

DISSECTION OF ISOTOPE EFFECTS. I. DISSECTED β -ISOTOPE EFFECTS IN THE SOLVOLYSIS
OF 2-OCTYL BROSYLATE IN 65% AQUEOUS ETHANOL

George A. Gregoriou* and Fannia S. Varveri

Department of Chemistry, N.R.C. "Demokritos", Greek Atomic Energy Commission, Athens, Greece

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One of the many consequences of the concept of carbonium ion intermediates and of the ionization hypothesis in general has been the establishment of the idea that the first step in such reactions is the rate determining one.¹ This idea, in turn, must have a cause and effect relation with the initial establishment of the practice of deriving mechanistic information in solvolyses from a comparison of effects on overall reaction rates, as for example in the case of isotope effects.² Obviously, if product formation is determined after a common and rate determining step, then isotopic or other effects measured on such rates would not be affected by the formation of different products nor by any change in their relative yields. In the reverse case, however, overall reaction rates and effects on them could prove to depend on the different products and their yields; hence, unless this factor is taken into account, effects on rates of solvolytic reactions including of course isotope effects could prove to be inconclusive or misleading. The ideas about solvolytic intermediates have undergone developments, but the acceptance of a rate limiting step preceding product determining ones in many solvolyses has survived.²⁻⁴ Similarly, and even more so, the practice of deriving mechanistic information from a comparison of effects on overall reaction rates has remained more or less in wide use³⁻⁵ even though it is recognized that the same steps may be determining both rates and products in many solvolyses involving intermediates and of course in those that do not.

Our long held objections to some aspects of the ionization hypothesis and resulting developments including the above practice⁶ led to the suggestion^{6a} that the study of effects on overall reaction rates would benefit if supplemented by the study of these effects on the partial rate constants for the formation of the individual reaction products, k_i (eq 1). This communication illustrates the suggested approach^{6a} as applied in the case of isotope effects, and specifically to β -effects in the solvolysis of 2-octyl brosylate (I) in 65% aqueous ethanol.

The pseudo first order solvolytic behavior of the title solvolysis allows the use of eq 1 which leads to eq 2. In these equations, k is the solvolytic rate constant for the overall reaction

$$k_i = k f_i \quad (1), \quad (k_i)_H / (k_i)_D = (k_H / k_D) [(f_i)_H / (f_i)_D] \quad (2)$$

while k_i and f_i are respectively the solvolytic partial rate constant and the mole fraction for the formation of the i th product. Equation 2 gives what will be referred to as "dissected isotope effects" (DIE), $(k_i)_H / (k_i)_D$, from rate and product data; specifically, from the kinetic isotope effect for the overall reaction, k_H / k_D , and the isotope effect on the mole fraction of each individual product $(f_i)_H / (f_i)_D$.

The suggested determination and comparison of such isotope effects on k_i 's, and of other effects on k_i values in solvolytic reactions, is a quite legitimate approach which does not depend on any debatable assumptions. The interpretation, however, of such values is another matter which depends on the mechanism of the reaction and particularly on the relation between rate and product determining steps. Nevertheless, we suggest as a "working approach" the determination and comparison of DIE's the very use and correlation of which should in itself contribute to their inter-

pretation as well as to a better understanding of isotope effects.

Following these considerations, 2-octyl brosylate (I), I-1,1,1-d₃, and I-3,3-d₂ were synthesized, and product and rate data for their solvolysis in 65% aqueous ethanol were determined (Table I).

2-Octanol-1,1,1-d₃ was prepared by the reaction of hexanal with the Grignard reagent of iodomethane-1,1,1-d₃. Ethyl caproate was reduced with lithium aluminum deuteride to give 1-hexanol-1,1-d₂ followed by treatment with phosphorus tribromide to yield 1-bromohexane-1,1-d₂ which reacted in turn as the Grignard reagent with acetaldehyde to give 2-octanol-3,3-d₂. The brosylates of these two alcohols and of 2-octanol were prepared by the usual procedure.

The kinetic isotope effects observed are $k_H/k_{\beta d_2} = 1.332$ for I-3,3-d₂, and $k_H/k_{\beta d_3} = 1.167$ for I-1,1,1-d₃. These effects are similar to the respective isotope effects in the aqueous ethanolysis of 2-pentyl and isopropyl brosylates which are: $k_H/k_{\beta d_2} = 1.317$ for 2-pentyl brosylate in 70% (V/V) aqueous ethanol; and $k_H/k_{\beta d_3} = 1.189$ for isopropyl brosylate in 50% (V/V) aqueous ethanol.^{2,7} The similarity of the β -isotope effects is in line with the accepted² similarity in the mechanistic pattern of solvolysis of these compounds. Thus, the interpretation given by Shiner^{2,7} to the isotope effects of 2-pentyl and isopropyl brosylates is obviously supposed to apply to our octyl system as well. According to this interpretation, the β -isotope effect in the solvolysis of 3-pentyl brosylate in 70% aqueous ethanol is of hyperconjugative origin. The significantly larger effect of the β -CD₂ group than of the β -CD₃ one has been explained as the result of a more effective hyperconjugation of a β -methylene group than that of the methyl group. β -Isotope effects have been discussed² also in terms of the percent of the maximum effect of 1.46⁸ (per β -CD₃ group) expected for limiting solvolyses. These percents have also been related to the limiting v_s S_N² nature of the reaction, although not as quantitatively and strictly as for α -isotope effects.² Additionally, these and other deuterium isotope effects have been examined lately in relation to different possible rate determining steps.²

We now wish to apply our aforementioned approach to the present solvolysis. Our isotope effect and product data allow the calculation of the "dissected isotope effects" (DIE's) given in Table I. Their examination indicates that they differ from the overall reaction kinetic isotope effect k_H/k_D as well as between them. Particularly pronounced is the difference between the DIE's for the pathways involving elimination at the position of deuterium substitution and those for the other elimination or substitution reaction pathways; e.g., I-3,3-d₂ gives a DIE of 2.305 for cis-2-octene as compared to 1.177 for 1-octene or 1.210 for 2-octyl ethyl ether. Substitution product formation is associated with DIE's which differ from those of the elimination products to an extent such as 1.134 vs. 1.193 which are the respective DIE's for 2-octyl ethyl ether and cis-2-octene from I-1,1,1-d₃. Differences between the DIE's are observed even between the substitution products themselves. However, the difference is small with a slightly higher effect for the alcohol than the ether product; e.g. I-1,1,1-d₃ gives a DIE for 2-octanol of 1.162 as compared to 1.134 for 2-octyl ethyl ether. Even between trans- and cis-2-octene formation there seems to be a slight difference in the DIE's which for I-1,1,1-d₃ are 1.170 for the trans-isomer as compared to 1.193 for the cis-one, and 2.268 vs. 2.305 respectively for I-3,3-d₂. The DIE's for the rearranged substitution products 3-octyl alcohol and ether are important since these products must be formed by 1,2 hydride shift. However, the very small yield of these products, only 0.33 and 0.14% respectively (Table I), reduces the significance of the values of their DIE's.⁹ With this reservation in mind, one can note that the DIE's for the formation of the two rearranged substitution products are high

TABLE I. Products and Isotope Effects in the Solvolysis of 2-Octyl Brosylate (I), I-1,1,1-d₃, and I-3,3-d₂ in 65% (Wt/Wt) Aqueous Ethanol at 54.0°

Product ^a	Yield, mol% ^{b,c} from:			$(k_{iH}/k_{iD})^{c,d}$ for:	
	I	I-1,1,1-d ₃	I-3,3-d ₂	I-1,1,1-d ₃	I-3,3-d ₂
Overall reaction				1.167 ± 0.008 ^e	1.332 ± 0.009 ^e
2-Octanol	50.43 ± 0.10	50.64 ± 0.14	55.06 ± 0.16	1.162 ± 0.009	1.220 ± 0.010
2-Octyl ethyl ether	29.10 ± 0.09	29.93 ± 0.17	32.01 ± 0.10	1.134 ± 0.011	1.210 ± 0.011
<u>trans</u> -2-Octene	11.41 ± 0.06	11.38 ± 0.09	6.70 ± 0.06	1.170 ± 0.014	2.268 ± 0.030
<u>cis</u> -2-Octene	7.00 ± 0.04	6.84 ± 0.06	4.04 ± 0.03	1.193 ± 0.014	2.305 ± 0.029
1-Octene	1.60 ± 0.01	0.73 ± 0.01	1.81 ± 0.02	2.55 ± 0.06	1.177 ± 0.018
3-Octanol	0.328 ± 0.006	0.334 ± 0.018	0.264 ± 0.010	1.14 ± 0.06	1.65 ± 0.07
3-Octyl ethyl ether	0.139 ± 0.004	0.143 ± 0.003	0.106 ± 0.005	1.13 ± 0.04	1.75 ± 0.09

^aProducts found stable to the reaction and GC conditions. ^bValues given in relative mol% (absolute recovery 100% within experimental error) represent each the average of over twenty GC determinations (from seven final runs) except for that of 3-octanol which is based on few measurements. ^cUncertainties are standard errors for a 95% confidence interval. ^dCalculated from eq 2 from the overall reaction isotope effect k_H/k_D (first entry in the column) and the mole fraction $(f_i)_H/(f_i)_D$ obtained from the respective product yields given in the Table. ^eThese overall reaction kinetic isotope effects k_H/k_D are obtained from our titrimetric rate constants for the solvolysis of I, I-1,1,1-d₃, and I-3,3-d₂ which are respectively (as $k \times 10^2 \text{ min}^{-1}$) 4.425 ± 0.023 , 3.793 ± 0.017 , and 3.323 ± 0.020 . These rate constants represent the average values from between twelve and eighteen rate constant determinations for each ester made by the pH-stat technique.

when the migrating hydrogen atom is substituted by deuterium, e.g., 1.65 and 1.75. However, they are not as high as the DIE's involving elimination of the same hydrogen atom to give the olefins which are of the order of 2.30. Finally, one can also note that the β -CD₂ group gives different DIE's than the β -CD₃ one; e.g., the DIE for the formation of 2-octanol from I-3,3-d₂ is 1.220 as compared to 1.162 from I-1,1,1-d₃. The respective values for the formation of the 2-ether product are 1.210 and 1.134.

As discussed in the introduction, the above determination and comparison of such "dissected isotope effects" is free from any debatable assumptions. We could thus terminate their discussion at this point since their interpretation would require information on the relation between rate and product determining steps which is not available; indeed, although a rate determining first step leading to an ion pair has been suggested,² a definite answer is not available.^{4b} However, and for the purpose of an eventual understanding of the DIE's and mechanism of this solvolysis it is worthwhile to attempt to interpret these DIE values by applying the assumption, introduced as a "working hypothesis and first approximation", that "rates and products are determined in the same steps" or that "the same factors are reflected equally or proportionally in determining rates and products". This assumption which also renders the DIE's in our system into kinetic effects as well allows their direct comparison with the overall reaction kinetic isotope effect k_H/k_D . However, it should be kept in mind that the results of this comparison can be only tentative ones (since a hypothesis is involved) and are a stimulus, and subject to further investigation. Such a comparison suggests the following: (i) The observed kinetic isotope effect $k_H/k_D = 1.332$ for I-3,3-d₂ (and to a smaller extent the value of 1.167 for I-1,1,1-d₃) does not represent a single or single reaction isotope effect nor just a secondary one, and is not just of hyperconjugative origin; instead it is a composite effect made up of widely different isotope effects for different reactions, ranging from a high value of 2.305 for the formation of cis-2-octene down to 1.177 for 1-octene,

and includes the contribution of primary isotope effects associated with the formation of *cis*- and *trans*-2-octenes; (ii) The secondary β -deuterium isotope effect of the β -CD₂ group, which is associated (mainly) with the formation of the 2-octyl alcohol and ether, is indeed larger than the respective isotope effect of the β -CD₃ group leading to the same products; however, the difference between them far from being as large as that of the observed kinetic isotope effects (1.332 vs 1.167) is only e.g. 1.220 vs 1.162 (for 2-octanol). The large difference between the former values is due mainly to the high contribution from primary isotope effects to the isotope effect of the β -CD₂ group (1.332); (iii) Our findings and suggestion that the true secondary β -deuterium isotope effects in our system are smaller than the observed k_4/k_D values introduces some doubts about the secondary nature assumed for the isotope effect of 1.46 observed^a in the trifluoroacetylolysis of isopropyl brosylate which is used as a reference and maximum expected secondary β -deuterium isotope effect (per CD₃ group);² hence, this suggestion may also modify the meaning and significance of the "percent of the maximum effect of 1.46", in terms of which β -effects are sometimes discussed.²

Additional comments and numerous implications of the present approach and findings will have to wait until an answer is offered to the aforementioned hypothesis. One of the lines of approach to this end amounts to extending the above dissection of isotope effects to other reaction conditions and systems. If a consistent and reasonable picture emerges from a correlation of such DIE's, this would in itself provide a test of, and evidence for this hypothesis and its significance; moreover, it would contribute to a better understanding of isotope effects and of the mechanism of solvolytic reactions. Work along these lines is in progress.

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9. The main source of ambiguity is the possibility that some of the rearranged product could be due to contamination of the ester with some 3-octyl ester. Exclusion of 3-octyl alcohol from the 2-octanol used in the synthesis of the esters, and the constancy of the yield of rearranged products which we observed in the solvolysis before and after additional recrystallizations of the esters used, minimize the above possibility but can not exclude it altogether if one takes into account the very small yield of the rearranged products.