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Kinetics of base-catalyzed cyclization of 2,6-dinitrophenylsulfanyl ethanenitrile and 2,4,6-trinitrophenylsulfanyl ethanenitrile[†]

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The kinetics of base catalyzed cyclization of 2,6-dinitrophenylsulfanyl ethanenitrile and 2,4,6-trinitrophenylsulfanyl ethanenitrile giving 2-cyano-7-nitrobenzo[*d*]thiazole-3-oxide and 2-cyano-5,7-dinitrobenzo[*d*]thiazole-3-oxide respectively was studied in methanolic methoxyacetate, acetate, trichlorophenoxide, *N*-methylmorpholine, and *N*-methylpiperidine buffers at 25 °C and $I = 0.1\ \mathrm{mol\,L^{-1}}$. It was found that reaction involves both general acid and general base catalyses whose manifestation depends on the pK_a of the acid-buffer component and the ratio of both buffer components. In weakly basic buffers the rate-limiting step is C—H bond breaking in the cyclic intermediate, while in strongly basic buffers the rate-limiting step is the general acid-catalyzed elimination of hydroxyl group from the intermediate. Copyright © 2008 John Wiley & Sons, Ltd.

Keywords: cyclization reactions; acid–base catalysis; reaction kinetics; mechanism; *N*-oxides

INTRODUCTION

In recent years we have dealt with the kinetics and mechanisms of intramolecular reactions of carbanions having an adjacent electron-deficient center,[1–5] most frequently a nitro group. The nucleophilic attack on the nitrogen atom of the nitro group proceeds easily, in such cases, when the intramolecular reaction can produce five- or six-membered rings. The ring closure reaction of *ortho*-substituted nitroarenes, involving the condensation reaction between a nitro group and nucleophilic center at the *ortho*-standing substituent, can be considered a standard way for the preparation of various heterocyclic *N*-oxides (nitrones).[6]

In our previous papers[1–5] we have dealt with structure–reactivity relationships of 6-substituted methyl 2,4-dinitrophenylsulfanyl ethanoates. When a carbanion is linked with 2,4-dinitro-6-Z-trisubstituted benzene ring by a sulfur-bridge substituted benzothiazole-*N*-oxide is formed in such cases where Z is an alkyl group,[3] halogen,[3] or another nitro group.[5] The reaction fails[7] for the parent derivative carrying hydrogen in position 6- (Z = H) but for methyl-2,6-dinitrophenylsulfanylethanoate (hydrogen in position 4-) proceeds smoothly.[5] The difference in behavior of the 2,4-dinitrophenyl derivative and the other derivatives is obviously due to steric effects. The substituents at 2- and 6-positions sterically enforce such a conformation of the side chain that approaches the arrangement of the transition state of cyclization step. This conformation of the starting compounds was proved by means of X-ray.[4]

Different behavior was observed in the case of the 6-methoxycarbonyl derivative[3] and 6-cyano derivative,[8] when the reaction gave – instead of the expected *N*-oxide – a product of attack at the methoxycarbonyl group or at the cyano group.

The aim of this work is to find out what effect, upon kinetics and mechanism of the cyclization, will result from substitution of the activating ester group by a nitrile group. It is well known that interaction of a nitrile group adjacent to carbanionic center considerably differs from that of the ester group bound in the same way. In the case of esters, their conjugated base is stabilized by both the negative inductive effect of the ester group and partial delocalization of the electron pair being released over the carbonyl group.[9] This delocalization is not synchronous with the C—H bond breaking, which results in an increase in energy of the transition state of proton transfer and lowers the rate of cleavage of the proton from the ester molecule as well as lowering the carbanion reverse protonation rate (the principle of nonperfect synchronization[10–13]). The interaction between a carbanion center and an α-cyano group is largely polar; stabilization of cyanocarbanions by transfer of negative charge onto the α-cyano group is relatively unimportant in comparison with their stabilization by the polar effect of the cyano group; the concentration of negative charge at carbon atom of a CH group in the carbanion is substantially higher in the case of a nitrile than in the case of an ester, and the proton transfer in both directions is substantially faster than that in the case of esters of comparable acidity.[14]

EXPERIMENTAL

Compounds

Preparation and characterization of 2,6-dinitrophenylsulfanyl ethanenitrile (**1**), 2-cyano-7-nitrobenzo[*d*]thiazole-3-oxide (**2**),

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[†] This paper is dedicated to the memory of Professor Otto Exner who passed away on 30 January 2008.

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Table 1. pK_a values of acid buffer components in methanol at 25°C and $I = 0.1$ mol L^{-1}

Buffer	pK_a
Acetate	9.52
Methoxyacetate	8.36
2,4,6-Trichlorophenoxide	10.52
N-methylmorpholine	9.12
N-methylpiperidine	11.05

2,4,6-trinitrophenylsulfanyl ethanenitrile (**3**), 2-cyano-5,7-dinitrobenzo[*d*]thiazole-3-oxide (**4**), and 2-carbamoyl-7-nitrobenzo-[*d*]thiazol-3-oxide (**5**) were described in Reference.[15]

pK_a values of acid buffer components

The pK_a values of methoxyacetic acid, *N*-methylmorpholinium, *N*-methylpiperidinium, and 2,4,6-trichlorophenol in methanol (Table 1) were determined spectrophotometrically from the absorptions of indicators (2-chloro-4-nitrophenol and 4-nitrophenol) using the procedure described in Reference.[2] The pK_a value of acetic acid in methanol[16] is 9.52. For calculation of the concentration of methoxide anion in buffers the value of pK_S(CH_3OH) = 16.916 was adopted.[17]

Kinetic measurements

Methanol (UV–Vis grade) was refluxed under argon to remove traces of carbon dioxide and was stored under an argon atmosphere. Its quality was checked by means of UV–Vis spectroscopy. Absorbance of the pure solvent against an empty cell was lower than 0.08 at wavelengths above $\lambda = 250$ nm, $l = 1$ cm.

Anhydrous sodium perchlorate p.a. for adjustment of ionic strength was dried at 100 °C/2.6 kPa for 6 h. Commercially available (Aldrich) acids and tertiary amines for buffers were distilled, and the fractions with b.p. 106–107 °C (*N*-methylpiperidine), b.p. 115–116 °C (*N*-methylmorpholine), and b.p. 202–203 °C (methoxyacetic acid) were used. 2,4,6-Trichlorophenol was recrystallized from aqueous methanol and filtered with charcoal, m.p. 65–66 °C. All buffers were prepared according to Reference.[5]

All the kinetic measurements were carried out using a HP 8453 Diode Array Spectrophotometer at 25 ± 0.1 °C and ionic strength $I = 0.1$ mol L^{-1} at the wavelengths of 375 and 308 nm (for compound **1**) and 381 nm (for compounds **3**) and at the substrate concentrations of *ca* 4×10^{-5} mol L^{-1}.

RESULTS AND DISCUSSION

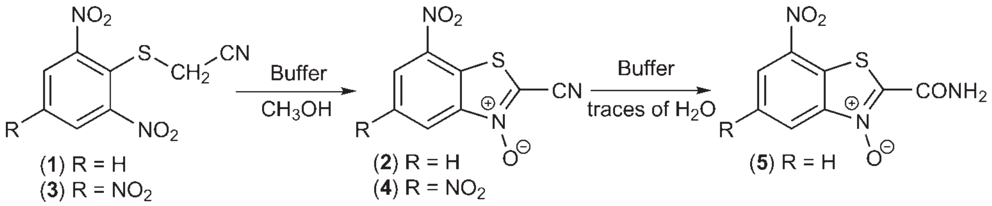
Kinetics of cyclization reaction of 2,6-dinitrophenylsulfanyl ethanenitrile (1)

The base-catalyzed cyclization of nitrophenylsulfanyl ethanenitriles **1** and **3** in buffers produces substituted 2-cyanobenzo[*d*]thiazole-3-oxides **2** and **4**, respectively (Scheme 1). In the case of compound **2** in basic *N*-methylpiperidine buffers, subsequent hydrolysis of the nitrile group to amide **5** was also observed.[15] This hydrolysis took place even if the methanol used was pre-dried with magnesium, and in more acidic buffers it was slower than the cyclization itself by several orders of magnitude.

The cyclization reaction kinetics were studied in methanolic solutions of methoxyacetate, acetate, trichlorophenoxide, *N*-methylmorpholine, and *N*-methylpiperidine buffers with the c_B/c_{BH} ratios ranging from 1:4 to 8:1. It was found that the dependences of the observed rate constants (k_{obs}) upon buffer concentration ($c_{Buffer} = c_{BH} + c_B$) are linear (except for those measured in the *N*-methylpiperidine buffers), and their slopes give the catalytic constant of the respective buffer (k_{Buff}). Extrapolation to zero buffer concentration gave the catalytic constants (k_{ext}). In this case, the only catalytic species is the methoxide anion, whose concentration is given by the ratio c_B/c_{BH} (Fig. 1). The values of rate constants k_{Buff} and k_{ext} are presented in Table 2.

Plotting of the extrapolated rate constants (k_{ext}) obtained in the individual buffers against the methoxide anion concentration in these buffers gave a nonlinear dependence (Fig. 2). In the case of cyclizations of methyl 2,6-dinitrophenylsulfanyl ethanoate[5] and methyl 2,4,6-trinitrophenylsulfanyl ethanoate,[2] these dependences were linear and their slopes gave the rate constants (k_{MeO}) for the rate-limiting breaking of the C—H bond in the starting esters by methoxide ion. In the case of 2,6-dinitrophenylsulfanyl ethanenitrile (**1**), this nonlinear dependence has a shape characteristic for reactions with an acid–base pre-equilibrium, which means that the rate-limiting step for the reaction **1** → **2** is preceded by a fast equilibrium producing a carbanion which subsequently undergoes intramolecular cyclization to give **In**$_1^-$ (Scheme 2).

The formation of the C—N bond in the cyclization of the conjugated base of 2,6-dinitrophenylsulfanyl ethanenitrile (**S**$^-$) giving **In**$_1^-$ is probably very fast. The reasons lie in the favorable arrangement of the interacting groups,[18] the high concentration of negative charge at the carbon atom in the carbanion **S**$^-$ (the extent of delocalization of lone electron pair in carbanions stabilized by an ester group is substantially higher than that in



Scheme 1.

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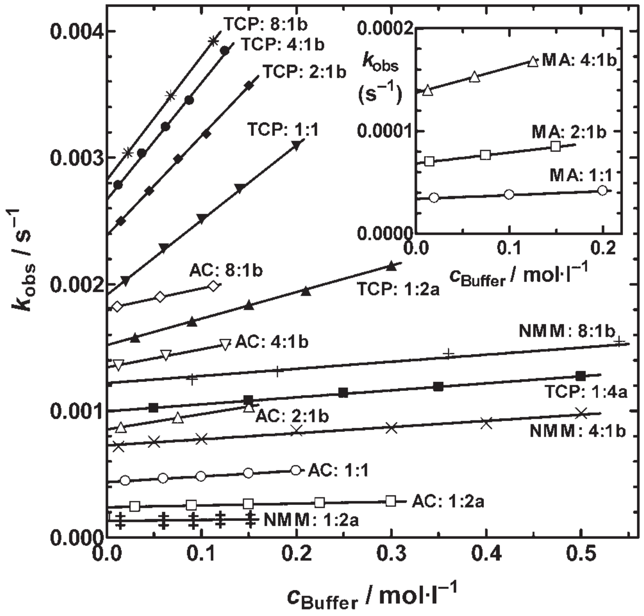

Figure 1. Dependence of the observed rate constant (k_{obs}) for the reaction **1** → **2** on the total buffer concentration ($c_{Buffer} = c_B + c_{BH}$) in acetate buffers (AC), 2,4,6-trichlorophenoxide buffers (TCP), and *N*-methylmorpholine buffers (NMM). Inset: methoxyacetate buffers (MA). *Note*: (1:1) and (2:1b) *N*-methylmorpholine buffers are omitted due to better clarity; a, acidic; b, basic

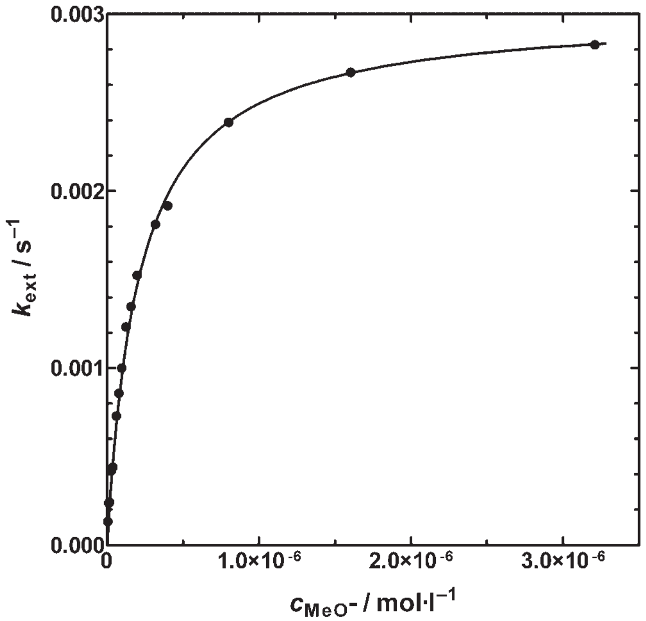

Figure 2. Dependence of the extrapolated rate constant k_{ext} (s^{-1}) *versus* c_{MeO^-} (mol L^{-1}) for the reaction **1** → **2** measured in acetate, *N*-methylmorpholine, and 2,4,6-trichlorophenoxide buffers

Table 2. Rate constants k_{ext} (s^{-1}) and k_{Buff} (L mol^{-1} s^{-1}) for cyclization of **1** in buffers with different ratio c_B/c_{BH}

	c_B/c_{BH}	k_{ext} (10^4)	k_{Buff} (10^4)	k^{corr}_{Buff} (10^3)
Methoxyacetate buffers	1:1	0.339	0.389	2.922
	2:1	0.684	1.070	4.073
	4:1	1.371	2.486	4.856
Acetate buffers	1:2	2.386	1.481	1.667
	1:1	4.362	4.508	2.763
	2:1	8.541	11.99	4.271
	4:1	13.43	14.35	3.276
	8:1	18.08	15.97	2.621
2,4,6-trichlorophenolate buffers	1:4	9.961	5.532	1.688
	1:2	15.20	20.93	4.240
	1:1	19.14	59.22	8.956
	2:1	23.85	78.58	9.873
	4:1	26.66	92.64	10.46
	8:1	28.23	97.78	10.41
N-methylmorpholine buffers	1:2	1.272	1.048	2.806
	1:1	2.337	2.333	3.239
	2:1	4.163	4.033	3.001
	4:1	7.258	4.879	2.056
	8:1	12.29	5.607	1.464
N-methylpiperidine buffers	1:4	24.49	140.4	22.54
	1:2	26.32	153.3	19.70
	1:1	29.39	157.2	18.10
	2:1	32.29	137.1	14.75
	4:1	31.92	128.8	13.37

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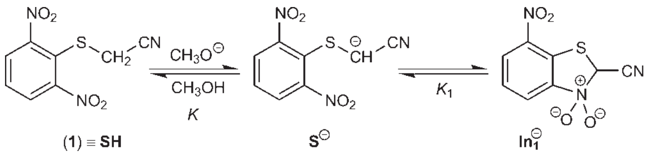


Scheme 2.

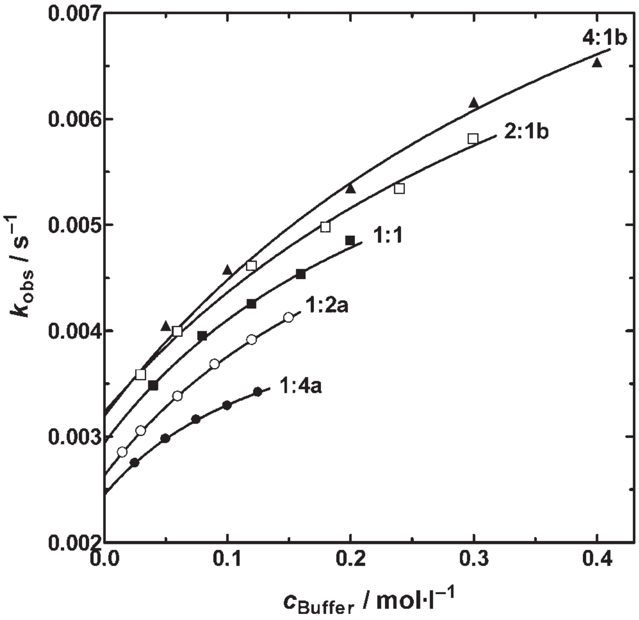


Figure 3. Dependence of the observed rate constant (k_{obs}) of reaction **1** → **2** on the total buffer concentration ($c_{Buffer} = c_B + c_{BH}$) in *N*-methylpiperidine buffers

carbanions stabilized by a nitrile group, which means that the electron density at the α-carbon atom in the carbanion is substantially higher in nitriles than in esters), the sterically enforced deviation of the *ortho*-nitro group out of the ring plane,[15] and the thermodynamically favorable formation of a five-membered ring.[19] The reverse breaking of this bond must be fast too, because in the case of the analogous 2,4-dinitrophenylsulfanyl ethanenitrile the reaction performed in the most basic *N*-methylpiperidine buffer gave no detectable amounts of the cyclization product even after several days. Therefore, it can be presumed that the fast acid–base pre-equilibrium is followed by formation of the negatively charged intermediate $\mathbf{In}_1^-$, this subsequent step being fast and reversible too (K_1).

The rate differences for cleavage of the proton from methyl di- and trinitrophenylsulfanyl ethanoate[2,5] and 2,6-dinitrophenylsulfanyl ethanenitrile (**1**) are in accordance with non-perfect synchronization principle. In the case of the ester the C—H bond breaking and its reverse formation is not synchronized[10–13] with the extent of delocalization of electron pair over the ester group and its reverse localization, which decelerates both the breaking and the formation of the C—H bond and hence also the rate constant of establishing of acid–base equilibrium. For the same reason, the formation of the C—N bond during the cyclization of methyl di- and trinitrophenylsulfanylethanoate[2,5] and its reverse breaking are decelerated too.

For reactions involving fast acid–base pre-equilibrium the kinetic Eqn (1) can be written, where K is the equilibrium constant of formation of $\mathbf{S}^-$, k the rate constant of transformation of $\mathbf{In}_1^-$ into the product, and K_1 is the equilibrium constant of the equilibrium between $\mathbf{In}_1^-$ and $\mathbf{S}^-$

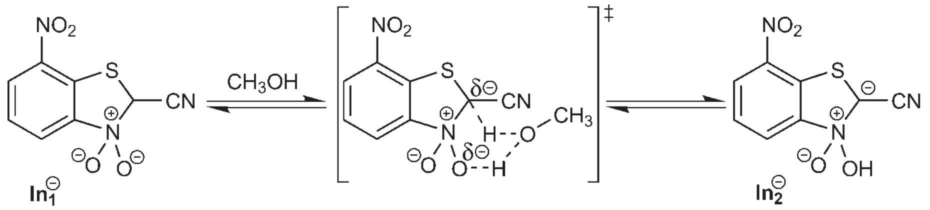
$$k_{ext} = \frac{k \cdot K_1 \cdot K \cdot [\mathrm{CH_3O^-}]}{1 + K \cdot [\mathrm{CH_3O^-}]} \qquad (1)$$

The nonlinear regression of the experimental points presented in Fig. 3 using Eqn (1) gave the values of $K = 4.8 \times 10^6\ \mathrm{L\ mol^{-1}}$ and $k \times K_1 = 3.013 \times 10^{-3}\ \mathrm{s^{-1}}$. The calculation using the equation $\mathrm{p}K_a = \mathrm{p}K + \mathrm{p}K_S(\mathrm{CH_3OH})$ gave the value of $\mathrm{p}K_a(\mathbf{1}) = 10.23$.

The transformation of the intermediate $\mathbf{In}_1^-$ into product (k) is catalyzed by methanol. If methoxide was also involved, then the value of k would increase with the buffer basicity (i.e., with methoxide concentration). The breaking of the C—H bond in $\mathbf{In}_1^-$ is so much facilitated by the presence of adjacent positively charged nitrogen atom that the methoxide virtually does not make itself felt. The transformation of $\mathbf{In}_1^-$ to product **2** involves the methanol-catalyzed C—H bond breaking, protonation of the negatively charged oxygen atom, subsequent methanol-catalyzed breaking of the N—OH bond, and concerted formation of the C=N double bond. The proton transfer from carbon to oxygen ($\mathbf{In}_1^- \rightarrow \mathbf{In}_2^-$) can take place in two steps or in one single step via a cyclic transition state (Scheme 3). This solvent-mediated proton switch[20] is made possible by the energy gain from the formation of a new O—H bond, which thus facilitates the C—H bond breaking.

In the presence of buffers, a similar fast pre-equilibrium exists; however, the transformation of $\mathbf{In}_1^-$ to product is also catalyzed by buffer, not only by methanol (Scheme 4), and k_{obs} increases linearly with the buffer concentration. In this case, the transformation of $\mathbf{In}_1^-$ to $\mathbf{In}_2^-$ proceeds in two steps via $\mathbf{In}_1^{2-}$:

The equilibrium between $\mathbf{In}_1^{2-}$ and $\mathbf{In}_2^-$ is also established very rapidly, because it involves a proton transfer between two electronegative atoms. Similar deviation in behavior of lyate anion (hydroxide in water or methoxide in methanol) and base



Scheme 3.

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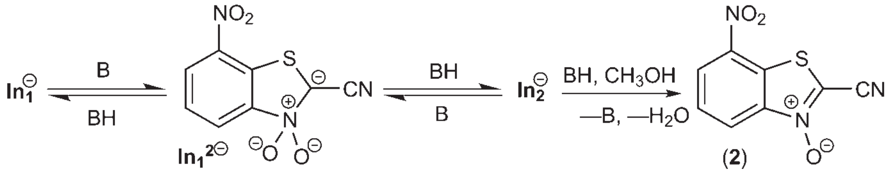

Scheme 4.

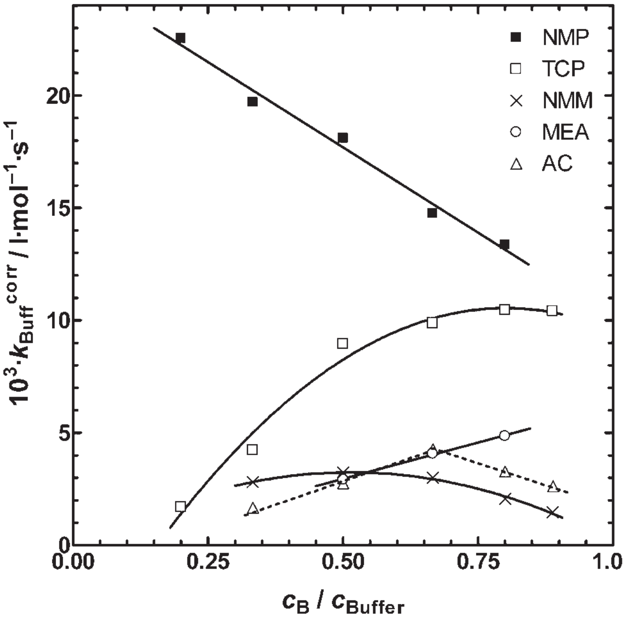

Figure 4. Dependence of the corrected rate constant k^{corr}_{Buf} (L mol^{-1} s^{-1}) for buffer catalyzed reaction **1** → **2** on the basic fraction of buffer (c_B/c_{Buffer}) in methoxyacetate (MA), acetate (AC), *N*-methylmorpholine (NMM), 2,4,6-trichlorophenoxide (TCP), and *N*-methylpiperidine (NMP) buffers

buffer component can often be observed in Brønsted plots where k_{OH} or k_{MeO} lie out of linear dependence.

In *N*-methylpiperidine buffers, the dependences of k_{obs} on c_{Buffer} are not linear, and the extrapolation to zero buffer concentration provides the rate constants k_{ext} (Fig. 3) again. The values of k_{ext} and k_{Buff} (Table 2) were obtained by nonlinear regression of the data using Eqn (2), where k^R_{Buff} is the rate constant of buffer-catalyzed reverse protonation of the intermediate, $\mathbf{In}_1^{2-} \rightarrow \mathbf{In}_1^-$, and k_p is the rate constant of the transformation $\mathbf{In}_1^{2-} \rightarrow \mathbf{2}$ (as shown in Scheme 4).

$$k_{obs} = k_{ext} + \frac{k_{Buff} c_{Buffer}}{1 + \frac{k^R_{Buff}}{k_p} c_{Buffer}} \qquad (2)$$

The relatively low value of pK_a(**1**) = 10.23 indicates that the substrate is dissociated to the extent given by the ratio of c_B/c_{BH} and pK_a(BH) in all buffers used. However, only the carbanion $\mathbf{S}^-$ is the reactive form, while the substrate itself does not undergo cyclization. Therefore, the obtained catalytic constants k_{Buff} have to be corrected using Eqn (3). The values of k^{corr}_{Buff} are presented in Table 2.

$$k^{corr}_{Buff} = k_{Buff}\left(1 + 10^{(pK_a(\mathbf{1}) - pK_a(BH) - \log[B]/[BH])}\right) \qquad (3)$$

Plotting of k^{corr}_{Buff} values against the ratio c_B/c_{Buffer} provides a linear dependence from which it is possible to determine[21] the catalytic constants of both buffer components. Extrapolation to $c_B/c_{Buffer} = 0$ and 1 gives the catalytic constants k_B and k_{BH}, respectively.

Similar linear plots (Fig. 4) were observed for the cyclization reaction of compound **1** in methoxyacetate buffers, where the slope was positive, and in *N*-methylpiperidine buffers, where – on the contrary – the slope was negative. This means that only the basic buffer component (methoxyacetate anion) is catalytically active in the methoxyacetate buffers, which agrees with the presumption that the rate-limiting step of the reaction is proton cleavage from $\mathbf{In}_1^-$ by a relatively weak base (pK_a = 8.36). In acetate, *N*-methylmorpholine and 2,4,6-trichlorophenoxide buffers, the dependence shows a very unusual break: at first the value of k^{corr}_{Buff} increases with increasing proportion of the basic form of the buffer, but from a certain ratio c_B/c_{Buffer} the value of k^{corr}_{Buff} decreases. This shape of the dependence of k^{corr}_{Buff} *versus* c_B/c_{Buffer} probably indicates a change in the rate-limiting step of the reaction. Increasing the strength of the basic component of the buffer (in terms of pK_a from 9.12 to 10.52) accelerates cleavage of the proton from $\mathbf{In}_1^-$, and the rate-limiting step gradually switches to the general acid-catalyzed cleavage of OH group from $\mathbf{In}_2^-$ giving **2**. In the most basic *N*-methylpiperidine buffers (pK_a = 11.05), the cleavage of the proton from $\mathbf{In}_1^-$ is fast, and the rate-limiting step changes to the general acid-catalyzed cleavage of OH group from $\mathbf{In}_2^-$ in all buffers.

The earlier break of the dependence in the *N*-methylmorpholine buffers is probably due to the fact that nitrogen bases operate more effectively than oxygen bases in the processes of proton transfer from a C-acid.

In *N*-methylpiperidine buffers, the value of k_{obs} increases with the concentration of the base faster at lower base concentrations than at higher base concentrations (Fig. 3). Even at very low concentrations of the basic form of the buffer, the rate of C—H bond breaking in $\mathbf{In}_1^-$ is considerably high and hence the catalysis by *N*-methylpiperidine operates side by side with the breaking of this bond catalyzed by methanol alone (k_0).

The fact that the cyclization of compound **1** needs also the acid component of buffer follows from the finding that no cyclization, giving product **2**, takes place in solutions of sodium methoxide alone.

Kinetics of cyclization of 2,4,6-trinitrophenylsulfanyl ethanenitrile (3)

The cyclization reaction of 2,4,6-trinitrophenylsulfanyl ethanenitrile (**3**) in methanolic methoxyacetate, acetate, and *N*-methylmorpholine buffers gives 5,7-dinitrobenzo[*d*]thiazole-3-oxide (**4**) as the only product. Compound **4** is produced by the cyclization of compound **3** even in methanol alone, the reaction half-life being about 15 min ($k_0 = 7.7 \times 10^{-4}$ s^{-1}).

Table 3. Rate constants k_{ext} (s^{-1}) and k_B ($L\,mol^{-1}\,s^{-1}$) of cyclization of **3** in buffers with the different ratio c_B/c_{BH}

	c_B/c_{BH}	k_{ext} (10^3)	k_{Buff} (10^3)	k_B (10^3)
Methoxyacetate buffers	1:4	0.753	0.9433	4.716
	1:2	1.099	3.820	11.46
	1:1	1.267	10.26	20.51
	2:1	1.689	13.77	20.65
	4:1	2.244	16.23	20.29
Acetate buffers	1:2	3.338	12.39	37.16
	1:1	4.851	18.45	36.89
	2:1	9.002	25.29	37.93
	4:1	17.14	30.44	38.05

The dependences of the observed rate constants (k_{obs}) upon buffer concentration (c_{Buffer}) or the concentration of its basic component (c_B) in methoxyacetate and acetate buffers are linear over the whole range of concentrations measured; their slopes give the values of k_{Buff} or k_B, respectively, and their intercepts give the values of k_{ext} (Table 3). The dependence of k_{ext} on methoxide anion concentration is linear in this case (Fig. 5), and its slope gives the catalytic rate constant for methoxide anion, $k_{MeO} = 9.97 \times 10^4\,L\,mol^{-1}\,s^{-1}$. Hence here it is impossible to determine the precise value of $pK_a(\mathbf{3})$, in contrast to what was described above for compound **1**. The values of k_B obtained in methoxyacetate buffers (Table 3) show an increase at the beginning but then, starting from the ratio of $c_B/c_{BH} = 1$, they are virtually the same. In more basic acetate buffers (Table 3) they exhibit oscillations about the value of $k_B = (37.5 \pm 0.6) \times 10^{-3}\,L\,mol^{-1}\,s^{-1}$. From this behavior it can be deduced that compound **3** is present in the form of its conjugated base (carbanion) in basic methoxyacetate buffers. The estimated value for the pK_a (**3**) ≈ 8 stands in accord with the acidifying effect of the additional nitro group on the benzene ring. Thus except for the acidic methoxyacetate buffers, the correction of constants k_{Buff} or k_B will not markedly change their values.

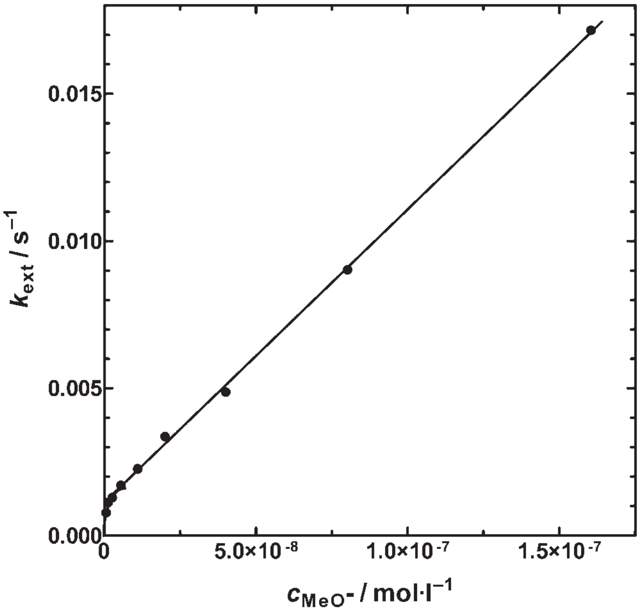

Figure 5. Dependence of extrapolated rate constants k_{ext} (s^{-1}) of cyclization of compound **3** in methoxyacetate buffers on methoxide concentration ($[CH_3O^-]$ ($mol\,L^{-1}$))

Like in the case of the 2,6-dinitro derivative **1**, the rate-limiting step of cyclization in methoxyacetate and acetate buffers is breaking of the C—H bond in intermediate $\mathbf{In}_1^-$ by methoxyacetate or acetate anion (k_B) or, as the case may be, also by methoxide anion (k_{MeO}). The rate of establishing of the equilibrium between substrate **3** and its conjugated base ($\mathbf{S}^-$) was investigated by means of a deuteration experiment. Almost all hydrogen of the —SCH_2— group of compound **3** was replaced by deuterium in an acidic acetate buffer ($[CH_3COOD]/[CH_3COONa] = 2{:}1$, $[CH_3COONa] = 0.05\,M$) in CD_3OD within a period of time in which only *ca* 35% of the cyclization had taken place. Of course, the equilibrium was reached much more rapidly in CH_3OH because:

a) when most of the hydrogen in CH_2 group of the substrate has been replaced by deuterium, it is predominantly deuterium that is removed by reaction with methoxide or acetate;
b) simultaneously, the methoxide-catalyzed cyclization reaction is taking place which is not accompanied by replacement of hydrogen by deuterium.

The dependence of k_{obs} on c_{Buffer} is also linear in the *N*-methylmorpholine buffers at higher buffer concentrations. A downward deflection is only observed at the lowest concentrations. In this case, the value of k_{ext} does not correspond to the catalytic action of methoxide ion. Therefore, Table 4 only presents the values of the catalytic constant k_{Buff} or its corrected value k_{Buff}^{corr} (the correction was carried out by means of Eqn (3) in which the value of $pK_a(\mathbf{3}) = 8$ was used). Plotting of k_{Buff}^{corr} against the c_B/c_{Buffer} ratio gives the graph presented in Fig. 6.

Table 4. Corrected rate constants k_{Buff} and k_{Buff}^{corr} ($L\,mol^{-1}\,s^{-1}$) for cyclization of **3**

	c_B/c_{BH}	k_{Buff} (10^3)	k_{Buff}^{corr} (10^3)
N-methylmorpholine buffers	1:4	22.80	33.77
	1:2	24.83	30.80
	1:1	24.75	27.73
	2:1	24.33	25.79
	4:1	17.44	17.96

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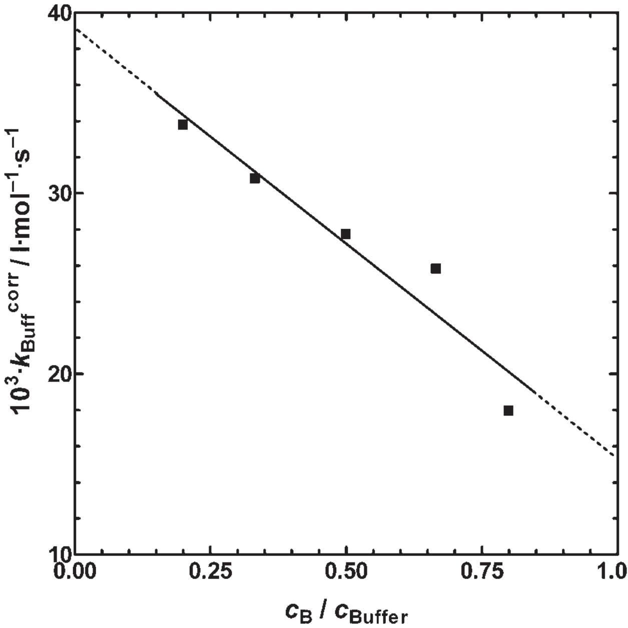

Figure 6. Dependence of the corrected rate constant k_{Buf}^{corr} (L mol^{-1} s^{-1}) for buffer catalyzed reaction **3** → **4** on the basic fraction of *N*-methylmorpholine buffer (c_B/c_{Buffer})

The value k_{Buff}^{corr} extrapolated to $c_B/c_{Buffer} = 1$ gives $k_B = 1.3 \times 10^{-2}$ L mol^{-1} s^{-1}, and that extrapolated to $c_B/c_{Buffer} = 0$ gives $k_{BH} = 3.96 \times 10^{-2}$ L mol^{-1} s^{-1}, which means that the rate-limiting step of the cyclization in *N*-methylmorpholine buffers consists in the cleavage of the OH group from $\mathbf{In}_2^-$.

CONCLUSIONS

The kinetics and mechanism of cyclization of 2,6-dinitrophenylsulfanyl ethanenitrile (**1**) and 2,4,6-trinitrophenylsulfanyl ethanenitrile (**3**) giving 2-cyano-7-nitrobenzo[*d*]thiazol-3-oxide (**2**) and 2-cyano-5,7-dinitrobenzo[*d*]thiazol-3-oxide (**4**), respectively, were studied in methanolic *O*-buffers (methoxyacetate, acetate, 2,4,6-trichlorophenolate) and tertiary amine *N*-buffers (*N*-methylmorpholine and *N*-methylpiperidine). In the case of cyclization of 2,6-dinitrophenylsulfanyl ethanenitrile (**1**), the dependence of the observed rate constants extrapolated to zero buffer concentration, k_{ext}, upon methoxide concentration in buffer had a shape characteristic of the existence of an acid–base pre-equilibrium. The calculated value was pK_a(**1**) = 10.23. Thereafter, the conjugated base of the substrate rapidly undergoes cyclization to give the negatively charged intermediate $\mathbf{In}_1^-$, which then much more slowly reacts to give the final product **3**, the reaction being catalyzed by methanol and/or both buffer components. While in methoxyacetate and acidic acetate, 2,4,6-trichlorophenoxide and *N*-methylmorpholine buffers the rate-limiting step involves cleavage of the C—H bond in the intermediate $\mathbf{In}_1^-$, in the basic acetate, 2,4,6-trichlorophenoxide, *N*-methylmorpholine, and all the *N*-methylpiperidine buffers the rate-limiting step involves expulsion of OH$^-$ from intermediate $\mathbf{In}_2^-$ by action of acidic component of buffer and methanol.

The cyclization of 2,4,6-trinitrophenylsulfanyl ethanenitrile (**3**) in methoxyacetate and acetate buffers is catalyzed by the basic component of the buffer and methoxide ion only, which means that, irrespective of the c_B/c_{BH} ratio, the reaction rate-limiting step is C—H bond breaking in intermediate $\mathbf{In}_1^-$. The value of pK_a(**3**) ≈ 8 can only be guessed from the region of change of the slope of dependence of k_{obs} *versus* c_B in buffers with varying c_B/c_{BH} ratio. In *N*-methylmorpholine buffers, the rate-limiting step of reaction is expulsion of OH$^-$ from intermediate $\mathbf{In}_2^-$ by action of acidic component of buffer and methanol.

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