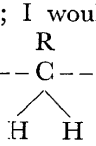
SESSION VI

II. INVESTIGATIONS OF ISOTOPE EFFECTS IN ORGANIC SYSTEMS (Part C)

Application of the Successive Labelling Technique to some Carbon, Nitrogen and Chlorine Isotope Effect Studies of Organic Reaction Mechanisms—A. FRY, *University of Arkansas, U.S.A.*

Question: Several years ago, Dr K. R. Lynn and I† published ^{13}C isotope effect values for cyanide ion and methylene carbon "labelling" in the cyanization of methyl iodide in aqueous solution. For cyanide carbon isotopy, (k_{12}/k_{13}) was $\simeq 1{\cdot}01$ and for methylene carbon isotopy it was $\simeq 1{\cdot}06$, values which correspond well with your values for the corresponding (k_{12}/k_{14}) in the benzyl chloride system. However, even after making allowance for the differences between methyl iodide and benzyl chloride, your ^{14}C isotope effects seem small in comparison with our ^{13}C isotope effects. Is there a simple explanation for the difference?

It does not appear difficult to explain a low isotope effect for cyanide ion isotopy, but I am confused by the size (in both the cases mentioned in my first question) of the isotope effect for carbon isotopy in the —CH_2— group; I would have regarded the transition state for this process as



NC---C---X, and would have expected a rather modest isotope effect, whereas a somewhat substantial one is observed by both of us. How do you interpret these experimental findings? P. YANKWICH, *University of Illinois, U.S.A.*

Answer: To the extent that the benzyl chloride reaction goes by an S_N1 mechanism (as seems to be indicated by a comparison of the size of the chlorine isotope effect and the other chlorine isotope effects mentioned here), we would expect a relatively smaller isotope effect for this compound than for the methyl system explained in the paper. Our value for the cyanide isotope effect is not much more than a rough estimate, and may, in fact, be comparable to your value. Alternatively, it might well be that a smaller effect would be expected in the benzyl system (S_N1-like) than in the methyl system (S_N2-like). Further refinement in our qualitative analysis would be required to make a definite statement on this point.

In line with the analysis presented in the paper, I would expect a large central carbon isotope effect for both the benzyl and methyl systems,

† Work cited in Reference 13.

with a value for the methyl compound (S_N2-like) considerably larger than that for the benzyl compound (S_N1-like). The main difference between the two systems will lie in the additional bonding (by resonance and solvation) in the benzyl (S_N1-like) activated complex compared with the methyl compound. The additional bonding (A - - - R interactions in our symbolic representation) will reduce the isotope effect for the benzyl compound. FRY

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Question: Have you been able to correlate your isotope-effect results for benzyl chloride reactions with kinetic evidence of a transition in mechanism, such as can be obtained by trapping experiments using, for instance, mixtures of nucleophiles? D. SAMUEL, *Weizmann Institute of Science, Israel*

Answer: We have not carried out the experiment you suggest, but have done a good deal of kinetic work on the system, and the kinetic- and isotope-effect results dovetail quite well. We plan additional kinetic experiments in connection with our benzyl carbon isotope-effect measurements. The kinetic work we have done so far is covered in some detail in Reference 15. FRY

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Comment: I think your statement that isotope effects are indicative of bonding changes at the isotopic position must be modified by saying that this conclusion can be reached only if the isotope effect is different from $\nu_{1L}^{\ddagger}/\nu_{2L}^{\ddagger}$ values which can be obtained without making force-constant changes at the isotopic position. M. WOLFSBERG, *Brookhaven National Laboratory, U.S.A.*

Kinetic Hydrogen Isotope Effects in the Hydration of Isobutene—V. M. GOLD and M. A. KESSICK, *University of London, England*

Comment: In a paper published several years ago, Bunton and I set out an alternative view of these systems, which does not appear to be in conflict with your views, but perhaps has a more mechanistic basis. It can be summarized in the statement that isotope fractionation at low tracer level gives the primary isotope effect due to frequency changes in the atom in the course of transfer between initial and transition states, whereas rate comparison between isotopically pure solvents gives a combination of this primary effect and a *secondary* effect mainly produced by isotopic substitution for the two hydrogen atoms of the hydronium ions which are *not* transferred. It is concluded that the ground-state frequencies for the tracer experiments are those of the water molecule and not the hydronium ion, whereas on comparing the rates in pure solvents at the same hydronium ion concentration, the hydronium ion should be considered the ground state. V. J. SHINER, JR., *Indiana University, U.S.A.*

Reply: My treatment also includes secondary isotope effects by isotopic substitution of the non-transferred hydrogen atoms of the hydroxonium ion.

When calculating isotope effects in mixed media, on the basis of empirical partition fractions, it is always possible to choose either the water molecule or the hydroxonium ion as the "ground state". It depends whether the measured isotope effect is expressed relative to isotopic abundance in water or in hydrogen ions. In the latter case, the isotope fractionation between water and hydrogen ions must be taken into account and, as this gives the mechanistically correct picture of a proton transfer from the hydrogen ion (rather than from water), this is the procedure we have chosen.

For a comparison between tracer-level T- and solvent D-isotope effects, consistency demands that H_2TO^+ should be taken as the ground state for triton transfer in H_2O, if D_3O^+ is taken for deuteron transfer (in D_2O). GOLD

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Comment: It is only important or relevant to consider the difference in the chemical bonding between the substrate and the transition state and all kinds of pre-equilibria are possible. In the present case, this leads to distinguishing quite clearly between two types of experiment—the tracer experiment and the experiment in pure media. Oversimplifying and assuming a reaction without acid catalysis, let us consider the cases of tracer-labelled water and pure water.

If, in an experiment with tracer-labelled water, the alcohol is isolated and the tracer can be seen in the CH-bond and all the tracer is washed out of the hydroxyl group in the product isolated, it is clear that on analysing the tracer in the CH-bond, only the rate ratio of the proton and its isotopic substituents in passing to the CH-bond will be measured.

In an experiment with, let us say, pure water and pure D_2O, there will be additional complication if, during the rate-determining stage, there is a change in the bonding of the proton in the hydroxyl group. J. BIGELEISEN, *Brookhaven National Laboratory, U.S.A.*

Reply: When we examined this problem we were, in fact, very careful to bear in mind the possibility that product-forming and rate-controlling steps in this reaction might be different. However, our results so far do not give grounds for such a view. GOLD

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Comment: In order not to revive the argument about mixed H_2O/D_2O media, let us accept the fact that by a suitable choice of parameters it would probably be possible to wash out the expected Gross–Butler "bulge" and get reasonable agreement with experimental results.

However, to one who is not convinced that the Gross–Butler treatment has theoretical validity, the situation seems to be as follows: The distinctive feature of the Gross–Butler equation is the "bulge" at low k_H/k_D values.

The only experimental indications of such a bulge of which I am aware are the rather unconvincing ones in the hydration studies carried out by Purlee and Taft, and these have just been shown to be almost totally unrelated to the question of proton solvation.

It follows, unless what I believe to be undue weight is placed on the relatively minor differences predicted by different models in the region of large k_H/k_D values, that there is no experimental support for the Gross–Butler equation. Consequently, as pointed out in the paper by Long, Paul and myself, very little mechanistic information can be obtained from mixed-medium studies of mechanism. E. A. HALEVI, *Institute of Technology, Israel*

Competitive Deuteration of Toluene and Toluene-α, α, α, α-d_3—W. M. LAUER and K. C. SENAN, *University of Minnesota, U.S.A.*

Comment: If there is no independent reason for rejecting the earlier results obtained by Koons and yourself (Reference 1), perhaps they are not really contradicted by your present data from the competitive method. In a direct kinetic study of the same type as you and Koons carried out, secondary isotope effects showed up where you found ordinary substituent effects; whereas in the competitive experiments ordinary substituent effects and secondary isotope effects both disappear. My reason for wanting to save the earlier results is that I have tried† to make some use of the difference between them and the lack of an isotope effect in the more acidic and less selective conditions in which Kresge and Satchell (Reference 3) worked, and also of the somewhat different behaviour observed by Swain, Knee and Kresge (Reference 2) in nitration and bromination. E. A. HALEVI, *Institute of Technology, Israel*

Reply: The results quoted were obtained in a lower aromatic hydrocarbon concentration than the 24·6 mole per cent value which showed the large difference as a function of molecular weight. We realized of course that if there were no differences in the competitive case, then perhaps, the large differences in the case of high aromatic hydrocarbon concentration would disappear on decreasing the concentration. This is, of course, true; *i.e.* one can substantially reproduce the competitive results with alkyl benzenes by selecting low concentrations, although this naturally leads to experimental difficulties, because of the very small amount of aromatic hydrocarbon then available. However, I am aware of no reason for eliminating the earlier results, other than the possibility of exchange due to the primary isotope effect on passing from tri-alpha deuteriotoluene to benzoic acid, and the fact that the mass-spectrometric values seem to be a little more direct. LAUER

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Question: I do not understand why the competitive results and the separate measurements give different substituent effects. V. J. SHINER, JR., *Indiana University, U.S.A.*

† E. A. Halevi. *Progress in Physical Organic Chemistry*, Vol. 1, Chapter IV, Interscience, New York (1963).

Answer: We attribute this to a solvent effect. These are molar percentages and as the concentration of aromatic hydrocarbon is increased molarwise the solvent becomes more hydrocarbon-like. In addition, there is undoubtedly association in the case of trifluoroacetic acid and all these factors affect the nature of the solvent. LAUER

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Comment: Might this process not involve something a little more fundamentally mechanistic? I am very surprised that Swain, Knee and Kresge did not find a larger hyperconjugative isotope effect in the experiments to which you referred and wonder if this does not in some way reflect the fact that this was a competitive experiment, whereas the others were not. There may be some clue here to the source of the difference. V. J. SHINER, JR., *Indiana University, U.S.A.*

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Comment: Acid-catalysed aromatic hydrogen exchange is a reaction with two rate-determining steps, in which the observed rate constant is a function of k_1, the rate constant for electrophilic attack, and an intramolecular isotope effect:

$$H'Ar + HA \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} H'ArH^+ + A^- \xrightarrow{k_2} ArH + H'A$$

$$k_{obs.} = \frac{k_1}{1 + k_{-1}/k_2}$$

The rate constant of importance for discussions of the type we are having here is k_1, but k_1 is not always directly proportional to $k_{obs.}$: k_1/k_2 can change from case to case. It is dangerous, therefore, to draw conclusions from small differences in observed aromatic exchange rates. A. J. KRESGE, *Illinois Institute of Technology, U.S.A.*

Effect of Deuterium Substitution on the Solvolysis Rates of (Methylcyclopropyl)-carbinyl Derivatives—D. E. SUNKO *et al.*, *Institute "Ruder Bošković", Yugoslavia*

Question: Are not different proportions of the products (olefins, substitution products and rearranged compounds) formed in the hydrolysis of the various cyclic tosylates? If so, does this not indicate different transition states for these compounds, making direct comparison of rate constants and isotope effects more difficult? D. SAMUEL, *Weizmann Institute of Science, Israel*

Answer: The product composition is different for the various substituted cyclopropyl derivatives and this naturally makes it possible that the transition states might be somewhat different. SUNKO