Mononuclear Heterocyclic Rearrangements. Part 7.[1] Evidence for General Base Catalysis in the Rearrangement of the *Z*-Phenylhydrazone of 3-Benzoyl-5-phenyl-1,2,4-oxadiazole into 2,5-Diphenyl-4-benzoylamino-1,2,3-triazole in Dioxan–Water

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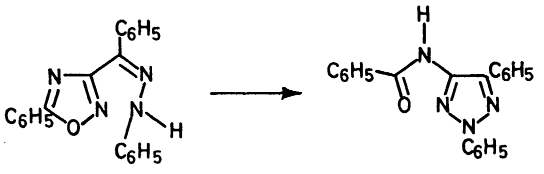
The title reaction has been studied at various pS^+ and buffer concentrations. Kinetic constants for uncatalysed and catalysed pathways have been calculated. A mechanism for the rearrangement is offered.

FROM a study of the mononuclear heterocyclic rearrangement (m.h.r.)[2,3] of the *Z*-phenylhydrazone of 3-benzoyl-5-phenyl-1,2,4-oxadiazole (I) into 2,5-diphenyl-4-benzoylamino-1,2,3-triazole (II) we recently showed[3a] the occurrence of two possible pathways for the rearrangement (I)⟶(II)



(I) (II)

The first, uncatalysed pathway occurs in the pS^+ range 3.8—6.5, the second, base-catalysed, predominates at p$S^+ > 8.0$; at pS^+ 6.5—8.0 both mechanisms operate. Moreover, we suggested that the base-catalysed reaction is probably governed by *general* catalysis.

In order to extend the information on the nature of base catalysis in our system we now report data on the influence of the type of buffer and of its concentration on the reaction rate at constant ionic strength and at constant or variable pS^+.

A rearrangement reaction subjected to general catalysis obeys the kinetic law (1)† where $(k_A)_R$ represents

$$(k_A)_R = k_u + \Sigma_i k_i[C_i] + \Sigma_{j,k} k_{j,k}[C_j][C_k] \qquad (1)$$

the apparent kinetic constant for the rearrangement, k_u the uncatalysed specific rate constant, and the terms $k_i[C_i]$ or $k_{j,k}[C_j][C_k]$ refer respectively to any bimolecular or termolecular catalysed reaction pathway. By using a suitable number of $(k_A)_R$ values under chosen experimental conditions it is possible to obtain all the coefficients pertaining to the single steps.

RESULTS AND DISCUSSION

We have studied the rearrangement (I) ⟶ (II) in the presence of two buffers, sodium borate–boric acid and sodium phenoxide–phenol, at various pS^+, buffer concentrations, and/or temperatures (Tables 1 and 2). At constant pS^+ the $(k_A)_R$ values increase with buffer concentration indicating general catalysis. Taking into account the pS^+ range considered and the observation that at pS^+ 3.6—6.5 the rearrangement rate is constant,[3] we have fitted (see Experimental section) the observed $(k_A)_R$ values to equation (2) where $k_{OH}[OH^-]$, $k_B[B]$, and

$$(k_A)_R = k_u + k_{OH}[OH^-] + k_B[B] + k_A[A] + k_{A,B}[A][B] + k_{B,OH}[B][OH^-] \qquad (2)$$

$k_A[A]$ represent the bimolecular reaction pathways with catalysis by hydroxide ion and by the basic (B) and the acidic (A) component of buffer, respectively; whereas $k_{A,B}[A][B]$ and $k_{B,OH}[B][OH^-]$ imply a termolecular reaction pathway with catalysis by both A and B or both B and OH^-, respectively. Of course, the terms depending on hydroxonium ion concentration have not been included in equation (2). The results of fitting at 298.15 K are in Table 3.

Since k_A, $k_{A,B}$, and $k_{B,OH}$ either give meaningless (negative) contributions to $(k_A)_R$ or have a high inherent uncertainty, the relevant terms in equation (2) have been neglected.

Using the criterion proposed by Hammett[4,‡] to identify the kind of catalysis it is possible to show that the rearrangement studied is general base-catalysed.

The values of k_u, which are the intercepts of the regression function, are affected by a large inherent uncertainty. The average value of k_u (2.3×10^{-7} s^{-1}) previously measured in the pS^+ independent range is certainly more reliable.

The values of k_{OH} obtained with the two buffers are very similar (3.8 and 4.2 l mol^{-1} s^{-1}).

Since the base is not consumed as the reaction proceeds, it also follows that an acid (water or each acid present in solution) must be involved in a fast step. Of course, this observation holds for all the base-catalysed pathways.

The catalytic constant of borate ion, as expected, is lower than k_{OH} ($k_{OH}/k_{H_2BO_3}$ *ca.* 400) but at any buffer concentration the term $k_{H_2BO_3}$ [$H_2BO_3^-$] gives a significant contribution to the rearrangement rate.

[†] The same law holds for nucleophilic or electrophilic catalysis.

[‡] 'A general base catalysis is recognizable if for some base B_i the rate of the catalysed reaction is significant compared both with the rate due to catalysis by the lyonium ion and with that due to the solvent.'

TABLE 1

Apparent kinetic constants and activation parameters calculated at 298.15 K for the rearrangement (I) ⟶ (II) at various pS^+ and borate buffer concentrations

pS^+ [a]	10.37	10.92	11.37	11.72	11.87	12.14			
$10^5(k_A)_R$ [b]	3.81	12.5	35.9	67.2	90.1	158			
$\Delta H^‡$ [c]	92	90	83	92	91	90			
$\Delta S^‡$ [d]	−21	−18	−32	2	2	3			
pS^+ [e]	9.62	10.13	10.30	10.64	10.87	11.12	11.40	11.62	11.90
$10^5(k_A)_R$ [b]	0.994	2.85	3.70	7.22	12.5	23.6	35.9	62.0	110
$\Delta H^‡$ [c]	90	89	93	94	91	87	89	90	90
$\Delta S^‡$ [d]	−38	−34	−18	−8	−14	−24	−13	−4	0
pS^+ [f]	9.70	9.98	10.11	10.48	10.72	11.12	11.31	11.55	11.98
$10^5(k_A)_R$ [b]	1.48	2.53	3.38	7.02	10.9	26.2	40.3	64.7	148
$\Delta H^‡$ [c]	90	92	90	92	95	89	90	87	88
$\Delta S^‡$ [d]	−37	−25	−27	−18	−4	−15	−9	−13	−3

[a] Total buffer concentration, 0.125 M. [b] $(k_A)_R/s^{-1}$, values calculated by activation parameters. The experimental rate constants were measured in the range 283—333 K and were reproducible to within ±3%. [c] kJ mol^{-1}; the maximum error is 2 kJ mol^{-1}. [d] J K^{-1} mol^{-1}; the maximum error is 8 J K^{-1} mol^{-1}. [e] Total buffer concentration, 0.025M. [f] Total buffer concentration, 0.05M.

TABLE 2

Apparent kinetic constants and activation parameters calculated at 298.15 K for the rearrangement (I) ⟶ (II) at various pS^+ and phenoxide buffer concentrations

pS^+ [a]	9.56	10.02	10.30	10.61	10.92	11.02	11.38	11.64
$10^5(k_A)_R$ [b]	0.699	1.85	3.40	6.55	12.4	15.6	33.2	58.6
$\Delta H^‡$ [c]	84	88	87	84	85	87	85	85
$\Delta S^‡$ [d]	−62	−41	−39	−44	−33	−26	−28	−21
pS^+ [e]	9.48	9.82	10.07	10.36	10.53	10.91	11.18	11.50
$10^5(k_A)_R$ [b]	0.667	1.36	2.31	4.40	6.19	13.9	24.0	47.3
$\Delta H^‡$ [c]	92	91	89	90	91	87	88	90
$\Delta S^‡$ [d]	−34	−32	−36	−26	−21	−25	−18	−8
pS^+ [f]	9.45	9.81	10.09	10.41	10.68	10.91	11.23	11.57
$10^5(k_A)_R$ [b]	0.803	1.70	3.05	5.76	10.3	16.7	32.4	65.5
$\Delta H^‡$ [c]	90	88	87	90	86	84	86	87
$\Delta S^‡$ [d]	−42	−41	−39	−23	−33	−34	−23	−14

[a—f] As in Table 1.

TABLE 3

Multiple linear regression analysis [a] of kinetic data according to equation (2) at 298.15 K

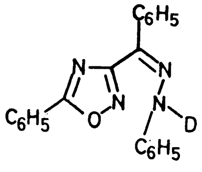
Buffer [b]	10^5k_u/ s^{-1}	$k_{OH} \pm s_{k_{OH}}$/ l mol^{-1} s^{-1}	$10^2(k_B \pm s_{k_B})$/ l mol^{-1} s^{-1}	$10^4(k_A \pm s_{k_A})$/ l mol^{-1} s^{-1}	$10^4(k_{A,B} \pm s_{k_{A,B}})$/ l^2 mol^{-2} s^{-1}	$k_{B,OH} \pm s_{k_{B,OH}}$/ l^2 mol^{-2} s^{-1}	R
1	0.35	3.6 ± 0.1	1.4 ± 0.1	0	−0.21 ± 0.04	0	0.9995
1	−0.59	3.8 ± 0.6	0.98 ± 0.07	0	0	0	0.9986
2	0.62	4.1 ± 0.3	0.87 ± 0.03	−0.63 ± 0.43	0	3.7 ± 2.9	0.9999
2	0.59	4.1 ± 0.3	0.90 ± 0.02	−0.71 ± 0.43	0	0	0.9999
2	0.39	4.2 ± 0.9	0.89 ± 0.02	0	0	0	0.9999

[a] s_{k_i}, $s_{k_{j,k}}$, standard deviations of k_i and $k_{j,k}$, respectively; R, multiple correlation coefficient. The number of points is 24 throughout. [b] Buffers: 1, sodium borate–boric acid; 2, sodium phenoxide–phenol.

The catalytic constant of phenoxide ion is again lower than k_{OH} (k_{OH}/k_{PhO} *ca.* 400). Due to the similarity of the pK_a values of boric acid and phenol, $k_{H_2BO_3}$ is similar to k_{PhO}. Also in this case, the term $k_{PhO}[PhO^-]$ makes a significant contribution to the rearrangement rate, at any buffer concentration.

The catalytic constants obtained for OH^-, $H_2BO_3^-$, and PhO^- allow further confirmation of general catalysis. In fact, we have applied the Brönsted relationship to our set of bases, including k_{H_2O},* and obtained β 0.46 (r 0.9997), *i.e.* a value which indicates general base catalysis.[4]

This is further supported by the results obtained from a study of kinetic isotope effects at various pS^+ values. The α-*N*-deuteriated *Z*-phenylhydrazone of 3-benzoyl-5-phenyl-1,2,4-oxadiazole (ID) readily exchanges deuterium with protium (and *vice versa*) in the presence of water, in accord with Brodskii's [6] observation that proton transfers between atoms with unshared electron pairs (involving a four-centre concerted process) are very rapid. The rearrangement of (ID) has been carried out in dioxan–D_2O. The relevant kinetic constants (see Table 4) have been measured at 313.15 K both in the pS^+-independent range and in the base-catalysed range. The Figure shows a comparison between the log $(k_A)_R$



(ID)

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* k_{H_2O} has been calculated from the relation $k_u = k_{H_2O}[H_2O] + k_{Dioxan}[Dioxan]$ using k_u measured in the pS^+-independent range (see above), k_{Dioxan},[5] and neglecting the mixing effect of the two solvents.

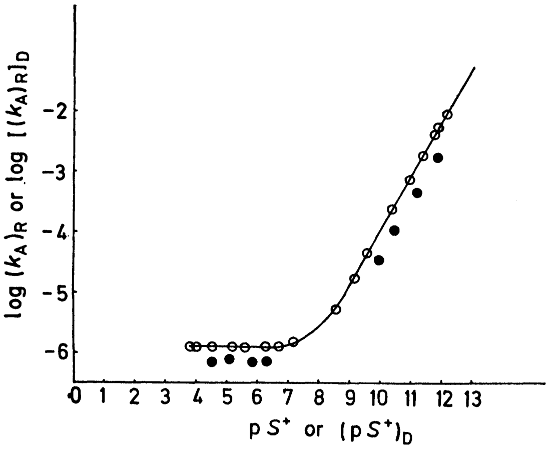
TABLE 4

Rate constants at 313.15 K for the rearrangement of (ID) in dioxan–D_2O (1 : 1 v/v)

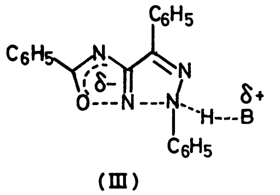
pS^+	4.50^a	5.08^a	5.85^a	6.28^a	9.95^b	10.48^b	11.18^b	11.85^b
$10^6[(k_A)_R]_D$ [c]	0.69	0.78	0.68	0.69	34.0	107	460	1 750
$[(k_A)_R]_H/[(k_A)_R]_D$	1.8	1.6	1.8	1.8	2.9	2.8	2.8	3.0

[a] Buffer: sodium citrate–citric acid. [b] Buffer: sodium borate–boric acid. [c] The rate constants are accurate to within ±3%.

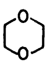
values for (I) and (ID) as a function of p^+S. The $[(k_A)_R]_H/[(k_A)_R]_D$ ratio is 1.8 in the pS^+-independent range and 2.9 in the base-catalysed range. These values indicate that the reaction is faster in H_2O than in D_2O and involves a proton transfer in the rate-controlling step.[6] The measured ratios agree with the different time of bond-breaking and -forming [N · · · H · · · B, see (III)] in the two ranges.



Plot of log $[(k_A)_R]_H$ (○) in dioxan–water and of log $[(k_A)_R]_D$ (●) in dioxan–D_2O, at 313.15 K, respectively, *versus* pS^+ and $(pS^+)_D$. $(pS^+)_D$ calculated from the relation $(pS^+)_D = pS^+ + 0.37$ according to A. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1975, 947



(III)

$B = H_2O$, , OH^-, $H_2BO_3^-$, PhO^-

The data agree with a general base-catalysed rearrangement with a transition state such as (III), similar to that proposed[3b] for the rearrangement of (I) in benzene promoted by piperidine.

EXPERIMENTAL

Synthesis and Purification of Compounds.—Compounds (I), (II), dioxan, and water were prepared and/or purified according to the methods reported.[3]

pS^+ *and Kinetic Measurements.*—An operational pH scale, pS^+,[7a] was established in aqueous dioxan by employing the pK_a values of acids determined by interpolation from the data reported by Harned and Owen.[7b] For dioxan–water (1 : 1 v/v) the meter reading after calibration against buffers was not significantly different from pS^+; in fact it was necessary to apply a correction of +0.16 to the meter reading.

The kinetics (at constant ionic strength 0.05M) were followed spectrophotometrically by measuring the disappearance of (I) at $\lambda_{max.}$ 366 nm (log ε 4.22 ± 0.02). Compound (II) does not absorb at this wavelength. In the range of pS^+ studied the spectra of (I) and (II) were practically pS^+-independent. The concentrations of (I) used were *ca.* 6×10^{-5}M.

At each studied pS^+ (I) rearranged to (II) in high yields (≥98%, as determined by u.v.–visible spectral analysis at infinity).

(Z)-α-N-*Deuteriated Phenylhydrazone of* 3-*Benzoyl*-5-*phenyl*-1,2,4-*oxadiazole* (ID).—To a solution of (I) (1 g) in dioxan (15 ml), an excess of deuterium oxide (*ca.* 8—10 ml) was added slowly and with stirring until the solid separated. The mixture was carefully heated until the solid dissolved and then left at room temperature. On standing, pure (ID) crystallised. An n.m.r. test confirmed complete (I) ⟶ (ID) isotope exchange.

pK_a *Determination of Boric Acid and Phenol in Water–Dioxan* (1 : 1, v/v).—The title determination was carried out using the experimental values of pS^+ for the considered acids at different buffer ratios (see Tables 5 and 6). Assuming γ_A 1 and using the activity coefficients extrapolated from the data of Harned and Owen,[7b] a least-squares treatment of data according to equation (3) gives equations (4) and (5).

$$\log a_B/a_A = pK_A + pS^+ \quad (3)$$

$$pK_{H_3BO_3} = 11.69 \pm 0.03 \ (r\ 0.994) \quad (4)$$

$$pK_{PhOH} = 11.93 \pm 0.03 \ (r\ 0.999) \quad (5)$$

Calculations.—The values of $(k_A)_R$ used in the least-squares treatment were calculated at 298.15 K from activation parameters. The values of hydroxide ion concentration were calculated using 15.80 as the pK_w value in dioxan–water (1 : 1 v/v)[8] and 0.545 as the mean activity coefficient in the same system.[7] The values of $[H_2BO_3^-]$, $[H_3BO_3]$, $[PhO^-]$, and [PhOH] were calculated from known total buffer concentrations and using pK_a 11.69 and 11.93, respectively, for boric acid and phenol (see above).

The values of k_i and $k_{j,k}$ in Table 3 were obtained using multiple linear regression analysis of the apparent kinetic constants, $(k_A)_R$, at 298.15 K using equation (2).

The program used computes a sequence of regression equations in a stepwise manner. At each step one variable is added to the regression equation. The variable added is the one which makes the greatest reduction in the error sum of squares. Variables with too low *F* values are automatically removed.

An examination of the results of correlations reported in Table 3, shows that experimental data are better described by a four- or five-parameter than by a three-parameter equation (compare lines 1 and 2, or 3—5). However, the

TABLE 5

Experimental values of pS^+ measured at different [sodium borate] : [boric acid] ratios

a_B/a_A [a]	0.046	0.074	0.136	0.363	0.817	1.272	2.180
pS^+	10.30	10.54	10.82	11.23	11.63	11.79	12.03

[a] Total buffer concentration, 0.025M.

TABLE 6

Experimental values of pS^+ measured at different [sodium phenoxide] : [phenol] ratios

a_B/a_A [a]	0.074	0.172	0.545	0.817	1.271	1.820
pS^+	10.75	11.17	11.65	11.82	12.05	12.20

[a] Total buffer concentration, 0.025M.

improvement is only apparent in that the confidence level does not change significantly. Moreover, a negative regression parameter has no physical meaning. Thus, in the Discussion section we have used the parameters obtained by the two-independent-variables fit.

In view of the numerous approximations involved in the calculations the agreement between experimental and calculated $(k_A)_R$ values has to be considered good. On the other hand we only comment on the relative magnitudes of k_i and $k_{j,k}$ rather than attach any particular meaning to their absolute values.

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