

## A Study of Competitive and Consecutive Second Order Reactions: N-Alkylation of Amines by Methyl Iodide

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The kinetics of alkylation of aniline, methyl aniline and dimethylaniline by methyl iodide have been determined in nitrobenzene. The mechanism of the process has been discussed. Second order process has been observed with secondary and tertiary amines, presumably monoalkylation is occurring. In the case of aniline, a consecutive second order process has been noted indicating dialkylation. Frost-Schwemer treatment has been utilised to compute the second order rate constants. This is the first kinetic report of dialkylation in the case of aniline and mono-alkylation in the case of secondary amines.

Alkylation of tertiary amines by alkyl iodides has been extensively studied by Brown<sup>1,2</sup> and others<sup>3,4,5</sup>. No work has been recorded with primary and secondary amines, probably because of the difficulty encountered in the separation of rate constants for the primary and the secondary amines. The study has been primarily intended to solve this difficult problem of separation of rate constants of a polyalkylation process of primary and secondary amines.

### EXPERIMENTAL

Nitrobenzene, the only solvent used, was purified by usual procedure and then distilled. The amines were distilled just before use. The b.p.s. and refractive indices are as follows: nitrobenzene, b.p. 210°, n, 1.5524; aniline, b.p. 183°, n, 1.5863; methylaniline, b.p. 193°, n, 1.5702, dimethylaniline, b.p. 193°, n, 1.5587. Methyl iodide used was of Biedel (Pure).

The reactions were followed by usual titrimetric techniques of precipitation reactions viz., Volhard's method.

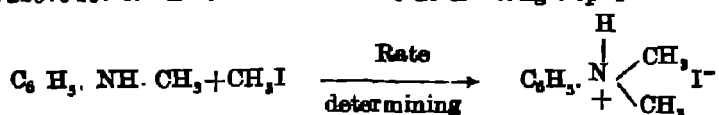
### RESULTS AND DISCUSSION

The second order rate constants of the reaction between N-methylaniline and methyl iodide are given below:—

Solvent: Nitrobenzene		Temp : 60°
Concentration of N-Methyl aniline.	Concentration of CH <sub>3</sub> I	K moles <sup>-1</sup> min <sup>-1</sup>
1. 0.0963M	0.0715M	$4.720 \times 10^{-2}$
2. 0.05150M	0.05121M	$4.529 \times 10^{-2}$

1. Brown, H. C. and Leroy, Nelson K., *J. Amer. Chem. Soc.*, 1953, 75, 24.
2. Brown, H. C. and Grayson, M., *ibid*, 1953, 75, 20.
3. Brown, W. G. and Fried, S., *ibid*, 1943, 65, 1841.
4. Baker, J. W., *J. Chem. Soc.*, 1936, 1449.
5. —*ibid*, 1935, 1840.

The above results indicate that the rate determining step is :



It is supported by the fact that the stoichiometry of the reaction is only equivalent amount ( $A_0=B_0$ ) and even when the reaction was performed with  $A_0=2B_0$ , the consumption of methyl iodide stopped at 42% of the methyl iodide and no further reaction took place even at 92°. This necessitates a revision of the earlier ideas that polyalkylation takes place with methyl iodide. It is established that the alkylation is not proceeding beyond the tertiary stage. The perfect second order rate constant obtained till even 60% of the reaction confirms the above view.

To support our conclusion from the above results, kinetics of alkylation of aniline was studied. A series of experiments were done with  $A_0=2B_0$  and  $A_0=3B_0$ . Stoichiometry showed that there is no consumption of methyl iodide more than two equivalents even at 92°. This shows probably a competitive two step consecutive second order process is occurring till the tertiary stage i.e., primary gets alkylated to secondary and then to tertiary and no further reaction takes place. This makes it necessary to separate the two rate constants by a procedure and the procedure adopted was that of Frost and Schwemer<sup>6-7</sup>.

Solvent: Nitrobenzene			Temp. 60°	
Concentration of Aniline	Concentration of $\text{CH}_3\text{I}$	$K_1$ moles <sup>-1</sup> min <sup>-1</sup>	$K_2$ moles <sup>-1</sup> min <sup>-1</sup>	$K_1/K_2$
.02565 M	.05035 M	$1.904 \times 10^{-4}$	.001228	15.5

The only limitation was that the time ratios that were used were only 50/30, 50/20 and 50/40, the reason being the reaction was slow and could not be proceeded further to compute other percentages.

This was further confirmed by two more runs at higher temperatures viz., 80° and 92°. Computation was by Frost and Schwemer method and in these runs all the time ratios could be computed.

Solvent	Temp.	Concn. of Aniline	Concn. of $\text{CH}_3\text{I}$	$K_1$ moles <sup>-1</sup> min <sup>-1</sup>	$K_2$ moles <sup>-1</sup> min <sup>-1</sup>	$K_1/K_2$
Nitrobenzene (Pure)	92°	.027365M	.0523M	0.06542	0.022	2.9
"	80°	.026M	.0507M	0.05537	0.006503	8.5

It may be pertinent to compare the rate constants computed by the use of ordinary second order rate expression for the initial stages of the reaction assuming that there is no incursion of the second step during the early phase and the value obtained by Frost-Schwemer method.

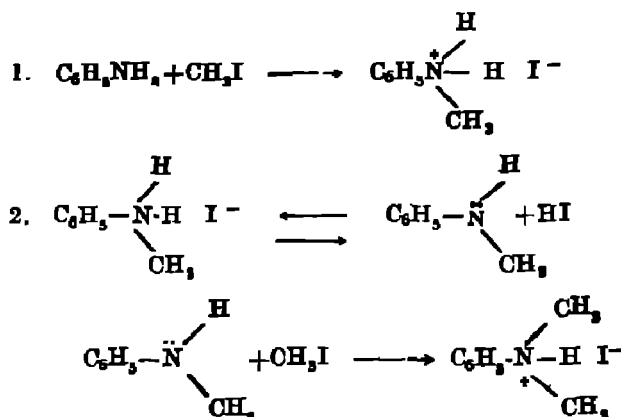
6. Frost, A. A. and Schwemer, W. G., *J. Amer. Chem. Soc.*, 1951, **73**, 4541., *ibid*, 1952, **74**, 1268.

7. —*ibid*, 1952, **74**, 1268.

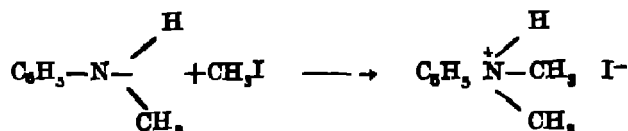
Solvent: Nitrobenzene (pure)		
Temp.	$K_1$ moles <sup>-1</sup> min <sup>-1</sup> value by F-S treatment	$K_1$ moles <sup>-1</sup> min <sup>-1</sup> for the initial stages upto 20% using ordinary second order rate expression.
60°	$1.90 \times 10^{-4}$	$2.215 \times 10^{-4}$
80°	$5.397 \times 10^{-4}$	$5.529 \times 10^{-4}$
92°	$6.542 \times 10^{-4}$	$6.823 \times 10^{-4}$

## MECHANISM

Aniline undergoes alkylation till the tertiary stage:



It may be mentioned that a separate run with N-methyl aniline confirms the above course.



The relative stabilities of the protonated species have to be explained.



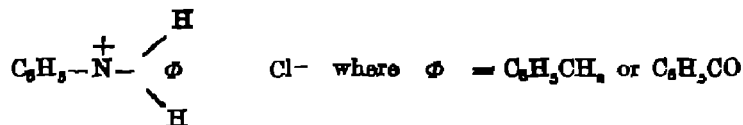
The species (b) is stable and no further alkylation is occurring. The species (a) is able to reversibly breakdown and reacts further till it becomes species (b).

One has to refer to the reactions of benzyl chloride<sup>8</sup> and benzoyl chloride<sup>9</sup> with aniline. The reactions stop at the mono stage. The probable reason, in addition to other factors

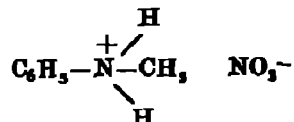
8. Baker, J.W., *J. Chem. Soc.*, 1936, 1448.

9. Williams and Hinselwood, C.N., *J. Chem. Soc.*, 1934, 1079.

like steric factors, may be the stability of the cation when the anion is a chloride e.g.:

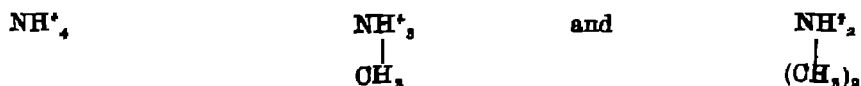


This stability of the cation stops the reaction at the mono stage. To confirm the above reasoning N-methyl aniline was treated with dil.  $\text{HNO}_3$  giving the salt;



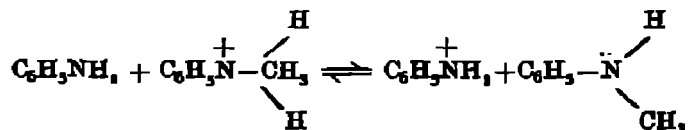
and the alkylation did not take place with  $\text{CH}_3\text{I}$ . This may be the reason why in all synthetic experiments of quaternization  $\text{Na}_2\text{CO}_3$ <sup>10</sup> is used to break up the protonated species and make available a free base for further alkylation.

But in the case of iodides we found that the species (a) was unstable where as the species (b) was stable. The breakdown of the iodides may be because of the partial ionic character being less compared to chlorides<sup>11</sup> and with consequent less stability of  $\text{N}^+$ -methyl anilinium cation in the case of iodides. The species (b) is made stabler as the alkyl groups hyper-conjugate with  $\text{N}^+$  and stabilize the cation. The species (a) is unable to be stabilized by a monoalkyl group and consequently breaks down. Such reasoning is in consonance with the discussion regarding the relative stabilities of cations:



where it is postulated that the introduction of the methyl groups results in a change in the electron-density at the nitrogen overcoming the loss in energy of solvation.

To explain the alkylation of amines, it is generally postulated by synthetic workers that the following equilibrium<sup>12</sup>.



is responsible for further alkylation. The above reasoning is erroneous as anilinium ion is not stable compared to methyl-anilinium ion which is due to their difference in basic character. The reason why alkylation occurs seems to be the less stable nature of the protonated species which reversibly breaks down to yield the free base.

10. Arnold, R. T., Webers, V. J. and Dodson R. M., *J. Amer. Chem. Soc.*, 1933, 74, 368.

11. Pauling, L., "The Nature of the Chemical Bond", P. 619, Cornell University Press (1960).

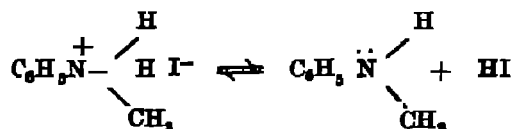
12. Packer and Vaughan, "A Modern Approach to Organic Chemistry", P. 619, Oxford University Press (1938).

Comparison of the rate constants of monomethyl aniline and second step of the aniline with  $\text{CH}_3\text{I}$ :—

Solvent: Nitrobenzene	Temp.: 60°
Base	Rate Constant
Monomethylaniline	0.04720
Aniline	0.001228*

\*Value for the second step.

The difference in rate constants certainly confirms the above postulates. In the case of methyl aniline it is the reaction of the free base with methyl iodide. In the case of the second step of aniline alkylation takes place after the breakdown of



which causes the lower kinetic rate.

Ratio of the rate constants for alkylation of aniline with  $\text{CH}_3\text{I}$  at different temperatures:

Temp.	60°	80°	92°
$K_1/K_2$	15.5	8.5	2.9

The decrease in the ratio of  $K_1/K_2$  with increase in temperature is because of the increase in  $K_2$  resulting from the breakdown of the protonated species with increase in temperature due to the increased instability.

Kinetics of alkylation of dimethyl aniline with  $\text{CH}_3\text{I}$ :—

Solvent: Nitrobenzene		Temp. 60°
Conc. of the base	Conc. of CH <sub>3</sub> I	K, mole <sup>-1</sup> min <sup>-1</sup>
0.0505 M	0.0548 M	4.293 × 10 <sup>-3</sup>

The rate determining step is definitely the quaternization of the base and the process is one of second order.

Comparative rate constants and basic character of aniline, methyl aniline and dimethyl aniline are given below.

Solvent: Nitrobenzene		Temp: 60°
Bases.	$K \times 10^{-3}$	pK <sub>a</sub>
Aniline	2.215*	4.58
Methylaniline	4.529	4.85
Dimethylaniline	4.293	5.06

\*Rate constant for the first step.

Though the order of the rate constants seems to be in consonance with the basic nature of the amines up to methyl aniline thus relating the reactivity with the basic character, the slight decrease in the rate constant for dimethyl aniline may probably be attributed to the steric effect of methyl groups causing retardation of the process.

#### Effect of Iodide Concentration.

Base	Concn. of the base	Concn. of $\text{CH}_3\text{I}$	Temp.	$k$ , moles <sup>-1</sup> min <sup>-1</sup>
Aniline	0.0189 M	0.0548 M	92°	.06661*
	0.02738 M	0.0523 M	92°	.06823*
Methyl aniline	0.0363 M	0.0715 M	60°	.04720
	0.0515 M	0.0512 M	60°	.0452

\*Values used are of the first step.

Constancy of rate constants, within experimental error, in the alkylation of the above mentioned bases proves beyond doubt the inert nature of the iodide concentration at a particular temperature for a particular step.

#### Effect of Temperature.

Increase of temperature, results in increase in kinetic rate. A plot of  $\log k$  vs  $1/T$  showed linearity for both the steps of alkylation of aniline. The energy of activation for the first step of alkylation of aniline is 9.827 k. cal and that for the second step is 19.83 k. cal which is reasonable for bimolecular reactions. Work is in progress with other substituted anilines and secondary amines.

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