

# Study of acid hydrolysis of some substituted derivatives of 3-phenyliminoxindole

<sup>a</sup>D. KALAVSKÁ, <sup>b</sup>S. KALAVSKÝ, <sup>c</sup>A. KOŠTURIÁK, and <sup>a</sup>A. SZALÓ

<sup>a</sup>Department of Analytical Chemistry, Faculty of Natural Sciences,  
Komenský University, 816 50 Bratislava

<sup>b</sup>Department of General Physics, Faculty of Natural Sciences,  
Komenský University, 816 31 Bratislava

<sup>c</sup>Department of Experimental Physics, Faculty of Natural Sciences,  
P. J. Šafárik University, 041 54 Košice

Received 17 February 1977

*Dedicated to Professor S. Stankoviansky on his 70th birthday*

The hydrolysis of ten substituted derivatives of 3-phenyliminoxindole in the pH region 2.5—5.0 and in the temperature range 10—80°C is described.

The reaction kinetics was investigated spectrophotometrically in the region 300—800 nm within the concentration range  $1 \times 10^{-4}$ — $6 \times 10^{-4}$  M in the presence of 15 volume % of 1-propanol.

The overall rate constants as well as the rate constants of noncatalyzed and by the H<sup>+</sup> ion catalyzed process were determined. The critical concentrations of catalyst were calculated. The activation parameters of the overall reaction and catalyzed hydrolysis were determined. The effect of substituent on the rate and course of hydrolysis was investigated. It has been proved that the acid hydrolysis of the derivatives of 3-phenyliminoxindole is a first-order reaction in the whole investigated range of temperature, concentration, and pH. The results of acid-catalyzed hydrolysis are confronted with the results obtained in the study of base-catalyzed hydrolysis and a view on the mechanism of hydrolytic reactions in the whole pH range is put forward.

Изучался гидролиз 10 замещенных производных 3-фенилиминоксиндола при pH 2,5—5,0 в интервале температур 10—80°C.

Кинетика реакции определялась спектрофотометрическим методом в области 300—800 нм в интервале концентраций  $1 \cdot 10^{-4}$ — $6 \cdot 10^{-4}$  М при добавлении 15 об. % пропилового спирта.

Были определены общие константы скорости, а также константы скорости некатализируемого и ионом  $H^+$  катализируемого процессов. Были найдены критические концентрации катализатора. Были определены параметры активации общей реакции и катализируемого гидролиза. Изучалось влияние заместителя на скорость и ход гидролиза. Доказано, что кислотный гидролиз производных 3-фенилиминоксиндола является реакцией первого порядка во всем интервале температур, концентраций и pH. Результаты кислотного гидролиза сравнивались с результатами изучения щелочного гидролиза и высказалось мнение о механизме реакций гидролиза в целом диапазоне pH.

This paper is a continuation of our preceding study of the alkaline hydrolysis of the substituted derivatives of 3-phenyliminoxindole [1—4] in which we have found that, besides the reversible hydrolysis of isatin ring giving rise to the derivatives of  $\alpha$ -anisatinic acid, an irreversible hydrolysis of the  $C=N$  bond proceeds in two parallel ways and depends on the concentration of the catalyzing  $OH^-$  particles, temperature, and the kind of substituent. In this paper, we confront these results with the new results of the study of acid hydrolysis, in order to obtain a wider view on the kinetics and mechanism of hydrolysis of the derivatives of 3-phenyliminoxindole.

The following derivatives of 3-phenyliminoxindole were investigated: 1. 4- $N(CH_3)_2$ , 2. 4- $NH_2$ , 3. 4- $OH$ , 4. 4- $OCH_3$ , 5. 4- $OC_2H_5$ , 6. 4- $CH_3$ , 7. 3- $CH_3$ , 8.  $-H$ , 9. 4- $Br$ , 10. 3- $Cl$ .

### Experimental

The substituted derivatives of 3-phenyliminoxindole were prepared and purified according to [5—8]. All other chemicals were anal. grade reagents or were purified by crystallization or distillation.

Spectrophotometric measurements were carried out on a Specord UV VIS spectrophotometer (Zeiss, Jena) by using a thermostated cell where the temperature was controlled accurate to  $\pm 0.5^\circ C$ .

The Britton—Robinson buffer solutions were used the ionic strength of which was adjusted to  $I = 0.2$  by means of KCl. The pH value of solutions was measured immediately in the reaction mixture with a pH-meter PHM 22r (Radiometer) by the use of a pair of electrodes (G 202 B and K 401). The solutions measured contained the substances in concentration  $1 \times 10^{-4}$ — $6 \times 10^{-4}$  M and 15 volume % of 1-propanol. The dependence of absorption spectra (300—800 nm) on time as well as the dependence of absorbance at  $\lambda_{max}$  on time was used for the investigation of the course of hydrolysis. The data obtained by both kinds of measurement were in good agreement. The measurements were repeated (3—5) times and all values obtained were statistically evaluated by using trivial programmes for linear regression on a computer Siemens 4004.

The final products of acid hydrolysis were isolated and identified by thin-layer chromatography by means of standard solutions of isatin and corresponding substituted derivatives of aniline.  $8 \mu\text{l}$  of  $4 \times 10^{-4}$  M solution of hydrolyzed 3-phenyliminoxindole and the same quantity of standard solutions were always put side by side on Silufol foils UV 254 (Cavalier, Votice). A 1:1 butanol—methanol mixture was used as an eluent. The  $R_f$  values of individual products of hydrolysis were in good agreement with the  $R_f$  values of corresponding standards.

## Results and discussion

By investigating the change in absorption spectra in the region 300—800 nm as a function of time, we have found for all derivatives that the absorption maximum continuously decreases and finally vanishes while any new maximum corresponding to hydrolysis products does not appear in the region of investigated wavelengths. By evaluating  $\log c/c_0$  vs.  $t$ , we obtain a straight line. The investigated reaction is a first-order reaction for all derivatives in the temperature region 10—80°C, in the pH range 2.5—5.0, and at concentrations ranging from  $1 \times 10^{-4}$  to  $6 \times 10^{-4}$  M. The overall rate constants of the investigated reaction are given in Table 1 and Fig. 1.

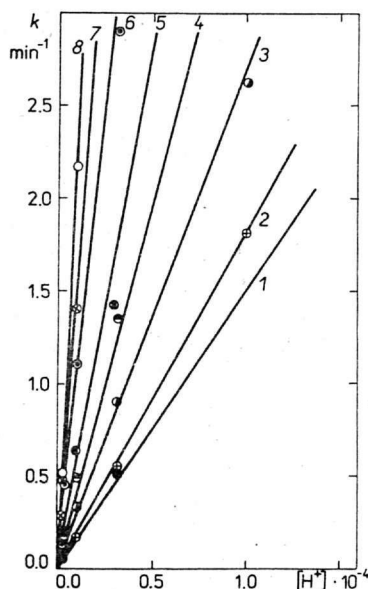


Fig. 1. Overall rate constant  $k$  as a function of the concentration of protons for 3-phenyliminoxindole.

$c = 3 \times 10^{-4}$  M, 15 volume % of 1-propanol,  $I = 0.2$ .

1. 283 K; 2. 293 K; 3. 303 K; 4. 313 K; 5. 323 K; 6. 333 K; 7. 343 K; 8. 353 K.

Table 1

Average values of the overall rate constants  $k$  for acid hydrolysis of the derivatives of 3-phenyliminox-indole,  $I=0.2$ , 15 volume % of 1-propanol

Substituent	pH	$k, \text{min}^{-1}$							
		283 K	293 K	303 K	313 K	323 K	333 K	343 K	353 K
4-N(CH <sub>3</sub> ) <sub>2</sub>	5.0							0.3318	
	4.5		0.0733	0.1083			0.5657		
4-NH <sub>2</sub>	5.0							0.4686	
	4.5		0.0818	0.0910			0.4686		0.6856
4-OH	5.0							0.4495	
	4.5		0.0952	0.1144			0.6578		
4-OCH <sub>3</sub>	5.0							0.2859	
	4.5		0.0855	0.1023			0.6593		
4-OC <sub>2</sub> H <sub>5</sub>	5.0							0.2513	
	4.5		0.0861	0.1090			0.4760		
4-CH <sub>3</sub>	5.0							0.2459	
	4.5		0.0835	0.1004			0.4737		
3-CH <sub>3</sub>	5.0							0.2478	
	4.5		0.0769	0.1017			0.4051		
—H	5.0		0.0299	0.0374	0.0736	0.1053	0.1587	0.2942	0.3750
	4.5	0.0505	0.0799	0.1018	0.1754	0.2514	0.4517	0.4730	0.5109
	4.0		0.1602	0.3327	0.4972	0.6456	1.1056	1.4069	2.1718
	3.5	0.5192	0.5303	0.8941	1.3486	1.4102	1.7926		
	3.0		1.8187	2.6224	2.7094				
	2.5	2.3720	4.0943						
	2.0								
3-Cl	5.0							0.2754	
	4.5		0.0476	0.0597			0.2418		
4-Br	5.0							0.2416	
	4.5		0.0602	0.1600			0.2512		

It is obvious from Table 1 that the reaction rate increases with temperature and increasing concentration of the protons and is considerably dependent on the kind of substituent. The overall rate constant  $k$  may be expressed in the form

$$k = k_1 + k_2[\text{H}_3\text{O}^+]$$

where  $k_1$  is the rate constant of the noncatalyzed process while the second term represents the contribution of the catalyzed hydrolysis. The values of  $k_1/k_2$  give the critical concentrations of catalyst, i.e. if the concentration of catalyst in solution is smaller than the critical value, the noncatalyzed hydrolysis prevails.

Table 2 shows that the critical concentration of catalyst decreases with increasing temperature and the contribution of the noncatalyzed process decreases. Similar

relationships were also obtained in the study of alkaline hydrolysis [3], but the critical values of catalyst were in the concentration range 0.03—1.3 M. The hydrolysis catalyzed by the  $H^+$  ions proceeds much easier than the hydrolysis catalyzed by the  $OH^-$  ions. For the acid hydrolysis of H derivative in the investigated temperature region, the concentration of catalyst sufficient to produce the reaction characterized by overall rate constant  $k \sim 0.03\text{--}4.10 \text{ min}^{-1}$  is  $[H^+] \sim 2 \times 10^{-4}\text{--}2 \times 10^{-6} \text{ M}$ . On the other hand, the necessary concentration of catalyzing particles in alkaline solutions is  $[OH^-] \sim 0.05\text{--}0.60 \text{ M}$  while the overall rate constant is in the interval  $(5 \times 10^{-3}\text{--}10^{-1}) \text{ min}^{-1}$  [3]. The values of activation energies also show that the acid hydrolysis proceeds much easier than the hydrolysis catalyzed with the  $OH^-$  ion [3, 4]. In acid solutions containing the catalyst in the concentrations  $10^{-5}\text{--}10^{-3} \text{ M}$ , the activation energy attains the values of 38.3—15.3  $\text{kJ mol}^{-1}$  while it attains the values of 131.1—75.8  $\text{kJ mol}^{-1}$  in alkaline hydrolysis if the concentration of catalyzing particles is  $10^{-2}\text{--}10^{-1} \text{ M}$  [1—4] (Tables 2 and 3, Figs. 2 and 3).

Table 2

Rate constants of the noncatalyzed ( $k_1$ ) and catalyzed ( $k_2$ ) acid hydrolysis of 3-phenyliminoxindole and the values of  $k_1/k_2$  characterizing the critical values of the concentration of catalyst

$T, K$	$k_2$ $\text{min}^{-1} \text{ mol}^{-1} \text{ l}$	$s_{k_2}$	$k_1$ $\text{min}^{-1}$	$s_{k_1}$	$R$	$N$	$k_1/k_2$ $\text{mol l}^{-1}$
283	704.8	77.7	0.1559	0.1420	0.9940	6	$2.2 \times 10^{-4}$
293	1 295.2	81.9	0.1216	0.1114	0.9921	12	$9.3 \times 10^{-5}$
303	2 593.3	41.8	0.0416	0.0197	0.9996	12	$1.6 \times 10^{-5}$
313	2 610.7	270.5	0.1996	0.1275	0.9843	10	$7.6 \times 10^{-5}$
323	4 146.3	364.8	0.1285	0.0607	0.9923	10	$3.1 \times 10^{-5}$
333	4 961.4	1 082.7	0.3107	0.1804	0.9555	8	$6.2 \times 10^{-5}$
343	12 675.2	1 041.5	0.1263	0.0633	0.9966	8	$9.9 \times 10^{-6}$
353	21 009.3	3 481.3	0.0274	0.0117	0.9865	6	$1.3 \times 10^{-6}$

The dependence of activation energy and frequency factor on the concentration of catalyst or pH range may be expressed for acid catalysis in the following form

$$E_a = -16.53 + 10.93 \text{ pH}$$

$$\log A_0 = 0.13 + 0.96 \text{ pH}$$

The activation parameters are little dependent on substituent. The dependence of logarithm of the rate constant on substituent at pH 4.5 and 293 K is to be expressed for derivatives 3—10 by the following equation

$$\log k = -0.409(\pm 0.057) \sigma - 1.103(\pm 0.014); \quad R = -0.9760; \quad N = 8$$

Table 3

Activation parameters of the overall acid hydrolysis of the derivatives of 3-phenyliminoxindole ( $A_0$ ,  $E_a$ ,  $\Delta H^\ddagger$ ,  $\Delta S^\ddagger$ ) and activation parameters of the catalyzed hydrolysis ( $A_{02}$ ,  $E_{a2}$ ,  $\Delta H_2^\ddagger$ ,  $\Delta S_2^\ddagger$ ) for 3-phenyliminoxindole

Substituent	pH	$A_0$ , min <sup>-1</sup>	$E_a$ , kJ mol <sup>-1</sup>	$N$	$R$	$\Delta S^\ddagger$ , J mol <sup>-1</sup> K <sup>-1</sup>	$\Delta H^\ddagger$ , kJ mol <sup>-1</sup>	$N$	$R$
4-N(CH <sub>3</sub> ) <sub>2</sub>	4.5	$(3.01 \pm 0.302) \cdot 10^6$	$42.91 \pm 2.52$	6	-0.9983	$-163.63 \pm 8.29$	$40.27 \pm 2.53$	6	-0.9980
4-NH <sub>2</sub>	4.5	$(2.69 \pm 0.199) \cdot 10^6$	$42.03 \pm 1.87$	6	-0.9990	$-164.59 \pm 6.15$	$39.44 \pm 1.87$	6	-0.9989
4-OH	4.5	$(4.73 \pm 0.601) \cdot 10^5$	$37.34 \pm 3.21$	6	-0.9963	$-179.08 \pm 10.59$	$34.74 \pm 3.22$	6	-0.9957
4-OCH <sub>3</sub>	4.5	$(1.07 \pm 0.135) \cdot 10^6$	$39.60 \pm 3.16$	6	-0.9968	$-172.25 \pm 10.34$	$37.01 \pm 3.16$	6	-0.9964
4-OC <sub>2</sub> H <sub>5</sub>	4.5	$(1.20 \pm 0.211) \cdot 10^6$	$40.35 \pm 3.27$	6	-0.9957	$-176.27 \pm 9.96$	$36.46 \pm 3.44$	6	-0.9955
4-CH <sub>3</sub>	4.5	$(7.98 \pm 0.102) \cdot 10^4$	$33.32 \pm 3.26$	6	-0.9953	$-193.83 \pm 10.47$	$30.73 \pm 3.24$	6	-0.9945
3-CH <sub>3</sub>	4.5	$(9.59 \pm 0.370) \cdot 10^4$	$34.26 \pm 0.98$	6	-0.9996	$-192.30 \pm 3.18$	$31.67 \pm 0.98$	6	-0.9995
-H	5.0	$(1.724 \pm 0.128) \cdot 10^5$	$38.26 \pm 1.97$	12	-0.9934	$-187.66 \pm 6.07$	$35.59 \pm 1.97$	12	-0.9934
-H	4.5	$(1.633 \pm 0.127) \cdot 10^4$	$29.83 \pm 2.03$	12	-0.9968	$-202.97 \pm 6.49$	$26.71 \pm 2.04$	12	-0.9968
-H	4.0	$(8.092 \pm 0.239) \cdot 10^3$	$27.10 \pm 1.67$	12	-0.9974	$-210.39 \pm 5.27$	$24.43 \pm 1.70$	12	-0.9974
-H	3.5	$(4.265 \pm 0.446) \cdot 10^3$	$21.41 \pm 2.67$	12	-0.9703	$-218.09 \pm 8.41$	$18.86 \pm 2.67$	12	-0.9700
-H	3.0	$(1.036 \pm 0.289) \cdot 10^3$	$15.33 \pm 3.36$	6	-0.9080	$-229.73 \pm 24.28$	$12.81 \pm 3.35$	6	-0.9080
3-Cl	4.5	$(1.560 \pm 0.248) \cdot 10^4$	$30.68 \pm 4.01$	6	-0.9915	$-207.42 \pm 13.19$	$28.08 \pm 3.99$	6	-0.9915
4-Br	4.5	$(2.740 \pm 0.378) \cdot 10^3$	$25.50 \pm 4.13$	4	-0.9700	$-207.33 \pm 17.20$	$22.90 \pm 4.11$	4	-0.9700

$E_{a2} = (36.91 \pm 3.39)$  kJ mol<sup>-1</sup>;  $A_{02} = 4.5 \times 10^9$  min<sup>-1</sup>;  $\Delta H_2^\ddagger = (34.29 \pm 3.35)$  kJ mol<sup>-1</sup>;  $\Delta S_2^\ddagger = (326.09 \pm 10.47)$  J mol<sup>-1</sup> K<sup>-1</sup>.

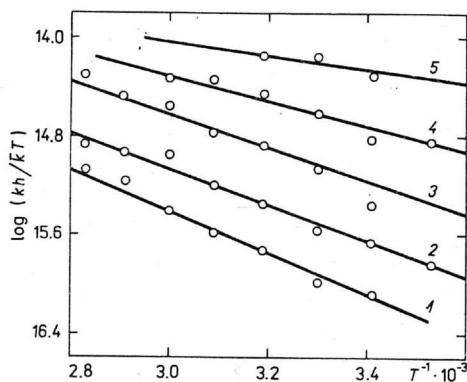


Fig. 2.  $\log k h/k T$  vs.  $T^{-1}$  for 3-phenylimin-oxindole.  
 $c = 3 \times 10^{-4}$  M, 15 volume % of 1-propanol,  
 $I = 0.2$ .  
 1. pH 5; 2. pH 4.5; 3. pH 4.0; 4. pH 3.5;  
 5. pH 3.0.

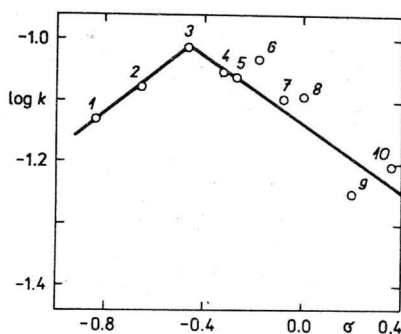
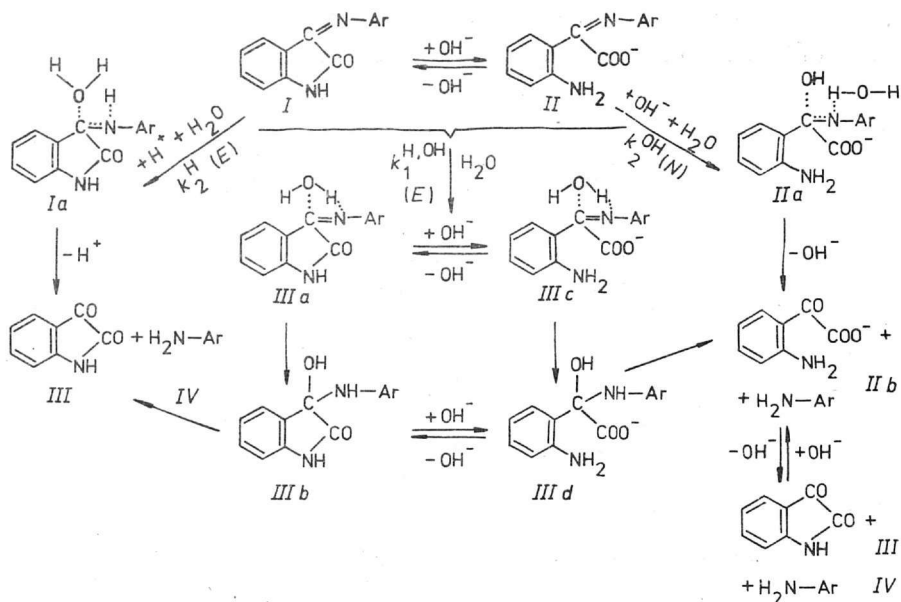


Fig. 3.  $\log k$  as a function of the  $\sigma$  constant.  
 293 K, pH 4.5,  $c = 3 \times 10^{-4}$  M,  $I = 0.2$ , 15 volume % of 1-propanol.

As evident from Fig. 3, derivatives 1 and 2 exhibit observable deviations from linear course. Analogous deviations were revealed for derivatives 1 and 2 in correlations  $\varepsilon_{\max}$  and  $\lambda_{\max}$  vs. the  $\sigma$  constant. Owing to a great electron-donor effect of substituent, it may be assumed that both derivatives enter into the reaction in different structure when compared with other derivatives. In these considerations, we must, however, take into account a different solvation ability of derivatives 1 and 2 with respect to derivatives 3–10, as shown in [8]. This view is also supported by the correlations  $\log k$  vs.  $\sigma$  constant for alkaline hydrolysis [3]. It ensues from the general character of hydrolysis in acid and alkaline solutions and from the mentioned relationships [1–4] that the hydrolysis catalyzed by protons as well as the noncatalyzed hydrolysis is an electrophilic reaction whereas the hydrolysis catalyzed by the  $\text{OH}^-$  ions in alkaline solutions [1–4] obeys a nucleophilic mechanism, as shown in Scheme 1.

The base-catalyzed hydrolysis proceeds most rapidly in case of manifest electron-acceptor substituents while the acid hydrolysis is enhanced by the electron-donor effects of substituents. On the basis of these results as well as information in [1–4], we may depict the hydrolysis of the derivatives of 3-phenyliminnoxindole within the whole pH range as follows (Scheme 1).

The fundamental form of compounds I is protonated in acid solutions. It takes a molecule of water to give Ia. The rate of formation of this product is rate-determining in this electrophilic hydrolysis which is characterized by the rate constant of the acid-catalyzed hydrolysis,  $k_2^{\text{H}}$ . In alkaline solutions, the reaction is catalyzed by the  $\text{OH}^-$  ions and is characterized by the rate constant  $k_2^{\text{OH}}$  while



Scheme 1

$\alpha$ -anilisinic acid *II* undergoes hydrolysis to give products *IIa* and *IIb*. Intermediates *Ia* and *IIb* rapidly decompose to yield final products *III* and *IV*.

The noncatalyzed hydrolysis which occurs as an electrophilic reaction in the whole pH range is characterized by the rate constant  $k_1^{H,OH}$ . This reaction starts with an electrophilic reaction of compound *I* or *II* with a molecule of water (in dependence on the pH of solution). Intermediates *IIIa*—*d* decompose to yield the final products, i.e. 2,3-dioxindole and substituted aniline.

## References

1. Zacharová-Kalavská, D. and Košturiak, A., *Collect. Czech. Chem. Commun.* **40**, 1504 (1975).
2. Košturiak, A. and Zacharová-Kalavská, D., *Chem. Zvesti* **29**, 34 (1975).
3. Košturiak, A., Stankoviansky, S., and Zacharová-Kalavská, D., *Collect. Czech. Chem. Commun.* **41**, 2582 (1976).
4. Košturiak, A. and Domanský, R., *Chem. Zvesti* **27**, 227 (1973).
5. Koevenagel, E., *J. Prakt. Chem.* **89**, 46 (1914).
6. Binz, A. and Heuter, R., *Ber.* **48**, 1038 (1915).
7. Vorländer, D., *Ber.* **40**, 1419 (1907).
8. Košturiak, A., Stankoviansky, S., and Zacharová-Kalavská, D., *Chem. Zvesti* **31**, 237 (1977).

Translated by R. Domanský