Introduction of Substituents in the Aromatic Nucleus. Exploration of its Mechanism by means of Isotopic Hydrogen

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The heavy isotopes of hydrogen, deuterium (^{2}H) and tritium (^{3}H), offer a means of determining the slow step of some of the common reactions by which substi-

difference for the initial bonds, and the latter being the predominating quantity will cause a measurable difference in reaction velocity.

Thus a substitution of the pure S_E2 type should show such a difference, and if a molecule carries hydrogen atoms of different mass in symmetrical positions, the light-weight atoms should be substituted more frequently than the heavy ones. The product will then contain a higher proportion of the heavy isotope than the starting material.

In the case of an addition mechanism of the »π-complex» type [1] two things may happen. Either of the two steps may be
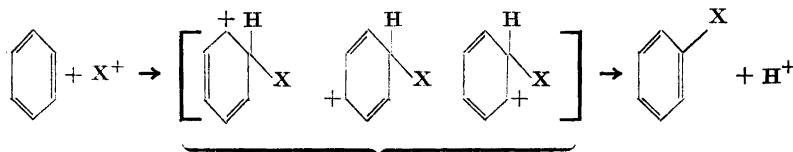
mesomerism
(written explicitly for the intermediate only)

tuents are introduced in the benzene nucleus. Hitherto it has not been settled whether the nitration, bromination, alkylation, *etc.* of benzene and related compounds are true substitutions (of the S_E2 type) or primarily additions of the positive ion to the aromatic nucleus by means of the π electrons of the latter [1]. (Hardly any other type of reaction seems to come into question. It seems quite certain that the substituting agent in these reactions is the corresponding cation.)

If the splitting off of hydrogen takes part in the rate-determining step of the reaction, a position carrying a heavy hydrogen isotope should react more slowly than one carrying protium, owing to the lower zero point energy of the former bond. Generally, the difference in zero point energy between the »activated complexes» of the two reactions only partly counterbalances the corresponding

rate-determining. Since the intermediate has never been caught in these cases, the second step is probably rapid. The first step is likely to determine the rate, and this addition should be practically independent of the mass of the hydrogen atom. According to this mechanism, light and heavy hydrogen should be substituted in the same proportion as they occur in the starting material, and the isotopic ratio should remain unchanged during the reaction.

A necessary condition for the realization of such experiments is that no hydrogen exchange between different reactants occurs.

By means of tracer amounts of tritium and comparison of the specific radioactivity [2] of the reactants and the products, it has been shown that the nitration of toluene [3] and benzene (two nitro groups introduced by means of nitric-

sulphuric acid mixture) follows the π-complex mechanism, as found in quite another way by Ingold *et al.*[4], who very kindly communicated this result to the writer. By the same tritium method it has been found that the introduction of a nitro group in *a* position in naphthalene by means of nitric acid follows the same mechanism.

Preliminary experiments seem to indicate that the bromination of benzene in the presence of iodine follows mainly the same course.

The chlorination of toluene in *a* position in the absence of catalyst and in the presence of light, in which chlorine atoms probably remove hydrogen atoms (in any case π-complex formation is impossible in this aliphatic substitution), has been found to prefer light atoms to heavy ones.

Other substitution reactions are being investigated in the same manner.

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2. Melander, L. *Acta Chem. Scand.* **2** (1948) 440.
3. Melander, L. *Nature*, in print.
4. Gillespie, R. J., Hughes, E. D., Ingold, C. K., Millen, D. J., and Reed, R. I. *Nature*, in print.