TABLE VII
S-ARYL DIMETHYLTHIOCARBAMATES

Compd	Mp, °C	Proton nmr τ values (no. of protons): Aromatic multiplet	$N(CH_3)_2$ Singlet	$Ar-CH_3$ singlet	$Ar-C(CH_3)_3$ singlet	Thiol ester carbonyl ir band, cm^{-1} [a]
B2	31–33[b]	2.50–2.96 (4 H)	6.97 (6 H)	7.65 (3 H)		1669
B4	c	2.50–2.67 (5 H)	6.98 (6 H)			1668
B5	81–83[d]	2.40–2.77 (4 H)	6.97 (6 H)			1660
B6	136–137.5[d]	2.32–2.83 (9 H)	6.98 (6 H)			1665
B7	c	2.73 (4 H)	6.94 (6 H)	7.67 (3 H)		1668
B8	35–37[b]	2.86 (3 H)	7.00 (6 H)	7.59 (6 H)		1664
B9	75–77[b]	2.45–3.00 (4 H)	7.07 (6 H)		8.53 (9 H)	1662
B10	70–73[d]	2.68–2.98 (3 H)	6.95 (6 H)	7.67 (3 H)	8.56 (9 H)	1662
B12	83–85[d]	2.68 (9 H)	7.19 (6 H)			1663
B13	127–129[d]	2.56–2.91 (13 H)	7.42 (6 H)			1660

[a] Reported as occurring near 1675 cm^{-1} by L. J. Bellamy, "The Infra-red Spectra of Complex Molecules," 2nd ed, John Wiley and Sons, Inc., New York, N. Y., 1958, p 188. [b] Recrystallized from 30–60° petroleum ether. [c] Liquid. [d] Recrystallized from ethanol.

TABLE VIII
REARRANGEMENT OF (2-*t*-BUTYL-4-METHL)PHENYL DIMETHYLTHIOCARBAMATE (A10) AT 258.2°

Time at 258.2°, min	% of A10 remaining	$k \times 10^5$ [a] sec^{-1}
0	100	
30	89.4	6.2
90	74.0	5.6
150	58.6	6.0
210	48.5	5.7
270	39.6	5.7
450	19.3	6.1
1350	*ca.* 0	Av $k = 5.9 \pm 0.2$

[a] Calculated from the equation $k = 2.303/t \times \log a/(a - x)$ where t = seconds, a = initial concentration, and $(a - x)$ = concentration at time t.

amounts of A and B isomers occurred over a period of days at room temperature. Duplicate runs in each case agreed within 4% (the precision of the nmr integrator). The rearrangements were followed kinetically to at least 75% completion and no drifts in the rate constants were noted. The results are listed in Table I.

In every case, after many half-lives, no O-aryl compound could be detected by nmr.

The results of a typical kinetic run are illustrated in Table VIII.

Registry No.—A2, 16241-02-4; B2, 7322-85-2; A4, 16241-04-6; B4, 7304-68-9; A5, 16241-06-8; B5, 7305-13-7; A6, 16241-08-0; B6, 16241-09-1; A7, 10345-39-8; B7, 7305-14-8; A8, 16241-12-6; B8, 16241-13-7; A9, 16241-14-8; B9, 16241-15-9; A10, 16214-91-8; B10, 16214-92-9; A12, 10345-41-2; B12, 16241-17-1; A13, 16241-18-2; B13, 16241-19-3.

Hydrolysis Kinetics for *p*-Dimethylaminophenyl Isocyanate in Aqueous Solutions

PAUL M. MADER

Research Laboratories, Eastman Kodak Company, Rochester, New York 14650

Received December 5, 1967

p-Dimethylaminophenyl isocyanate hydrolyzes, giving *p*-dimethylaminoaniline. The rate-limiting reaction at pH <9 is hydration of the isocyanate to give the carbamic acid (or carbamate ion). Rate data for the hydration indicate three reaction paths which are first order in unprotonated isocyanate: (1) pH independent; (2) first order in $[H^+]$; (3) first order in $[OH^-]$. Approach of the rate to pH independence as the pH is lowered is attributed to protonation of the isocyanate. The rate decreases with increasing acetate buffer concentration. In phosphate buffers, fast reaction of the phosphate with the isocyanate competes with hydration. An interpretation of the yields of *p*-dimethylaminoaniline in phosphate buffers indicates that there is no important catalysis of isocyanate hydrolysis by phosphate. The yield experiments also gave the rate constant for the reaction of the isocyanate with *p*-dimethylaminoaniline to form 1,3-bis(*p*-dimethylaminophenyl)urea. Arsenate reacts with the isocyanate even more rapidly than does phosphate. The product goes to *p*-dimethylaminoaniline very rapidly. Above pH 9, decarboxylation of the carbamate ion is the rate-limiting reaction in the hydrolysis of the isocyanate. It is proposed that decarboxylation proceeds *via* protonation of the nitrogen of the carbamate group.

Hydrolysis kinetics for organic isocyanates in aqueous solution appear not to have been reported. The present communication describes the hydrolysis kinetics for *p*-dimethylaminophenyl isocyanate in aqueous solutions containing 1% acetonitrile. This isocyanate gave a product (*p*-dimethylaminoaniline) that could be monitored conveniently at a rotating platinum anode, and reaction rates were not prohibitively high. Since the rotating electrode is a very sensitive analytical probe, low isocyanate concentrations could be used. It was thus possible to avoid almost completely the reaction of the isocyanate with *p*-dimethylaminoaniline to give 1,3-bis(*p*-dimethylaminophenyl)urea.[1] Eliminating this reaction simplified the kinetics.

Results and Discussion

Below pH 11, reactions were monitored with the rotating platinum electrode. At higher pH values, reactions were slow and were best followed spectrophotometrically. Observed pseudo-first-order rate constants, k_{obsd}, were calculated from slopes of log $(X_\infty$

---

[1] H. Staudinger and R. Endle, *Ber.*, **50**, 1042 (1917); C. Naegeli, A. Tyabji, L. Conrad, and F. Litwan, *Helv. Chim. Acta*, **21**, 1100 (1938).

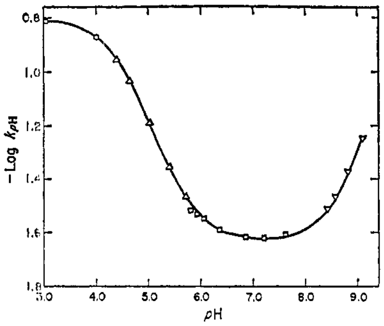


Figure 1.—pH dependence for the hydration of *p*-dimethylaminophenyl isocyanate at 25° and ionic strength 0.1 *M*: ○, hydrochloric acid solutions; △, acetate buffers; □, phosphate buffers; ▽, borate buffers.

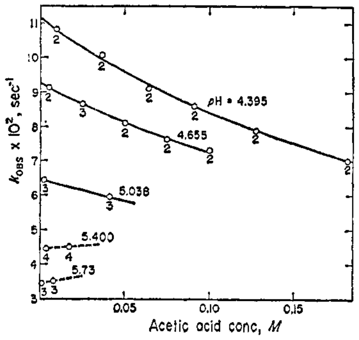


Figure 2.—Pseudo-first-order rate constants for the formation of *p*-dimethylaminoaniline from *p*-dimethylaminophenyl isocyanate in acetate buffers at 25° and ionic strength 0.1 *M*. Each point gives the average value of k_{obsd} for the number of kinetic runs indicated beneath the point. The solid lines were calculated with eq 2. The maximum acetate concentration at each pH was 0.1 *M*.

minus X_t) *vs.* time plots, where X is the experimental variable monitored.

Near pH 9 there was a change in the rate-limiting step, resulting in nonlinear induction periods in the first-order plots. In these cases, k_{obsd} values were obtained from the slopes of the linear portions of the plots following the induction periods. Below pH 9, the rate-limiting reaction is hydration of the isocyanate to give carbamic acid or carbamate ion (RNHCOOH or $RNHCOO^-$). Above pH 9, decarboxylation of the carbamate ion is rate limiting. The accumulation of carbamate as an intermediate in the conversion of phenyl isocyanate into aniline has been described by Mohr.[2]

pH Dependence of Isocyanate Hydration.—Reactions were run at 25° in dilute hydrochloric acid solutions and in acetate, phosphate, arsenate, and borate buffers. Ionic strength was adjusted to a calculated value of 0.1 *M*. The values of k_{obsd} depended on the concentrations of the buffers. Extrapolation of k_{obsd} to zero buffer concentration gave values designated k_{pH} (for the hydrochloric acid solutions, k_{obsd} is identical in meaning with k_{pH}). The log k_{pH}–pH profile is shown in Figure 1. A theoretical model that can duplicate this profile consists of three parallel reactions, each first-order in unprotonated isocyanate. The first is pH independent, the second is first-order in hydrogen ion, and the third is first-order in hydroxide ion. The approach toward pH independence as pH is lowered is associated with substantial protonation of the isocyanate. This model leads to eq 1 where k_1, k_2, and k_3 are the rate con-

$$k_{pH} = (k_1 + k_2 10^{-pH} + k_3 K_w 10^{pH})(1 + K_1^{-1} 10^{-pH})^{-1} \quad (1)$$

stants for the three parallel reactions, K_1 is the acid dissociation constant for the protonated isocyanate, and K_w is the ion product for water. Values for the parameters of eq 1, determined by nonlinear regression, are given in Table I. The value found for K_1 does not seem unreasonable for the acid dissociation constant of the protonated isocyanate. Calculated and experimental k_{pH} values agree well. The standard error of fit of log k_{pH} (calcd) to log k_{pH} (exptl) is 0.0089 log unit. The maximum deviation is 0.019 log unit.

TABLE I

PARAMETER VALUES FOR 25° AND IONIC STRENGTH 0.1 *M* (OR 0.5 *M* AS INDICATED)

Eq	Parameter	pH[a]	Value[b]	Units
1	k_1		$(2.31 \pm 0.02) \times 10^{-2}$	sec^{-1}
1	k_2		$(7.35 \pm 0.08) \times 10^{3}$	$M^{-1}\,sec^{-1}$
1	k_3k_w		$(2.78 \pm 0.08) \times 10^{-11}$	$M\,sec^{-1}$
1	K_1		$(2.17 \pm 0.09) \times 10^{-5}$	M
2	a	4.395	29.3 ± 1.5	$M^{-1}\,sec$
2	a	4.655	29.6 ± 1.8	$M^{-1}\,sec$
2	a	5.038	32.0 ± 5.9	$M^{-1}\,sec$
3, 4	K_2		$\sim 3 \times 10^{-6}$	M
3, 5	K_3		~ 0.7	M^{-1}
6	k_4		0.692 ± 0.031	$M^{-1}\,sec^{-1}$
6	k_5		$(1.231 \pm 0.039) \times 10^{6}$	$M^{-2}\,sec^{-1}$
7	b	5.823	63.5 ± 1.0	M^{-1}
7	b	6.860	32.3 ± 0.6	M^{-1}
7	b	7.202	28.8 ± 0.4	M^{-1}
7	b	7.616	27.8 ± 0.4	M^{-1}
7	c	5.823	$(1.12 \pm 0.06) \times 10^{3}$	M^{-1}
7	c	6.860	$(4.87 \pm 0.07) \times 10^{3}$	M^{-1}
7	c	7.202	$(6.34 \pm 0.09) \times 10^{3}$	M^{-1}
7	c	7.616	$(6.57 \pm 0.13) \times 10^{3}$	M^{-1}
8	k_4		0.657 ± 0.016	$M^{-1}\,sec^{-1}$
8	k_5		$(0.920 \pm 0.050) \times 10^{6}$	$M^{-2}\,sec^{-1}$
9	k_6	5.823	35.9	$M^{-1}\,sec^{-1}$
9	k_6	6.860	118	$M^{-1}\,sec^{-1}$
9	k_6	7.202	152	$M^{-1}\,sec^{-1}$
9	k_6	7.616	161	$M^{-1}\,sec^{-1}$
10	k_7		172	$M^{-1}\,sec^{-}$
10	K_4		3.7×10^{-7}	M
14, 15	$k_w[H_2O]$		$(5.134 \pm 0.096) \times 10^{-5}$	sec^{-1}
			$(5.198 \pm 0.125) \times 10^{-5}$[c]	sec^{-1}
14, 15	k_{H^+}		$(1.501 \pm 0.014) \times 10^{8}$	$M^{-1}\,sec^{-1}$
			$(1.097 \pm 0.016) \times 10^{8}$[c]	$M^{-1}\,sec^{-1}$
14, 15	$k_{H_2CO_3}/K_6$		$(4.49 \pm 0.29) \times 10^{8}$	$M^{-2}\,sec^{-1}$
14, 15	$k_{HCO_3^-}$		0.1326 ± 0.0078	$M^{-1}\,sec^{-1}$
14	K_5/k_{10}		0.875×10^{-9}[d]	$M\,sec$
			$(1.137 \pm 0.040) \times 10^{-9}$[c]	$M\,sec$

[a] No entry means that the parameter is theoretically independent of pH. [b] Limits are estimates of the standard errors. [c] Ionic strength, 0.5 *M*. [d] Fixed at this value.

Hydration of the Isocyanate in Acetate Buffers.—Observed pseudo-first-order rate constants are plotted *vs.* acetic acid concentration in Figure 2. In the lower part of the pH range, there is significant inhibition of the reaction by the buffers. At the upper end of the pH range, there may be a barely perceptible catalysis. The inhibition can be accounted for quantitatively by assuming that (a) an acetic acid–isocyanate adduct forms in a reversible reaction; (b) equilibrium with respect to this reaction is maintained during the course of the isocyanate hydration; (c) the adduct is basic, *i.e.*, it can be protonated; (d) the only reaction of the adduct is its dissociation to give back the isocyanate; and (e) there is no catalysis by acetate buffers of *p*-dimethylaminoaniline formation. The theoretical rela-

---

(2) E. Mohr, *J. Prakt. Chem.*, **73**, 177 (1906).

tionship between the observed rate constants and the acetic acid concentration is given in eq 2. The parameter a is given by eq 3 where K_3, the formation con-

$$k_{\text{obsd}}^{-1} = k_{\text{pH}}^{-1} + a[\text{HOAc}]. \qquad (2)$$

$$a = K_3(1 + 10^{-\text{pH}}K_2^{-1})(k_1 + k_2 10^{-\text{pH}} + k_3 K_w 10^{\text{pH}})^{-1} \cong K_3(1 + 10^{-\text{pH}}K_2^{-1})(k_1 + k_2 10^{-\text{pH}})^{-1} \qquad (3)$$

stant for the acetic acid–isocyanate adduct is given by K_3 = [unprotonated adduct][HOAc]$^{-1}$ [unprotonated isocyanate]$^{-1}$, K_2 is the acid dissociation constant for the protonated adduct, and the other constants have the same significance and values as in eq 1. For the acetate buffers, the term headed by k_3 in the expression for a is very small and can be omitted.

Equation 2 predicts that at constant pH the reciprocal of the observed rate constant is linearly related to the acetic acid concentration, a prediction in accord with the experimental results. Values for the parameter a, determined by regression, are given in Table I. The value of a is approximately independent of pH. This result is not a necessary consequence of the theoretical model. Rather, it indicates the fortuitous relationship in eq 4. Substitution of approximation 4 in eq 3 and solving for K_3 give the relationship in eq 5.

$$K_2 \cong k_1/k_2 \qquad (4)$$

$$K_3 \cong k_1 a \qquad (5)$$

Values for K_2 and K_3 calculated with approximations 4 and 5 and with the known values of k_1, k_2, and a are given in Table I.

Consider now the structure of the proposed acetic acid–isocyanate adduct. Naegeli and Tyabji believed that the more stable of the adducts formed from isocyanates and carboxylic acids in inert solvents are mixed anhydrides, RNHCOOCOR′.[3] However, they did not accept this structure for the adducts that formed reversibly. Two structures that can be considered for the adduct proposed here to explain the kinetic data are a hydrogen-bonded complex and a mixed anhydride. Comparison of the values of K_2 and K_1 indicates that the adduct is a stronger base than the isocyanate. This is not the result expected for a hydrogen-bonded complex of the isocyanate with acetic acid. Therefore, the mixed anhydride structure is preferred. If the interpretation of the kinetics in the acetate buffers is correct, we have an example of a mixed carbamic carboxylic anhydride that forms rapidly and reversibly. Thus, Naegeli and Tyabji may not have been entirely justified in rejecting the mixed anhydride structure for certain carboxylic acid–isocyanate adducts just on the basis of the looseness of the adducts.

Hydration of the Isocyanate in Phosphate Buffers.—As shown by measurements of p-dimethylaminoaniline yields, hydration was not the only reaction of the isocyanate in phosphate buffers. A competing reaction of the isocyanate with the phosphate gave a product that went only very slowly to p-dimethylaminoaniline. This product is presumably a mixed phosphoric carbamic anhydride resulting from nucleophilic attack of phosphate at the carbon of the isocyanate group. Cramer and Winter have isolated such products from acetonitrile solution.[4]

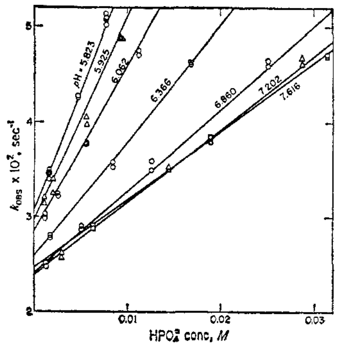


Figure 3.—Pseudo-first-order rate constants for the formation of p-dimethylaminoaniline from p-dimethylaminophenyl isocyanate in phosphate buffers at 25° and ionic strength 0.1 M. The lines were calculated with eq 6.

The observed pseudo-first-order constants, k_{obsd}, for the hydration of the isocyanate are given in Figure 3. These k_{obsd} values obey eq 6, where k_{pH} is given by eq 1.

$$k_{\text{obsd}} = k_{\text{pH}} + (k_4 + k_5 10^{-\text{pH}})[\text{HPO}_4^{2-}] \qquad (6)$$

The values of k_4 and k_5 are given in Table I. Interpretation of p-dimethylaminoaniline yields shows that the term containing HPO_4^{2-} in eq 6 can be accounted for on the basis of the isocyanate–phosphate reaction just mentioned. There is no important contribution to this term by catalytic reaction paths leading to p-dimethylaminoaniline. The form of this term shows that there is more than one path involved in the isocyanate–phosphate reaction.

Yields of p-dimethylaminoaniline, based on initial isocyanate, are given in Tables II and III. These yields were measured after the reaction of the isocyanate had gone essentially to completion but before noticeable hydrolysis of the phosphoric carbamic anhydride had occurred. The competitive reaction of the phosphate with the isocyanate shows itself in the decreasing yields with increasing buffer concentration. The analytical method used in these experiments dictated higher initial isocyanate concentrations than sufficed in the kinetic experiments. Consequently, there was appreciable reaction of p-dimethylaminoaniline with the isocyanate to give 1,3-bis(p-dimethylaminophenyl)-urea. For this reason, the yields of p-dimethylaminoaniline do not extrapolate to 100% at zero buffer concentration.

The yields have been interpreted on the basis of the model shown in Scheme I where A and P represent the isocyanate and p-dimethylaminoaniline, respectively (protonated and unprotonated). This model leads to eq 7 where the values for b and c are calculated in eq 8 and 9 and Y is the per cent yield of p-dimethylaminoaniline.

Scheme I

$$\text{A} \xrightarrow{k_{\text{pH}}} \text{P}$$

$$\text{A} + \text{HPO}_4^{2-} \xrightarrow{k_4 + k_5 10^{-\text{pH}}} \text{mixed anhydride}$$

$$\text{A} + \text{P} \xrightarrow{k_6} \text{symmetrical urea}$$

$$1 + 0.01Y + \frac{2 + b[\text{HPO}_4^{2-}]}{c[\text{A}]_0} \ln\left(1 - \frac{0.01Yc[\text{A}]_0}{1 - c[\text{P}]_0}\right) = 0 \qquad (7)$$

$$b = (k_4 + k_5 10^{-\text{pH}})/k_{\text{pH}} \qquad (8)$$

$$c = k_6/k_{\text{pH}} \qquad (9)$$

---

[3] C. Naegeli and A. Tyabji, *Helv. Chim. Acta*, **18**, 142 (1935).

[4] F. Cramer and M. Winter, *Chem. Ber.*, **92**, 2761 (1959).

TABLE II
YIELDS OF *p*-DIMETHYLAMINOANILINE FROM *p*-DIMETHYLAMINOPHENYL ISOCYANATE IN PHOSPHATE BUFFERS AT 25° AND IONIC STRENGTH 0.1 *M*.
INITIAL CONCENTRATION OF *p*-DIMETHYLAMINOANILINE = 0

pH	$10_5[\mathrm{A}]_0$,[a] *M*	$10^2[\mathrm{HPO_4^{2-}}]$, *M*	Yield, % Found	Yield, % Calcd
5.823	4.23	0.1523	87.3	87.60
		0.266	81.4	82.46
		0.380	77.8	77.90
		0.494	73.8	73.80
		0.646	68.7	68.95
	7.44	0.1523	84.6	85.11
		0.1523	85.5	85.11
		0.228	82.0	81.87
		0.266	81.0	80.32
		0.304	78.8	78.84
		0.380	76.0	76.02
		0.494	72.1	72.14
		0.646	67.5	67.54
		0.761	64.8	64.42
6.860	3.09	0.248	80.9	81.95
		0.619	74.3	74.95
		0.992	68.8	68.98
		1.487	61.8	62.33
		1.98	57.1	56.85
		2.48	52.7	52.18
	5.86	2.48	49.3	49.52
	6.42	0.248	72.7	73.36
		0.618	67.2	67.90
		0.992	62.8	63.10
		1.487	57.8	57.65
		1.98	53.2	53.03
		2.48	49.3	49.02
	12.6	0.248	61.3	61.86
		0.619	57.3	58.10
		0.992	54.3	54.71
		1.487	50.3	50.72
		1.98	47.3	47.24
		2.48	44.7	44.13
7.202	2.90	0.283	80.3	79.92
		0.934	69.6	69.98
		2.83	51.6	51.10
	5.86	0.1415	72.6	72.58
		0.283	70.9	70.70
		0.934	62.8	63.07
		1.70	55.5	55.85
		2.83	47.6	47.65
7.616	4.23	0.623	70.0	70.48
		1.09	64.6	64.94
		1.555	59.4	60.16
		2.02	55.8	56.03
		2.65	51.1	51.21
		3.11	48.2	48.17
	7.44	0.623	62.8	62.70
		0.623	62.9	62.70
		1.09	58.6	58.41
		1.555	54.7	54.65
		2.33	49.4	49.27
		3.11	45.8	44.77

[a] Initial isocyanate concentration.

TABLE III
YIELDS OF *p*-DIMETHYLAMINOANILINE FROM *p*-DIMETHYLAMINOPHENYL ISOCYANATE (6.42×10^{-5} *M*) IN THE PRESENCE OF ADDED *p*-DIMETHYLAMINOANILINE. PHOSPHATE BUFFER AT pH 6.860, 25°, AND IONIC STRENGTH 0.10 *M*

$10^5[\mathrm{P}]_0$,[a] *M*	$10^2[\mathrm{HPO_4^{2-}}]$, *M*	Yield, % Found	Yield, % Calcd
2.02	0.248	65.3	62.47
	0.992	56.0	54.05
3.78	0.248	53.5	53.87
	0.992	45.7	46.81
6.30	0.248	43.2	42.81
	0.992	37.4	37.48

[a] Initial *p*-dimethylaminoaniline concentration.

aminoaniline, $[\mathrm{A}]_0$ is the initial isocyanate concentration, and $[\mathrm{P}]_0$ is the concentration of *p*-dimethylaminoaniline added at the beginning of the reaction. A computer was used to find values for the parameters b and c for each of the four experimental pH levels. The program involved solving eq 7 for Y by a reiterative procedure and adjusting b and c to minimize the sum of the squares of the differences between experimental and calculated Y values. The values of b and c are given in Table I. The Y values calculated with these parameters and eq 7 are shown in Tables II and III, where they may be compared with the experimental yields.

The intercept and slope of the regression line for a plot of $k_{\mathrm{pH}}b$ *vs.* $10^{-\mathrm{pH}}$, where k_{pH} was calculated with eq 1, gave values for k_4 and k_5 (see eq 8). These values are shown in Table I. The rather good agreement between these constants derived partly from yield measurements and those obtained entirely from kinetic measurements supports the validity of the theoretical model for the yield experiments. The success of this model, which does not incorporate phosphate catalysis, is the basis for the earlier statement that phosphate catalysis is unimportant.

Values for k_6, the second-order rate constant for the reaction of the isocyanate with protonated plus unprotonated *p*-dimethylaminoaniline, were obtained with eq 9, the k_{pH} values being calculated with eq 1. This rate constant decreases with decreasing pH (see Table I). If it is assumed that this decrease is associated with protonation of the *p*-dimethylaminoaniline and that the rate for the protonated amine is zero, and, if any effect of the small degree of protonation of the isocyanate in the phosphate buffers is ignored, then k_6 is given theoretically by eq 10 where k_7 is the rate

$$k_6 = k_7K_4/(K_4 + 10^{-\mathrm{pH}}), \qquad (10)$$

constant for the reaction of unprotonated *p*-dimethylaminoaniline with the isocyanate, and K_4 is the acid dissociation constant for the protonated *p*-dimethylaminoaniline. Values for k_7 and K_4, determined from the k_6 values and eq 10 by regression, are given in Table I. The agreement between the value of K_4 and the value determined independently by spectrophotometry ($K_4 = 3.2 \times 10^{-7}$ *M* at 25° and μ 0.1 *M*) indicates that the assumptions leading to eq 10 are valid.

As mentioned, hydrolysis of the phosphoric carbamic anhydride was very slow in the phosphate buffers. The rate was independent of buffer concentration and of pH in the range 6.88–7.63. The reaction is first order and has a half-time of 0.97 day at 25°.

The theoretical model used above in the analysis of the yield experiments leads to the expression given in eq 11 for the per cent yield, based on isocyanate, of

$$Y_{\mathrm{anh}} = b(100 + Y)[\mathrm{HPO_4^{2-}}]/(2 + b[\mathrm{HPO_4^{2-}}]), \qquad (11)$$

the phosphoric carbamic anhydride where Y and b have the same significance as in eq 7. Values of Y_{anh} calculated with eq 11 and with Y and b values taken

TABLE IV

THEORETICAL YIELDS, Y_{anh}, OF PHOSPHORIC CARBAMIC ANHYDRIDE IN pH 6.86 PHOSPHATE BUFFERS. YIELDS, Y_{slow}, OF p-DIMETHYLAMINOANILINE FORMED IN THE SLOW HYDROLYSIS OF THE PHOSPHORIC CARBAMIC ANHYDRIDE

$10^2[HPO_4^{2-}]$, M	$10^5[A]_0$, M[a]	Y_{anh}, %[b]	Y_{slow}, %[a]
0.248	6.42	6.7	6.8
0.618	6.42	15.3	15.7
1.487	6.42	30.5	29.5
2.48	5.86	42.8	41.0

[a] Initial isocyanate concentration. [b] Yields based on the initial isocyanate concentration.

from Table I are given in Table IV along with experimental yields, also based on isocyanate, of *p*-dimethylaminoaniline formed in the slow hydrolysis of the phosphoric carbamic anhydride. Comparison of the two sets of yield values indicates that conversion of the anhydride into the amine was close to quantitative.

Hydration of the Isocyanate in Arsenate Buffers.—Because of an experimental difficulty apparently associated with the arsenate buffers (high background current at the rotating platinum electrode), only one kinetic run was made (0.00125 M $H_2AsO_4^-$; 0.0025 M $HAsO_4^{2-}$; 25°; μ 0.1 M; pH 7.06). The formation of *p*-dimethylaminoaniline was close to pseudo first order (k_{obsd} = 0.0357 sec^{-1}). This rate constant is substantially larger than k_{pH} (0.0239 sec^{-1} at pH 7.06). This difference is probably not due to general acid–base catalysis by arsenate, since such catalysis was not important in solutions of $H_2PO_4^-$–HPO_4^{2-}, a couple having very nearly the same pK_a as $H_2AsO_4^-$–$HAsO_4^{2-}$. Therefore, augmentation of k_{obsd} by arsenate must result from a reaction of arsenate with the isocyanate, perhaps leading to an arsenate carbamate anhydride.

It was of interest to see if the arsenate–isocyanate product is as long lived as the phosphoric carbamic anhydride. Measurements of *p*-dimethylaminoaniline yields indicated that the arsenate–isocyanate product is very short lived. As in the yield experiments with phosphate buffers, the initial isocyanate concentration (6.38 × 10^{-5} M) was high enough to give noticeable diminution of yield owing to the reaction of the *p*-dimethylaminoaniline with the isocyanate. Yields were measured shortly after the initial fast reaction of the isocyanate and then at times up to a day later. There was no slow increase in yield, as when phosphate buffers were used, and the yield increased with increasing arsenate buffer concentration (Table V). These observations show that the arsenate–isocyanate product had gone to *p*-dimethylaminoaniline prior to the earliest yield measurement. In the single kinetic experiment, there was no indication of any further formation of the amine following the initial fast first-order reaction. Apparently the arsenate–isocyanate product went to and amine about as fast as it formed. In effect, then, arsenate catalyzes the conversion of the isocyanate into *p*-dimethylaminoaniline.

TABLE V

YIELDS OF p-DIMETHYLAMINOANILINE FROM p-DIMETHYLAMINOPHENYL ISOCYANATE IN ARSENATE BUFFERS AT pH 7.062, 25°, AND IONIC STRENGTH 0.1 M

$10^2[AsO_4^{2-}]$, M	Yield, %
0.125	77.7
0.25	79.9
0.50	83.3
0.825	86.7
1.50	91.0
2.50	94.0

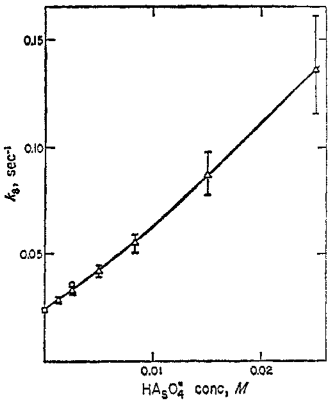


Figure 4.—Pseudo-first-order rate constants for the formation of *p*-dimethylaminoaniline from *p*-dimethylaminophenyl isocyanate in arsenate buffers at pH 7.06, 25°, and ionic strength 0.1 M: ○, observed kinetically; △, calculated from *p*-dimethylaminoaniline yields with eq 12 and 10 (the limits show the effect on the calculated rate constants of ±1% errors in the yields); □, calculated with eq 1.

The yields have been interpreted on the basis of the model which is shown in Scheme II where A and P represent the isocyanate and *p*-dimethylaminoaniline, respectively, k_8 is the pH- and arsenate-dependent pseudo-first-order rate constant for conversion of A into P, and k_6 is given by eq 10. Equation 12

SCHEME II

$$A \xrightarrow{k_8} P$$

$$A + P \xrightarrow{k_6} \text{symmetrical urea}$$

$$(1 + 0.01Y)[A]_0 = -2(k_8/k_6) \ln \{1 - 0.01Y[A]_0(k_8/k_6)^{-1}\} \quad (12)$$

was derived for this model where Y is the per cent yield of *p*-dimethylaminoaniline based on isocyanate, and $[A]_0$ is the initial concentration of isocyanate.

Equation 12 was solved by reiteration to obtain values of k_8/k_6 corresponding to the Y values of Table V. These k_8/k_6 values were multiplied by k_6 (eq 10 gives k_6 = 139 for pH 7.06) to obtained k_8. A plot of k_8 *vs.* $HAsO_4^{2-}$ concentration is shown in Figure 4. The plot is not linear, possibly owing to errors in Y. As shown in the figure, small errors in Y can give large errors in k_8. As expected, the plot extrapolates to a value close to k_{pH} from eq 1. It also passes close to the observed rate constant for the single kinetic experiment. If one assumes that the nonlinearity of the plot is an artifact, k_8 can be expressed in a form analogous to eq 6 for reactions in phosphate buffers. See eq 13 where k_9 is the rate constant, of unknown pH

$$k_8 = k_{pH} + k_9[HAsO_4^{2-}] \quad (13)$$

dependence, for the reaction of $HAsO_4^{2-}$ with the isocyanate at pH 7.06. The value of k_9 from the slope of the k_8 *vs.* $[HAsO_4^{2-}]$ plot is approximately 5.0 M^{-1} sec^{-1}. An idea of the relative nucleophilicities of arsenate and phosphate toward the isocyanate can be

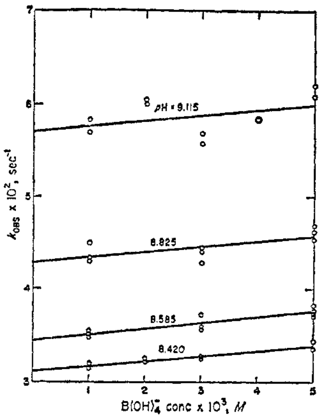


Figure 5.—Pseudo-first-order rate constants for the formation of *p*-dimethylaminoaniline from *p*-dimethylaminophenyl isocyanate in borate buffers at 25° and ionic strength 0.1 *M*.

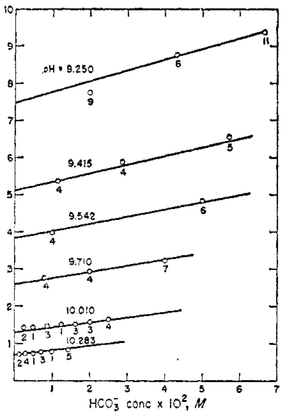


Figure 6.—Pseudo-first-order rate constants for the decarboxylation of *p*-dimethylaminophenylcarbamate ion in carbonate buffers at 25° and ionic strength 0.1 *M*. Each point gives the average value of k_{obsd} for the number of kinetic runs indicated beneath the point. The lines were calculated with eq 14.

gained by comparing k_9 with the coefficient of $[HPO_4^{2-}]$ in eq 6. At pH 7.06, the value of this coefficient is 0.80 M^{-1} sec^{-1}. Thus, arsenate is more nucleophilic than phosphate. A similar difference was observed for the attack of arsenate and phosphate on *p*-nitrophenyl acetate.[5]

Hydration of the Isocyanate in Borate Buffers.—Very dilute buffers were used to avoid significant polymerization of the borate ion. Owing to this precaution, the maximum observed effect of buffer dilution on pH was only 0.025 units (for the pH 9.115 buffer). To obtain k_{obsd}, the experimental rate constants were corrected for the small changes in pH accompanying dilution. The largest correction amounted to 2.5%. The others were less than 1%. The positive slopes of the k_{obsd} *vs.* $[B(OH)_4^-]$ plots (Figure 5) may indicate a reaction of the borate ion with the isocyanate having a rate constant of about 0.6 M^{-1} sec^{-1}.

Decarboxylation of the Carbamate Ion.—Observed pseudo-first-order rate constants for the decarboxylation in carbonate-buffered solutions and in sodium hydroxide solutions are given in Figures 6 and 7. Over much of the pH range, the reaction of the carbamate ion is close to first order in hydrogen ion. The data for the carbonate-buffered solutions indicate acid catalysis of the reaction by H_2CO_3 and HCO_3^-.

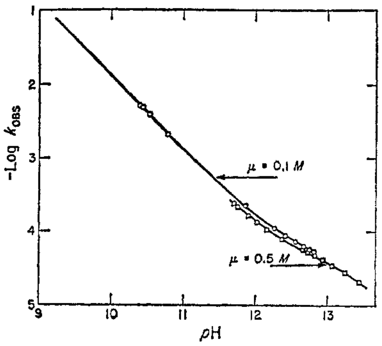


Figure 7.—pH dependence for the decarboxylation of *p*-dimethylaminophenylcarbamate ion at 25°. The points are for runs in sodium hydroxide solutions. The lines were calculated with eq 14.

To extend the pH to higher values than available at ionic strength 0.1 *M*, experiments were also run at ionic strength 0.5 *M* in unbuffered sodium hydroxide solutions. The log k_{obsd}-pH profile has an inflection at pH ~ 12.5 (Figure 7). The rate constants measured by Christenson for the decarboxylation of phenyl carbamate ion in sodium hydroxide solutions (μ not held constant) also give such an inflection.[6] Spectrophotometry revealed no change in the molar extinction of the substrate throughout the experimental pH range. Therefore, the inflection is not associated with an acid-base reaction of the substrate.

The experimental results can be explained on the basis of the acid catalysis mechanism discussed by Bell[7]

$$S^- + \Sigma_i A_i \underset{k_r}{\overset{k_f}{\rightleftharpoons}} SH + \Sigma_i B_i$$

$$SH \xrightarrow{k_{10}} p\text{-dimethylaminoaniline}$$

where S^- is the carbamate ion, SH is protonated carbamate ion, and $\Sigma_i A_i$ and $\Sigma_i B_i$ represent all the acids and their conjugate bases, respectively. The pseudo-first-order constants k_f and k_r are given by $k_f = \Sigma_i k_i[A_i]$ and $k_r = \Sigma_i k_i'[B_i]$, where k_i is the rate constant for proton transfer from acid A_i to S^-, and k_i' is the rate constant for proton transfer from SH to base B_i.

If $k_f \ll k_r$, the steady-state approximation for SH can be used, giving eq 14 where K_5 is the acid dissociation constant for SH. For the kinetic experiments eq 15 applies, where $K_6 = 10^{-pH}[HCO_3^-]/[H_2CO_3]$. Of course, the last term of eq 15 is zero for experiments in the unbuffered sodium hydroxide solutions. Regression with a computer was used to fit eq 14 to the 13 k_{obsd} values for ionic strength 0.5 *M*. The resulting constant parameter values are given in Table I. Calculated and experimental k_{obsd} values agree closely. The standard error of fit of log k_{obsd} (calcd) to log k_{obsd} (exptl) is only 0.0069 log unit. The largest deviation is 0.0109 log unit. Multiple regression (both pH and $[HCO_3^-]$ varied) was used to fit eq 14 to k_{obsd} for ionic strength 0.1 *M*. All the 108 k_{obsd} values for

$$1/k_{obsd} = 1/\Sigma_i k_i[A_i] + K_5/(k_{10}10^{-pH}) \qquad (14)$$

$$\begin{aligned}\Sigma_i k_i[A_i] = {} & k_w[H_2O] + k_{H^+}10^{-pH} + k_{H_2CO_3}[H_2CO_3] + \\ & k_{HCO_3^-}[HCO_3^-] = k_w[H_2O] + k_{H^+}10^{-pH} + \\ & [(k_{H_2CO_3}/K_6)10^{-pH} + k_{HCO_3^-}][HCO_3^-] \qquad (15)\end{aligned}$$

---

(5) W. P. Jencks and J. Carriulo, *J. Amer. Chem. Soc.*, **82**, 1778 (1960).

(6) I. Christenson, *Acta Chem. Scand.*, **18**, 904 (1964).

(7) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, pp 136, 137.

carbonate-buffered solutions and unbuffered sodium hydroxide solutions were included in this one regression. In this regression, the value of K_5/k_{10} was fixed, since the data did not extend to high enough pH to allow evaluation of this parameter from the data. The value of K_5/k_{10} was set equal to 0.77 times the value of this parameter for ionic strength 0.5 *M*. The factor 0.77 is an estimate of the salt effect for K_5/k_{10} in going from ionic strength 0.5 to 0.1 *M*. Parameter values resulting from the regression are given in Table I. The standard error of fit of log k_{obsd} (calcd) to log k_{obsd} (exptl) for ionic strength 0.1 *M* is 0.0115 log unit. The maximum deviation for any k_{obsd} is 0.0299 log unit. The deviation exceeds 2σ for only 4 out of the 108 k_{obsd} values.

As expected for a reaction involving an uncharged reactant (H_2O), the value of k_w is insensitive to change in ionic strength. The value of k_{H^+}, on the other hand, decreases with increasing ionic strength, consistent with the reaction of oppositely charged species (carbamate anion and hydronium cation). The change in k_{H^+} is close to that predicted by the empirical expression[8] given below.

$$\Delta \log k_{H^+} = -\Delta[\sqrt{\mu}/(1 + \sqrt{\mu}) - 0.20\,\mu]$$

Bell[7] has pointed out an interesting prediction based on the mechanism for acid catalysis described above. The mechanism predicts that k_{obsd} will not approach k_w [H_2O], the water-catalyzed rate, as the hydrogen-ion concentration approaches zero. Rather, the rate will go to zero, as is apparent from eq 14. That this prediction is borne out for carbamate decarboxylation is shown more clearly in the k_{obsd} *vs.* $10^{-\text{pH}}$ plot of Figure 8 than in the logarithmic plot of Figure 7. Lacking data for the lower hydrogen-ion concentrations, as in the case of the experiments at ionic strength 0.1 *M*, one might erroneously assume k_{obsd} to be given by the linear eq 16 which is the equation for general acid

$$k_{\text{obsd}} = \pi_w[H_2O] + \pi_{H^+}10^{-\text{pH}}, \qquad (16)$$

catalysis when water and hydrogen ion are the only acids present. The intercepts and slopes of straight lines through those k_{obsd} values showing near-linear dependence on $10^{-\text{pH}}$ give $\pi_w[H_2O]$ and π_{H^+} values that differ from the values of $k_w[H_2O]$ and k_{H^+} resulting from the fitting of eq 14 to the k_{obsd} values. The proper choice of mechanism is important if correct values for the catalytic constants are desired.

In the mechanism leading to eq 14, the position of protonation in SH is not specified and is a matter of conjecture. In the derivation of eq 14, the conversion of SH into *p*-dimethylaminoaniline was assumed to be a pH-independent, irreversible reaction. Of the sites available for protonation in the carbamate ion, the carbamate nitrogen is the one whose protonation would seem most likely to lead to such a reaction. Owing to the very low concentration of CO_2 in the experiments, the position of the equilibrium in Scheme III, part b, is assumed to lie far to the right. In effect, then, the reaction is considered to be irreversible.

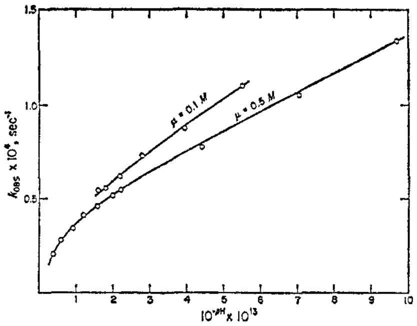
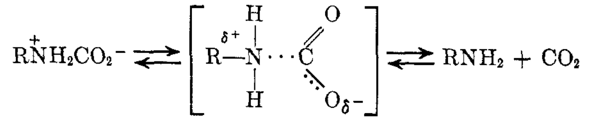


Figure 8.—Dependence of decarboxylation rate on $10^{-\text{pH}}$ at 25°.

Scheme III

$$RNHCO_2^- + \Sigma_i A_i \rightleftharpoons R\overset{+}{N}H_2CO_2^- + \Sigma_i B_i \qquad (a)$$



$$R\overset{+}{N}H_2CO_2^- \rightleftharpoons \left[R\overset{\delta+}{-}N(H)_2\cdots C(=O)\cdots O^{\delta-} \right] \rightleftharpoons RNH_2 + CO_2 \qquad (b)$$

Experimental Section

p-Dimethylaminophenyl isocyanate was prepared by the method of Staudinger and Endle.[1] The material distilled at 100° (~3 mm) and solidified in the receiver, mp 35–36.5° uncor. Reagent grade or Acculate[9] standard volumetric solutions were used for the buffers. The acetate and borate buffers were prepared from the respective acids and sodium hydroxide. The phosphate and carbonate buffers were prepared from the appropriate sodium salts, and the arsenate buffer was made with Na_2HAsO_4 and hydrochloric acid. Sodium sulfate was employed to maintain the ionic strength at 0.1 *M* for the diluted buffers and for the sodium hydroxide solutions. Sodium nitrate was used to maintain the ionic strength for the hydrochloric acid solutions. Sodium hydroxide solutions were brought to ionic strength 0.5 *M* with sodium chloride.

In the kinetic experiments, the temperature was held at 25.0 ± 0.2°. The apparatus used to follow the formation of *p*-dimethylaminoaniline electrochemically was designed by W. R. Ruby, of these laboratories. A water-jacketed beaker was fitted with a Teflon cover, nitrogen inlet tube and exit port, and the conventional configuration of rotating platinum-disk working electrode and platinum-disk auxiliary electrode. The external saturated calomel reference electrode was connected through an agar-saturated sodium nitrate bridge. A modified version of the Adams potentiostat was used to supply constant voltage to the cell and to amplify the current.[10] The amplified current was recorded *vs.* time with a Moseley Autograf Model 2D-2 X-Y recorder. The potential applied to the working electrode was between 200 and 430 mV *vs.* the S. C. E. higher potential was needed at the lower pH values to give adequate current.

Over the course of a number of kinetic runs, there was a gradual downward drift in the current associated with a given concentration of *p*-dimethylaminoaniline. This effect was due to a change in the electrode surface that could be reversed by polishing the electrode. The change in the electrode during a kinetic experiment was of no apparent consequence, provided the total time that voltage was applied to the cell did not exceed about 15 min. For the slow reactions in the vicinity of pH 10.5, the voltage was interrupted after about two half-lives and re-established after about ten half-lives. The electrochemical method was not used for pH values higher than 10.78.

The buffer (75 ml) was placed in the cell and purged with nitrogen. The working voltage was applied to the cell until the current was constant, and then 0.75 ml of a stock solution of the isocyanate (~6×10^{-4} *M*) in Eastman Spectro Grade acetonitrile was added rapidly with a syringe. The stirring of the solution by the rotating electrode gave complete mixing in 2 sec or less. Nitrogen was passed over the surface of the solution during the reaction. Although no special precautions were taken to remove or exclude water from the acetonitrile stock solutions of the isocyanate, these solutions were surprisingly stable. There was no indication of change in a week.

---

[8] C. W. Davies, "Progress in Reaction Kinetics," Vol. 1, Pergamon Press Inc., New York, N. Y., 1961, p 161.

[9] Obtained from Anachemia Chemicals, Ltd.

[10] J. R. Alden, J. Q. Chambers, and R. N. Adams, *J. Electroanal. Chem.*, **5**, 152 (1963).

Preliminary experiments with the acetate buffers gave results indicating that an impurity was oxidizing or catalyzing the oxidation of the *p*-dimethylaminoaniline. This reaction was prevented by adding 0.1–0.2 ml of 0.03 M Na_2EDTA to the reaction mixtures. The oxidation was apparently not a serious problem; eliminating it caused only a small decrease in the measured rate constants.

The increase in rate with decreasing acetate buffer concentration was not associated with the use of sodium sulfate to maintain the ionic strength. Sodium nitrate gave the same result.

The reaction product in the kinetic experiments was not isolated. That *p*-dimethylaminoaniline was formed was confirmed by determination of the polarographic wave at the end of the reaction at pH 10.28.

Kinetic runs at pH values higher than 10.78 were monitored spectrophotometrically. The reaction vessel was a Teflon beaker with a tight-fitting Teflon cover having nitrogen inlet and exit tubes and a port for removing samples. The sodium hydroxide solution (100 ml) was purged with nitrogen that had been passed through 0.1 M sodium hydroxide solution and 0.1 M sodium chloride solution. Reaction was started by adding 1 ml of a stock solution ($\sim 6 \times 10^{-3}$ M) of the isocyanate in Eastman Spectro Grade acetonitrile. Nitrogen was passed through the solution during the course of the reaction. Samples were removed and absorbances were measured at 260 and 274 mμ with the Beckman DU spectrophotometer. The absorbances decreased with time, making a first-order approach to values very close to those of *p*-dimethylaminoaniline. Rate constants were calculated for both the 260- and 274-mμ data and averaged. Agreement between the constants for the two wavelengths was generally excellent.

Reactions were monitored spectrophotometrically for as long as 4 days. Simply passing nitrogen through the solutions did not suffice to protect the very labile *p*-dimethylaminoaniline from noticeable autoxidation during such a long time. Consequently, 0.04 g of sodium sulfite was included in each reaction mixture. This agent very effectively inhibited the autoxidation. The *p*-dimethylaminoaniline in turn would have been expected to inhibit the autoxidation of the sulfite, an important point, since this oxidation is accompanied by a change in absorbance at 260 and 274 mμ. As an extra precaution against oxidation of the sulfite, 0.03 g of Na_4EDTA was included in the solutions.

Measurements of the pH values of the reaction mixtures were made at the end of each kinetic experiment. A Corning Model 12 pH Meter was used. For pH values below 11, a Beckman glass electrode (Cat. No. 1190-80) was employed, and the Corning Triple-Purpose electrode was used for higher pH values. A Beckman reference calomel electrode was used. The electrodes were calibrated with 0.01 M sodium tetraborate, and their linearity was checked with Corning pH 7.00 buffer. Dilute sodium hydroxide solutions were protected from atmospheric CO_2 during the pH measurements with nitrogen. Sodium ion corrections were made.

The following relationships exist between the sodium hydroxide concentrations and the corrected experimental pH values greater than 11: pH = 13.829 + 0.979 log[NaOH] for ionic strength 0.1 M; pH = 13.746 + 0.994 log[NaOH] for ionic strength 0.5 M. The standard error of fit of the experimental to the calculated pH values is 0.004 pH unit. The maximum deviation is 0.008 pH unit. The fact that the coefficients of log NaOH are close to unity indicates that ion activity coefficients remained almost unchanged as sodium hydroxide concentration was varied at constant ionic strength.

For the experiments in which yields of *p*-dimethylaminoaniline were determined, reactions were carried out in rubber-stoppered glass bottles fitted with nitrogen inlet and exit tubes and a port for sampling. Isocyanate stock solution (Eastman Spectro Grade acetonitrile) (1 ml) was delivered from a calibrated volumetric pipet into 100 ml of nitrogen-purged buffer. Analysis for *p*-dimethylaminoaniline was carried out as follows. A 5-ml sample of the reaction mixture was added to a mixture of 2 ml of a buffer designed to give pH $\sim$7 and v ml of 5×10^{-4} M aqueous 1-naphthol solution. Then there was added v ml of 2×10^{-3} M aqueous potassium ferricyanide solution, followed by 1 ml of 15% Triton X-100 solution. Finally, the solution was made up to a total weight of 10.00 g with water. The volume v was chosen to be about 0.2 ml in excess of the volume theoretically required to convert the *p*-dimethylaminoaniline into the blue indoaniline dye. If v was much larger, significant amounts of colored 1-naphthol oxidation products were formed. Owing to the Triton X-100, the dye followed Beer's law in the solutions.[11] The amount of *p*-dimethylaminoaniline in the sample was calculated from the absorbance at 600 mμ. The calculations were based on the results of calibration experiments. Analyses were generally carried out in duplicate and sometimes in triplicate. The values given in Tables II–V are the averages.

In the yield experiments having the highest initial isocyanate concentration (1.26×10^{-4} M), traces of crystalline solid formed in the reaction mixtures. The amount of this material, estimated visually, decreased with increasing phosphate concentration, and therefore it correlated with the expected yields of 1,3-bis(*p*-dimethylaminophenyl)urea. The material melted partially in the 250–260° range. Staudinger and Endle give 258–259° dec for the melting point of the urea.[1]

Registry No.—*p*-Dimethylaminophenyl isocyanate, 16315-59-6; *p*-dimethylaminoaniline, 99-98-9.

Acknowledgment.—The author wishes to thank Mr. E. A. Sylvestre, of the Eastman Kodak Co., for carrying out the computations.

---

(11) L. K. J. Tong and M. Carol Glesmann, *J. Amer. Chem. Soc.*, **79**, 4305 (1957).