KINETICS AND MECHANISM OF ALKALINE HYDROLYSIS OF (*Z*)-O-(N-4-NITROPHENYLCARBAMOYL)BENZALDOXIMES IN 30% AQUEOUS ETHANOL

Jaromír MINDL, František RADONSKÝ, Jiří KLICNAR and Miroslav VEČEŘA

Organic Chemistry Department,
Institute of Chemical Technology, 53210 Pardubice

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Alkaline hydrolysis of (*Z*)-O-(N-4-nitrophenylcarbamoyl)benzaldoximes (*I*), the configuration of which was verified by IR spectra, produces a mixture of *Z* and *E*-benzaldoximates *II* and *III*, benzonitrile *IV*, and 4-nitrophenylcarbamate ion (*V*). In subsequent reactions *II* and *III* are hydrolyzed to benzaldehyde *VI*, and *III* and *IV* give finally benzoate *VII*. The carbamate *V* is decarboxylated to 4-nitroaniline (*VIII*). The compound *I* is hydrolyzed to oxime and 4-nitroaniline (*VIII*) in neutral medium. The hydrolysis rates of three compounds type *I* have been measured in 30% aqueous ethanol at pH 4 to 14. Character of the hydrolysis course in alkaline medium corresponds to a reaction of ElcB type. In neutral medium spontaneous hydrolysis with water takes place and the reaction rate is independent of concentration of hydrogen ion.

Brady and coworkers[1,2] hydrolyzed (Z)-O-(N-phenylcarbamoyl)benzaldoxime with aqueous 2M sodium hydroxide and isolated from the products benzonitrile besides (Z)-benzaldoxime and sodium benzoate. Later Hauser and Jordan found that (Z)-O-acylbenzaldoximes in basic medium also give benzonitrile besides (Z)-benzaldoxime, their ratio depending on the reaction conditions[3] (Eq. (*A*)). So far no detailed kinetic study of mechanism of these reactions has been carried out.

$$\mathrm{Y{-}CO{-}O{-}N{=}CHAr} \xrightarrow{\mathrm{H_2O/NaOH}} \mathrm{Y{-}CO{-}ONa} + \mathrm{ArCN} + \mathrm{ArCH{=}N{-}ONa} + \mathrm{ArCO_2Na}\,, \qquad (A)$$

where Y = ArNH, CH_3, CH_3O

The present communication represents a continuation of our previous study of hydrolysis of isomeric (*E*)-O-(N-4-nitrophenylcarbamoyl)benzaldoximes[4]. Our aim was to use the model of (Z)-O-(N-4-nitrophenylcarbamoyl)benzaldoximes and estimate composition of the hydrolysis products as well as effect of substituents on rate and mechanism of the hydrolysis in 30% aqueous ethanol at various pH values. The 4-nitro substituent in the group Y of the substrate was chosen with respect to easy spectrophotometric measurement of the reaction rate.

EXPERIMENTAL

Reagents

The substituted (Z)-O-(N-4-*nitrophenylcarbamoyl)benzaldoximes*: Solution of 0·05 mol 4-nitrophenyl isocyanate in 30 ml benzene was mixed with solution of 0·05 mol substituted (*Z*)-benzaldoxime in 50 ml benzene. The mixture was heated on a bath to boiling with stirring 15 min. The product separated on cooling was filtered off. A part of the product was dissolved in benzene and submitted to chromatography on a silica gel column (benzene–ethyl acetate) to remove the present starting substances and small amounts of the benzonitrile formed. The individual fractions were checked and compared with standard samples by TLC on Silufol (detection with solution of stannous chloride and the Ehrlich reagent). The product was obtained by crystallization from the respective fraction. Yields of the mentioned products were 65—78%. Their melting points and results of elemental analyses are given in Table I. Pure (*Z*)-O-(4-nitrophenylcarbamoyl)benzaldoximes in solid state are slowly decomposed to benzonitriles on action of light. The (*Z*)-benzaldoximes were prepared according to Beckmann[5].

Analytical Methods

The hydrolysis of (*Z*)-O-(N-4-nitrophenylcarbamoyl)benzaldoximes and (*Z*)-benzaldoximes was carried out in the same way as in our previous work[4]. Composition of the products was determined by TLC on Silufol after hydrolysis of these substances in media of pH 13·8, 10·9 and 6·4. The products of alkaline hydrolysis were analyzed by withdrawing samples at definite time intervals in the reaction course. Sodium 4-nitrophenylcarbamate and 4-nitroaniline were determined by UV spectrophotometry using a Unicam SP 800 B apparatus (comparison with standard

TABLE I

Melting Points and Results of Elemental Analyses of (*Z*)-O-(N-4-Nitrophenylcarbamoyl)benzaldehydoximes

Compound substituent	Formula (mol.wt.)	M.p., °C	Calculated/Found		
			% C	% H	% N
Id H	$C_{14}H_{11}N_3O_4$ (285·3)	120—121	58·65 58·94	4·13 3·89	14·60 14·73
Ib 3-Cl	$C_{14}H_{10}ClN_3O_4$ (319·7)	90— 91·5	52·36 52·59	3·43 3·15	13·30 13·14
Ic 4-NO_2	$C_{14}H_{10}N_4O_6$ (330·2)	112—113·5	51·05 50·92	3·16 3·05	16·59 16·97
Id 4-CH_3	$C_{15}H_{13}N_2O_4$ (299·3)	123—124	60·58 60·21	4·58 4·39	13·43 14·05
Ie 4-OCH_3	$C_{15}H_{13}N_2O_5$ (315·3)	120—121	57·31 57·14	4·37 4·15	13·23 13·33

substances). The IR spectra of the aldoximes and their carbamates were measured in Nujol using a Spectromom 2000 apparatus (Mom, Budapest), the wave numbers being calibrated with the use of polystyrene.

Kinetic Measurements

For the measurements solutions in 30% aqueous ethanol and phosphate, borax and acetate buffers were used. In alkaline medium the measurement was started by injecting about 10 μl ethanolic substrate solution in 2 ml 30% aqueous–ethanolic buffer solution. The measurement was discontinuous, the reaction vessels were temperated at 25 or 55°C. The carbamate concentration in the reaction mixture was $1{\cdot}2 \cdot 10^{-5}$M at the moment of the injection. At pre-chosen time intervals the reaction was quenched by acidification with aqueous sulphuric acid to pH 3–4 and cooling. At these pH values the hydrolysis was very slow and the formed sodium 4-nitrophenyl carbamate decarboxylated[6] readily to 4-nitroaniline the concentration of which was followed spectrophotometrically in the region of 385 nm. The kinetic measurements were carried out with the use of a VSU-2 spectrophotometer (Zeiss, Jena). The pH values of the solutions were determined with a pH-Meter 4c (Radiometer, Copenhagen) at 25°C.

RESULTS AND DISCUSSION

Configuration of Starting Substances

The configuration of the (Z)-benzaldoximes was verified with the use of the band of valence vibration ν(C=N) which is IR-inactive for the *E* isomer[7]. The solid *E* isomers

TABLE II
Wave Numbers of Bands (cm^{-1}) in IR Spectra of *Z* and *E* Benzaldoximes

Sample		ν(O—H)[a]	ν(C=N)	ν(N—O)	γ(C—H)		δCC
H	*Z*	3 180 s	1 657 m	956 vs	852 s	765 s	697 vs
	E	3 320 vs	—	969 vs	871 vs	765 s	698 vs
3-Cl	*Z*	3 160 s	1 654 m	967 s	886 m	767 s	687 m
	E	3 220 s	—	987 vs	885 m	786 s	687 m
4-CH_3	*Z*	3 140 s	1 643 m	945 s	805 s		—
	E	3 340 s	—	957 s	807 s		—
4-NO_2	*Z*	3 180 s	1 644 w 1 662 w	965 m	845 s		—
	E	3 320 s	—	778 s	857 s		—
4-OCH_3	*Z*	3 165 s	1 642 m	949 vs	826 vs		—
	E	3 260 s	—	963 vs	819 vs		—

[a] vs very strong, s strong, m medium, w weak band.

show higher values of wave numbers of the bands[8] ν(O—H), γ(C—H) and δCC of benzene nucleus[9]. For differentiation between the two isomers the data of the region 690 to 900 cm^{-1} are less suitable, with the *Z* and *E* benzaldoximes only the band γ(C—H) is different (852 and 871 cm^{-1}, respectively), with the 3-chloro derivatives the only differing band is assigned to deformation vibration γ(C—H) of the three neighbouring hydrogen atoms (767 and 786 cm^{-1}, respectively). With the 4-methyl derivative the difference makes only 2 cm^{-1}, and the *Z* isomer of the 4-methoxy derivative has even higher value than the *E* isomer. Table II also gives the frequencies ν(N—O) belonging to a very intensive band which seems to be more suitable criterion for differentiation of the both isomers.

These results were applied for determination of sterical correspondence of (*Z*)-O-(N-4-nitrophenylcarbamoyl)benzaldoximes *Ia* to *Ie*, too. The 4-nitro derivative *Ic* was not involved in the measurements due to its low stability. The other derivatives prepared from (*Z*)-benzaldoximes showed lower values (N—O) as compared with the respective *E* isomers (Table III). Identical results are also obtained from the spectral region of out-of-plane deformation vibrations of C—H bonds and deformations of the aromatic nucleus δCC where the bands due to 4-nitrophenyl group could be differentiated from those of phenyl group at oxime group. Compared with the respective spectral region of benzaldoximes, the carbamoyl derivatives of the *Z* and *E* isomers show greater frequency differences for the bands γCH and δCC in accord with the presumption that the *Z* isomers should exhibit lowering of frequencies due to interactions with the adjacent C=N group[10].

Table III also gives wave number values of the bands ν (N—H) and ν(C=O) of the amide group. The substituent effects make themselves felt rather in the carbonyl frequency than in that of the bonds C=N and NH. The wave numbers of the band ν(C=N) are lower than those of the corresponding benzaldoximes, the vibration is active with the *E* isomers, too. Table III also gives the values for the amide II band, the bands of nitro and methoxy groups were found at usual wave numbers.

Analysis of the Hydrolysis Products

Material-balance experiments of the hydrolysis of (*Z*)-O-(N-4-nitrophenylcarbamoyl) benzaldoximes (*I*) were carried out in alkaline and neutral regions. The products and the hydrolysis course are summarized in Scheme (*B*).

At pH 13·8 and 25°C the reaction mixture contained (according to chromatographical analysis) both *E* and *Z* benzaldoximates (*II*, *III*), benzonitrile (*IV*), sodium 4-nitrophenylcarbamate (*V*), 4-nitroaniline (*VIII*) and sodium benzoate (*VII*). In this medium the hydrolysis half-life was below 1 s, and the ratio of the *E* to *Z* oximes in the reaction product was 1 : 5, the concentration of the *Z*-isomer *III* being decreased far faster with time than that of the *E*-isomer *II*. From time analysis of the products it follows that the *Z*-isomer is partly isomerized to the *E*-configuration,

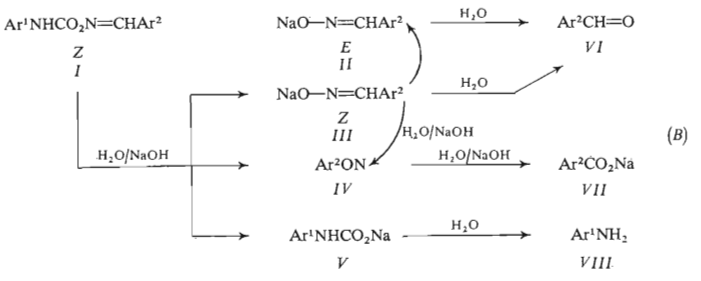
TABLE III

Wave Numbers of Bands (cm^{-1}) in IR Spectra of (*Z*) and (*E*)-O-(N-4-Nitrophenylcarbamoyl)benzaldoximes *I*

Formula		ν(N—H)[a]	ν(C=O)	ν(C=N)	Amid II	ν(N—O)	γ(C—N)		δCC
							4-NO_2Ph	subst. Ph	
Ia	*Z*	3 330 m	1 750 vs	1 640 m	1 537 vs	855 s	855 s	750 s	690 m
	E	3 340 m	1 750 vs	1 622 m	1 560 m	943 m	862 s	762 s	700 m
Ib	*Z*	3 350 m	1 778 vs	1 610 m	1 560 m	907 vs	844 s	746 s	696 m
	E	3 375 m	1 780 vs	1 620 m	1 548 s	947 s	848 s	755 s	704 m
Id	*Z*	3 340 m	1 750 vs	1 620 m	1 542 vs	906 s	847 s	807 s	—
	E	3 300 m	1 740 vs	1 610 m	1 560 s	928 m	849 s	812 s	—
Ie	*Z*	3 345 m	1 745 vs	1 627 m	1 530 vs	906 s	842 s	826 s	—
	E	3 350 m	1 750 vs	1 617 s	1 555 s	937 m	854 s	829 s	—

[a] See footnote a in Table II.

partly hydrolyzed to the aldehyde *VI*, and partly transformed *via* elimination to the nitrile *IV* which is hydrolyzed to the benzoate *VII*. Besides the *Z*-isomer *III* also *E*-benzaldoxime can be hydrolyzed to benzaldehyde, this reaction is very slow[4]. As a further product we identified the carbamate *V* which, at room temperature, slowly hydrolyzed to 4-nitroaniline. At pH 10·9 the reaction mixture contained the substances *I* to *V*, *VII* and *VIII* as in the above case. The hydrolysis of the carbamate *V* was faster (the decarboxylation to 4-nitroaniline was complete after 2 h). At pH 6·4 the hydrolysis product contained, besides the unreacted starting substance, only (*Z*)-benzaldoxime (*III*) and 4-nitroaniline (*VIII*). For comparison we also hydrolyzed (*E*)-O-(N-4-nitrophenylcarbamoyl)-benzaldoxime at pH 13·8 and found, among the reaction products, the compounds *V* and *VIII* besides both (*E*) and (*Z*)-benzaldoximes. Hydrolysis of (*Z*)-benzaldoximes (*III*) in the same medium resulted in isomerization, and the both isomers gave benzaldehyde *VI* and benzoate *VII* after 10 h boiling. Hydrolysis of the (*E*)-isomer *II* only gave the aldehyde *VI* under these conditions. From our experiments it follows that the substrate *I* is not isomerized before hydrolysis, but transformation of *Z* into *E* isomer takes place first in the phase of the oximate. In accord therewith (*E*)-O-(N-4-nitrophenylcarbamoyl)-benzaldoxime was not found in the reaction mixture. Furthermore, it is obvious that the hydrolysis at pH 6·4 and higher is a complex reaction in which the substrate *I* is transformed first to the compounds *II* to *V* which are subject to further hydrolytical reactions. According to our findings, formation of *E*-isomer of the oximate *II* is practically irreversible, which is supported by the fact that the ratio of the both isomers is changed much faster during the reaction, and the oximate *Z III* is decreasing (Scheme (*B*)). Besides that, (*E*)-O-(N-4-nitrophenylcarbamoyl)benzaldoxime does not produce benzonitrile under the same conditions[4]. The benzoate *VII* is produced by hydrolysis of benzonitrile *IV*, but it could be formed by disproportionation of the benzaldehyde *VI*, too. However, as benzoate is formed faster than benzaldehyde by 5 orders of magnitude under the same conditions[4], the above possibility is little



likely. In the hydrolysis products of the oximate *III* we could not find the nitrile *IV*. We presume that the nitrile hydrolysis is faster than its formation from oxime, and benzoate is the final product. As we could detect the presence of the nitrile *IV* in the hydrolysis of the carbamate *I*, it must be presumed that the former can be produced by direct elimination from the latter (Scheme (*B*)).

The subsequent reaction of the carbamate *V* to the amine *VIII* is acid catalyzed[6]. Therefore, sodium 4-nitrophenylcarbamate was only found in alkaline medium. At pH 6·4 the decarboxylation is so fast that the carbamate *V* cannot be trapped.

Kinetics and Mechanism of Hydrolysis of (*Z*)-O-(N-4-*Nitrophenylcarbamoyl*)-*benzaldoximes*

Fig. 1 gives the pH dependence of logarithm of the rate constants of the compound series *Ia* to *Ic* (Table I) in 30% aqueous ethanol at 25°C. The hydrolysis rates were followed by the increase of 4-nitroaniline concentration. The calculation of the rate constants did not take into account the side reaction of the substrate *I* to the nitrile *IV* which makes less than 5% with respect to concentrations of the oximates. From analogy with the hydrolysis mechanism of carbamates[4] of *E* configuration it is presumed that the carbamates *Ia* to *Ic* with *Z* configuration are hydrolyzed *via* ElcB mechanism. The both pH profiles are given in Fig. 1. In accordance with this mechanism, in the pH region of the fully ionized substrate (*i.e.* above pH 12) the hydrolysis rate does not change with increasing pH value. Within pH 12 to 9 concentration of the conjugated base (*i.e.* the reacting species) is decreased, and in accord therewith log k_{obs} decreases with the slope equal to unity. The hydrolysis rate of the 3-chloro derivative *Ib* was followed within pH 5 to 9 and found pH-independent (Fig. 1). For this spontaneous solvolysis a mechanism *via* the tetrahedral inter-

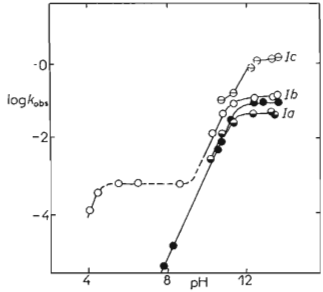
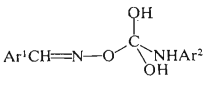


FIG. 1

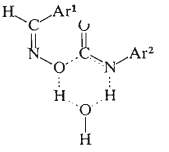
pH Dependence of Logarithm of Hydrolysis Rate Constants of the Studied Oximes

◒ *Ia*; ○ *Ib*; ◓ *Ic*; ●(*E*)-O-(N-4-Nitrophenylcarbamoyl)-3-chlorobenzaldehydroxime.

mediate *Ix* can be suggested, or alternatively a cyclic process with intramolecular catalysis *Iy* can be considered (Scheme (*C*)). In acid medium below pH 5 the 3-chloro derivative *Ib* shows a decrease of the hydrolysis rate which is proportional to increasing concentration of hydroxonium ion. This behaviour is ascribed to protonation of the neutral substrate with formation of the less reactive conjugate acid, the probable protonation site being the oxime nitrogen.



Ix



Iy

(*C*)

Furthermore from Fig. 1 it is seen that behaviour of *Z* and *E* carbamates *Ib* in alkaline medium is very similar (the same being true for the substituent effects; the $\varrho_{(Z)}$ and $\varrho_{(E)}$ estimates[4] are 1·36 and 1·42, respectively), whereas in neutral region their hydrolysis character is considerably differing. Whereas the *Z* isomer is subject to spontaneous solvolysis, the *E* isomer is more stable in this medium, and if it is subject to spontaneous hydrolysis at all, then its rate is lower by more than 2 orders of magnitude. This different hydrolytical stability has not yet been explained.

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