EFFECT OF MEDIUM ON ACID-CATALYZED DECOMPOSITION OF *N*-(PHENYLAZO)-SUBSTITUTED NITROGEN HETEROCYCLES

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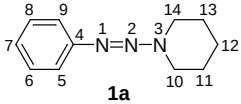
Dedicated to Professor Otto Exner on the occasion of his 75th birthday in recognition of his contribution to physical organic chemistry and chemometrics. We are proud to have had the possibility to collaborate with him for a long time.

Four *N*-(phenylazo)-substituted saturated nitrogen heterocyclics were synthesized and their structure was confirmed by ^{1}H and ^{13}C NMR spectroscopy. The kinetics of their acid-catalyzed decomposition were studied at various concentrations of the catalyst (pivalic acid) in 40, 30, and 20% (v/v) aqueous ethanol at 25 °C. The values obtained for the observed rate constants were processed by the non-linear regression method according to the suggested kinetic models and by the method of principal component analysis (PCA). The interpretation of the results has shown that the acid-catalyzed decomposition of the heterocyclics under the conditions used proceeds by the mechanism of general acid catalysis, the proton being the dominant catalyst particle of the rate-limiting step. The decrease in the observed rate constant at higher concentrations of the catalyst was explained by the formation of a non-reactive complex composed of the undissociated acid and the respective *N*-(phenylazo)heterocycle. The effect of medium and steric effect of the heterocyclic moiety on the values of catalytic rate constant are discussed.

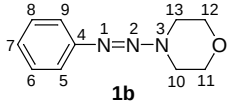
Key words: Reaction kinetics; Mechanism; Solvent effects; Triazenes; Chemometrics.

The investigation of relationships between the structure of organic compounds and their reactivity involving the effect of medium is an important task of physical organic chemistry. Suitable model systems for experimental measurements with the purpose of elucidation of these relationships involve compounds with triazene skeleton. These derivatives are readily soluble in most organic solvents (amfiprotic, protic) and various water–organic solvent mixtures. Triazenes exhibit high reactivity toward various reagents. There have been published for example studies of base-catalyzed cyclization of 1-[2-(methoxycarbonyl)phenyl]-3-(2-substituted phenyl)triazenes in

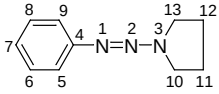
aqueous methanolic buffers with pH 7.5–11.7 (ref.[1]) going by $B_{Ac}2$ mechanism with specific base catalysis. Majority kinetic studies of structurally related triazenes exhibit high reactivity toward electrophilic reagents, the proton in particular. In the present paper, we have chosen the *N*-(phenylazo)heterocycles **1a**–**1d** as the model compounds.



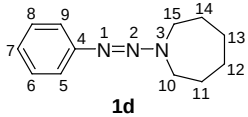
1a



1b



1c



1d

This work follows our previous papers focusing upon acid-catalyzed decomposition of various triazenes in various type of media (for example refs[2–5]).

The triazenes of this type have not yet received much attention in the literature; indeed, *N*-(phenylazo)perhydroazepine has not been cited at all. The other derivatives are biologically active. Antiviral and insecticidal properties were found[6] with *N*-(phenylazo)piperidine and *N*-(phenylazo)-pyrrolidine. They are effective against mosaic viruses, domestic flies, red spider mites, and bean beetles. Rondestvedt and Davis[7] dealt in a complex way with studies of 3,3-dialkyl-1-phenyltriazenes, *i.e.*, compounds with the same basic skeleton as that in the *N*-(phenylazo)heterocycles chosen by us. Some of these derivatives showed anti-tumour activity. Active tumour inhibition was proved in the case of 3,3-dimethyl-1-phenyltriazene itself or in its derivatives having 4-nitro, 4-methoxy, 2-methyl, and 3-trifluoromethyl groups in the phenyl ring. However, this activity was not found with *N*-(phenylazo)heterocycles. Some triazenes appear as intermediates in syntheses of aryl iodides from anilines[8], these syntheses being distinguished by high degrees of conversion. Also described was a method of preparation of aryl iodides involving *N*-(arylazo)pyrrolidine as intermediate. A reaction of *N*-(phenylazo)piperidine with tin radicals has been reported[9] to produce phenyl radicals.

A general method of preparation of triazenes consists in the azo coupling of the corresponding diazonium salt to amine in neutral to mildly basic medium[7]. This procedure is also applicable to preparations of the model *N*-(phenylazo)heterocycles chosen by us. The starting materials for these

syntheses are the corresponding saturated nitrogen heterocycles and benzenediazonium chloride.

Compounds with triazene skeleton are very easily decomposed in acid media. Protonation of the molecule can take place at any of the three nitrogen atoms present, as it follows from the electron density distribution[10–12], but the triazene chain is only split after the protonation at N-3 atom, where there is no double bond. The protonations at the two remaining nitrogen atoms are only side equilibria. On the basis of findings in paper[3] dealing with similar problems of pivalic acid-catalyzed decomposition of 3,3-dialkyl-1-phenyltriazenes in 40% (v/v) aqueous ethanol, we can consider two mechanisms[13,14] of acid-catalyzed decomposition of the model *N*-(phenylazo)heterocycles in aqueous ethanolic media: the specific acid catalysis (A1) and the general acid catalysis (A-S_E2). The former presumes the protonation at N-3 atom of triazene skeleton as a rapid pre-equilibrium and subsequent decomposition of the protonated intermediate as the rate-limiting step. The latter involves simultaneous proton transfer to N-3 and the N-2–N-3 bond splitting in the rate-limiting step. In both the cases, the products are the corresponding diazonium salts and heterocyclics, *i.e.*, the compounds used in the preparation of the model substances.

An analysis of mechanism of specific acid catalysis leads to the conclusion that increasing steric requirements on the part of the heterocyclic moieties could possibly cause an acceleration of decomposition of the protonated substrate and hence also an acceleration of the whole reaction. This conclusion directly follows from the definition of A1 mechanism: it involves the proton transfer from the acid catalyst to sterically hindered N-3 atom in a rapid pre-equilibrium step; therefore, the steric effects of heterocyclic moieties (hindering the access of the acid to the reaction centre) do not affect the overall reaction rate.

In the general acid catalysis, which was confirmed for compounds with triazene skeleton by measuring the kinetics of decomposition of substituted 3-methyl-1,3-diphenyltriazenes and subsequent mathematical modelling of this reaction[13,14], there are two possible pathways: the catalysis by the proton and that by general acid. The catalysis by the dimer of carboxylic acid is not considered likely in aqueous ethanolic media. In the case of general acid catalysis, an increasing slowing down of the reaction with increasing steric requirements of the heterocyclic moieties should be observable, because this mechanism involves the proton transfer from a sterically hindered acid to the reaction centre in the rate-limiting step, the steric hindrance at the reaction centre thus being fully manifested.

EXPERIMENTAL

Spectroscopy

The ^1H and ^{13}C NMR spectra of the *N*-(phenylazo)heterocyclics prepared were measured on an AMX 360 spectrometer (Bruker) at 360.14 and 90.56 MHz, respectively, as 5% $CDCl_3$ pyrrolidine and morpholine derivatives or $(CD_3)SO$ piperidine and perhydroazepine derivatives solutions. The UV-VIS spectra of the *N*-(phenylazo)heterocyclics dissolved in 40% (v/v) aqueous ethanol were measured on a diode-array spectrophotometer HP 8452A (Hewlett–Packard). The NMR chemical shifts, referenced to the solvent used, the wavelengths of the longest-wave UV-VIS maxima are presented below.

Syntheses of Intermediates and Model Substances

Preparation of Perhydroazepine by Reduction of Hexano-6-lactam (Modified According to ref.[15])

Synhydride (272.5 ml, 0.99 mol) was placed in a 1-liter Erlenmeyer flask equipped with an Y-part with a reflux condenser and a dropping funnel. A solution of hexano-6-lactam (19.1 g, 0.41 mol) in toluene (200 ml) was added dropwise into the reducing agent stirred with a magnetic stirrer (the reaction is strongly exothermic). After adding all the lactam, the reaction mixture was stirred for another 2 h and then refluxed. After cooling and pouring into a mixture of hydrochloric acid and ice (500 ml; 1 : 1), the organic phase was separated and extracted with dilute hydrochloric acid (2 × 200 ml; 1 : 1). The aqueous phase was mixed with the two extracts and the resulting mixture was extracted with ether. The extract was evaporated on a vacuum evaporator to a small volume, alkalinized with concentrated sodium hydroxide solution, and steam-distilled. The distillate was saturated with solid potassium hydroxide, and the separated perhydroazepine was extracted with ether (200 ml). The ethereal extract was evaporated and the residue was distilled to give 35 ml (0.31 mol) perhydroazepine (75% yield).

Preparation of N-(Phenylazo)heterocycles – (General Procedure Modified According to ref.[16])

A solution of sodium acetate (16.4 g, 0.2 mol) in water (20 ml) was mixed with the corresponding heterocyclic (0.2 mol) in a 500 ml beaker. The solution thus formed was stirred at a temperature below 5 °C, and a cold solution of benzenediazonium chloride (0.2 mol) prepared in a usual way was added, maintaining the pH of reaction mixture at about 7. The separated solid was collected by suction, washed with water, dried, and purified by recrystallization.

N-(Phenylazo)piperidine (**1a**). Yellow crystals. Yield: 16%, m.p. 38–40 °C (benzene), (ref.[17] gives 43 °C). For $C_{11}H_{15}N_3$ (189.3) calculated: 69.81% C, 7.99% H, 22.20% N; found: 69.98% C, 8.06% H, 22.88% N. ^1H NMR: 7.20 m, 1 H (H-7); 7.38–7.41 m, 4 H (H-5, H-6, H-8, H-9); 1.66 s, 6 H (H-11, H-12, H-13); 3.77 s, 4 H (H-10, H-14). ^{13}C NMR: 120.23, 2 C (C-5, C-9); 125.51, 1 C (C-7); 128.89, 2 C (C-6, C-8); 150.36, 1 C (C-4); 23.77, 5 C (C-10, C-11, C-12, C-13, C-14). UV: 314 nm.

N-(phenylazo)morpholine (**1b**). Orange crystals. Yield: 19%, m.p. 25–27 °C (benzene), (ref.[18] gives 29–30 °C). For $C_{10}H_{13}N_3O$ (191.2) calculated: 62.81% C, 6.85% H, 21.97% N; found: 62.94% C, 6.93% H, 21.95% N. ^1H NMR: 7.17 m, 1 H (H-7); 7.31–7.35 m, 2 H (H-6, H-8);

7.42–7.45 m, 2 H (H-5, H-9); 3.73–3.76 m, 4 H (H-11, H-12); 3.80–3.83 m, 4 H (H-10, H-13). ^{13}C NMR: 121.15, 2 C (C-5, C-9); 126.42, 1 C (C-7); 128.84, 2 C (C-6, C-8); 150.04, 1 C (C-4); 47.94, 2 C (C-10, C-13); 66.31, 2 C (C-11, C-12). UV: 290 nm.

N-(phenylazo)pyrrolidine (**1c**). Yellow crystals. Yield: 12%, m.p. 47–49 °C (diethyl ether), (ref.[7] gives 47–49 °C). For $C_{10}H_{13}N_3$ (175.2) calculated: 68.54% C, 7.48% H, 23.98% N; found: 68.85% C, 7.44% H, 23.17% N. ^{1}H NMR: 7.10 m, 1 H (H-7); 7.28–7.32 m, 2 H (H-6, H-8); 7.38–7.40 m, 2 H (H-5, H-9); 1.98–2.02 m, 4 H (H-11, H-12); 3.77 s, 4 H (H-10, H-13). ^{13}C NMR: 120.32, 2 C (C-5, C-9); 125.11, 1 C (C-7); 128.79, 2 C (C-6, C-8); 150.39, 1 C (C-4); 23.79, 4 C (C-10, C-11, C-12, C-13). UV: 314 nm.

N-(phenylazo)perhydroazepine (**1d**). Yellow crystals. Yield: 16%, m.p. 19–21 °C (diethyl ether). For $C_{12}H_{17}N_3$ (203.3) calculated: 70.90% C, 8.43% H, 20.67% N; found: 71.23% C, 8.51% H, 20.70% N. ^{1}H NMR (^{a} axial, ^{e} equatorial): 7.14 m, 1 H (H-7); 7.35–7.36 d, 4 H (H-5, H-6, H-8, H-9); 1.58–1.61m, 4 H (H-12, H-13); 1.77 s and 1.87 s, 2 H and 2 H (H-11^a, H-14^a and H-11^e, H-14^e); 3.76 t and 4.00 t, 2 H and 2 H (H-10^a, H-15^a and H-10^e, H-15^e). ^{13}C NMR: 120.09, 2 C (C-5, C-9); 124.79, 1 C (C-7); 128.80, 2 C (C-6, C-8); 150.90, 1 C (C-4); 24.41, 27.68, 28.38, 29.69, 4 C (C-11, C-12, C-13, C-14); 48.04, 53.61, 2 C (C-10, C-15). UV: 310 nm.

Kinetic Measurements, Determination of pK_{HA} of Acid Catalyst

Pivalic acid (analytical grade, Fluka) was dissolved in 40, 30, or 20% (v/v) aqueous ethanol to obtain the highest concentration and (by diluting with the same solvents) the lower concentrations used for kinetic measurement. The concentration of acid catalyst was then determined titrimetrically with 0.1 M tetrabutylammonium hydroxide using Titralab3 automatic titrator with potentiometric indication (Radiometer) and a glass and SCE electrodes with saturated methanolic KCl solution.

The same apparatus was also used to determine the pK_{HA} value of pivalic acid in the respective water–ethanol mixtures (40%, pK_{HA} = 6.33; 30%, pK_{HA} = 5.95; 20%, pK_{HA} = 5.65), using benzoic acid as the standard (its pK_{HA} values were taken from ref.[19]: 40%, pK_{HA} = 5.35; 30%, pK_{HA} = 5.07; 20%, pK_{HA} = 4.80).

The pivalic acid-catalyzed decomposition of *N*-(phenylazo)heterocyclics was measured in 40, 30, or 20% (v/v) aqueous ethanolic solution using the same spectrophotometer as above. The measurements were carried out at the wavelengths of the respective longest-wave UV-VIS maxima. A 1-cm quartz cell was charged with *ca* 2 ml of a pivalic acid and, after attaining the temperature of 25.0 ± 0.1 °C in the cell compartment, 1–10 µl of *N*-(phenylazo)-heterocyclic compound solution in dioxane was injected with a Hamilton syringe, and the cell content was thoroughly mixed. The absorbance decrease was followed at the above-mentioned wavelength for a period of four half-lives of the reaction. The experimental data obtained were evaluated and the rate constants were obtained using the optimization program included in the program set OPGM. We also carried out measurements to confirm the fact that the acid-catalyzed decomposition of the *N*-(phenylazo)heterocyclics proceeds as a pseudo-first-order reaction. In connection with our previous paper[3] dealing with the acid-catalyzed decomposition of 3,3-dialkyl-1-phenyltriazenes with pivalic acid in 40% (v/v) aqueous ethanol at 25 °C, we have now also measured acid-catalyzed decomposition of 3,3-dicyclohexyl-1-phenyltriazene in 30 and 20% (v/v) aqueous ethanol under the same conditions. The observed rate constants of all decompositions are given in Table I.

TABLE I
Observed rate constants for acid-catalyzed decomposition of *N*-(phenylazo)heterocyclics **1a**–**1d** in various solvents

40% (v/v) aqueous ethanol, $k_{obs} \cdot 10^3$, s^{-1}						
Substrate/c_{HA}	0.0101	0.0308	0.0503	0.1007	0.1510	0.1985
1a	0.4878	1.0750	1.8460	2.3220	2.1800	2.8690
1b	0.4545	0.7740	1.3470	1.7310	1.9740	1.9920
1c	1.1205[a]	1.9643[a]	2.6170	3.0930	3.3730	4.1200[a]
1d	0.3989	0.6718[a]	0.9306[a]	1.0380	1.1450	1.4550
Substrate/c_{HA}	0.2489	0.2992	0.3300	0.3607	0.3999	0.4502
1a	2.8930	2.9460	2.8850	2.8620	2.7130	2.5860
1b	2.1410	2.1540	2.0930	2.1160	2.0560	1.9870
1c	4.6250[a]	4.8610	4.7980	4.5970	4.1930[a]	4.2980[a]
1d	1.5940	1.5670	1.5320	1.4115[a]	1.3240[a]	1.3500
Substrate/c_{HA}	0.5006	0.5593	0.5872	0.6432	0.6966	
1a	2.4990	2.3625[a]	2.3150	2.2110	2.1420	
1b	2.0770	1.9830	1.8980	1.9280	1.8990[a]	
1c	3.9760	3.6490[a]	3.7880[a]	3.6460	3.5500[a]	
1d	1.2730	1.0610[a]	1.1160	1.0830	0.9766	
30% (v/v) aqueous ethanol, $k_{obs} \cdot 10^2$, s^{-1}						
Substrate/c_{HA}	0.0101	0.0309	0.505	0.1010	0.1515	0.1992
1a	0.4059	0.5819	0.7698	0.9188	1.0230	1.0380
1b	0.2848	0.4311	0.5262	0.6246[a]	0.7396	0.7698
1c	0.3758	0.6466	0.8015	0.9748	1.0140	1.0370
1d	0.1768	0.2536	0.3187	0.4088[a]	0.4208[a]	0.3938
DCTAZ[b]	1.8770	3.5190	4.2870	5.5700	6.9800	6.5980
Substrate/c_{HA}	0.2497	0.3002	0.3507	0.4012	0.4517	0.5022
1a	1.0080	0.9181	0.7224	0.6488	0.5799	0.5847
1b	0.7641	0.6970	0.6397	0.5820	0.5392	0.5195[a]
1c	1.0160	1.0120	0.9455	0.8850	0.8326	0.8302
1d	0.3927	0.3800	0.3585	0.3030	0.2605	0.2562
DCTAZ[b]	6.4110	5.3650	4.5470	2.8920	2.6390	2.3380

TABLE I
(*Continued*)

30% (v/v) aqueous ethanol, $k_{obs} \cdot 10^2$, s^{-1}						
Substrate/c_{HA}	0.5611	0.5892	0.6453	0.7014		
1a	0.5239	0.5020	0.4676	0.4398		
1b	0.4652[a]	0.4785	0.4273[a]	0.3924[a]		
1c	0.7909	0.7654	0.7305	0.6586[a]		
1d	0.2295	0.2211	0.2076	0.1817		
DCTAZ[b]	1.6850	1.6410	1.4120	1.2300		
20% (v/v) aqueous ethanol, $k_{obs} \cdot 10^2$, s^{-1}						
Substrate/c_{HA}	0.0101	0.0302	0.0504	0.0907	0.1492	0.1996
1a	0.9313	1.6660	2.0540	2.4990	2.9280	3.1720
1b	0.6200	1.0500	1.2380	1.4390	1.7730	1.9230
1c	0.8040	1.2120	1.5250	2.0820	2.1840	2.5090
1d	0.4251	0.6910	0.8197	0.9588	1.0420	1.0440
DCTAZ[b]	0.0993	0.1668	0.3264[a]	0.4851[a]	0.6138	0.7294
Substrate/c_{HA}	0.2500	0.3004	0.3508	0.3991		
1a	3.3370	3.3220	3.0630	2.9495[a]		
1b	2.0140	2.0580	1.9370	1.7410		
1c	2.5220	2.5550	2.4900	2.4630		
1d	1.0380	0.9085	0.7718	0.6020[a]		
DCTAZ[b]	0.8024	0.9491	1.1183[a]	0.9485[a]		

[a] Average value from more measurements; [b] 3,3-dicyclohexyl-1-phenyltriazene.

RESULTS AND DISCUSSION

Syntheses, Spectral and Kinetic Results

The synthesis of *N*-(phenylazo)heterocyclics was accomplished by the classic azo coupling of benzenediazonium salt and the corresponding saturated nitrogen heterocycle. Aqueous sodium acetate proved to be the best coupling medium for all the four derivatives prepared. pH ≈ 7 had to be kept throughout the coupling reaction with particular attention to avoid its low-

ering to the acid region. It was also important to keep the mixture cold to prevent the diazonium salt from decomposition, especially at the beginning of the coupling reaction. Otherwise, the reaction proper presented no problems.

The structure of *N*-(phenylazo)heterocyclics was confirmed by their ^{1}H and ^{13}C NMR spectra. The results of NMR measurements along with assignment of individual chemical shifts to the corresponding hydrogen or carbon atoms are given in Experimental. In the NMR spectra of *N*-(phenylazo)-heterocycles, some chemical shifts of hydrogen or carbon atoms coalesce into a single signal due to dynamic changes in the molecule. On the other hand, the ^{1}H NMR spectrum of *N*-(phenylazo)perhydroazepine clearly differentiates between axial and equatorial hydrogen atoms. In the ^{1}H NMR spectrum of *N*-(phenylazo)morpholine, chemical shifts of the pairs of chemically equivalent hydrogen atoms in the morpholine moiety are very close, which prevents their unambiguous assignment.

For the acid-catalyzed decomposition of *N*-(phenylazo)heterocyclics measured in 40, 30, or 20% (v/v) aqueous ethanol, we chose pivalic acid as a catalyst because of its considerable steric requirements. The observed rate constants k_{obs} of the acid-catalyzed decomposition of *N*-(phenylazo)-heterocycles with pivalic acid in 40, 30, and 20% (v/v) aqueous ethanol are presented in Table I along with the values found for 3,3-dicyclohexyl-1-phenyltriazene in 30 and 20% (v/v) aqueous ethanol. A graphical representation for *N*-(phenylazo)morpholine decomposition in 30% (v/v) aqueous ethanol is given as an example in Fig. 1 as a plot of k_{obs} *vs* the pivalic acid concentration. The experimental k_{obs} values are given as points.

The graphical treatment of experimentally measured data shows that increasing concentration of pivalic acid causes a virtually linear increase in

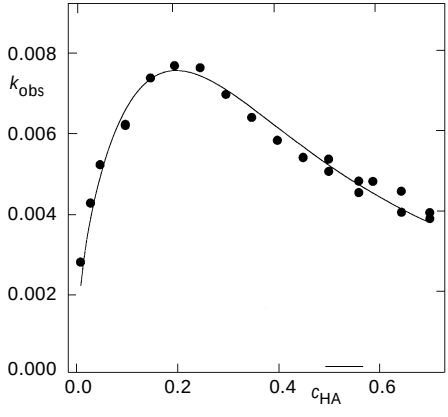


FIG. 1
The relation between c_{HA} and k_{obs} for *N*-(phenylazo)morpholine in 30% aqueous ethanol; ● experimental data, calculated functional dependence (*20*)

k_{obs} up to a certain concentration which depends on the solvent used. This limiting concentration lies in the interval from 0.15 to 0.30 mol l^{-1} for all the media. Above this limiting concentration, the k_{obs} value increases no longer with increasing concentration of pivalic acid but it begins to decrease. Curves of similar shape were also found[3] in the case of acid-catalyzed decomposition of 3,3-dialkyl-1-phenyltriazenes with pivalic acid as a catalyst in 40% (v/v) aqueous ethanol.

For all the derivatives studied and all the concentrations used, the k_{obs} values in 40% (v/v) aqueous ethanol are generally the lowest, increasing with the decreasing ethanol content in the reaction mixture. The acid-catalyzed decomposition is the fastest in 20% (v/v) aqueous ethanol. The largest ratio of the maximum k_{obs} values in 20 and 40% (v/v) aqueous ethanol, 11.4, was found with *N*-(phenylazo)piperidine. The ratios of the other compounds decrease in the order: *N*-(phenylazo)morpholine 9.6, *N*-(phenylazo)perhydroazepine 6.6, and *N*-(phenylazo)pyrrolidine 5.3.

When comparing the k_{obs} values depending on the concentration of the acid catalyst c_{HA} for a series of *N*-(phenylazo)heterocycles in 40% (v/v) aqueous ethanol, we can see that an exchange of the heterocycle affects the decomposition rate. The order of k_{obs} values for the whole concentration range of pivalic acid is as follows: k_{obs} (*N*-(phenylazo)pyrrolidine) > k_{obs} (*N*-(phenylazo)piperidine) > k_{obs} (*N*-(phenylazo)morpholine) > k_{obs} (*N*-(phenylazo)-perhydroazepine). This order corresponds to the increasing ring size of the heterocycles. Although the morpholine and piperidine rings are of the same size, the k_{obs} values obtained for *N*-(phenylazo)morpholine were lower, obviously due to a reduced electron density on N-3 atom. The electronegative oxygen atom in the morpholine ring makes the N-3 nitrogen atom in *N*-(phenylazo)morpholine less nucleophilic and less basic than that in *N*-(phenylazo)piperidine (pK_B = 11.12 and 8.49 for piperidine and morpholine, respectively[20]). This order is in accordance with the finding of our previous paper[3] concerning the dialkyl derivatives of the Ph–N=N–NR_2 type where the following order of rate constant values was obtained for alkyl groups R: k_{obs} (methyl) ≈ k_{obs} (ethyl) > k_{obs} (isopropyl) > k_{obs} (butyl) > k_{obs} (cyclohexyl).

If the decomposition of *N*-(phenylazo)heterocyclics is measured in 30% (v/v) aqueous ethanol, then the order remains unchanged: k_{obs} (*N*-(phenylazo)pyrrolidine) > k_{obs} (*N*-(phenylazo)piperidine) > k_{obs} (*N*-(phenylazo)morpholine) > k_{obs} (*N*-(phenylazo)perhydroazepine). However, the differences between the individual dependences are smaller. *N*-(Phenylazo)piperidine behaves almost identically with *N*-(phenylazo)-pyrrolidine up to the concentration of 0.22 mol l^{-1} of pivalic acid, but

above that (0.5–0.7 mol l^{-1}), its k_{obs} values are almost identical with those of *N*-(phenylazo)morpholine. This is probably due to a combination of solvation effects of the mixed solvent and complex formation with the undissociated acid.

In 20% (v/v) aqueous ethanol, it is no longer true that the decomposition of the compounds with the smallest heterocycle is the fastest, and that the increase in the ring size is associated with slowing down of the acid-catalyzed decomposition. The order of rate constants is: k_{obs} (*N*-(phenylazo)piperidine) > k_{obs} (*N*-(phenylazo)pyrrolidine) > k_{obs} (*N*-(phenylazo)morpholine) > k_{obs} (*N*-(phenylazo)perhydroazepine). The changes in the order are obviously due to specific solvation effects of water, which generally makes less operative other effects manifested in solvents with a higher content of organic component.

When comparing the dependences of k_{obs} *vs* c_{HA} in individual mixtures, one arrives at interesting results. In 40% (v/v) aqueous ethanol, the dependences for individual compounds reach their maxima at the concentration of acid catalyst about 0.3 mol l^{-1}, whereas those in 30% (v/v) aqueous ethanol at about 0.2 mol l^{-1} and those in 20% (v/v) aqueous ethanol at about 0.25 mol l^{-1}. At these concentrations, we determined the differences between the experimental k_{obs} values of the individual dependences. In 40% (v/v) aqueous ethanol, the largest difference is between the dependences for *N*-(phenylazo)pyrrolidine and *N*-(phenylazo)piperidine (0.0019 s^{-1}), whereas the difference between *N*-(phenylazo)piperidine and *N*-(phenylazo)morpholine is only 0.0008 s^{-1}, and that between the dependences for *N*-(phenylazo)morpholine and *N*-(phenylazo)perhydroazepine is still smaller, only 0.0006 s^{-1}. On the other hand, in 30% (v/v) aqueous ethanol this trend is opposite. The difference between the dependences for *N*-(phenylazo)pyrrolidine and *N*-(phenylazo)piperidine is zero, that between *N*-(phenylazo)piperidine and *N*-(phenylazo)morpholine is 0.0027 s^{-1}, that between *N*-(phenylazo)morpholine and *N*-(phenylazo)-perhydroazepine being the highest, 0.0038 s^{-1}. In 20% (v/v) aqueous ethanol, the highest k_{obs} values are shown by *N*-(phenylazo)piperidine, the difference between *N*-(phenylazo)piperidine and *N*-(phenylazo)pyrrolidine being 0.0082 s^{-1}.The difference between the dependences for *N*-(phenylazo)pyrrolidine and *N*-(phenylazo)morpholine amounts 0.0051 s^{-1}, and that between *N*-(phenylazo)morpholine and *N*-(phenylazo)perhydroazepine 0.0098 s^{-1}.

Of interest are the dependences for 3,3-dicyclohexyl-1-phenyltriazene in 40 (ref.[3]), 30, and 20% (v/v) aqueous ethanol. This compound differs from the *N*-(phenylazo)heterocyclics, because the above-mentioned rule, *viz.* that

in 40% (v/v) aqueous ethanol, the acid-catalyzed decomposition of all the five substrates considered is the slowest and it increases with decreasing ethanol content, does not hold unambiguously here. The trend is roughly retained up to the concentration of acid catalyst of 0.23 mol l^{-1}, but at higher concentrations, an abrupt decrease in k_{obs} for 20 and 30% (v/v) aqueous ethanol occurs and the order of compounds is changed. A comparison of k_{obs} for 3,3-dicyclohexyl-1-phenyltriazene with that for the *N*-(phenylazo)heterocyclics in the individual mixtures reveals that the decomposition of dicyclohexyl derivative is the fastest in 40% (v/v) aqueous ethanol, whereas in 30% (v/v) aqueous ethanol it is between *N*-(phenylazo)morpholine and *N*-(phenylazo)perhydroazepine. In 20% (v/v) aqueous ethanol, the slowest reaction takes place at the concentration of c_{HA}= 0.30 mol l^{-1}.

Mathematical Modelling of k_{obs} vs c_{HA} Dependence

As already stated above, the decomposition of *N*-(phenylazo)heterocyclics can proceed by either of two basic mechanisms[13,14]. In the first one, the substrate S is split into products P by the A-S_E2 mechanism either by the reaction of the substrate with the proton

$$S + H^+ \xrightarrow{k_H} P , \qquad (1)$$

or with the undissociated acid HA

$$S + HA \xrightarrow{k_{HA}} P . \qquad (2)$$

The existence of a dimeric form of the acid catalyst is improbable in the media studied.

The second mechanism is specific acid catalysis (A1)

$$S + H^+ \overset{K_H}{\rightleftharpoons} SH^+ \xrightarrow{k} P . \qquad (3)$$

The mechanisms given, however, cannot explain the decrease in observed rate constant at higher concentrations of the pivalic acid catalyst. This decrease is probably due to the lowering of concentration of the reac-

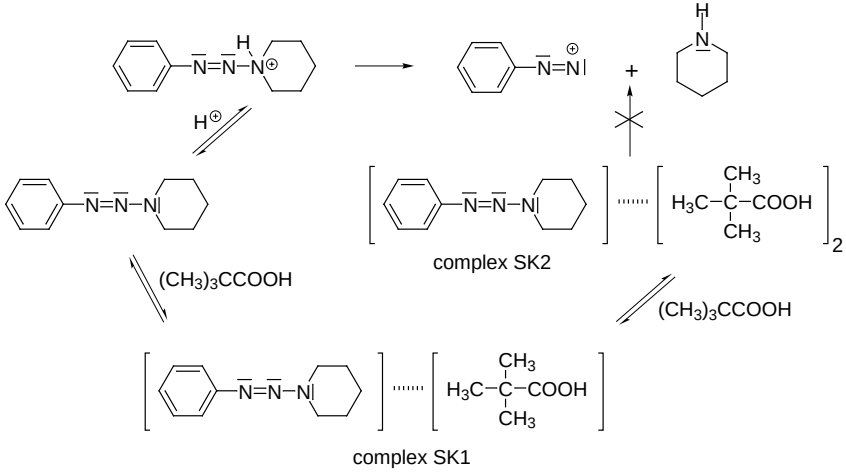
tive form of *N*-(phenylazo)heterocyclic compound in the reaction mixture caused by formation of a little reactive complex. This complex can be composed of *N*-(phenylazo)heterocycle and the undissociated acid in the ratios of 1 : 1, 1 : 2, 1 : 3 *etc.*[21]. The formation of such complexes, denoted as SK1, SK2, SK3, can be expected in fast pre-equilibria followed by very slow product-forming processes.

$$\mathrm{S} + \mathrm{HA} \overset{K_{\mathrm{SK1}}}{\rightleftharpoons} \mathrm{SK1} \xrightarrow{k'_{\mathrm{HA}}} \mathrm{P} \qquad (4)$$

$$\mathrm{S} + \mathrm{SK1} \overset{K_{\mathrm{SK2}}}{\rightleftharpoons} \mathrm{SK2} \xrightarrow{k''_{\mathrm{HA}}} \mathrm{P} \qquad (5)$$

$$\mathrm{S} + \mathrm{SK2} \overset{K_{\mathrm{SK3}}}{\rightleftharpoons} \mathrm{SK3} \xrightarrow{k'''_{\mathrm{HA}}} \mathrm{P} \qquad (6)$$

Proposed mechanism for *N*-(phenylazo)piperidine with formation of complexes SK1 and SK2 is schematically suggested in Scheme 1. Then the concentrations of pivalic acid and *N*-(phenylazo)heterocycle in Eqs (*1*)–(*6*) can be expressed as follows.



SCHEME 1

$$c_{HA} = [H^+] + [HA] + [SK1] + [SK2] + [SK3] + [SH^+] \quad (7)$$

$$c_S = [S] + [SK1] + [SK2] + [SK3] + [SH^+] \quad (8)$$

$$K_{SK1} = [SK1]/[HA][S] \quad (9)$$

$$K_{SK2} = [SK2]/[HA][SK1] = [SK2]/K_{SK1}[HA]^2[S] \quad (10)$$

$$K_{SK2} = [SK3]/[HA][SK2] = [SK3]/K_{SK1}K_{SK2}[HA]^3[S] \quad (11)$$

$$K_H = [SH^+]/[H^+][S] \quad (12)$$

$$K_{HA} = [H^+][A^-]/[HA] = [H^+]^2/[HA] \quad (13)$$

Using Eqs (*7*)–(*12*) along with the reaction rate equation the overall relationship for the dependence of the observed rate constant on concentrations of pivalic acid and proton can be derived (Eq. (*14*)). Of that, the concentrations of all species on the right-hand side of Eq. (*7*), except for [HA], were neglected relative to experimentally determined dissociation constants of pivalic acid in 40, 30, and 20% (v/v) aqueous ethanol (K_{HA} = $5.012 \cdot 10^{-7}$, $1.122 \cdot 10^{-6}$, and $2.139 \cdot 10^{-6}$, respectively) and of the concentration ratio of *N*-(phenylazo)heterocycle and acid catalyst in the reaction mixture.

$$k_{obs} = \frac{k'''_{HA}K_{SK3}K_{SK2}K_{SK1}c_{HA}^3 + k''_{HA}K_{SK2}K_{SK1}c_{HA}^2 + (k'_{HA}K_{SK1} + k_{HA})c_{HA} + (kK_H + k_H)[H^+]}{1 + K_{SK3}K_{SK2}K_{SK1}c_{HA}^3 + K_{SK2}K_{SK1}c_{HA}^2 + K_{SK1}c_{HA} + K_H[H^+]} \quad (14)$$

Though being complex, the equation makes it possible to set up a number of models with the acid catalyst concentrations raised to different powers in both the numerator and denominator. Using Eq. (*13*) and an

experimentally determined dissociation constant of pivalic acid in given media (see Experimental), it is then possible to write the proton concentrations in the media as follows:

$$\text{in 40\% (v/v) aqueous ethanol ... } [H^+] = 0.000684 \sqrt{c_{HA}} \qquad (15)$$

$$\text{in 30\% (v/v) aqueous ethanol ... } [H^+] = 0.00106 \sqrt{c_{HA}} \qquad (16)$$

$$\text{in 20\% (v/v) aqueous ethanol ... } [H^+] = 0.00150 \sqrt{c_{HA}} \ . \qquad (17)$$

The lowering of the k_{obs} values at high concentrations of the acid catalyst can be due to the existence of SK1, SK2 or SK3 complexes only if these complexes do not react further or react much more slowly than the other species (*i.e.* $k'_{HA} = k''_{HA} = k'''_{HA} = 0$). The reaction according to Eq. (*3*) will not proceed either hence $k_{HA} = 0$. On the basis of these facts, Eq. (*14*) can be simplified to Eq. (*18*).

$$k_{obs} = \frac{\left(kK_H + k_H\right)\left[H^+\right]}{1 + K_{SK3}K_{SK2}K_{SK1}c_{HA}^3 + K_{SK2}K_{SK1}c_{HA}^2 + K_{SK1}c_{HA} + K_H\left[H^+\right]} \qquad (18)$$

Equation (*18*) was solved by non-linear regression obtaining a negative value of parameter K_H (physically meaningless). Therefore, the terms involving the K_H parameter were excluded, *i.e.*, the mechanism of specific acid catalysis described by Eq. (*3*) does not show up ($k = 0$). By gradual excluding the statistically insignificant parameters, we obtained the resulting mathematical model with two parameters containing the term $\sqrt{c_{HA}}$ in the numerator (after introducing for $[H^+]$ from Eqs (*15*), (*16*), or (*17*)) and the term $\sqrt{c_{HA}}$, c_{HA}, c_{HA}^2, or c_{HA}^3 in the denominator. These models were applied to the dependences of k_{obs} *vs* c_{HA} for the respective compounds. For the *N*-(phenylazo)heterocyclics, the suitable model involves the c_{HA}^2 term in the denominator (Eqs (*19*), (*20*), and (*21*) for 40, 30, and 20% (v/v) aqueous ethanol, respectively); hence the mechanism only involves non-reactive complexes SK1 and SK2. For the acid-catalyzed decomposition of *N*-(phenylazo)heterocyclics in 20% (v/v) aqueous ethanol, a suitable model seems to involve the SK3 complex (Eq. (*22*)). In this medium, it is impossi-

ble to unambiguously decide which of the models is most probably valid because the existence of non-reactive complex is manifested particularly in the region of decreasing dependence of k_{obs} *vs* c_{HA}. This part of curve, however, is not sufficiently depicted, since the dependence can only be measured up to the catalyst acid concentration $c_{HA} = 0.4$ mol l^{-1} (it is impossible to prepare the solutions of higher concentrations). Obviously, more probable is a model involving the non-reactive complexes formed by a lower number of molecules of the undissociated acid.

$$k_{obs} = \frac{0.000684 k_H \sqrt{c_{HA}}}{1 + K_K c_{HA}^2} \text{ , where } K_K = K_{SK1} K_{SK2} \qquad (19)$$

$$k_{obs} = \frac{0.00106 k_H \sqrt{c_{HA}}}{1 + K_K c_{HA}^2} \text{ , where } K_K = K_{SK1} K_{SK2} \qquad (20)$$

$$k_{obs} = \frac{0.00150 k_H \sqrt{c_{HA}}}{1 + K_K c_{HA}^2} \text{ , where } K_K = K_{SK1} K_{SK2} \qquad (21)$$

$$k_{obs} = \frac{0.00150 k_H \sqrt{c_{HA}}}{1 + K_K c_{HA}^3} \text{ , where } K_K = K_{SK1} K_{SK2} K_{SK3} \qquad (22)$$

The results obtained by non-linear regression, the catalytic rate constants k_H, the complex stability constants K_K, their standard deviations, and residual sums of squares (RSS) for the *N*-(phenylazo)heterocyclics in the given media are given in Table II. An example of interpretation of the results is the dependence of k_{obs} *vs* c_{HA} in Fig. 1 (the curve is the functional dependence of k_{obs} on c_{HA} calculated according to the respective model, the points showing the experimental values).

In 40% (v/v) aqueous ethanol, the catalytic rate constant k_H decreases with increasing size of heterocyclic moiety, which unambiguously confirms the effect of substituents at the N-3 atom on the rate of acid-catalyzed decomposition of the *N*-(phenylazo)heterocyclic. The effect observed can be interpreted by steric hindrance to the approach of solvated proton to the N-3 atom, which supports the claim of bimolecular reaction mechanism with general acid catalysis. Although the piperidine and morpholine rings are of the same size, the k_H value is higher for *N*-(phenylazo)piperidine than for *N*-(phenylazo)morpholine. Obviously, this is due to a lower nucleophilicity and basicity of the N-3 atom in *N*-(phenylazo)morpholine compared

with *N*-(phenylazo)piperidine as a consequence of the presence of the electronegative oxygen atom in the morpholine ring and the change in electron density distribution. In 30 and 20% (v/v) aqueous ethanol, the catalytic rate constant k_H does not decrease any longer with increasing ring size of the heterocyclic moiety. Obviously, here the steric requirements of bulky substituents are outweighed by specific solvation effects of water which generally lower the influence of other effects operating in 40% (v/v) aqueous ethanol (*i.e.*, a solvent with higher proportion of ethanol). In 40, 30, and 20% (v/v) aqueous ethanol, the mixed complex stability constant

TABLE II
Optimized parameters k_H (l mol^{-1} s^{-1}), K_K (l^2 mol^{-2}), their standard deviations (*s*), residual sum of squares (*RSS*) and number of experimental points (*n*) obtained by non-linear regression

Substrate	k_H	$s(k_H)$	K_K	$s(K_K)$	$RSS \cdot 10^7$	*n*
			40% (v/v) aqueous ethanol, model (*19*)			
1a	10.93	0.328	4.34	0.255	2.29	17
1b	7.38	0.221	2.87	0.244	2.25	17
1c	15.75	0.315	3.42	0.201	10.69	25
1d	5.60	0.168	4.77	0.354	13.64	22
DCTAZ[b]	17.46	0.370	2.30	0.157	3.52	22
			30% (v/v) aqueous ethanol, model (*20*)			
1a	32.60	0.978	12.91	0.796	33.52	16
1b	21.22	0.424	8.19	0.359	15.95	21
1c	29.28	1.171	6.69	0.524	69.56	18
1d	13.30	0.266	11.82	0.570	4.42	18
DCTAZ[b]	18.51	0.370	40.04	2.570	25.82	16
			20% (v/v) aqueous ethanol, model (*21*)			
1a	59.23	1.185	5.65	0.397	9.26[d]	11
1b	35.59	1.068	5.50	0.567	14.87[d]	10
1c	44.98	1.349	4.91	0.494	7.15[d]	10
1d	25.47	1.019	16.27	1.422	3.03[d]	11

[a] 3,3-Dicyclohexyl-1-phenyltriazene; [b] experimental data from ref.[8]; [c] model (*23*); [d] $RSS \cdot 10^6$.

K_K of SK1 and SK2 complexes is not only related to the steric requirements of heterocyclic moieties but also significantly affected by the participation of solvating molecules of water and ethanol.

The method of non-linear regression was also used for the experimental data of acid-catalyzed decomposition of 3,3-dicyclohexyl-1-phenyltriazene. In 40% (v/v) aqueous ethanol, the dependence of k_{obs} on c_{HA} for this compounds was described in a previous paper[3] by application of a model involving SK1 and SK2 (Eq. (*19*)). However, for the dependence in 30% (v/v) aqueous ethanol, the model (*20*) is no longer sufficient. We have found a suitable model involving, besides SK1 and SK2, also the SK3 complex and described by Eq. (*23*).

$$k_{obs} = \frac{0.00106 k_H \sqrt{c_{HA}}}{1 + K_K c_{HA}^3}, \text{ where } K_K = K_{SK1} K_{SK2} K_{SK3} \qquad (23)$$

The data for 20% (v/v) aqueous ethanol resisted all optimization attempts for any of the models, the complex stability parameter K_K always being statistically insignificant. This is a consequence of an insufficient range of measurement of the k_{obs} *vs* c_{HA} dependence. However, the experimental data allow a conclusion that a further increase in the acid catalyst concentration would cause a very steep decrease in k_{obs}, and the curve of this shape could then be fit by a model involving apparently a non-reactive complex containing three or even more molecules of the undissociated acid. The complex stability constant K_K would be high.

The kinetic data obtained for the *N*-(phenylazo)heterocyclics were also treated by the method of principal component analysis[22] (PCA). The source matrix for the given medium was arranged in such a way that the rows and columns corresponded to the individual substrates and the acid catalyst

TABLE III
Values of score vectors ***t*** from PCA calculation in various solvents

Substrate	40% Ethanol	30% Ethanol	20% Ethanol
1a	0.461	0.740	1.000
1b	0.248	0.478	0.410
1c	1.000	1.000	0.673
1d	0.000	0.000	0.000

concentrations, respectively. The matrix was filled to 100%. According to the statistical criteria, only one latent variable is significant in all the media, describing 97.8, 94.8, and 98.9% of variability in 40, 30, and 20% (v/v) aqueous ethanol, respectively. From the order of values in the score vectors (Table III), it is obvious that the single latent variable describing the variability of source matrix involves both the steric effect of the heterocyclic moiety and the solvent effect. Obviously, in 40% (v/v) aqueous ethanol the order of values in the score vector is given predominantly by the ring size of the heterocycle which is associated with steric requirements. In 30% (v/v) aqueous ethanol, the order remains the same, but in 20% (v/v) aqueous ethanol, the solvent effect of the mixture probably begins to be apparent in addition to the steric effect, which alters the order of the given substrates. The same conclusion and the same order of substrates followed from the qualitative description of the k_{obs} *vs* c_{HA} dependence, too.

CONCLUSION

Results obtained on proposed mathematical models with unambiguous chemical meaning show that acid-catalyzed decomposition under used condition proceeds by mechanism A-S_E2 (general acid catalysis). The proton is dominant catalyst affecting in rate limiting step. Very interesting situation of decreasing of observed rate constant at higher concentration of acid catalyst was explained by the formation of non-reactive complex of two (in same cases three) molecules of undissociated acid catalyst and the respective model heterocyclic triazene. Values of catalytic rate constants and results of PCA shows that the ring size of heterocyclic moiety affecting substantially on reaction rate.

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