenyl-4-benzoylamino-1,2,3-triazole (II) have been measured in dioxane/water (50:50, v:v) in the range of pS^+ 3.8-12.2 at various temperatures and the activation parameters determined. On the basis of the results obtained, we present evidence for the occurrence of two different types of reaction: the first, base-catalyzed; the second, pS^+ -independent. In the base-catalyzed range the catalysis is of the general type.

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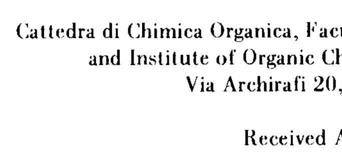
In a study (1) of the behaviour of the phenylhydrazone of the 3-benzoyl-5-phenyl-1,2,4-oxadiazole (I) on heating it above its melting point or in solution in the presence of an acid or a base, in every case the rearrangement into 2,5-diphenyl-4-benzoylamino-1,2,3-triazole (II) was observed.



To obtain information about the mechanism of this transformation, a typical mononuclear heterocyclic rearrangement (2), we have undertaken a program of research on the rearrangement (oxadiazole → triazole) extended to the study of the behaviour of various substituted oxadiazoles in different solvents (protic or aprotic, polar or apolar) and in different conditions of pS^+.

In this first paper we report kinetic data on the study of the rearrangement I → II in dioxane/water (50:50 v:v) in the range of pS^+ 3.8-12.2 at different temperatures.

EXPERIMENTAL

Synthesis and Purification of Compounds.

The phenylhydrazone of the 3-benzoyl-5-phenyl-1,2,4-oxadiazole (I) (1) and of 3-benzoyl-1,2,4-oxadiazole (IV) (1), the 2,5-diphenyl-4-benzoylamino-1,2,3-triazole (II) (1), 2,5-diphenyl-4-formylamino-1,2,3-triazole (V) (1) and 3-benzoyl-5-phenyl-1,2,4-oxadiazole (III) (6), water and dioxane (7) were prepared and/or purified according to the methods reported.

pS^+ Measurements.

An operational pH scale, pS^+ (8), was established in aqueous dioxane by employing the pK_a of acids determined by interpolation from the data reported by Harned and Owen (9). For dioxane/water (50:50, v:v) the meter reading after calibration against aqueous buffers was not significantly different from pS^+; in fact it was necessary to apply a correction of + 0.16 to the meter reading.

pS^+ Measurements were made by using a Radiometer PHM 63 digital pH-meter. Variations of pS^+ values before and after any run in the buffered solutions of reaction were lower than 0.03 unity: the mean value of pS^+ was used for calculations.

Kinetics Measurements.

The kinetics of the rearrangement I → II and IV → V were followed spectrophotometrically by measuring respectively the disappearance of I and IV at the wave length of their maximum (366 nm, log ϵ = 4.22 ± 0.02 and 360 nm, log ϵ = 4.26 ± 0.02, respectively) at which II and V did not absorb. Ionic strength of the buffered solutions was kept constant at the value of 0.05 through addition of potassium chloride. In the range of pS^+ studied, the spectra of I, II, IV and V in dioxane/water measured in the range 220-500 nm were pS^+ -independent (only slight random variations were observed). The concentrations employed were 6 x $10^{-5}M$ for I and 7.6 x 10^{-5} M for IV.

Discussion

Chemical and Kinetic Data.

We have collected kinetic data in the range of pS^+ 3.8-

Table I

Kinetic Data and Activation Parameters for the Rearrangement I → II in Dioxane/Water (50:50, v:v)

pS^+	10^6k, sec^{-1}, at various temperatures (°C) (a)			-log k (b)	$\Delta H^{\neq}$(c) kcal mol^{-1}	$\Delta S^{\neq}$(d) u.e.
3.81 (e)	1.30 (40.05)	3.41 (50.10)	9.51 (60.20)	5.896	19.9	-22.3
3.99 (e)	1.28 (40.05)	3.24 (50.10)	8.75 (60.20)	5.904	19.2	-24.4
4.50 (e)	1.30 (40.35)	3.53 (50.15)	9.16 (60.10)	5.902	19.8	-22.0
5.16 (e)	1.20 (40.07)	3.00 (48.50)	8.93 (60.10)	5.919	20.2	-21.3
5.57 (e)	1.27 (40.07)	3.04 (48.50)	9.50 (60.10)	5.903	20.3	-20.8
6.26 (e)	1.32 (40.07)	2.82 (47.50)	10.2 (60.10)	5.886	20.5	-20.0
6.67 (e)	1.40 (40.05)	3.53 (50.00)	10.6 (60.10)	5.873	20.4	-20.4
7.16 (e)	1.60 (40.05)	4.33 (50.00)	13.1 (60.10)	5.818	21.4	-17.0
8.52 (f)	5.46 (40.17)	19.8 (51.40)	51.3 (60.20)	5.272	22.6	-10.6
9.12 (f)	18.0 (40.17)	66.0 (51.20)	174 (60.20)	4.752	22.9	-7.5
9.57 (f)	45.7 (40.18)	168 (51.40)	409 (60.20)	4.344	22.2	-7.7
10.37 (f)	73.6 (30.10)	228 (40.00)	841 (51.20)	3.626	22.0	-5.0
10.92 (f)	65.8 (19.95)	235 (30.06)	758 (40.15)	3.126	21.5	-4.3
11.37 (f)	57.4 (9.97)	204 (20.10)	630 (29.98)	2.727	21.4	-2.7
11.72 (f)	347 (20.00)	1290 (30.00)	4150 (40.10)	2.382	21.9	+0.5
11.87 (f)	468 (20.00)	1720 (30.00)	5460 (40.10)	2.263	21.7	+0.3
12.14 (f)	822 (20.00)	3010 (30.00)	9310 (40.10)	2.029	21.4	+0.5

(a) The rate constants are accurate to better than ± 3%. (b) At 40°, values calculated from activation parameters. (c) At 40°, the probable error is 0.6 kcal mol^{-1}. (d) At 40°. (e) Buffer, citrate. (f) Buffer, borate.

12.2, where the only reaction was the rearrangement I → II. At pS^+ lower than 3.8 and in the conditions used, hydrolysis of I to 3-benzoyl-5-phenyl-1,2,4-oxadiazole (III) and phenylhydrazine (VI) was a significative competitive reaction; research on this point is in progress.

$$\mathrm{III+VI} \xleftarrow[\text{(partial reaction)}]{pS^+<3.8} \mathrm{I} \xrightarrow[pS^+<3.8\ \text{(partial reaction)}]{pS^+>3.8\ \text{(practically unique reaction)}} \mathrm{II}$$

The apparent first order kinetic constants at any pS^+, calculated by plotting the logarithms of the optical densities versus time, and the thermodynamic parameters are reported in Table I. Since the rate constant values were strongly affected by the pS^+, the control of pS^+ was fulfilled by means of a series of buffers (see Table I and Figure 1).

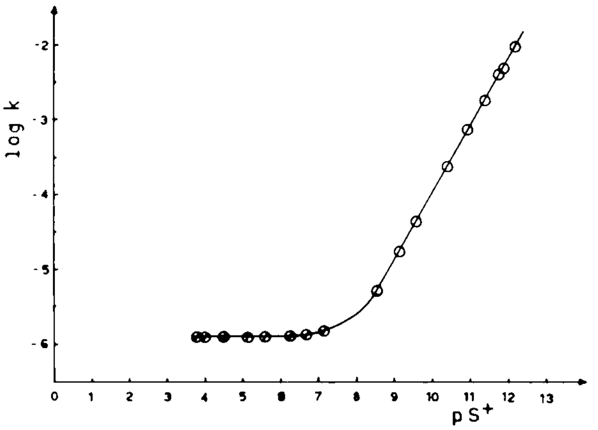


Figure 1: Plot of log k, at 40°, for the rearrangement I → II versus pS^+ in dioxane/water (50:50, v:v) with buffer citrate ⊘ and borate ○.

A plot of log k versus pS^+ (see Figure 1) showed a sharp decrease of the reactivity with pS^+, up to range of pS^+ 6.8-3.8 at which the rate of reaction was practically pS^+-independent. The curve obtained (Figure 1) indicates two different types of reaction corresponding to the two different ranges of pS^+, the first (starting from the highest value of pS^+) a base-catalyzed reaction, the second a pS^+-independent one.

Using different buffers for the same range of pS^+ (see Tables II and III, and Figure 2) we observed that the kinetic constant values were affected by the nature of the buffer used, thus indicating a general base catalysis. Therefore there cannot be a rate limit at least until I gives its anion, and this is possible for the $pS^+ \geqslant (pK_a)_I$.

Table II

Kinetic Data for the Rearrangement I → II in Dioxane/Water (50:50, v:v) at 40°, Glycine Buffer

pS^+	10^6k, sec^{-1} (a)	-log k
8.70	3.55	5.450
9.75	20.6	4.686
10.00	44.0	4.357
10.70	251	3.600
11.05	694	3.159
11.75	5080	2.294

(a) The rate constant are accurate to better than ± 3%.

Table III

Kinetic Data and Activation Parameters for the Rearrangement I → II in Dioxane/Water (50:50, v:v), Phosphate Buffer

pS^+	10^6k, sec^{-1}, at various temperatures (°C) (a)			-log k (b)	$\Delta H^{\neq}$(c) kcal mol^{-1}	$\Delta S^{\neq}$(d) u.e.
7.52	1.77 (40.03)	5.37 (50.00)	16.8 (60.10)	5.760	22.7	-12.6
8.20	2.58 (40.03)	8.63 (50.00)	26.9 (60.00)	5.590	23.7	-8.5
8.80	7.88 (41.32)	24.7 (50.00)	82.6 (60.00)	5.177	25.6	-0.7
9.16	17.0 (41.32)	50.7 (50.00)	189 (60.00)	4.856	26.2	+2.8
9.53	13.4 (29.95)	47.8 (39.97)	186 (50.20)	4.297	24.7	+0.6
9.90	34.2 (30.00)	140 (40.15)	573 (51.30)	3.868	25.3	+4.3

(a) The rate constante are accurate to better than ± 3%. (b) At 40°, values calculated from acrivation parameters. (c) At 40°, the probable error is 0.6 kcal mol^{-1}. (d) At 40°.

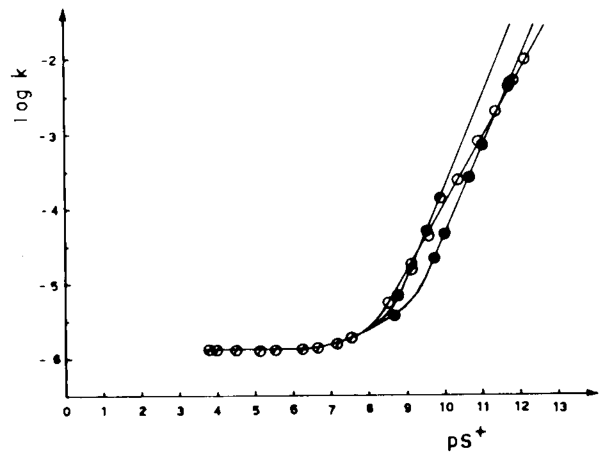


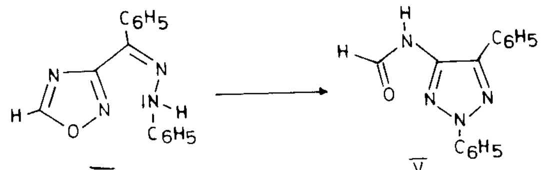
Figure 2: Plot of log k, at 40°, for the rearrangement I → II versus pS^+ in dioxane/water (50:50, v:v) with buffer citrate ⊘, borate ○, phosphate ◑ and glycine ●.

In the base-catalyzed range it is possible to indicate a mechanism for the rearrangement through a van't Hoff complex (10) where SH and PH indicate respectively I and II, where the rate determining step is the first one which requires (see after) the partial loss of resonance stabilization

$$SH + B \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} S{*}\text{---}H\text{---}B \xrightarrow{k_2} P^- + BH \xrightarrow{k_3} PH + B$$

energy of the 1,2,4-oxadiazole ring. In the third step P^- can accept the proton from conjugate acid of the base used as well as from the protic solvent.

To confirm this point, we have studied the kinetics of the rearrangement of the phenylhydrazone of 3-benzoyl-1,2,4-oxadiazole (IV) into 2,5-diphenyl-4-formylamino-1,2,3-triazole (V) in experimental conditions (pS^+ 7.3-9.5 phosphate buffer) similar to those used for rearrangement I → II. Table IV gives the kinetic data and the corresponding activation parameters.



IV V

A comparison of kinetic data for the two process (I → II and IV → V) shows that in the range of pS^+ studied the rearrangement IV → V is faster (k_{IV}/k_I ca. 10 at any pS^+) than I → II. Looking at the activation parameters we can observe that the difference of reactivity ($\delta\Delta G^{\neq}$ ca. 2 kcal mol^{-1}) depends on a variation of activation enthalpies whereas activation entropies permain constant.

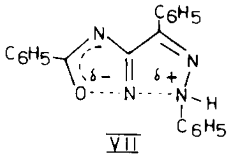
Table IV

Kinetic Data and Activation Parameters for the Rearrangement IV → V in Dioxane/Water (50:50, v:v), Phosphate Buffer

pS^+	10^6k, sec^{-1}, at various temperatures (°C) (a)			-log k (b)	$\Delta H^{\neq}$(c) kcal mol^{-1}	$\Delta S^{\neq}$(d) u.e.
7.30	7.58 (40.60)	21.0 (50.00)	64.8 (60.20)	5.156	22.1	-11.6
8.45	3.04 (19.85)	12.8 (30.05)	45.8 (40.00)	4.335	23.9	-2.0
9.42	31.3 (20.00)	124 (29.97)	436 (40.10)	3.362	23.3	+0.4

(a) The rate constants are accurate to better than ± 3%. (b) At 40°, values calculated from activation parameters. (c) At 40°, the probable error is 0.6 kcal mol^{-1}. (d) At 40°.

This observation agrees with the higher thermodynamic stability of I with respect to IV, deriving from the presence in I of a diaryloid system (I is a derivative of 5-phenyl-1,2,4-oxadiazole): obviously the higher stabilization energy of resonance of I affects the position and the shape of the transition state in the reaction coordinate.



VII

The rate and the activation parameters of the rearrangement I → II are scarcely affected by pS^+ value in the range 3.8-6.8, thus indicating a unique mechanism of reaction, probably of the S_Ni type (5), with a highly solvated transition state. This hypothesis agrees with the zwitterionic nature of the transition state (VII), which reflects on the values (large) of activation entropies.

In the base-catalyzed range, according to the nature of the transition state, the activation entropies are low.

In the whole range studied (3.8-12.2) the activation enthalpies were high, confirming that formation of the transition state is associated with partial loss of stabilization resonance energy of the 1,2,4-oxadiazole ring only in part balanced by the gain deriving from the incipient formation of the new heterocyclic ring (1,2,3-triazole).

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