241. *Mechanism of Substitution at a Saturated Carbon Atom. Part LIX.* Kinetics and Mechanism of the Reaction of Methyl Bromide with Pyridine in Benzene.*

By Y. Pocker.

In contrast to the S_N1 substitutions of triphenylmethyl chloride in benzene, as described in the preceding papers, the reaction of methyl bromide with pyridine is of first order in each reagent, and is subject to only very weak catalysis by hydroxy-compounds, and to weakly accelerative effects of salts, including a common-ion salt (bromide). All the forms of catalysis are ascribed to macroscopic medium effects of added polar molecules or saline ion-pairs, and it is concluded, contrary to Swain and Eddy, that an S_N2 mechanism is under observation.

The rates and their thermodynamic factors, reported here and by Winkler and Hinshelwood, for Menschutkin reactions in benzene, are compared with those, given by de la Mare *et al.*, for Finkelstein reactions in acetone. The similar effects of structure show that both substitutions have the same molecularity, *i.e.*, that both are S_N2 reactions.

Swain and Eddy [1] investigated the interaction of methyl bromide with pyridine in solvent benzene, and included it as an example of Swain's " push-pull termolecular " mechanism. The writer concurs with Hughes and Ingold [2] in regarding it as an S_N2 substitution, but one subject to co-solvent accelerative effects when dipolar substances are added to the non-polar solvent, benzene, because charges are being created in the reaction, and therefore its transition state is more polar than its initial state :

$$C_5H_5N + CH_3Br \longrightarrow \left[C_5H_5\overset{\delta+}{N} \cdots CH_3 \cdots \overset{\delta-}{Br}\right] \longrightarrow \left\{C_5H_5\overset{+}{N}CH_3\right\}\overset{-}{Br}$$

The reaction goes at a convenient speed at 100°, and its product is thermodynamically stable enough to enable the kinetics of the forward process to be investigated without trouble from reversibility. The present re-investigation of the reaction seemed desirable in order to bring out the contrasts, which Swain and Eddy's paper do not make clear, between its kinetics, and the kinetics of those S_N1 substitutions in benzene, which form the subject of the immediately preceding papers.

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[*] Part LVIII, preceding paper.

[1] Swain and Eddy, *J. Amer. Chem. Soc.*, 1948, **70**, 2989.

[2] Ingold, " Structure and Mechanism in Organic Chemistry," G. Bell, London, 1953, p. 357.

(1) *Kinetics and Mechanism of the Reaction of Methyl Bromide with Pyridine in Benzene.*—The first contrast is that, whilst the reactions of triphenylmethyl chloride are of first order in this substance, and of zeroth order in substituting agents at low concentration, the reaction of methyl bromide with pyridine is of first order in each reagent. This is established by the constancy of the second-order rate coefficients in runs with different initial concentrations of either reactant as shown in Table 1, and also (in agreement with Swain and Eddy) by the kinetic course of the individual runs, as illustrated in Table 6.

TABLE 1. *Second-order rate-constants (k_2 in sec.$^{-1}$ mole^{-1} l.) of the reaction of methyl bromide with pyridine in benzene at* 100°.

Run	[MeBr]	[C_5H_5N]	10^4k_2	Run	[MeBr]	[C_5H_5N]	10^4k_2
48	0·06	0·20	4·70	49	0·12	0·20	4·70
1	0·12	0·10	4·69	3	,,	0·30	4·72
2	,,	0·20	4·70	4	0·24	,,	4·75

The catalytic effects of added alcohols and phenol are much smaller in this reaction than in the investigated substitutions of triphenylmethyl chloride. Thus whilst 0·1M-methyl alcohol produces a 1700% increase in the rate of alcoholysis of triphenylmethyl chloride, and a 14,000% increase in the rate of its halide exchange, it leads only to a 14% increase in the rate of reaction of methyl bromide with pyridine. Further illustrations of the contrast are given in Table 2.

Benzyl alcohol, phenol, and also nitrobenzene accelerate the reaction as much as, or more than, methyl alcohol does; but none of these accelerations is really large, as can be seen from the general comparison in Table 3. Neither the alcohols nor phenol reacts with methyl bromide in benzene in the absence of pyridine at rates which are significant in comparison with the rates of the reaction with pyridine.

TABLE 2. *Effect of added methyl alcohol on the second-order rate-constants (k_2 in sec.$^{-1}$ mole^{-1} l.) of reaction of methyl bromide with pyridine in benzene at* 100°; *and comparison of the percentage accelerations produced by methyl alcohol in this reaction and in substitutions of triphenylmethyl chloride in benzene at* 25° (*cf. Parts LIV and LVI*).

Initially, [MeBr] = 0·12M and [C_5H_5N] = 0·20M, throughout.

MeBr + pyridine			Increase (%) of rate		
Run	MeOH	10^4k_2	MeBr + Py	Ph_3CCl + MeOH	Ph_3CCl + M^+Cl^-
2, 49	0·00	4·70	0	0	0
19	0·01	4·75	1	23	—
17	0·02	4·80	2	110	55·5
20	0·05	5·00	6	530	—
18	0·10	5·35	14	1700	14,000
16	0·20	6·00	28	11,400	—
21	0·50	7·95	69	123,000	—

TABLE 3. *Effect of molecular addenda on the second-order rate-constants (k_2 in sec.$^{-1}$ mole^{-1} l.) of reaction of methyl bromide with pyridine in benzene at* 100°.

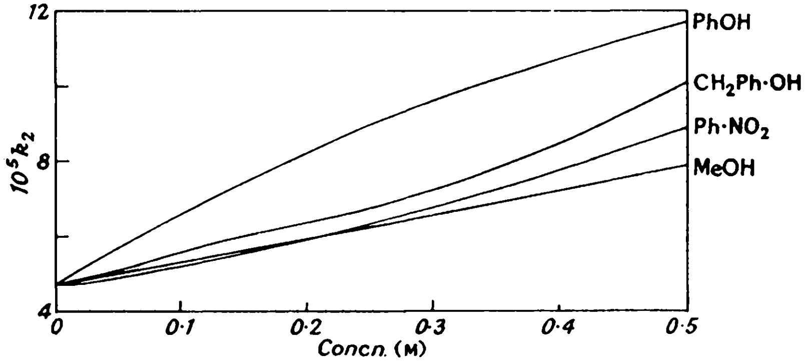
(Initial concns. as in Table 2.)

	MeOH	$CH_2Ph{\cdot}OH$		PhOH		$Ph{\cdot}NO_2$	
[Addendum]	10^4k_2	Run	10^4k_2	Run	10^4k_2	Run	10^4k_2
0·01	4·75	24	4·75	4	4·85	11	4·70
0·02	4·80	22	4·80	8	5·10	—	—
0·05	5·00	25	5·07	5	5·68	14	4·95
0·10	5·35	23	5·60	6	6·60	12	5·27
0·20	6·00	26	6·37	7	8·26	15	6·00
0·50	7·95	27	10·0	10	11·7	13	8·85

As all these catalytic effects are somewhat small, it is not to be expected that they would deviate strikingly from linearity; but that they are in general non-linear will be clear from the rate–concentration curves shown in the Figure. It is difficult, therefore, to agree with Swain and Eddy in their arguments, (*a*) that the accelerative effects of added hydroxy-compounds are too large to admit of interpretation as polar co-solvents effects, and (*b*) that the accelerative effects are to be regarded as linear, in accordance with Swain's termolecular theory. It should be said that these authors offer no acceptable experimental evidence in support of these conclusions, and, in particular, no proof of the assumed constancy of reaction-order in the added substances. In illustrating their discussion, they formulate the termolecular theory with phenol as the third molecule; but they record only one experiment with added phenol.

An examination has been made of the kinetic effect of three salts, *viz.*, tetra-*n*-butylammonium perchlorate, nitrate, and bromide. All these salts show a weakly accelerative effect, even the bromide, which would, of course, be a common-ion salt for reactions of methyl bromide, were an S_N1-type mechanism in operation. The results are in Table 3.

Effect of molecular addenda in various concentrations on the second-order rate-constants, k_2, of reaction of methyl bromide with pyridine in benzene at 100°. (The curves are drawn strictly through the experimental points, but the points themselves are not shown, because so many of them are very nearly coincident.)



The accelerations are approximately linear at the salt concentrations employed, but because of the small magnitude of the effects, only a limited significance can be attached to the observed linearity. However, the figures convey no suggestion of a dependence of the accelerations on the square-root of salt concentration (cf. Part LVI).

TABLE 4. *Effect of added salts on the second-order rate-constants (k_2 in sec.$^{-1}$ mole^{-1} l.) of reaction of methyl bromide with pyridine in benzene at* 100°.

(Initial concns. as in Table 2.)

	$Bu^n_4NClO_4$		$Bu^n_4NNO_3$		Bu^n_4NBr	
[Salt]	Run	10^4k_2	Run	10^4k_2	Run	10^4k_2
0·0001	—	—	32	4·70	—	—
0·001	52	4·80	33	4·75	—	—
0·005	51	5·00	34	4·85	53	4·80
0·01	37, 50	5·35	35	5·05	54	4·90

Run 39 : 0·005M-$Bu^n_4NClO_4$ + 0·005M-$Bu^n_4NNO_3$ .... 10^4k_2 = 5·20
,, 38 : 0·01M ,, + 0·001M ,, ... ,, 5·40
,, 56 : 0·005M ,, + 0·001M-Bu^n_4NBr .... ,, 5·02
,, 55 : ,, ,, + 0·005M ,, ... ,, 5·10
,, 57 : ,, ,, + 0·010M ,, ... ,, 5·20

The largest of these kinetic effects is that of the perchlorate; but it is much smaller than any of the effects which this salt produces in the reactions of triphenylmethyl chloride with alcohols. Thus a concentration of 10^{-3}M, which increases the rate of the triphenylmethyl chloride reactions by ratios up to 20-fold, does not increase that of the methyl bromide reaction by more than 2%. The effects of the nitrate and bromide are successively smaller still. Whereas in the reactions of triphenylmethyl chloride with alcohols, the introduction of tetra-*n*-butylammonium perchlorate, together with tetra-*n*-butylammonium nitrate (or together with any second salt which, when alone, has a weaker catalytic effect than the perchlorate), leads to a smaller rate than the perchlorate alone would have given, the joint effect of tetra-*n*-butylammonium perchlorate and nitrate on the reaction of methyl bromide with pyridine seems to be approximately additive.

The great contrast between the present salt effects, and those described in the preceding papers for reactions of triphenylmethyl chloride, is consistent with the basic difference of mechanism which the author assumes. There are far too few simple ions in benzene appreciably to affect the energy of a bimolecular transition state, and the weak, approximately linear, approximately additive, effects which one does observe seem best ascribed to a macroscopic medium effect of the salts in their stable ion-pair forms.

(2) *Effects of Alkyl Structure on Rates of Menschutkin Reactions: Comparison with Finkelstein Substitutions.*—The second-order rate-constant here given for the reaction of methyl bromide with pyridine at 100° in benzene, 4·70 × 10^{-4} sec.$^{-1}$ mole^{-1} l., is in satisfactory agreement with that obtained by Swain and Eddy, *viz.*, (4·82 ± 0·25) × 10^{-4} sec.$^{-1}$ mole^{-1} l. Now Winkler and Hinshelwood [3] have determined rate-constants for the reactions of ethyl and *n*-propyl bromide in benzene at the same temperature. Their data permit the following structural comparison of $10^4 k_2$ values for these Menschutkin reactions: MeBr, 4·70 (100·0°); EtBr, 0·249 (99·8°); Pr^{n}Br, 0·101 (99·7°). The rate-ratio Me : Et is thus about 20 : 1, and the ratio Et : Pr^n is about 2·5 : 1.

Since the present conclusion is that these reactions are bimolecular, it is legitimate to compare the above ratios with those obtained by de la Mare, Fowden, Hughes, Ingold, and Mackie [4] for the bimolecular Finkelstein substitutions of the same alkyl bromides in acetone. The point of the comparison is that the rates of the latter group of S_N2 reactions were analysed, practically and theoretically, with considerable quantitative success, for their polar and steric, energetic and entropic, factors. For example, entropies of transition states were calculated on the assumption that these were bimolecular, with results which agreed well with experiment, but which would be completely upset if in fact the transition states were termolecular.

Table 5 shows the comparison, for the two groups of reaction, not only of the rate-ratios, but also of the corresponding differences, $\Delta G^{\ddagger}$, in the free-energy of activation, and, where possible, the differences in the enthalpic and entropic components $\Delta H^{\ddagger}$ and $T\Delta S^{\ddagger}$ of the free-energy, the former component being identified, as an approximation, with the Arrhenius energy of activation, ΔE_A.

TABLE 5. *Rate-ratios and activation-energy differences, for some nucleophilic substitutions of simple alkyl bromides at 100°.*

			Activation energy terms (kcal./mole)					
	Rate-ratios		Diff. (Et − Me)			Diff. (Pr^n − Et)		
Substituting agent	Me : Et	Et : Pr^n	$\Delta H^{\ddagger}$	$-T\Delta S^{\ddagger}$	$\Delta G^{\ddagger}$	$\Delta H^{\ddagger}$	$-T\Delta S^{\ddagger}$	$\Delta G^{\ddagger}$
C_5H_5N	20	2·5	—	—	2·2	0·3	0·4	0·7
Cl^-	34	1·6	1·9	0·7	2·6	0·1	0·4	0·5
Br^-	32	2·0	1·7	0·9	2·6	0·0	0·5	0·5
I^-	72	1·4	2·5	0·7	3·2	−0·1	0·4	0·3

In the above-mentioned analysis of the kinetics of the Finkelstein substitutions, it was shown that, on passing from methyl to ethyl bromide the major part of the decrease in rate is derived from an increase in $\Delta H^{\ddagger}$, which in turn arises as the sum of comparable polar and steric energy contributions; whilst a minor, but still important, part of the rate decrease arises from an increase in $-T\Delta S^{\ddagger}$, which itself is the sum of a minor steric and a major ponderal entropy contribution. It was shown further that, on passing from ethyl

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[3] Winkler and Hinshelwood, *J.*, 1935, 1147.

[4] de la Mare, Fowden, Hughes, Ingold, and Mackie, *J.*, 1955, 3169 *et seq.* (8 papers).

to *n*-propyl bromide, there should theoretically be scarcely any increase in $\Delta H^{\ddagger}$, as was not inconsistent with the observations, having regard to the accuracy of the relevant experiments; so that practically the whole of this rate decrease was to be ascribed to the increase in $-T\Delta S^{\ddagger}$, which, in turn, had a negligible steric component, and arose almost wholly from the ponderal entropic effect. Although kinetic analysis of the Menschutkin reactions has not yet been carried as far as that of the Finkelstein substitutions, it does seem almost certain, from the figures in Table 5, that such an analysis of the former group of reactions would give very similar results.

It seems equally clear that the Finkelstein and Menschutkin substitutions are similar in mechanism, and that, since a quantitative treatment of the kinetics of the former confirms their bimolecular nature, we must infer, in agreement with the conclusion derived from kinetic form and catalysis in Section 1, that the Menschutkin reactions of simple alkyl bromides in benzene are S_N2 substitutions.

EXPERIMENTAL

Materials.—The preparation or purification of most of the substances here used is described in Part LIV. Methyl bromide was purified by passing it as vapour through sulphuric acid wash-towers, and then condensing it with exclusion of moisture. Tetra-*n*-butylammonium bromide, prepared as already described for the iodide (Part LIV), had m. p. 120° (Found: Br, 24·8. Calc. for $C_{16}H_{36}NBr$: Br, 24·8%).

Method.—Sets of sealed tubes, each containing 5 ml. of the reaction mixture, were placed in the thermostat at 100·0°, and, severally, at intervals, were withdrawn and cooled, the first such withdrawal marking the kinetic zero. In the contents of each tube, bromide ion was determined, either by Volhard's method or by potentiometric titration, the two methods giving identical results.

Kinetics.—The solubility of methylpyridinium bromide is not above 0·002M at 100°, and therefore this salt became precipitated early during the runs. However, this seemed to make no difference to the rates of the reactions, which gave good second-order constants. Surface catalysis appears to be small, inasmuch as the rates were not appreciably affected, either by adding initially an excess of solid methylpyridinium bromide, or by packing the reaction tubes with glass wool.

Rate constants were calculated by the integrated formula for an irreversible reaction of second order. The details of some sample runs are given in Table 6.

TABLE 6. *Illustrative experiments on the reaction of methyl bromide with pyridine, without or with added substances, in benzene at* 100·0°.

[In all the runs recorded in this table, the initial concentration of methyl bromide was 0·12M, and of pyridine 0·20M. The concentrations *x* of product are in mole l.$^{-1}$, and are reckoned as excesses over the small amounts found at the kinetic time-zero. The times *t* are in min., and the corresponding integrated rate-constants k_2 are in sec.$^{-1}$ mole^{-1} l.]

Run 2			Run 18			Run 15			Run 35		
Nothing added			[MeOH] = 0·10M			[$PhNO_2$] = 0·20M			[Bu_4NNO_3] = 0·01M		
t	10^2x	10^4k_2	*t*	10^2x	10^4k_2	*t*	10^2x	10^4k_2	*t*	10^2x	10^4k_2
15	0·95	4·69	15	1·05	5·34	15	1·20	6·04	15	1·00	4·96
30	1·80	4·73	30	2·00	5·35	30	2·20	5·97	30	1·92	5·11
60	3·18	4·67	60	3·52	5·35	45	3·10	6·05	60	3·37	5·05
90	4·32	4·68	90	4·70	5·32	60	3·83	5·96	90	4·51	5·00
120	5·25	4·70	120	5·70	5·36	90	5·10	6·00	120	5·48	5·03
150	6·05	4·74	150	6·48	5·35	120	6·14	6·10	150	6·29	5·15
180	6·67	4·69	180	7·12	5·33	150	6·92	6·02	180	6·93	5·05
210	7·27	4·70	210	7·70	5·38	180	7·50	5·91	210	7·48	5·05
240	7·70	4·70	240	8·18	5·38	210	8·07	6·00			

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WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, GOWER ST., LONDON, W.C.1.

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