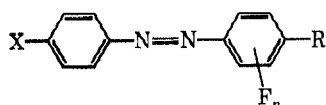TABLE IV

RELATIVE AMOUNTS[a] OF PROTONATED TAUTOMERS
OF FLUORINATED 4-AB DERIVATIVES



$n = 2,4$

| Positions of $F_n$ | X | R | Ammonium form, % | Azonium form, % |
|---|---|---|---|---|
| 3,5 | H | NH$_2$ | 48 | 53 |
| 3,5 | H | NHCH$_3$ | 65 | 30 |
| 3,5 | H | N(CH$_3$)$_2$ | 100 | 5 |
| 3,5 | Et | NH$_2$ | 46 | 52 |
| 3,5 | Et | NHCH$_3$ | 65 | 34 |
| 3,5 | Et | N(CH$_3$)$_2$ | 100 | 2 |
| 2,6 | H | NH$_2$ | 14 | 81 |
| 2,6 | H | NHCH$_3$ | 9 | 94 |
| 2,6 | H | N(CH$_3$)$_2$ | 8 | 96 |
| 2,6 | Et | NH$_2$ | 14 | 78 |
| 2,6 | Et | NHCH$_3$ | 9 | 89 |
| 2,6 | Et | N(CH$_3$)$_2$ | 9 | 97 |
| 2,3,5,6 | H | NH$_2$ | 86 | 25 |
| 2,3,5,6 | H | NHCH$_3$ | 35 | 63 |
| 2,3,5,6 | H | N(CH$_3$)$_2$ | 82 | 5 |
| 2,3,5,6 | Et | NH$_2$ | 75 | 28 |
| 2,3,5,6 | Et | NHCH$_3$ | 35 | 67 |
| 2,3,5,6 | Et | N(CH$_3$)$_2$ | 78 | 5 |

[a] Based as described in text on method of Ryan.[14]

times with H$_2$O, taken up in Et$_2$O, and dried over Na$_2$SO$_4$ and then molecular sieves (type 4A). The crude product from four batches of 30.2 g of 4-ethylnitrobenzene[20] was distilled at 4.5 mm under a blanket of N$_2$. The product (which decomposes when steam distilled) was collected at 64–65°: yield 33 g (30%); mp 17–18°; $n^{25}$D 1.5550; ir (neat) 1508 cm$^{-1}$.

*Anal.* Calcd for C$_8$H$_9$NO: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.23; H, 6.67; N, 10.09.

**3,5-Difluoro-4'-ethylazobenzene. A. Deamination of 3,5-**

Difluoro-4'-ethyl-AB.—The named AB was deaminated as described[1b] for 3,5-difluoro-AB in 45% yield, mp 81–82°.

*Anal.* Calcd for C$_{14}$H$_{12}$F$_2$N$_2$: C, 68.28; H, 4.91; N, 11.37. Found: C, 68.39; H, 4.95; N, 11.37.

**B.**—The foregoing compound was also synthesized by method A in the next paragraph in 64% yield (melting point, mixture melting point with product in previous paragraph, and ir spectra all identical).

**Methods, as Indicated in Table I. A.**—Arylene diamines were condensed with nitrosobenzene, or 4-ethylnitrosobenzene, in the general way described previously.[1b] For most of these condensations we used temperatures of 32–38°. For optimum yields of the tetrafluorinated[21] dyes the reaction was continued for 10 days at temperatures of 40–43°.

**Method B.**—4-Formamidoazo dyes were methylated with CH$_3$I in alcoholic KOH followed by hydrolysis in added aqueous NaOH.[1b]

**Method C.**—Dimethylation of aminoazo dyes was carried out in (CH$_3$O)$_2$PO, CH$_3$I, and Na$_2$CO$_3$.[1b,22]

**Method D.**—A mixture of 12 g of 4-acetamido-2,6-difluoro-aniline[1b] and 5.7 g of nitrosobenzene[20] or 7.3 g of p-ethylnitroso-benzene in 30 ml of absolute ethanol and 15 ml of glacial acetic acid was flushed with N$_2$ and allowed to stand at 37° ± 2° for 14 days. The reaction mixture was stirred into water and the supernatant was decanted from gummy material. The latter was dried, dissolved in benzene, and put through an alumina column. After the eluent was evaporated, the product in the major red band was rechromatographed, giving the yields and melting points recorded in Table I.

**Method E. 2,3,5,6-Tetrafluoro-MAB.**—A mixture 2 g of 4-acetamido-2,3,5,6-tetrafluoroazobenzene, 20 ml of EtOH, 0.7 g of KOH, and 3 g of CH$_3$I was boiled under reflux for 4 hr; 10 ml of 20% aqueous NaOH was added; and refluxing was continued for 1 hr. The reaction mixture was poured into water and the red precipitate was filtered off and dried. The product was passed through an alumina column (C$_6$H$_6$). Upon evaporation of the solvent and addition of 1 drop of MeOH, red crystals formed, mp 141–153°. Recrystallization from alcohol raised the melting point (Table I).

**Registry No.**—p-Ethyl nitrosobenzene, 22955-65-3; 3,5-difluoro-4'-ethylazobenezne, 22955-66-4.

(20) Aldrich Chemical Co., Milwaukee, Wis.

(21) Tetrafluoro-p-phenylenediamine was purchased from Whittaker Corp., San Diego, Calif.

(22) H.-L. Pan and T. L. Fletcher, *J. Org. Chem.*, **27**, 3639 (1962).

---

# Electrolyte Effects upon the Reactions of Nitrohalobenzenes with Amines[1]

C. A. BUNTON AND L. ROBINSON

*Department of Chemistry, University of California, Santa Barbara, California 93106*

Specific salt effects have been observed for reactions between 2,4-dinitrofluorobenzene and aniline or the anions of glycine, glycylglycine, and glycylglycylglycine in water, and for the reactions of 2,4-dinitrochlorobenzene and aniline or the glycylglycinate ion. The overall salt effects can be separated into those on the activity coefficient of the substrate, and on the relative activity coefficients of the nucleophile and the transition state. The transition-state effects are smaller for reactions of the amines than of hydroxide ion. Anions of high charge density, *e.g.*, SO$_4^{2-}$, assist reaction by destabilizing the substrate even though they destabilize the transition state relative to the nucleophile, whereas low charge density anions and cations, *e.g.*, ClO$_4^-$ or (CH$_3$)$_4$N$^+$, stabilize both the substrate and the transition state.

The reactions between nucleophiles and 2,4-dinitro-fluoro- and -chlorobenzene involve initial addition to give an intermediate which then loses the halide ion. For general discussions of these reactions, see ref 2. In polar hydroxylic solvents loss of the halide ion is generally rapid, so that the rate-limiting step is nucleophilic addition, but in favorable cases loss of fluoride ion

may be slow,[2] and in one system slow loss of chloride has been observed.[3]

Aromatic substitutions by nucleophilic anions are subject to large specific salt effects,[4–6] whereas the Debye–Hückel relationship predicts that they should be absent, and the Hughes–Ingold extension of this

(1) Support of this work by the National Science Foundation is gratefully acknowledged.

(2) J. F. Bunnett, *Quart. Rev.* (London), **12**, 1 (1958); S. D. Ross, *Progr. Phys. Org. Chem.*, **1**, 31 (1963); J. F. Bunnett and R. H. Garst, *J. Amer. Chem. Soc.*, **87**, 3875, 3879 (1965); J. Miller, *Aust. J. Chem.*, **22**, 921 (1969).

(3) R. L. Toranzo, R. V. Caneda, and J. Brieux, *J. Amer. Chem. Soc.*, **88**, 3651 (1966).

(4) J. D. Reinheimer, J. T. Gerig, and J. C. Cochran, *ibid.*, **83**, 2873 (1961), and references cited therein.

(5) C. A. Bunton and L. Robinson, *ibid.*, **90**, 3965 (1968).

(6) C. A. Bunton and L. Robinson, *J. Org. Chem.*, **34**, 780 (1969).

treatment predicts that the effects should be small and negative.[7] However, many of the results have been obtained for organic solvents, some of them of low polarity, so that ion pairing and interactions between the ions and the nitro groups of the aromatic substrate could have been important.[4]

We found similar salt effects for reactions of hydroxide and thiophenoxide ions with 2,4-dinitrochlorobenzene,[5] and hydroxide ion with 2,4-dinitrofluorobenzene,[6] in aqueous solvents, and for reaction in water the effects could be separated into those upon the activity coefficient of the substrate and the ratio of the activity coefficients of the hydroxide ion and the transition state. A similar treatment was applied to the salt effects upon the reaction between aniline and 2,4-dinitrochlorobenzene,[5] where the salt effects are different from those upon the hydroxide ion reactions. In the present work we compare the salt effects upon the reactions of hydroxide ion and aniline with 2,4-dinitrofluoro- and -chlorobenzenes (Ia and b) with those upon the corresponding reactions of the anions of glycine, glycylglycine, and glycylglycylglycine so that we can find out whether the salt effects are affected by an overall negative charge upon the nucleophile even though this charge is not at the reaction center, and whether kinetic salt effects are dependent upon the
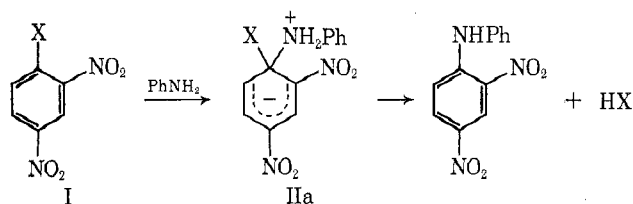


overall structure of the reagents, or merely upon the nature of the reaction center. In addition we hoped to be able to extend our observations on the extent to which these salt effects depended upon changes in the activity coefficients of the substrates.[5,6]



X = F, Cl
n = 0, 1, 2
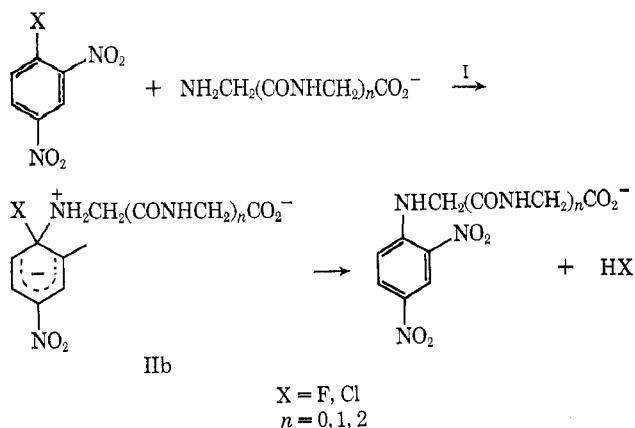
Salt effects upon the reaction of aniline and 2,4-dinitrochlorobenzene are different from those found for the corresponding reactions of hydroxide ion with 2,4-dinitrofluoro- and -chlorobenzene, but part of this effect could have been caused by the differences in temperature between that of 85.0° used for the reaction of aniline with 2,4-dinitrochlorobenzene and that of 25.0° used for the other reactions.[5,6] 2,4-Dinitro-

fluorobenzene is much more reactive toward amines than is the chlorobenzene, and its reactions with aniline and anions of the amino acids can be studied at 25.0°.[2,8] Therefore, we could compare the salt effects under identical conditions for the reactions of the amino acid anions and halobenzenes with those of hydroxide ion and aniline.

Insofar as kinetic salt effects are often used as mechanistic tests, and attempts are made to eliminate the effects of added electrolytes by working at constant ionic strength, it seemed important to decide to what extent salt effects depend on mechanism and to what extent on charge type and the chemical nature of the reactants.[7] In addition, 2,4-dinitrofluorobenzene is often used in protein modification, and its reactions with amino acid and peptide anions are simple models for these protein reactions.[8]

## Experimental Section

**Kinetics.**—The reactions were followed spectrophotometrically in water using a Gilford spectrophotometer as already described.[5,6] The reactions between aniline and 2,4-dinitrofluorobenzene were followed at 3650 Å, those of glycine at 3625 Å, and those of glycylglycine and glycylglycylglycine at 3550 Å. The reagent concentrations were $10^{-5}$–$10^{-4}$ $M$ for the halobenzenes and 0.025–0.055 $M$ for the amines. Because of the insolubility of the product, we had to use lower substrate concentrations for the aniline reactions, and the absorbance changes for the overall reaction were small (0.06 OD units), compared with 0.1 OD for the other reactions.

Under the conditions used the reaction between hydroxide ion and the substrates is relatively unimportant,[5,6] except for the reaction between 2,4-dinitrochlorobenzene and the glycylglycinate ion at 85.0°, where the hydroxide ion reaction makes a contribution of ca. 10% to the overall reaction based on the values of $k_2$ for the reaction of hydroxide ion with 2,4-dinitrochlorobenzene,[5] and the rate constants are therefore less reliable for this than for the corresponding reactions of 2,4-dinitrofluorobenzene.

The solutions were maintained at pH 9.0 for the reactions of glycylglycine with 2,4-dinitrochlorobenzene at 85.0° and glycylglycylglycine with 2,4-dinitrofluorobenzene, 9.5 for the other reactions of glycylglycine at 25.0°, and 10.5 for the reactions of glycine, using 0.015 $M$ borate or carbonate buffer. These reactions of halobenzenes and amines follow second-order kinetics in aqueous solvents,[2] and the second-order rate constants, $k_2$, were obtained by dividing the first-order rate constants by the nucleophile concentration. Good first-order rate constants were obtained for over 2 half-lives, except for reaction of aniline with 2,4-dinitrofluorobenzene, where there was scatter in the points for the latter part of the reaction.

## Results

**Kinetics.**—The values of the second-order rate constants are given in Tables I–III. Because of the relative unreactivity of 2,4-dinitrochlorobenzene toward amines, we followed its reactions at a much higher temperature than that used for the other reactions and therefore we did most of our work with 2,4-dinitrofluorobenzene. The relative reactivities of the various nucleophiles toward 2,4-dinitrofluorobenzene at 25.0° follow: aniline, 1; glycylglycylglycinate anion, 0.9; glycylglycinate anion, 1.1; glycinate anion, 5.5; and OH⁻, 4.0. For 2,4-dinitrochlorobenzene at 85.0° the following obtain: aniline, 1; glycylglycinate anion, 1.6; and OH⁻, 11. The spread of reactivities of these nucleophiles is much greater for reactions with aryl

(7) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chapter VII.

(8) D. G. Herries, W. Bishop, and F. M. Richards, *J. Phys. Chem.*, **68**, 1842 (1964).

TABLE I

SECOND-ORDER RATE CONSTANTS FOR REACTIONS OF 2,4-DINITROFLUOROBENZENE WITH AMINO ACID AND PEPTIDE ANIONS[a]

| | Reagent | | | | | |
|---|---|---|---|---|---|---|
| | NH₂CH₂CO₂⁻ [b] | | NH₂CH₂COHNCH₂CO₂⁻ [c] | | NH₂(CH₂CONH)₂CH₂CO₂⁻ [d] | |
| Salt | 1.0[e] | 2.0[e] | 1.0[e] | 2.0[e] | 1.0[e] | 2.0[e] |
| LiCl | 1.02 | 1.06 | 1.05 | 1.07 | 1.07 | 1.31 |
| NaCl | 1.29 | 1.60 | 1.17 | 1.52 | 1.30 | 1.65 |
| KCl | 1.46 | 1.69 | 1.27 | 1.59 | 1.40 | 1.85 |
| (CH₃)₄NCl | 1.24 | 1.64 | 1.27 | 1.61 | 1.43 | 2.08 |
| NaBr | 1.26 | 1.46 | 1.31 | 1.54 | 1.26 | 1.46 |
| NaNO₃ | 1.20 | 1.30 | 1.21 | 1.43 | 1.19 | 1.39 |
| NaClO₄ | 1.00 | 1.01 | 1.00 | 1.00 | 1.07 | 1.24 |
| Na₂SO₄ | 1.37 | 2.00 | 1.11 | 1.92 | 1.20 | 1.84 |

[a] Values of $k_2{}^s/k_2{}^0$ in water at 25.0° with 0.025 $M$ reagent. [b] $k_2{}^0 = 16.6 \times 10^{-2}$ l. mol⁻¹ sec⁻¹. [c] $k_2{}^0 = 3.35 \times 10^{-2}$ l. mol⁻¹ sec⁻¹. [d] $k_2{}^0 = 2.79 \times 10^{-2}$ l. mol⁻¹ sec⁻¹. [e] Ionic strength.

TABLE II

SECOND-ORDER RATE CONSTANTS FOR
REACTION OF 2,4-DINITROCHLOROBENZENE WITH
GLYCYLGLYCINATE ANION[a]

| Salt | 1.0[b] | 2.0[b] |
|---|---|---|
| LiCl | 0.84 | 0.78 |
| NaCl | 1.08 | 1.35 |
| KCl | 1.24 | 1.68 |
| (CH₃)₄NCl | 1.31 | 1.96 |
| NaBr | 1.03 | 1.23 |
| NaNO₃ | 1.02 | 1.15 |
| NaClO₄ | 0.85 | 0.81 |
| Na₂SO₄ | 1.15 | 1.53 |

[a] Values of $k_2{}^s/k_2{}^0$ in water at 85.0° with 0.025 $M$ reagent; $k_{20} = 9.44 \times 10^{-3}$ l. mol⁻¹ sec⁻¹, in the absence of added salts. [b] Ionic strength.

TABLE III

SECOND-ORDER RATE CONSTANTS FOR
REACTION OF 2,4-DINITROFLUOROBENZENE WITH ANILINE[a]

| Salt | 1.0[b] | 2.0[b] |
|---|---|---|
| NaCl | 1.30 (1.38) | 1.67 (1.76) |
| KCl | 1.33 (1.37) | 1.62 (1.73) |
| (CH₃)₄NCl | | 0.98 (1.20) |
| NaBr | | 1.32 (1.44) |
| NaNO₃ | 1.03 (1.14) | 1.28 (1.25) |
| C₇H₇SO₃Na | 1.15 | 1.37 |
| NaClO₄ | 0.96 (0.94) | 0.87 (0.83) |
| Na₂SO₄ | 1.69 (1.72) | |
| LiClO₄ | 0.73 (0.80) | 0.63 (0.70) |

[a] Values of $k_2{}^s/k_2{}^0$ in water at 25.0° with 0.05 $M$ aniline; with no salt $k_2{}^0 = 3.0 \times 10^{-2}$ l. mol⁻¹ sec⁻¹. Values in parentheses are for the reaction of 2,4-dinitrochlorobenzene at 85.0° (ref 5). [b] Ionic strength.

acetates, although this spread decreases with increasing ester reactivity.[9] For the amino acid anions $k_2$ increases with increasing basicity of the amino group,[10] but aniline is more and hydroxide ion less reactive than expected from the basicities.

**Activity Coefficients.**—The salt effects upon the activity coefficients were literature values.[5,6]

## Discussion

The kinetic salt effects upon the reactions of hydroxide ion with 2,4-dinitrofluoro- and -chlorobenzenes are very similar, and are not affected by changing the temperature from 25 to 45°.[5,6] So far as comparisons can be made, salt orders are similar for reactions of aniline and 2,4-dinitrofluoro- and -chlorobenzene,

despite the different temperatures of the experiments, and qualitatively the salt effects upon the reactions of the halobenzenes with the anions of the amino acids and peptides are closer to those found for aniline than for hydroxide ion (Tables I–III and ref 5 and 6).

Kinetic salt effects can in principle be separated into initial and transition-state effects,[11–14] although, because of the problems in measuring and the uncertainties in calculating[15] single ion activities, we calculate the salt effects upon the activity coefficient of the transition state relative to that of the nucleophile.[5,6] The Brønsted–Bjerrum rate equation applied to these reactions of the halobenzenes with the nucleophile, Y, gives

$$\frac{k_2{}^s}{k_2{}^0 f_{ArX}} = \frac{f_Y}{f^*}$$

(where $k_2{}^s$ and $k_2{}^0$ are the second-order rate constants in the presence and absence of added electrolyte, and $f^*$ is the activity coefficient of the transition state).

The values of the relative activity coefficients, $f_Y/f^*$, are given in Tables IV and V. These values are less accurate than those of the rate constants because of the errors in the activity coefficients of the halobenzenes; there is ca. 10% uncertainty for most of the values; and the uncertainties are greatest for reactions of 2,4-dinitrochlorobenzene with glycylglycinate anion because of the contributions of the hydroxide ion reaction and for reactions of 2,4-dinitrofluorobenzene with aniline. The values of $f_Y/f^*$ for reactions of 2,4-dinitrochloro- or -fluorobenzene with a given nucleophile are very similar, despite some differences in temperature.

These results show, as did earlier results,[5,6,11–14] that in general salt effects as mechanistic criteria should where possible be supplemented by the separation of initial and transition-state effects, and we noted that part of the kinetic salt effects upon substitutions by small anionic nucleophiles could be interpreted in terms of the effects of electrolytes upon the relative free energies of low and high charge density nucleophile and transition state, respectively.[5,6]

Salt effects upon $f_X/f^*$ are similar for reactions of glycinate and the peptide ions, but they are different for the corresponding reactions of hydroxide ion, and kinetic salt effects upon the hydroxide ion reactions are

(9) W. P. Jencks and J. Gilchrist, *J. Amer. Chem. Soc.*, **90**, 2622 (1968).

(10) R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," Butterworth, London, 1959, Appendix 12.

(11) D. McIntyre and F. A. Long, *J. Amer. Chem. Soc.*, **76**, 3240 (1954).

(12) G. A. Clarke and R. W. Taft, *ibid.*, **84**, 2295 (1962).

(13) C. A. Bunton, J. H. Crabtree, and L. Robinson, *ibid.*, **90**, 1258 (1968).

(14) C. A. Bunton, N. A. Fuller, S. G. Perry, and I. Pitman, *J. Chem. Soc.*, 4478 (1962).

(15) J. N. Butler, "Ionic Equilibrium," Addison Wesley Publishing Co., Inc., Reading, Mass., 1964, p 435.

TABLE IV

SALT EFFECTS UPON RELATIVE ACTIVITY COEFFICIENTS FOR REACTIONS OF 2,4-DINITROFLUOROBENZENE[a]

| | 1.0[b] | | | | | 2.0[b] | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | OH⁻ | Glycinate anion | Glycyl-glycinate anion | Glycylglycyl-glycinate anion | PhNH₂ | OH⁻ | Glycinate anion | Glycyl-glycinate anion | Glycylglycyl-glycinate anion | PhNH₂ |
| LiCl | 0.45 | 0.76 | 0.78 | 0.79 | | 0.24 | 0.56 | 0.57 | 0.68 | |
| NaCl | 0.68 | 1.03 | 0.94 | 1.04 | 1.04 | 0.47 | 0.93 | 0.88 | 0.96 | 0.97 |
| KCl | 1.03 | 1.36 | 1.19 | 1.29 | 1.23 | 1.13 | 1.53 | 1.44 | 1.68 | 1.47 |
| (CH₃)₄NCl | 1.77 | 1.50 | 1.53 | 1.73 | | 2.75 | 2.18 | 2.12 | 2.78 | 1.28 |
| NaBr | 0.67 | 1.14 | 1.16 | 1.13 | | 0.61 | 1.29 | 1.35 | 1.29 | 1.16 |
| NaNO₃ | 0.87 | 1.38 | 1.39 | 1.37 | 1.19 | 0.87 | 1.69 | 1.86 | 1.80 | 1.66 |
| NaClO₄ | 1.05 | 1.58 | 1.58 | 1.69 | 1.52 | 1.34 | 2.38 | 2.36 | 2.91 | 2.05 |
| Na₂SO₄ | 0.58 | 0.64 | 0.54 | 0.56 | 0.79 | 0.39 | 0.53 | 0.51 | 0.49 | |

[a] Values of $f_Y/f^*$; the values for OH⁻ are from ref 6. [b] Ionic strength.

TABLE V

SALT EFFECTS UPON RELATIVE ACTIVITY COEFFICIENTS FOR REACTIONS OF 2,4-DINITROCHLOROBENZENE[a]

| | 1.0[b] | | | 2.0[b] | | |
|---|---|---|---|---|---|---|
| Salt | OH⁻ [c] | Glycyl-glycinate anion[d] | PhNH₂[e] | OH⁻ [c] | Glycyl-glycinate anion[d] | PhNH₂[e] |
| LiCl | 0.42 | 0.63 | | 0.26 | 0.49 | |
| NaCl | 0.66 | 0.83 | 1.06 | 0.51 | 0.88 | 1.13 |
| KCl | 0.97 | 1.17 | 1.30 | 0.95 | 1.60 | 1.63 |
| (CH₃)₄NCl | 1.87 | 1.51 | 1.25 | 3.00 | 2.53 | 1.56 |
| NaBr | 0.67 | 0.91 | 1.10 | 0.57 | 0.98 | 1.20 |
| NaNO₃ | 0.75 | 1.06 | 1.18 | 0.72 | 1.25 | 1.73 |
| NaClO₄ | 0.86 | 1.19 | 1.33 | 0.84 | 1.37 | 1.40 |
| Na₂SO₄ | 0.53 | 0.56 | 0.62 | 0.41 | 0.47 | |

[a] Values of $f_Y/f^*$. [b] Ionic strength. [c] At 25.0 and 45.0° (ref 5). [d] At 85.0°. [e] At 85.0° (ref 5).

similar to those found for reactions of other nucleophilic anions.[5] On the other hand, the kinetic salt effects, and those upon $f_X/f^*$, are similar for the reactions of all the amines, irrespective of their net charge.

The effects of added salts upon the relative free energies of the nucleophile and the transition state are indicated by the changes in $f_Y/f^*$ (Tables IV and V), and the similarity of these values for the various glycinate ions suggests that they are not sensitive to changes in the structure of the nucleophile away from the reaction center, as expected if the environment of the carboxylate residue of the amino acid anion does not change in going to the transition state. We therefore assume that interactions between the carboxylate ion and the forming ammonium ion are relatively unimportant in the transition state, or in the intermediate (II). This assumption is supported by the similarity of the nucleophilicities of glycinate anion, glycineamide, glycylglycinate anion, and glycylglycylglycinate anion (Tables I–III and ref 8).

In general the values of $f_Y/f^*$ (relative to reaction in the absence of added salts) are smaller for reactions of hydroxide than of the other nucleophiles; however, the opposite is the situation for tetramethylammonium chloride. In our earlier work we noted the ability of the bulky tetramethylammonium ion to stabilize the bulky transition state relative to a high charge density anion such as hydroxide.[5,6] Most of the salts stabilize the transition state relative to the nucleophilic amine, in contrast to their effects in the hydroxide ion reactions, but in agreement with qualitative theories.[7] In one case, that of sodium sulfate, the transition states are destabilized relative to the nucleophiles, although this rate-retarding effect is overcome by the greater destabilization of the substrate. Differences between the

salt effects upon the reactions of hydroxide ion and the amines are to be expected. For reactions of hydroxide ion, a small, high charge density ion, which should strongly order water molecules, generates a low charge density, anionic transition state, whereas with the amines an uncharged nucleophile generates a transition state in which the positively charged ammonium ion center can itself order the water molecules.

These results confirm the earlier conclusions that in moderately concentrated salt solutions the kinetic effects depend upon the nature of the electrolyte rather than upon the ionic strength of the solution and the charge type of the reaction.[5,6] These effects could be exerted directly or indirectly *via* changes in the water structure,[16] although their persistence in aqueous organic solvents in which the water structure has been destroyed[5,17] suggests that direct interactions between the electrolytes and the initial and transition states may be important,[5] and there is thermodynamic evidence for interactions between some large cations and polar, organic nonelectrolytes in water.[18]

The results on these nucleophilic aromatic substitutions support the earlier suggestion that specific salt effects in water are related to mechanism as well as structure of the reagents, and can therefore be related to transition-state structure.[5,6,13,19]

**Registry No.**—I (X = F), 70-34-8; I (X = Cl), 97-00-7; aniline, 62-53-3.

(16) H. S. Frank and M. G. Evans, *J. Chem. Phys.*, 13, 507 (1945); R. K. McMullan and G. A. Jeffrey, *ibid.*, 31, 1231 (1959); G. R. Choppin and and K. Buijs, *ibid.*, 39, 2042 (1963).

(17) A. Fratiello and D. G. Douglass, *J. Mol. Spectrosc.*, 11, 465 (1963); D. N. Glew, H. D. Mark, and N. S. Rath, *Chem. Commun.*, 265 (1968).

(18) E. Grunwald, G. Baughman, and G. Kohnstarn, *J. Amer. Chem. Soc.*, 82, 5801 (1960).

(19) C. A. Bunton and E. Humeres, *J. Org. Chem.*, 34, 572 (1969).