# Kinetic and equilibrium studies of the proton and deuteron transfer reaction between diarylcyanomethanes and 1,2-bis-(dialkylaminomethyl)benzene in acetonitrile

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## Abstract

Equilibrium and rate constants, primary deuterium isotope effects, and activation parameters have been determined for the proton-transfer reactions of 4-nitrophenyl-phenyl-cyanomethane and 4-bromophenyl-4-nitrophenylcyanomethane with 1,2-bis(dimethylaminomethyl)benzene and 1,2-bis(diethylaminomethyl)benzene in acetonitrile. The reaction was followed spectrophotometrically using the stopped-flow technique. Large kinetic isotope effects at 25°C  $k_{\rm H}/k_{\rm D}$  = 16.8 – 18.8 were observed for studied reactions. The multistep mechanism of the reactions was proposed.

#### INTRODUCTION

The basicity of the following three groups of nitrogen bases is much greater than that of aliphatic or aromatic amines: guanidines, macrobicyclic amines and 1,8-diaminonaphthalenes [1].



Guanidine compounds and their derivatives  $(pK_a = 20-24$  in acetonitrile) owe their basicity to the delocalization of positive charge over the whole molecule after protonation [2].

The basic properties of macrobicyclic amines (p $K_a = 24-27$  in acetoni-

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trile) are due to the presence of three stereoisomeric forms in diprotonated bases: out-out, out-in and in-in [3].

The third group of strong nitrogen bases, 1,8-diaminonaphthalenes  $(pK_a = 17-19 \text{ in acetonitrile})$  have basic properties resulting from a significant steric hindrance which only allows the addition of a single proton at a central position between two nitrogen atoms [4].

Recently, a new group of nitrogen bases derived from benzene, 1,2bis(dialkylaminomethyl)benzenes, have been synthesized:



The determined  $pK_a$  values in acetonitrile for the 1,2-bis(di-Raminomethyl)benzenes are: R = methyl, 18.70; ethyl, 19.98; propyl, 18.47; butyl, 11.89; hexyl 11.80 [5]. Only the first three bases have exceptional basic properties similar to those of 1,8-diaminonaphthalene, while the last two derivatives (R = butyl and hexyl) behave as ordinary alkyl amines [4]. Recently it was also found that, in comparison with 1,8-dimethylaminonaphthalene, the three new bases favour the deprotonation of various acids at the same time as the strength of intramolecular NHN<sup>+</sup> hydrogen bonds diminishes [5].

The large values of the kinetic isotope effect for the reaction of proton transfer from C-acids to 1,8-diaminonaphthalene derivatives observed in acetonitrile [6,7], and a complex character of proton transfer from its protonated forms to the free bases [8–10], stimulated us to undertake studies on the kinetics of proton transfer from diarylcyanomethanes to 1,2-bis(di-R-aminomethyl)benzenes (R = methyl and ethyl) in acetonitrile.

# EXPERIMENTAL

1,2-bis(dimethylaminomethyl)benzene and 1,2-bis(diethylaminomethyl)benzene were prepared as previously described [11].

4-nitrophenyl-phenylcyanomethane, and 4-bromophenyl-4-nitrophenylcyanomethane and deuterated analogues were prepared using the method of Hojatti and Leffek [12].

Acetonitrile was purified by the standard method with final distillation over  $P_2O_5$  (81.5–82.0°C) [13].

# Equilibrium and kinetic measurements

The kinetic runs and equilibrium measurements were carried out using Specord UV-vis and stopped-flow spectrophotometers with the cell block thermostated to  $\pm 0.1^{\circ}$ C. The kinetic runs were completed under pseudo-

## TABLE 1

Equilibrium constant K (dm<sup>3</sup>mol<sup>-1</sup>) and molar absorptivity  $\varepsilon$  at 25°C for the proton-transfer reaction to give an ion pair product

Substrate C-acid	Base	K	£
1	1	$108 \pm 30$	38000
1	2	$300 \pm 50$	38000
2	1	$150 \pm 50$	40000
2	2	$480~\pm~50$	39000

first-order conditions with the base concentration in excess. The observed rate constants were calculated from traces of absorbance vs. time using the Guggenheim method and second-order rate constants for the forward (k) and backward  $(k_{-})$  reactions were calculated by a linear least-squares fit of the variation of  $k_{\rm obs}$  with base concentration  $(k_{\rm obs} = k[B] + k_{-})$ . The activation parameters were calculated by a linear least-squares fit of  $\ln k/T$  vs. 1/T.

The equilibrium constant for the reaction was determined by the Benesi-Hildebrand method [14] from the optical densities.

#### **RESULTS AND DISCUSSION**

The reactions of 4-nitrophenyl-phenylcyanomethane (C-acid 1) and 4bromophenyl-4-nitrophenylcyanomethane (C-acid 2) with 1,2-bis(di-Raminomethyl)benzenes (R = methyl (base 1) and ethyl (base 2)) in acetonitrile, gives a colour product characterized by  $\lambda_{max} = 580$  and 590 nm, respectively.

Table 1 presents the equilibrium constants and molar absorbance coefficients determined for the studied system from the Benesi-Hildebrand equation [14] for an acid concentration of  $1 \times 10^{-5} \text{ mol dm}^{-3}$  and base concentrations of  $10^{-3}$ - $10^{-2} \text{ mol dm}^{-3}$ . The equilibrium constants for the reaction of C-acid 1 with bases 1 and 2 are greater by a factor of about 100 than those for the reaction of C-acid 1 with 1,8-diaminonaphthalenes [6, 7]. However, equilibrium constants determined for the studied reactions are considerably lower than those obtained for the reaction of C-acids 1 and 2 with the strong base tetramethylguanidine (p $K_a = 23.3$ ).

Table 2 presents the rate constants of the studied reactions of proton and deuteron transfer for a C-acid concentration of  $1 \times 10^{-5}$  mol dm<sup>-3</sup> and base concentrations between  $5 \times 10^{-4}$  and  $50 \times 10^{-4}$  mol dm<sup>-3</sup>.

The values of the observed rate constants were used to calculate secondorder rate constants for the forward and backward reaction, as well as the kinetic equilibrium constant and deuterium kinetic isotope effect. All these

# TABLE 2

Observed rate constants for the proton- and deuteron-transfer reactions between diarylcyanomethanes (C-acids 1 and 2) and 1,2-bis(dialkylaminomethyl)benzenes (bases 1 and 2) in acetonitrile

Reaction	Temp. (°C)	10⁴[ <i>B</i> ] (M)	$egin{aligned} m{k}_{ ext{obs}}^{ ext{H}}\ ( ext{s}^{-1}) \end{aligned}$	$k^{ m D}_{ m obs} \ ({ m s}^{-1})$
C-acid 1 + base 1	5	550	1.65-2.18	0.072-0.101
	10	5-50	2.20 - 2.95	0.092-0.132
	15	5-50	2.65 - 3.55	0.104 - 0.158
	20	5-50	3.25 - 4.50	0.113-0.189
	25	5-50	4.10- 5.60	0.141-0.229
C-acid 1 + base 2	5	5-50	1.32 - 2.68	0.086-0.158
	10	5-50	1.68- 3.61	0.105-0.206
	15	5-50	2.10- 4.80	0.113-0.264
	20	5-50	2.63- 6.25	0.138-0.335
	25	550	3.20- 7.75	0.152 - 0.410
C-acid 2 + base 1	5	5-50	3.51 - 6.52	0.124-0.262
	10	5-50	4.50-8.20	0.135-0.315
	15	5-50	5.70-9.70	0.153-0.364
	20	5-50	7.00-11.50	0.172-0.405
	25	5-50	8.56-13.30	0.191-0.451
C-acid $2 + base 2$	5	5-50	2.80- 7.40	0.105-0.322
	10	5-50	3.50- 9.40	0.123-0.412
	15	5-50	4.30-11.90	0.147-0.523
	20	550	5.10-14.70	0.166-0.646
	25	5-50	6.01 - 17.65	0.181-0.792

values are collected in Table 3. The values of the kinetic equilibrium constants for all studied reactions calculated at a temperature of 25°C are comparable with the values of the thermodynamical equilibrium determined by the Benesi-Hildebrand method [14]. Such a result proves that a multistep reaction is controlled by the step determining the equilibrium process. Furthermore, Table 3 shows that for forward reactions, the usual Brønsted dependence between reaction rate and basicity of the bases is observed. In the case of base 2 the rate constants are larger.

The contribution of the backward reaction to the total process of formation of the reaction product in reactions of C-acids 1 and 2 with bases 1 and 2 is considerable. This is observed for both the proton- and deuteron-transfer reactions. The rate constants for the backward deuteron-transfer reactions are larger than that for isotopic exchange D/H in the ion pair. This result is in good agreement with theoretical models discussing the influence of two extreme cases of fast and slow isotopic exchange D/H in

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Rate constants, equilibrium constants and deuterium isotope effects for the proton-transfer reactions between diarylcyanomethanes (C-acids 1 and 2) and 1.2-bis(dialkvlaminomethvl)benzenes (bases 1 and 2) in acetonitrile

(C-ACIUS I AIIU Z) AIIU	1,2-015(UIA1		IZETICS (DASCS I AT	IN 2) III ACCOUNTING			
Reaction	Temp. (°C)	$k_{\rm H} \ ({ m dm}^3 { m mol}^{-1}{ m s}^{-1})$	$k_{ m H}^{-}$ (s <sup>-1</sup> )	$k_{\rm D} \ ({ m dm}^3 { m mol}{ m -1}{ m s}^{-1})$	$rac{10^2k_{ m D}^-}{ m (s^{-1})}$	$K_{ m H}^{ m (dm^3mol^{-1})}$	$k_{ m H}/k_{ m D}$
C-acid 1 + base 1	20 11 22 20 12	$117 \pm 8 \\ 159 \pm 18 \\ 205 \pm 7 \\ 285 \pm 11 \\ $	$\begin{array}{c} 1.62 \pm 0.02 \\ 2.24 \pm 0.05 \\ 2.53 \pm 0.02 \\ 3.09 \pm 0.03 \\ 0.02 \\ 0.$	$\begin{array}{c} 6.5 \pm 0.6 \\ 9.1 \pm 0.4 \\ 11.5 \pm 0.8 \\ 18.1 \pm 1.3 \\ 1.1.3$	$\begin{array}{c} 6.7 \pm 0.3 \\ 8.7 \pm 0.1 \\ 9.8 \pm 0.1 \\ 10.1 \pm 0.4 \\ 10.1 \pm 0.4 \\ 10.1 \pm 0.4 \end{array}$	72 + 5 70 + 8 82 + 3 92 + 4	$18.0 \pm 2.0 \\ 17.5 \pm 2.1 \\ 17.8 \pm 1.4 \\ 15.8 \pm 1.3 \\ 15.6 \pm 1.3 \\ 15.6 \pm 1.3 \\ 15.6 \pm 1.7 \\ 15.6 \pm 1.7 \\ 17.7 \\ 1$
C-acid 1 + base 2	5 2 1 1 1 2 1 2 2 2 2 2 2 2 2 2 2 2 2 2	$330 \pm 20$ $307 \pm 13$ $422 \pm 15$ $592 \pm 15$ $805 \pm 26$	$\begin{array}{c} 3.36 \pm 0.06 \\ 1.09 \pm 0.05 \\ 1.48 \pm 0.05 \\ 1.75 \pm 0.07 \\ 2.17 \pm 0.08 \\ 2.17 \pm 0.08 \\ 2.07 \pm 0.08 \\ 0.08 \end{array}$	$\begin{array}{c} 13.0 \pm 1.7\\ 16.0 \pm 0.7\\ 22.1 \pm 1.4\\ 33.2 \pm 1.4\\ 46.1 \pm 1.0\\ 26.1 \pm 0.6\\ 20.1 \pm 0.6\end{array}$	$\begin{array}{c} 13.4 \pm 0.0 \\ 7.7 \pm 0.1 \\ 9.9 \pm 0.4 \\ 10.9 \pm 1.3 \\ 12.1 \pm 0.5 \\ $	282 ± 18 282 ± 18 338 ± 16 370 ± 19 271 ± 19	$\begin{array}{c} 19.2 \pm 1.2 \\ 19.2 \pm 1.2 \\ 19.2 \pm 1.4 \\ 17.9 \pm 0.9 \\ 17.5 \pm 0.7 \\ 17.5 \pm 0.7 \\ 12.5 \pm 0.7 \\ 12.6 \pm 0.9 \end{array}$
C-acid 2 + base 1	20 20 20 20 20 20 20 20 20 20 20 20 20 2	655 ± 3 655 ± 3 826 ± 8 886 ± 5 1005 ± 8 1067 ± 15	$\begin{array}{c} 2.70 \pm 0.03\\ 3.20 \pm 0.07\\ 4.09 \pm 0.02\\ 5.26 \pm 0.02\\ 6.39 \pm 0.13\\ 7.90 \pm 0.10\end{array}$	$\begin{array}{c} 0.0.2 \\ 32.2 \\ 46.0 \\ 1 \\ 2.4 \\ 51.1 \\ 1 \\ 2.0 \\ 58.0 \\ 1 \\ 2.0 \end{array}$	$\begin{array}{c} 1.0.0 \pm 0.0 \\ 11.5 \pm 0.2 \\ 13.3 \pm 0.5 \\ 14.5 \pm 0.5 \\ 16.2 \pm 0.5 \\ 16.2 \pm 0.5 \end{array}$	$204 \pm 9$ $204 \pm 9$ $168 \pm 1$ $159 \pm 8$ $135 \pm 6$	$\begin{array}{c} 20.3 \pm 1.4 \\ 20.3 \pm 1.4 \\ 21.2 \pm 1.8 \\ 19.2 \pm 0.8 \\ 19.7 \pm 1.1 \\ 18.3 \pm 1.0 \end{array}$
C-acid 2 + base 2	5 15 25 25	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{rrrr} 47.8 \pm 1.6 \\ 66.1 \pm 2.1 \\ 84.1 \pm 4.5 \\ 108.0 \pm 4.0 \\ 137.0 \pm 4.0 \end{array}$	$\begin{array}{l} 8.5 \ \pm \ 0.5 \\ 8.4 \ \pm \ 0.7 \\ 9.8 \ \pm \ 1.4 \\ 10.0 \ \pm \ 1.0 \\ 10.1 \ \pm \ 1.0 \end{array}$	$\begin{array}{rrrr} 440 \pm 20 \\ 467 \pm 10 \\ 486 \pm 10 \\ 533 \pm 5 \\ 540 \pm 6 \end{array}$	$\begin{array}{rrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrrr$

the reaction product on the kinetics of the proton-transfer process [6,7,9, 10,15].

The values of the kinetic isotope effects obtained for the studied reactions were relatively large and dependend on the diarylocyanomethane used; consequently, for the stronger C-acid 2 the values of  $k_{\rm H}/k_{\rm D}$  are larger by 2 units. This result demonstrates that the transition state of this reaction is more symmetrical than that of the reaction of C-acid 1 with the studied bases.

The values of  $k_{\rm H}/k_{\rm D}$  are almost the same as those obtained in the reaction of C-acids 1 and 2 with 1,8-diaminonaphthalene in acetonitrile [7].

The values of the kinetic isotope effect can also be considered in terms of a contribution of the tunnelling effect to the observed rate constants for studied reactions of the process of proton transfer. However, the large value of the rate constant for the backward reaction in the formation process of the reaction product makes it very difficult to carry out a reliable interpretation.

Table 4 presents the activation parameters for the reactions of proton and deuteron transfer between C-acids 1 and 2, and bases 1 and 2. The significantly negative values of the entropy of activation obtained indicate an ionic character of the transition state of the reaction of neutral substrates. Moreover, the higher steric demands of the C-acids and the bases are reflected by the large negative values of entropy of activation. The enthalpies of activation  $\Delta H^{\ddagger}$  are compensated by the entropy of activation,  $\Delta S^{\ddagger}$ . The values of  $\Delta G^{\ddagger}$  in Table 4 are characteristic of ionogenic bimolecular reactions in polar aprotic solvents [16,17].

The difference  $\Delta H_D^{\ddagger} - \Delta H_H^{\ddagger}$ , which is another criterion of the occurrence of tunnelling proton transfer besides the isotope effect, is for all studied reactions lower than 5 kJ mol<sup>-1</sup> and within the range of classical values.

Table 5 presents the activation parameters of the reverse reaction of the ion pair product into substrates. The values of free entropy of activation for these reactions are by about  $12 \text{ kJ mol}^{-1}$  greater than for the reaction of proton transfer from C-acids 1 and 2 to bases 1 and 2.

Bases 1 and 2 can occur in various conformations in acetonitrile, but only one of them is able to bond a proton centrally via two nitrogen atoms.



Furthermore, the molecules of the C-acids are relatively large and, due to steric reasons, the protonation of free bases 1 and 2 can occur at only one nitrogen atom in the slow process; then the next fast step gives a stable

bis(dialkylaminometh	yl)benzenes (bases	and uceron-transfer 1 and 2) in acetonitrile	reactions between	dıarylcyanometha	nes (C-acids 1 an	d <b>2</b> ) and 1,2-
	Proton transfe	er		Deuteron transfer		
Reaction	∆H <sup>‡</sup> (kJ mol <sup>-1</sup> )	$\Delta S^{\ddagger}$ (J mol <sup>-1</sup> K <sup>-1</sup> )	ΔG <sup>‡</sup> (kJ mol <sup>-1</sup> )	ΔH <sup>t</sup> (kJ mol <sup>-1</sup> )	$\frac{\Delta S^{\ddagger}}{(\mathrm{J}\mathrm{mol}^{-1}\mathrm{K}^{-1})}$	$\Delta G^{\ddagger}$ (kJ mol <sup>-1</sup> )
C-acid 1 - base 1 C-acid 1 - base 2 C-acid 2 - base 1 C-acid 2 - base 2	$34.4 \pm 2.0$ $39.4 \pm 1.3$ $13.8 \pm 2.5$ $30.2 \pm 0.8$	$ \begin{array}{rcrcrc} -81 \pm 7 \\ -55 \pm 5 \\ -140 \pm 8 \\ -78 \pm 3 \end{array} $	$\begin{array}{l} 58.5 \ \pm \ 2.0 \\ 55.5 \ \pm \ 1.5 \\ 55.5 \ \pm \ 3.0 \\ 53.4 \ \pm \ 1.0 \end{array}$	$\begin{array}{l} 37.6 \ \pm \ 3.8 \\ 44.4 \ \pm \ 1.5 \\ 17.6 \ \pm \ 1.3 \\ 33.5 \ \pm \ 0.9 \end{array}$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{c} 65.3 \pm 4.0 \\ 63.2 \pm 1.6 \\ 62.6 \pm 2.0 \\ 60.9 \pm 1.0 \end{array}$

pug 6 Activation parameters for the proton- and deuteron-transfer reactions between diarylcyanomethanes (C-acids 1 and bis(dialkylaminomethyl)benzenes (bases 1 and 2) in acetonitrile

**TABLE 4** 

#### TABLE 5

Activation parameters for the backward reaction of the proton-transfer reaction between diarylcyanomethanes (C-acids 1 and 2) and 1,2-bis(dialkylaminomethyl)benzenes (bases 1 and 2) in acetonitrile

Reaction	$\Delta H^{\ddagger}$	$\Delta S^{\ddagger}$	$\Delta G^{\ddagger}$
			(Komor)
C-acid 1 – base 1	$26.8 \pm 2.2$	$-144 \pm 8$	$69.7 \pm 2.4$
C-acid 1 – base 2	$28.1~\pm~1.3$	$-143 \pm 5$	$70.7 \pm 1.5$
C-acid $2 - base 1$	$28.5 \pm 0.8$	$-132 \pm 6$	$67.8~\pm~1.0$
C-acid $2$ – base $2$	$\textbf{22.6} ~\pm~ \textbf{0.7}$	$-155 \pm 3$	$68.8~\pm~1.0$

product with the central proton between two nitrogen atoms. The opposite reaction to that being studied in this work has demonstrated that the process of proton transfer from protonated 1,8-diaminonaphthalene to oxygen bases [9,10] has two steps, and is controlled by the  $K_1$  equilibrium constant of process 1 and the rate constant  $k_2$  of process 2:



On the basis of the significant values of the isotope effects and activation parameters, the following mechanism of the reaction of 1,2bis(dialkylaminomethyl)benzenes with diarylcyanomethanes is proposed:



The first slow step is followed by a fast process of cyclization to a

thermodynamically very stable system  $(N \cdots H \cdots N)^+$ . The obtained results prove an analogy between proton sponges of the type 1,8-diaminonaphthalene, and the studied dinitrogen bases 1 and 2.

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