is isotope dependent since $Q^D/Q^H = 1.3$–1.4 for indole compounds and unquenched L-trp (Figure 1).[2,3,6] The third process involves intramolecular quenching by the acid form of the amino group of L-trp ($NH_3^+ = X$), and the fraction of molecules carrying NH_3^+ is α. The effect of isotope substitution on this quenching process can arise from differences in the transfer rate of D^+ and H^+ from $-ND_3^+$ and $-NH_3^+$, respectively. In the absence of quencher (un-ionized amino group)

$$Q_0 = \frac{k_1}{k_1 + k_2} = k_1\tau_f \quad (4)$$

where $\tau_f = 1/(k_1 + k_2)$; in the presence of quencher (ionized amino group)

$$Q = \frac{k_1}{k_1 + k_2 + k_3\alpha} \quad (5)$$

Combination of eq 4 and 5 results in

$$\frac{Q_0}{Q} - 1 = k_3\tau_f\alpha \quad (6)$$

The deuterium isotope effect can be expressed as an effect on the rate constant ratio k_3^H/k_3^D, obtained from eq 6 for the two solvents, H_2O and D_2O. This leads to

$$k_3^H/k_3^D = \frac{\tau_f^D\alpha^D[(Q_0/Q)^H - 1]}{\tau_f^H\alpha^H[(Q_0/Q)^D - 1]} \quad (7)$$

At neutral pH, $\alpha^D = \alpha^H = 1$. The lifetime ratio, $\tau_f^D/\tau_f^H = 1.37$, is obtained from the data for L-trp (Figure 1) since quantum yields in these systems are proportional to lifetime.[2,3] In good agreement with this value, a lifetime ratio of 1.39 was obtained from studies of I^- quenching of L-trp at pH 11 in H_2O and D_2O.[20] From eq 7, $k_3^H/k_3^D = 2.7$. This is in reasonable agreement with the value 3.0 calculated by Eisinger and Navon for L-trp at higher temperatures,[4] and is characteristic of isotope effects for nonclassical proton transfer observed in other systems.[21] In the case of L-trp-L-tyr, the slightly larger quantum yield ratio observed in the plateau region compared to the peak region also indicates a similar mechanism. The intramolecular quenching of indole-3-acetamide by glycine and the large isotope effect observed also provide evidence for the proton transfer mechanism in these systems.

A shift of the fluorescence spectrum to shorter wavelengths is associated with the protonation of the amino and carboxyl groups of tryptophyl peptides. Shifts in nmr spectra[22] and in absorption spectra[23] caused by the same ionization changes for glycyl and tryptophyl peptides have been explained by inductive effects. In agreement with the absorption study, smaller shifts were observed for dipeptides when an additional peptide bond was situated between the ionizing group and the indole side chain. It is known that the fluorescence of indole in polar solvents at room temperature is shifted to longer wavelengths due to an excited state interaction with the solvent.[4,24,25] Inductive effects which perturb the electronic transitions may alter the interaction of the fluorophor with the polar solvent during the excited state and cause a shift of fluorescence spectrum.

Although the first observation that intramolecular viscosity-dependent processes are involved in the quenching of tryptophan was made by Weber,[7] Weinryb and Steiner stressed the importance of proton transfer from amino groups in determining quantum yield.[17] It has recently also been shown that the quantum yield of tryptophyl-containing compounds is markedly viscosity dependent only if the compound has a free amino group.[26]

The work reported here provides further evidence for the importance of quenching by proton transfer to a fluorophor and suggests that mechanisms of this type which may occur in proteins can be profitably studied in D_2O.

Acknowledgment. I am grateful for the excellent technical assistance of Mrs. Grace Kerwar and to Professor R. Bersohn for critically reading the manuscript.

(20) S. S. Lehrer and G. Kerwar, unpublished results.
(21) R. P. Bell, *Discussions Faraday Soc.*, **39**, 16 (1965).
(22) W. J. Horsley and H. Sternlicht, *J. Amer. Chem. Soc.*, **90**, 3738 (1968).
(23) J. W. Donovan, M. Laskowski, Jr., and H. A. Scheraga, *ibid.*, **83**, 2686 (1961).
(24) M. S. Walker, T. W. Bednar, and R. Lumry, *J. Chem. Phys.*, **47**, 1020 (1967).
(25) J. W. Longworth, *Biophys. J.*, **9**, A-217 (1969).
(26) I. Weinryb, *Biochem. Biophys. Res. Commun.*, **34**, 865 (1969).

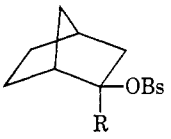
Communications to the Editor

α-Deuterium Isotope Effects on the Solvolyses of Norbornyl Brosylates and Synthesis of Labeled Norbornyl Derivatives[1]

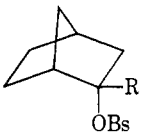
Sir:

The nonclassical[2] and classical[3] ion theories of the behavior of norbornyl brosylates were not differentiated by earlier α-deuterium isotope effect studies. Lee and Wong suggested two interpretations of the lower α-isotope effect on acetolysis of *exo*-norbornyl-2-*d* brosylate (I-2-*d*) relative to *endo*-norbornyl-2-*d* brosylate (II-2-*d*).[4] In the nonclassical ion interpretation the low isotope effect could result from anchimeric assistance, which confers SN2 character to C_2 (III). SN2 reactions (IV) have nil α-isotope effects.[5] Par-

(1) Supported by the National Science Foundation.
(2) (a) S. Winstein, E. Clippinger, R. Howe, and E. Vogelfanger, *J. Amer. Chem. Soc.*, **87**, 376 (1965); (b) S. Winstein, *ibid.*, **87**, 381 (1965).
(3) H. C. Brown, *Chem. Brit.*, **2**, 199 (1966); *Chem. Eng. News*, **45**, 87 (Feb 13, 1967).
(4) C. C. Lee and E. W. C. Wong, *J. Amer. Chem. Soc.*, **86**, 2753 (1964); *Can. J. Chem.*, **43**, 2254 (1965).
(5) V. J. Shiner, Jr., *J. Amer. Chem. Soc.*, **74**, 5285 (1952); A. Streitwieser, R. H. Jagow, R. C. Fahey, and S. Suzuki, *ibid.*, **80**, 2326 (1958).

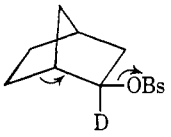


I, R = H
I-2-*d*, R = D

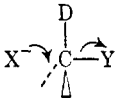


II, R = H
II-2-*d*, R = D

ticipation is not involved in the ionization of II so the



III



IV

α-isotope effect is higher. These ideas motivated the original experiments.[4]

In the classical ion interpretation it was suggested that, because internal return would scramble deuterium originally at C_2 to C_1 and because isotopic substitution at C_1 would have no effect on ionization to a classical norbornyl cation,[6] the lower isotope effect for I-2-*d* might be the result of scrambling.[4]

We present evidence that excludes scrambling as the cause of the low α-isotope effect along with evidence that isotopic scrambling can accompany conversion of deuterated *endo*-norbornyl brosylates to *exo*-norbornyl acetates with tetramethylammonium acetate in acetone.

According to the classical ion scrambling hypothesis, if internal return could be eliminated the α-isotope effect of I-2-*d* would equal that of II-2-*d*. Although internal return cannot be eliminated entirely, it can be reduced sufficiently to test the scrambling hypothesis. In acetic acid 22% of the ion pairs solvolyze and 78% return with equilibration of C_1 and C_2.[7] In 80% ethanol, 65% solvolyze and only 35% return.[7,8] If scrambling were the cause of the low isotope effect on acetolysis, the isotope effect on ethanolysis should be higher.[9]

We have measured the solvolysis rates of I-2-*d* in 80% ethanol and, as a check on our methods, in buffered acetic acid (Table I). Our acetolysis results are in accord with earlier work.[4] The α-isotope effect on aqueous ethanolysis is, in fact, the same as for acetolysis and not higher. That our technique is sufficiently sensitive to detect any decrease in isotope effect is assured by observation of a lower isotope effect on acetolysis than ethanolysis of *exo*-norbornyl-3,3-d_2 brosylate,[10] in which internal return scrambles deuterium from C_3 to C_7. There is evidence that deuterium substitution at C_7 shows a smaller isotope effect than

(6) V. J. Shiner, Jr., and J. S. Humphrey, Jr., *J. Amer. Chem. Soc.*, **85**, 2416 (1963).

(7) Reference 2a, footnote 5.

(8) B. L. Murr, A. Nickon, T. D. Swartz, and N. Werstiuk, *J. Amer. Chem. Soc.*, **89**, 1730 (1967).

(9) The solvolytic isotope effect is $k_H/k_D = (k_1^H/k_1^D)(F_H/F_D)$, where k_1^H is the ionization rate constant and F_H is the fraction of ion pairs that solvolyze for the hydrogen compound. The quantities k_1^D and F_D are defined similarly for the deuterium compound. Because k_1^H/k_1^D is solvent independent for *endo*-norbornyl brosylates, we assume that k_1^H/k_1^D is solvent independent for *exo*-norbornyl brosylates. We further assume that the ratio of $(F_H/F_D)_{HOAc}$ for acetic acid to $(F_H/F^D)_{EtOH}$ for aqueous ethanol is not greater than 1.02. The justification for this assumption is that the isotope effects on solvolysis of C_6-deuterated *exo*-norbornyl brosylates are the same in acetolysis and aqueous ethanolysis.[8]

(10) B. L. Murr and J. A. Conkling, *J. Amer. Chem. Soc.*, **92**, 3464 (1970).

Table I. α-Isotope Effects on the Solvolyses of *exo*- and *endo*-Norbornyl Brosylates

Compound	k_H/k_D[a] 80% ethanol	k_H/k_D[a] HOAc-KOAc
exo-Norbornyl brosylate (25°)	1.124 ± 0.010	1.118 ± 0.013 1.11 ± 0.01[b]
endo-Norbornyl brosylate (55°)	1.193 ± 0.014	1.20 ± 0.01[b]

[a] Averages and average deviations of four or five determinations of the isotope effect by monitoring the protium and deuterium compounds simultaneously in the same thermostated spectrophotometer compartment by the method of C. G. Swain and C. R. Morgan, *J. Org. Chem.*, **29**, 2097 (1964). [b] Data of Lee and Wong.[4]

substitution at C_3.[11] We conclude that the isotope effect at C_2 must be considerably less than 1.20 and we adopt the observed value of 1.12 pending completion of precise conductance rate determinations.

Another conclusion can be drawn from the equality of the α-isotope effects on acetolysis and ethanolysis of I-2-*d*. If the α-isotope effect on ethanolysis is as low as 1.12, then the isotope effect at C_1 must be substantial (>1.05) because deuterium scrambling is essentially complete after one acetolysis half-life. This conclusion was anticipated from the C_6 isotope effects on I.[8] An interpretation of C_6 isotope effects requires weakening of the C_1–C_6 bond in the transition state, which weakens the C–H bonds at C_6. However weakening the C_1–C_6 bond should also weaken the C–H bond at C_1. If I ionized to a classical cation, there should be no isotope effect at C_1 because the C–H bond is almost orthogonal to the developing p orbital.[6] Thus, all of the isotope effects on the face of the *exo*-norbornyl system bearing the leaving group are α-isotope effects in kind. α-Isotope effects appear to be relatively independent of charge. In the α-phenylethyl system the α-isotope effects are essentially the same on formation of carbonium ion,[12a] radical,[12b] and carbanion.[12c]

The difference in the α-isotope effects of I-2-*d* and II-2-*d*, while in accord with the nonclassical theory outlined above, cannot distinguish the classical and nonclassical theories for two reasons: the I-2-*d* isotope effect is not abnormally small compared to isotope effects of unactivated secondary sulfonates;[13] the II-2-*d* isotope effect might be unusually large. The I-2-*d* isotope is equal to the *ionization* isotope effect of benzhydryl benzoate.[14] Schaefer found an extraordinarily large α-isotope effect for *endo*-norbornyl-2-*d* bromide (1.28).[11] If the bromide is abnormal the brosylate could be too. While the magnitude of the I-2-*d* isotope effect does not distinguish between the two theories the *equality* of the acetolysis and ethanolysis I-2-*d* isotope effects does.

In our hands the literature procedure (Chart I) for the preparation of several labeled *exo*-norborneols afforded substantial isotopic rearrangement.[4] The rearrangement was shown to occur during the dis-

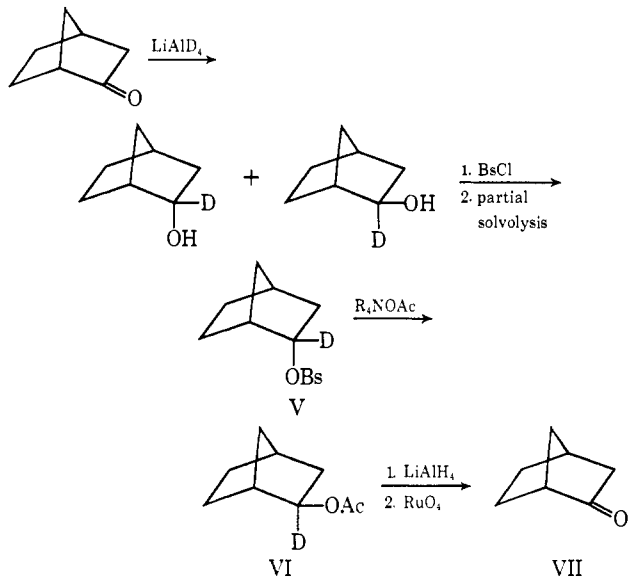
(11) J. P. Schaefer, M. J. Dagani, and D. S. Weinberg, *ibid.*, **89**, 6938 (1967).

(12) (a) V. J. Shiner, W. E. Buddenbaum, B. L. Murr, and G. Lamaty, *ibid.*, **90**, 418 (1968); (b) S. Seltzer, *ibid.*, **83**, 2625 (1961); **85**, 14 (1963); (c) A. Streitwieser and D. E. Van Sickle, *ibid.*, **84**, 254 (1962).

(13) K. T. Leffek, J. A. Llewellyn, and R. E. Robertson, *Can. J. Chem.*, **38**, 1505 (1960); K. Mislow, S. Borčić, and V. Prelog, *Helv. Chim. Acta*, **40**, 2477 (1957); V. J. Shiner, Jr., R. Fisher, and W. Dowd, *J. Amer. Chem. Soc.*, **91**, 7748 (1969).

(14) B. L. Murr and M. F. Donnelly, paper in preparation.

Chart I



placement reaction on V in acetone with tetramethylammonium acetate. In the preparation of *exo*-norbornyl-2-*d* acetate (VI), if the scheme functioned without rearrangement, the norcamphor VII isolated from the cycle in Chart I should contain no deuterium. In practice we found variable amounts of nonexchangeable deuterium in VII (usually 9–13%) by mass spectral analysis. These figures correspond to ionization of 18–26% of the *endo*-brosylate. The method may not always fail, but we were unable to control the reaction.[15] The difficulty was circumvented by use of tetra-*n*-butylammonium acetate in refluxing benzene. This process is much faster than its acetone counterpart (3 hr *vs.* 12 days).

The C_3-labeled compounds employed in our studies were also prepared by use of the new displacement conditions.[10] Another necessary ingredient in the preparation of the C_3-labeled compounds was the ability to oxidize *exo*-norborneol-3-*d* without significant loss of deuterium. This was accomplished with ruthenium tetroxide in Freon-11 at 0°.[16] Immediate work-up afforded ketone with less than 2% loss of deuterium (by mass spectrum). When the reaction mixture was allowed to stand overnight the ketone showed 25% loss of deuterium. *exo*-3-Deuterium was introduced by deuterioboration. *endo*-3-Deuterium was introduced by $LiAlD_4$ reduction of *exo*-norbornene oxide. Norcamphor-3,3-d_2 was prepared by exchange.[11] All deuterium in the C_3-deuterated norborneols was shown to be in that position by oxidation, exchange with trifluoroacetic acid,[11] and mass spectral analysis.

Acknowledgment. We thank Professor A. Nickon for helpful criticism and Professor H. C. Brown for suggesting deuterioboration to introduce *exo*-3-deuterium.

(15) Spectral analysis by nmr suggested that little or no rearrangement accompanied one tetramethylammonium acetate–acetone run. Professor C. C. Lee has informed us that he has also detected the rearrangement.

(16) E. J. Corey, J. Casanova, Jr., P. A. Vatakencherry, and R. Winter, *J. Amer. Chem. Soc.*, **85**, 169 (1963).

(17) National Science Foundation Cooperative Fellow, 1965-1969.

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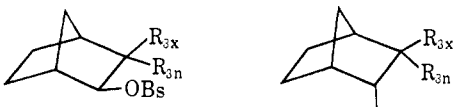
β-Deuterium Isotope Effects on the Solvolyses of Norbornyl Brosylates[1]

Sir:

The small isotope effect on *ionization* (k_α) caused by C_3 dideuteration of *exo*-norbornyl bromide (k_H/k_D = 1.09) was attributed to participation, which imparts SN2 character to C_2 and lowers the demand for hyperconjugative electron release.[2] The even smaller effect on *solvolysis* (k_H/k_D = 1.04) was ascribed to isotopic scrambling to C_7 by internal return.[2] A low isotope effect (k_H/k_D = 1.014) was also reported for *exo*-norbornyl-3,3-d_2 brosylate.[3] The latter isotope effect is extraordinary because secondary bromides invariably have shown smaller isotope effects than corresponding arenesulfonates.

In this note we report identification of a heretofore unrecognized cause for the low C_3 isotope effect on solvolysis of *exo*-norbornyl derivatives. The known geometric dependence of the β-isotope effect[4,5] and the particular geometry of the nonclassical norbornyl cation suggested that low β-isotope effects might result from a low *endo*-3-*d* isotope effect due to its unfavorable geometric orientation in the nonclassical transition state. This would result in a substantial effect for an *exo*-3-*d* and a low effect for an *endo*-3-*d*. Epimeric C_3-deuterated *endo*-norbornyl brosylates that ionize to a classical cation should both show substantial isotope effects.

We have determined isotope effects (Table I) on aqueous ethanolysis and acetolysis of *exo*-norbornyl-3-*exo*-*d* brosylate (I-3-*exo*-*d*), *exo*-norbornyl-3-*endo*-*d* brosylate (I-3-*endo*-*d*), *exo*-norbornyl-3,3-d_2 brosylate (I-3,3-d_2), *endo*-norbornyl-3-*exo*-*d* brosylate (II-3-*exo*-*d*), *endo*-norbornyl-3-*endo*-*d* brosylate (II-3-*endo*-*d*), and *endo*-norbornyl-3,3-d_2 brosylate (II-3,3-d_2).[6]



I
I-3-*exo*-*d*
I-3-*endo*-*d*
I-3,3-d_2

II
II-3-*exo*-*d*
II-3-*endo*-*d*

{$R_{3x} = R_{3n} = H$}
{$R_{3x} = D$; $R_{3n} = H$}
{$R_{3x} = H$; $R_{3n} = D$}
{$R_{3x} = R_{3n} = D$}

Entries 1–4 (Table I, 80% ethanol) show that essentially the entire isotope effect of I-3,3-d_2 is caused by the *exo*-3-*d*. The isotope effects, however, for II-3-*exo*-*d* and II-3-*endo*-*d* are both substantial (entries 5–7) and similar to values recently reported for *trans*- and *cis*-cyclopentyl-2-*d* brosylates (entries 8 and 9).[7]

(1) This work was supported by the National Science Foundation.

(2) J. P. Schaefer, M. J. Dagani, and D. S. Weinberg, *J. Amer. Chem. Soc.*, **89**, 6938 (1967).

(3) J. M. Jerkunica, S. Borčić, and D. E. Sunko, *Chem. Commun.*, 1302 (1967).

(4) V. J. Shiner, Jr., and J. S. Humphrey, Jr., *J. Amer. Chem. Soc.*, **85**, 2416 (1963).

(5) V. J. Shiner, Jr., B. L. Murr, and G. Heinemann, *ibid.*, **85**, 2413 (1963).

(6) Compounds were prepared by methods given in the preceding paper: B. L. Murr and J. A. Conkling, *ibid.*, **92**, 3462 (1970). See also ref 7 of this paper.

(7) J. O. Stoffer and J. D. Christen, *ibid.*, **92**, 3190 (1970). The au-