Mononuclear Heterocyclic Rearrangements. Part 10.[1] Kinetic Study of the Amine-catalysed Rearrangement of the *Z*-*p*-Nitrophenylhydrazone of 3-Benzoyl-5-phenyl-1,2,4-oxadiazole into 4-Benzoylamino-2-*p*-nitrophenyl-5-phenyl-1,2,3-triazole in Benzene

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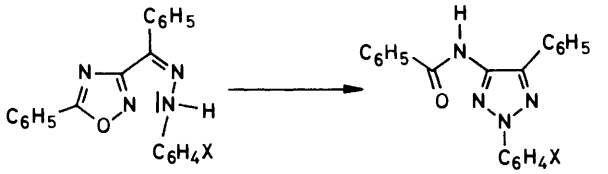
The kinetics of the title reaction have been measured in the presence of primary, secondary, and tertiary amines and of primary diamines. The following relationships have been observed: $k_A = k_{IV}[B]^3$ with primary amines and with 1,6-diaminohexane, $k_A = k_{III}[B]^2$ with secondary cyclic amines and the other primary diamines, and $k_A = k_{II}[B]$ with diazabicyclo[2.2.2]octane (DABCO). The reaction has also been studied in the presence of pairs of amines [butylamine (piperidine) and triethylamine (DABCO)], in which case 'mixed' terms such as k'_{IV} [BuA][DABCO]^2 and k'_{III}[PIP][DABCO] also occur. On the basis of the results the kinetic laws observed have been ascribed to catalysis of catalysis which depends on the nature and the structure of the amine used.

The *Z*-arylhydrazones of 3-acyl-1,2,4-oxadiazoles (I) rearrange into 4-acylamino-2-aryl-1,2,3-triazoles (II) in solution or by heating.[2] Recently we reported kinetic data[3] on the effect of some amines [piperidine (PIP), triethylamine (TEA), and other secondary amines] on the mononuclear heterocyclic rearrangement (m.h.r.)[2,4] of the *Z*-*p*-nitrophenylhydrazone of 3-benzoyl-5-phenyl-1,2,4-oxadiazole, (Ia), in benzene and showed that the effect of steric requirements (s.r.) of the amine can dominate over its basicity in determining both the reactivity and the catalysis law (linear or quadratic dependence of the rate constant on amine concentration).

In order to gain further insight into the mechanism of catalysis by amines, with special regard to the catalysed reaction pathways requiring more than one molecule of amine, we have collected data on the m.h.r. of the above phenylhydrazone in benzene in the presence of 20 amines: seven secondary cyclic amines, seven primary amines, one tertiary amine, and five primary diamines. Some experiments in the presence of pairs of amines [PIP and TEA; PIP and diazabicyclo[2.2.2]octane (DABCO); n-butylamine (BuA) and TEA; BuA and DABCO] have also been performed.



(I) (II)

a; X = *p*-NO_2
b; X = H

Results

For each amine the apparent first-order kinetic constant for the rearrangement, k_A, increases with increasing amine concentration (Table 1). Depending on the class of amines, different catalysis laws have been observed. As expected on account of the uncatalysed m.h.r. of the phenylhydrazone of 3-benzoyl-5-phenyl-1,2,4-oxadiazole, (Ib), in benzene[5] and of the rate-depressing effect of the *p*-nitro-group,[6] the uncatalysed reaction pathway for (Ia) escaped detection.

Secondary Cyclic Amines.—The secondary cyclic amines are characterized by different s.r. and basicities as a function of the ring size [pyrrolidine (PYR), PIP, hexamethyleneimine (HEXA), and heptamethyleneimine (HEPTA)] or of the endocyclic heteroatoms [morpholine (MOR), piperazine (PIZ), and *N*-methylpiperazine (MPIZ)], or of the substituent at the carbon atom adjacent to the basic nitrogen atom [2-methylpiperidine (MPIP)]. Nevertheless, these amines all give the same catalysis law † (see Table 2) as piperidine [equation (1)].[5,‡]

$$k_A = k_{III}[B]^2 \quad (1)$$

Based on the large range of association constants, K_B, for the formation of ion-pairs between these amines and 2,4-dinitrophenol in benzene (*e.g.*, K_{MOR} 70 and K_{PYR} 7 630),[7] it is possible to attempt a linear free energy correlation between log k_A and log K_B. The good correlation obtained for all the secondary cyclic amines but 2-methylpiperidine (Figure a; slope 1.45, *n* 7, *r* 0.986) shows that similar factors (electronic as well as steric) affect both the basicities and the catalytic efficiencies of the amines.

Although in the case of non-cyclic secondary amines the s.r. can determine not only the reactivity for m.h.r. but also the catalytic pattern [for example, di-n-propylamine and di-isobutylamine catalyse the m.h.r. of (Ia) according to dif-

† k_{II}, k_{III}, and k_{IV} refer, respectively, to the reaction pathways involving one molecule of substrate, (Ia) and one, two, or three molecules of amine.

‡ While the piperidine-catalysed m.h.r. of (Ia) follows equation (1), the corresponding reaction of (Ib) obeys equation (4), though with a high k_{III}/k_{II} ratio. This different behaviour can be reasonably related to the different positions, along the reaction co-ordinate, of the transition states involved; thus the later transition state for (Ia) requires two molecules of piperidine whereas the earlier transition state for (Ib) can involve one or two molecules of piperidine.

Table 1. Apparent first-order kinetic constants [a] for the rearrangement (Ia) ⟶ (IIa), k_A, in benzene at 313.15 K in the presence of various amines

[Morpholine]/M	0.190	0.290	0.465	0.561	0.670	0.802	0.910	1.00	1.12	1.26		
$10^6\ k_A/s^{-1}$	0.380	0.842	2.28	3.25	4.64	6.75	8.58	10.3	13.1	16.6		
[1-Methylpiperazine]/M	0.200	0.280	0.370	0.450	0.540	0.610	0.690	0.770	0.900	0.990		
$10^4\ k_A/s^{-1}$	0.101	0.210	0.354	0.512	0.748	0.961	1.23	1.53	2.12	2.55		
[Piperazine]/M	0.080	0.155	0.210	0.265	0.335	0.385	0.425	0.477	0.565			
$10^4\ k_A/s^{-1}$	0.172	0.670	1.18	1.87	3.03	4.01	4.94	6.16	8.73			
[Heptamethyleneimine]/M	0.122	0.212	0.320	0.429	0.592	0.698	0.790	0.892	1.02			
$10^4\ k_A/s^{-1}$	0.156	0.480	1.09	1.96	3.68	5.26	6.55	8.30	10.9			
[2-Methylpiperidine]/M	0.155	0.260	0.375	0.518	0.648	0.805	0.895	1.01	1.12			
$10^5\ k_A/s^{-1}$	0.554	1.67	3.37	6.45	9.93	15.3	18.7	24.0	29.8			
[Hexamethyleneimine]/M	0.105	0.220	0.325	0.410	0.515	0.600	0.700	0.800	0.920	0.990		
$10^4\ k_A/s^{-1}$	0.212	0.983	2.13	3.28	5.15	6.94	9.42	12.6	16.5	19.0		
[Pyrrolidine]/M	0.070	0.102	0.170	0.235	0.360	0.428	0.480	0.539	0.600			
$10^4\ k_A/s^{-1}$	0.586	1.28	3.45	6.60	15.2	21.6	27.0	34.1	42.4			
[Benzylamine]/M	0.120	0.220	0.348	0.405	0.514	0.588	0.720	0.807	0.920	1.01		
$10^5\ k_A/s^{-1}$	0.011	0.068	0.268	0.421	0.854	1.28	2.35	3.30	4.91	6.47		
[2-Phenylethylamine]/M	0.120	0.217	0.330	0.410	0.500	0.618	0.760	0.817	0.924	1.02		
$10^5\ k_A/s^{-1}$	0.065	0.393	1.37	2.58	4.78	9.19	16.9	20.6	30.4	41.1		
[3-Phenylpropylamine]/M	0.110	0.205	0.313	0.395	0.490	0.575	0.705	0.800	0.935	1.00		
$10^5\ k_A/s^{-1}$	0.093	0.606	2.21	4.42	8.25	13.6	25.1	36.8	59.0	70.4		
[n-Propylamine]/M	0.120	0.200	0.270	0.380	0.465	0.545	0.645	0.710	0.790	0.860	0.915	0.990
$10^4\ k_A/s^{-1}$	0.017	0.084	0.202	0.593	1.08	1.80	2.96	3.97	5.39	7.03	8.59	10.8
[n-Butylamine]/M	0.089	0.150	0.210	0.280	0.402	0.480	0.562	0.649	0.740	0.820	0.910	1.04
$10^4\ k_A/s^{-1}$	0.011	0.050	0.142	0.331	0.975	1.68	2.74	4.14	6.04	8.40	11.4	17.1
[n-Pentylamine]/M	0.094	0.190	0.260	0.370	0.470	0.540	0.640	0.710	0.795	0.865	0.935	1.03
$10^4\ k_A/s^{-1}$	0.014	0.112	0.293	0.857	1.67	2.61	4.31	5.97	8.29	10.8	13.6	18.2
[n-Hexylamine]/M	0.100	0.200	0.292	0.395	0.495	0.550	0.635	0.710	0.795	0.935	1.00	
$10^4\ k_A/s^{-1}$	0.018	0.141	0.433	1.06	2.09	2.87	4.38	6.20	8.68	14.1	17.3	
[1,2-Diaminoethane]/M	0.050	0.075	0.095	0.140	0.200	0.275	0.310	0.420	0.470	0.535		
$10^4\ k_A/s^{-1}$	0.255	0.564	1.08	2.47	5.16	9.59	12.8	23.1	29.3	37.5		
[1,3-Diaminopropane]/M	0.040	0.060	0.075	0.093	0.137	0.175	0.225	0.255	0.287			
$10^4\ k_A/s^{-1}$	0.386	0.851	1.35	2.09	4.76	7.64	12.7	16.1	20.7			
[1,4-Diaminobutane]/M	0.030	0.062	0.086	0.112	0.140	0.186	0.200	0.230	0.260			
$10^4\ k_A/s^{-1}$	0.282	1.24	2.34	4.01	6.27	11.0	12.8	16.9	21.5			
[1,5-Diaminopentane]/M	0.026	0.045	0.060	0.072	0.096	0.113	0.138	0.165	0.198	0.226	0.258	
$10^5\ k_A/s^{-1}$	0.680	2.03	3.47	5.24	9.23	12.8	18.9	27.3	38.4	50.9	66.9	
[1,6-Diaminohexane]/M	0.120	0.168	0.205	0.266	0.315	0.350	0.380	0.452	0.500			
$10^4\ k_A/s^{-1}$	0.361	1.00	1.81	3.98	6.45	9.08	11.6	19.5	26.3			
[DABCO]/M	0.0202	0.0450	0.105	0.145	0.197	0.250						
$10^5\ k_A/s^{-1}$	0.125	0.251	0.611	0.867	1.17	1.49						

[a] The rate constants are accurate to within ±3%. [(Ia)] 1.5—2.0 × 10^{-4}M. At $\lambda_{max.}$ 398 nm, log ε 4.50 ± 0.02.

ferent catalysis laws *], for a cyclic secondary amine the influence of a methyl group α to the basic centre is not so dramatic: in fact the only effect observed here is a lowering of reactivity. It is well known that dialkylamines are sterically more hindered than secondary cyclic amines, probably because of the rigidity of the six-membered ring structure (chair conformation): thus a methyl group controls only the selection of conformation in order to minimize, in particular, interactions with the 'substituent' lone pair on nitrogen.

Primary Amines.—All the amines tested obey equation (2) (see Table 2), and an excellent linear free energy correlation

$$k_A = k_{IV}[B]^3 \qquad (2)$$

exists between log k_A and log K_B (Figure b; slope 1.59, *n* 7, *r* 0.996). It is noteworthy that although secondary cyclic amines and primary amines obey different kinetic laws, they show similar β values.

Primary Diamines.—All the diamines studied, with the exception of 1,6-diaminohexane, follow the catalysis law expressed by equation (1) (see Table 2). 1,6-Diaminohexane behaves like the primary amines [equation (2)] but although it has much the same basicity in water † as the n-alkylamines, it displays more catalytic efficiency ‡ [$(k_{III})_{diamine}/(k_{III})_{alkylamines}$ 12—30].

DABCO.—This tertiary amine behaves like TEA [3] and obeys equation (3) (see Table 2). DABCO and TEA show

$$k_A = k_{II}[B] \qquad (3)$$

similar basicities in benzene but the first is the more efficient catalyst [$(k_{II})_{DABCO}/(k_{II})_{TEA}$ 6].

* This fact demonstrates the critical role played in non-cyclic amines by branching at the carbon atom β to nitrogen.

† Measurements of K_B for ion pairing of diamines with 2,4-dinitrophenol in benzene could not be carried out because of experimental difficulty.[7]

‡ This behaviour of diamines has some precedents: *e.g.* in the aminolysis of *p*-nitrophenyl acetate [8] or of benzylpenicillin,[9] the diamines are better catalysts than other amines of comparable basicity. This has been interpreted by taking into account intramolecular hydrogen-bond formation. Moreover, while in the aminolysis and amidinolysis of *p*-nitrophenyl acetate the primary amines give third-order kinetics (second order in amine), diamines or benzamidine show second-order kinetics (first order in amine).

Table 2. Linear correlations [a] for the rearrangement (Ia) ⟶ (IIa) in benzene at 313.15 K in the presence of various amines

B	Equation $k_A/[B] = k_{II} + k_{III}[B]$ $10^4(k_{II} \pm s_{II})$	$10^4(k_{III} \pm s_{III})$	r	n	log K_B [b]
Piperidine [c]	−0.06 ± 0.12	28.6 ± 0.2	0.9997	12	3.65
Diethylamine [c]	0.00 ± 0.01	1.21 ± 0.01	0.9997	11	3.18
Di-n-propylamine [c]	0.0474 ± 0.0021	0.291 ± 0.003	0.9995	9	2.97
Di-n-butylamine [c]	0.0560 ± 0.0012	0.254 ± 0.002	0.9998	10	2.94
Morpholine	0.00 ± 0.00	0.105 ± 0.001	0.9998	10	1.85
1-Methylpiperazine	−0.01 ± 0.01	2.61 ± 0.02	0.9997	10	2.82
Piperazine [d]	−0.06 ± 0.07	27.3 ± 0.2	0.9998	9	3.29
Heptamethyleneimine	0.06 ± 0.06	10.5 ± 0.1	0.9997	9	3.30
2-Methylpiperidine	0.01 ± 0.01	2.35 ± 0.02	0.9998	9	3.41
Hexamethyleneimine	0.10 ± 0.09	19.3 ± 0.2	0.9998	10	3.48
Pyrrolidine	0.44 ± 0.14	117 ± 0	1.0000	9	3.88
1,2-Diaminoethane	−1.68 ± 0.38	135 ± 1	0.9997	10	
1,3-Diaminopropane	−0.73 ± 0.31	253 ± 2	0.9998	9	
1,4-Diaminobutane	0.00 ± 0.15	319 ± 1	1.0000	9	
1,5-Diaminopentane	−0.02 ± 0.10	99.8 ± 0.7	0.9998	11	
	Equation $k_A/[B]^2 = k_{III} + k_{IV}[B]$				
B	$10^4(k_{III} \pm s_{III})$	$10^4(k_{IV} \pm s_{IV})$	r	n	log K_B [b]
Benzylamine	0.00 ± 0.00	0.626 ± 0.001	1.0000	10	1.23
2-Phenylethylamine	−0.02 ± 0.02	3.87 ± 0.03	0.9998	10	1.71
3-Phenylpropylamine	−0.01 ± 0.04	7.15 ± 0.06	0.9997	10	1.85
n-Propylamine	−0.21 ± 0.04	11.3 ± 0.1	0.9998	12	2.00
n-Butylamine	0.00 ± 0.05	15.2 ± 0.1	0.9998	12	2.04
n-Pentylamine	−0.04 ± 0.06	16.6 ± 0.1	0.9998	12	2.13
n-Hexylamine	0.04 ± 0.03	17.2 ± 0.1	1.0000	11	2.16
1,6-Diaminohexane	−0.24 ± 0.50	211 ± 2	0.9998	9	
	Equation $k_A = k_{II}[B] + i$				
B	$10^5(k_{II} \pm s_{II})$	$i \pm s_i$	r	n	log K_B [b]
Di-isobutylamine [c]	0.142 ± 0.001	0.00 ± 0.00	0.9997	9	
Triethylamine [c]	1.01 ± 0.00	0.00 ± 0.00	0.9999	9	3.43
DABCO	5.99 ± 0.05	−0.01 ± 0.01	0.9999	6	3.39

[a] s_{II}, s_{III}, and s_{IV} are the standard deviations of the regression parameters k_{II}, k_{III}, and k_{IV}, respectively; n is the number of experimental points; r is the correlation coefficient; i is the intercept of the regression line with the ordinate [B] = 0. All the correlations are statistically significant at better than the 0.1% level. [b] See text. Data from ref. 7. [c] Data from ref. 3. [d] Values corrected for statistical factor.

Discussion

A previous study of the m.h.r. of (Ia) in the presence of some secondary amines [PIP, diethylamine (DEA), di-n-propylamine (DPA), di-n-butylamine (DBA), and di-isobutylamine (DiBA)] and of TEA in benzene has shown a second-order dependence on the amine concentration in the case of PIP, DEA, DPA, or DBA.[3] This was related * to interaction of the amine with the C(5)–N(4) bond of the 1,2,4-oxadiazole ring (which favours the rearrangement) or, alternatively, to catalysis of catalysis.

Bearing in mind the results obtained for the m.h.r. of (Ib) in dioxan–water [10] and in methanol [1] (which show the occurrence of general base catalysis) and those for a number of solvents,[1] we propose the following rationalization of the catalysis of m.h.r. in benzene operated by the 26 amines studied.

For DABCO, TEA, and DiBA (two tertiary amines and a secondary amine with high s.r.) only one reaction pathway has been observed, *i.e.* that requiring one molecule of amine [equation (3)]: in this case the amine acts as a general base favouring the rearrangement by abstraction of the hydrogen of arylhydrazone. Since the cyclic secondary amines and DEA show a reaction pathway requiring two molecules of amine [equation (1)], the secondary amines with an s.r. intermediate between DEA and DiBA follow both reaction pathways [equation (4)].[3]

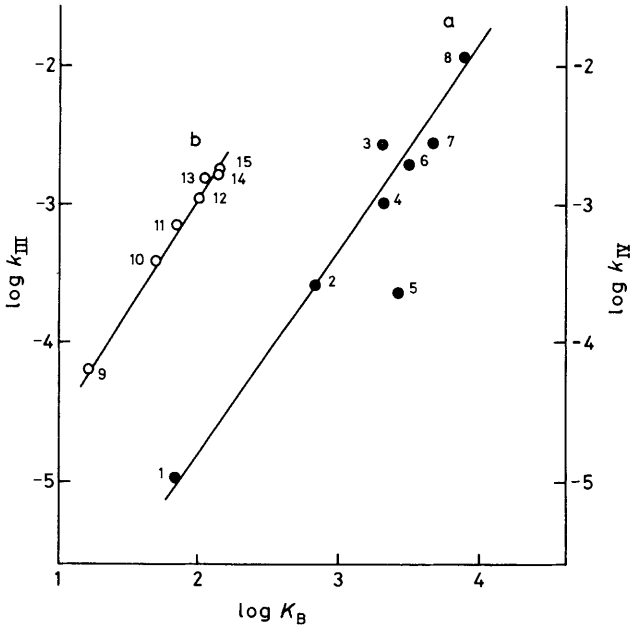
$$k_A = k_{II}[B] + k_{III}[B]^2 \qquad (4)$$

The catalysis mechanism for primary amines involves three molecules of amine. The need for the third molecule of amine agrees with catalysis of catalysis depending on the number of hydrogen atoms bound to nitrogen. Thus, when the base is a secondary amine catalysis requires a second molecule of amine; when it is a primary amine two other molecules of amine are required. Of course the tertiary amines and the amines with high s.r. cannot involve additional base molecules.

Indeed, the behaviour of primary amines might also be accounted for on the grounds of an interaction with the 1,2,4-oxadiazole ring at the C(5)–N(4) bond with the formation of a six-membered ring without charge separation as depicted in (V; R^1 = n-alkyl, R^2 = H). Since this effect should also operate in the case of secondary amines [(V; $R^1 = R^2$ = n-alkyl)] and it is not observed, we do not favour the above interpretation.

If one considers the possibility of a hydrogen-bond inter-

* We have excluded the possibility that the amine behaves as a dimer because, in other reactions catalysed by aliphatic secondary amines, (*e.g.* aromatic nucleophilic substitutions or proton abstraction reactions), this kind of dependence on amine concentration is not usually observed.



Brønsted-type plot of log k_{III} or log k_{IV} *versus* log K_B for the rearrangement (Ia) ⟶ (IIa) in the presence of various secondary cyclic amines (●) and primary amines (○), respectively. (1, MOR; 2, MPIZ; 3, PIZ; 4, HEPTA; 5, MPIP; 6, HEXA; 7, PIP; 8, PYR; 9, benzylamine; 10, 2-phenylethylamine; 11, 3-phenylpropylamine; 12, n-propylamine; 13, BuA; 14, n-pentylamine; 15, n-hexylamine)

quence we have observed that the reactivity increases with chain lengthening up to 1,4-diaminobutane and then is markedly reduced for 1,5-diaminopentane. 1,6-Diaminohexane does not behave as the other diamines examined and therefore it acts as a primary amine following equation (2).

Catalysis by Pairs of Amines.—The kinetic data discussed hitherto seems better understandable on the basis of catalysis of catalysis rather than of an addition to the C(5)–N(4) bond. However, in order to obtain definitive evidence we have studied the m.h.r. of (Ia) in the presence of the following pairs of amines at various concentrations: PIP and DABCO, PIP and TEA, BuA and DABCO, and BuA and TEA.

The presence of two catalysing amines could make operative the kinetic laws (5) and (6), where some of the catalytic constants can occasionally give a negligible contribution. A stepwise multiple linear regression analysis [10] of the kinetic

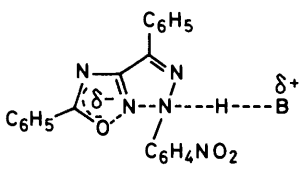
$$k_A = k_{II}[TA] + k_{III}[PIP]^2 + k'_{III}[TA][PIP] \quad (5)$$

$$k_A = k_{II}[TA] + k_{IV}[BuA]^3 + k'_{IV}[BuA][TA]^2 + k''_{IV}[BuA]^2[TA] \quad (6)$$

TA = DABCO or TEA

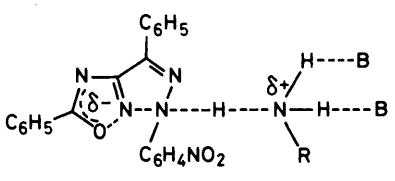
data* according to equations (5) and (6) has furnished the results of equations (7)—(9).

$$10^4 k_A = (0.66 \pm 0.25)[DABCO] + (28.5 \pm 0.07)[PIP]^2 + (48.7 \pm 1.0)[DABCO][PIP] \quad (7)$$
(i 0.00 ± 0.03, n 31, R 0.999 94)



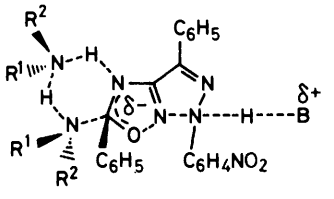
(III)

B = DABCO, TEA, or DiBA



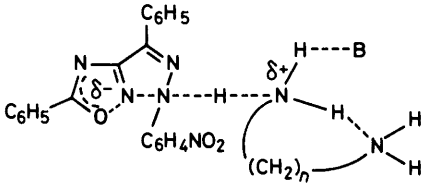
(IV)

B = RNH_2 or $H_2N(CH_2)_6NH_2$



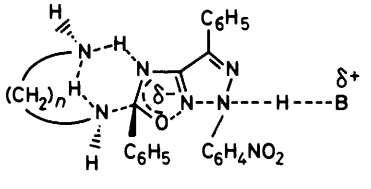
(V)

B = R^1R^2NH



(VI)

B = $H_2N(CH_2)_nNH_2$



(VII)

B = $H_2N(CH_2)_nNH_2$

action between the two amino-groups of the same molecule, the relevant catalysis mechanisms for primary diamines should parallel those of primary amines, as in (VI) and (VII).

An examination of molecular models shows that the probability of 'internal' interaction in (VI) or in (VII) increases on going from 1,2-diaminoethane to 1,4-diaminobutane, through 1,3-diaminopropane, decreases in 1,5-diaminopentane, and is very low with 1,6-diaminohexane. In conse-

$$10^4 k_A = (0.61 \pm 0.08)[DABCO] + (15.2 \pm 0.0)[BuA]^3 + (35.9 \pm 1.9)[BuA][DABCO]^2 + (40.0 \pm 0.8)[BuA]^2[DABCO] \quad (8)$$
(i 0.00 ± 0.01, n 34, R 0.999 98)

* The kinetic constants used in correlations are those shown in Tables 1 and 3.

Table 3. Apparent first-order kinetic constants [a] for the rearrangement (Ia) ⟶ (IIa), k_A, in benzene at 313.15 K in the presence of pairs of amines

[DABCO]/M [b]	0.0251	0.0502	0.0730	0.104	0.150	0.200	0.245	0.280	
$10^4k_A/s^{-1}$	0.368	0.468	0.570	0.719	0.983	1.32	1.65	1.95	
[n-Butylamine]/M [c]	0.0830	0.152	0.202	0.264	0.324	0.388	0.452	0.515	
$10^4k_A/s^{-1}$	0.212	0.424	0.641	1.01	1.52	2.28	3.15	4.24	
[Triethylamine]/M [d]	0.0620	0.124	0.248	0.412	0.570	0.720	0.865	1.04	
$10^5k_A/s^{-1}$	1.65	1.82	2.18	2.65	3.06	3.46	3.85	4.42	
[n-Butylamine]/M [e]	0.0520	0.125	0.208	0.270	0.354	0.416	0.478	0.520	
$10^4k_A/s^{-1}$	0.0304	0.0717	0.210	0.406	0.843	1.32	1.96	2.49	
[DABCO]/M [f]	0.0224	0.0520	0.102	0.156	0.208	0.240	0.280		
$10^4k_A/s^{-1}$	1.47	1.85	2.33	2.94	3.49	3.84	4.28		
[Piperidine]/M [g]	0.0440	0.0950	0.202	0.310	0.420	0.550			
$10^4k_A/s^{-1}$	0.344	0.790	2.23	4.33	7.17	11.5			
[Triethylamine]/M [h]	0.052	0.104	0.210	0.320	0.405	0.505			
$10^4k_A/s^{-1}$	1.98	1.96	1.95	2.00	2.01	2.04			
[Triethylamine]/M [i]	0.051	0.102	0.204	0.325	0.480	0.605	0.760	0.880	1.02
$10^5k_A/s^{-1}$	6.14	6.21	6.25	6.09	6.15	6.10	6.14	6.25	6.28

[a] As in Table 1. [b] At [n-Butylamine] 0.262M. [c] At [DABCO] 0.155M. [d] At [n-Butylamine] 0.210M. [e] At [Triethylamine] 0.252M. [f] At [Piperidine] 0.208M. [g] At [DABCO] 0.105M. [h] At [Piperidine] 0.262M. [i] At [Piperidine] 0.145M.

$$10^4k_A = (0.096 \pm 0.013)[TEA] + (15.2 \pm 0.0)[BuA]^3 + (4.68 \pm 0.22)[BuA]^2[TEA] \quad (9)$$
$$(i\ 0.00 \pm 0.01,\ n\ 37,\ R\ 0.999\ 98)$$

The different contribution to the mixed terms from DABCO and TEA can be easily rationalized by considering that general base catalysis is subject to steric hindrance. As a consequence the tertiary amines can be effective catalysts only if the steric interactions are low. As a matter of fact, while DABCO is present in all possible mixed terms, there is no such term as [TEA][PIP] * and TEA is present only in a term depending on two molecules of BuA and one molecule of TEA.

Among the mixed terms the occurrence of a term such as k'_{IV}[BuA][DABCO]^2 cannot be easily accounted for by addition to the C(5)–N(4) bond of the 1,2,4-oxadiazole ring and therefore the catalysis of catalysis mechanism is strongly supported.

Conclusion

The data of this and the preceding paper strongly support a general base-catalysed mechanism for the m.h.r. of aryl-hydrazones (Ia and b) of 3-benzoyl-5-phenyl-1,2,4-oxadiazole. Catalysed pathways requiring more than one molecule of amine have been definitely established in the framework of catalysis of catalysis.

Experimental

Synthesis and Purification of Compounds.—Compounds (Ia) and (IIa) [6] and benzene [11] were prepared and/or purified according to the methods reported. Amines (reagent standard) were all purified by standing over potassium hydroxide (24 h) and twice fractionally distilled.

Kinetic Measurements.—The kinetics were followed spectrophotometrically as previously described.[3]

* This is evident from a consideration of data in Table 3 which shows that the m.h.r. of (Ia) catalysed by piperidine is unaffected by the addition of TEA.

Acknowledgements

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