LETTERS TO THE EDITORS

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Medical and Other Patents for the Use of Mankind

BEFORE the War my laboratory was supported by the Josiah Macy Jr. Foundation, New York, receiving 3,000 dollars a year. This help enabled me to work without limitation and publish without restriction. During the War, this help ceased and forced me to seek the help of industry. I worked out a method for the preparation of a substance of high biological importance and therapeutic value, a substance which has found no application yet for lack of a suitable method of preparation. As a recompense for the help obtained, I had to offer this method to industry and keep it secret. The result is that for the sake of 10,000 dollars a substance is inaccessible which could relieve much human suffering. In the present financial conditions of my country, the State is unable to give necessary support for research; and I, having greatly extended my laboratory, am compelled to seek further collaboration with industry. Possibly my work will lead shortly to the discovery of new, highly important substances, and I shall be unable to talk about them freely. The other laboratories and research workers of my country are in a similar condition and the free, generous, international spirit of science is endangered. Maybe my country, being small and poor, does not matter much; but such trends spread easily and should be suppressed at their roots.

I wish to submit this problem to readers of *Nature*. I wonder whether the United Nations Educational, Scientific and Cultural Organisation could do something in this matter, perhaps suggesting to chemical industries the creation of an international fund for the support of research and for purchasing patents for the common use of mankind or, at least, for the use of the contributors, enabling at the same time researchers to work and publish freely. I expect most research workers would prefer to offer their work and results to such a body, which may even solve the old problem of how scientific men can be protected from exploitation and enjoy the fruits of their own work without disadvantage to the human community.

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Reactions of Organic Halides in Solution

DR. A. G. EVANS has recently discussed those bimolecular and unimolecular substitutions in which a nucleophilic reagent displaces halogen as halide ion from an alkyl halide[1].

With reference to the bimolecular reactions (S_{N2}), he ascribes to us the view that the diminution of rate along the series Me, Et, *i*-Pr, *t*-Bu is entirely due to the polar effect of the alkyl group. This is a mistaken presentation of our ideas. For, in the first place, we regard the polar and steric effects as both contributing to the structural influence on rate: we stated this qualitatively in 1935[2], and have more recently indicated means of assessing quantitatively the separate effects[3]; furthermore, in 1937[4] we emphasized the special importance of steric hindrance (which has its physical basis in the exclusion principle) in relation to the spatial orientation of bimolecular substitution, contrary to an earlier idea[5] that polarity was determinative in this connexion. The second important point is that, as we have repeatedly insisted, the polar effect in bimolecular reactions is itself ambiguous[6]: it includes a polarizability effect, and therefore depends (for substitutions) not only on the compound substituted, but also on the substituting agent and the solvent. For example, in substitutions of alkyl halides in polar solvents by simple anionic reagents, such as halide or alkoxide ions, the polar effect may be expected to lead to rate differences in the direction illustrated; but this inference from simple electrostatic considerations does not embrace corresponding substitutions by such neutral reagents as pyridine. Our picture of the situation has been explained at length in our papers, and is not susceptible of the type of simplification with which Evans has tried to represent it.

Evans himself takes the extreme view that the polar effect envisaged by us is completely absent from the bimolecular substitutions, though steric hindrance remains important[7]. That the polar effect is not absent in general from bimolecular nucleophilic substitutions is consistent with the result of exchanging the electron-releasing methyl substituents for electron-attracting groups: here, in the case of substitution by anionic reagents, we find that the effect of the substituent, in spite of steric hindrance, is often accelerative. We pointed this out in 1935, using the illustrations then available: several new examples have since been recorded. For an assessment of the relative importance of polar and steric effects in cases in which both reduce reaction-rate, we again refer to our general discussion[3]. We agree that steric hindrance is present in the bimolecular substitutions of α-methylallyl halides: Catchpole had pointed this out[8], and the case is included by implication in our general consideration of steric hindrance by alkyl groups. The conclusion does not, however, follow logically from Evans's argument, which, by carrying over a rate comparison of two compounds from one reaction mechanism to another, ignores the duplex nature of polarity and the dependence of polarizability effects on mechanism[6].

Turning to the unimolecular substitutions (S_{N1}), the rates of which are controlled by the rates of ionization of the alkyl halides, Evans concludes that the increase of rate along the alkyl series Me, Et, *i*-Pr, *t*-Bu is 'due to' the decrease of ionization potential of the alkyl radical. We agree that the two phenomena are related, but would prefer to express the relationship by saying that the increase of ionization-rate and the decrease of ionization potential (in other words, the ease with which an alkyl cation separates, on one hand, from an anion, and on the other, from an electron) are analogous manifestations of the same structural causes.

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June 14.

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Friedel–Crafts Catalysts and Polymerization

IN an earlier communication[1], evidence was given upon which the following conclusion was based. In the dimerization of di-isobutene and the polymerization of isobutene, it is essential that a trace of some third component, X, shall be present in addition to the monomer and the Friedel–Crafts catalyst, in order that the reaction shall proceed at an appreciable rate. It was suggested then that this third component was probably water. We have continued this line of investigation by studying the boron trifluoride-catalysed polymerization of isobutene in the gas phase using high-vacuum technique. The polymerization reaction was followed by mixing the boron trifluoride and the isobutene in the gas phase and measuring the fall in pressure with time. We may summarize the results as follows:

(*a*) The unpurified isobutene, taken straight from the cylinder, reacts rapidly when its pressure is greater than a certain value (Curve *A*).

(*b*) Isobutene, purified by many distillations from − 80° C. to liquid air *in vacuo*, reacts very slowly under conditions which are otherwise identical with those for the experiments described in (*a*) (Curve *B*).

(*c*) The purified isobutene reacts rapidly if mixed with vapour of the residue from the distillation described in (*b*) (Curve *C*).

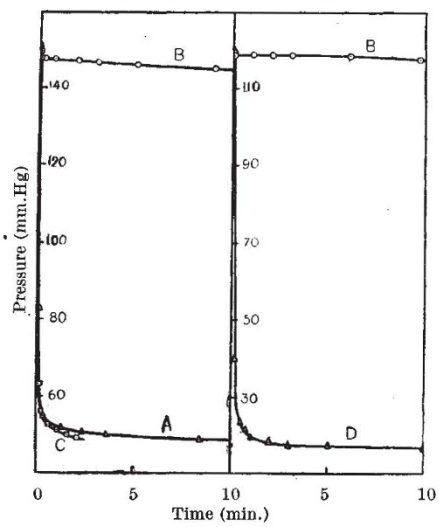
(*d*) This residue was identified as water by measurements of vapour pressure and freezing point.

(*e*) Purified isobutene reacts rapidly if previously mixed with water vapour. So little as 10^{-1} mm. of water vapour is sufficient to give the rapid reaction (Curve *D*).

(*f*) When water is present with the isobutene in the gas phase, part of the boron trifluoride which is introduced into the mixture is removed by combination with the water. The boron trifluoride and water combine in practically equal molar quantities.

(*g*) When water had been added to purified isobutene to cause the rapid reaction in one experiment, the addition of boron trifluoride to the purified isobutene alone in the subsequent experiment was sometimes found to lead to rapid reaction. If the reaction vessel was pumped out for about half an hour between the two experiments, however, the purified isobutene used alone in the second experiment did not give the rapid reaction on addition of boron trifluoride.

We conclude from these experiments that for isobutene to be rapidly polymerized in the gas phase, the presence of both BF_3X and excess boron trifluoride are necessary. In the experiments described in this communication, the third component, X, is water.



A, UNPURIFIED ISOBUTENE; *B*, DISTILLED ISOBUTENE; *C*, DISTILLED ISOBUTENE PLUS 1% RESIDUE VAPOUR; *D*, DISTILLED ISOBUTENE PLUS 0·1% WATER VAPOUR