

# THE ROLE OF SOLVENT IN CHEMICAL REACTIONS

## Part II.\* The Reaction between Aniline and Methyl Iodide in Different Solvents

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In the previous part<sup>1</sup> were reported some observations on the influence of solvents on the reaction between pyridine and methyl iodide. The present studies deal with the alkylation of a primary amine. While the first reaction was comparatively simple, here there are two complications—consecutive reactions of progressive alkylation, replacing the hydrogen atom of the primary amine and then formation of the quaternary ammonium compound. While the two substitution reactions may involve comparable activation energies, the formation of the quaternary ammonium compound may involve a lower activation energy. Cox<sup>2</sup> has studied the reaction between aniline and  $\omega$ -bromo acetophenone in several solvents while Hawkins<sup>3</sup> has studied the reaction between pyridine and allyl bromide in different solvents. Neither worker has been able to notice any specific correlation between any of the physical properties of the solvent and the reaction rate. The reactions had also been studied by these workers under conditions in which heterogeneity could not be excluded. Subsequent work also indicates the use of benzyl bromide<sup>4</sup> and allyl chloride<sup>5</sup> in the reaction with pyridine and it has been observed that the influence of dielectric constant is sometimes in opposite directions when the different halides are compared. It was felt that the use of methyl halides in the first instance will simplify the situation and serve as a starting point in the analysis of solvent influences.

The reaction between aniline and methyl iodide proceeded under homogeneous conditions in both acetone and ethyl alcohol but in nitrobenzene and carbon tetrachloride solutions even in very dilute solutions separation of a solid product was evident quite early in the course of the reaction. The

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analysis of both precipitate and solution from time to time for nitrogen as well as iodide contents showed clearly that the solid separating was primarily aniline hydriodide while the solution contained the products of progressive alkylation, depending on the duration of the reaction. The reaction apparently did not go to completion, the amount of methyl iodide used up being only about 87% at about 35° C. even after eight months.

Irrespective of the solvent used, the initial rate, whether one takes the value obtained by graphical extrapolation of experimental data or actual calculated value for the first 10% of the reaction, differed to varying extents, from the mean value of the rate constant. The reaction was found to be best considered as a second order one even though there was a pronounced drift in the value. For purpose of discussion, the values are collected together in Tables I, II, III and the drift in the values of the rate constants illustrated in Figs. 1 and 2 below:

TABLE I

*The reaction in nitrobenzene*

[Aniline]: [methyl iodide]	Tempe- rature ° C.	Initial value of bimolecular rate constant $\times 10^4$	Mean value of bimolecular rate constant $\times 10^4$
1.50	50	2.33	2.80
1.53	60	4.29	4.69
1.15	40	1.62	1.73
1.26	50	2.29	2.63
0.85	45	1.62	1.88
0.74	50	2.31	2.72
0.89	50	2.45	2.71
0.87	55	3.46	3.74
0.87	60	5.39	5.02

TABLE II  
*The reaction in acetone*

[Aniline]: [methyl iodide]	Tempe- rature ° C.	Initial value of bimolecular rate constant $\times 10^4$	Mean value of bimolecular rate constant $\times 10^4$
1.44	40	2.70	3.11
1.28	50	5.74	6.03
0.79	40	1.87	1.64
0.88	40	2.37	2.41
0.88	45	3.30	3.35
0.91	50	4.81	4.50
0.86	50	4.22	4.57
0.87	55	6.11	6.18

TABLE III

Solvent	Temperature° C.	% Reaction	$k_2 \times 10^4$	$k_1 \times 10^4$
Nitrobenzene ..	40	8.49	1.618	1.478
		27.57	1.646	1.345
		43.03	1.706	1.236
		55.76	1.738	1.132
		63.95	1.793	1.063
95% Ethyl alcohol ..	60	28.39	16.82	
		48.12	17.55	
		62.10	17.51	
Acetone .. ..	50	13.11	4.81	
		29.38	4.75	
		39.62	4.55	
		47.37	4.49	
		57.10	4.35	

*N.B.*:—In all the tables, concentrations are approx. M/10, all rate constants in moles. litre and the unit of time is the second.

2. In Table III,  $k_1$ -First order rate const. calcd. with respect to methyl iodide.

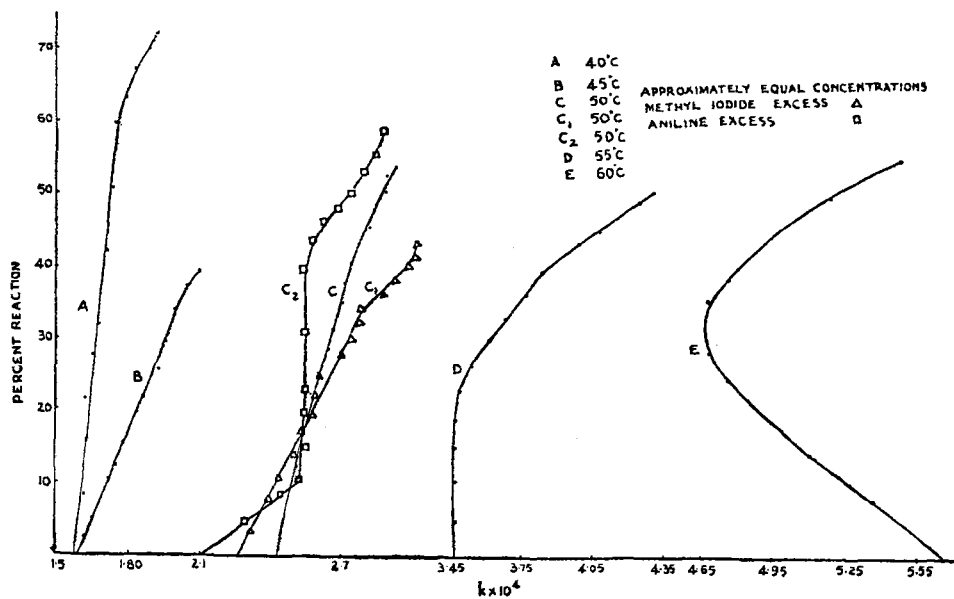


FIG. 1. Reaction in Nitrobenzene

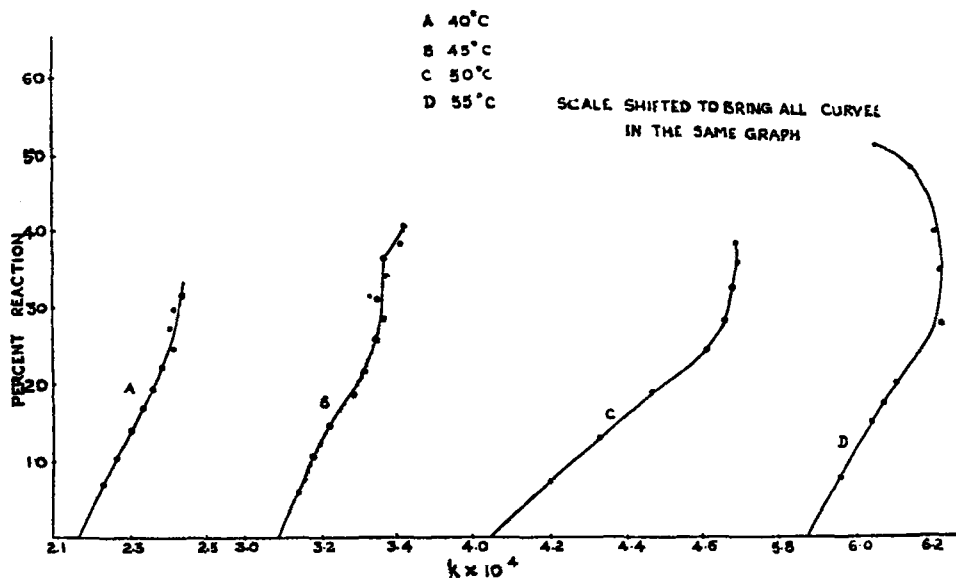


FIG. 2. Reaction in Acetone

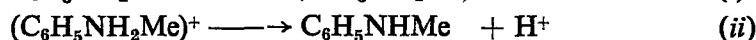
Grant and Hinshelwood<sup>6</sup> in their study of benzoylation of aniline found that the best constants were obtained when the proportion of amine to acyl

halide was 2 : 1, the second molecule of the amine serving to prevent the reversal of the reaction. If similar conditions were to hold good in the alkylation studied here, with the consumption of methyl iodide as the measured quantity, one might expect that the rate expression of the type:

$$dx/dt = k_2 (a - x) (b - 2x)$$

will apply but calculations showed that no constant could be obtained using the integrated form of this equation. The formation of aniline hydrochloride as well as the drift in the rate constant call for a different explanation.

The following stages can be visualised for the reaction:



Ionisation of methyl iodide is unlikely to be first stage in reaction since the rate is found to be quite dependent on the initial concentration. The first reaction is clearly the rate-determining step and the general trend of rate constants is that of a second order. (ii) and (iii) are reversible reactions and in the presence of an adequate quantity of aniline, reaction (iii) will be negligible. The reversibility could be readily demonstrated by starting with an alkyl aniline hydrochloride. After contact with a solution of aniline in the different solvents, the final product analysed to indicate the interchange, the solid being essentially aniline hydrochloride.

TABLE IV

Solvent	Dielectric constant at 20° C.	Bimolecular rate constants $\times 10^4$					Arrhenius parameters	
		40° C.	45° C.	50° C.	55° C.	60° C.	E K. Cals.	$\log_{10} PZ$
Acetone ..	31.0	2.17	3.09	4.06	5.88	..	13.23	5.59
Ethyl alcohol (95%) ..	40	4.07	..	8.86	..	17.7	15.37	7.35
Nitrobenzene	35.79	..	1.60	2.44	3.46	5.67	16.83	7.80

*N.B.*—The rate constants in acetone and nitrobenzene have been obtained from experiments in which the ratio Aniline: Methyl iodide was in the region 0.85–0.90.

Since the reaction appeared to be sensitive to even small changes in the concentrations, the order of the reaction could be computed only by van't

Hoff's differential method and these indicate that the reaction is of the first order with reference to aniline but the reaction order with respect to methyl iodide is only half. Since the measured quantity is only the change in methyl iodide concentrations and part of the iodide is fixed as aniline hydriodide, further work is needed to indicate the path of the reaction in full. With this limitation, however, we can analyse the influence of the solvent.

For reasons already indicated, comparison could be made using the initial value of the bimolecular rate constant (obtained by extrapolating  $k_2$ -% reaction graph to 0% reaction), in the different solvents at different temperatures. Some justification for this procedure is the observation that the  $\log k - 1/T$  graph showed very good linear relationship (Fig. 3).

It is clear that while there is a corresponding change in both Arrhenius' parameters similar to that indicated by Fairclough and Hinshelwood,<sup>7</sup> there does not appear to be any correlation with dielectric constant, of the type expected for a dipole-dipole reaction. Solvation of the transition state, removal of the proton as a solvated ion in the second stage of the reaction, changes in the dielectric constant with temperature (which have not been taken note of in the present calculations), solubility of the different products—all are relevant factors to be taken into account and further information is clearly needed. As a first step, solvent mixtures might be expected to give useful data and these are considered in the next part. The complex nature of specific solvent influences are shown clearly by the rate constant, the reaction being fastest with 95% ethyl alcohol even though the activation energy in this solvent is much higher than in acetone.

If the solvent is to take part in proton removal, the alternative question arises: Is there any unimolecular change with ionisation of methyl iodide as the rate determining step? This step cannot be ruled out on account of the high dielectric constant of the media. Hughes, Ingold and Shapiro<sup>8</sup> have shown, for instance, that where, as in the case of Isopropyl halides, both  $S_N1$  and  $S_N2$  mechanisms are possible, the rate constant may show a continuous rise. This feature is present in the present reaction at the lower temperatures but at the highest temperatures studied and probably at the later stage in the reaction the trend is reversed and there is a sign of decrease. At the present stage, it is not possible to isolate the two types of reaction and with a primary amine further alkylations which also consume the alkyl halides, are unavoidable so that the consumption of methyl iodide appears to be more than can be accounted for by the first stage of the alkylation. In either case, it is clear that the introduction of an alkyl group is analogous to the formation of 'Onium compounds'.

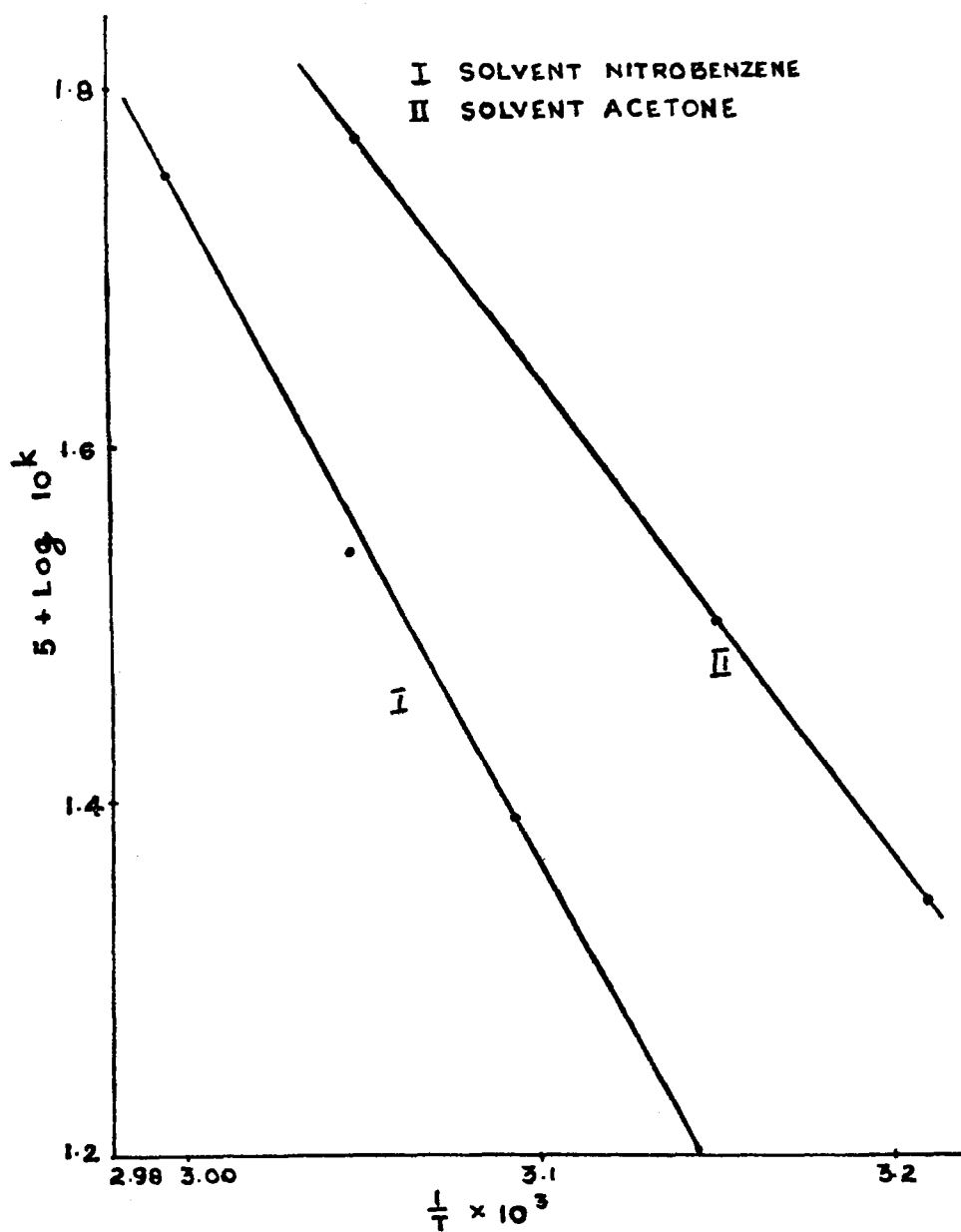


FIG. 3

## EXPERIMENTAL

Aniline, redistilled, B.D.H., was distilled once, kept over Analar potassium hydroxide for a week and then redistilled with the minimum exposure to light. Even diffuse daylight was found to cause the deepening in the colour

of the distillate. Rejecting large head and tail fractions, only the middle fraction was collected, B.P. 183° C./760 mm.

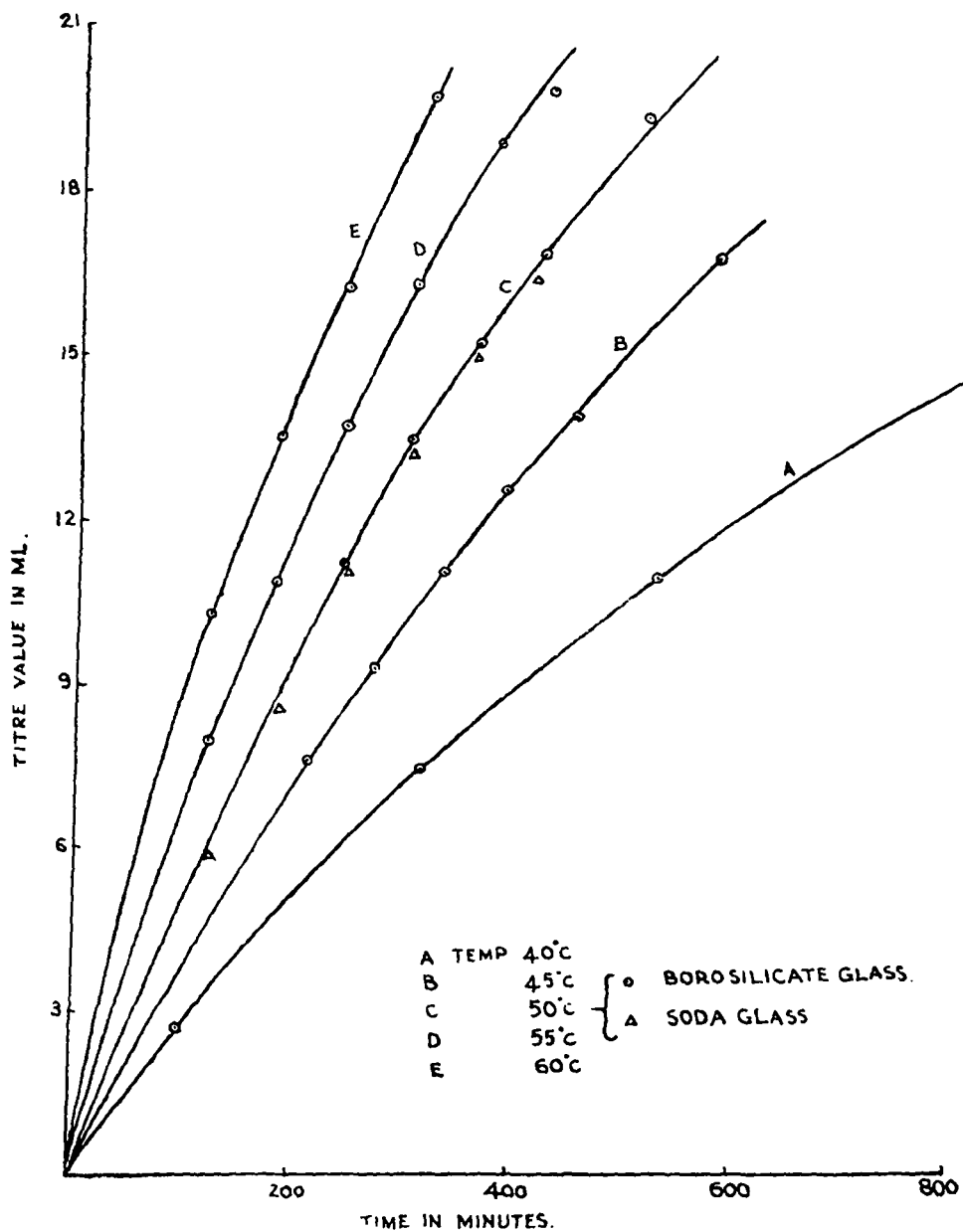


FIG. 4. Solvent : Nitrobenzene



Methyl iodide was purified as in the previous part.<sup>1</sup>

Nitrobenzene, pure redistilled, B.D.H., was shaken repeatedly with small portions of sodium carbonate solution till the aqueous portion was colourless, then washed repeatedly with distilled water, left over anhydrous calcium chloride in the dark for a week and then fractionated, only the middle fraction being used, B.P. 210° C./760 mm. Moelwyn-Hughes<sup>9</sup> considered that this drying agent was not adequate but it was found that by using long periods of drying and rejecting large head and tail fractions, contamination by moisture is negligible. The amine hydriodides formed in the reaction are found to be appreciably soluble even in the presence of minute amounts of water in the solvent and a test for the absence of water in the solvents is the ready precipitation of the salts even in the most dilute solutions. Further, it was observed that freshly distilled nitrobenzene is very pale in colour which deepens with the absorption of moisture.

Acetone of Laboratory Reagent quality was purified as in the previous part.<sup>1</sup>

Carbon tetrachloride of redistilled grade was left over mercury, shaken at frequent intervals until there was no further formation of mercuric sulphide, then washed thoroughly with sodium bicarbonate and then with distilled water, and finally dried over anhydrous calcium chloride and fractionated B.P. 75.6° C./760 mm.

*Preliminary experiments.*—Aniline and methyl iodide reacted vigorously with considerable evolution of heat. In nitrobenzene, the reaction was still exothermic but much slower. Leafy white crystals with no sharp melting are generally obtained. Estimation of the iodide content gave a value nearer to aniline hydriodide than to the alkylated product. (In the course of these studies, it has been found that estimations using Fajans' method with eosin as the indicator gave more consistent results.) The results show clearly that the product separating out was essentially aniline hydriodide with about 3% of methyl aniline hydriodide. Nitrogen estimations by microkjeldahl methods gave identical results. Relative proportions did not alter the nature of the precipitated product. The examination of the mother liquor indicated the presence of alkylated products at all stages of methylation. The reaction in carbon tetrachloride was slower and the precipitate obtained had as before no sharp melting point. Estimation of iodide content indicated that invariably it was of mixed composition. Similar results were obtained using chloroform and acetic acid as solvents, the reaction being extremely slow in the last named solvent,

Typical results of analyses are presented in Table V.

TABLE V

	Nitrobenzene solutions			Carbon tetrachloride solutions	
		Precipitate	Mother liquor		
Experiment No.	4	5	45	11	50 (Left over for 8 months)
Concentration of aniline ..	M/10	M/5	M/5	M/10	M/5
Concentration of methyl iodide .. ..	M/10	M/10	M/5	M/10	M/5
Per cent. nitrogen ..	6.352	6.305		..	..
Per cent. iodine ..	57.35		48.67	56.15	56.08 & 56.74

Aniline hydriodide requires nitrogen 6.339% and iodine 57.46%.

*Kinetic studies.*—The reactions were studied in a large thermostat, electrically operated and maintained at the requisite temperature with a tolerance of  $\pm 0.005$  at  $40^\circ$ ,  $\pm 0.01$  at  $50^\circ$  and  $\pm 0.015$  at  $60^\circ$  C. The reactant solutions were prepared by weighing both solvent and solute and thoroughly mixing the two in well-stoppered bottles. Measured equal volumes of these were pipetted into bulbs of borosilicate glass and sealed. A number of these sealed tubes were kept in the thermostat, and from time to time taken out and analysed.

The contents of the bulb were transferred to a separating funnel, rinsing the bulb with ice-cold distilled water, shaken with benzene sufficient to form an upper layer dissolving the reaction mixture. The aqueous layer was tapped off and the benzene layer extracted four times with ice-cold water. All the aqueous portions were combined and the iodide content estimated by Fajans' method using eosin as indicator.

Where the solvent was miscible with water, the contents of the bulb were taken up with ice-cold water to which sufficient acetic acid was added to chill the reaction and the iodide estimated with silver nitrate solution.

Typical runs in the different solvents are presented in Tables VI to IX.

TABLE VI  
*Reaction in nitrobenzene*

Temperature	40° C.		50° C.		60° C.	
Aniline concentration	0.09434 mol./l.		0.03466 mol./l.		0.1074 mol./l.	
Methyl iodide concentration ..	0.08414 „		0.01839 „		0.07004 „	
Strength of AgNO <sub>3</sub> solution ..	0.0255 N		0.01048 N		0.02462 N	
	Time	V	Time	V	Time	V
	5880	2.75	19780	2.50	3600	4.15
	18876	7.55	43890	5.50	7200	7.95
	31600	11.15	49855	6.10	10800	10.45
	74830	18.85	59800	7.25	14400	12.65
	103500	21.85	77650	8.75	18000	14.98
	132400	24.20	95940	9.93	21600	16.75

TABLE VII  
*Reaction at 50° C. in nitrobenzene for elucidating reaction order*

Concentration of aniline	0.09674 mol./l.	0.09674 mol./l.	0.09731 mol./l.	0.1390 mol./l.				
Concentration of methyl iodide	0.09491 mol./l.	0.13060 mol./l.	0.1098 mol./l.	0.1098 mol./l.				
Strength of AgNO <sub>3</sub> solution	0.02514 N in all the four experiments							
	Time	V	Time	V	Time	V	Time	V
	9000	6.85	9300	9.10	14400	11.25	10800	12.40
	12600	8.95	12600	12.10	18300	13.60	14400	15.40
	16200	10.75	16200	14.40	21600	15.30	18000	17.95
	19800	12.60	19800	16.95	25200	17.00	21600	20.25
	23400	14.35	23400	19.25	30600	19.50	25200	22.45
	27000	16.20	27000	20.28	34200	20.00	28800	24.60
	30600	17.05	30600	22.55	43200	23.25	32400	25.55

TABLE VIII  
Reaction in 95% ethyl alcohol

Temperature °C.	40	50	60			
Concentration of aniline	0·09408 mol./l.	0·08732 mol./l.	0·1075 mol./l.			
Concentration of methyl iodide	0·08553 „	0·08839 „	0·08543 „			
Strength of AgNO <sub>3</sub> solution	0·02550 N.	0·02504 N	0·02462 N.			
	Time	V	Time	V	Time	V
	7725	7·90	7200	12·70	2100	9·85
	14890	12·60	10800	16·15	4500	16·70
	22270	16·10	14400	18·75	7500	21·55
	29540	18·60	18000	20·65	9300	23·65
	36850	20·30	21600	22·18	11700	25·75
	44080	21·6			14100	27·08
	62090	24·3			16500	24·40

TABLE IX  
Reaction in acetone

Temperature °C.	40	50		
Concentration of aniline	0·08935 mol./l.	0·08650 mol./l.		
Concentration of methyl iodide	0·08946 „	0·08688 „		
Strength of AgNO <sub>3</sub> solution	0·02550 N.	0·02496 N.		
	Time	V	Time	V
	9218	5·55	7825	9·30
	16460	9·30	14400	13·05
	23570	11·85	25200	17·35
	32700	14·25	39600	20·90
	47130	17·35	61200	23·60
	76320	21·25		

Time in Seconds; V, Titre value in ml.

Examples of the general trend with other concentrations are illustrated in Figs. 5 and 6.

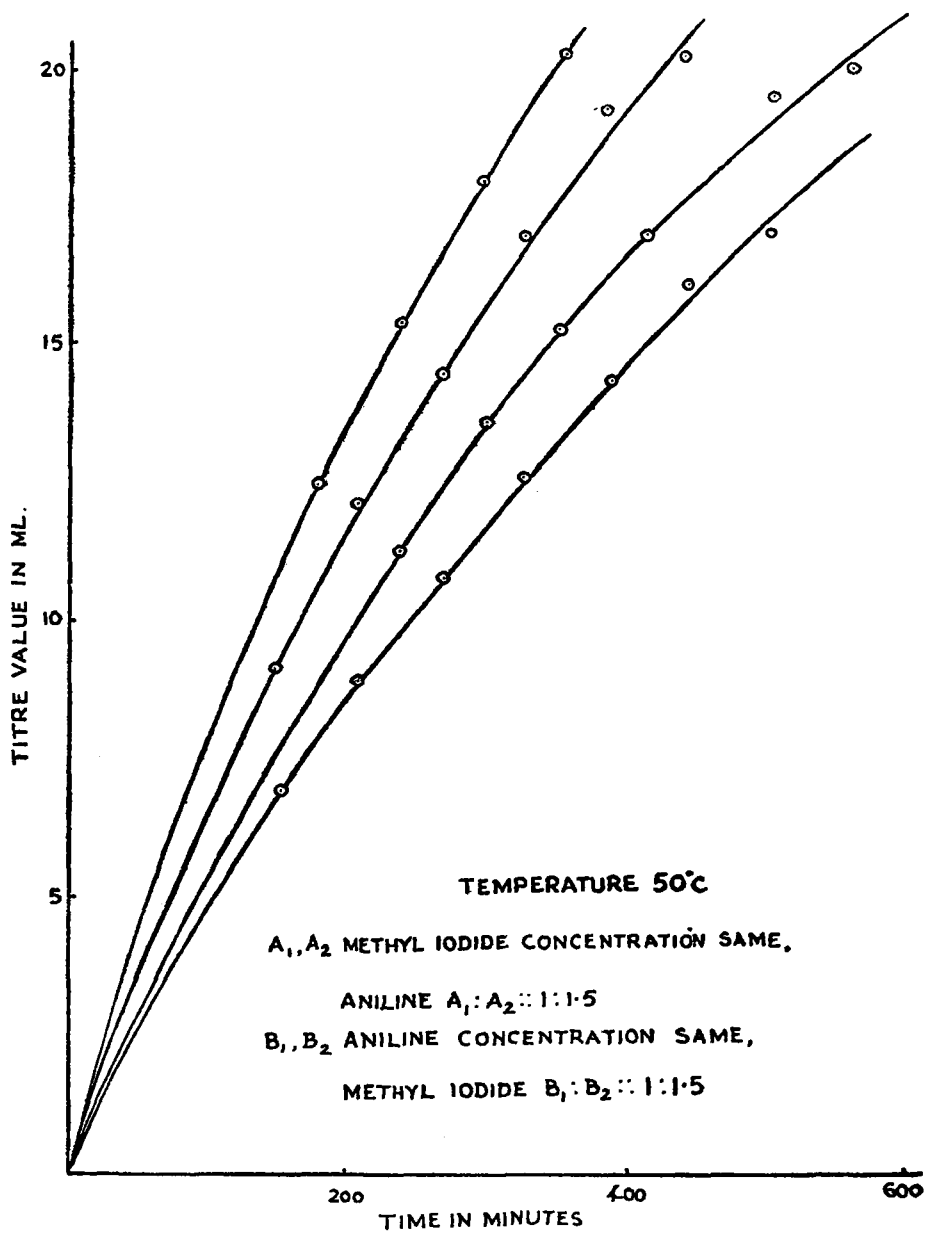


FIG. 5. Solvent Nitrobenzene

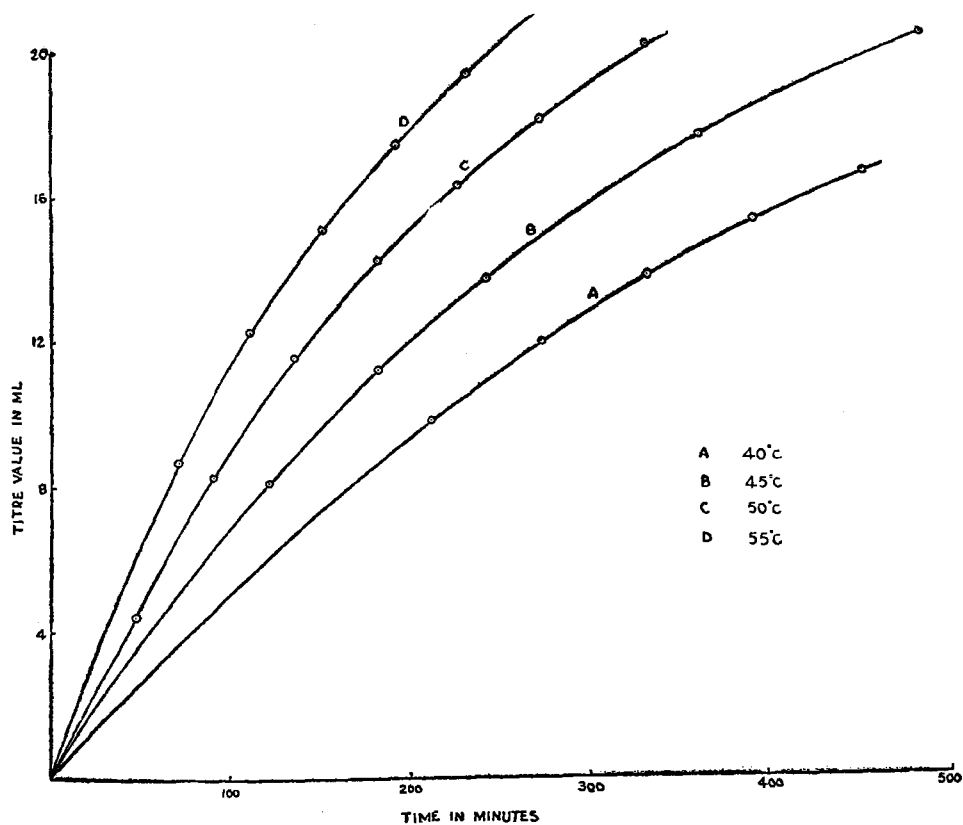


FIG. 6. Reaction in acetone

No kinetic studies were made in pure carbon tetrachloride as it was not possible even in the most dilute solutions to have homogeneous conditions. Similarly no kinetic studies were made in glacial acetic acid as the extent of reaction was small even after weeks.

#### SUMMARY

The reaction between aniline and methyl iodide has been studied at four different temperatures in 95% ethyl alcohol, acetone, nitrobenzene and carbon tetrachloride. The complications arising from progressive alkylations as well as from the crystallisation have been minimised under the experimental conditions in the initial stages. The observed changes in the rate constants and in the Arrhenius parameters are discussed.

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