

$$\left(\frac{k_H}{k_D}\right)_t = \frac{1}{(t_2 - t_1)} \int_{t_1}^{t_2} \left(\frac{k_H}{k_D}\right)_t dt = \frac{4k_H}{(A+B)(k_\alpha - k_t)(t_2 - t_1)} \times \ln \left[ \frac{(A+B) + (3A-B)e^{-(k_\alpha - k_t)t_2}}{(A+B) + (3A-B)e^{-(k_\alpha - k_t)t_1}} \right] + \frac{4k_H}{(A+B)} \quad (4)$$

and Wong<sup>2b</sup> for 2-*d*-II), we have calculated the values of  $(k_H/k_D)_t$  through one and three half-lives of solvolysis and at  $t = \infty$  for 6-*endo-d*-I and for 6-*exo-d*-I, assuming that there is no isotope effect for D at C-1, C-6, and C-6' (entries 1 and 5, Table II). Clearly, even at infinite time,  $(k_H/k_D)_t$  does not attain the measured values of 1.09 and 1.11. If a more realistic extent of scrambling were used, the calculated isotope effects through one and three half-lives would be even lower.<sup>8,9</sup> If, in addition to  $k_H/k_{D2} = 1.20$ , one takes an isotope effect at C-1 of 1.10,<sup>11</sup>  $(k_H/k_D)_t$  still falls short of the measured values (entries 2 and 6, Table II). It is necessary to take  $k_H/k_{D2} = 1.20$  and two other isotope effects of 1.10 (or the equivalent of this combination) to achieve agreement with the acetolysis experiments (e.g., entries 3 and 4). The aqueous ethanolysis data impose further restrictions. If one supposes that only one C-H bond at C-6 exhibits an isotope effect, then (e.g., entries 7 and 8) the calculated average value through three half-lives is 1.10 for 6-*exo-d*-I, but it is at most 1.040 for 6-*endo-d*-I (entry 8).<sup>12</sup>

We conclude that an isotope effect of  $1.10 \pm 0.02$  (within the limits of our present precision) must be operative for D at both sites, C-6 and C-6', to account for the behavior of brosylates I in aqueous ethanol; and because solvent effects on secondary isotope effects are known to be small,<sup>13</sup> these same isotope effects must operate in acetolysis. Furthermore, the major contribution to the isotope effect must necessarily be on the ionization of the brosylate.<sup>14</sup> We plan to determine these isotope effects by precision conductance to measure any difference between the *exo* and *endo* positions at C-6.

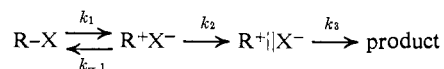
Our observed  $\gamma$ -isotope effects for the *endo*-brosylates II are those expected of a transition state for ionization to a classical cation.<sup>16</sup> However, the extraordinarily

(11) Note that, for a transition state to a classical ion, the isotope effect at the bridgehead, C-1, is expected to be small or inverse [V. J. Shiner and J. S. Humphrey, *J. Am. Chem. Soc.*, **85**, 2416 (1963)].

(12) The magnitude of the discrepancy may be seen by calculation of the value of  $k_H/k_{D2}$  necessary to attain the observed  $(k_H/k_D)_t$  through three half-lives if there were no isotope effects at C-1, C-6, and C-6'. This requires (1)  $(k_H/k_{D2}) \geq 1.50$  for acetolysis; (2)  $(k_H/k_{D2}) > 4$  for aqueous ethanolysis; and (3) an upward drift of ca. 10% in  $(k_D)_t$  through three half-lives. No drift was detected.

(13) G. J. Frisone and E. R. Thornton, *J. Am. Chem. Soc.*, **86**, 1900 (1964).

(14) The accepted scheme for solvolysis of *exo*-norbonyl brosylate is



Product forms inevitably from solvent-separated ion pair.<sup>6b</sup> The fraction,  $F$ , of intimate ion pairs that suffers dissociation is  $k_2/(k_2 + k_{-1})$ . There can be no isotope effect on  $F$  if there is no isotope effect on  $k_1$ . Even with an isotope effect on  $k_1$ , isotope effects on  $F$  are expected to be negligible.<sup>15</sup>

(15) J. G. Evans and G. Y. S. Lo, *J. Am. Chem. Soc.*, **88**, 2118 (1966).

large  $\gamma$ -isotope effects on the solvolysis of 6-*exo-d*-I and 6-*endo-d*-I are not expected on the basis of the "classical transition state" hypothesis, at least in its present form.<sup>19,19a</sup>

(16) For example, the reported  $\gamma$ -isotope effect on acetolysis of III is  $(k_H/k_D) = 1.00$  for six deuterium atoms,<sup>17</sup> and other reported  $\gamma$ -isotope effects are slightly inverse.<sup>18</sup>



OTs

III

(17) S. Winstein and J. Takahashi, *Tetrahedron*, **2**, 316 (1958).

(18) K. T. Leffek, J. A. Llewellyn, and R. E. Robertson, *J. Am. Chem. Soc.*, **82**, 6315 (1960); S. Borčić, M. Nikoletic and D. E. Sunko, *ibid.*, **84**, 1615 (1962).

(19) H. C. Brown, *Chem. Brit.*, **2**, 199 (1966).

(19a) NOTE ADDED IN PROOF. Torsional effects in the norbornyl system as recently discussed (P. von R. Schleyer, *J. Am. Chem. Soc.*, **89**, 699, 701 (1967)) would not account for our isotope effects at C-6.

(20) National Institutes of Health Predoctoral Fellow, 1962-1966.

(21) Du Pont Teaching Fellow, 1963-1965.

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## Secondary Deuterium Kinetic Isotope Effects in Acetolysis of 2-Norbonyl-6-*d* Brosylates

Sir:

It has been proposed<sup>1-4</sup> that solvolyses of *exo*-2-norbonyl brosylate, in contrast to the *endo* epimer, proceed with anchimeric assistance leading to a nonclassical norbornonium ion (V) in the rate-determining step. This view has been challenged by Brown, *et al.*<sup>5,6</sup> According to these authors, the solvolysis rate of the *exo*-brosylate is not abnormally large, and the difference in rates between the two epimeric brosylates is to be sought in the slow reaction rate of the *endo*-brosylate. The cause of the latter deceleration is seen in the steric hindrance to ionization. The *endo*-6-hydrogen should, because of its vicinity, hinder the departure of the sulfonate ester group at C<sub>2</sub> from the same side of the molecule. On these grounds and owing to the smaller size of deuterium, it was predicted<sup>7</sup> that the solvolysis of compound II would proceed with an inverse ( $k_H/k_D < 1.00$ ) kinetic isotope effect.

We now wish to report the acetolysis rate constants for compounds I-IV, which were prepared according to the procedure of Nickon, *et al.*<sup>8,9</sup> The acetolysis rates were followed by continuous titration of the liberated acid by means of a pH-stat (Radiometer, Copenhagen, Model TTT1). Thus, complete rate curves with a very large number of points were obtained. Moreover, only a small amount of the sulfonate ester

(1) S. Winstein and D. S. Trifan, *J. Am. Chem. Soc.*, **71**, 2953 (1949).

(2) J. D. Roberts and C. C. Lee, *ibid.*, **73**, 5009 (1951).

(3) S. Winstein and D. S. Trifan, *ibid.*, **74**, 1147, 1154 (1952).

(4) J. D. Roberts, C. C. Lee, and W. H. Saunders, Jr., *ibid.*, **76**, 4501 (1954).

(5) H. C. Brown, F. J. Chloupek, and M.-H. Rei, *ibid.*, **86**, 1248 (1964).

(6) H. C. Brown and G. L. Tritle, *ibid.*, **88**, 1320 (1966).

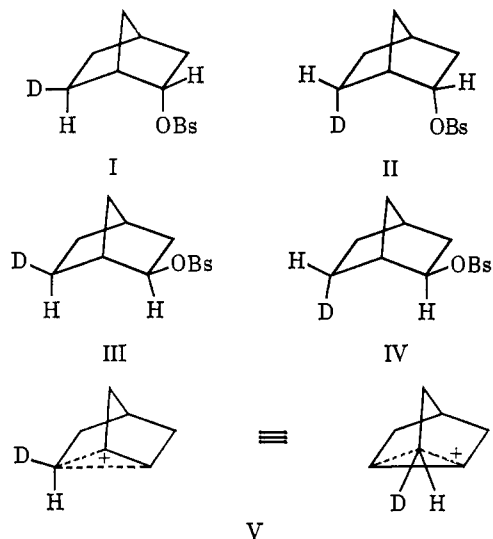
(7) H. C. Brown, Special Publication No. 16, The Chemical Society, London, 1962, p 140.

(8) A. Nickon, J. H. Hammons, J. L. Lambert, and R. O. Williams, *J. Am. Chem. Soc.*, **85**, 3713 (1963); A. Nickon, J. L. Lambert, R. O. Williams, and N. H. Werstiuk, *ibid.*, **88**, 3354 (1966).

(9) B. L. Murr, A. Nickon, T. D. Swartz, and N. H. Werstiuk, *ibid.*, **89**, 1730 (1967).

was needed for a single run, allowing several repeated determinations of the rate constants and an accurate statistical analysis.

In our previous work<sup>10,11</sup> it was suggested that the replacement of a hydrogen by deuterium at the 6



position has about the same retarding effect upon the acetolysis of the *exo*-2-norbornyl brosylate, regardless of whether the deuterium is *exo* or *endo*. It was, however, recognized that the internal rearrangement (occurring simultaneously with the acetolysis) of the brosylate would epimerize deuterium at the 6 position and could thus obscure the results. The method used for rate measurements in this work minimizes such complications. Thus, it was possible to measure very accurately instantaneous acetolysis rates in the initial stages of the reaction (by simple scale expansion on the recorder) before an important amount of deuterium epimerization due to internal return could have occurred. If the stereochemistry of deuterium at carbon 6 had a significant influence on solvolysis rate, an increasing or decreasing trend in the isotope effect should have been observed.

The results, given in Tables I, II, and III, indicate (a) that acetolyses of both deuterated *endo*-2-norbornyl brosylates (I and II) proceed *without* a significant kinetic isotope effect and (b) that acetolyses of both deuterated *exo*-2-norbornyl brosylates (III and IV) proceed *with a similar* kinetic isotope effect, irrespective of the stereochemistry of deuterium.

These results are in perfect agreement with a rate-determining formation of the norbornonium ion in the acetolysis of *exo*-2-norbornyl brosylate, but not of *endo*-2-norbornyl brosylate.<sup>1-4</sup> First, it is quite plausible that a participation of the C<sub>1</sub>-C<sub>6</sub> bond electrons, such as formulated by V, could cause vibrational changes of the C<sub>6</sub>-H(D) bonds from which originate the kinetic isotope effects observed. Second, it is to be assumed that the transition states in the reactions of III and IV resemble the intermediate norbornonium ion.<sup>12</sup> In this cation the distinction between the *exo* and *endo* hydrogen (deuterium) at C<sub>6</sub> is lost. On these

grounds, it is possible to rationalize the fact that both III and IV display about the same isotope effect upon acetolysis.

In the solvolysis of *exo*-2-norbornyl brosylate the possibility of a C<sub>6</sub>-H participation has been considered.<sup>2,4</sup> The results reported herein do not support this hypothesis. Compared to cases where such a participation was established,<sup>13</sup> our measured isotope effects are much too small.<sup>10</sup>

The results obtained do not lend support to the expressed opinion of a steric hindrance to ionization in solvolysis of I and II.<sup>5,6</sup> With respect to isotope effects the acetolysis of *endo*-2-norbornyl brosylate has to be considered as "normal." The prediction regarding the solvolysis rate of II<sup>4</sup> has not been fulfilled.

Table I. Acetolysis Rate Constants of 6-Deuterated *endo*-2-Norbornyl Brosylates at 65.0°<sup>a</sup>

Compd	$k \times 10^6, \text{sec}^{-1b}$	$k_H/k_D^b$
H	5.30 ± 0.04	
I <sup>c</sup>	5.19 ± 0.05	1.021 ± 0.012
II <sup>d</sup>	5.31 ± 0.03	0.998 ± 0.009

<sup>a</sup> Acetic acid containing 1% acetic anhydride. <sup>b</sup> Uncertainty are standard errors. <sup>c</sup> Prepared from the corresponding ketone containing 67% monodeuterated molecules (determined by mass spectroscopy). <sup>d</sup> Prepared from the corresponding ketone containing 84.5% monodeuterated molecules (determined by mass spectroscopy).

Table II. Acetolysis Rate Constants of 6-Deuterated *exo*-2-Norbornyl Brosylates at 44.4°<sup>a</sup>

Compd	$k \times 10^4, \text{sec}^{-1b}$	$k_H/k_D^b$	$k_H/k_D \text{ cor}^{b,d}$
H	8.98 ± 0.08		
III <sup>c</sup>	8.18 ± 0.03	1.097 ± 0.011	1.149 ± 0.016
H <sup>f</sup>	9.58 ± 0.02		
IV <sup>e,f</sup>	8.86 ± 0.07	1.082 ± 0.009	1.097 ± 0.011

<sup>a-c</sup> See corresponding footnotes in Table I. <sup>d</sup> Corrected to 1 atom of deuterium/molecule. <sup>e</sup> Prepared from the corresponding ketone containing 82% monodeuterated molecules (determined by mass spectroscopy). <sup>f</sup> Slightly different experimental conditions for rate measurements were used: acetic acid containing 0.7% acetic anhydride and rates at 44.3°.

Table III. Instant Isotope Effects in Acetolysis of 6-Deuterated *exo*-2-Norbornyl Brosylates at 44.4°<sup>a</sup>

Compd	% solvolysis completion <sup>f</sup>	$k_H/k_D^b$
III <sup>c</sup>	2.4	1.106 ± 0.018
	4.8	1.089 ± 0.010
	7.1	1.104 ± 0.009
	9.3	1.097 ± 0.008
	11.5	1.095 ± 0.007
IV <sup>d,e</sup>	13.7	1.096 ± 0.007
	2.6	1.084 ± 0.019
	5.1	1.084 ± 0.014
	7.6	1.077 ± 0.013
	10.0	1.076 ± 0.012
	12.3	1.076 ± 0.011
	14.6	1.078 ± 0.011

<sup>a-c</sup> See corresponding footnotes in Table I. <sup>d</sup> See footnote e, Table II. <sup>e</sup> See footnote f, Table II. <sup>f</sup> It was estimated that less than 5% of the total added brosylate could have solvolyzed before the measurements were started.

While the work reported here was in progress, we learned that research along very similar lines was being performed by Professors A. Nickon and B. L. Murr

(13) S. Winstein and J. Takahashi, *Tetrahedron*, 2, 316 (1958).

(10) K. Humski, S. Borčić, and D. E. Sunko, *Croat. Chem. Acta*, 37, 3 (1965).

(11) S. Borčić, V. Belanić-Lipovac, and D. E. Sunko, *ibid.*, 33, 35 (1961).

(12) G. S. Hammond, *J. Am. Chem. Soc.*, 77, 334 (1955).

at The Johns Hopkins University. An exchange of comments and experimental data greatly helped us in our work, which is fully acknowledged. The very similar results obtained by their group<sup>9</sup> and ours using different experimental procedures is a good check on the accuracy of the data.

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## A Nuclear Magnetic Resonance Study of OH··· $\pi$ Hydrogen Bonding<sup>1</sup>

Sir:

Jackman<sup>2</sup> has stated that "because of the magnitude of the shifts associated with hydrogen bonding, nuclear magnetic resonance will doubtless prove to be a valuable alternative to infrared spectroscopy for the investigation of structural features which permit such an interaction." Intramolecular OH··· $\pi$  hydrogen bonding has been aptly demonstrated in the infrared,<sup>3a</sup> but limited study of such interactions has been extended to nmr.<sup>3b</sup> The initial results on an nmr study of the hydrogen-bonding tendencies of 13 norbornanols are summarized in Table I. During the course of this research

lower fields than **1** and **2**, presumably due to the inductive effect of phenyl. This effect falls off with distance as shown by comparison of **3** and **4** with **5**.

(2) Phenyl-substituted secondary alcohols which are incapable of intramolecular OH··· $\pi$  bonding show slopes related to dimer-monomer equilibria which are equal to and greater than those for the unsubstituted parent compounds. The values of 30, 42, and 58 for **4**, **3**, and **5**, respectively, suggest an order of decrease in steric factors which presumably raises the energy difference between the monomeric and dimeric species.<sup>5</sup>

(3) Particularly noteworthy are the  $\gamma_0$  positions for **7-10**, all of which show essentially complete bonding to the benzene ring in their infrared spectra at infinite dilution. The  $\gamma_0$ 's all occur at higher fields relative to those incapable of such interactions. In addition, while **7**, **9**, and **10** show approximately equivalent  $\Delta\mu$ 's indicative of the strength of the OH··· $\pi$  bond, their  $\gamma_0$ 's occur at quite different fields, the magnitudes of the differences being reflected by  $\sigma_H$ .

(4) All secondary alcohols which demonstrate complete OH··· $\pi$  bonding in the infrared exhibit very small slopes relative to the other secondary alcohols. The values range from 2.8 to 5.4 and reflect a reduction in the energy difference between the monomer and dimer. That this reduction in energy is due to both the intramolecular interaction lowering the energy of the mono-

Table I. Hydrogen Bonding Data for Some Norbornanols

Compd	Norbornanol <sup>a</sup>	( $d\gamma/dx$ ) <sub>x=0</sub>	$\gamma_0$ , ppm	$\Delta_i^b$	$\sigma_H^c$	$\Delta\mu$ , cm <sup>-1</sup> <sup>d</sup>
<b>1</b>	<i>exo</i> -	34	0.82	.....	....	...
<b>2</b>	<i>endo</i> -	33	0.83	.....	....	...
<b>3</b>	<i>3-endo-Ph-2-exo</i> -	42	1.10	0.28	....	...
<b>4</b>	<i>3-exo-Ph-2-endo</i> -	30	1.20	0.37	....	...
<b>5</b>	<i>7-anti-Ph-2-exo</i> -	58	0.90	0.08	....	...
<b>6</b>	<i>1-Ph-2-endo</i> -	12	1.14	0.31	0.06	19 <sup>e</sup>
<b>7</b>	<i>1-Ph-2-exo</i> -	2.8	0.91	0.09	0.19	30 <sup>e</sup>
<b>8</b>	<i>3-endo-Ph-2-endo</i> -	5.4	1.02	0.19	0.18	10
<b>9</b>	<i>3-exo-Ph-2-exo</i> -	2.9	0.58	-0.24	0.52	30
<b>10</b>	<i>7-syn-Ph-2-exo</i> -	4.0	0.26	-0.56	0.64	28
<b>11</b>	<i>2-exo-Ph</i> -	7.2	1.24	0.41	....	...
<b>12</b>	<i>2-endo-Ph</i> -	11	1.30	0.48	....	...
<b>13</b>	<i>1-Cyclohexyl-2-exo</i> -	17	0.81	-0.01	....	...

<sup>a</sup> The O-H resonance frequencies were determined for six to eight concentrations of alcohol ranging from *ca.* 0.10 to below 0.01 mole fraction. <sup>b</sup>  $\Delta_i$  is the difference between the O-H signal at infinite dilution and the O-H signal for the parent alcohol, **1** or **2**. <sup>c</sup>  $\sigma_H$  is the difference between the O-H signal at infinite dilution and that observed for **3**, **4**, or **5**. This was done to compensate for the inductive effect of phenyl. <sup>d</sup> Infrared. <sup>e</sup> D. C. Kleinfelter, Ph.D. Thesis, Princeton University, 1960, p 94.

it was learned in conversation with Collins and Benjamin that they too have observed the phenomenon to be discussed in one compound, *7-syn-phenylnorbornane-7-anti,2-exo-diol*.<sup>4</sup>

A number of structural features related to inductive, steric, conformational, and  $\pi$ -interaction effects can be revealed by an examination of the magnitude of the slope ( $d\gamma/dx$ )<sub>x=0</sub> and the position of  $\gamma_0$ . These are summarized as follows:

(1) Those bicyclic secondary alcohols incapable of intramolecular OH··· $\pi$  bonding have their  $\gamma_0$ 's at

(1) This research was supported in part by a grant from the National Science Foundation.

(2) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959, p 68.

(3) (a) P. von R. Schleyer, D. S. Trifan, and R. Bacskai, *J. Am. Chem. Soc.*, **80**, 6691 (1958); (b) M. Oki and H. Iwamura, *Bull. Chem. Soc. Japan*, **35**, 1552 (1962); R. J. Ouellette, D. L. Marks, and D. Miller, *J. Am. Chem. Soc.*, **89**, 913 (1967).

(4) C. J. Collins and B. M. Benjamin, *ibid.*, **89**, 1652 (1967).

mer and a steric effect raising the energy of the dimer was shown from the slope of 17 exhibited by **13**, the 1-cyclohexyl analog of **7**. Assuming that the bulk of a cyclohexyl group is larger than that of phenyl, then the OH··· $\pi$  bond in **7** causes at least a sixfold decrease in the slope.

The reasons for the relative equivalence of the  $\Delta\mu$ 's for alcohols **7**, **9**, and **10** and the variance of their  $\gamma_0$  values stem from the differences between the infrared and nmr absorption processes. An examination of Dreiding models and measurements of both the approximate distance and the angle from the center of the benzene ring to the hydroxyl hydrogen aids in explaining these differences. The measurements are included in Table II.

In both the infrared and nmr the maximum interaction is experienced when the OH bond is oriented

(5) B. G. Somers and H. S. Gutowsky, *ibid.*, **85**, 3065 (1963).