

SESSION IV

II. INVESTIGATIONS OF ISOTOPIC EFFECTS IN ORGANIC SYSTEMS

(Part A)

Secondary Isotope Effects on pi-complex Formation—E. A. HALEVI and B. RAVID, *Institute of Technology, Israel*

Question: Are you suggesting that there is an influence on the small inductive effect of alkyl groups (due to the presence of a counter-ion, for example) which is not characteristic of the larger inductive effects of other groups, indicated by their σ' constants! V. J. SHINER, JR., *Indiana University, U.S.A.*

Answer: Yes, but the suggestion is hardly original. The electron-releasing effect of a substituent depends on its intrinsic polarity and its polarizability.

In a substituent like-NH₃⁺, the former is predominant and the latter may be neglected by comparison. In the case of alkyl groups, which have only slight intrinsic polarity, polarizability (or what Ingold calls "interaction polarization") should predominate. I believe that this is what causes much of the confusion about the assignment of σ , σ' , and σ^* values to alkyl substituents. HALEVI

Steric origin of some Secondary Isotope Effects—V. F. RAAEN and C. J. COLLINS, *Oak Ridge National Laboratory, U.S.A.*

Question: Your experiments show a precision in the data for ¹²C/¹⁴C isotope effect which is about an order of magnitude better than most data in the literature. Could you kindly elaborate on the precision, accuracy and reproducibility of your individual experiments, and state the number of completely independent measurements made? I am thinking particularly of different samples of tracer-marked material purified by various processes. This point is the source of one of the most important problems in the study of isotope effects. J. BIGELEISEN, *Brookhaven National Laboratory, U.S.A.*

Answer: The errors were determined by computer with an accuracy within 0.2 per cent, averaged over 3 or 4 determinations, each of which involves several factors. The carbon-14 values were obtained with ion chambers, which, in our opinion, give the most accurate figures obtainable. We do not use Braun tubes as we work with fairly high levels of activity, usually of the order of 6–10 mc/mole. Instead, we use meter relays to determine the timing sequence, so that we can start and stop our clocks without

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worrying about the large driving mechanism, which is a source of some uncertainty in the Braun tube. This, I think, helps us to secure accuracy. Our samples are burnt by a dry combustion technique which is a modification of Tolbert's technique.

Moreover, the fact that the deuterium will exchange over a certain period makes it necessary to carry out all the experiments in one day, so as to ensure consistent results. We believe that this keeps exchange to within 1 per cent. One experiment, including weighing and computing, can be completed in 20 minutes. RAAEN

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Question: The beta secondary ^{14}C isotope effects which you determined had values of 1.0085 and 1.0038 respectively in acetophenone- β - ^{14}C and acetophenone-phenyl-1- ^{14}C . Although it is possible that there are sufficiently large force-constant changes at the carbon positions, under your conditions, to yield isotope effects of this magnitude (and they would then have to be different at the two different beta carbons), perhaps these isotope effects reflect largely $\nu_{1\text{L}}^\ddagger/\nu_{2\text{L}}^\ddagger$ values (see the paper by Wolfsberg and Stern, *Pure Appl. Chem.* **8**, 225, 325, 1964) and may therefore throw interesting light on the reaction motion here. If the values of the isotope effects do reflect $\nu_{1\text{L}}^\ddagger/\nu_{2\text{L}}^\ddagger$, it is to be expected that they will be fairly temperature-independent. Temperature-dependence measurements of these effects would thus be of great interest. Matters may be complicated by having effects which reflect both $\nu_{1\text{L}}^\ddagger/\nu_{2\text{L}}^\ddagger$ and force-constant changes. M. WOLFSBERG, *Brookhaven National Laboratory, U.S.A.*

Answer: It is difficult to determine isotope effects of the order of magnitude observed for the secondary carbon-14 effects. I believe that moderate temperature effects could be detected in the reaction of acetophenone-methyl- ^{14}C (with 2,4-dinitrophenylhydrazine), over the practical temperature range of -70 to $+70^\circ$. The suggestion is certainly worth consideration. RAAEN

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Comment: The isotope effect of deuterium substitution adjacent to the carbonyl group in your reaction is very close to the inverse of a similar isotope effect observed by Cross and Shiner for the acid-catalysed hydrolysis of ketals. Since the rate-determining step which you propose for your reaction is essentially the inverse of the rate-determining step in the hydrolysis of ketals, the experimental results are consistent. Further, I do not believe that hyperconjugation can be ruled out as an important contributing factor for these effects—though it does not of course, contribute to the effects caused by deuterium substitution further away from the reaction centre.

With regard to Dr Wolfberg's suggestion, it should be pointed out that, some years ago, Professor Streitwieser suggested that the hyperconjugative interaction was principally due to an influence on the bending mode. V. J. SHINER, JR., *Indiana University, U.S.A.*

Reply: The reaction is complex and we have been forced to make two assumptions: first, that the rate-determining step is the attack by the base; and, secondly, that no change in mechanism occurs on going from one ketone to another. If, instead of limiting ourselves to steric effect, we consider also inductive and hyperconjugative effects; we must assume that both effects operate for methyl- d_3 propiophenone and that only hyperconjugative effects are involved for the remaining ketones and methyl- d_3 -*o*-tolualdehyde. For the latter, the hyperconjugative effect—if operative—should be larger. RAAEN

Comment: I support Dr Shiner's comment on the possible importance of the methyl bending motions in "hyperconjugative" isotope effects. The striking feature in the infrared spectrum of the hexamethylbenzene-chloramil complex is the enhanced intensity of the symmetric methyl bending mode†, which must mean that this motion is associated with large shifts of charge. Since the complex is a charge-transfer one, these effects must be related to the stability of the complex. The secondary isotope effects in this type of system are in the hyperconjugative direction‡. E. A. HALEVI, *Institute of Technology, Israel*

Question: Using the range benzaldehyde to α -naphthaldehyde, Dr Raaen obtained results for deuterium varying from an inverse isotope effect to no isotope effect. Using tritium, we found a normal isotope effect in the case of the β -naphthaldehyde§. What is the reason for this change in the direction of the isotope effect? H. SIMON, *Technische Hochschule, Munich, Germany*

Answer: The only tentative explanation I can suggest for the change in mechanism is that the dehydration does apply partly and that it operates in the opposite direction. RAAEN

Detection and Computation of Isotope Fractionation in the Adsorption Chromatography of Dual-labelled Compounds—P. D. KLEIN *et al.*, *Argonne National Laboratory, U.S.A.*

Comment: In one of your experiments, you used dihydrolanosterol prepared by catalytic tritiation of the side-chain double bond. I consider it a well-established experimental fact that this method of labelling is not specific. D. SUNKO, *Ruder Bošković Institute, Yugoslavia*

Answer: The hydrogenation of lanosterol over Raney nickel in dioxan has been shown by Bloch to be a mild, non-bond-transforming process which preserves the $\Delta^{8,9}$ bond. It was for this reason that lanosterol was labelled by this means during its conversion to dihydrolanosterol. The fact that the sample was randomized as well as reduced is irrelevant, since tritium was introduced in order to obtain labelled sterol of known purity by *chemical* as opposed to *biological* means. KLEIN

† *cf.* E. A. Halevi and B. Ravid. These proceedings, *Pure Appl. Chem.* 8, 339 (1964).

§ H. Simon and D. Palm. Cited in the paper as Reference 7.