853. *Mechanism of Substitution at a Saturated Carbon Atom. Part LXI.* Addendum on the Finkelstein Reaction, and Reply to Farhat-Aziz and Moelwyn-Hughes.*

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Repetition of the work of Hughes, Ingold, and Mackie on the reaction of methyl iodide and lithium chloride in acetone, with and without added lithium perchlorate, has confirmed that the disturbances alleged by Farhat-Aziz and Moelwyn-Hughes in Hughes, Ingold, and Mackie's rates do not exist, that the salt effects the latter authors found are real, and that the enormous discrepancy that Farhat-Aziz and Moelwyn-Hughes saw in Hughes, Ingold, and Mackie's rates arises from Farhat-Aziz and Moelwyn-Hughes's having temporarily forgotten the difference between a rate and a rate-constant.

As part of a comparative study of the effect of alkyl structure on the rates of Finkelstein reactions, Hughes, Ingold, and Mackie [1] examined the rates of reaction of lithium chloride in acetone with a series of alkyl iodides, among them methyl iodide. The reactions, though reversible, went well forward in the conditions used, and were of simple second-order form over considerable parts of their course in the presence of sufficient lithium perchlorate to buffer specific salt effects:

$$\mathrm{RI} + \mathrm{LiCl} \rightleftharpoons \mathrm{RCl} + \mathrm{LiI}$$

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* Part LX, *J.*, 1960, 806.

[1] Hughes, Ingold, and Mackie, *J.*, 1955, 3177.

This was accordingly a convenient method of comparing the kinetic effects of different alkyl groups on the reaction.

Farhat-Aziz and Moelwyn-Hughes[2] have published a study of the rate of one of the reverse reactions, that between methyl chloride and lithium iodide in acetone. They did not measure the rate of our forward, *i.e.*, their reverse, reaction, but deduced it on certain assumptions. However, at the outset of their paper, they refer to it, as if measured, in the words: " The rate of the reverse reaction is greater . . . than that found by other workers (Hughes, Ingold, and Mackie) by a factor of more than 1000."

We do not habitually comment on inapplicable criticisms, but we do comment in this case, because the sweeping assertion quoted, followed, as it is, by a succession of incorrect " explanations," obscures the circumstance that the essential cause of the large factor mentioned is that Farhat-Aziz and Moelwyn-Hughes have temporarily forgotten the difference between a rate, which is observational, and a rate-constant, which depends on the kind of constant, *i.e.*, on the formula by which it is calculated.

Farhat-Aziz and Moelwyn-Hughes, however, account for the alleged discrepancy in several ways, which are alike in assuming faulty work on our part. So let us examine how far they are correct.

Their first explanation is that Hughes, Ingold, and Mackie " used sealed ampoules with an unspecified volume of vapour," thereby " permitting the escape of vapours of methyl iodide and methyl chloride into the gas-space in contact with their solutions."

We thought we had called attention to this source of error and how to avoid it, in rate measurements on alkyl halides, first, and often enough in papers of this series to make clear that it is routine with us to check its significance and take evasive measures if necessary. Actually the error never attains significance except in poor solvents for alkyl halides, notably water, and at temperatures high for the volatility of the alkyl halide. Two records, taken from related papers, will suffice to show its insignificance in the present case. The rate of reaction of methyl bromide at 100° in aqueous formic acid was reduced by about 20% by a gas space 3 times the liquid volume, and this error became undetectable when the gas-space was reduced to a small fraction of the liquid volume.[3] Without any special precautions, *i.e.*, with our usual approximate 15% of gas-space, as also with more than twice that, no detectable disturbance due to the gas-space occurred in the reaction of methyl bromide at 55° in " 80% " aqueous ethanol.[4] It was therefore obvious that no detectable error of this kind could arise in the reaction of less volatile methyl iodide, in the better solvent anhydrous acetone, at the still lower temperatures used by Hughes, Ingold, and Mackie, who, nevertheless, protected themselves against it experimentally.[5] For demonstration in face of the assertion made, and not because there could be any doubt, we have now re-examined the point as follows. Some rate measurements in Hughes, Ingold, and Mackie's conditions, as specified at the top of Table 1, were conducted (*a*) in ampoules with 0·5 ml. of gas-space, (*b*) in 100 ml. flasks with 5—95 ml. of gas-space, and (*c*) in a 1000 ml. flask with 910—990 ml. of gas-space. As Table 1 shows, no difference of rate was detected, so criticism on this score is finally invalidated.

Farhat-Aziz and Moelwyn-Hughes's second explanation of the alleged discrepancy is that it arises " owing to their [Hughes, Ingold, and Mackie's] not allowing for the kinetic consequences of the reverse reaction." They say that Hughes, Ingold, and Mackie " dismissed " the retrograde reaction.

This is a strange charge; first, because Farhat-Aziz and Moelwyn-Hughes also conclude that the rate of the retrograde reaction is smaller than that of the forward reaction " by a factor of about 4000." If this were true, if the reverse reaction really went so very much more slowly, its dismissal would be justified.

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[2] Farhat-Aziz and Moelwyn-Hughes, *J.*, 1959, 2635.

[3] Bateman and Hughes, *J.*, 1940, 947.

[4] Bateman, Cooper, Hughes, and Ingold, *J.*, 1940, 934.

[5] Mackie, Thesis, London, 1952, p. 98.

In fact, the reverse reaction does not qualify for dismissal quite so completely; and the second, and more serious answer to Farhat-Aziz and Moelwyn-Hughes is that Hughes, Ingold, and Mackie did not dismiss it. They explained that their reactions went so far forward that they could follow proportions up to 70% of the stoicheiometrically possible forward process without interference from the back-reaction; and that when, additionally, salt effects were buffered with excess of lithium perchlorate, second-order constants, calculated as for an irreversible reaction, were good over the stated ranges. We have again checked this matter by taking three runs, nos. 2, 3, and 4 of Table 1, to equilibrium, as in the example set out in Table 2. Equilibrium was reached after 94·1, 94·2, and 94·8% of reaction in the respective cases (mean, 94·4%). The stoicheiometric equilibrium constants, [MeCl][LiI]/[MeI][LiCl], were therefore 15·1, 15·4, and 17·5 (mean $K = 16{\cdot}0$). The stoicheiometric rate constants were in fact steady to rather beyond the 70% given as a working limit by Hughes, Ingold, and Mackie. Within that range the reverse reaction had no significance. Well beyond it, the kinetic effect of the reverse reaction can indeed be seen.

TABLE 1. *Showing the absence of Farhat-Aziz and Moelwyn-Hughes's alleged effect of vapour space on the rate of reaction between methyl iodide and lithium chloride in anhydrous acetone at 25·20°.*

(In all four runs the initial concentrations were: a = [MeI] = 0·05725, b = [LiCl] = 0·02960, [$LiClO_4$] = 0·09475M. Aliquot parts of 6·81 ml. were titrated electrometrically with 0·0200M-$AgNO_3$ for I^- and for total Hal^-. The constants, in sec.$^{-1}$ mole^{-1} l., were calculated from $k_2 = [2{\cdot}303/t(a - b)] \log_{10} [b(a - x)/a(b - x)]$. In the runs in flasks, the vapour space increased as samples were withdrawn, but k_2 did not drift, as is further illustrated in Table 2. Runs 3 and 4 were performed together, so that nothing differed except the size of the flasks.)

Run	Vessel(s)	Initial vol. soln. (ml.)	Approx. vol. vapour (ml.)	Mean 10^3k_2	Std. devn.	No. of readings *
1	7·3 ml. ampoules	6·81 each	0·5	5·33	0·26	9
2	" 100 ml." flask	100	5—95	5·49	0·13	8
4	" 100 ml." flask	100	5—95	5·40	0·12	8
3	" 1000 ml." flask	100	910—990	5·33	0·12	7

* Number giving k_2 values, of which means and standard deviations are quoted; not counting " zero " and " infinite " time readings.

TABLE 2. *Showing the insignificance, over more than* 70% *of the reaction between methyl iodide and lithium chloride in acetone, of Farhat-Aziz and Moelwyn-Hughes's alleged kinetic disturbance by the back-reaction.*

(Run 2: Initial conditions, analytical method, and calculations, as noted at the head of Table 1.)

t (min.)	Reaction (%)	10^3k_2	t (min.)	Reaction (%)	10^3k_2	t (min.)	Reaction (%)	10^3k_2
0·0	4·9	—	24·0	37·0	5·56	150	83·7	5·18
4·0	11·1	5·51	36·0	46·0	5·25	260	89·0	3·43 *
6·0	14·8	5·84	50·0	56·6	5·47	800	93·7, 94·6	—
12·0	23·3	5·68	100	76·8	5·42	900	94·0	—

Mean k_2 (excluding value marked *), 5·49 × 10^{-2} sec.$^{-1}$ mole^{-1} l. Mean reaction at 20—22 half-lives, 94·1%.

Hughes, Ingold, and Mackie pointed out that, when the constant excess of lithium perchlorate was omitted, the second-order rate-constants diminished as reaction continued, but from the beginning, whereas they had found, as we have confirmed, that, in the initial range and for quite a long way forward, the back-reaction had no inportance. They interpreted the drift as arising from a negative salt effect, such as is general to, and expected for, bimolecular Finkelstein reactions, and in particular from the replacement of a weaker by a stronger salt as reaction proceeds. Therefore they added, in constant excess, the chemically inert salt, lithium perchlorate, which, as expected, reduced the rate and cut out the drift: this was obviously the simplest way for those authors to fulfil their purpose, which was to set up standard conditions for comparing the kinetic effects of different alkyl groups on the reaction.

Farhat-Aziz and Moelwyn-Hughes's next allegation is that Hughes, Ingold, and Mackie have misdescribed the drift. They claim that there is no drift due to salt effects, and that the drift observed by Hughes, Ingold, and Mackie arises from the back-reaction. They admit that the effect of added lithium perchlorate is " difficult to interpret " satisfactorily on that basis. They add, however, that " the treatment for opposing bimolecular reactions satisfactorily fits the facts, and no drift can be detected in either velocity coefficient."

This statement, so far as it concerns the velocity coefficient of the reaction between methyl iodide and lithium chloride, is not only unsupported by any data that we can find in Farhat-Aziz and Moelwyn-Hughes's paper, but also is in conflict both with Hughes, Ingold, and Mackie's findings and with the present re-investigation. In order to test the point, we have carried out four new experiments on the reaction between methyl iodide and lithium chloride in acetone, in the absence of lithium perchlorate (nos. 5—8). An example is given in Table 3. In all these runs, we observed the downward drift, as reported by Hughes, Ingold, and Mackie, in the stoicheiometric second-order rate-constant throughout the first 70% of reaction, where, as we have seen, the kinetic effect of the reverse reaction is insignificant. As Hughes, Ingold, and Mackie found, this drift not only sets in much too early to be understood on the basis of the known equilibrium, but also is eliminated, with lowered rates, in parallel runs in the presence of excess of lithium perchlorate.

TABLE 3. *Confirming the salt effect in the reaction between methyl iodide and lithium chloride, by showing that the progressive negative effect sets in earlier than the equilibrium could account for, and is suppressed by excess of lithium perchlorate.*

(Expt. 6. In anhydrous acetone at 25·20°. Initially, [MeI] = 0·02862 and [LiCl] = 0·01480M. Analytical procedure and calculations as noted at the head of Table 1.)

Run 6a. Without $LiClO_4$.			Run 6b. $[LiClO_4]$ = 0·09475M.		
(min.)	Reaction (%)	10^3k_2	t (min.)	Reaction (%)	10^3k_2
0·0	22·1	—	0·0	3·9	—
1·0	26·5	37·8	8·0	9·0	5·32
2·0	30·7	38·4	12·0	13·1	6·17
4·0	36·5	34·0	25·0	23·0	5·83
7·0	44·5	33·1	45·0	35·0	5·80
9·0	47·7	31·3	85·0	53·2	5·73
13·0	56·5	31·8	115	62·6	5·71
21·0	65·7	28·9	165	73·6	5·67
27·0	70·7	27·6	220	80·5	5·40
200	94·1	—	∞	94·5 *	—

* Calculated from equilibrium constant $K = 16$ (runs 2—4).

Farhat-Aziz and Moelwyn-Hughes purport to summarise Hughes, Ingold, and Mackie's interpretation of these phenomena in the following statement. " They claim that the reaction is subject to a salt effect, which is said to be generic to Finkelstein substitutions, negative in sign, and specific with respect to the cation." Hughes, Ingold, and Mackie did not signalise, or even separately mention, a specific effect of the cation: both ions matter. In part, the salt effect on bimolecular Finkelstein reactions is a special case of the medium effect, theoretically described by Hughes and Ingold in 1935. When we make a medium more polar, whether we do so by changing the solvent, or by dissolving ions in a weakly polar solvent, we stabilise the initial state more than the transition state, in which the ionic charge is more diffuse; and therefore the reaction goes more slowly—very much more slowly, for example, in water than in acetone.

Farhat-Aziz and Moelwyn-Hughes make yet another insubstantial allegation. This is that " Hughes, Ingold, and Mackie treat lithium chloride in acetone solution as completely ionised (or dissociated)." In fact, Hughes, Ingold, and Mackie did not treat the electrochemical condition of lithium chloride at all: they did not need to, concerned, as they were, only with a comparison of the kinetic effect of alkyl groups.*

If they had treated it, they would not have used, as Farhat-Aziz and Moelwyn-Hughes do, Acree's " dual " theory of 1915,† affected as this is, in such an application, by the Bjerrum theory of 1926. For in acetone, the Bjerrum distance is 13—14 Å (depending on temperature), more than 5 times the touching distance of the counter-ions, and, like the distance for a coulombic equipartition energy, of the same order of magnitude as an average solute–particle separation corresponding to the range of concentration used. It is therefore impossible that the functions of the salt can be accurately described in terms of only two sharply differentiated but inherently uniform species, called " associated " and " dissociated," with all chemical and electrochemical activity concentrated exclusively in the latter—which is then, strangely enough, taken as an ideal solute, *i.e.*, as ions without coulombic forces. The door of dissociation in acetone is not restricted to being shut or open, but can be ajar to a continuous distribution of extents, each Boltzmann-weighted extent having its proper chemical and electrochemical activity, and all measurements being of appropriate averages.‡

It was in recognition of this situation that Hughes, Ingold, and Mackie compared their alkyl groups on the basis of stoicheiometric rate-coefficients, as well as for the more general reason for which stoicheiometric coefficients are usually quoted, *viz.*, that they best summarise, because they can be simply back-converted to, the observational rates—as is the function of rate-coefficients. However, it was open to Farhat-Aziz and Moelwyn-Hughes to divide Hughes, Ingold, and Mackie's rates by concentrations other than stoicheiometric, if they wanted to for the purpose of comparison with their own figures. They should certainly not have compared numerically two quite differently defined rate-coefficients. Still more, they should not have called the resulting mismatch a comparison of rates.

We can now see how the magnitude of the grave error, which Farhat-Aziz and Moelwyn-Hughes attempted to fasten on to Hughes, Ingold, and Mackie's rates, is built up. In an equilibrium medium, the rates of the opposing reactions are indubitably equal. We can deduce the rate of one reaction from that of the other more generally (at the same temperature) if we can make the proper allowances for changes in medium composition. In

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* A paper by Winstein, Sevedoff, and Smith has just appeared,[6] which cites that by Farhat-Aziz and Moelwyn-Hughes and repeats their mistake of treating incomplete salt dissociation as a mutually exclusive alternative to a salt effect, as well as repeating their complaint that Hughes, Ingold, and Mackie neglected the former. Neither of the two other groups of authors seems to have realised that the term " salt effect " is phenomenological (one adds a salt and it has an effect), with no limitation of physical mechanism, except the implication, common to all medium effects (solvent or salt) of a differential interaction with an initial state and a transition state. If we build up the concept of a Finkelstein reaction, starting from the essential bond-change, say, $Cl^- + RI \longrightarrow ClR + I^-$, at first without reference to solvation shells or close gegen-ions, and then in imagination add a more polar solvent, *e.g.*, water to acetone, a retardation will ensue; and we shall explain that on the basis that the water associates more with the initial-state ion Cl^- than with the transition-state ion $(ClRI)^-$. If, instead of adding water, we add lithium ion, replacing some large cation by this small one, a retardation will again ensue; and we can analogously say that Li^+ associates more with Cl^- than with $ClRI^-$; or, neglecting the strict differential aspect, we could say, simply, that Li^+ associates with Cl^-. However, the latter statement is an approximation to the former, not a contrary alternative.

† Farhat-Aziz and Moelwyn-Hughes do not cite Acree's original papers on this subject, but do cite a paper by Evans and Sugden,[7] which applies the theory and cites its literature.

‡ There are, of course, circumstances in which the use of a crude model, such as that of Acree in ion-pairing solvents, would be justified as the simplest approach to a broad comparison; it would be justified, for example, in a comparison of nucleophilic powers among a variety of anions. Here we are merely pointing out that no considerations were before Hughes, Ingold, and Mackie which would require them to adopt such a model.

[6] Winstein, Sevedoff, and Smith, *Tetrahedron Letters*, 1960, **9**, 24

[7] Evans and Sugden, *J.*, 1949, 270.

Acree-type calculations on Farhat-Aziz and Moelwyn-Hughes's runs, it emerges that the ratio [LiCl]/[" dissociated " Cl^- as calculated], at equilibrium, always amounts to some hundreds: in the one fully recorded kinetic run, it is close to 300. Hence the ratio, $k_{\text{Acree}} : k_{\text{stoicheiometric}}$, of the two coefficients by which one might alternatively describe the same rate of the same reaction is here about 300. And since at equilibrium the rates of the opposing reactions are equal, one *can*, if one feels justified, apply one figure to one reaction and the other to the opposing one. This provides the main component of the claimed rate discrepancy. Then, the standard excess of lithium perchlorate, in the presence of which Hughes, Ingold, and Mackie made their comparisons, reduced their rates, and likewise their rate-coefficients, by a factor of about 4. Apparently, Farhat-Aziz and Moelwyn-Hughes even felt justified in taking that in, so using the product of the factors in order to compose their alleged discrepancy " by a factor of more than 1000," which, well confused with baseless detailed criticisms, they laid, inapplicably, to Hughes, Ingold, and Mackie's account.

EXPERIMENTAL

Materials.—Methyl iodide was decolorised by means of mercury, dried (K_2CO_3), and distilled; it had b. p. 42—43°/750 mm. A stock solution in acetone was prepared, and, after 2 weeks, was free from iodide ion and acid on dilution with water, but gave 100·0% of both on hydrolysis at 100°. Lithium chloride and lithium perchlorate were crystallised from acetone–benzene, collected under dry nitrogen, and dried in a vacuum at 120° over phosphoric oxide. Stock solutions of the salts in acetone underwent no change in 2 weeks, and gave, respectively, 100·0% and 0·0% of chloride ion. " AnalaR " acetone was distilled from magnesium perchlorate. Parallel rate measurements in the original and dried solvent gave identical results, and hence no more extensive drying was attempted.

Kinetics.—Runs were done in ampoules and in volumetric flasks. The contents of ampoules were enclosed in them at 0°, and 5 min. with shaking were allowed to bring them to thermostat temperature. The components of mixtures to be made in volumetric flasks were separately brought to thermostat temperature first, and thus the time zero could be taken somewhat sooner after making the mixtures. Samples were quenched by pouring them into ice-cold water. They were titrated electrometrically with silver nitrate, after addition of enough solid barium nitrate to make a solution 5% in that salt. A duplicate titration on a sample kept for 15 min. in ice-water gave the same content of iodide and chloride ion, thus showing that the quenching was effective. Our practice was to measure iodide, total halide ion, and pH. The total halide and the pH (5·2—5·4) remained constant throughout each run.

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