Intramolecular General Base Catalysis and the Rate-determining Step in the Nucleophilic Cleavage of Ionized Phenyl Salicylate with Primary and Secondary Amines

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The nucleophilic second-order rate constants for the reactions of ionized phenyl salicylate (PS^-) with primary and secondary amines have revealed Brønsted plots of slopes $\beta_{nuc_1} = 0.52 \pm 0.06$ and $\beta_{nuc_2} = 0.27 \pm 0.05$, respectively. The suggested stepwise reaction mechanism involves the intramolecular proton transfer from cationic nitrogen to the anionic phenolic oxygen to form the monoanionic tetrahedral addition intermediate as the rate-determining step. The low value of β_{nuc_2} is attributed to the extensive of proton transfer in the late transition state while the large value of β_{nuc_1} is ascribed to the proton transfer in the early transition state of the rate-determining step. However, these low and high values of β_{nuc_2} and β_{nuc_1}, respectively, are also compatible with the occurrence of respective early and late transition states in the rate-determining step involving concerted intramolecular general base-catalysed nucleophilic attack at the carbonyl carbon of PS^-. Significantly large positive deviations from Brønsted plots have been observed for the reactivities of α-nucleophiles toward PS^-. Monoprotonated ethane-1,2-diamine is *ca.* 20-fold more reactive than would be expected from its basicity, and this is attributed to the occurrence of the intramolecular general acid catalysis. The reactions of PS^- with hydroxylamine and *N*-methylhydroxylamine involve *ca.* $\geqslant$70% aminolysis and $\leqslant$30% transesterification while those with tris-(2-hydroxyethyl)amine involve 100% transesterification. The extremely low reactivity of ammonia compared with that of primary amines of similar basicity indicates that it does not belong to a series of homologous primary amines in its nucleophilic reactivity toward PS^-.

Mechanistic elucidation of intramolecular general acid- and base-catalysed reactions has become of considerable importance since it has become apparent that such catalyses are involved in many enzymatic reactions.[1] Intramolecular general base catalysis has been shown to accelerate the rates of hydrolysis of salicylate esters by a factor of *ca.* 10^6.[2] The mechanistic details of the hydrolysis of the salicylate esters have been investigated by many workers[3–10] and the most convincing mechanism of these reactions involves intramolecular general base catalysis.

The butylaminolyses of methyl salicylate[11] and phenyl salicylate[12] were studied in non-hydroxylic solvents. The proposed mechanism for butylaminolysis of phenyl salicylate in acetonitrile involves an intramolecular general acid catalysis coupled with an intermolecular general base catalysis. Recent studies of the aminolysis of methyl salicylate in aqueous media indicated that various secondary amines were completely unreactive while several primary amines were significantly reactive toward ionized methyl salicylate (MS^-).[13] In our earlier study on the aminolysis of phenyl salicylate,[14] it was observed that both secondary and primary amines were highly reactive toward ionized phenyl salicylate (PS^-). In this study,[14] however, only three primary amines were considered and the observed points for two of them, ethane-1,2-diamine and glycine, were found to deviate negatively from the Brønsted plot drawn through the observed points for secondary amines. The respective presence and absence of nucleophilic reactivity of secondary amines toward PS^- and MS^- indicate that the nucleophilic reactivity of both primary and secondary amines toward PS^- may not be expected to constitute a single Brønsted plot. In order to test this hypothesis, we studied the nucleophilic cleavage of PS^- with several primary amines and a number of secondary amines and the results obtained are described in this paper.

Experimental

Materials.—All chemicals used were of reagent grade and were obtained from Aldrich, BDH, and Fluka AG. D_2O with minimum isotopic purity of 99.7% was obtained from BDH. Glass-distilled water was used in the entire kinetic studies. The stock solutions of phenyl salicylate in acetonitrile were frequently prepared.

Kinetic Measurements.—The reaction rates of aminolysis and hydrolysis of phenyl salicylate were studied by monitoring the disappearance of phenyl salicylate at either 350 or 340 nm. The kinetics of the reactions of phenyl salicylate with tris-(2-hydroxyethyl)amine were also studied by monitoring the appearance of product(s) at 280 nm. The details of the procedure are described elsewhere.[14] The observed data were found to obey equations (1) and (2) for the reactions where disappearance of reactant and appearance of product(s), respectively, were monitored as a function of time (t). In equations (1) and (2), A_{obs}, A_∞, and A_0 represent absorbance at any time, t, at $t = \infty$, and $t = 0$, respectively,

$$A_{obs} = \varepsilon_{app}[X]_0 \exp(-k_{obs}t) + A_\infty \quad (1)$$

$$A_{obs} = \varepsilon_{app}[X]_0[1 - \exp(-k_{obs}t)] + A_0 \quad (2)$$

ε_{app} is the apparent molar absorption coefficient, $[X]_0$ is the initial concentration of phenyl salicylate, and k_{obs} is the observed pseudo-first-order rate constant. The three unknown parameters, k_{obs}, ε_{app}, and A_∞ or A_0 were calculated from equations (1) or (2) by the use of the non-linear least-squares technique.* The observed data were found to fit reasonably well

* Non-linear and linear least-squares computer programs in BASIC were developed and entire computations were carried out on either a Commodore Professional 3016 or a VAX 11 digital computer.

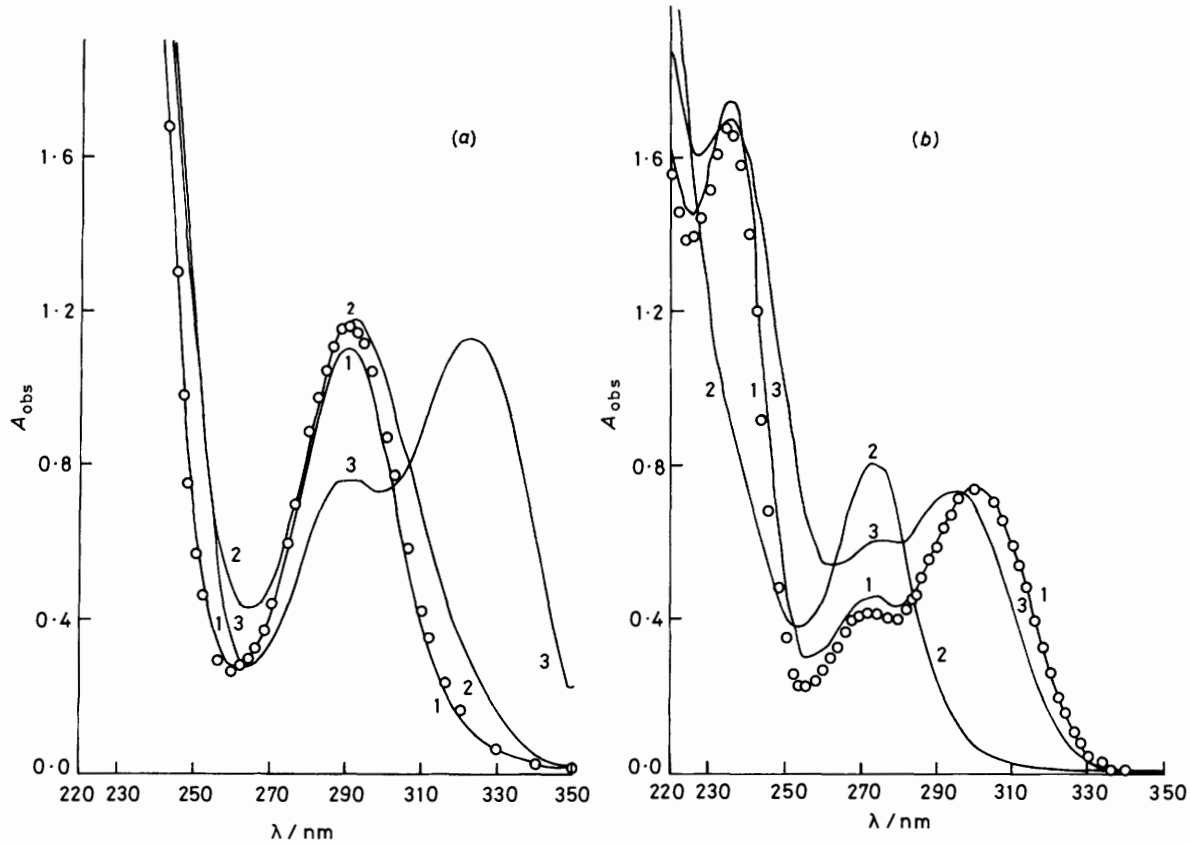


Figure 1. (*a*) Spectra of the products of hydrolysis and aminolysis of phenyl salicylate (PSH) at pH > 11.5. Unless otherwise stated, ionic strength = 1.0 mol l^{-1}, [phenyl salicylate]$_0$ = 2 × 10^{-4} mol l^{-1}, MeCN = 1%. 1, Hydrolysis: spectrum was obtained after 8 half-lives of the reaction. Observed points (○) were obtained for an authentic mixture of salicylic acid (2 × 10^{-4} mol l^{-1}) and phenol (2 × 10^{-4} mol l^{-1}) at pH > 11.5; 2, morpholinolysis: 0.2M-morpholine. Spectrum was obtained after 15 half-lives of the reaction; 3, propylaminolysis: 2.04 × 10^{-4}M-PSH, 0.10M-propylamine. Spectrum was recorded after 15 half-lives of the reaction. (*b*) Spectra of the products of hydrolysis and aminolysis of phenyl salicylate (PSH) at pH < 1.5. Unless otherwise stated, ionic strength, [phenyl salicylate]$_0$, and MeCN as in (*a*). The hydrolysis (at 0.1M-NaOH), morpholinolysis (at pH > 11.5), and propylaminolysis (at pH > 11.5) of PSH were carried out for 6.5, 13.5, and 15 half-lives, respectively, and the product mixtures acidified by adding known and sufficient amounts of HCl such that the pH of the resulting product mixtures was <1.5. The spectra 1, 2, and 3 of these acidified product mixtures were quickly recorded. 1, Hydrolysis: [phenyl salicylate]$_0$ = 1.96 × 10^{-4} mol l^{-1} and observed points (○) were obtained for an authentic mixture of salicylic acid (2 × 10^{-4} mol l^{-1}) and phenol (2 × 10^{-4} mol l^{-1}) at pH < 1.5; 2, morpholinolysis: 0.15M-morpholine; 3, propylaminolysis: 0.1M-propylamine

to equations (1) or (2) for almost all the kinetic runs. The percentage deviations between the observed and calculated absorbance values were less than 2% for up to 3—6 half-lives for most of the kinetic runs.

Determination of pK_a.—The concentration pK_a of protonated *N*-methylhydroxylamine was determined by potentiometric-titration techniques. The value of pK_a at 30 °C and 1 mol l^{-1} strength was found to be 6.24 ± 0.01 which is comparable to literature values of 6.15[15] and 6.25[16] obtained at 25 °C and 0.5 mol l^{-1} ionic strength. The ionization constant, K_a, of the conjugate acid of 2-aminopyridine was determined by spectrophotometric techniques[14] and the value of K_a obtained was (6.13 ± 0.25) × 10^{-8} mol l^{-1} at 30 °C and 1 mol l^{-1} ionic strength.

Product Characterization.—In order to find out whether the cleavage of PS^-, in buffered solutions of primary and secondary amines, involves amines acting as nucleophiles or general base catalysts, we carried out the following spectral studies. If the amines acted as general base catalysts for hydrolytic cleavage of PS^-, then the expected products would be salicylate and phenolate ions in an alkaline medium. On the other hand, the expected products would be *N*-substituted salicylamides and phenolate ion if the amines were acting as nucleophiles. We studied the cleavage of PS^- in the presence of 0.10M-propylamine and 0.006M-NaOH. The progress of the reaction was monitored by observing the decrease in absorbance values at 350 nm (A_{obs}^{350}). When the reaction appeared to be over (*i.e.* when there was no further change in A_{obs}^{350} within *ca.* 30—60 min), the spectrum of the reaction products was recorded as shown in Figure 1(*a*). The reaction mixture was then acidified to pH < 1.5 with a known amount of HCl (using stock solution of *ca.* 11M-HCl). The spectrum of the acidified reaction products was quickly recorded as shown in Figure 1(*b*). Similar spectra in both acidic and basic media were obtained for the reaction products of PS^- with morpholine and hydroxide ion and are shown in Figure 1(*a*) and 1(*b*). The spectra of the authentic mixtures containing equal amounts of salicylic acid and phenol were also obtained under essentially similar experimental conditions and are shown by open circles in Figure 1(*a*) and 1(*b*). The spectra of the products of the reactions of PS^- with morpholine and pyrrolidine were identical in both acidic and basic media. Similarly, the spectra of the reaction products of PS^- with propylamine, Tris, and 2-methoxyethylamine were identical under similar experimental conditions. The spectra of the products of alkaline hydrolysis of PS^- were found to be identical in the absence and presence of 0.02M-pyrrolidine.

It is evident from the spectra shown in Figures 1(*a*) and 1(*b*) that the products of the cleavage of PS^- in the presence of primary and secondary amines are not the same as the products of hydrolysis of PS^-. The products (*N*-substituted salicylamides) of the reactions of PS^- with primary amines show significant absorption at 350 nm [Figure 1(*a*) and Table 2]. The extinction coefficient of products of propylaminolysis of PS^- at 270 nm in acidic media is 2 900 l mol^{-1} cm^{-1} which may be compared with the extinction coefficient (2 460 l mol^{-1} cm^{-1} at 270 nm) of the products of butylaminolysis of PSH in non-hydroxylic solvents. Furthermore, the possibility of the primary and secondary amines acting as general base catalysts may be ruled out by the fact that sterically less hindered tertiary amines such as 1,4-diazabicyclo[2.2.2]octane and trimethylamine did not show any detectable catalysis in the cleavage of PS^-.[17] If, for example, morpholine, piperazine, and *N*-methylpiperazine are effective catalysts then it is difficult to explain why 1,4-diazabicyclo[2.2.2]octane did not exhibit detectable catalysis.

Results

Hydrolysis.—A series of kinetic runs was carried out within the [NaOH] range 0.01—1.00 mol l^{-1} at 30 °C. The ionic strength was kept constant at 1.0 mol l^{-1} using KCl. The observed pseudo-first-order rate constants, k_{obs}, were found to fit to equation (3)

$$k_{obs} = k_0 + k_{OH}[OH^-] \quad (3)$$

where k_0 and k_{OH} represent pH-independent first-order and OH^--catalysed second-order rate constants, respectively. The least-squares calculated values of $k_0^{H_2O}$ [$\equiv k_0$ in equation (3)] and k_{OH} are (3.60 ± 0.05) × 10^{-4} s^{-1} and (12.4 ± 0.1) × 10^{-4} l mol^{-1} s^{-1}, respectively. The fitting of the observed data to equation (3) is evident from the standard deviations associated with the values of k_0 and k_{OH}. The cleavage of PS^- was also studied at 30 °C within [OD^-] range of 0.005—0.1 mol l^{-1} in a solvent with minimum isotopic and MeCN contents of 98.7 and 1%, respectively. The observed data obeyed equation (3) and the least-squares-calculated values of $k_0^{D_2O}$ [$\equiv k_0$ in equation (3)] and k_{OD} [k_{OH} in equation (3)] were (2.30 ± 0.01) × 10^{-4} s^{-1} and (12.7 ± 0.2) × 10^{-4} l mol^{-1} s^{-1}, respectively. The observed solvent isotope effect ($k_0^{H_2O}/k_0^{D_2O}$) of 1.6 (for solvent-catalysed cleavage of PS^-) may be compared with analogous reported values of 1.7 for phenyl salicylate[4] and 1.68 for *p*-nitrophenyl 5-nitrosalicylate.[3]

Reaction with Primary and Secondary Amines.—The nucleophilic cleavage of phenyl salicylate buffered solutions of dimethylamine and diethylamine were studied at various pH. The observed data revealed reasonably good fit to equation (4)

$$k_{obs}^{corr} = k_n[Am]_T \quad (4)$$

where $[Am]_T$ and k_n represent the total amine buffer concentration and apparent second-order nucleophilic rate constant, respectively. $k_{obs}^{corr} = k_{obs} - k'_0$ where buffer-independent rate constants, k'_0, at different pH values were calculated from equation (5).

$$k'_0 = \frac{k_0^{H_2O}K'_a}{a_H + K'_a} \quad (5)$$

In equation (5), $k_0^{H_2O} = 3.60 \times 10^{-4}$ s^{-1} and K'_a (= 5.67×10^{-10})[14] is the ionization constant of phenyl salicylate. The values of k_n as summarized in Table 1 were calculated from equation (4) using a linear least-squares technique. The fitting of the observed data to equation (4) is evident from the standard deviations of k_n values.

The general rate law for the nucleophilic cleavage of phenyl salicylate in buffered amine solutions may be given as

$$\text{rate} = -\frac{d[Sub]_T}{dt} = (k'_0 + k_{OH}[OH^-])[Sub]_T + k_1[PS^-][Am] + k_2[PSH][Am] \quad (6)$$

where $[Sub]_T$ represents the total concentration of substrate (phenyl salicylate). $[Am]_T$, [PSH], and $[PS^-]$ represent the concentrations of free amine base, non-ionized, and ionized phenyl salicylate, respectively. The other probable kinetic terms such as $k_3[PS^-][Am][OH^-]$ and $k_4[PSH][Am][OH^-]$ were ignored on the basis as described elsewhere.[14] The observed rate law (rate = $k_{obs}[Sub]_T$) and equation (6) give equation (7)

$$k_{obs} = k'_0 + k_{OH}[OH^-] + \frac{k_1K_aK'_a + k_2K_aa_H}{(a_H + K'_a)(a_H + K_a)} \quad (7)$$

where K_a is the ionization constant of the protonated amine. The hydroxide-ion-catalysed term, $k_{OH}[OH^-]$, appeared to be negligible compared with k'_0 for the reactions carried out at pH ≤ 11.50. Under such experimental conditions, equations (4) and (7) result in equation (8)

$$k_nQ = k_1K_aK'_a + k_2K_aa_H \quad (8)$$

where $Q = (a_H + K'_a)(a_H + K_a)$. The respective least-squares-calculated values of $k_1K_aK'_a$ and k_2K_a are (26.4 ± 0.3) × 10^{-22} mol l^{-1} s^{-1} and (4.04 ± 0.68) × 10^{-12} s^{-1} for dimethylamine and (14.9 ± 0.9) × 10^{-24} mol l^{-1} s^{-1} and (−4.6 ± 123.0) × 10^{-15} s^{-1} for diethylamine. The negative value of k_2K_a with standard deviations of >100% for diethylamine revealed an insignificant contribution of $k_2K_aa_H$ compared with $k_1K_aK'_a$ in equation (8) under the present experimental conditions. Similar results were obtained with several other amines.[14] Although the standard deviation associated with the calculated value of k_2K_a for dimethylamine is not so high as to rule it out completely, the maximum contribution of $k_2K_aa_H$ toward k_nQ [equation (8)] obtained at the lowest pH (10.03) is only <13%. Values of $k_1K_aK'_a$ and k_2K_a were used to calculate k_1 and k_2 with known values of K_a and K'_a and the respective values thus obtained were 0.522 ± 0.006 and 0.453 ± 0.076 l mol^{-1} s^{-1}. The value of k_2 of 0.453 l mol^{-1} s^{-1}, although not very reliable, is comparable to that derived from the Brønsted plot obtained in an earlier study.[14] If we ignore the term $k_2K_aa_H$ in equation (8), the calculated values of $k_1K_aK'_a$ turned out to be (27.8 ± 1.4) × 10^{-22} and (14.9 ± 1.0) × 10^{-24} mol l^{-1} s^{-1} for dimethylamine and diethylamine, respectively. These values of $k_1K_aK'_a$ were used to calculate k_1 as summarized in Table 2. The value of k_1 for dimethylamine was found to increase by less than *ca.* 6% if the $k_2K_aa_H$ term is ignored in equation (8).

The values of k_1 for several other amines were determined by carrying out the kinetic runs within the pH range of *ca.* 11.0—12.3 and at total amine concentration $[Am]_T$ range as shown in Table 2. Under the experimental conditions of the reactions of these amines with phenyl salicylate, the concentrations of non-ionized phenyl salicylate and protonated amines appeared to be negligible and hence the contribution of the k_2 term is apparently negligible compared with the k_1 term in equation (6). The observed data obeyed equation (9)

$$k_{obs} - k'_0 - k_{OH}[OH^-] = \frac{k_1K_a[Am]_T}{a_H + K_a} \quad (9)$$

Table 1. Apparent second-order rate constants for the reactions of phenyl salicylate with amine nucleophiles[a]

Amine	pH	$10^3 k_n$/l mol^{-1} s^{-1}	$[Am]_T$ range[b]	No. of runs
Dimethylamine	10.03	44.1 ± 0.3[c]	0.05—0.30	6
	10.24	70.1 ± 0.3	0.05—0.30	6
	10.50	116 ± 1	0.05—0.30	6
	10.74	169 ± 2	0.025—0.150	6
	10.98	242 ± 2	0.025—0.150	6
	11.21	301 ± 2	0.025—0.150	6
Diethylamine	10.89	1.44 ± 0.06	0.20—0.50	4
	11.07	1.64 ± 0.07	0.16—0.48	4
	11.36	2.42 ± 0.11	0.20—0.70	4
	11.57	2.99 ± 0.11	0.16—0.48	4
	11.76	3.66 ± 0.18	0.08—0.28	4

[a] Conditions: [Phenyl Salicylate]$_0$ = 1.8 × 10^{-4} mol l^{-1}; 0.8% MeCN in the aqueous reaction mixtures; 1 mol l^{-1} ionic strength and 30 °C; λ = 340 nm. [b] Total amine buffer concentration range. [c] Error limits are standard deviations.

where k_{OH} = 12.4 × 10^{-4} l mol^{-1} s^{-1}. The values of k'_0 and [OH$^-$] at different pH values were obtained from equation (5) and the relationship [OH$^-$] = 10$^{pH}K_w/\nu_{OH}$, respectively. The values of K_w and activity coefficient of hydroxide ion, ν_{OH}, at 1 mol l^{-1} ionic strength were considered to be 1.449 × 10^{-14} mol^2 l^{-2} [18] and 0.70,[19] respectively. The values of k_1 for various amines calculated from equation (9) are summarized in Table 2. The fitting of the observed data to equation (9) is evident from the standard deviations associated with the values of k_1.

Solvent Isotope Effect on Aminolysis of PS$^-$.—The rates of reactions of PS$^-$ with Tris, 2-methoxyethylamine, propylamine, morpholine, and pyrrolidine were studied by carrying out kinetic runs in a solvent containing 1% MeCN and more than 98.7% D_2O. The observed pseudo-first-order rate constants, $k_{obs}^{D_2O}$, obtained within the pD range 11.7—12.90, reasonably fit equation (10)

$$k_{obs}^{D_2O} - k_0^{D_2O} - k_{OD}[OD^-] = k_1^{D_2O}[Am]_T \qquad (10)$$

where $k_0^{D_2O}$ = 2.30 × 10^{-4} s^{-1}, k_{OD} = 12.7 × 10^{-4} l mol^{-1} s^{-1} and [OD$^-$] = 10$^{pD}K_{D_2O}/\nu_{OD}$ with $K_{D_2O} = a_D a_{OD}$. The ionic product of D_2O, K_{D_2O}, is equal to K_w/6.53 where K_w is the ionic product of H_2O. The values of the activity coefficients of OD$^-$, ν_{OD}, and OH$^-$, ν_{OH}, were assumed to be the same at ionic strength 1.0 mol l^{-1}. The nucleophilic second-order rate constants, $k_1^{D_2O}$, were calculated from equation (10) and are summarized in Table 2.

Transesterification of Phenyl Salicylate in Alkaline Amino Alcohol Solutions.—The reaction kinetics carried out in alkaline solutions of hydroxylamine and *N*-methylhydroxylamine at varying total amine concentrations were found to be complicated by the slow degradation of the *O*-acylated product. In these reactions, true first-order kinetics were found only up to 80—89% reaction. Thus the k_1 values obtained for these two amines are the sum of the second-order rate constants for the nucleophilic attack by the *N*- and *O*- sites of these amines. However, as described in the Appendix, the contribution due to *O*-attack is ≤30% under the experimental conditions imposed. The *O*-attack-corrected nucleophilic second-order rate constants are also shown in Table 2. Transesterification could not be detected in the reactions of 3-aminopropan-1-ol, 2-aminoethanol, bis-(2-hydroxyethyl)amine, and Tris with PS$^-$. We have recently observed that the rate of methanolysis of PS$^-$ is *ca.* 20 and 40 times faster than that of ethanolysis and propanolysis of PS$^-$, respectively.[13] It is interesting to note that the estimated rate constants for *O*-attack in the reactions of hydroxylamine and *N*-methylhydroxylamine with PS$^-$ are 26.3 × 10^{-3} and 22.8 × 10^{-3} l mol^{-1} s^{-1}, respectively (Appendix). These rate constants when converted into first-order units at 0.24 mol l^{-1} amine concentration are *ca.* 10—12 times larger than the first-order rate constant (5.20 × 10^{-4} s^{-1}) for methanolysis of PS$^-$ at 0.24 mol l^{-1} MeOH, obtained under essentially similar experimental conditions. The absence of transesterification of PS$^-$ with the other amino alcohols of the present study is most probably a result of the predominant *N*-attack, as compared with *O*-attack, of these nucleophiles.

Reaction with Tris-(2-hydroxyethyl)amine (THEA).—The nucleophilic cleavage of PS$^-$ was studied at various concentrations of tris-(2-hydroxyethyl)amine, $[THEA]_T$, within the pH range 11.01—11.79 and 10.92—11.77 at 280 and 350 nm, respectively. The rates of the reactions appeared to be dependent on $[THEA]_T$ and true first-order kinetics could be obtained up to 99 and 71—94% reaction when studied at 280 and 350 nm, respectively.

Bender *et al.*[3] and Capon *et al.*[4] did not observe an intramolecular general base-catalysed rate enhancement in the reactions of ionized salicylate esters with nucleophiles bearing no mobile proton at the nucleophilic site. We also did not observe any detectable nucleophilic reactivity of trimethylamine, 1,4-diazabicyclo[2.2.2]octane, and triethylamine toward PS$^-$.[17] In view of these observations, the nitrogen of THEA cannot be the site of reaction between PS$^-$ and THEA. The hydroxy group of THEA must therefore be acting as the nucleophile in these reactions. The transesterified product *N*,*N*-bis-(2-hydroxyethyl)aminoethyl salicylate, thus formed, hydrolysed slowly in the latter phase of the reaction which slightly complicated the first-order kinetics of transesterification. The observed pseudo-first-order rate constants calculated from the initial phase of the reactions (up to 99 and 71—94% reaction when studied at 280 and 350 nm, respectively) were found to obey equation (9). The calculated values of k_1 (Table 2) obtained from the rate studies at 280 and 350 nm are essentially the same. It is interesting to note that the value of k_1 (Table 2) is approximately equal to the rate constant (=6.26 × 10^{-4} l mol^{-1} s^{-1} at 30 °C)[13] obtained for ethanolysis of PS$^-$ if the former is corrected by a factor of 3 to allow for the fact that there are 3 reactive OH groups in THEA.

During the rate studies carried out at 280 and 350 nm, the kinetics of the terminal phase of the reactions were also studied by monitoring the disappearance of the transesterified product at 340 and 350 nm, respectively. The observed pseudo-first-order rate constants calculated from equation (1) are summarized in Table 3. The rate constants (Table 3) appear to be independent of $[THEA]_T$ and pH. These rate constants are comparable to

Table 2. Second-order rate constants (k_1) for the reactions of PS^- with primary and secondary amines[a]

Amine	pK_a[b]	pH or pD range[c]	$10^3 k_1$/l mol^{-1} s^{-1}	A_∞ range at 350 nm[d]	t_∞ range/min	$[Am]_T$ range[e]	No. of runs
Hydrazine	8.15[f]	11.68—12.46	114 ± 1[g]	0.218—0.230	60—24	0.05—0.30	6
		11.51—12.14	107 ± 1	0.221—0.231	55—28	0.05—0.25	5
Hydroxylamine	5.97[f]	11.23—11.77	101 ± 1	0.328—0.266	4—1	0.08—0.32	9
			74.7[h]				
3-Aminopropan-1-ol	10.16[i]	11.53—12.18	36.3 ± 0.2	0.192—0.230	*ca.* 114	0.05—0.30	6
2-Hydroxyethylamine	9.60[j]	11.34—11.84	22.8 ± 0.1	0.211—0.270	76—30	0.10—0.60	6
2-Methoxyethylamine	9.45[k]	11.34—12.24	16.8 ± 0.2	0.208—0.260	106—31	0.10—0.60	6
		12.33—12.84	16.2 ± 0.2[l]	0.297—0.335	21—14	0.20—0.60	4
Butane-1,4-diamine	10.77[m] (pK_2)	11.71—12.25	95.2 ± 0.4	0.174—0.212	74—30	0.03—0.18	6
Propane-1,3-diamine	10.62[m] (pK_2)	11.55—12.11	79.6 ± 0.3	0.185—0.213	69—30	0.03—0.18	6
Ethylamine	10.72[f]	11.58—12.12	46.4 ± 0.4	0.151—0.195	99—32	0.03—0.18	6
Propylamine	10.79[n]	11.54—12.11	50.0 ± 0.3	0.145—0.186	63—22	0.03—0.18	6
		12.36—12.87	59.4 ± 0.5	0.230—0.261	40—12	0.04—0.20	5
Ammonia	9.21[o]	11.14—11.74	0.658 ± 0.008	0.073—0.256	310—207	0.10—0.90	6
Tris	8.14[f]	11.07—11.74	3.16 ± 0.06	0.198—0.373	*ca.* 1 380	0.12—0.60	5
		11.32—11.84	3.10 ± 0.04	0.291—0.385[p]	100—65	0.20—0.60	4
		11.94—12.45	1.96 ± 0.001[l]	0.301—0.387	110—95	0.20—0.60	4
Methylamine	10.85		204[q]				
Glycine	9.63		19.7[q]				
Ethane-1,2-diamine	10.18(pK_2)		55.3[q]				
	7.53(pK_1)		36.3[q]				
Dimethylamine	11.05[o]		581 ± 6				
Diethylamine	11.07[r]		4.46 ± 0.14				
N-Methylhydroxylamine	6.24[s]	11.04—11.66	81.4 ± 0.6	0.190—0.216	10—5	0.08—0.48	6
			58.6[h]				
		10.92—11.44	76.0 ± 0.6	0.227—0.428	9	0.08—0.32	5[t]
			54.7[h]				
Diethanolamine	9.04[s]	11.19—11.87	2.86 ± 0.07	0.005—0.010	130—89	0.12—0.60	5
Pyrrolidine	11.32[f]	11.51—11.92	550 ± 18	0.012—0.048	50—22	0.016—0.022	6
		12.42—12.67	638 ± 23[l]	0.026—0.028	15—10	0.014—0.028	4
Morpholine	8.60		86.3[q]				
		11.69—12.63	91.4 ± 1.0[l]	0.029—0.025	18—7	0.05—0.20	4
			77.7[q]				
Piperidine	11.23		231[q]				
N-Methylpiperizine	9.10(pK_2)		118[q]				
Piperizine	9.83(pK_2)		311[q]				
	5.57(pK_2)		27.5[q]				
2-Aminopyridine	7.21[s]	11.51—12.29	−0.07 ± 0.01[u]	0.010—0.020	*ca.* 1 320	0.12—0.60	5
Triethanolamine	8.15[v]	11.02—11.80	1.66 ± 0.03	*w*	120—68	0.12—0.60	5
		10.93—11.77	1.61 ± 0.08	0.175—0.427	37	0.12—0.60	3

[a] Conditions $[\text{phenyl salicylate}]_0 = 1.6 \times 10^{-4}$ mol l^{-1}; 0.8% MeCN in the aqueous reaction mixtures; 1 mol l^{-1} ionic strength; 30 °C; λ = 350 nm. [b] pK_a of conjugate acids of amines. [c] pD = pH meter reading + 0.4 (P. J. Glasoe and F. A. Long, *J. Phys. Chem.*, 1960, **64**, 188). [d] The observed values of A_∞ at t_∞ ($t = \infty$). [e] Total amine concentration range. [f] A. R. Becker, D. J. Richardson, and T. C. Bruice, *J. Am. Chem. Soc.*, 1977, **99**, 5058. [g] Error limits are standard deviations. [h] *O*-Attack-corrected value. [i] M. N. Khan, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1977. [j] T. H. Fife and B. R. DeMark, *J. Am. Chem. Soc.*, 1977, **99**, 3075. [k] T. H. Fife, R. J. Bambery, and B. R. De Mark, *J. Am. Chem. Soc.*, 1978, **100**, 5500. [l] Obtained in D_2O and $[\text{phenyl salicylate}]_0 = 2.0 \times 10^{-4}$ mol l^{-1}. [m] T. C. Bruice and R. C. Willis, *J. Am. Chem. Soc.*, 1965, **87**, 531. [n] J. J. Morris and M. I. Page, *J. Chem. Soc., Perkin Trans. 2*, 1980, 220. [o] D. Z. Rogers and T. C. Bruice, *J. Am. Chem. Soc.*, 1979, **101**, 4713. [p] $[\text{phenyl salicylate}]_0 = 2 \times 10^{-4}$ mol l^{-1}. [q] Obtained from M. N. Khan, *J. Org. Chem.*, 1983, **48**, 2046. [r] M. N. Khan, *J. Chem. Soc., Perkin Trans. 2*, 1987, 819. [s] This study. [t] λ = 340 nm. [u] Calculated from the relationship $k_{obs} = k_0 + k_1[Am]_T$ where $k_1 = (3.79 \pm 0.05) \times 10^{-4}$ s^{-1}. [v] M. N. Khan, *J. Chem. Soc., Perkin Trans 2*, 1985, 891. [w] λ = 280 nm.

those obtained for pH-independent hydrolyses of methyl salicylate ($k_{obs} = 1.07 \times 10^{-4}$ s^{-1} at 30 °C [13] and 2.44×10^{-4} s^{-1} at 37 °C [20]), ethyl salicylate ($k_{obs} = 1.20 \times 10^{-4}$ s^{-1} at 30 °C and 2.33×10^{-4} s^{-1} at 37 °C [20]), 2-hydroxyethyl salicylate ($k_{obs} = 1.23 \times 10^{-4}$ s^{-1} at 30 °C [13]), and 2-ethoxyethyl salicylate ($k_{obs} = 1.24 \times 10^{-4}$ s^{-1} at 30 °C [13]).

The Cleavage of PS^- in Alkaline Solutions of 2-Aminopyridine.—The cleavage of phenyl salicylate was also studied at different concentrations of 2-aminopyridine within the pH range 11.51—12.29. The observed rate constants appeared to be independent of the concentrations of 2-aminopyridine. It is apparent that a detectable nucleophilic reactivity of 2-aminopyridine toward PS^- could be expected only if the basicity of primary amino-group ($-NH_2$) nitrogen is larger than that of pyridine nitrogen. The NH_2 group will therefore act as the nucleophile rather than the pyridine nitrogen which does not carry the required mobile proton for intramolecular general base catalysis. These observations thus indicate that the pyridine nitrogen is presumably more basic than the nitrogen of NH_2 group. This is conceivable for at least one reason, *i.e.* the basicity of the pyridine nitrogen is expected to be greatly increased by the electron-donating ability of NH_2 group toward pyridine nitrogen through resonance, whereas no such direct resonance effect is expected by pyridine nitrogen toward the nitrogen of NH_2 group.

Discussion

The dependence of the nucleophilic second-order rate constants, k_1, upon the basicities of the amine nucleophiles is

Table 3. Observed pseudo-first-order rate constants, $k_{obs\,2}$, for aqueous cleavage *N*,*N*-bis-(2-hydroxyethyl)aminoethyl salicylate formed in the reactions of PS^- with tris-(2-hydroxyethyl)amine[a]

	λ = 350 nm				λ = 340 nm			
$[THEA]_T$[b]/mol l^{-1}	pH	Time range[c]/10^3 s	$10^4 k_{obs\,2}/s^{-1}$	R[d]	pH	Time range[c]/10^3 s	$10^4 k_{obs\,2}/s^{-1}$	R[d]
0.12	10.93	7.2—82.8	0.922 ± 0.081[e]	6	11.02	7.2—97.2	1.10 ± 0.07[e]	5
0.24					11.38	7.0—97.2	1.02 ± 0.05	7
0.36	11.54	4.2—82.8	1.13 ± 0.06	9	11.57	7.0—97.2	1.07 ± 0.09	9
0.48					11.71	7.0—97.2	1.06 ± 0.05	11
0.60	11.77	4.2—82.8	1.07 ± 0.05	12	11.80	7.0—97.2	1.08 ± 0.05	13

[a] Conditions: $[X]_0 = 1.6 \times 10^{-4}$ mol l^{-1}, 1 mol l^{-1} ionic strength, 30 °C, and 0.8% MeCN in the aqueous reaction mixture. [b] Total concentration of tris-(2-hydroxyethyl)amine. [c] The range of time intervals on the time (t) *versus* observed absorbance (A_{obs}) plot which could be used to calculate $k_{obs\,2}$ from equation (1) (with k_{obs} replaced by $k_{obs\,2}$). [d] $R = k_{obs\,1}/k_{obs\,2}$ where $k_{obs\,1}$ and $k_{obs\,2}$ represent the observed pseudo-first-order rate rate constants for the cleavage of phenyl salicylate and *N*,*N*-bis-(2-hydroxyethyl)aminoethyl salicylate respectively, at constant $[THEA]_T$. [e] Error limits are standard deviations.

shown in Figure 2 from which it appears that the rate constants for the reactions of PS^- with primary and secondary amines constitute Brønsted plots of different slope. These observations are in contrast with the results obtained for the nucleophilic cleavage of phenyl acetate with amine nucleophiles, where all primary, secondary, and tertiary amines constituted a single Brønsted plot,[21–23] The rate constants, k_1, for the reactions of PS^- with primary amines were found to fit to equation (11)

$$\log k_1 = \beta_{nuc_1} pK_a + C_1 \qquad (11)$$

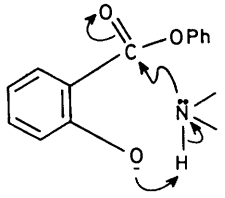
with least-squares-calculated values of β_{nuc_1} and C_1 of 0.52 ± 0.06 and −6.67 ± 0.65 l mol^{-1} s^{-1}, respectively. In the calculation of β_{nuc_1}, the customary statistical corrections were made to k_1 and pK_2 for diamines. Ammonia was not included in the calculation of β_{nuc_1} and C_1 simply because it appeared to deviate from the Brønsted plot (Figure 2) by a factor of *ca.* 16. Similarly, monoprotonated ethane-1,2-diamine, hydroxylamine, and hydrazine were also not included in the calculation of β_{nuc_1} and C_1. In our recent studies on the nucleophilic cleavage of maleimide, where primary,[24] secondary,[25] and tertiary[26] amines appeared to react with different mechanisms, ammonia was found to be significantly less reactive compared with primary amines of similar basicity. In the aminolysis of phenyl acetate with various amines, where primary, secondary, and tertiary amines appeared to constitute a single Brønsted plot, ammonia did not show any significant deviation.[22,23] The rate constant, k_1, for Tris seems to fall on the Brønsted plot of slope β_{nuc_1} (Figure 2) within the limits of the experimental error. This is surprising in view of its significantly large steric requirements for nucleophic attack.

The rate constants, k_1, for the reactions of PS^- with secondary amines obeyed the Brønsted equation with slope (β_{nuc_2}) 0.27 ± 0.05 and intercept (C_2) −3.37 ± 0.49 l mol^{-1} s^{-1}. Statistical corrections were applied to pK_2 and k_1 for piperazine in the treatment of observed data to the Brønsted equation. The value for β_{nuc_2} of 0.27 is slightly different from the previously reported value of 0.18 which was derived from the observed points for both primary and secondary amines.[14] In the calculation of β_{nuc_2}, the rate constants, k_1, for *N*-methylhydroxylamine and monoprotonated piperazine were not considered. The observed points for bis-(2-hydroxyethyl)amine and diethylamine negatively deviated from the Brønsted plot of slope β_{nuc_2} (for secondary amines) by a factor of *ca.* 40. Such a large negative deviation can most probably be attributed to steric effects. However, a straight line drawn through the points for bis-(2-hydroxyethyl)amine and diethylamine revealed a slope of *ca.* 0.10 which is comparable to β_{nuc_2}. Thus, it may be concluded that the reactions of PS^- with all the secondary amines of the present study follow the same mechanism.

The α-effect nucleophiles, hydroxylamine and hydrazine, deviated positively from the Brønsted plot of β_{nuc_1} by factors of *ca.* 275 and 31, respectively. Similarly, a 3-fold positive deviation from the Brønsted plot of slope β_{nuc_2} was observed for *N*-methylhydroxylamine. The nucleophilic reactivities of α-effect nitrogen nucleophiles toward phenyl and *p*-nitrophenyl acetate were found to be larger than those of primary amines of comparable basicity by factors of 30—2 500.[27] Hydrazine revealed a similar rate increase in its reactions with benzylpenicillin[28] and maleimide.[24] In these reactions, the proposed mechanism does not involve nucleophilic attack as the rate-determining step. Morris and Page[29] have shown that the α-effect in hydrazinolysis of benzylpenicillin is manifested by a 15-fold increase in the rate constant for nucleophilic attack and a 22-fold decrease in the rate constant for the expulsion of the nucleophile from the tetrahedral addition intermediate. This study indicates that the kinetic α-effect (15-fold) is significantly smaller than that of thermodynamic α-effect (*ca.* 350-fold), *i.e.* the α-effect manifested in the equilibrium constant for the formation of the tetrahedral addition intermediate. Recently, Palling and Jencks[30] have observed small rate increases for the reactions of acetyl chloride with α-effect nitrogen nucleophiles, compared with other primary amines of comparable basicity. In these reactions, the nucleophilic attack is shown to be the rate-determining step. It is interesting to note that a straight line drawn through the two points involving only hydroxylamine and hydrazine gave a slope (β_{nuc}) of *ca.* 0.1.

The first-order rate constant, k_0, for pH-independent aqueous cleavage of PS^- is *ca.* 3 times larger than that of ionized methyl salicylate (MS^-). But the values of $(k_1^{PS^-}/k_1^{MS^-})_{RNH_2}$ where $k_1^{PS^-}$ and $k_1^{MS^-}$ represent the nucleophilic second-order rate constants for the reactions of RNH_2 with PS^- and MS^-, respectively, are 223 for $MeNH_2$, 170 for $HOCH_2CH_2CH_2NH_2$, 250 for $MeOCH_2CH_2NH_2$, 60 for NH_2OH, 22 for NH_2NH_2, 60 for $H_3N^+CH_2CH_2NH_2$, 300 for $H_2NCH_2CH_2NH_2$, 230 for $H_2N[CH_2]_3NH_2$, and 280 for $H_2N[CH_2]_4NH_2$. These results indicate that the pK_a of the leaving group has significant effect on aminolysis compared with hydrolysis of ionized salicylate esters.

The reaction of PS^- with primary and secondary amines may be expected to involve either intramolecular general base catalysis (mechanism I) or intramolecular general acid catalysis (mechanism II). The probable occurrence of such kinetically equivalent mechanisms in the hydrolysis of salicylate esters has been resolved and the involvement of mechanism I has been convincingly ascertained.[2–4] We did not observe nucleophilic reactivity of trimethylamine, triethylamine, 1,4-diaza-



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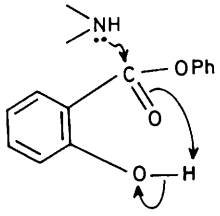
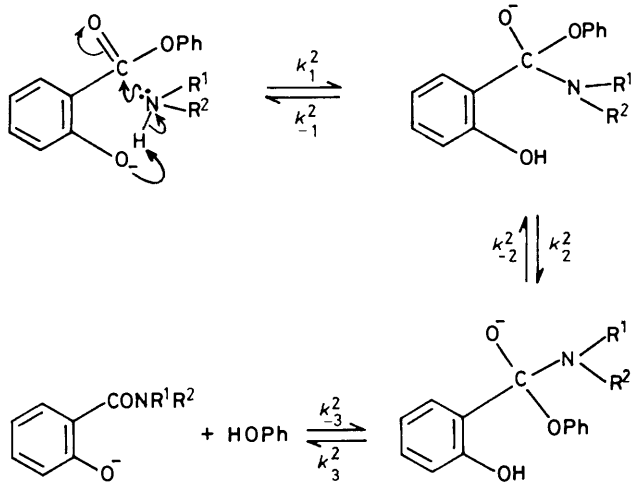
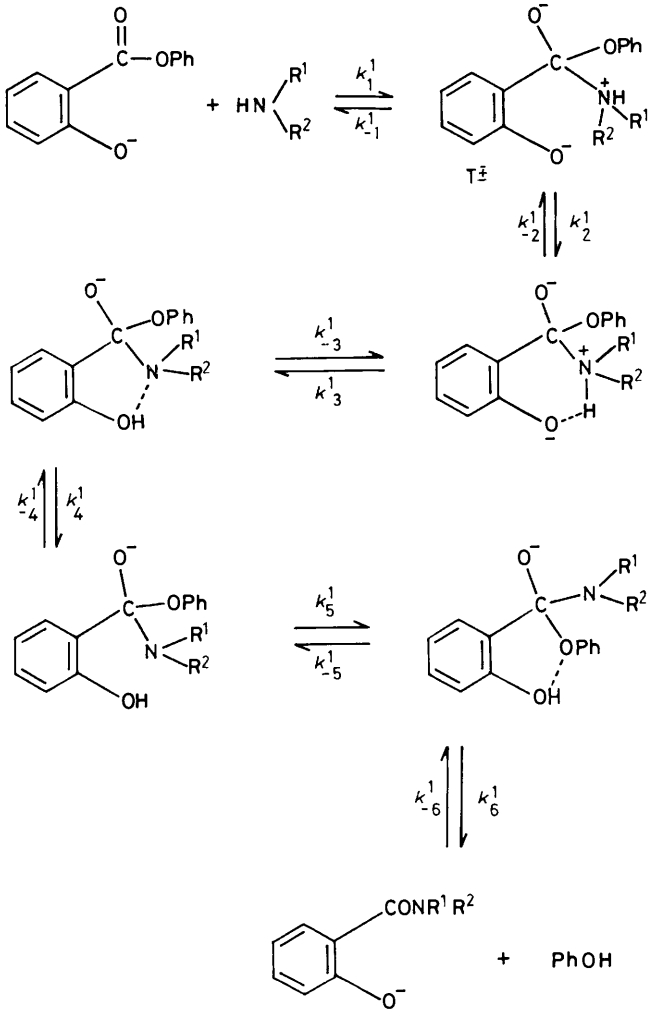


II



Scheme 2.



Scheme 1.

bicyclo[2.2.2]octane toward PS^-.[17] Similarly, enhanced nucleophilic reactivity of imidazole and azide ion toward ionized phenyl and *p*-nitrophenyl salicylates, respectively, could not be detected by other workers.[3,4] Enhanced nucleophilic reactivity would be expected in the reactions of phenyl salicylate with tertiary amines if mechanism II is operative. These observations thus support the occurrence of intramolecular general base catalysis (I) in the aminolysis of phenyl salicylate.

The value of β_{nuc_1} (0.52) is significantly different from that of β_{nuc_2} (0.27) which indicates the occurrence of two different types, or locations, of transition states on the reaction co-ordinate in the critical rate-determining step(s). The value of β_{nuc_1} of 0.52 may be compared with β_{nuc} values of 0.73 [23,31] and 0.96 [32] obtained for nucleophilic attack by primary and secondary amines on phenyl acetate [23,31] and phenyl quinoline-6-carboxylate,[32] respectively. A β_{nuc} value of 0.9 ± 0.1 (for the reactions of primary, secondary, and tertiary amines with aryl acetates) has been attributed to the rate-determining expulsion of the leaving group from the dipolar tetrahedral addition intermediate.[33]

The present data are not sufficient to rule out completely the possible occurrence of either stepwise mechanism (Scheme 1) or the alternative concerted mechanism (Scheme 2).

It has been elegantly argued by Jencks [34] and Williams [35] that the magnitude of β_{nuc} obtained for nucleophilic substitutions may be a measure of the positive charge development on the attacking atom in the critical transition state. Although this proposal is not free from objections,[34] if we assume its validity, then the magnitude of β_{nuc_1} of 0.52 indicates the development of 0.52 charge on nitrogen atom of the nucleophile in the transition state. The simplest stepwise mechanism that could explain the value of β_{nuc_1} of 0.52 may be that shown in Scheme 1.

A value for β_{nuc_1} of 0.52 may be attributed to either k_1^1 step as being rate-determining with a late transition state on the reaction co-ordinate, or to the k_3^1 step being rate-determining with little proton transfer taking place in the transition state (*i.e.* an early transition state). In Scheme 1, rate constants k_2^1, k_{-2}^1, k_4^1, and k_{-4}^1 correspond to the conformational changes of the reactive intermediates. Similarly, $\beta_{nuc_2} = 0.27$ may be ascribed to either k_1^1 step as being rate-determining in which little bond formation between nucleophilic and electrophilic centres has occurred in the transition state, or to the k_3^1 step as being rate-determining, with a late transition state on the reaction co-ordinate. The proposal that the reactions of PS^- with primary and secondary amines reveal the different locations of the transition states in the critical rate-determining step on the reaction co-ordinate may be valid, since the occurrence of these

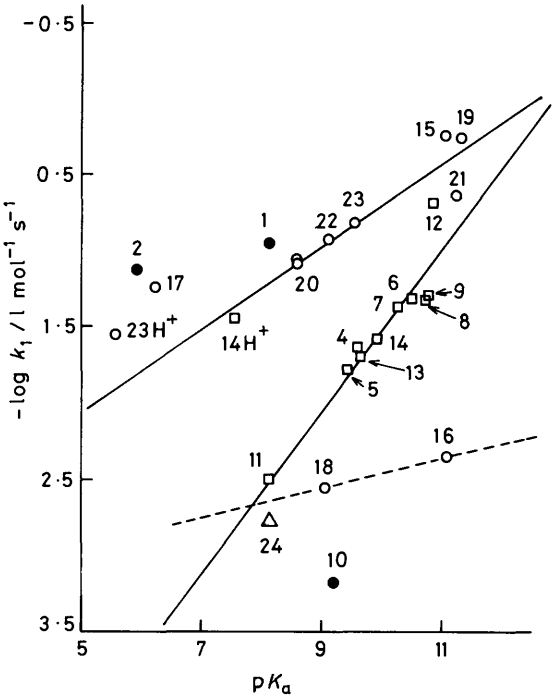


Figure 2. The dependence of the nucleophilic second-order rate constants, k_1, for the reactions of ionized phenyl salicylate (PS^-) with primary amines (□) and secondary amines (○) on the pK_a of the conjugate acid of the amine at 30 °C. The solid lines are drawn through the least-squares-calculated points from Brønsted equation [equation (11)] with $\beta_{nuc_1} = 0.52$, $C_1 = -6.67$ l mol^{-1} s^{-1} for (□), and $\beta_{nuc_2} = 0.27$, $C_2 = -3.37$ l mol^{-1} s^{-1} for (○). In the Brønsted plots: 1, hydrazine (●); 2, hydroxylamine (●); 3, 3-aminopropan-1-ol; 4, 2-hydroxyethylamine; 5, 2-methoxyethylamine; 6, butane-1,4-diamine; 7, propane-1,3-diamine; 8, ethylamine; 9, propylamine; 10, ammonia (●); 11, Tris; 12, methylamine; 13, glycine; 14, ethane-1,2-diamine; $14H^+$, monoprotonated ethane-1,2-diamine; 15, dimethylamine; 16, diethylamine; 17, *N*-methylhydroxylamine; 18, bis-(2-hydroxyethyl)-amine; 19, pyrrolidine; 20, morpholine; 21, piperidine; 22, *N*-methylpiperazine; 23, piperazine; $23H^+$, monoprotonated piperazine; and 24, tris-(2-hydroxyethyl)amine (△). Statistical corrections to pK_2 and to k_1 for the reactivity of 6, 7, 14, and 23 were made in the Brønsted plots

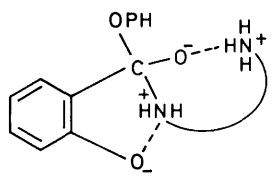
reactions appears to depend upon the conformational requirements of the reacting species. The Brønsted slope (β_{nuc}) of 0.81 obtained in the nucleophilic reactions of primary amines with ionized methyl salicylate[13] (MS^-) may be compared with β_{nuc_1}, however we could not detect any nucleophilic reactivity of various secondary amines toward MS^-.[13] The explanation of these observations apparently lies in the conformational requirements or stereoelectronic controlled mode of these reactions.

In the alternative concerted mechanism (Scheme 2), the high and low values of β_{nuc_1} and β_{nuc_2} could be attributed to the occurrence of the late and early transition states, respectively, in the critical rate-determining k_1^2 step.

The values of $k_1^{H_2O}/k_1^{D_2O}$ for the reactions of PS^- with 2-methoxyethylamine, morpholine, propylamine, pyrrolidine, and Tris are 1.03, 0.95, 0.84, 0.86, and 1.60, respectively. An almost insignificant solvent isotope effect obtained for all the amines studied, except Tris, reveals that nucleophilic attack (k_1^1 step in Scheme 1 or k_1^2 in Scheme 2) is most likely to be the rate-determining step. However, the absence of a solvent isotope effect on the aminolysis of PS^- as support for nucleophilic attack being the rate-determining step is not completely free from ambiguity. Solvent isotope effect would be expected only if the k_3^1 step (Scheme 1) is the rate-determining step, and if intramolecular proton transfer in the k_3^1 step is slower than intermolecular proton transfer between $T^{\pm}$ and OD^- (from solvent), *i.e.* intramolecular general base catalysis is less effective compared with intermolecular general base or specific base catalysis. In fact, we did not observe the intermolecular general base-catalysed term, $k'_3[Am]^2[PS^-]$ or the specific base-catalysed term $k'_4[Am][OH^-][PS^-]$, in the rate law for aminolysis of PS^-. Also, intramolecular reactions are generally much faster than their intermolecular counterparts.[36] Thus, it seems unlikely that intermolecular proton exchange between $T^{\pm}$ and the solvent molecule (D_2O) would be faster than intramolecular proton exchange, and consequently a solvent isotope effect may not be expected in these reactions. However, it is not clear at the moment why there is a significant solvent isotope effect in the reaction of Tris with PS^-.

The k_5^1 and k_6^1 steps (Scheme 1) and k_1^2 and k_3^2 steps (Scheme 2) which involve conformational changes followed by the intramolecular general acid-catalysed expulsion of the leaving group were included merely to cover the possibility of the occurrence of the intramolecular general base catalysis in the reverse reaction. The occurrence of the k_6^1 step or k_3^2 step reveals that an enhanced rate of nucleophilic cleavage of the un-ionized salicylate ester compared with that of the corresponding 2-methoxybenzoate ester could be expected provided that the leaving-group expulsion is the rate-determining step. The involvement of such intramolecular general acid catalysis cannot be detected kinetically if nucleophilic attack is the rate-determining step. Bender *et al.*[3] observed a *ca.* 10-fold increase in the nucleophilic second-order rate constants for the reactions of azide ion with un-ionized *p*-nitrophenyl 5-nitrosalicylate and *p*-nitrophenyl salicylate compared with those of *p*-nitrophenyl 2-methoxy-5-nitrobenzoate and *p*-nitrophenyl 2-methoxybenzoate, respectively. In contrast, only a *ca.* 1.8-fold rate enhancement could be observed in the reaction of imidazole with *p*-nitrophenyl salicylate compared with that with *p*-nitrophenyl 2-methoxybenzoate. Similar observations have been observed by Capon *et al.*[4] in the reactions of imidazole with phenyl salicylate and phenyl 2-methoxybenzoate.

The rate constants, k_1, for the reaction of PS^- with monoprotonated ethane-1,2-diamine appeared to be *ca.* 20-fold larger than that expected from the Brønsted plot of slope of 0.52 (Figure 2). This high reactivity can be attributed to the probable occurrence of intramolecular general acid catalysis as shown by mechanism III. Such catalysis would not be expected in the



III

reaction of PS^- with monoprotonated piperazine because of the structural rigidity of the piperazine. The observed rate constant, k_1, for this reaction is only *ca.* 3 times larger than that expected from the Brønsted plot of slope 0.27 (β_{nuc_2}).

Appendix

Calculation of the Fractions of O-*Attack and* N-*Attack in the Reactions of PS$^-$ with Hydroxylamine and* N-*Methylhydroxylamine.*—The observed absorbance, A_∞, (Table 2) obtained at 350 nm and at $t = \infty$, is presumed to be the sum of the absorptions contributed by the products formed by the attacks of OH (*i.e. O*-attack) and NH_2 (*i.e. N*-attack) groups at the

Table 4. The calculated values of the fractions of *O*-attack (ψ) in the reactions of PS^- with hydroxylamine and *N*-methylhydroxylamine[a]

		NH_2OH			MeNHOH			
$[Am]_T$[b]/mol l^{-1}	ε_1/l mol^{-1} cm^{-1}	ε_2/l mol^{-1} cm^{-1}	A_∞	ψ	ε_2/l mol^{-1} cm^{-1}	A_∞	ψ	ψ[c]
0.08	3 700	1 400	0.328	0.28	169	0.190	0.29	0.32
0.16	3 700	1 400	0.314	0.24	250	0.209	0.31	0.35
0.24	3 700	1 400	0.316	0.25	331	0.215	0.30	0.36
0.32	3 700	1 400	0.266	0.12	412	0.214	0.28	0.36
0.40	3 700				488	0.214	0.26	0.36
0.48	3 700				562	0.216	0.25	0.36

[a] $[X]_0 = 1.6 \times 10^{-4}$ mol l^{-1}. [b] Total amine concentration. [c] Values of ψ when $\varepsilon_2 = 0.0$.

carbonyl carbon of PS^-. If ψ represents the fraction of *O*-attack, then

$$\psi\varepsilon_1 + (1 - \psi)\varepsilon_2 = A_\infty/[X]_0 \quad \text{(i)}$$

where ε_1 and ε_2 represent the molar absorption coefficients of ionized *O*-salicylylhydroxylamine or *O*-salicylyl-*N*-methylhydroxylamine (the products formed from *O*-attack) and *N*-salicylylhydroxylamine or *N*-salicylyl-*N*-methylhydroxylamine (the products formed due to *N*-attack), respectively and $[X]_0$ is the initial concentration of phenyl salicylate. The rearrangement of equation (i) gives equation (ii).

$$\psi = \frac{(A_\infty/[X]_0) - \varepsilon_2}{\varepsilon_1 - \varepsilon_2} \quad \text{(ii)}$$

We were unable to obtain authentic samples of *O*-salicylylhydroxylamine and *O*-salicylyl-*N*-methylhydroxylamine to calculate ε_1, therefore the values of ε_1 were obtained by assuming that the molar absorption coefficients (at 350 nm) of ionized *O*-salicylylhydroxylamine and *O*-salicylyl-*N*-methylhydroxylamine approximate that of ionized methyl salicylate (MS^-). This assumption may not be unreasonable (at least for qualitative purposes) since the molar absorption coefficients of the ionized salicylate esters of methanol, ethanol, and ethane-1,2-diol at 340 nm are nearly same within the limits of experimental error. The observed molar absorption on coefficient of MS^- and 350 nm is $(3.70 \pm 0.09) \times 10^3$ l mol^{-1} cm^{-1}. It is evident from the observed values of A_∞ (Table 2) obtained at 350 nm for the reactions of PS^- with primary amines that these A_∞ values are nearly the same within the limits of identical total amine concentration range for almost all the primary amines. The values of A_∞ obtained in the reactions of PS^- with hydrazine appear to be independent of the total hydrazine concentration within the range of 0.05—0.30 mol l^{-1}. These values of A_∞ were used to calculate the molar absorption coefficient of 1.40×10^3 l mol^{-1} cm^{-1} (at 350 nm) for ionized *N*-salicylylhydrazine. The molar absorption coefficients at 350 nm for ionized *N*-salicylylhydroxylamine and *N*-salicylylhydrazine were assumed to be same, hence the value of ε_2 is 1.40×10^3 l mol^{-1} cm^{-1}. The observed values of A_∞ at different total hydroxylamine concentrations (Table 2) were used to calculate the values of ψ from equation (ii) with $\varepsilon_1 = 3.70 \times 10^3$ l mol^{-1} cm^{-1}, $\varepsilon_2 = 1.40 \times 10^3$ l mol^{-1} cm^{-1} and $[X]_0 = 1.6 \times 10^{-4}$ mol l^{-1} and the results obtained are summarized in Table 4.

The values of A_∞ at 350 nm (Table 2) obtained for the reactions of secondary amines with PS^- are almost negligible. However, the values of ε_2 derived from the *N*-salicylylpyrrolidine and the values of A_∞ (Table 2) were used to calculate ψ from equation (ii) for the reactions of PS^- with *N*-methylhydroxylamine. The results obtained are shown in Table 4.

Although these calculated values of ψ for both hydroxylamine and *N*-methylhydroxylamine are not very reliable because of the uncertainty in the magnitudes of both ε_1 and ε_2, these values of ψ could be used to calculate the pseudo-first-order rate constants for transesterification, k_{est}, of 6.31×10^{-3} and 5.47×10^{-3} s^{-1} at 0.24M-hydroxylamine and *N*-methylhydroxylamine, respectively, ($k_{est} = \psi k_{obs}$ where k_{obs} is the observed pseudo-first-order rate constant for the cleavage of PS^- at 0.24M-hydroxylamine or *N*-methylhydroxylamine). These estimated values of k_{est} are comparable to k_{est} of 5.20×10^{-4} s^{-1} obtained at 0.24M-MeOH for the methanolysis of PS^- under essentially similar experimental conditions.

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