

HYDROLYSIS KINETICS AND MECHANISM OF ACYL-1,3-DIPHENYLTRIAZENES

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The hydrolysis rate constants of 3-(N-methylcarbamoyl)-1,3-diphenyltriazene (*I*), 3-(N-phenylcarbamoyl)-1,3-diphenyltriazene (*II*) and 3-acetyl-1,3-diphenyltriazene (*III*) have been determined in aqueous media within pH 0 to 14, H_0 to 3 and H_- to 15. The hydrolyses at $pH < 2$ and $pH > 11$ show specific acid and base catalysis, respectively, whereas within pH 2 to 11 non-catalyzed hydrolysis takes place. Activation parameters of the non-catalyzed and catalyzed hydrolyses have been determined. Quantum-chemical calculation of 3-carbamoyltriazene (*IV*) has been carried out by the MINDO/2 method. Hydrolysis mechanism of the studied compounds is suggested for the non-catalyzed, specific acid catalyzed and specific base catalyzed hydrolysis.

The ureas *I*, *II* and amide *III* investigated in the present paper are described synthetically elsewhere¹⁻⁴. The urea *I* exhibits herbicidal activity¹, the urea *II* was proposed as a carcinostatic² and additive to polymers³. So far, however, the practically important hydrolytic stability has not been studied. Molecules of the compounds *I-III* contain several reactive centres, so that mechanism of hydrolytic decomposition can be inferred from analogy with similar types of compounds. In acid medium the hydrolysis mechanism of the compounds *I-III* can resemble that of 1,3-diphenyltriazene⁵⁻⁹ or that of ureas¹⁰⁻¹³ or amides¹⁴⁻¹⁹. In case of the specifically base catalyzed hydrolysis two kinetically indistinguishable mechanisms can be considered, *viz.* $B_{Ac}2$ (refs^{10,14,15,20-31}) and $ElcB$ (refs³²⁻³⁹). There is, however, no analogy for mechanism of the non-catalyzed hydrolysis.

The aim of this work was to measure hydrolysis kinetics of the compounds *I-III* in acid, neutral and alkaline media and to suggest mechanisms of the respective reactions.

EXPERIMENTAL

Reagents. The ureas *I* and *II* were prepared by reaction of 0.1 mol 1,3-diphenyltriazene dissolved in 50 ml n-heptane with 0.1 mol methylisocyanate and phenylisocyanate, respectively. After one hour standing at room temperature the separated solid was crystallized from light petroleum (m.p. 103–105°C with decomposition in accord with ref.¹; yield 71.6%). The compound *II* was crystallized from cyclohexane-dioxane mixture (10 : 1) (m.p. 123–125°C with decom-

position, ref.² 124–125°C; yield 63·8%). The amide *III* was prepared⁴ by five hours boiling of 0·5 mol 1,3-diphenyltriazene with 0·6 mol acethanhydride in 300 ml ether, yield 63·3%. Crystallization from chloroform–ether mixture (1 : 10) (m.p. 127–129°C, ref.⁴ 129–130°C).

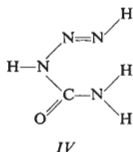
Kinetic measurements. 2 ml aqueous buffer solution (or sulphuric acid or sodium hydroxide of required concentration) was tempered in a 1 cm cell in Unicam SP 800 B or Specord UV VIS spectrophotometer at $25\cdot0 \pm 0\cdot1^\circ\text{C}$ for 5 min. Then 2–5 μl 0·2M respective substrate solution in dioxane was injected, and the mixture in the cell was mixed. Absorbance changes were followed up to 2–3 reaction half-lives at wavelength of the maximum of main absorption band (λ , nm: *I* = 290, *II* = 290, *III* = 286). Experimental points of the kinetics were processed according to our optimization program⁴⁰ to give values of pseudomonomolecular rate constant k_{obs} (Eq. (1)) and the absorbance values at $t = 0$ and $t = \infty$. The pH values were measured with a PHM-4 apparatus. The values H_0 and H_- were taken from refs^{41,42} according to the acid and base concentrations found titrimetrically. The activation parameters were determined at 5–7 temperature values within 25 to 55°C, the pH's of the hydrolyzing media being *I*: 1·00, 3·56, 13·48; *II*: 0·15, 3·56, 12·16; *III*: 1·10, 3·56, 12·46.

Identification of products. The hydrolysis products of the urea *II* in neutral medium were identified as follows: 0·02 g *II* was dissolved in 10 ml dioxane and the solution was poured into 50 ml 20% aqueous dioxane. The mixture was left to stand at room temperature 4 h. The separated solid was washed with water several times and dried. M.p. 239°C, mixed m.p. with *N,N'*-diphenyl-urea 238°C.

5 ml buffer pH 6·84 was mixed with 0·2 μl dimethylaniline in a 2 cm cell; the mixture was shaken and tempered at 25·0°C. Thereto, 1 μl 0·1M solution of the urea *I* or amide *III* in dioxane was added, and absorbance increase of the azo dyestuff formed was followed (λ 445 nm). After the reaction was finished, the dyestuff was extracted in ether and identified by chromatographical comparison (Silufol) with authentic 4-(*N,N*-dimethylamino)azobenzene.

10 μl 0·1M solution of the urea *II* in dioxane was injected into 5 ml 0·1M solution of 4-(*N,N*-dimethylamino)benzaldehyde in 1M- H_2SO_4 tempered at 25·0°C, whereupon the decomposition kinetics and electronic spectrum of the products were measured. The experiment was repeated with 10 and 20 μl 0·1M aniline solution in dioxane, and spectrum of the product was compared with that of the above kinetic experiment.

Quantum-chemical calculations. Due to bad convergency of the MINDO/2 method in calculation of the urea *I* we chose a simpler model — 3-carbamoyltriazene (*IV*) — for the calculation. The parametrization by Dewar^{43–45} and standard bond lengths (pm: (N=N) = 125, (N–N) = 134, (N–C) = 138, (N–H) = 102, (C=O) = 122) (ref.⁴⁵) and bond angles (120°) were used. The molecule was considered planar with the conformation *IV*.



RESULTS AND DISCUSSION

All the acceptable mechanisms fit Eq. (1) in which $[S]$ means actual concentration of the substrate. Fig. 1 gives pH dependence of the rate constants k_{obs} of the compounds *I–III*. The experimental points are interlined by the curve which can be described by Eq. (2), where k_{H} and k_{OH} are composed constants.

$$v = k_{\text{obs}}[S] \quad (1)$$

$$k_{\text{obs}} = k_{\text{H}}a_{\text{H}^+} + k_0 + k_{\text{OH}}K_{\text{W}}/a_{\text{H}^+} \quad (2)$$

The term $k_{\text{H}}a_{\text{H}^+}$ concerns specific acid catalysis, the second and the third terms expressing the contributions of the non-catalyzed hydrolysis and specific base catalysis, respectively. Values of the constants of Eq. (2) were obtained by statistical treatment of experimental results (Table I).

Hydrolysis in Acid Medium

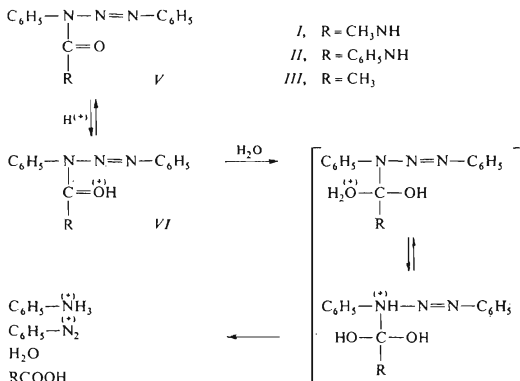
Several mechanisms can operate in specifically acid catalyzed hydrolysis of the ureas *I* and *II* and amide *III*. The first one described with ureas^{10–13} and amides^{14–19} is characterized by protonation of oxygen of carbonyl groups, subsequent attack by water, and decomposition of the formed tetrahedral intermediate (Scheme 1). The second mechanism consists in spontaneous decomposition of the substrate which also is protonated at oxygen of the carbonyl group (*VI*) and subsequent tautomerization (Scheme 2). The last given mechanism is analogous to that of acid catalyzed hydrolysis of triazenes^{7–9} and cannot be differentiated from the second mechanism kinetically or by products (Scheme 3).

TABLE I

Rate Constants of Eq. (2) for Compounds *I–III* in Water at 25°C

Constant	<i>I</i>	<i>II</i>	<i>III</i>
$k_{\text{H}} 10^3, \text{l mol}^{-1} \text{s}^{-1}$	5.72	2.75 ^a	34.5
$k_0 10^4, \text{s}^{-1}$	5.96	29.2	15.8
$k_{\text{OH}} 10^2, \text{l mol}^{-1} \text{s}^{-1}$	0.691	88.4	172

^a Slope of section of the pH-profile $\alpha = 0.728$, a statistically significant difference from $\alpha = 1$.



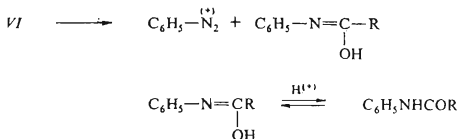
SCHEME 1

The first suggested mechanism is indirectly excluded by the fact that aniline was proved among the hydrolysis products of the urea *II*. The same conclusion also follows from the activation entropies ΔS^\ddagger (Table II) which are positive (*II* and *III*) or small and negative (*I*) in contrast to the high negative values found with urea¹⁰ ($-58.6 \text{ J mol}^{-1} \text{ K}^{-1}$) or benzamide¹⁴ ($-61.5 \text{ J mol}^{-1} \text{ K}^{-1}$, 60% ethanol). In the two latter cases the first type of mechanism is significant.

TABLE II

Activation Parameters of Hydrolysis of the Compounds *I–III* in Aqueous Neutral, Acid and Alkaline Media at 25.0°C

Parameter	Compound	Acid	Neutral	Alkaline
ΔH^\ddagger , kJ mol ⁻¹	<i>I</i>	80.03 ± 2.26	89.40 ± 2.13	96.98 ± 2.05
	<i>II</i>	97.82 ± 1.59	80.57 ± 1.51	82.08 ± 4.94
	<i>III</i>	84.09 ± 2.89	76.59 ± 1.72	39.09 ± 1.67
ΔS^\ddagger , J mol ⁻¹ K ⁻¹	<i>I</i>	-23.44 ± 7.41	-8.16 ± 6.78	39.47 ± 6.66
	<i>II</i>	23.10 ± 4.69	-23.23 ± 4.77	30.89 ± 16.03
	<i>III</i>	80.45 ± 9.33	-41.98 ± 5.48	-111.92 ± 5.48



SCHEME 2

The quantum-chemical calculation of the molecule *IV* by the MINDO/2 method provided, among others, information on distribution of electron density represented by orbital population and total charge (Table III only gives the p_z populations independent of geometry). If the presumption is accepted that the electron distribution is not qualitatively changed by the structural simplification carried out, then oxygen atom of the carbonyl group appears to be most easily protonated (the same is true in calculation of urea by the PPP method⁴⁶). This result agrees with the first two mechanisms (Schemes 1 and 2). As compared with amides and ureas, the hydrolysis of the investigated compounds proceeds at milder conditions in spite of the fact that the presence of the electron-acceptor phenylazo group lowers basicity (pK: N-methyl-

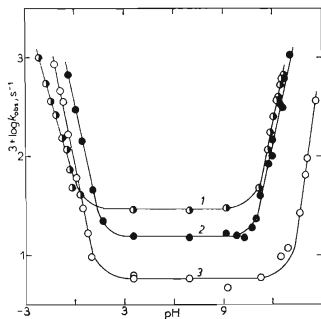


FIG. 1
pH Dependence of Logarithm of Hydrolysis Rate Constants of the Compounds *I*, *II*, *I* and *III* 2 at 25.0°C

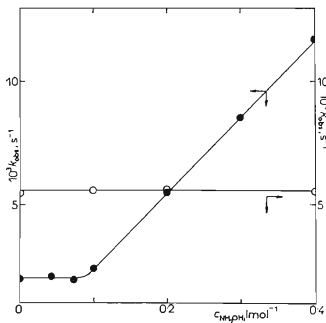
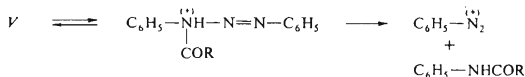


FIG. 2
Dependence of Hydrolysis Rate Constants of the Compounds *I* and *III* on Hydroxylamine Concentration

pH = 9.70–10.05; $I = 1.0$; $c_I = 1.0 \cdot 10^{-4} M$; $c_{III} = 5.9 \cdot 10^{-5} M$; $I \circ$, $III \bullet$.

acetamide⁴⁷ - 1.00; ethyl N-methylcarbamate⁴⁸ - 2.72; N-methylbenzamide⁴⁹ - 1.47). A possible explanation lies in high reactivity of the protonated substrate, spontaneous decomposition being more likely (Schemes 2 and 3).



SCHEME 3

In all the mechanisms discussed the solvent (water) acts as solvating medium of the reactants and, in the first case (Scheme 1), as a reactant as well. Participation of water in the activated complex could not be proved by measurements in concentrated acids (water activity is lowered) due to disappearance of the bands useful for kinetic measurements from the electronic spectrum.

Hydrolysis in Neutral Region

Among the hydrolysis products of the urea *I* and amide *III* diazonium salt was proved by azo coupling, the hydrolysis products of the urea *II* contained N,N'-di-phenylurea. Hence, splitting of the molecule takes place outside the carbonyl group in the triazene chain. The lowered carbonyl reactivity is also documented by reaction

TABLE III

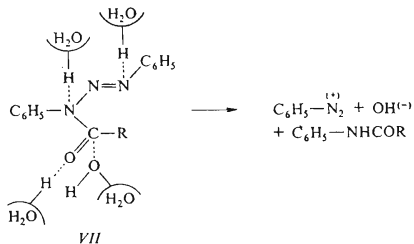
p_z Orbital Populations and Total Charges Calculated by MINDO/2 Method^a for 3-Carbamoyl-triazene (*IV*)

Atom	N1	N2	N3	C4	O5
P_{p_z}	1.206	0.918	1.544	0.627	1.568
q	-0.337	+0.179	-0.428	+0.992	-0.680

Atom	N6	H1	H3	H6	H6'
P_{p_z}	1.861	—	—	—	—
q	-0.663	+0.221	+0.237	+0.252	+0.228

^a The MINDO/2 method somewhat overestimates the charge distribution.

with hydroxylamine (Fig. 2) which, being a strong nucleophile, only reacts with 3-acetyl-1,3-diphenyltriazene (*III*) ($k_{\text{catal}} = 2.27 \cdot 10^{-2} \text{ l mol}^{-1} \text{ s}^{-1}$) but not with *I*. This result contrasts with great electron deficit at carbonyl carbon atom (Table III, a prerequisite of high reactivity). A possible explanation is hydration in the region of the carbonyl (connected with a partial electron transfer from oxygen atom of water to carbonyl carbon atom and with sterical hindrance). Decomposition is not likely, because anion of 1,3-diphenyltriazene represents a bad leaving group⁵⁰ ($\text{p}K_{\text{A}} = 13.27$, 20% ethanol⁵¹).



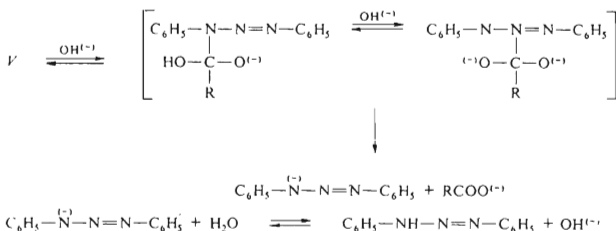
SCHEME 4

The $\text{N}_{(2)}\text{—N}_{(3)}$ bond splitting in the triazene chain, which agrees with the found products, must be assisted by a proton donor, *i.e.* water molecule. With respect to small negative activation entropies ΔS^\ddagger (Table II) the water molecule is obviously coordinated to the substrate molecule in a form of hydrated complex. These complexes can be schematically represented by formula *VII* (respecting the electron distribution; Table III), and the reaction is described by Scheme 4. In accord with the suggested mechanism, measurement in deuterium oxide has no influence on the rate constant.

Hydrolysis in Alkaline Media

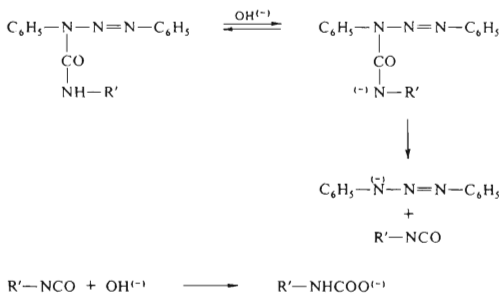
In case of specific base catalyzed hydrolysis of the investigated ureas two kinetically indistinguishable mechanisms can be considered, *viz.* $\text{B}_{\text{Ac}}2$ (Scheme 5) and ElcB (Scheme 6), whereas for the amide *III* the former one only is possible. The $\text{B}_{\text{Ac}}2$ mechanism is well-known with esters^{20–27}, amides^{13,14,28–30} and ureas^{10,31}. The ElcB mechanism was found with the substrates containing acidic hydrogen at the neighbouring atom to carbonyl group. This mechanism is observed most often with carbamic acid derivatives^{32–39}. The criteria differentiating between the

$B_{Ac}2$ and $ElcB$ mechanisms involve the activation entropy, its value being positive with $ElcB$ and negative with $B_{Ac}2$, e.g. ΔS^\ddagger ($J \text{ mol}^{-1} \text{ K}^{-1}$): 4-nitrophenyl *N*-phenylcarbamate + 138 (water-dioxane 4 : 1)³⁴; 1-naphthyl *N*-methylcarbamate³⁷ + 2.5;



SCHEME 5

4-nitrophenyl *N*-phenyl-*N*-methylcarbamate⁵² -117.2; benzamide -112.2 (60% ethanol)¹⁴; phenyl acetate -80.4 (60% acetone)²¹; urea³¹ -83.7 and -89.6. Comparison of the literature data with the values of Table II leads to a conclusion that the amide *III* is hydrolyzed by the $B_{Ac}2$ mechanism (the only possibility, because there are no acidic hydrogen atoms at α -position of acyl; Scheme 5), whereas the values ΔS^\ddagger indicate the $ElcB$ mechanism in case of the ureas *I* and *II* (Scheme 6).



SCHEME 6

No kinetic isotopic effect was found with the ureas *I* and *II* (its value should be $k_{OD_2}/k_{OH_2} = 0.65$ and 1 for $B_{Ac}2$ and ElcB, respectively, according to Tobias and Kézdy²⁷). However, with 4-nitrophenyl N-phenylcarbamate (ElcB) the ratio $k_{OD}/k_{OH} = 1.8$ was found³⁴. Hence, application of this criterion is questionable. One of the currently used criteria for proving the ElcB mechanism, *viz.* blocking of α -hydrogen by substitution, could not be used, because we failed in preparing the necessary 3-(N,N-disubstituted carbamoyl)-1,3-diphenyltriazene. However, base hydrolysis of the ureas *I* and *II* *via* ElcB mechanism is supported by the already discussed reaction with hydroxylamine (Fig. 2) and by high predicted acidity of α -hydrogen (Table III) as compared with *e.g.* water molecule (0.12; 0.13)^{53,54}.

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