ture was kept at its reflux temperature for 2 hours after the addition of the amine salt solution had been completed. At this point a yellow oil had separated from the solution. This was removed and the aqueous layer was extracted three times with 100-ml. portions of ether. The combined ether extracts and oil were washed with 100 ml. of 5% sodium hydroxide, then with 100 ml. of water and dried in contact with anhydrous sodium sulfate. The ether solution of amino sulfide was filtered, cooled in an ice-bath, and while being stirred was carefully treated with hydrogen chloride gas. The white hydrochloride salt was removed by filtration and the filtrate was tested with gaseous hydrogen chloride for complete precipitation of the amine salt. The use of excess hydrogen chloride had to be avoided as it caused the amine hydrochlorides to become sticky and very difficult, if not impossible, to recrystallize. After recrystallization from isopropyl alcohol, 21.8 g. (78% yield) of a white crystalline product was obtained which melted at 123–124.5°. Analytical results are given in Table III.

Acetylated Aminophenyl ω-(N,N-Dialkylamino)-alkyl Sulfide Methyl Iodides.—In a typical experiment, 12.5 g. (0.1 mole) of *p*-aminothiophenol was dissolved in 100 ml. of 20% by weight sodium hydroxide contained in a flask fitted with a stirrer, reflux condenser, dropping funnel and a nitrogen gas delivery tube. To this alkaline solution was added 16.5 g. (0.096 mole) of diethylaminoethyl chloride hydrochloride dissolved in 100 ml. of water. The stirred reaction mixture was heated mildly for a 4-hour period while a gentle stream of nitrogen was bubbled through it. After cooling the reaction mixture it was extracted with three 100-ml. portions of ether which were combined, washed with 100 ml. of 10% sodium hydroxide, then with 100 ml. of water and dried in contact with anhydrous sodium sulfate and filtered. After removal of the ether by evaporating, 20 ml. (0.20 mole) of acetic anhydride was added to the residual oil and the mixture was heated to its boiling point and then poured into water. The resulting solution was made slightly alkaline with sodium hydroxide, causing an oil to separate, which was extracted with ether and dried with anhydrous magnesium sulfate. The ether was removed by evaporation and the free amine was treated with methyl iodide to yield a brown solid, which on recrystallization from absolute ethanol yielded 5.2 g. (21% yield) of the quaternary methyl iodide salt melting at 155–56°. Analytical results are given in Table I.

East Lansing, Michigan

[Contribution from the Severance Chemical Laboratory, The College of Wooster]

The Salt Effect in the Aromatic Nucleophilic Substitution Reaction[1a,b]

By John D. Reinheimer, William F. Kieffer, Stanley W. Frey, John C. Cochran and Edward W. Barr

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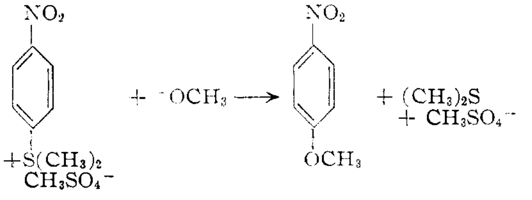
The effect of added salts on the rate constant of the ion dipole reaction, $MOCH_3$ + 2,4-dinitrochlorobenzene, was investigated. The rates were studied in absolute methanol as a function of the reactant ($LiOCH_3$, $KOCH_3$ and $NaOCH_3$) in the presence of added lithium, sodium and potassium salts. The change in rate constant is not due to ionic strength alone, but an additional factor which is believed to be ion pairing must be involved.

The effect of ionic strength upon aromatic nucleophilic substitution reactions has been investigated.[2] The Debye–Hückel relationship of

$$\log k/k_0 = 2AZ_aZ_b\sqrt{u} \qquad (1)$$

is obeyed for the replacement of bromine on an aromatic cation, 4-bromo-3-nitro-N,N,N-trimethylanilinum chloride, by the methoxide ion.[2a] This is an example of reaction of ions of opposite charge in which the center of charge of the aryl cation is not the site of the reaction. Another example is the ion–ion reaction



(2)

in which the anion attacks the aryl carbon directly attached to the positive sulfur.[2b] "The linear relationship of Debye–Hückel law is obeyed in this reaction, though the slope does not agree precisely with that calculated from theory." The salt effect for the ion–dipole nucleophilic reaction was investigated by Lulofs.[2c] He added water and salts to the reaction mixture of 2,4-dinitrobromobenzene and sodium ethoxide. The addition of NaAc had little effect upon the rate constant, but addition of NaBr resulted in a decreased reaction rate. In solvents that contained more water, the change in reaction rate constant was greater. The purpose of the present research was to explore the effect of added salts upon the ion–dipole reaction of $MOCH_3$ and 2,4-dinitrochlorobenzene (2,4-DNCB).

Experimental

Materials.—Methanol, Fisher certified, A.C.S., was dried over Drierite two times and distilled in all-glass apparatus.[3] Drying tubes containing Drierite and NaOH were used to exclude HOH and CO_2 during distillation. The acidity of the distillate was checked.

2,4-Dinitrochlorobenzene, Eastman Kodak Co., white label, was recrystallized once from ethanol, then from benzene. A second sample was recrystallized twice from ether. No difference in rate constant was observed with these samples.

All salts, except the hydrates, were dried at 75° in a vacuum apparatus; LiCl, $LiNO_3$, NaCl, NaBr, KI, KBr, KAc and NaI were A.C.S. reagent grade compounds; $NaClO_4 \cdot HOH$ and $LiClO_4 \cdot 3HOH$ were C.P.; while $LiI \cdot 3HOH$, $LiAc \cdot 2HOH$, $LiBr \cdot n HOH$ were purified grades. The $LiBr \cdot n HOH$ was dried to constant weight in the vacuum apparatus before use.

Solutions.—Salt solutions were prepared by placing the salt into a weighed volumetric flask, reweighing and diluting to volume. This method was necessary since the anhy-

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[1] (a) This research supported by a grant from the Petroleum Research Fund administered by the American Chemical Society and the donors of which are the Shell Oil Co., Inc., Standard Oil Co. of California, Standard Oil Co. (Indiana), Standard Oil Co. (New Jersey), The Texas Co., N. V. de Bataafsche Petroleum Maatschappij and Phillips Petroleum Company. (b) A preliminary report was given in This Journal, **79**, 1263 (1957).

[2] (a) B. Bolto, M. Liveris and J. Miller, *J. Chem. Soc.*, 750 (1956). (b) B. Bolto and J. Miller, *Australian J. Chem.*, **9**, 74 (1956); (c) M. P. K. Lulofs, *Rec. trav. chim.*, **20**, 292 (1901).

[3] J. A. Riddick and E. E. Toops, Jr., "Technique of Organic Chemistry," Vol. 7, 2nd Ed., Interscience Publishers, Inc., New York, N. Y., 1955, p. 335.

drous lithium salts were hygroscopic. All salt solutions were checked for acidity prior to each kinetic run. Less concentrated salt solutions were prepared by dilution of the stock solution.

2,4-Dinitrochlorobenzene solutions were prepared by weighing the solid to the nearest milligram on a powder paper and transferring to a 250-ml. volumetric flask.

Methoxide solutions were prepared by dissolving 1 mole of the metal in one liter of methanol. The concentrated solution was stored under nitrogen in a glass-stoppered flask fitted with a siphon. The sample was removed by applying 1–2 lb. pressure with dry nitrogen. The concentrated methoxide was diluted and the diluted solution was standardized against HCl. Occasional spot checks of the molarity of diluted $MOCH_3$ showed that concentrated methoxide solution did not vary with time.

Precautions.—(1) All flasks were dried in a vacuum oven. (2) Dry nitrogen was used to push methanol from drying flasks to the distilling flask in closed systems to exclude moisture and CO_2. (3) HCl was standardized with Na_2CO_3, then compared to the NaOH which had been standardized against potassium acid phthalate. These results agreed to 0.3/1000. (4) All solutions including acids and bases were kept in constant temperature-bath for 10–15 minutes before dilution to volume or final mixing. (5) Temperature was controlled to 24.90 ± 0.03°. (6) Pipets, burets and thermometers were calibrated.

Procedure.—The methoxide and salt solution were placed in one flask and 2,4-DNCB solution in another. Concentrations of 2,4-DNCB and $NaOCH_3$ were equal. A right angle bend with two male 24/40 ₸ joints was used to connect these two flasks. The contents were mixed by inversion and zero time was marked when one-half the contents of the methoxide flask had entered the 2,4-DNCB flask. After 3 or 4 inversions (about 20 seconds) the flask was returned to the constant temperature-bath. Samples were removed by pipet and the time was marked when the pipet was half discharged into a known amount of standard aqueous HCl. The reaction was followed by a standard acid–base back-titration procedure[4] or by Cl^- evolution. The evolution of Cl^- was followed by Shiner's[5] potentiometric procedure when the anion of the added salt was not a halide. In this method the reaction was stopped by pipeting the sample into dilute chloride free acetic acid. The rate constants were determined by graphical methods. Agreement between these two methods was good, as shown in Table I.

TABLE I

REACTION RATE CONSTANT OF 2,4-DINITROCHLOROBENZENE AND $MOCH_3$ IN ABSOLUTE METHANOL AT 24.90°

Methoxide used	Substance added	Rate, $K \times 10^2$, l. mole^{-1} sec.$^{-1}$	Titration method
Na	None	2.64	Acid–base
		2.60	Chloride
		2.56	Acid-base
		2.62	Chloride
		2.61	Acid–base
	Av.	2.61	
	2 ml. H_2O/150 ml.	2.69	Acid–base
		2.70	Cl^- titration
Li	None	2.38	Chloride
		2.41	Acid–base
		2.38	Chloride
		2.45	Acid-base
	Av.	2.41	
	2 ml. H_2O/150 ml.	2.44	Cl^- titration
		2.48	Acid–base
K	None	2.80	Acid–base
		2.80	Chloride
		2.82	Acid–base
		2.78	Chloride
		2.77	Acid–base
		2.78	Chloride
	Av.	2.79	
	2 ml. H_2O/150 ml.	2.86	Acid–base
		2.86	Chloride
K	LiAc·2HOH (0.10 *M*)	2.41	Chloride
	(0.10 *M*)	2.44	Acid–base

The data for a typical run are given in Table II. The reaction is: $LiOCH_3$ + 2,4-DNCB at 24.90°; potassium acetate, 0.235 *M*, was added and 10.00-ml. samples were taken. Concentrations of $LiOCH_3$ and 2,4-DNCB were equal and were 0.0292 *M*.

TABLE II

Sample	Time, sec.	Ml. $AgNO_3$, 0.02379 *M*	Normality 2,4-DNCB	1/*C*
0	0	0	0.02932	34.1
I	199	2.13	.02426	40.2
II	396	3.54	.02090	47.9
III	595	4.65	.01827	54.7
IV	796	5.50	.01625	61.5
V	998	6.19	.01464	68.3
VI	1199	6.77	.01323	75.5
VII	1398	7.23	.01213	82.3
VIII	1600	7.60	.01126	89.0

$K_2 = 3.45 \times 10^{-2}$ l. mole^{-1}sec.$^{-1}$ (graph).

Results

This investigation was divided into three parts: The effect of added lithium, sodium and potassium salts upon the reaction of (1) $LiOCH_3$ and 2,4-DNCB, (2) $NaOCH_3$ and 2,4-DNCB and (3) $KOCH_3$ and 2,4-DNCB. It was not possible to use nitrates and perchlorates with $KOCH_3$ due to the slight solubility of KNO_3 and $KClO_4$ in methyl alcohol. The results are summarized in Figs. 1–3 and Tables I and III.

TABLE III

SODIUM METHOXIDE AND 2,4-DINITROCHLOROBENZENE AT 24.90° IN ABSOLUTE METHANOL[a]

Original concn., mole/liter	Rate constant $\times 10^2$, l. mole^{-1} sec.$^{-1}$
0.0136	2.65
	2.66
.0272	2.61
	2.61
.0408	2.57
	2.58
.0813	2.67
	2.67
Av.	2.63 ± 0.03

[a] Acid–base titrations.

Since the salt effects observed are not large, a brief discussion of the quality of the data is given. The reaction rate constants were followed by acid–base titration and by Cl^- evolution to give typical data as presented in Table I. The chloride titration could not be utilized whenever a halide salt was added; however, the rate constants obtained by both methods with added acetates, perchlorates and nitrates agreed within experimental error. As a routine check, the rate of the $MOCH_3$ + 2,4-DNCB reaction was run whenever a new sample of 2,4-DNCB was used, or if a new stock solution of

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(4) J. F. Bunnett, *et al.*, THIS JOURNAL, **75**, 642 (1953).

(5) V. J. Shiner and M. L. Smith, *Anal. Chem.*, **28**, 1043 (1956).

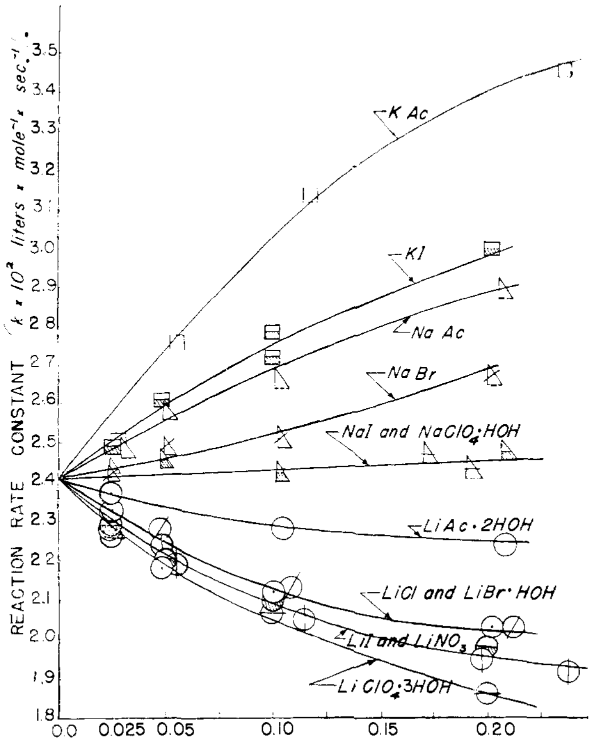

Fig. 1.—Lithium methoxide and 2,4-dinitrochlorobenzene in absolute methanol at 24.90°.

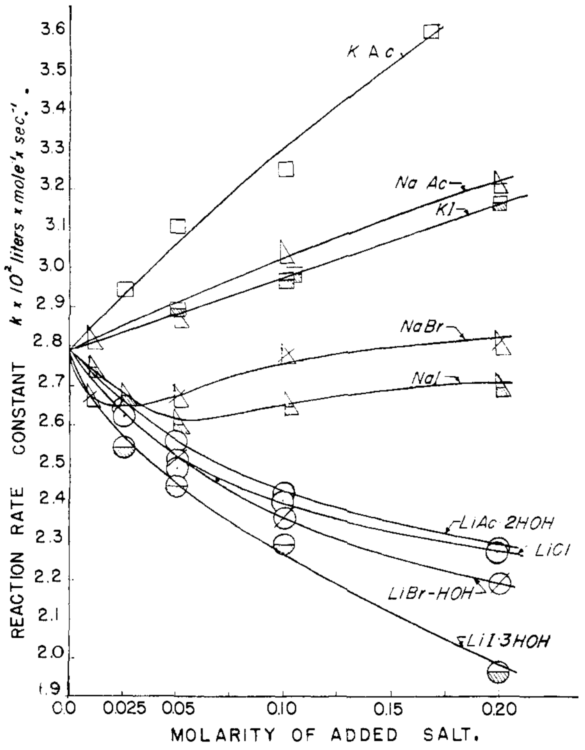

Fig. 2.—Potassium methoxide and 2,4-dinitrochlorobenzene in absolute methanol at 24.90°.

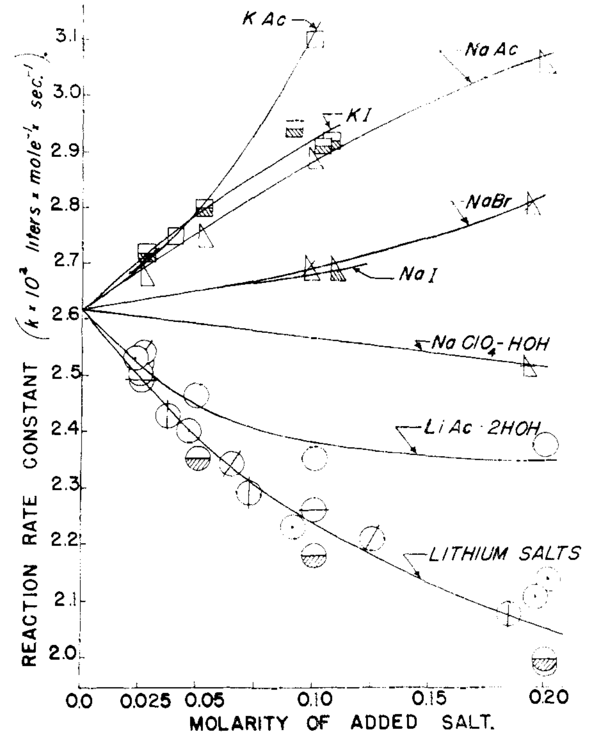

Fig. 3.—Sodium methoxide and 2,4-dinitrochlorobenzene in absolute methanol at 24.90°.

HCl, NaOH or $MOCH_3$ was prepared. These checks showed no drift in the rate constant over a period of two years. In general, there was very little scatter of points in an individual run. The method of mixing reagents was rapid, so that the time of sampling was accurately known. The rate constants were reproducible to ±1%.

Comparison of the average value in Table I with literature values shows only moderate agreement. Bunnett[6] has assembled previous results and commented upon their lack of agreement. At 25.0° values are 0.0245 (Bunnett), 0.0250 (Holleman), 0.0296 (Miller). Eliel's[7] result of 0.0257 ±0.0015 and our value of 0.0261 complete the list. One possible explanation for these rates is that each worker used different concentrations. Such a "salt effect" was observed by Lulofs[8] in the reaction of sodium ethoxide and 2,4-DNCB. The results of this research obtained by varying the concentration of reactants given in Table III do not support this hypothesis. Temperature variations do not seem to be involved, for our thermometer was calibrated against a calorimeter thermometer (°F.) which was certified by N.B.S., while Bunnett reported the use of calibrated thermometers. Indeed, temperature errors of the order of 2° would be required to account for the extreme differences, and these seem highly unlikely. The purity of 2,4-DNCB samples seems to be the most reasonable cause; we did not go to extreme measures to ensure purity, but recrystallized two times. Since our data were self-consistent, the differences due to added salts were significant, hence comparison with previous work does not invalidate our results.

Several features of interest may be observed in

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(6) J. F. Bunnett, H. Moe and D. Knutson, This Journal, **76**, 3938 (1954).

(7) E. Eliel and K. W. Nelson, *J. Org. Chem.*, **20**, 1685 (1955).

(8) J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 296 (1951).

the accompanying graphs. (a) The addition of lithium salts decreased the reaction rate constant with each methoxide. The decrease is a function of the amount of salt added. (b) The addition of potassium salts increased the reaction rate constant with each methoxide. (c) The results with sodium salts were more complex. The addition of sodium salts to the sodium methoxide reaction had a slight effect upon the reaction rate constant. Sodium salt addition decreased the reaction rate with potassium methoxide and increased the rate with lithium methoxide. The effect of added sodium acetate was to increase reaction velocity more than any other sodium salt. (d) Approximately the same rate constant was observed for the reactions $MOCH_3 + M'X$ and $MX + M'OCH_3$ where the concentrations were 0.025 M or less. (The concentrations of $MOCH_3$ and 2,4-DNCB were equal and varied from 0.025–0.029 M in all reactions.)

Since some of the salts were hydrated, the effect of added water upon the reaction rate constant was investigated. When small amounts of water were added (1.7% by weight, 2.00 ml./150 ml. of solution) the reaction rate constant was increased by 0.08 l. mole^{-1} sec.$^{-1}$ or less for each methoxide. Attempts to obtain rate constants in solvents containing 10 and 20% water gave poor reproducibility. However, the increase in reaction rate constant was greater at higher percentages of water. Since the most concentrated solution of hydrated salts (0.20 M $LiClO_4 \cdot 3HOH$) contained 0.7 g. of HOH/150 ml., the increase in rate constant due to water of hydration is negligibly small.

Discussion of Results

The observed salt effects cannot be explained upon the basis of ionic strength. If this rate expression were followed, the rate constant change should be in the same direction for all added salts, which is contrary to experiment. One may postulate that the effective charge on the activated form of 2,4-DNCB is small compared to unity, so that the $(Z_a \times Z_b)$ factor of equation 1 is nearly zero. Hence the change in rate constant due to ionic strength is overshadowed by other factors.

The possibility that the anions of added salts are acting as nucleophilic reagents in competition with $^-OCH_3$ exists. However, the products which were isolated from many of the reaction mixtures gave the literature melting point for 2,4-dinitroanisole. In addition, the rate of replacement of Cl in 2,4-DNCB by I^-, Br^- and benzoate is much too slow to be significant.[9]

It would seem reasonable that the phenomenon of ion pairing will have a prominent place in the interpretation of the data. Kraus[10] has indicated that considerable ion pairing is to be expected in solvents of dielectric constant between 35 and 50. Evers and Knox[11] have determined dissociation constants for KI, KBr, KCl, KNO_3 and KCNS in methanol to be 0.100, 0.076, 0.068, 0.0275 and 0.0780 respectively. Preliminary experiments on the salt effect in a 50% v./v. of benzene (D = 2.27), and methanol (D = 32.6) by Cochran and Reinheimer[12] indicate that the change in rate constant with added salts is greater in this medium of lower dielectric constant. Thus, the addition of 0.05 M $LiI \cdot 3HOH$ to the reaction of $NaOCH_3$ and 2,4-DNCB gave a change in rate constant of 0.30×10^{-2} l./mole sec. in methanol and 1.15×10^{-2} l./mole sec. in methanol–benzene, a nearly 4-fold increase.

Two alternative hypotheses based on ion pairing may be advanced to partially account for the salt effect. Both assume that the contribution of the anion to the over-all salt effect is small or that the salt effect is mainly due to the added cation.[13] Both utilize the equilibrium

$$M^+ + {}^-OCH_3 \rightleftarrows (M^+, {}^-OCH_3) \text{ ion pairs} \quad (3)$$

If one assumes that there are two reactive species in solution, $^-OCH_3$ and ion pair $(M^+, {}^-OCH_3)$, the reaction rate that is observed depends upon both. Similar assumptions were made by Olsen[14] and by Acree.[15] Three cases exist, $K_1 = K_2$, $K_1 > K_2$,

$$\begin{aligned} K_{obs} &= K_1[{}^-OCH_3] + K_2[M^+, {}^-OCH_3] \\ &= K_1(\alpha) + K_2(1 - \alpha) \end{aligned} \quad (4)$$

where α = fraction of salt ionized

$K_1 < K_2$. If $K_1 = K_2$, there is no salt effect. The addition of M^+ forces the equilibrium 3 to form ion pairs, but though the kind of reactive species is changed, each new ion pair reacts as fast as the methoxide ion from which it was formed. If $K_1 > K_2$, the reaction rate will be decreased by addition of M^+, for a less active species replaces the methoxide ion. On the other hand, if $K_1 < K_2$, the rate observed when M^+ is added will increase.

Applying this scheme to the data, one finds $K_1 = K_2$ for $NaOCH_3$, $K_1 < K_2$ for $KOCH_3$, $K_1 > K_2$ for $LiOCH_3$. If we assume that the tendency for intimate ion pair formation is lithium > sodium > potassium, the order of observed rate constant for $M^+, {}^-OCH_3$ + 2,4-DNCB is obtained. The addition of Na^+ salts to $NaOCH_3$ should cause little change in rate constant, the addition of Li^+ salts to $LiOCH_3$ should cause a decrease, while K to $KOCH_3$ should cause an increase. The addition of

$$\begin{tikzcd} (K^+, {}^-OCH_3) + Li^+ + X^- \arrow[r, shift left] \arrow[d, shift left] & (Li^+, {}^-OCH_3) + K^+ + X^- \arrow[l, shift left] \arrow[d, shift left] \\ K^+ + {}^-OCH_3 \arrow[u, shift left] & {}^+Li + {}^-OCH_3 \arrow[u, shift left] \end{tikzcd} \quad (5)$$

a non-common ion salt may be expressed by an equilibrium such as above. The competition of the added Li^+ and the K^+ for free $^-OCH_3$ will result in the formation of some new $(Li^+, {}^-OCH_3)$ ion pairs. These, being a less reactive species, cause a decrease in the observed rate constant. The anion of the added salt will pair with the added cation, hence the observed rate decrease is a measure

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(9) G. M. Bennett and I. H. Vernon, *J. Chem. Soc.*, 1783 (1938); L. R. Parks and G. S. Hammond, THIS JOURNAL, **77**, 2903 (1955).

(10) C. A. Kraus, *J. Phys. Chem.*, **58**, 673 (1954).

(11) E. C. Evers and A. G. Knox, THIS JOURNAL, **73**, 1939 (1951).

(12) John Cochran, Thesis submitted to the faculty of The College of Wooster, in partial fulfillment of requirements for the B.A. degree, April, 1957.

(13) A. R. Olsen and T. R. Simonson, *J. Chem. Phys.*, **17**, 1167 (1949).

(14) A. R. Olsen, L. D. Frashin and F. J. Spieth, *J. Phys. Chem.*, **55**, 860 (1951).

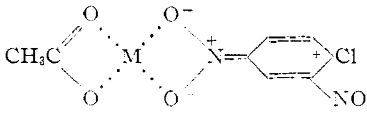
(15) S. F. Acree, THIS JOURNAL, **37**, 1909 (1915).

of the cation attraction of X^-. Another way of saying this is the free Li^+ added depends upon the cation of the lithium salt used. The order of ion-pair forming power becomes $Ac^- > Cl^-$, $Br^- > I^-$, $NO_3^- > ClO_4^-$. The converse would be true if KX were added to (Li^+, $^-OCH_3$). In this case, a more reactive species would be formed and the reaction rate increased.

The second hypothesis is that there is only one reactive species in solution, namely, the methoxide ion, or that $K_1 >> K_2$ in equation 4. A similar assumption has been made by Verhoek[16] in the decarboxylation of trichloroacetic acid. If the formation of intimate ion pairs again follows the order $Li^+ > Na^+ > K^+$, then the largest free methoxide ion concentration will be found in the potassium methoxide solution. The predicted reaction rate constant at equal concentrations of the three methoxides should follow the experimental order of $KOCH_3 > NaOCH_3 > LiOCH_3$. If a common cation is added to the reaction, equilibrium 3 will be forced to the right, reducing the concentration of the methoxide and decreasing the reaction rate. This is observed when a lithium salt is added to lithium methoxide, and the same order of anion attraction for M^+ is obtained as given above. Whenever a salt whose methoxide is more strongly ion paired than the starting alkali methoxide is added, the reaction rate decreases. Thus, lithium salts added to $KOCH_3$ and $NaOCH_3$ show this effect. The equilibrium constant for equation 5 must be somewhat greater than unity for these reactions. The increase in rate constant when sodium or potassium salts are added to lithium methoxide again involves equation 5. The equilibrium is forced to the left by the addition of comparatively large amounts of KX, hence forming (K^+, $^-OCH_3$) which in turn dissociates into more free methoxide ions.

Neither of the above hypotheses seems completely satisfactory, though the authors prefer the second. It is difficult to understand how (M^+, $^-OCH_3$) ion pairs could attack the 2,4-DNCB. In addition there is no place in the first hypothesis for the specific effect of the acetate ion. The second fails to account for the increase in rate constant above K_0, the reaction rate with no salts added. If simple ion pairing is the only cause of the changed rate, why does the addition of sodium salts to sodium methoxide and potassium salts to potassium methoxide cause rate increases? While the hypothesis of ion pairing explains a good part of the data, an additional factor must be involved in these latter rate increases.

A tentative explanation for the specific effect of the acetate ion involves 2,4-DNCB. If the acetate ion and the nitro group are involved in structures such as I



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the positive charge on carbon 1 will be enhanced, facilitating the attack of the nucleophilic agent. This type of ion complex should be formed by the anion with the strongest cation attractive powers. Some support for the acetates of unusual attractive powers is given by the salt effects observed by Winstein and Clippinger.[17] The possibility of the formation of potassium complex about the potassium ion of coördination number 4 may be an important factor in comparative stability of acetate complex with respect to other anions. Brady and Krause[18] have found that K^+ has this coördination number in aqueous solution.

Acknowledgments.—The authors thank Dr. J. F. Bunnett of the University of North Carolina for many significant conversations concerning this research.

WOOSTER, OHIO

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(16) G. A. Hall and F. H. Verhoek, THIS JOURNAL, **69**, 613 (1947).

(17) S. Winstein and E. Clippinger, *ibid.*, **78**, 2785 (1956).

(18) G. W. Brady and J. T. Krause, *J. Chem. Phys.*, **27**, 304 (1957).