Kinetics of the alkaline hydrolysis of 2-thioaryl-3, 5-dinitropyridine derivatives in 50% v/v DMSO–water

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The kinetics of the alkaline hydrolysis of substituted 2-thioaryl-3,5-dinitropyridine have been studied in 50% DMSO– water. The observed rate constants and the second order rate constants were calculated. The thermodynamic parameters for the unsubstituted compound reveals the activating power of the two nitro- and aza-groups .

Keywords: substituted 2-thioaryl-3,5-dinitropyridine, kinetics, DMSO–water

Nucleophilic substitution in heteroaromatics is a subject of ongoing interest in our laboratory and especially the behaviour of substituted nitro pyridines towards different nucleophiles has attracted our attention.[1-6] It was reported that the alkaline hydrolysis of both 2-chloro-5-nitropyridine and 2-chloro-3,5-dinitropyridine often involves an S_N(ANRORC) mechanism which starts by addition of the nucleophile (usually at the *meta* position to the leaving group) followed by ring opening and ring closure.[7]

Recently the reactions of 2-chloro-5-nitropyridine, 2-chloro-3-nitropyridine, 2-chloro-3,5-dinitropyridine, with arene thiolates,[1,2] morpholine,[3,4] piperidine,[4] aniline derivatives[5] and aryloxide ions[6] were reported. The substitution product was found to be formed via the $S_N(AE)^{ipso}$ mechanism. In continuation of these researches, we have examined the effect of the 2-substituent on the mechanism of the alkaline hydrolysis reaction of 2-thioaryl-3,5-dinitropyridines[2] since they do not appear to have been studied.[8,9]

Experimental

Material: Substituted 2-thioaryl-3,5-dinitropyridines 1a-h were prepared as reported earlier.[2] Carbonate free sodium hydroxide was prepared as reported.[10]

General procedure: 2-thioaryl-3,5-dinitropyridines 1a-h (0.5 g) were treated with sodium hydroxide (10ml DMSO-H_2O v/v) 1:100 respectively and refluxed at 40°C for 1 h. Upon cooling and acidification a mixture of diaryl disulfide,[11-13] (Table 1) and 3,5- dinitro-2-pyridone was obtained which was separated by fractional crystallisation.

Kinetic measurements: The solvent used for kinetic runs was of reagent grade (Aldrich). The rate constants were measured in the thermostated cell compartment of a Shimadzu 160-A UV–VIS. spectrophotometer. Repetative scans of the reaction mixture showed the disappearance of activated complex which absorbed at λ 470 nm in 50% v/v DMSO–H_2O. Good pseudo-first order kinetics were measured at different concentrations of NaOH (5×10^{-4}– 5×10^{-3} M) and 2-thioaryl-3,5-dinitropyridine (5×10^{-5}M). The first order rate constants k_{obs} were calculated using equation (1), where A_o, A_t, and A are the values of absorbance at zero time, time t, and the end of the reaction respectively

$$\ln (A_t - A) = - k_{obs}\, t + \ln (A_o - A) \qquad (1)$$

A second order reaction rate k_2 was calculated from the obtained straight lines passing through the origin as a result of the plots of the reaction rate constant k_{obs} values versus sodium hydroxide concentration (in the range 5×10^{-4}– 5×10^{-3} M), while the concentration of the compounds **1a–h** remained constant (5×10^{-5}M)

Results and discussion

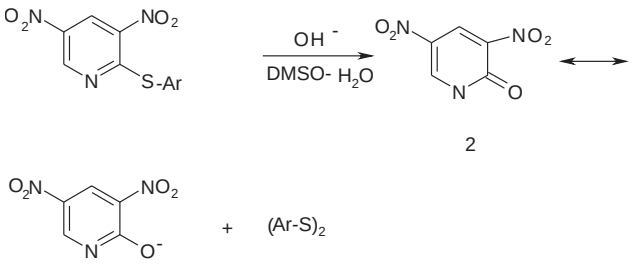
The present work studies the kinetic of the alkaline hydrolysis of the titled compounds in 50% v/v DMSO–H_2O that gave 3,5-dinitro-2-pyridone and the corresponding disulfides, Scheme 1.

This reaction may involve different pathways, Scheme 2. The first one is the ring opening and subsequent ring closure[7,8] pathway (a). The hydroxide ion adds to the unsaturated 6-position,[7] **3.** The formation of 3,5-dinitropyridine–(1H), **2**, involves the intermediacy of the formyl cyanodinitropropenoid salt **4**, being formed by ring opening of the initially formed Meisenhemer adduct **3**. The conversion of **3**→**4**→**5** and **6** take place with an excess of hydroxide ion to give product[7] **2**. The absorbance (of a strong yellow colour) at λ_{max} 426 nm that corresponds to the delocalised anion **4** rejects mechanism of pathway (a).

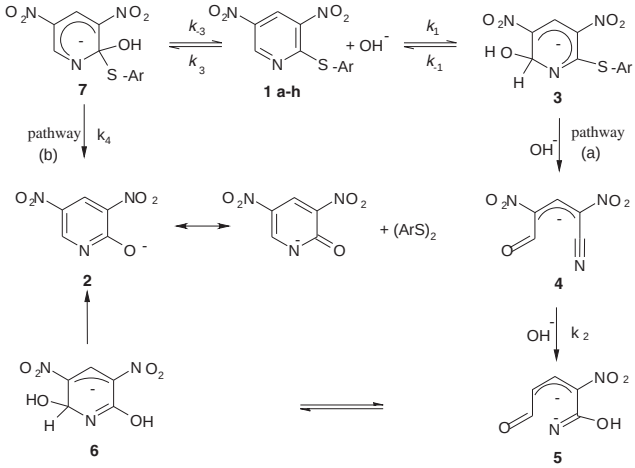
The mechanism of pathway (b) involves exclusively attack of hydroxide ion to the C-2 position [$S_N(AE)^{ipso}$] to form a Meisenhemer complex **7.** Otherwise, the reaction involves the addition of hydroxide ion to the unsubstituted 6-position,[7] **3**. The identity of the intermediate may be the C-2 complex **7**, mechanism of pathway (b), or may be the attack of C-6 **3** as reported[7]. If the latter is the case, then the C-2 complex is not observed at all, since we see only one coloured intermediate. The reaction would then follow the pathway (b)

Table 1 Physical properties of diaryl disulfides

Disulfide	Yield/%	Melting point/°C
$(PhS)_2$	80	60(lit. ref.10) 61
$(4\text{-}CH_3PhS)_2$	78	58(lit. ref.11) 57
$(4\text{-}CH_3OPhS)_2$	72	48(lit. ref.2) 46
$(4\text{-}BrPhS)_2$	89	114(lit. ref.12)112
$(4\text{-}ClPhS)_2$	85	74(lit. ref.10) 73



Scheme 1
1a, Ar = -C_6H_5; **1b**, Ar = 3-Cl-C_6H_4; **1c**, Ar = 4-Cl-C_6H_4; **1d**, Ar = 3-Br-C_6H_4; **1e**, Ar = 4-Br-C_6H_4; **1f**, Ar = 3-MeO-C_6H_4; **1g**, Ar = 4-MeO-C_6H_4; **1h**, Ar = 4-Me-C_6H_4



Scheme 2

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Table 2 Second order rate constants (k_2 l mol^{-1}s^{-1}) for the reaction of 2-thioaryl-, 3,5-dinitropyridine (5×10^{-5}M) and sodium hydroxide (5×10^{-4}- 5×10^{-3} M) in 50% DMSO-water (v/v)

		[OH$^-$] 10^3 / k_{obs} 10^4						k_2
Cpd	Ar	0.5	1.0		2.0	3.0	4.0	5.0
1a	C_6H_5	0.58	1.24	3.15	5.19	6.91	8.44	0.17
1b	3-Cl-C_6H_4	1.00	3.07	7.00	12.00	16.30	22.03	0.41
1c	4-Cl-C_6H_4	0.70	1.45	4.76	7.67	10.70	13.50	0.26
1d	3-Br-C_6H_4	0.83	2.17	6.36	11.89	17.13	19.19	0.39
1e	4-Br-C_6H_4	0.54	2.57	5.14	9.94	13.30	16.80	0.33
1f	3-MeO-C_6H_4	0.56	1.99	5.18	6.53	-	13.19	0.25
1g	4-MeO-C_6H_4	0.41	0.88	1.80	3.30	5.10	6.70	0.10
1h	4-Me-C_6H_4	0.95	1.80	3.40	5.00	6.60	8.10	0.16

Where, ρ value is 0.85 (r = 0.95).

mechanism, where k_1>> k_3. Since the C-2 complex **7** is generally thermodynamically more stable than the C-6 complex, **3**, k_3 must be small and k_4 large if the C-6 complex **3** is not observed.

When solutions of **1a–h** and an excess of sodium hydroxide (1:100) in 50% DMSO-water are mixed, a pale to deep yellow colour (depending on the R-substituent) appears immediately which changes slowly to colourless. The values of λ_{max} for all substituents are constant because their effects are small on the pyridyl moiety through the sulfur atom of intermediates **7a–h**. The extinction coefficient at this wavelength has a different value for each of these intermediates. Therefore, the fast step cannot be studied kinetically because the formation of yellow colour at λ_{max} 470 nm is to fast to be followed with a stopped-flow spectrophotometer. The pseudo rate constant at 30°C for the formation of the product **2** was followed by the decreasing in absorbance with time of the intermediate **7** at λ_{max} 470nm using UV spectrum pathway (b). The kinetic measurement of the product **2** at λ_{max} 345 (nm) cannot be measured because of overlapping with other species at this wavelength.

The kinetic runs were carried out for the reaction of sodium hydroxide with each 2-thioaryl-3,5-dinitropyridine derivative in 50% v/v DMSO-water at 30°C, Table 2.

Table 2 shows that the rate constants (k_2 l mol^{-1}s^{-1}) at 30°C depends on the nature of the position of the leaving group, where electron-attracting substituents in the thioaryl moiety increase the reaction rate constants, whereas electron donating substituents decrease the rate constant. The small difference between rate constants of various substituents indicates that the activated complex contains a partial negative charge Fig. 1.

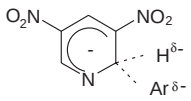

Fig. 1

The sign and magnitude of the charge of the activated complex can be calculated from the plot of log k_2 against σ Hammett constants. The slope gave ρ = +0.85 indicating a partial negative charge in the transition state, conforming this proposal. Therefore, the S_N(ANRORC) mechanism, Scheme 1, pathway(a), was not the case, since the ρ value would be higher than observed, beside the slight substituent effects in addition to the absence of the absorbance of the open intermediate **4.**[7]

We have measured the rate constants under pseudo first order conditions for 2-thiophenyl-3, 5-dinitropyridine **1a** at different temperatures (25–40°C), Table 3.

Table 3 reveals that the rate constants k_{obs} s^{-1} increases as the temperature is elevated. The overall second order rate constants k_2 (l mol^{-1} s^{-1}) were calculated by eqn (2)

$$k_2 = k_{obs} / [OH^-] \qquad (2)$$

However, log k_{obs} versus log [OH$^-$] gave straight lines but their slopes are slightly higher or lower than one (slopes 0.93 ± 0.01– 1.40 ± 0.09)

Table 3 Rate constants k_{obs} (s^{-1}) and k_2 (l mol^{-1}s^{-1}) and thermodynamic parameters for the 2-thiophenyl-3, 5-dinitropyridine 1a (5×10^{-5}M) and sodium hydroxide (5×10^{-3}M) (1:100)

t/ºC	10^4k_{obs}/s^{-1}	10^2 k_2/l mol^{-1}s^{-1}
25	4.52	9.04
30	8.44	16.88
35	12.27	24.53
40	17.70	35.40

Where, $\Delta H^{\#}$ = 67.07 kJ mol^{-1}, $\Delta S^{\#}$ = -83.42 J mol^{-1} at 25°C.

implying that the rate is proportional to the power of OH$^-$ concentration. This is because OH$^-$ ions can presumably be slightly involved in pathway (a), Scheme 2.

The large activating power of the two nitro and aza groups with the strong nucleophilicity of OH$^-$ is expected to give a small enthalpy of activation for the decomposition of the intermediate.[7] The value of entropy of activation $\Delta s^{\#}$ indicates that the reaction is bimolecular reaction and is consistent with the ordered activated complex,[7] pathway (b), Scheme 2.

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