Mononuclear Heterocyclic Rearrangement. Part 6 (1). Studies on Base Catalysis of the Rearrangement of the (*Z*)-*p*-Nitrophenylhydrazone of 3-Benzoyl-5-phenyl-1,2,4-oxadiazole in Benzene: Effect of Piperidine, Triethylamine and of Some Secondary Amines

Vincenzo Frenna and Nicolò Vivona

Institute of Organic Chemistry, University of Palermo, Via Archirafi 20, Palermo 90123, Italy

Domenico Spinelli and Giovanni Consiglio

Cattedra di Chimica Organica, Faculty of Pharmacy, University of Bologna, Via Zanolini 3, Bologna 40126, Italy

Received November 3, 1980

The kinetics of the title reaction catalyzed by various secondary and tertiary amines have been measured at 40° in benzene. The catalysis laws which were observed confirm the previous hypothesis about the mechanism of the mononuclear heterocyclic rearrangements.

J. Heterocyclic Chem., **18**, 723 (1981).

In studying the piperidine-catalyzed isomerization and rearrangement (2) of both the (*E*)- and (*Z*)-phenylhydrazone of 3-benzoyl-5-phenyl-1,2,4-oxadiazole (I-*E* and I-*Z*) in benzene, we observed (1) that the experimental kinetic results for the mononuclear heterocyclic rearrangement of I-*Z* (the corresponding reaction for I-*E* could not be detected) obey the following kinetic law

$$(k_A)_R = k_1[PIP] + k_2[PIP]^2$$

where $k_2/k_1 \cong 24$, thus indicating that in the range of concentrations which were studied ([PIP] 0.2 − 1.0 *M*), the third-order reaction pathway is always the more important one.

In order to gain additional information concerning this reaction mechanism, we have now studied the behaviour of the (*Z*)-*p*-nitrophenylhydrazone of 3-benzoyl-5-phenyl-1,2,4-oxadiazole (II-*Z*) with one tertiary amine (triethylamine: TEA), four secondary amines (diethylamine: DEA; di-*n*-propylamine: DPA; di-*n*-butylamine: DBA; diisobutylamine: DiBA) and one cyclic amine (piperidine: PIP). The amines which were chosen show similar basicities but differ greatly in steric requirements (SR) (3). The choice of the *p*-nitroderivative instead of the unsubstituted phenylhydrazone allowed us to have more convenient reaction times.

Kinetic Results and Discussion.

Under the experimental conditions used, II-*Z* rearranged to III in high yields (≥ 98%). In each case the apparent kinetic constant depends on the amine concentration (Table 1); the three following different kinetic laws have been observed (Table 2).

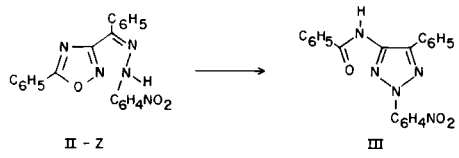
$$(k_A)_R = k_1[B] \text{ for TEA and DiBA}$$
$$(k_A)_R = k_1[B] + k_2[B]^2 \text{ for DPA and DBA}$$
$$(k_A)_R = k_2[B]^2 \text{ for PIP and DEA}$$

Based on this data, the first observation which can be made is that in the reaction of II-*Z* with piperidine as a catalyst, the reaction pathway requiring only one mole of amine [which was the less important one for I-*Z* also (1)] is absent. This fact agrees with the greatly reduced nucleophilicity of the arylhydrazone nitrogen of II-*Z* when compared with I-*Z*, thus necessitating the intervention of the second molecule of base.

Comparing the apparent rate constants at [B] = 1.0 *M* (Table 2) we observed a strong decrease (by a factor of 2000) of reactivity with increasing the SR of the amines. In fact, PIP, a cyclic amine with no strain and with the lowest SR, is by far the most efficient catalyst; moreover, the efficiency of catalysis strongly decreases going from DEA to DiBA through DPA, DBA and TEA. The reactivity does not seem to be correlated with the basicity of the amines, measured by the pK_a values in water (4), the basicity variation being very low *inter alia*.

The calculated k_2 values change greatly as a function of the amines used ($2.5 - 285 \cdot 10^{-5}$ l^{2}mol^{-2}s^{-1}). On the contrary the k_1 values, where observed, are very close to each other ($0.14 - 1.0 \cdot 10^{-5}$ l mol^{-1}s^{-1}), according to the similar basicity of the amines used.

The absence of the k_1 term could only be apparent in the reactions with PIP and DEA. In fact, due to the high values of the slope, the statistical uncertainties for the intercepts are high. Thus, the values of k_1 are not statistically different from zero.



0022-152X/81/040723-03$02.25

© HeteroCorporation

Table 1

Apparent First-Order Constants $(k_A)_R$ (a) for the Rearrangement of II-*Z* in Benzene at 40° in the Presence of Various Amines

[PIP]/*M*	0.095	0.190	0.250	0.297	0.347	0.396	0.500	0.600	0.700	0.800	0.890	1.010
$10^4(k_A)_R/s^{-1}$	0.25	1.03	1.82	2.45	3.40	4.36	7.15	10.2	14.3	18.3	22.4	29.0
[DEA]/*M*	0.100	0.203	0.285	0.404	0.520	0.575	0.640	0.715	0.808	0.930	0.995	
$10^5(k_A)_R/s^{-1}$	0.12	0.50	0.98	1.95	3.32	4.00	4.79	6.21	7.93	10.5	11.9	
[DPA]/*M*	0.120	0.210	0.320	0.420	0.530	0.650	0.730	0.830	1.010			
$10^5(k_A)_R/s^{-1}$	0.10	0.22	0.46	0.70	1.09	1.54	1.88	2.39	3.45			
[DBA]/*M*	0.125	0.205	0.325	0.425	0.525	0.635	0.735	0.830	0.940	1.025		
$10^5(k_A)_R/s^{-1}$	0.11	0.22	0.45	0.70	0.99	1.40	1.78	2.19	2.79	3.24		
[DiBA]/*M*	0.200	0.335	0.420	0.510	0.610	0.715	0.825	0.910	1.010			
$10^6(k_A)_R/s^{-1}$	0.28	0.49	0.58	0.72	0.86	1.02	1.18	1.28	1.44			
[TEA]/*M*	0.110	0.200	0.350	0.500	0.610	0.700	0.870	1.000	1.120			
$10^6(k_A)_R/s^{-1}$	1.11	2.01	3.53	5.12	6.18	7.14	8.82	10.2	11.3			

(a) The rate constants are accurate to within ± 3%.

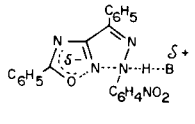
Table 2

Linear Regression Analysis of Apparent First-Order Constants $(k_A)_R$ for the Rearrangement of II-*Z* in Benzene at 40° in the Presence of Various Amines by the Equation $(k_A)_R = k_1[B] + k_2[B]^2$ (a)

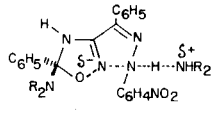
Amine	$10^5(k_1 \pm s_1)$	$10^5(k_2 \pm s_2)$	*r*	*n*	$10^5(k_A)_R$ (b)
PIP	−0.3 ± 1.2	285 ± 2	0.9997	12	285
DEA	−0.03 ± 0.07	12.1 ± 0.1	0.9996	11	12.1
DPA	0.46 ± 0.02	2.93 ± 0.03	0.9997	9	3.39
DBA	0.56 ± 0.01	2.54 ± 0.02	0.9998	10	3.10
DiBA	0.14 ± 0.01		0.9998	9	0.14
TEA	1.01 ± 0.01		0.9999	9	1.01

(a) The C.L. values for the significance of k_1 and k_2 are all better than 99.9%; s_1 and s_2 are standard deviations, respectively, of k_1 and k_2; *r* = correlation coefficient; *n* = number of experimental points. (b) Values calculated at [amine] = 1.0 *M*.

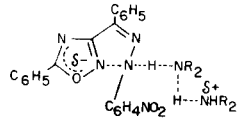
With TEA the unique observed reaction pathway requires only one mole of amine and this agrees with the mechanism proposed by us (1,5). In fact, a tertiary amine can only act as a general base which catalyzes the rearrangement by favouring the abstraction of the arylhydrazone hydrogen and can neither give an interaction



with 1,2,4-oxadiazole ring (1), *e.g.*, as the addition at the



C_5-N_4 bond proposed by Harsanyi (6), nor catalysis of catalysis (1,7).



Secondary amines with low SR (PIP and DEA) apparently show only the reaction pathway implying two moles of amines; increasing the SR (DPA and DBA) increases the role of the pathway implying one mole of amine (k_2/k_1 are 6.4 and 5.5, respectively, with DPA and DBA according to the increase of SR). Finally, the secondary amine with the highest SR (DiPA) recalls the behaviour of TEA. In fact, a high SR opposes the addition at the C_5-N_4 bond as well as the catalysis of catalysis.

In conclusion, the results collected in this work strongly support our previous hypothesis about the reaction mechanism (1).

EXPERIMENTAL

Synthesis and Purification of Compounds.

Compound II-*Z* (5a), compound III (5a), benzene (8) and the amines (9) were prepared and/or purified according to the methods reported.

Kinetic Measurements.

The kinetics were followed spectrophotometrically as previously indicated (1) by quenching the samples in benzene/acetic acid and measuring the disappearance of II-*Z* at the wavelength of its absorption maximum (398 nm, log ε 4.50), where III parctically does not absorb. Because

of the influence of light on the reactivity, the reaction vessels were wrapped in aluminum sheets.

Acknowledgement.

We thank the C.N.R. for support.

REFERENCES AND NOTES

(1) V. Frenna, N. Vivona, D. Spinelli and G. Consiglio, *J. Heterocyclic Chem.*, **17**, 861 (1980).

(2) On mononuclear heterocyclic rearrangements, see A. J. Boulton, A.R. Katritzky and A. M. Hamid, *J. Chem. Soc. C*, 2005 (1967); A. J. Boulton, "Lectures in Heterocyclic Chemistry", HeteroCorporation, Provo, Utah, 1973; A. S. Afridi, A. R. Katritzky and C. A. Ramsden, *J. Chem. Soc., Perkin Trans. I*, 315 (1976).

(3) H. K. Hall Jr., *J. Am. Chem. Soc.*, **79**, 5441, 5444 (1957).

(4) Obviously the basicity of the amines in water can only give rough information, if any, concerning their behaviour in benzene.

(5a) D. Spinelli, V. Frenna, A. Corrao and N. Vivona, *J. Chem. Soc., Perkin Trans. II*, 19 (1978); (b) D. Spinelli, A. Corrao, V. Frenna, N. Vivona, M. Ruccia and G. Cusmano, *J. Heterocyclic Chem.*, **13**, 357 (1976); D. Spinelli, V. Frenna, A. Corrao, N. Vivona and M. Ruccia, *ibid.*, **16**, 359 (1979).

(6) K. Harsanyi, *ibid.*, **10**, 957 (1973).

(7) J. F. Kirsch and W. P. Jencks, *J. Am. Chem. Soc.*, **86**, 833 (1964); A. Arcoria, E. Maccarone, G. Musumarra and G. A. Tomaselli, *Tetrahedron*, **31**, 2523 (1975).

(8) A. I. Vogel, "Practical Organic Chemistry", 3rd Ed., Longmans, London, 1961, p. 173.

(9) Amines, reagent degree, were all purified by standing on potassium hydroxide (24 hours) and twice fractionally distilled.