Kinetics and Mechanism for the Formation of *o*-Carboxy(*N*-methyl)benzohydroxamic Acid in the Cleavage of Ethyl *N*-[*o*-(*N*-Methyl-*N*hydroxycarbamoyl)benzoyl]carbamate in *N*-Methylhydroxylamine, Acetate, and Phosphate Buffers

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ABSTRACT: The rate of cleavage of ethyl *N*-[*o*-(*N*-methyl-*N*-hydroxycarbamoyl)benzoyl]-carbamate (ENMBC) in the buffer solutions containing *N*-methylhydroxylamine, acetate + *N*-methylhydroxylamine, and phosphate + *N*-methylhydroxylamine followed an irreversible consecutive reaction path: ENMBC $\xrightarrow{k_{1}$ obs} \mathbf{A} \xrightarrow{k_{2}obs} \mathbf{B} where \mathbf{A} and \mathbf{B} represent *N*-hydroxyl group cyclized product of ENMBC and *o*-(*N*-methyl-*N*-hydroxycarbamoyl)benzoic acid, respectively.

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Both rate constants $k_{1 \text{ obs}}$ and $k_{2 \text{ obs}}$ showed the presence of buffer catalysis, but buffer catalysis turned out to be weak in the presence of *N*-methylhydroxylamine buffer, while it was strong in the presence of acetate and phosphate ones. Buffer-independent rate constants k_{10} and k_{20} increased linearly with the increase in a_{OH} with definite intercepts. The values of molar absorption coefficient of **A**, obtained under varying total buffer concentrations at a constant pH, showed the presence of a fast equilibrium: $\mathbf{A} + \text{CH}_3$ NHOH \leftrightarrows **C**, where **C** represents *N*-[*o*-(*N*-methyl-*N*-hydroxycarbamoyl)methyl]benzohydroxamic acid. © 2003 Wiley Periodicals, Inc. Int J Chem Kinet 35: 427–437, 2003

INTRODUCTION

The aqueous cleavage of phthalimide and substituted phthalimides in the presence of primary and secondary amines involves rather complex reaction mechanisms [1–8]. Isolation of intermediates and end products in these reactions provides a fruitful insight about the mechanisms of these reactions. But the fine details of these complex mechanisms are expected to be achieved only from a systematic kinetic study that can indirectly give support for the presence of highly reactive intermediates of extremely short lifetimes (say $\sim 10^{-10}$ s).

The cleavage of N-ethoxycarbonylphthalimide (NCPH) in aqueous buffers of N-methylhydroxylamine has been found to follow an irreversible consecutive reaction path: NCPH $\xrightarrow{k_1}$ ENMBC $\xrightarrow{k_2}$ A $\xrightarrow{k_3}$ B where ENMBC, A, and B represent ethyl N-[o-(Nmethyl-N-hydroxycarbamoyl)benzoyl]carbamate, Nhydroxyl group cyclized product of ENMBC, and o-carboxy(N-methyl)benzohydroxamic acid, respectively [9]. The mechanistic details of k_1 step have been studied earlier [10]. The consecutive nature of this reaction has been kinetically analyzed by monitoring the change in the concentrations of NCPH and A spectrophotometrically as a function of a reaction time [9]. In this study, the use of considerably high concentrations of N-methylhydroxylamine buffer was restricted because of the kinetic profiles, $k_1 \gg k_2$ and k_3 . This experimental problem allowed to attain only a maximum of <0.025 M free amine. Under such conditions, the buffer effects on k_2 and k_3 (if any) could not be detected. The present study was initiated with an aim to find out the occurrence or nonoccurrence of buffer catalysis in k_2 step and k_3 step by covering considerably high total buffer concentration range. The results and probable explanation(s) are described in this paper.

EXPERIMENTAL

Materials

All the chemicals used were of a reagent grade and were obtained from Aldrich or Fluka. Buffer solutions of N-methylhydroxylammonium chloride of desired

pH's were prepared by adding the required amounts of NaOH just before the start of kinetic runs. Standard solution (0.02 M) of NCPH was prepared in acetonitrile.

Kinetic Measurements

The rate of the title reaction was studied spectrophotometrically by monitoring the change in absorbance of the reaction mixture at 300 nm as a function of reaction time. The reactant ENMBC was generated by reacting NCPH with *N*-methylhydroxylamine under the reaction conditions in which the rate of formation of ENMBC was more than 75- and 10-fold larger than that of cyclization of ENMBC to form intermediate in the presence of *N*-methylhydroxylamine and acetate buffer, respectively. The details of the kinetic procedures were same as previously described [10].

In view of the earlier reports on this reaction [9,10], a brief reaction scheme for the title reaction may be expressed by Eq. (1)

$$NCPH \xrightarrow{\text{very fast}} ENMBC \xrightarrow{k_{1}obs} \mathbf{A} \xrightarrow{k_{2}obs} \mathbf{B}$$
(1)

where **A** and **B** represent benzo-3-methyl-2,3-oxazine-1,4-dione (*N*-hydroxyl group cyclized product of ENMBC) and *o*-(*N*-methyl-*N*-hydroxycarbamoyl)benzoic acid, respectively.



Both NCPH and A absorb strongly, while both EN-MBC and B do not exhibit a detectable absorption

at 300 nm. Thus, the observed absorbance (A_{obs}) at 300 nm is essentially due to intermediate **A** because, under the present reaction conditions, more than 99.9% conversion of NCPH to ENMBC occurred within <100 and 200 s in the presence of *N*-methylhydroxylamine and acetate buffer, respectively. The observed data, A_{obs} versus *t*, were found to fit to Eq. (2)

$$A_{\rm obs} = \frac{E_{\rm app}[X]_0 k_{1\,\rm obs}}{(k_{2\,\rm obs} - k_{1\,\rm obs})} [\exp(-k_{1\,\rm obs}t) - \exp(-k_{2\,\rm obs}t)] + A_0$$
(2)

where $[X]_0 = [NCPH]_0$ (initial concentration of NC-PH), $E_{app} = E_A - E$, $A_0 = E[X]_0$ with $E = E_{ENMBC}$ and $E_{\text{ENMBC}} \approx E_{\text{B}}$. The notations E_{ENMBC} , E_{A} , and $E_{\rm B}$ represent the molar absorption coefficients of EN-MBC, A, and B, respectively. The assumption that $E_{\text{ENMBC}} \approx E_{\text{B}}$ at 300 nm is supported by the fact that the values of A_{∞} (= $E_{\mathbf{B}}[\mathbf{X}]_0$) obtained in the present study are similar to the corresponding values of A_{∞} $(=E_{\text{ENMBC}}[X]_0 \equiv A_0$ in the present study) obtained in a separate study where disappearance of NCPH was monitored spectrophotometrically as a function of reaction time at 300 nm [10]. The values of $k_{1 \text{ obs}}$, $k_{2 \text{ obs}}$, and E_{app} were calculated from Eq. (2) by using the nonlinear least-squares technique. The observed data fit to Eq. (2) reasonably well as evident from a typical plot of A_{obs} versus reaction time (t) shown in Fig. 1. The product **B** has been previously characterized as the sole end product in the cleavage of NCPH under the aqueous buffer solution of CH₃NHOH [10]. A qualitative experimental evidence for formation of the intermediate A through the cleavage of ENMBC under the present



Figure 1 Plot showing the dependence of observed absorbance (A_{obs} at 300 nm) versus reaction time (t) for the cleavage ENMBC at total *N*-methylhydroxylamine buffer concentration ([Am]_T) = 0.1 M, pH 6.86, and 30°C. The solid line is drawn through the data points calculated by the least-square method using Eq. (2) and parameters listed in Table I.

experimental conditions has been previously described [9].

RESULTS AND DISCUSSION

Effects of *N*-Methylhydroxylamine Buffer on $k_{1 \text{ obs}}$, $k_{2 \text{ obs}}$, and E_{app}

Four to five kinetic runs were carried out within the total *N*-methylhydroxylamine buffer concentration ([Am]_T where [Am]_T = [CH₃NHOH] + [CH₃NH₂OH⁺]) range of ≥ 0.10 to ≤ 0.50 M at a constant pH. The values of $k_{1 \text{ obs}}$, $k_{2 \text{ obs}}$, and E_{app} were calculated from Eq. (2) and these values of kinetic parameters at different [Am]_T and pH are summarized in Table I. The values of $k_{1 \text{ obs}}$ and $k_{2 \text{ obs}}$ were kinetically analyzed by using Eqs. (3) and (4), respectively,

$$k_{1\,\rm obs} = k_{10} + k_{1b} [\rm Am]_{\rm T} \tag{3}$$

$$k_{2 \text{ obs}} = k_{20} + k_{2b} [\text{Am}]_{\text{T}}$$
 (4)

where k_{10} and k_{20} are buffer-independent first-order rate constants and k_{1b} and k_{2b} are buffer-dependent second-order rate constants. The linear least-square method was applied to estimate the values of k_{10} , k_{20} , k_{1b} , and k_{2b} at different pH's, as summarized in Table II. The fitting of observed data to Eqs. (3) and (4) seems reasonably good as demonstrated in the least-squares calculated values of rate constants $k_{1 \text{ cld}}$ and $k_{2 \text{ cld}}$ as shown in Table I and from the standard deviations associated with the calculated values of k_{10} , k_{20} , k_{1b} , and k_{2b} , as shown in Table II.

The values of k_{1b} and k_{2b} are less reliable as compared to the corresponding values of k_{10} and k_{20} because the maximum contributions of k_{1b} [Am]_T and k_{2b} [Am]_T toward $k_{1 obs}$ and $k_{2 obs}$ in Eqs. (3) and (4), respectively (obtained at the maximum values of [Am]_T), are <50%. However, the values of k_{1b} are more reliable at lower pH as compared to those at higher pH. The rate of cyclization of ENMBC to **A** appears to involve specific base (HO⁻), general base (CH₃NHOH), and general acid (CH₃NH₂OH⁺) catalysis as shown by Eq. (5).

$$\text{ENMBC} = \frac{k_{\text{IoH}}^{k_{\text{Iw}}}}{k_{\text{IoH}} \text{CH}_{3}\text{NHOH}} \mathbf{A} \qquad (5)$$

Thus, Eqs. (1) and (5) can lead to Eq. (6)

$$k_{1 \text{ obs}} = k_{1 \text{w}} + k_{1 \text{OH}} a_{\text{OH}} + (k_{1 \text{gb}} f_a^{\text{Am}} + k_{1 \text{ga}} f_{a\text{H}}^{\text{Am}}) [\text{Am}]_{\text{T}}$$
(6)

pН	$[\mathrm{Am}]_{\mathrm{T}}^{b}(\mathrm{M})$	A_0	$k_{1 \text{ obs}} (10^{-4} \text{ s}^{-1})$	$k_{1 \text{ cld}}^{c}$ (10 ⁻⁴ s ⁻¹)	$k_{2 \text{ obs}} (10^{-4} \text{ s}^{-1})$	$k_{2 \text{ cld}}^{d}$ (10 ⁻⁴ s ⁻¹)	E_{app} (M ⁻¹ cm ⁻¹)	$\frac{E_{\rm appcld}^{e}}{({\rm M}^{-1}~{\rm cm}^{-1})}$
5.86	0.10	0.037	8.40 ± 0.17^{f}	8.23	3.70 ± 0.27^{f}	3.81	1499 ± 29^{f}	1477
5.88	0.15	0.063	9.54 ± 0.25	9.63	4.11 ± 0.39	3.98	1299 ± 31	1322
5.87	0.20	0.065	10.7 ± 0.2	11.0	4.22 ± 0.61	4.14	1133 ± 23	1152
5.87	0.25	0.061	12.7 ± 0.4	12.4	4.22 ± 0.61	4.31	1008 ± 33	988
6.28	0.10	0.017	17.1 ± 1.6	18.5	5.62 ± 0.38	5.58	1696 ± 107	1578
6.29	0.20	0.029	23.6 ± 1.2	21.9	5.70 ± 0.22	5.83	1231 ± 41	1357
6.28	0.30	0.059	26.1 ± 3.0	25.4	6.45 ± 0.68	6.08	1076 ± 82	1100
6.26	0.40	0.054	27.9 ± 1.9	28.8	5.81 ± 0.35	6.33	815 ± 35	870
6.24	0.50	0.109	32.2 ± 2.7	32.3	6.81 ± 0.52	6.58	773 ± 41	685
6.66	0.10	0.027	30.5 ± 1.7	32.1	7.23 ± 0.36	6.82	1743 ± 65	1687
6.66	0.15	0.044	33.6 ± 2.0	32.4	7.58 ± 0.44	8.22	1493 ± 60	1554
6.66	0.20	0.049	35.0 ± 1.4	32.8	9.65 ± 0.34	9.62	1364 ± 37	1400
6.66	0.25	0.071	31.2 ± 1.7	33.1	11.2 ± 0.6	11.0	1282 ± 51	1241
6.86	0.10	0.028	44.7 ± 1.6	43.8	10.2 ± 0.4	10.8	1681 ± 39	1673
6.87	0.15	0.032	41.6 ± 0.9	43.1	12.6 ± 0.2	11.5	1542 ± 22	1555
6.89	0.20	0.075	42.9 ± 2.9	42.5	11.7 ± 0.7	12.1	1420 ± 64	1416
6.89	0.25	0.088	42.1 ± 2.3	41.8	12.6 ± 0.7	12.7	1272 ± 47	1270
6.90 ^g	0.10	0.056	45.4 ± 1.4	46.1	9.62 ± 0.22	9.69	1600 ± 31	1573
6.90 ^g	0.15	0.064	49.0 ± 1.8	49.1	10.5 ± 0.3	10.3	1384 ± 30	1412
6.90 ^g	0.20	0.100	54.2 ± 2.2	52.0	10.8 ± 0.3	10.9	1212 ± 29	1235
6.91 ^g	0.25	0.100	53.6 ± 2.1	55.1	11.6 ± 0.3	11.6	1088 ± 25	1064
7.04	0.10	0.020	64.3 ± 2.3	65.4	9.08 ± 0.27	8.98	1735 ± 33	1722
7.05	0.15	0.045	69.4 ± 3.2	67.4	9.99 ± 0.41	10.7	1505 ± 37	1544
7.05	0.20	0.059	68.5 ± 3.4	69.4	13.7 ± 0.5	12.5	1388 ± 40	1349
7.06	0.25	0.081	71.3 ± 1.9	71.4	13.7 ± 0.3	14.3	1147 ± 17	1161
7.53	0.10	0.060	185 ± 5	186	17.4 ± 0.3	17.7	1481 ± 19	1482
7.53	0.15	0.094	178 ± 3	180	18.7 ± 0.3	18.4	1290 ± 11	1284
7.54	0.20	0.114	182 ± 4	175	19.6 ± 0.3	19.2	1073 ± 12	1082
7.55	0.25	0.148	166 ± 5	172	19.5 ± 0.5	19.9	905 ± 15	900

Table I Values of Unknown Parameters, $k_{1 \text{ obs}}$, $k_{2 \text{ obs}}$, and $E_{\mathbf{B}}$, Calculated from Eq. (2)^{*a*}

^{*a*} Unless otherwise noted conditions: $[NCPH]_0 = [X]_0 = 3.2 \times 10^{-4} \text{ M}$; ionic strength 1.0 M (maintained by KCl); 30°C; $\lambda = 300 \text{ nm}$; the aqueous solvent for each kinetic run contained 1.6% v/v CH₃CN.

^b $[Am]_T (= [CH_3NHOH] + [CH_3NH_2OH^+])$ is total N-methylhydroxylamine buffer concentration.

^{*c*} Calculated from Eq. (3) as described in the text.

^d Calculated from Eq. (4) as described in the text.

^{*e*} Calculated from Eq. (9) with empirical parameters, E_{app}^{0} and K, listed in Table III.

^{*f*} Error limits are standard deviations.

^{*e*} Conditions: $[NCPH]_0 = [X]_0 = 6.4 \times 10^{-4} \text{ M}$; ionic strength 1.0 M (maintained by KCl); 30°C; $\lambda = 300 \text{ nm}$; the aqueous solvent for each kinetic run contained 3.2% v/v CH₃CN.

where $[Am]_T = [CH_3NHOH] + [CH_3NH_2OH^+], f_a^{Am} = K_a^{Am}/(a_H + K_a^{Am}), f_{aH}^{Am} = 1 - f_a^{Am}, and K_a^{Am} = ([CH_3NHOH]a_H)/[CH_3NH_2OH^+].$ Comparison of Eqs. (3) and (6) gives

$$k_{10} = k_{1w} + k_{1OH}a_{OH} \tag{7}$$

$$k_{1b} = k_{1gb} f_{a}^{Am} + k_{1ga} f_{aH}^{Am}$$
(8)

Although most of the k_{1b} values are unreliable as mentioned earlier, a linear plot of k_{1b}/f_a^{Am} versus a_H yielded $10^3 k_{1gb} = 3.95 \pm 1.75 \text{ M}^{-1} \text{ s}^{-1}$ and $k_{1ga}/K_a^{Am} =$ $(3.96 \pm 2.65) \times 10^3 \text{ M}^{-2} \text{ s}^{-1}$. The value of k_{1ga}/K_a^{Am} $(=3.96 \times 10^3 \text{ M}^{-2} \text{ s}^{-1})$ gave $10^3 k_{1ga} = 2.28 \text{ M}^{-1} \text{ s}^{-1}$ with $pK_a^{\text{Am}} = 6.24$ [11].

The values of k_{2b} , although not very reliable as concluded earlier in the text, seem to follow a kinetic equation similar to Eq. (8) with the replacement of k_{1b} , k_{1gb} , and k_{1ga} by k_{2b} , k_{2gb} , and k_{2ga} , respectively, where $k_{2ga} = 0$. The calculated values of k_{2b} gave the value of k_{2gb} as $(2.01 \pm 1.38) \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$.

The values of E_{app} show a decrease with the increase in [Am]_T at a constant pH (Table I). These data were found to fit to the following empirical equation

$$E_{\rm app} = E_{\rm app}^0 / \left(1 + K [\rm Am]_T^2 \right) \tag{9}$$

рН	$k_{10} (10^{-4} \mathrm{s}^{-1})$	$k_{10 \text{ cld}}^{b}$ (10 ⁻⁴ s ⁻¹)	$(10^{-4} \text{ M}^{-1} \text{ s}^{-1})$	100Y ₁ ^c	k_{20} (10 ⁻⁴ s ⁻¹)	$k_{20 \text{ cld}}^{d}$ (10 ⁻⁴ s ⁻¹)	$(10^{-4} \text{ M}^{-1} \text{ s}^{-1})$	$100Y_2^{e}$
N-Methylhyd	lroxylamine buff	er						
5.87 ± 0.01	5.41 ± 0.54^{f}	6.67	28.1 ± 3.0^{f}	56	3.48 ± 0.24^{f}	3.44	3.33 ± 1.32^{f}	19
6.27 ± 0.02	15.0 ± 1.5	12.0	34.5 ± 4.5	53	5.33 ± 0.40	3.87	2.49 ± 1.26	19
6.66 ± 0.00	31.4 ± 4.1	25.0	7.0 ± 22.4	5	4.02 ± 0.91	4.93	28.0 ± 4.9	64
6.88 ± 0.02	45.1 ± 2.2		-13 ± 12		9.57 ± 1.6	6.10	12.6 ± 8.6	25
	42.8 ± 1.4	39.4	0	0				
6.90 ± 0.01	40.1 ± 3.1	41.1	59.6 ± 16.9	27	8.45 ± 0.28	6.24	12.5 ± 1.5	27
7.05 ± 0.01	61.3 ± 2.9	56.8	40.2 ± 15.5	14	5.47 ± 1.8	7.52	35.1 ± 9.6	62
7.54 ± 0.01	196 ± 10		-106 ± 52		16.3 ± 0.8	16.6	14.4 ± 4.5	18
	178 ± 8	169	0	0				
Acetate buffe	r							
5.45 ± 0.01	6.97 ± 0.66		20.9 ± 1.1	73	2.15 ± 0.09		0.43 ± 0.15	15
	$(4.46)^{g}$	4.47			$(1.87)^{g}$	3.26		
5.66 ± 0.06	7.01 ± 0.45		20.1 ± 0.7	72	2.53 ± 0.06		1.64 ± 0.10	37
	(4.38)	5.31			(2.11)	3.33		
5.88 ± 0.08	9.90 ± 1.29		20.6 ± 2.1	65	3.63 ± 0.43		3.02 ± 0.69	43
	(7.11)	6.76			(3.03)	3.49		
Phosphate bu	ffer							
6.84 ± 0.11	35.0 ± 3.2		160 ± 10	69	5.65 ± 0.70		48.8 ± 2.1	81
	(33.6)	36.2			(5.01)	5.84		
7.28 ± 0.16	75.2 ± 16.1		351 ± 48	69	3.62 ± 2.96		97.1 ± 8.9	93
	(73.7)	94.3			(2.88)			

Table II Values of Buffer-Independent First-Order Rate Constants, k_{10} and k_{20} , and Buffer-Dependent Second-Order Rate Constants, k_{1b} and k_{2b} , Calculated from Eqs. (3) and (4)^{*a*}

^a Reaction conditions are described in Tables I and IV.

^b Calculated from the relationship $k_{1 \text{ cld}} = k_{1\text{w}} + k_{1\text{OH}}a_{\text{OH}}$ with $10^4 k_{1\text{w}} = 3.13 \text{ s}^{-1}$ and $10^{-4} k_{1\text{OH}} = 3.31 \text{ M}^{-1} \text{ s}^{-1}$ as described in the text.

 $^{c}Y_{1} = k_{1b} [Buf]_{Tax}^{max}/(k_{10} + k_{1b} [Buf]_{Tax}^{max})$ where $[Buf]_{Tax}^{max}$ represents the maximum total buffer concentration attained in the study.

^d Calculated from the relationship $k_{2 \text{ cld}} = k_{2 \text{w}} + k_{2 \text{OH}} a_{\text{OH}}$ with 10⁴ $k_{2 \text{w}} = 3.15 \text{ s}^{-1}$ and 10⁻⁴ $k_{2 \text{OH}} = 0.270 \text{ M}^{-1} \text{ s}^{-1}$ as described in the text. ^e $Y_2 = k_{2b} [\text{Buf}]_{\text{Tax}}^{\text{max}} / (k_{20} + k_{2b} [\text{Buf}]_{\text{Tax}}^{\text{max}})$ where $[\text{Buf}]_{\text{Tax}}^{\text{max}}$ represents the maximum total buffer concentration attained in the study.

^{*f*} Error limits are standard deviations.

^g Parenthesized values stand for corrected k_{10}^{cor} or k_{20}^{cor} where $k_{10}^{cor} = k_{10} - (k_{1gb} f_a^{Am} + k_{1ga}^{Am})[Am]_T$ with $[Am]_T = 0.1$ M and 0.04 M for acetate and phosphate buffer, respectively; $k_{20}^{cor} = k_{20} - k_{2gb} f_a^{Am} [Am]_T$ with $[Am]_T = 0.1$ M and 0.04 M for acetate and phosphate buffer, respectively.

where E_{app}^{0} and *K* are empirical constants. The nonlinear least-squares technique was used to calculate E_{app}^{0} and *K* and these calculated values at different pH are summarized in Table III. Although the data seem to fit to Eq. (9) reasonably well as evident from the least-squares calculated values of E_{app} shown in Table I as $E_{app cld}$ and from the standard deviations associated with the values of E_{app}^{0} and *K* (Table III), the absolute magnitude of *K* at different pH are not very reliable for the fact that the maximum contributions of $K[\text{Am}]_{T}^{2}$ toward $1 + K[\text{Am}]_{T}^{2}$ in Eq. (9) are <50% at all pH values except at pH 6.27 where it is nearly 60%. This notion may be seen in the values of *K* at pH 6.88 and 6.90, which differ from each other by nearly 50% (Table III).

The decrease in E_{app} with increase in $[Am]_T$ at a constant pH may be attributed to the occurrence of the

following reaction paths in the title reaction.



where $[Am]_T = [CH_3NHOH] + [CH_3NH_2OH^+]$ and **C** exists in a fast equilibrium with **A** during the course of the reaction (i.e. $k_a[Am]_T^2 \gg k_{2 \text{ obs}}$ and $k_{-a} \gg k_{1 \text{ obs}}$ with

pН	$E_{\rm app}^0 ({\rm M}^{-1} {\rm cm}^{-1})$	$K ({ m M}^{-2})$	$K_1 ({ m M}^{-1})$	$K_2 (M^{-1})$
N-Methylhydroxyl	lamine buffer ^b			
5.87 ± 0.01^{c}	1631 ± 35^{c}	10.4 ± 0.6^{c}		
6.27 ± 0.02	1669 ± 104	5.7 ± 0.6		
6.66 ± 0.00	1812 ± 80	$7.4 \pm 0.1.3$		
6.88 ± 0.02	1780 ± 13	6.4 ± 0.2		
6.90 ± 0.01	1731 ± 43	10.0 ± 0.7		
7.05 ± 0.01	1896 ± 49	10.1 ± 0.8		
7.54 ± 0.01	1690 ± 11	14.0 ± 0.2		
Acetate buffer ^d				
5.45 ± 0.01	1914 ± 57		2.71 ± 0.30^{c}	0.56 ± 0.08^{c}
	$(1712 \pm 52)^{e}$		$(1.59 \pm 0.12)^{e}$	
5.66 ± 0.06	2062 ± 35		1.93 ± 0.15	0.58 ± 0.06
	(1891 ± 48)		(1.14 ± 0.08)	
5.88 ± 0.08	2035 ± 18		0.55 ± 0.05	-0.13 ± 0.08
	(2062 ± 15)		(0.64 ± 0.02)	
Phosphate $buffer^{f}$				
6.84 ± 0.11	(3180 ± 81)		(0.49 ± 0.10)	
7.28 ± 0.16	(2932 ± 58)		(0.22 ± 0.07)	

Table III Values of Unknown Parameters, E_{app}^{0} and K, at Different pH, Calculated from Eq. (9)^{*a*}

^a Reaction conditions are described in Tables I and IV.

^b The values of E_{app}^0 and K were calculated from Eq. (9) as described in the text.

^c Error limits are standard deviations.

^d The values of E_{app}^0 , K_1 and K_2 were calculated from Eq. (22) as described in the text.

^e Parenthesized values were calculated from Eq. (23).

^f The values of E_{app}^0 and K_1 were calculated from Eq. (23) as described in the text.

 $k_a/k_{-a} = K$). The formation of **A** from ENMBC and C involves hydroxide-ion-catalyzed intramolecular nucleophilic addition-elimination mechanism and the rates of such reactions are highly sensitive and almost insensitive to the pK_a of conjugate acids of leaving groups and nucleophiles, respectively [2,5,12,13]. The value of second-order rate constant for hydroxide-ion-catalyzed cyclization reaction of o-(N-hydroxycarbamoyl)benzohydroxamic acid is $\sim 1 \times$ $10^7 \,\mathrm{M^{-1} \, s^{-1}}$ at 30°C [5]. The values of pK_a of conjugate acids of leaving groups in the cyclization reactions of C and o-(N-hydroxycarbamoyl)benzohydroxamic acid should be nearly same and hence $k_{-a} \approx 7.4 \times 10^{-2} \, {
m s}^{-1}$ at pH 5.87, which is nearly 100-fold larger than $k_{1 \text{ obs}}$ at pH 5.87 (Table I). An approximate value of k_{-a} (7.4 × 10^{-2} s^{-1}) and the value of $K = 10.4 \text{ M}^{-2}$ (Table III) give $k_a [Am]_T^2 \ge 7.4 \times 10^{-3} \text{ s}^{-1}$ at $[Am]_T \ge 0.1 \text{ M}$ and pH 5.87, which is approximately \geq 20-fold larger than $k_{2 \text{ obs}}$ (Table I). The value of k_{a} [Am]_T² = 7.4 × 10⁻³ s⁻¹ at $[Am]_T = 0.1$ M and pH 5.87 may be compared with $k_{\rm obs} = 5.9 \times 10^{-2} \text{ s}^{-1}$ obtained for the reaction of NCPH with CH₃NHOH in N-methylhydroxylamine buffer ($[Am]_T = 0.1 \text{ M}$) of pH 5.80 [9].

In view of Eq. (10), $A_{obs} = E_{ENMBC}[ENMBC] + E_{A}[A] + E_{B}[B]$ and $[X]_{0} = [ENMBC] + [A] + [B]$. Thus, $A_{obs} = E_{ENMBC}[X]_{0} + (E_{A} - E_{ENMBC})[A] + (E_{A} - E_{ENMBC})[A]$ $(E_{\mathbf{B}} - E_{\text{ENMBC}})[\mathbf{B}]$. As concluded earlier, $E_{\mathbf{B}} \approx E_{\text{ENMBC}}$ and also $E_{\mathbf{A}} \gg E_{\text{ENMBC}}$ at 300 nm and these conclusions lead to the relationship

$$A_{\rm obs} = E_{\rm A}[{\rm A}] + E_{\rm ENMBC}[{\rm X}]_0.$$
(11)

But Eq. (10) shows that $[\mathbf{A}]_{\mathrm{T}} = [\mathbf{A}] + [\mathbf{C}]$ and hence

$$[\mathbf{A}] = [\mathbf{A}]_{\mathrm{T}} / (1 + K [\mathrm{Am}]_{\mathrm{T}}^2)$$
(12)

Thus, Eqs. (10), (11), and (12) lead to Eq. (2), with E_{app} represented by Eq. (9) where $E_{app}^0 = E_A$. It is thus apparent that E_{app}^0 should be independent of pH because it is the molar absorption coefficient of **A**. The values of E_{app}^0 are almost independent of pH (Table III).

Although reasonably good fit of observed data to Eq. (9) indicates the occurrence of general acid–base (GA–GB) catalysis in *N*-methylhydroxylaminolysis of **A**, i.e. k_a step (formation of **C** from **A**) in Eq. (10), it is further supported by the significant effect of the concentration of acetate buffer on E_{app} at a constant value of [Am]_T (=0.1 M) and pH. The occurrence of GA– GB catalysis in k_a step [Eq. (10)] is conceivable for the reason that these catalyses have been found to occur in the reaction of CH₃NHOH with NCPH [9,10] and both NCPH and **A** are highly and almost equally reactive toward nucleophile HO⁻. Despite an earlier conclusion that K values are not very reliable, an attempt has been made to analyze K values in terms of conceivable mechanism(s). The most plausible mechanism for the term $K[Am]_T^2$ in Eq. (9) is the occurrence of GB catalysis in k_a step (i.e. the formation of **C** from A) and specific base (SB) catalysis in k_{-a} step (i.e. the formation of A from C). The occurrence of such GB and SB catalysis in respect to k_a and k_{-a} steps predict a linear plot of $K(a_{\rm H} + K_{\rm a})^2$ versus $a_{\rm H}$ with slope = $(k_{\rm gb})^2$ $K_{\rm a}^{\rm Am}K_{\rm a}^{\rm Am})/(k_{\rm sb}K_{\rm w})$, where $k_{\rm gb}$ and $k_{\rm sb}$ represent GBcatalyzed third-order and SB-catalyzed second-order rate constants, respectively. Such a plot did appear to be linear within the pH range of 5.87–6.90, with some significant scattering in the observed and calculated data points. The value of K at pH 7.54 showed extremely large positive deviation from the theoretical line. The slope $[=(k_{gb}K_a^{Am}K_a^{Am})/(k_{sb}K_w)]$ of the linear plot turned out to be $(26.0 \pm 3.6) \times 10^{-6} \text{ M}^{-1}$, which gives $k_{gb} = 8 \text{ M}^{-2} \text{ s}^{-1}$ with $k_{sb} = 1 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}$ [5], $pK_a^{Am} = 6.24$, and $pK_w = 14$. Although the value of k_{gb} of 8 M⁻² s⁻¹ is expected to contain large uncertainty, it is not inconceivable in view of the reported value of $k_{\rm gb}$ of 54 M⁻² s⁻¹ for the GB-catalyzed formation of ENMBC from NCPH in the presence of CH₃NHOH buffer [9].

An alternative reaction scheme as shown by Eq. (13) and suggested in the earlier report [9], to explain the effects of $[Am]_T$ on E_{app} , may be ruled out for the following reasons. It can be easily shown

ENMBC
$$\xrightarrow{k_1} \mathbf{A} \xrightarrow{k_{2 \text{ obs}}} \mathbf{B}$$

 $k_3 \text{ [Am]}_T \qquad \mathbf{B}$
(13)

that Eq. (13) can lead to the relationships (i) $k_{1 \text{ obs}} = k_1 + k_3[\text{Am}]_{\text{T}}$ and (ii) $E_{\text{app}} = E_{\text{app}}^0 / (1 + (k_3/k_1)[\text{Am}]_{\text{T}})$. But the relationship (ii) is not exactly similar to Eq. (9) and the ratio $k_3/k_1 [\equiv k_{1b}/k_{10}$ in view of Eq. (3)] should be negligible at pH \geq 6.66. Thus, E_{app} should be independent of [Am]_{\text{T}} at pH \geq 6.66 but such prediction does not agree with E_{app} values summarized in Table I.

Effects of Acetate and Phosphate Buffers (Buf) on $k_{1 \text{ obs}}$, $k_{2 \text{ obs}}$, and E_{app} in the Presence of a Constant Value of $[Am]_T$

Five kinetic runs were carried out within the total buffer concentration ([Buf]_T) range of ≥ 0.08 to ≤ 0.90 M at a constant pH, [Am]_T(=[CH₃NHOH] + [CH₃NH₂OH⁺]), and temperature (30°C). Such observations were obtained at different pH ranging from ≥ 5.45 to ≤ 7.28 for both acetate and phosphate buffers. Pseudo-first-order rate constants $k_{1 \text{ obs}}$ and $k_{2 \text{ obs}}$, as shown in Table IV, were found to fit to Eqs. (3) and (4), respectively, with $[Am]_T$ replaced by $[Buf]_T$. The least-squares calculated values of k_{10} , k_{1b} , k_{20} , and k_{2b} at different pH are summarized in Table II. The extent of reliability of the fit of observed data to Eqs. (3) and (4) is evident from the least-squares calculated values of rate constants $k_{1 \text{ cld}}$ and $k_{2 \text{ cld}}$ (Table IV) and from the standard deviations associated with the calculated parameters k_{10} , k_{1b} , k_{20} , and k_{2b} (Table II).

The rate of formation of **A** from ENMBC and **B** from **A** in the presence of $[Am]_T$ and $[Buf]_T(=[BH] + [B^-])$, where BH and B⁻ represent respective acid and base components of buffer) may be given by Eqs. (14) and (15), respectively.

Rate₁ =
$$(k_{1w} + k_{1OH}a_{OH} + k_{1gb}[Am] + k_{1ga}[AmH^+]$$

+ $k'_{1gb}[B^-] + k'_{1ga}[BH])[ENMBC]$ (14)

$$\operatorname{Rate}_{2} = (k_{2w} + k_{2OH}a_{OH} + k_{2gb}[\operatorname{Am}] + k'_{2gb}[B^{-}] + k'_{2ga}[\operatorname{BH}])[\mathbf{A}]$$
(15)

Thus, Eqs. (1), (14), and (15) can lead to Eqs. (16) and (17)

$$k_{1 \text{ obs}} = k_{1\text{w}} + k_{1\text{OH}}a_{\text{OH}} + (k_{1\text{gb}}f_{a}^{\text{Am}} + k_{1\text{ga}}f_{a\text{H}}^{\text{Am}})[\text{Am}]_{\text{T}} + (k_{1\text{gb}}'f_{a}^{\text{Buf}} + k_{1\text{ga}}'f_{a\text{H}}^{\text{Buf}})[\text{Buf}]_{\text{T}}$$
(16)

 $k_{2\,\text{obs}} = k_{2\text{w}} + k_{2\text{OH}}a_{\text{OH}} + k_{2\text{gb}}f_{\text{a}}^{\text{Am}}[\text{Am}]_{\text{T}}$

+
$$(k'_{2gb}f_a^{Buf} + k'_{2ga}f_{aH}^{Buf})[Buf]_T$$
 (17)

where $[Buf]_T = [BH] + [B^-]$, $f_a^{Buf} = K_a^{BH}/(a_H + K_a^{BH})$, $f_{aH}^{BH} = 1 - f_a^{BH}$, and $K_a^{BH} = ([B^-]a_H)/[BH]$. Comparison of respective Eqs. (3) and (4) with (16) and (17) gives

$$k_{10} = k_{1w} + k_{1\text{OH}}a_{\text{OH}} + (k_{1\text{gb}}f_{a}^{\text{Am}} + k_{1\text{ga}}f_{a\text{H}}^{\text{Am}})[\text{Am}]_{\text{T}}$$
(18)

$$k_{1b} = k'_{1gb} f_a^{Buf} + k'_{1ga} f_{aH}^{Buf}$$
(19)

$$k_{20} = k_{2w} + k_{2OH}a_{OH} + k_{2gb}f_{a}^{Am}[Am]_{T} \quad (20)$$

$$k_{2b} = k'_{2gb} f_{a}^{Buf} + k'_{2ga} f_{aH}^{Buf}$$
(21)

The values of k_{1b} for acetate buffer show that the values of k_{1b}/f_a^{Buf} increase from 21.9×10^{-4} to 24.4×10^{-4} M⁻¹ s⁻¹ with the decrease in pH from 5.88 to 5.45. The linear plot of k_{1b}/f_a^{Buf} versus a_H gave intercept (= k'_{1gb}) and slope (= k'_{1ga}/K_a^{BH}) as (20.1 ± 0.9) × 10⁻⁴ M⁻¹ s⁻¹ and 116 ± 34 M⁻² s⁻¹, respectively. The value of k'_{1ga}/K_a^{BH} is less reliable for the fact that it is associated with considerably large standard deviation (~30%), and the maximum contribution of (k'_{1ga}/K_a^{BH}) a_H toward k_{1b}/f_a^{Buf} in Eq. (19), obtained

	[Buf] _T ^b		$k_{1 \text{ obs}}$	$k_{1 \text{cld}}^{c}$	$k_{2 \text{ obs}}$	$k_{2 \text{cld}}^d$	E_{app}	$E_{app cld}^{e}$
pН	(M)	A_0	(10^{-4} s^{-1})	(10^{-4} s^{-1})	(10^{-4} s^{-1})	(10^{-4} s^{-1})	$(M^{-1} cm^{-1})$	$(M^{-1} cm^{-1})$
Acetate buffer ^f								
5.44	0.15	0.060	10.2 ± 1.2^g	10.1	2.19 ± 0.27^g	2.22	1392 ± 115^g	1392
								$(1382)^{h}$
5.45	0.45	0.077	16.5 ± 2.0	16.4	2.34 ± 0.26	2.34	965 ± 68	969
								(997)
5.44	0.60	0.081	19.5 ± 1.9	19.5	2.43 ± 0.23	2.41	873 ± 47	863
5 45	0.75	0 100	21.0 1.2.2	22 (2.59 0.24	2.47	770 42	(875)
5.45	0.75	0.100	21.8 ± 2.2	22.6	2.58 ± 0.24	2.47	7.19 ± 42	/8/ (780)
5 4 5	0.90	0.068	26.4 ± 1.8	25.8	2.44 ± 0.23	2 54	732 ± 28	(780)
5.15	0.90	0.000	20.1 ± 1.0	23.0	2.11 ± 0.23	2.51	152 ± 20	(703)
5.58	0.15	0.050	9.92 ± 0.80	10.0	2.74 ± 0.21	2.78	1629 ± 97	1629
								(1616)
5.64	0.45	0.050	16.2 ± 1.1	16.1	3.30 ± 0.18	3.27	1219 ± 54	1222
								(1251)
5.67	0.60	0.047	19.4 ± 1.2	19.1	3.53 ± 0.19	3.52	1117 ± 42	1110
- - -	0.75	0.070	215 1 1 5	22.1		2.74	1020 + 42	(1125)
5.72	0.75	0.072	21.5 ± 1.5	22.1	3.82 ± 0.22	3.76	1020 ± 42	1027
5 71	0.00	0.054	25.3 ± 1.4	25.1	3.04 ± 0.10	4.01	066 ± 31	(1021)
5.71	0.90	0.054	25.5 ± 1.4	23.1	5.94 ± 0.19	4.01	900 ± 51	(935)
5.75	0.15	0.046	13.3 ± 1.0	13.0	3.82 ± 0.27	4.08	1875 ± 132	1876
								(1881)
5.88	0.45	0.062	18.5 ± 1.3	19.2	5.42 ± 0.30	4.99	1616 ± 80	1609
								(1601)
5.91	0.60	0.063	23.2 ± 1.6	22.3	5.32 ± 0.32	5.45	1488 ± 69	1495
.		0 0 -				- 00		(1499)
5.94	0.75	0.076	23.9 ± 1.5	25.3	6.20 ± 0.32	5.90	1391 ± 58	1393
5.04	0.00	0.046	20.2 ± 1.8	28.4	6.02 ± 0.24	6 25	1202 ± 40	(1393)
5.94	0.90	0.040	29.3 ± 1.0	20.4	0.02 ± 0.34	0.55	1302 ± 49	(1308)
Dhaan	hata huffad							(1500)
6 66		0.092	50.3 ± 1.0	47.9	9.73 ± 0.20	9.55	3009 ± 42	(3059)
6.81	0.24	0.134	50.5 ± 1.0 70.0 ± 0.6	73.5	17.5 ± 0.1	17.4	2926 ± 17	(2843)
6.87	0.32	0.151	84.6 ± 1.4	86.3	21.0 ± 0.3	21.3	2772 ± 30	(2745)
6.91	0.40	0.186	101 ± 2	99.2	24.4 ± 0.4	25.2	2644 ± 34	(2655)
6.95	0.48	0.210	113 ± 2	112	29.8 ± 0.5	29.1	2520 ± 31	(2570)
7.01	0.08	0.096	105 ± 1	103	13.2 ± 0.1	11.4	2877 ± 13	(2880)
7.26	0.24	0.144	152 ± 1	160	25.8 ± 0.2	26.9	2806 ± 14	(2783)
7.32	0.32	0.173	184 ± 3	188	32.8 ± 0.3	34.7	2743 ± 21	(2736)
7.37	0.40	0.191	237 ± 3	216	40.4 ± 0.4	42.4	2620 ± 15	(2691)
7.42	0.48	0.226	232 ± 13	244	53.4 ± 2.2	50.2	2692 ± 81	(2648)

Table IV Values of Unknown Parameters, $k_{1 \text{ obs}}$, $k_{2 \text{ obs}}$, and E_{app} , Calculated from Eq. (2)^{*a*}

^{*a*} Conditions: $[NCPH]_0 = [X]_0 = 5.6 \times 10^{-4}$ M; ionic strength 1.0 M (maintained by KCl); 30°C; $\lambda = 300$ nm; the aqueous solvent for each kinetic run contained 1.6% v/v CH₃CN.

^b $[Buf]_T(=[B^-] + [BH]]$ where B^- = acetate anion or phosphate di-anion and BH = acetic acid or phosphate mono-anion) is total buffer concentration.

^c Calculated from Eq. (3) as described in the text.

^{*d*} Calculated from Eq. (4) as described in the text.

^{*e*} Calculated from Eq. (22) with empirical parameters E_{app}^0 , K_1 , and K_2 listed in Table III. ^{*f*} Acetate buffer contains 0.1 M CH₃NHOH for each kinetic run.

^g Error limits are standard deviations.

^h Parenthesized values were calculated from Eq. (23) with empirical parameters E_{app}^{0} and K_{1} , listed in Table III.

ⁱ Phosphate buffer contains 0.04 M CH₃NHOH for each kinetic run.

at the lowest pH 5.45, is only $\sim 20\%$. However, the value of k'_{1ga}/K_a^{BH} (=116 M⁻² s⁻¹) gave 10⁴ k'_{1ga} = 24.2 M⁻¹ s²⁶, with $pK_a^{BH} = 4.68$ [10]. The values of k_{1b}/f_a^{Buf} increase with the increase in pH, which show the absence of GA catalysis (i.e. $k'_{1ga} f^{Buf}_{aH} \approx 0$ in Eq. (19)) in the presence of phosphate buffer. These data suggest the presence of GB–SB catalyzed term k'_{1gb}^{sb} [B⁻] [HO⁻] [ENMBC] in the rate law for the formation of A from ENMBC. Although 2 data points linear plot cannot give reliable values of intercept and slope, significantly larger value of k_{1b}/f_a^{Buf} (=0.0399 M⁻¹ at pH 7.28 than that at pH 6.84 $(k_{1b}/f_a^{Buf} = 0.0221 \text{ M}^{-1}$ s⁻¹) asserts the definite existence of both k'_{1gb} [B⁻] [ENMBC] and k'_{1gb} ^{sb} [B⁻] [HO⁻] [ENMBC] terms in the rate law for the formation of A from ENMBC. The most plausible general mechanism for the catalvzed formation of A from ENMBC in the presence of N-methylhydroxylamine, acetate, and phosphate buffers may be shown in Scheme 1 where $k'_{1gb}^{sb} = 0$ for both N-methylhydroxylamine and acetate buffers and $k'_{1ga} = 0$ for phosphate buffer.

The values of k_{2b}/f_a^{Buf} for both acetate and phosphate buffers increased with the increase in pH (Table II). These data show the presence of $k'_{2gb}[B^-][A]$ and $k'_{2gb}{}^{sb}[B^-][HO^-][A]$ terms in the rate law for the formation of **B** from **A** under both acetate and phosphate buffers. The linear plots of k_{2b}/f_a^{Buf} versus a_{OH} , containing only 3 and 2 data points for acetate and phosphate buffer, respectively, yielded respective k'_{2gb} and $k'_{2gb}{}^{sb}$ as $(-9.7 \pm 3.3) \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$ and $(5.34 \pm 0.61) \times 10^4 \text{ M}^{-2} \text{ s}^{-1}$ for acetate buffer as well as $42.5 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$ and $3.59 \times 10^4 \text{ M}^{-2} \text{ s}^{-1}$ for phosphate buffer. The negative value of k'_{2gb} with $\sim 34\%$ standard deviation for acetate buffer merely

shows that it is not statistically different from zero. The value of k'_{2gb}^{sb} turned out to be $(3.33 \pm 1.34) \times 10^4 \text{ M}^{-2} \text{ s}^{-1}$ for acetate buffer with $k'_{2gb} = 0$. A general mechanism for catalyzed formation of **B** from **A** may be shown in Scheme 2 where $k'_{2gb}^{sb} = 0$ for *N*-methylhydroxylamine buffer.

The values of E_{app} show a considerably large and small decrease with the increase in $[Buf]_T$ for acetate and phosphate buffer, respectively, at a constant pH and $[Am]_T$ (Table IV). The reaction mechanism for k_{-a} step in Eq. (10) (i.e. the reaction step involving the formation of A from C) may be expected to be similar to that for $k_{1 \text{ obs}}$ step in Eq. (10) (i.e. the reaction step involving the formation of A from ENMBC) in the presence of the same buffer. Similarly k_a step in Eq. (10) (i.e. the reaction step involving the formation of C from A) should involve GB catalysis for the nucleophilic reaction of CH₃NHOH with A to form C. These probable mechanisms, involved in forward reaction (i.e. k_a step) and backward reaction (i.e. k_{-a} step) of the equilibrium process between A and C in Eq. (10), and the conclusions described earlier in the text may lead to the relationship between E_{app} and $[Buf]_T$ at a constant $[Am]_T$ and pH as shown by Eq. (22)

$$E_{\rm app} = \frac{E_{\rm app}^0}{1 + \frac{K_1[{\rm Buf}]_{\rm T}}{1 + K_2[{\rm Buf}]_{\rm T}}}$$
(22)

where $E_{app}^0 = E_{app}$ at $[Buf]_T = [Am]_T = 0$ as well as K_1 and K_2 are the functions of rate constants, pH, and $[Am]_T$. Thus, E_{app}^0 , K_1 , and K_2 are constants at a constant pH and $[Am]_T$.

The values of E_{app} at different [Buf]_T (Buf = acetate buffer) and at a constant pH and [Am]_T(=0.1 M) were



 B^{-} = general base , $D = H_2NCOOCH_2CH_3$ BH = general acid



B = general base

BH = general acid

Scheme 2

treated with Eq. (22) and the nonlinear least-squares calculated values of E_{app}^0 , K_1 , and K_2 are summarized in Table III. Although the observed data fit reasonably well to Eq. (22) as evident from the calculated values of E_{app} shown as $E_{app \, cld}$ in Table IV and from the standard deviations associated with the calculated values E_{app}^0 , K_1 , and K_2 (Table III), the values of K_2 are less reliable for the reason that the maximum contribution of $K_2[Buf]_T$ is only ~35% compared to 1 in Eq. (22). Thus, if $K_2[Buf]_T$ is negligible compared to 1 under the present experimental conditions, then Eq. (22) should reduce to Eq. (23).

$$E_{\rm app} = \frac{E_{\rm app}^0}{1 + K_1 [\rm Buf]_T}$$
(23)

The values of E_{app}^0 and K_1 were also calculated from Eq. (23) by the use of nonlinear least-squares technique and the results obtained are summarized in Table III. The values of $E_{app cld}$ as shown in Table IV are not significantly different from the corresponding values of $E_{app cld}$ obtained by the use of Eq. (22) (Table IV). The values of K_1 , obtained at three different pH, can be explained in terms of suggested probable mechanisms which led to derive Eq. (22). The calculated values of E_{app}^0 are almost independent of pH which are in agreement with Eq. (22) or (23).

An attempt to fit E_{app} values for phosphate buffer to Eq. (22) was unsuccessful probably for the reason that the change in E_{app} with change in [Buf]_T from 0.08 to 0.48 M is very small (Table IV). However, these data appear to fit to Eq. (23) as evident from the $E_{app cld}$ values summarized in Table IV. The least-squares calculated values of E_{app}^{0} and K_{1} are summarized in Table III. The lower value of $K_{1}(=0.22 \text{ M}^{-1})$ at pH 7.28 than that at pH 6.84 ($K_{1} = 0.49 \text{ M}^{-1}$) is conceivable in view of the expected mechanisms involved in the forward and backward reactions of equilibrium process between A and C in Eq. (10).

The values of k_{10} and k_{10}^{cor} (in the presence of acetate and phosphate buffers) at different pH fit to the relationship $k_{10} = k_{1w} + k_{10H}a_{0H}$ (where $a_{0H} = 10^{pH-pK_w}$ with $pK_w = 13.84$ [14]). The least-squares calculated values of k_{1w} and k_{10H} are $(3.1 \pm 2.9) \times 10^{-4}$ s⁻¹ and $(3.31 \pm 1.60) \times 10^4$ M⁻¹ s⁻¹, respectively. The extent of reliability of the linear fit of k_{10} and k_{10}^{cor} with a definite intercept is evident from $k_{10\,cld}$ values summarized in Table II. The value of k_{1w} is associated with considerably large (~100%) standard deviation and hence it is not reliable. The value of k_{10H} is comparable with the corresponding values for related intramolecular nucleophilic addition–elimination reactions [5,12].

The values of k_{20} and k_{20}^{cor} at different pH (Table II) appeared to fit to the relationship $k_{20} = k_{2w} + k_{2OH}a_{OH}$. The least-squares calculated values of k_{2w} and k_{2OH} are $(3.15 \pm 0.67) \times 10^{-4} \text{ s}^{-1}$ and $(0.270 \pm 0.039) \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$, respectively. Both k_{2w} and k_{2OH} are not significantly different from the corresponding values of k_w (=2.6 × 10⁻⁴ s⁻¹) and k_{OH} (=0.20 × 10⁴ M⁻¹ s⁻¹) for hydrolysis of NCPH [15]. It has been shown elsewhere [9] that the p K_a of conjugate acid of leaving group in the hydrolysis of NCPH.

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